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Cancer, COVID-19 and Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the coronavirus that causes COVID-19 (coronavirus disease 2019), the respiratory illness responsible for the ongoing COVID-19 pandemic. The virus was previously referred to by its provisional name, 2019 novel coronavirus (2019-nCoV), and has also been called human coronavirus 2019 (HCoV-19or hCoV-19). First identified in the city of Wuhan, Hubei, China, the World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020. SARS-CoV-2 is a positive-sense single-stranded RNA virus that is contagious in humans. As described by the US National Institutes of Health, it is the successor to SARS-CoV-1, the virus that caused the 2002–2004 SARS outbreak. SARS-CoV-2 is a virus of the species *severe acute respiratory syndrome–related coronavirus* (SARSr-CoV). It is believed to have zoonotic origins and has close genetic similarity to bat coronaviruses, suggesting it emerged from a bat-borne virus. Research is ongoing as to whether SARS-CoV-2 came directly from bats or indirectly through any intermediate hosts. The virus shows little genetic diversity, indicating that the spillover event introducing SARS-CoV-2 to humans is likely to have occurred in late 2019. This article introduces recent research reports as references in the related studies.
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1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[2] is the coronavirus that causes COVID-19 (coronavirus disease 2019), the respiratory illness responsible for the ongoing COVID-19 pandemic.[3] The virus was previously referred to by its provisional name, 2019 novel coronavirus (2019-nCoV),[4][5][6][7] and has also been called human coronavirus 2019 (HCoV-19or hCoV-19).[8][9][10][11] First identified in the city of Wuhan, Hubei, China, the World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020.[12][13] SARS-CoV-2 is a positive-sense single-stranded RNA virus[14] that is contagious in humans.[15] As described by the US National Institutes of Health, it is the successor to SARS-CoV-1, the virus that caused the 2002–2004 SARS outbreak.[16]

SARS-CoV-2 is a virus of the species *severe acute respiratory syndrome–related coronavirus* (SARSr-CoV).[2] It is believed to have zoonotic origins and has close genetic similarity to bat coronaviruses, suggesting it emerged from a bat-borne virus.[9][17] Research is ongoing as to whether SARS-CoV-2 came directly from bats or indirectly through any intermediate hosts.[18] The virus shows little genetic diversity, indicating that the spillover event introducing SARS-CoV-2 to humans is likely to have occurred in late 2019.[19]

Epidemiological studies estimate that, in December 2019 — September 2020 period, each infection resulted in an average of 2.4 to 3.4 new ones when no members of the community are immune and no preventive measures are taken.[20] The virus primarily spreads between people through close contact and via aerosols and respiratory droplets that are exhaled when talking, breathing, or otherwise exhaling, as well as those produced from coughs or sneezes.[21][22] It mainly enters human cells by binding to angiotensin converting enzyme 2

(ACE2), a membrane protein that regulates the renin-angiotensin system.[23][24]

During the initial outbreak in Wuhan, China, various names were used for the virus; some names used by different sources included "the coronavirus" or "Wuhan coronavirus".[25][26] In January 2020, the World Health Organization recommended "2019 novel coronavirus" (2019-nCov)[5][27] as the provisional name for the virus. This was in accordance with WHO's 2015 guidance[28] against using geographical locations, animal species, or groups of people in disease and virus names.[29][30]

On 11 February 2020, the International Committee on Taxonomy of Viruses adopted the official name "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2).[31] To avoid confusion with the disease SARS, the WHO sometimes refers to SARS-CoV-2 as "the COVID-19 virus" in public health communications[32][33] and the name HCoV-19 was included in some research articles.[8][9][10]

Infection and transmission

Human-to-human transmission of SARS-CoV-2 was confirmed on 20 January 2020 during the COVID-19 pandemic.[15][34][35][36] Transmission was initially assumed to occur primarily via respiratory droplets from coughs and sneezes within a range of about 1.8 metres (6 ft).[37][38] Laser light scattering experiments suggest that speaking is an additional mode of transmission[39][40] and a far-reaching[41] and under-researched[42] one, indoors, with little air flow.[43][44] Other studies have suggested that the virus may be airborne as well, with aerosols potentially being able to transmit the virus.[45][46][47] During human-to-human transmission, between 200 and 800 infectious SARS-CoV-2 virions are thought to initiate a new infection.[48][49][50] If confirmed, aerosol transmission has biosafety implications because a major concern associated with the risk of working with emerging viruses in the laboratory is the generation of aerosols from various laboratory activities which are not immediately recognizable and may affect other scientific personnel.[51] Indirect contact via contaminated surfaces is another possible cause of infection.[52] Preliminary research indicates that the virus may remain viable on plastic (polypropylene) and stainless steel (AISI 304) for up to three days, but it does not survive on cardboard for more than one day or on copper for more than four hours.[10] The virus is inactivated by soap, which destabilizes its lipid bilayer.[53][54] Viral RNA has also been found in stool samples and semen from infected individuals.[55][56]

The degree to which the virus is infectious during the incubation period is uncertain, but research has indicated that the pharynx reaches peak viral load approximately four days after infection[57][58] or in the first week of symptoms and declines thereafter.[59] The duration of SARS-CoV-2 RNA shedding is generally between 3 and 46 days after symptom onset.[60]

A study by a team of researchers from the University of North Carolina found that the nasal cavity is seemingly the dominant initial site of infection, with subsequent aspiration-mediated virus-seeding into the lungs in SARS-CoV-2 pathogenesis.[61] They found that there was an infection gradient from high in proximal towards low in distal pulmonary epithelial cultures, with a focal infection in ciliated cells and type 2 pneumocytes in the airway and alveolar regions respectively.[61]

Studies have identified a range of animals—such as cats, ferrets, hamsters, non-human primates, minks, tree shrews, raccoon dogs, fruit bats, and rabbits—that are susceptible and permissive to SARS-CoV-2 infection.[62][63][64] Some institutions have advised that those infected with SARS-CoV-2 restrict their contact with animals.[65][66]

Asymptomatic transmission

On 1 February 2020, the World Health Organization (WHO) indicated that "transmission from asymptomatic cases is likely not a major driver of transmission".[67] One meta-analysis found that 17% of infections are asymptomatic, and asymptomatic individuals were 42% less likely to transmit the virus.[68]

However, an epidemiological model of the beginning of the outbreak in China suggested that "pre-symptomatic shedding may be typical among documented infections" and that subclinical infections may have been the source of a majority of infections.[69] That may explain how out of 217 on board a cruise liner that docked at Montevideo, only 24 of 128 who tested positive for viral RNA showed symptoms.[70] Similarly, a study of ninety-four patients hospitalized in January and February 2020 estimated patients shed the most virus two to three days before symptoms appear and that "a substantial proportion of transmission probably occurred before first symptoms in the index case".[71]

Reinfection

There is uncertainty about reinfection and long-term immunity.[72] It is not known how common reinfection is, but reports have indicated that it is occurring with variable severity.[72]

The first reported case of reinfection was a 33-year-old man from Hong Kong who first tested positive on 26 March 2020, was discharged on 15 April 2020 after two negative tests, and tested positive again on 15 August 2020 (142 days later), which was confirmed by whole-genome sequencing showing that the viral genomes between the episodes belong to different clades.[73] The findings had the implications that herd immunity may not eliminate the virus if reinfection is not an uncommon occurrence and that vaccines may not be able to provide lifelong protection against the virus.[73]

Another case study described a 25-year-old man from Nevada who tested positive for

SARS-CoV-2 on 18 April 2020 and on 5 June 2020 (separated by two negative tests). Since genomic analyses showed significant genetic differences between the SARS-CoV-2 variant sampled on those two dates, the case study authors determined this was a reinfection.[74] The man's second infection was symptomatically more severe than the first infection, but the mechanisms that could account for this are not known.[74]

Reservoir and origin

The first known infections from SARS-CoV-2 were discovered in Wuhan, China.[17] The original source of viral transmission to humans remains unclear, as does whether the virus became pathogenic before or after the spillover event.[9][19][75] Because many of the early infectees were workers at the Huanan Seafood Market,[76][77] it has been suggested that the virus might have originated from the market.[9][78] However, other research indicates that visitors may have introduced the virus to the market, which then facilitated rapid expansion of the infections.[19][79] A March 2021 WHO-convened report stated that human spillover via an intermediate animal host was the most likely explanation, with direct spillover from bats next most likely. Introduction through the food supply chain and the Huanan Seafood Market was considered another possible, but less likely, explanation.[80] An analysis in November 2021, however, said that the earliest-known case had been misidentified and that the preponderance of early cases linked to the Huanan Market argued for it being the source.[81]

For a virus recently acquired through a cross-species transmission, rapid evolution is expected.[82] The mutation rate estimated from early cases of SARS-CoV-2 was of 6.54×10^{-4} per site per year.[80] Coronaviruses in general have high genetic plasticity,[83] but SARS-CoV-2's viral evolution is slowed by the RNA proofreading capability of its replication machinery.[84] For comparison, the viral mutation rate in vivo of SARS-CoV-2 has been found to be lower than that of influenza.[85]

Research into the natural reservoir of the virus that caused the 2002–2004 SARS outbreak has resulted in the discovery of many SARS-like bat coronaviruses, most originating in horseshoe bats. Phylogenetic analysis indicates that samples taken from *Rhinolophus sinicus* show a resemblance of 80% to SARS-CoV-2.[86][87][88] Phylogenetic analysis also indicates that a virus from *Rhinolophus affinis*, collected in Yunnan province and designated RaTG13, has a 96.1% resemblance to SARS-CoV-2.[17][89] This sequence was the closest known to SARS-CoV-2 at the time of its identification,[80] but it is not its direct ancestor.[90] Other closely-related sequences were also identified in samples from local bat populations.[91]

Bats are considered the most likely natural reservoir of SARS-CoV-2.[80][92] Differences between the bat coronavirus and SARS-CoV-2 suggest that humans may have been infected via an intermediate host;[78] although the source of introduction into humans remains unknown.[93][94]

Although the role of pangolins as an intermediate host was initially posited (a study published in July 2020 suggested that pangolins are an intermediate host of SARS-CoV-2-like coronaviruses[95][96]), subsequent studies have not substantiated their contribution to the spillover.[80] Evidence against this hypothesis includes the fact that pangolin virus samples are too distant to SARS-CoV-2: isolates obtained from pangolins seized in Guangdong were only 92% identical in sequence to the SARS-CoV-2 genome (matches above 90 percent may sound high, but in genomic terms it is a wide evolutionary gap[97]). In addition, despite similarities in a few critical amino acids,[98] pangolin virus samples exhibit poor binding to the human ACE2 receptor.[99]

Phylogenetics and taxonomy

SARS-CoV-2 belongs to the broad family of viruses known as coronaviruses.[26] It is a positive-sense single-stranded RNA (+ssRNA) virus, with a single linear RNA segment. Coronaviruses infect humans, other mammals, including livestock and companion animals, and avian species.[100] Human coronaviruses are capable of causing illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome (MERS, fatality rate ~34%). SARS-CoV-2 is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HKU1, MERS-CoV, and the original SARS-CoV.[101]

Like the SARS-related coronavirus implicated in the 2003 SARS outbreak, SARS-CoV-2 is a member of the subgenus *Sarbecovirus* (beta-CoV lineage B).[102][103] Coronaviruses undergo frequent recombination.[104] The mechanism of recombination in unsegmented RNA viruses such as SARS-CoV-2 is generally by copy-choice replication, in which gene material switches from one RNA template molecule to another during replication.[105] SARS-CoV-2 RNA sequence is approximately 30,000 bases in length,[106] relatively long for a coronavirus (which in turn carry the largest genomes among all RNA families)[107] Its genome consists nearly entirely of protein-coding sequences, a trait shared with other coronaviruses.[104]

A distinguishing feature of SARS-CoV-2 is its incorporation of a polybasic site cleaved by furin,[98] which appears to be an important element enhancing its virulence.[108] It was suggested that the acquisition of the furin-cleavage site in the SARS-CoV-2 S protein was essential for zoonotic transfer to humans.[109] The furin protease recognizes the canonical peptide sequence RX[R/K]R↓X where the cleavage site is indicated by a down arrow and X is any amino acid.[110][111] In SARS-CoV-2 the recognition site is formed by the incorporated 12 codon nucleotide sequence CCT CGG CGG GCA

which corresponds to the amino acid sequence PRRA.[112] This sequence is upstream of an arginine and serine which forms the S1/S2 cleavage site (PRRAR↓S) of the spike protein.[113] Although such sites are a common naturally-occurring feature of other viruses within the Subfamily Orthocoronavirinae,[112] it appears in few other viruses from the Beta-CoV genus,[114] and it is unique among members of its subgenus for such a site.[98] The furin cleavage site PRRAR↓ is identical to that of the feline coronavirus, an alphacoronavirus 1 strain.[115]

Viral genetic sequence data can provide critical information about whether viruses separated by time and space are likely to be epidemiologically linked.[116] With a sufficient number of sequenced genomes, it is possible to reconstruct a phylogenetic tree of the mutation history of a family of viruses. By 12 January 2020, five genomes of SARS-CoV-2 had been isolated from Wuhan and reported by the Chinese Center for Disease Control and Prevention (CCDC) and other institutions;[106][117] the number of genomes increased to 42 by 30 January 2020.[118] A phylogenetic analysis of those samples showed they were "highly related with at most seven mutations relative to a common ancestor", implying that the first human infection occurred in November or December 2019.[118] Examination of the topology of the phylogenetic tree at the start of the pandemic also found high similarities between human isolates.[119] As of 21 August 2021, 3,422 SARS-CoV-2 genomes, belonging to 19 strains, sampled on all continents except Antarctica were publicly available.[120]

On 11 February 2020, the International Committee on Taxonomy of Viruses announced that according to existing rules that compute hierarchical relationships among coronaviruses based on five conserved sequences of nucleic acids, the differences between what was then called 2019-nCoV and the virus from the 2003 SARS outbreak were insufficient to make them separate viral species. Therefore, they identified 2019-nCoV as a virus of *Severe acute respiratory syndrome–related coronavirus*.[121]

In July 2020, scientists reported that a more infectious SARS-CoV-2 variant with spike protein variant G614 has replaced D614 as the dominant form in the pandemic.[122][123]

Coronavirus genomes and subgenomes encode six open reading frames (ORFs).[124] In October 2020, researchers discovered a possible overlapping gene named *ORF3d*, in the SARS-CoV-2 genome. It is unknown if the protein produced by *ORF3d* has any function, but it provokes a strong immune response. *ORF3d* has been identified before, in a variant of coronavirus that infects pangolins.[125][126]

Phylogenetic tree

A phylogenetic tree based on whole-genome sequences of SARS-CoV-2 and related coronaviruses is:[127][128]

There are many thousands of variants of SARS-CoV-2, which can be grouped into the much larger clades.[135] Several different clade nomenclatures have been proposed. Nextstrain divides the variants into five clades (19A, 19B, 20A, 20B, and 20C), while GISAID divides them into seven (L, O, V, S, G, GH, and GR).[136]

Several notable variants of SARS-CoV-2 emerged in late 2020. The World Health Organization has currently declared five variants of concern, which are as follows:[137]

- **Alpha**: Lineage B.1.1.7 emerged in the United Kingdom in September 2020, with evidence of increased transmissibility and virulence. Notable mutations include N501Y and P681H.
  - An E484K mutation in some lineage B.1.1.7 virions has been noted and is also tracked by various public health agencies.
- **Beta**: Lineage B.1.351 emerged in South Africa in May 2020, with evidence of increased transmissibility and changes to antigenicity, with some public health officials raising alarms about its impact on the efficacy of some vaccines. Notable mutations include K417N, E484K and N501Y.
- **Gamma**: Lineage P.1 emerged in Brazil in November 2020, also with evidence of increased transmissibility and virulence, alongside changes to antigenicity. Similar concerns about vaccine efficacy have been raised. Notable mutations also include K417N, E484K and N501Y.
- **Delta**: Lineage B.1.617.2 emerged in India in October 2020. There is also evidence of increased transmissibility and changes to antigenicity.
- **Omicron**: Lineage B.1.1.529 emerged in Botswana in November 2021.

Other notable variants include 6 other WHO-designated variants under investigation and Cluster 5, which emerged among mink in Denmark and resulted in a mink euthanasia campaign rendering it virtually extinct.[138]

Virology

Structure

Each SARS-CoV-2 virion is 50–200 nanometres (2.0×10^{-6}–7.9×10^{-6} in) in diameter.[77] Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope.[139] Coronavirus S proteins are glycoproteins and also type I membrane proteins (membranes containing a single transmembrane domain oriented on the extracellular side).[109] They are divided into two functional parts (S1 and S2).[100]

In SARS-CoV-2, the spike protein, which has been imaged at the atomic level using cryogenic electron microscopy,[140][141] is the protein responsible for allowing the virus to attach to and fuse with the membrane of a host cell;[139] specifically, its S1 subunit catalyzes attachment, the S2 subunit fusion.[142]

Genome

SARS-CoV-2 has a linear, positive-sense, single-stranded RNA genome about 30,000 bases long.[100] Its genome has a bias against cytosine (C) and guanine (G) nucleotides like other coronaviruses.[143] The genome has the highest composition of U (32.2%), followed by A (29.9%), and a similar composition of G(19.6%) and C (18.3%).[144] The nucleotide bias arises from the mutation of guanines and cytosines to adenosines and uracils, respectively.[145] The mutation of CG dinucleotides is thought to arise to avoid the zinc finger antiviral protein related defense mechanism of cells,[146] and to lower the energy to unbind the genome during replication and translation (adenosine and uracil base pair via two hydrogen bonds, cytosine and guanine via three).[145] The depletion of CG dinucleotides in its genome has led the virus to have a noticeable codon usage bias. For instance, arginine's six different codons have a relative synonymous codon usage of AGA (2.67), CGU (1.46), AGG (.81), CGC (.58), CGA (.29), and CGG (.19).[144] A similar codon usage bias trend is seen in other SARS–related coronaviruses.[147]

Replication cycle

Virus infections start when viral particles bind to host surface cellular receptors.[148] Protein modeling experiments on the spike protein of the virus soon suggested that SARS-CoV-2 has sufficient affinity to the receptor angiotensin converting enzyme 2 (ACE2) on human cells to use them as a mechanism of cell entry.[149] By 22 January 2020, a group in China working with the full virus genome and a group in the United States using reverse genetics methods independently and experimentally demonstrated that ACE2 could act as the receptor for SARS-CoV-2.[17][150][151][152] Studies have shown that SARS-CoV-2 has a higher affinity to human ACE2 than the original SARS virus.[140][153] SARS-CoV-2 may also use basigin to assist in cell entry.[154]

Initial spike protein priming by transmembrane protease, serine 2 (TMPRSS2) is essential for entry of SARS-CoV-2.[23] The host protein neuropilin 1 (NRP1) may aid the virus in host cell entry using ACE2.[155] After a SARS-CoV-2 virion attaches to a target cell, the cell's TMPRSS2 cuts open the spike protein of the virus, exposing a fusion peptide in the S2 subunit, and the host receptor ACE2.[142] After fusion, an endosome forms around the virion, separating it from the rest of the host cell. The virion escapes when the pH of the endosome drops or when cathepsin, a host cysteine protease, cleaves it.[142] The virion then releases RNA into the cell and forces the cell to produce and disseminate copies of the virus, which infect more cells.[156]

SARS-CoV-2 produces at least three virulence factors that promote shedding of new virions from host cells and inhibit immune response.[139] Whether they include downregulation of ACE2, as seen in similar coronaviruses, remains under investigation (as of May 2020).[157]

Treatment and drug development

Very few drugs are known to effectively inhibit SARS-CoV-2. Masitinib is a clinically safe drug and was recently found to inhibit its main protease, 3CLpro and showed >200-fold reduction in viral titers in the lungs and nose in mice. However, it is not approved for the treatment of COVID-19 in humans as of August 2021.[158]

Epidemiology

Retrospective tests collected within the Chinese surveillance system revealed no clear indication of substantial unrecognized circulation of SARS-CoV-2 in Wuhan during the latter part of 2019.[80]

A meta-analysis from November 2020 estimated the basic reproduction number of the virus to be between 2.39 and 3.44.[20] This means each infection from the virus is expected to result in 2.39 to 3.44 new infections when no members of the community are immune and no preventive measures are taken. The reproduction number may be higher in densely populated conditions such as those found on cruise ships.[159] Many forms of preventive efforts may be employed in specific circumstances to reduce the propagation of the virus.[124]

There have been about 96,000 confirmed cases of infection in mainland China.[160] While the proportion of infections that result in confirmed cases or progress to diagnosable disease remains unclear,[161] one mathematical model estimated that 75,815 people were infected on 25 January 2020 in Wuhan alone, at a time when the number of confirmed cases worldwide was only 2,015.[162] Before 24 February 2020, over 95% of all deaths from COVID-19 worldwide had occurred in Hubei province, where Wuhan is located.[163][164] As of 1 December 2021, the percentage had decreased to 0.062%.[160]

As of 1 December 2021, there have been 262,699,410 total confirmed cases of SARS-CoV-2 infection in the ongoing pandemic.[160] The total number of deaths attributed to the virus is 5,214,403.[160]

https://en.wikipedia.org/wiki/Severe_acute_respiratory_syndrome_coronavirus_2.

The following introduces recent reports as references in the related studies.

Addeo, A., et al. (2021). "Immunogenicity of SARS-CoV-2 messenger RNA vaccines in patients with cancer." Cancer Cell **39**(8): 1091-1098 e1092.

Patients with cancer experience a higher burden of SARS-CoV-2 infection, disease severity, complications, and mortality, than the general population. SARS-CoV-2 mRNA vaccines are highly effective in the general population; however, few data are available on their efficacy in patients with cancer. Using a prospective cohort, we assessed the seroconversion rates and anti-SARS-CoV-2 spike protein antibody titers following the first and second dose of BNT162b2 and mRNA-1273 SARS-CoV-2 vaccines in patients with cancer in US and Europe from January to April 2021. Among 131 patients, most (94%) achieved seroconversion after receipt of two vaccine doses. Seroconversion rates and antibody titers in patients with hematological malignancy were significantly lower than those with solid tumors. None of the patients with history of anti-CD-20 antibody in the 6 months before vaccination developed antibody response. Antibody titers were highest for clinical surveillance or endocrine therapy groups and lowest for cytotoxic chemotherapy or monoclonal antibody groups.

Allegra, A., et al. (2020). "Cancer and SARS-CoV-2 Infection: Diagnostic and Therapeutic Challenges." Cancers (Basel) **12**(6).

In late December 2019, a new infectious viral disease appeared. A new betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), has been recognized as the pathogen responsible for this infection. Patients affected by tumors are more vulnerable to infection owing to poor health status, concomitant chronic diseases, and immunosuppressive conditions provoked by both the cancer and antitumor therapies. In this review, we have analyzed some lesser known aspects of the relationship between neoplasms and SARS-CoV-2 infection, starting from the different expression of the ACE2 receptor of the virus in the various neoplastic pathologies, and the roles that different cytokine patterns could have in vulnerability to infection and the appearance of complications. This review also reports the rationale for a possible use of drugs commonly employed in neoplastic therapy, such as bevacizumab, ibrutinib, selinexor, thalidomide, carfilzomib, and PD-1 inhibitors, for the treatment of SARS-CoV-2 infection. Finally, we have highlighted some diagnostic challenges in the recognition of SARS-CoV-2 infection in cancer-infected patients. The combination of these two health problems-tumors and a pandemic virus-could become a catastrophe if not correctly handled. Careful and judicious management of cancer patients with SARS-Cov-2 could support a better outcome for these patients during the current pandemic.

Al-Mozaini, M., et al. (2021). "SARS-CoV-2 Viral Load Is Correlated With the Disease Severity and Mortality in Patients With Cancer." Front Oncol **11**: 715794.

The correlation between severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) viral load and risk of disease severity in cancer patients is poorly understood. Given the fact that cancer patients are at increased risk of severe coronavirus disease 2019 (COVID-19), analysis of viral load and disease outcome in COVID-19-infected cancer patients is needed. Here, we measured the SARS-CoV-2 viral load using qPCR cycle threshold (Ct) values collected from 120 noncancer and 64 cancer patients' nasopharyngeal swab samples who are admitted to hospitals. Our results showed that the in-hospital mortality for high viral load cancer patients was 41.38%, 23.81% for medium viral load and 14.29% for low viral load patients ($p < -0.01$). On the other hand, the mortality rate for noncancer patients was lower: 22.22% among patients with high viral load, 5.13% among patients with medium viral load, and 1.85% among patients with low viral load ($p < 0.05$). In addition, patients with lung and hematologic cancer showed higher possibilities of severe events in proportion to high viral load. Higher attributable mortality and severity were directly proportional to high viral load particularly in patients who are receiving anticancer treatment. Importantly, we found that the incubation period and serial interval time is shorter in cancer patients compared with noncancer cases. Our report suggests that high SARS-CoV-2 viral loads may play a significant role in the overall mortality and severity of COVID-19-positive cancer patients, and this warrants further study to explore the disease pathogenesis and their use as prognostic tools.

Alpalhao, M., et al. (2020). "Persistent SARS-CoV-2 infection and the risk for cancer." Med Hypotheses **143**: 109882.

The current SARS-CoV-2 has put significant strain on healthcare services worldwide due to acute COVID-19. However, the potential long-term effects of this infection haven't been extensively discussed. We hypothesize that SARS-CoV-2 may be able to cause persistent infection in some individuals, and should this be the case, that in a few years we may see a rise in cancer incidence due to carcinogenic effects of this coronavirus. Non-retroviral RNA viruses such as Coronaviridae have been shown to cause persistent infection in hosts. Empirical evidence of viral genomic material shedding weeks after apparent clinical and laboratorial resolution of COVID-19 may be an indirect proof for persistent viral infection. Furthermore, tropism towards certain immune-privileged territories may facilitate immune evasion by this virus. Structural homology with SARS-CoV-1 indicates that SARS-CoV-2 may be able to directly impair pRb and p53, which are key gatekeepers with tumor suppressor functions. Additionally, COVID-19 features preeminent inflammatory response with marked oxidative stress, which acts as both as

initiator and promotor of carcinogenesis. Should there be a carcinogenic risk associated with SARS-CoV-2, the implications for public health are plenty, as infected patients should be closely watched during long periods of follow-up. Additional investigation to establish or exclude the possibility for persistent infection is paramount to identify and prevent possible complications in the future.

Al-Tabba, A., et al. (2020). "Ethical Considerations for Treating Cancer Patients During the SARS-CoV-2 Virus Crisis: To Treat or Not to Treat? A Literature Review and Perspective From a Cancer Center in Low-Middle Income Country." Front Med (Lausanne) **7**: 561168.

Providing routine healthcare to patients with serious health illnesses represents a challenge to healthcare providers amid the SARS-CoV-2 pandemic. Treating cancer patients during this pandemic is even more complex due to their heightened vulnerability, as both cancer and cancer treatment weaken the immune system leading to a higher risk of both infections and severe complications. In addition to the need to protect cancer patients from unnecessary exposure to SARS-CoV-2 infection during their routine care, interruption, and discontinuation of cancer treatment can result in negative consequences on patients' health, in addition to the ghost of rationing healthcare resources in high demand during a global health crisis. This article aims to explore the ethical dilemmas faced by decision-makers and healthcare providers caring for cancer patients during the SARS-CoV-2 pandemic. This includes setting triage criteria for non-infected cancer patients, fairly allocating limited healthcare resources between cancer patients and SARS-CoV-2 patients, prioritizing SARS-CoV-2 treatment or vaccine, once developed, for cancer patients and non-cancer patients, patient-physician communication on matters such as end-of-life and do-not-resuscitate (DNR), and lastly, shifting physicians' priorities from treating their own cancer patients to treating critically ill SARS-CoV-2 infected patients. Ultimately, no straightforward decision can be easily made at such exceptionally difficult times. Applying different ethical principles can result in very different scenarios and consequences. In the end, we will briefly share the experience of the King Hussein Cancer Center (KHCC), the only standalone comprehensive cancer center in the region.

Amere Subbarao, S. (2021). "Cancer vs. SARS-CoV-2 induced inflammation, overlapping functions, and pharmacological targeting." Inflammopharmacology **29**(2): 343-366.

Inflammation is an intrinsic defence mechanism triggered by the immune system against infection or injury. Chronic inflammation allows the host to recover or adapt through cellular and humoral responses, whereas acute inflammation leads to cytokine storms resulting in tissue damage. In this review, we present the overlapping outcomes of cancer inflammation with virus-induced inflammation. The study emphasises how anti-inflammatory drugs that work against cancer inflammation may work against the inflammation caused by the viral infection. It is established that the cytokine storm induced in response to SARS-CoV-2 infection contributes to disease-associated mortality. While cancer remains the second among the diseases associated with mortality worldwide, cancer patients' mortality rates are often observed upon extended periods after illness, usually ranging from months to years. However, the mortality rates associated with COVID-19 disease are robust. The cytokine storm induced by SARS-CoV-2 infection appeared to be responsible for the multi-organ failure and increased mortality rates. Since both cancer and COVID-19 disease share overlapping inflammatory mechanisms, repurposing some anticancer and anti-inflammatory drugs for COVID-19 may lower mortality rates. Here, we review some of these inflammatory mechanisms and propose some potential chemotherapeutic agents to intervene in them. We also discuss the repercussions of anti-inflammatory drugs such as glucocorticoids and hydroxychloroquine with zinc or antiviral drugs such as ivermectin and remdesivir against SARS-CoV-2 induced cytokine storm. In this review, we emphasise on various possibilities to reduce SARS-CoV-2 induced cytokine storm.

Anantharaman, A., et al. (2021). "SARS-CoV-2 Clinical Outcomes in Patients with Cancer in a Large Integrated Health Care System in Northern California." Oncologist **26**(3): e500-e504.

The SARS-CoV-2 (COVID-19) pandemic continues to affect many lives globally. Patients with cancer undergoing potentially immunosuppressive therapies appear to be at particular risk for the disease and its complications. Here, we describe the experience of patients with cancer within Kaiser Permanente, a large, integrated health system in Northern California. Between February 25, 2020, and June 8, 2020, 4,627 patients were diagnosed with COVID-19, of whom 33 had active cancer treatment within 180 days and 214 had a history of cancer. Patients with active cancer treatment had a statistically higher risk of requiring noninvasive ventilation (odds ratio [OR], 2.57; confidence interval [CI], 1.10-6.01), and there was a nonsignificant trend toward higher risk of death (OR, 2.78; CI, 0.92-8.43). Those with a history of cancer had comparable outcomes to those without cancer. These data demonstrate an increased risk of complications from COVID-19 for patients with active cancer treatment.

Andersen, P. A., et al. (2021). "The impact and prevalence of SARS-CoV-2 in patients with head and neck cancer and acute upper airway infection in a tertiary otorhinolaryngology referral center in Denmark." Eur Arch Otorhinolaryngol **278**(9): 3409-3415.

PURPOSE: To determine the prevalence of SARS-CoV-2 at a Danish tertiary referral otorhinolaryngology clinic during the first wave of the COVID-19 pandemic among patients with suspected acute upper airway infection (UAI) and patients operated for head and neck cancer (HNC), respectively. To monitor changes in the number of patient encounters for acute UAI and the number of referrals for the workup of HNC. TRIAL REGISTRATION: NCT-04356560 (Clinicaltrials.gov). METHODS: Prospective enrolled case series of all patients with suspected acute UAI (n = 88) and of patients undergoing surgery for HNC (n = 96), respectively, from March 23rd to May 5th, 2020, at a public tertiary referral otorhinolaryngology clinic in Denmark. SARS-CoV-2 was diagnosed with nasopharyngeal and oropharyngeal swabbing. Patients with suspected acute UAI had symptoms and definitive diagnoses registered in a database. Trends in the number of referrals and patient encounters were retrieved from an electronic patient journal system and analyzed retrospectively. RESULTS: Eighty-eight patients with acute UAI were enrolled including 55 men and 34 women, median age of 31 years (range: 10 months to 82 years). One patient (1.1%) tested positive. Among 96 patients operated for HNC, zero tested positive. The number of referrals for HNC workup, and patient encounters for peritonsillar abscesses, decreased markedly in the first 3 weeks. CONCLUSION: The prevalence of SARS-CoV-2 during the first 6 weeks of the first wave was minimal among patients with acute UAI and zero among patients operated for HNC. The decrease in referrals for the workup of HNC may increase time to treatment initiation and patient morbidity.

Arab, M., et al. (2021). "Evaluation of Serologic Changes of IgG and IgM Antibodies Associated with SARS-COV-2 in Cancer Patients: A Cohort Seroprevalence Study." Asian Pac J Cancer Prev **22**(6): 1667-1670.

BACKGROUND: While the coronavirus disease 2019 (COVID-19) pandemic spreads, there is increasing evidence to suggest the elevated risk of SARS-CoV-2 infection and following morbidity and mortality in cancer patients. Serology testing using ELISA proposes major advantages as a diagnostic and preventive tool to control the present SARS-CoV-2 outbreak. This cohort study was to determine the SARS-CoV-2 seroconversion in asymptomatic cancer patients. METHODS: Patients in all age groups and with any type of cancer who have been in remission or have stable disease and received their latest anticancer therapy over 2 months ago included in the study. All patients were evaluated for COVID-19 symptoms and only asymptomatic patients were enrolled for serologic screening for SARS-CoV-2. Serum samples evaluated serologically for SARS-CoV-2 antibodies by enzyme-linked immunosorbent assay. RESULTS: A total of 168 asymptomatic cancer patients were included in the study. Of the 168 cases with a history of cancer who were asymptomatic for Covid-19, 29 cases (17.26%) had a positive serological test. CONCLUSION: In conclusion, in the present study asymptomatic cancer patients revealed 17% seropositivity, approximately equal to the general population of the same age, sex, geographic region, and epidemic status. Asymptomatic infections should further be investigated and considered as playing an important role in the COVID-19 transmission chain.

Arnold, C. C., et al. (2021). "Risk stratification by anamnesis increases SARS-CoV-2 test efficiency in cancer patients." Strahlenther Onkol.

PURPOSE: To evaluate the impact of testing asymptomatic cancer patients, we analyzed all tests for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) before and during radiotherapy at a tertiary cancer center throughout the second wave of the pandemic in Germany. METHODS: Results of all real-time polymerase chain reaction (RT-PCR) tests for SARS-CoV2 performed at our radio-oncology department between 13 October 2020 and 11 March 2021 were included. Clinical data and anamnestic information at the time of testing were documented and examined for (i) the presence of COVID-19-related symptoms and (ii) virus-related anamnesis (high-risk [prior positive test or contact to a positive tested person within the last 14 days] or low-risk [inconspicuous anamnesis within the last 14 days]). RESULTS: A total of 1056 SARS-CoV2 tests in 543 patients were analyzed. Of those, 1015 tests were performed in asymptomatic patients and 41 tests in patients with COVID-19-associated symptoms. Two of 940 (0.2%) tests in asymptomatic patients with low-risk anamnesis and three of 75 (4.0%) tests in asymptomatic patients with high-risk anamnesis showed a positive result. For symptomatic patients, SARS-CoV2 was detected in three of 36 (8.3%) low-risk and three of five (60.0%) high-risk tests. CONCLUSION: To the best of our knowledge, this is the first study evaluating the correlation between individual risk factors and positivity rates of SARS-CoV2 tests in cancer patients. The data demonstrate that clinical and anamnestic assessment is a simple and effective measure to distinctly increase SARS-CoV2 test efficiency. This might enable cancer centers to adjust test strategies in asymptomatic patients, especially when test resources are scarce.

Assaad, S., et al. (2020). "High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR." Eur J Cancer **135**: 251-259.

BACKGROUND: Cancer patients presenting with COVID-19 have a high risk of death. In this work, predictive factors for survival in cancer patients with suspected SARS-COV-2 infection were investigated. METHODS: PRE-COVID-19 is a retrospective study of all 302 cancer patients presenting to this institute with a suspicion of COVID-19 from March 1st to April 25th 2020. Data were collected using a web-based tool within electronic patient record approved by the Institutional Review Board. Patient characteristics symptoms and survival were collected and compared in SARS-COV-2 real-time or reverse-transcriptase PCR (RT-PCR)-positive and RT-PCR-negative patients. RESULTS: Fifty-five of the 302 (18.2%) patients with suspected COVID-19 had detectable SARS-COV-2 with RT-PCR in nasopharyngeal samples. RT-PCR-positive patients were older, had more frequently haematological malignancies, respiratory symptoms and suspected COVID-19 pneumonia of computed tomography (CT) scan. However, respectively, 38% and 20% of SARS-COV-2 RT-PCR-negative patients presented similar respiratory symptoms and CT scan images. Thirty of the 302 (9.9%) patients died during the observation period, including 24 (80%) with advanced disease. At the median follow-up of 25 days after the first symptoms, the death rate in RT-PCR-positive and RT-PCR-negative patients were 21% and 10%, respectively. In both groups, independent risk factors for death were male gender, Karnofsky performance status <60, cancer in relapse and respiratory symptoms. Detection of SARS-COV-2 on RT-PCR was not associated with an increased death rate ($p = 0.10$). None of the treatment given in the previous month (including cytotoxics, PD1 Ab, anti-CD20, VEGFR2...) correlated with survival. The survival of RT-PCR-positive and -negative patients with respiratory symptoms and/or COVID-19 type pneumonia on CT scan was similar with a 18.4% and 19.7% death rate at day 25. Most (22/30, 73%) cancer patients dying during this period were RT-PCR negative. CONCLUSION: The 30-day death rate of cancer patients with or without documented SARS-COV-2 infection is poor, but the majority of deaths occur in RT-PCR-negative patients.

Avanzato, V. A., et al. (2020). "Case Study: Prolonged Infectious SARS-CoV-2 Shedding from an Asymptomatic Immunocompromised Individual with Cancer." Cell **183**(7): 1901-1912 e1909.

Long-term severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) shedding was observed from the upper respiratory tract of a female immunocompromised individual with chronic lymphocytic leukemia and acquired hypogammaglobulinemia. Shedding of infectious SARS-CoV-2 was observed up to 70 days, and of genomic and subgenomic RNA up to 105 days, after initial diagnosis. The infection was not cleared after the first treatment with convalescent plasma, suggesting a limited effect on SARS-CoV-2 in the upper respiratory tract of this individual. Several weeks after a second convalescent plasma transfusion, SARS-CoV-2 RNA was no longer detected. We observed marked within-host genomic evolution of SARS-CoV-2 with continuous turnover of dominant viral variants. However, replication kinetics in Vero E6 cells and primary human alveolar epithelial tissues were not affected. Our data indicate that certain immunocompromised individuals may shed infectious virus longer than previously recognized. Detection of subgenomic RNA is recommended in persistently SARS-CoV-2-positive individuals as a proxy for shedding of infectious virus.

Ayhan, A., et al. (2021). "Perioperative SARS-CoV-2 infection among women undergoing major gynecologic cancer surgery in the COVID-19 era: A nationwide, cohort study from Turkey." Gynecol Oncol **160**(2): 499-505.

OBJECTIVE: The objective of this study was to determine the rate of perioperative SARS-CoV-2 infection among gynecologic cancer patients undergoing major surgery. METHODS: The database of the Turkish Ministry of Health was searched in order to identify all consecutive gynecologic cancer patients undergoing major surgery between March 11, 2020 and April 30, 2020 for this retrospective, nationwide, cohort study. The inclusion criteria were strictly founded on a final histopathological diagnosis of a malignant gynecologic tumor. COVID-19 cases were diagnosed by reverse transcriptase- polymerase chain reaction testing for SARS-CoV-2. The rate of perioperative SARS-CoV-2 infection and the 30-day mortality rate of COVID-19 patients were investigated. RESULTS: During the study period, 688 women with gynecologic cancer undergoing major surgery were identified nationwide. The median age of the patients was 59 years. Most of the surgeries were open (634/688, 92.2%). There were 410 (59.6%) women with endometrial cancer, 195 (28.3%) with ovarian cancer, 66 (9.6%) with cervical cancer, 14 (2.0%) with vulvar cancer and 3 (0.4%) with uterine sarcoma. The rate of SARS-CoV-2 infections confirmed within 7 days before or 30 days after surgery was 46/688 (6.7%). All but one woman was diagnosed postoperatively (45/46, 97.8%). The rates of intensive care unit admission and invasive mechanical ventilation were 4/46 (8.7%) and 2/46 (4.3%), respectively. The 30-day mortality rate was 0%. CONCLUSION: In the COVID-19 era, gynecologic cancer surgery may be performed with an acceptable rate of perioperative SARS-CoV-2

infection if the staff and the patients strictly adhere to the established infection control measures.

Banna, G., et al. (2020). "How we treat patients with lung cancer during the SARS-CoV-2 pandemic: primum non nocere." ESMO Open **5**(2): e000765.

New cases of the novel coronavirus, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continue to rise worldwide. A few reports have showed that mortality due to SARS-CoV-2 is higher in elderly patients and other active comorbidities including cancer. To date, no effective treatment has been identified and management for critically ill patients relies on management in intensive care units. Patients with lung cancer are at risk of pulmonary complications from COVID-19. Furthermore, the use of chemotherapy might have a negative impact in patient's outcome. Therefore, the risk/benefit ratio of systemic anticancer treatment (SACT) has to be considered. For each patient, several factors including age and comorbidities, as well as the number of hospital visits for treatment, can influence this risk. Each hospital around the world has issued some internal policy guidelines for oncologists, aiming to limit risks during this difficult time. We hereby propose a tool to support oncologists and physicians in treatment decision for patients with lung cancer. There are several variables to consider, including the extent of the epidemic, the local healthcare structure capacity, the risk of infection to the individual, the status of cancer, patients' comorbidities, age and details of the treatment. Given this heterogeneity, we have based our suggestions bearing in mind some general factors There is not easy, universal solution to oncological care during this crisis and, to complicate matters, the duration of this pandemic is hard to predict. It is important to weigh the impact of each of our decisions in these trying times rather than rely on routine automatisms.

Barbieri, A., et al. (2020). "Can Beta-2-Adrenergic Pathway Be a New Target to Combat SARS-CoV-2 Hyperinflammatory Syndrome?-Lessons Learned From Cancer." Front Immunol **11**: 588724.

SARS-CoV-2 infection is a new threat to global public health in the 21(st) century (2020), which has now rapidly spread around the globe causing severe pneumonia often linked to Acute Respiratory Distress Syndrome (ARDS) and hyperinflammatory syndrome. SARS-CoV-2 is highly contagious through saliva droplets. The structural analysis suggests that the virus enters human cells through the ligation of the spike protein to angiotensin-converting enzyme 2 (ACE2). The progression of Covid-19 has been divided into three main stages: stage I-viral response, stage II-pulmonary phase, and stage III-hyperinflammation phase. Once the patients enter stage III, it will likely need ventilation and it becomes difficult to manage. Thus, it will be of paramount importance to find therapies to prevent or slow down the progression of the disease toward stage III. The key event leading to hyperinflammation seems to be the activation of Th-17 immunity response and Cytokine storm. B2-adrenergic receptors (B2ARs) are expressed on airways and on all the immune cells such as macrophages, dendritic cells, B and T lymphocytes. Blocking (B2AR) has been proven, also in clinical settings, to reduce Th-17 response and negatively modulate inflammatory cytokines including IL-6 while increasing IFNgamma. Non-selective beta-blockers are currently used to treat several diseases and have been proven to reduce stress-induced inflammation and reduce anxiety. For these reasons, we speculate that targeting B2AR in the early phase of Covid-19 might be beneficial to prevent hyperinflammation.

Barriere, J., et al. (2021). "Current perspectives for SARS-CoV-2 vaccination efficacy improvement in patients with active treatment against cancer." Eur J Cancer **154**: 66-72.

A higher risk of death from coronavirus disease 19 has been shown for patients with solid cancers or haematological malignancies (HM). Thanks to the accelerated development of anti-SARS-SoV-2 vaccines in less than a year since the start of the global pandemic, patients with cancer were quickly prioritised in early 2021 for vaccination, however dependent on the very unequal availability at the global level. Impaired immunogenicity of SARS-CoV-2 mRNA vaccines in immunocompromised patients was rapidly reported as early as April 2021, although the vaccination fortunately appears to be generally effective without increasing the spacing. Worryingly, the humoral response of the SARS-CoV-2 vaccination is, however, considered insufficient in patients followed for HM, in particular when they are on anti-CD20 treatment. Thus, improving vaccination coverage by strengthening immune stimulation should be evaluated in patients under active treatment against cancer. Here, we discuss three different approaches: a third dose of early vaccine (repeated immune stimulation), heterologous prime-boost vaccination (multimodal immune stimulation) and a double-dose strategy (maximisation of immune response). Dedicated therapeutic trials, currently almost non-existent, seem rapidly necessary.

Basse, C., et al. (2021). "Characteristics and Outcome of SARS-CoV-2 Infection in Cancer Patients." JNCI Cancer Spectr **5**(1): pkaa090.

Background: Concerns have emerged about the higher risk of fatal coronavirus disease 2019 (COVID-19) in cancer patients. In this article, we review the experience of a comprehensive cancer center. Methods: A prospective registry was set up at Institut Curie at the beginning of the COVID-19

pandemic. All cancer patients with suspected or proven COVID-19 were entered and actively followed for 28 days. Results: Among 9842 patients treated at Institut Curie between March 13 and May 1, 2020, 141 (1.4%) were diagnosed with COVID-19, based on reverse transcription polymerase chain reaction testing and/or computerized tomography scan. In line with our case mix, breast cancer (40.4%) was the most common tumor type, followed by hematological and lung malignancies. Patients with active cancer therapy or/and advanced cancer accounted for 87.9% and 68.9% of patients, respectively. At diagnosis, 78.7% of patients had COVID-19-related symptoms, with an extent of lung parenchyma involvement inferior to 50% in 95.8% of patients. Blood count variations and C-reactive protein elevation were the most common laboratory abnormalities. Antibiotics and antiviral agents were administered in 48.2% and 6.4% of patients, respectively. At the time of analysis, 26 patients (18.4%) have died from COVID-19, and 100 (70.9%) were cured. Independent prognostic factors at the time of COVID-19 diagnosis associated with death or intensive care unit admission were extent of COVID-19 pneumonia and decreased O2 saturation. Conclusions: COVID-19 incidence and presentation in cancer patients appear to be very similar to those in the general population. The outcome of COVID-19 is primarily driven by the initial severity of infection rather than patient or cancer characteristics.

Benderra, M. A., et al. (2021). "Clinical Characteristics, Care Trajectories and Mortality Rate of SARS-CoV-2 Infected Cancer Patients: A Multicenter Cohort Study." Cancers (Basel) **13**(19).

BACKGROUND: COVID-19 may be more frequent and more severe in cancer patients than in other individuals. Our aims were to assess the rate of COVID-19 in hospitalized cancer patients, to describe their demographic characteristics, clinical features and care trajectories, and to assess the mortality rate. METHODS: This multicenter cohort study was based on the Electronic Health Records of the Assistance Publique-Hopitaux de Paris (AP-HP). Cancer patients with a diagnosis of COVID-19 between 3 March and 19 May 2020 were included. Main outcome was all-cause mortality within 30 days of COVID-19 diagnosis. RESULTS: A total of 29,141 cancer patients were identified and 7791 (27%) were tested for SARS-CoV-2. Of these, 1359 (17%) were COVID-19-positive and 1148 (84%) were hospitalized; 217 (19%) were admitted to an intensive care unit. The mortality rate was 33% (383 deaths). In multivariate analysis, mortality-related factors were male sex (aHR = 1.39 [95% CI: 1.07-1.81]), advanced age (78-86 y: aHR = 2.83 [95% CI: 1.78-4.51] vs. <66 y; 86-103 y: aHR = 2.61 [95% CI: 1.56-4.35] vs. <66 y), more than two comorbidities (aHR = 2.32 [95% CI: 1.41-3.83]) and C-reactive protein >20 ng/mL (aHR = 2.20 [95% CI: 1.70-2.86]). Primary brains tumors (aHR = 2.19 [95% CI: 1.08-4.44]) and lung cancer (aHR = 1.66 [95% CI: 1.02-2.70]) were associated with higher mortality. Risk of dying was lower among patients with metabolic comorbidities (aHR = 0.65 [95% CI: 0.50-0.84]). CONCLUSIONS: In a hospital-based setting, cancer patients with COVID-19 had a high mortality rate. This mortality was mainly driven by age, sex, number of comorbidities and presence of inflammation. This is the first cohort of cancer patients in which metabolic comorbidities were associated with a better outcome.

Berghoff, A. S., et al. (2020). "SARS-CoV-2 Testing in Patients With Cancer Treated at a Tertiary Care Hospital During the COVID-19 Pandemic." J Clin Oncol **38**(30): 3547-3554.

PURPOSE: To analyze the prevalence of SARS-CoV-2 infection in patients with cancer in hospital care after implementation of institutional and governmental safety measurements. METHODS: Patients with cancer routinely tested for SARS-CoV-2 RNA by nasal swab and real-time polymerase chain reaction between March 21 and May 4, 2020, were included. The results of this cancer cohort were statistically compared with the SARS-CoV-2 prevalence in the Austrian population as determined by a representative nationwide random sample study (control cohort 1) and a cohort of patients without cancer presenting to our hospital (control cohort 2). RESULTS: A total of 1,688 SARS-CoV-2 tests in 1,016 consecutive patients with cancer were performed. A total of 270 of 1,016 (26.6%) of the patients were undergoing active anticancer treatment in a neoadjuvant/adjuvant and 560 of 1,016 (55.1%) in a palliative setting. A total of 53 of 1,016 (5.2%) patients self-reported symptoms potentially associated with COVID-19. In 4 of 1,016 (0.4%) patients, SARS-CoV-2 was detected. At the time of testing at our department, all four SARS-CoV-2-positive patients were asymptomatic, and two of them had recovered from symptomatic COVID-19. Viral clearance was achieved in three of the four patients 14-56 days after testing positive. The estimated odds ratio of SARS-CoV-2 prevalence between the cancer cohort and control cohort 1 was 1.013 (95% CI, 0.209 to 4.272; P = 1), and between control cohort 2 and the cancer cohort it was 18.333 (95% CI, 6.056 to 74.157). CONCLUSION: Our data indicate that continuation of active anticancer therapy and follow-up visits in a large tertiary care hospital are feasible and safe after implementation of strict population-wide and institutional safety measures during the current COVID-19 pandemic. Routine SARS-CoV-2 testing of patients with cancer seems advisable to detect asymptomatic virus carriers and avoid uncontrolled viral spread.

Bertuzzi, A. F., et al. (2020). "Low Incidence of SARS-CoV-2 in Patients with Solid Tumours on

Active Treatment: An Observational Study at a Tertiary Cancer Centre in Lombardy, Italy." Cancers (Basel) **12**(9).

Background: The incidence and prognosis of SARS-CoV-2-positive cancer patients on active oncologic treatment remain unknown. Retrospective data from China reported higher incidence and poorer outcomes with respect to the general population. We aimed to describe the real-word incidence of SARS-CoV-2 in cancer patients and the impact of oncologic therapies on the infection. Materials & Methods: In this study, we analysed all consecutive cancer patients with solid tumours undergoing active intravenous treatment (chemotherapy, immunotherapy, targeted therapy, alone or in combination) between 21 February and 30 April 2020, in a high-volume cancer centre in Lombardy, Italy. We focused on SARS-CoV-2-positive patients, reporting on the clinical characteristics of the cancer and the infection. Results: We registered 17 SARS-CoV-2-positive patients among 1267 cancer patients on active treatment, resulting in an incidence of 1.3%. The median age was 69.5 years (range 43-79). Fourteen patients (82%) required hospitalisation for COVID-19 with a median in-hospital stay of 11.5 days (range 3-58). Fourteen of the seventeen (82%) were treated for locally advanced or metastatic disease. We could not demonstrate any correlation between SARS-CoV-2 infection and tumour or treatment type. The COVID-19-related fatality rate was 29% (5/17), which was higher than that of the general population cared for in our centre (20%). Conclusions: Active oncologic treatments do not represent a risk factor for SARS-CoV-2 infection in cancer patients. However, the prognosis of infected cancer patients appears to be worse compared with that of the non-oncologic population. Given the low number of SARS-CoV-2-positive cases and the uncertainties in risk factors that may have an impact on the prognosis, we advocate for the continuum of cancer care even during the current pandemic.

Bhari, V. K., et al. (2020). "SARS-CoV-2 cell receptor gene ACE2 -mediated immunomodulation in breast cancer subtypes." Biochem Biophys Rep **24**: 100844.

The recent outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has impacted the world severely. The binding of the SARS-CoV-2 virus to the angiotensin-converting enzyme 2 (ACE2) and its intake by the host cell is a necessary step for infection. ACE2 has garnered widespread therapeutic possibility as it is entry/interactive point for SARS-CoV-2, responsible for coronavirus disease 2019 (COVID-19) pandemic and providing a critical regulator for immune modulation in various disease. Patients with suffering from cancer always being on the verge of being immune compromised therefore gaining knowledge about how SARS-CoV-2 viruses affecting immune cells in human cancers will provides us new opportunities for preventing or treating virus-associated cancers. Despite COVID-19 pandemic got center stage at present time, however very little research being explores, which increase our knowledge in context with how SARS-CoV-2 infection affect cancer a cellular level. Therefore, in light of the ACE-2 as an important contributor of COVID-19 global, we analyzed correlation between ACE2 and tumor immune infiltration (TIL) level and the type markers of immune cells were investigated in breast cancer subtypes by using TIMER database. Our findings shed light on the immunomodulatory role of ACE2 in the luminal A subtype which may play crucial role in imparting therapeutic resistance in this cancer subtype.

Binet, Q., et al. (2021). "Nonbacterial thrombotic endocarditis in a patient with gastric cancer and SARS-CoV-2 infection." Clin J Gastroenterol **14**(4): 1031-1035.

Nonbacterial thrombotic endocarditis, formerly known as marantic endocarditis, is a very rare complication of advanced malignancy and other hypercoagulable states in which sterile, fibrin vegetations develop on heart valve leaflets. The most common malignancies associated with this entity are lung, pancreatic and gastric cancer. It has also been described as a presentation of COVID-19, which is known to be frequently complicated with coagulopathy and thromboembolic events. We report the case of a 62 year-old female patient newly diagnosed with stage IV gastric cancer and acute SARS-CoV-2 infection, presenting with confusion and homonymous hemianopsia in the setting of multiple acute ischemic strokes complicating a nonbacterial thrombotic mitral endocarditis. Herein, we discuss the underlying pathophysiology and make the hypothesis that SARS-CoV-2 infection could have participated in the pathogenesis of nonbacterial thrombotic endocarditis in our patient suffering from a gastric cancer.

Burgio, S., et al. (2021). "SARS-CoV-2 in patients with cancer: possible role of mimicry of human molecules by viral proteins and the resulting anti-cancer immunity." Cell Stress Chaperones **26**(4): 611-616.

A few reports suggest that molecular mimicry can have a role in determining the more severe and deadly forms of COVID-19, inducing endothelial damage, disseminated intravascular coagulation, and multiorgan failure. Heat shock proteins/molecular chaperones can be involved in these molecular mimicry phenomena. However, tumor cells can display on their surface heat shock proteins/molecular chaperones that are mimicked by SARS-CoV-2 molecules (including the Spike protein), similarly to what happens in other bacterial

or viral infections. Since molecular mimicry between SARS-CoV-2 and tumoral proteins can elicit an immune reaction in which antibodies or cytotoxic cells produced against the virus cross-react with the tumor cells, we want to prompt clinical studies to evaluate the impact of SARS-CoV-2 infection on prognosis and follow up of various forms of tumors. These topics, including a brief historical overview, are discussed in this paper.

Buscarini, E., et al. (2021). "Changes in digestive cancer diagnosis during the SARS-CoV-2 pandemic in Italy: A nationwide survey." Dig Liver Dis **53**(6): 682-688.

BACKGROUND: The SARS-CoV-2 pandemic has had a huge impact on healthcare systems, resulting in many routine diagnostic procedures either being halted or postponed. AIMS: To evaluate whether the diagnoses of colorectal, gastric and pancreatic cancers have been impacted by the SARS-CoV-2 pandemic in Italy. METHODS: A survey designed to collect the number of histologically-proven diagnoses of the three cancers in gastroenterology services across Italy from January 1 to October 31 in 2017-2020. Non-parametric ANOVA for repeated measurements was applied to compare distributions by years and macro-areas. RESULTS: Compared to 2019, in 2020 gastric cancer diagnoses decreased by 15.9%, CRC by 11.9% and pancreatic by 9.9%. CRC distributions showed significant differences between all years, stomach cancer between 2018 and 2020 and 2019-2020, and pancreatic cancer only between 2017 and 2019. The 2019-2020 comparison showed fewer CRC diagnoses in the North (-13.7%), Center (-16.5%) and South (-4.1%), fewer stomach cancers in the North (-19.0%) and South (-9.4%), and fewer pancreatic cancers in the North (-14.1%) and Center (-4.7%), with an increase in the South (+12.3%). Distributions of CRC and gastric cancer were significantly different between all years in the North. CONCLUSIONS: This survey highlights the concerning effects of the COVID-19 pandemic on the diagnostic yield of gastroenterology services for stomach, colorectal and pancreatic cancers in Italy.

Busetto, G. M., et al. (2020). "SARS-CoV-2 Infection and High-Risk Non-Muscle-Invasive Bladder Cancer: Are There Any Common Features?" Urol Int **104**(7-8): 510-522.

BACKGROUND: The new severe acute respiratory syndrome virus (SARS-CoV-2) outbreak is a huge health, social and economic issue and has been declared a pandemic by the World Health Organization. Bladder cancer, on the contrary, is a well-known disease burdened by a high rate of affected patients and risk of recurrence, progression and death. SUMMARY: The coronavirus disease (COVID-19 or 2019-nCoV) often involves mild clinical symptoms but in some cases, it can lead to pneumonia with acute respiratory distress syndrome and multiorgan dysfunction. Factors associated with developing a more severe disease are increased age, obesity, smoking and chronic underlying comorbidities (including diabetes mellitus). High-risk non-muscle-invasive bladder cancer (NMIBC) progression and worse prognosis are also characterized by a higher incidence in patients with risk factors similar to COVID-19. Immune system response and inflammation have been found as a common hallmark of both diseases. Most severe cases of COVID-19 and high-risk NMIBC patients at higher recurrence and progression risk are characterized by innate and adaptive immune activation followed by inflammation and cytokine/chemokine storm (interleukin [IL]-2, IL-6, IL-8). Alterations in neutrophils, lymphocytes and platelets accompany the systemic inflammatory response to cancer and infections. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio for example have been recognized as factors related to poor prognosis for many solid tumors, including bladder cancer, and their role has been found important even for the prognosis of SARS-CoV-2 infection. Key Messages: All these mechanisms should be further analyzed in order to find new therapeutic agents and new strategies to block infection and cancer progression. Further than commonly used therapies, controlling cytokine production and inflammatory response is a promising field.

Cabezon-Gutierrez, L., et al. (2020). "Seroprevalence of SARS-CoV-2-specific antibodies in cancer outpatients in Madrid (Spain): A single center, prospective, cohort study and a review of available data." Cancer Treat Rev **90**: 102102.

BACKGROUND: Coronavirus disease in 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has emerged as a global pandemic. Published data suggests that patients with a history of or active malignancy are at increased risk of infection and developing COVID-19 related complications. To date, the published data has analyzed the seroprevalence of COVID-19 infection in the general population, but not in cancer patients. Here we present the results of prevalence of IgG and IgM antibodies against SARS-CoV-2 in cancer patients from the University Hospital of Torrejon (Torrejon de Ardoz, Madrid, Spain). METHODS: SARS-CoV-2 IgG and IgM antibodies was assessed using a commercially available rapid test (Testsealabs(R) IgG/IgM Rapid Test Cassette) and collect the result from cancer outpatients who attended the medical oncology consult at University Hospital of Torrejon between June 1st and June 19th, 2020. FINDINGS: We analyzed the serological test results of 229 cancer patients. We estimated an overall seroprevalence (IgG or IgM positive) of 31.4%. The probability of

SARS-CoV-2 seropositivity was similar between men and women, type of treatment and cancer stage. The probability of seropositivity was significantly higher in cancer patients with pneumonia compared with cancer patients without pneumonia (Odds Ratio (OR) 7.65 [95% confidence interval (CI) 1,85-31,58]). INTERPRETATION: Our results show a higher rate of SARS-CoV-2 antibodies in cancer patients than in the general population. The role of those antibodies in the immune response against the virus infection is unclear.

Cai, Y., et al. (2020). "Considerations in treating patients with advance lung cancer during the epidemic outbreak of novel coronavirus (SARS-CoV-2)." Med Oncol **37**(9): 78.

The outbreak of pneumonia caused by novel coronavirus (SARS-CoV-2) in Wuhan, China, at the end of 2019 quickly escalated into a global health emergency. Since its outbreak until the 29th of April 2020, the pandemic has affected more than 3 million of people and caused 207,973 deaths globally. SARS-CoV-2 belongs to the beta-coronavirus genus of the Coronavirus family, and it shares the same subfamily with severe acute respiratory syndrome-associated coronavirus (SARS-CoV) and Middle East respiratory syndrome-associated coronavirus (MERS-CoV), all of which lead to severe pneumonia. For cancer patients, especially those with lung cancers, their immune systems are compromised due to the disease itself as well as the treatment for cancer. The weakened immunity of these patients puts them at a higher risk of not only developing diseases but severe diseases. In this study, through a literature review and data collection, we focus on the selection and consideration of antitumor treatment strategies for advanced lung cancer during the coronavirus disease 2019 (COVID-19) epidemic.

Cai, Y. C., et al. (2020). "Treating head and neck tumors during the SARS-CoV-2 epidemic, 2019 to 2020: Sichuan Cancer Hospital." Head Neck **42**(6): 1153-1158.

Since December 2019, a number of patients with novel coronavirus pneumonia (NCP) have been identified in Wuhan, Hubei Province, China. NCP has rapidly spread to other provinces and cities in China and other countries in the world. Due to the rapid increase in reported cases in China and around the world, on January 30, 2020, the World Health Organization (WHO) Emergency Committee announced that NCP is a Public Health Emergency of International Concern (PHEIC). However, there are relatively few suggestions and measures for tumor patients, especially patients with head and neck tumors. This article summarizes the prevention and control of disease in our medical institution to provide a reference for front-line head and neck surgeons.

Calvo, V., et al. (2021). "Cancer and SARS-CoV-2 Infection: A Third-Level Hospital Experience." Clin Epidemiol **13**: 317-324.

Introduction: Madrid has been the epicenter of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in Spain. We analyzed our experience with SARS-CoV-2 infected and cancer patients. Patients and Methods: We included patients from March 1 to April 30 2020 at Hospital Universitario Puerta de Hierro, Majadahonda, Madrid (Spain). The inclusion criteria were diagnosis of SARS-CoV-2 infection made by reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal specimens in cancer patients who were admitted to the hospital due to the need for respiratory support. The exclusion criteria were suspected cases not confirmed. The primary objective was to analyze the mortality rates of patients with cancer, especially those with lung cancer and COVID-19. Results: Overall in-hospital mortality of cancer patients with coronavirus disease 2019 (COVID-19) was 15.2% similar to 12.7% of the global COVID-19 hospitalized population (p=0.615) and greater than that of patients admitted without SARS-CoV-2 infection during the same period 4.3% (p<0.001). Among 653 patients receiving active cancer therapy during the study period, 24 (3.7%) developed COVID-19 and required admission, 4.2% of those receiving chemotherapy, 9.5% immunotherapy and 2.1% targeted therapies. Lung and breast cancer were the most frequent cancer types (26.1%), followed by colorectal cancer (19.6%). Mortality in patients with lung cancer was 25%. The univariate analysis comparing patients who developed a serious event to those who did not showed that the higher Brescia index, CURB-65 scale, lactate dehydrogenase (LDH) or C-reactive protein (CRP) were the risk factors of developing severe complications. Conclusion: Patients with cancer, especially lung cancer, and SARS-CoV-2 infection have a worse overall prognosis than the general population.

Cantini, L., et al. (2021). "Seroprevalence of SARS-CoV-2-Specific Antibodies in Cancer Patients Undergoing Active Systemic Treatment: A Single-Center Experience from the Marche Region, Italy." J Clin Med **10**(7).

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence in cancer patients may vary widely dependent on the geographic area and this has significant implications for oncological care. The aim of this observational, prospective study was to assess the seroprevalence of SARS-CoV-2 IgM/IgG antibodies in solid cancer patients referred to the academic institution of the Marche Region, Italy, between 1 July and 26 October 2020 and to determine the accuracy of the rapid serological test. After performing 3767 GCCOV-402a rapid serological tests on a total of 949 patients,

seroconversion was initially observed in 13 patients (1.4%). Ten (77% of the total positive) were IgG-positive, 1 (8%) were IgM-positive and 2 (15%) IgM-positive/IgG-positive. However, only 7 out of 13 were confirmed as positive at the reference serological test (true positives), thus seroprevalence after cross-checking was 0.7%. No false negatives were reported. The kappa value of the consistency analysis was 0.71. Due to rapid serological test high false positive rate, its role in assessing seroconversion rate is limited, and the standard serological tests should remain the gold standard. However, as rapid test negative predictive value is high, GCCOV-402a may instead be useful to monitor patient immunity over time, thus helping to assist ongoing vaccination programs.

Carvalho, K. M., et al. (2021). "Oral cancer management in the SARS-CoV-2 Pandemic-Indian scenario." J Family Med Prim Care **10**(3): 1090-1094.

The global burden of oral cancer rests on India's shoulders. Distant metastasis and extensive loco-regional spread result in a dismal 5-year prognosis. Tobacco chewing is the leading etiological factor. A lack of education among the masses combined with an inundated cancer care system account for high morbidity and mortality rates. The SARS-CoV-2 shows tropism for the oral mucosa. This viral tropism is thought to get augmented in oral cancer because of the upregulation of oral mucosal receptors and enzymes which enhance viral attachment and entry. The COVID-19 disease has caused a heavy blow to the cancer care sector in India because of paucity of COVID-19 centred health care regulations. This review highlights the need for the prompt creation of a national health policy which would prioritize and allow for the resumption of oral onco-surgical in light of COVID-19 pandemic.

Cavalcanti, E., et al. (2021). "Vaccination strategy and anti - SARS-CoV-2 S titers in healthcare workers of the INT - IRCCS "Fondazione Pascale" Cancer Center (Naples, Italy)." Infect Agent Cancer **16**(1): 32.

BACKGROUND: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and the resulting disease, coronavirus disease 2019 (COVID-19), have spread to millions of people globally, requiring the development of billions of different vaccine doses. The SARS-CoV-2 spike mRNA vaccine (named BNT162b2/Pfizer), authorized by the FDA, has shown high efficacy in preventing SARS-CoV-2 infection after administration of two doses in individuals 16 years of age and older. In the present study, we retrospectively evaluated the differences in the SARS-CoV-2 humoral immune response after vaccine administration in the two different cohorts of workers at the INT - IRCCS "Fondazione Pascale" Cancer Center (Naples, Italy): previously infected to SARS-CoV-2 subjects and not infected to SARS-CoV-2 subjects. METHODS: We determined specific anti-RBD (receptor-binding domain) titers against trimeric spike glycoprotein (S) of SARS-CoV-2 by Roche Elecsys Anti-SARS-CoV-2 S immunoassay in serum samples of 35 healthcare workers with a previous documented history of SARS-CoV-2 infection and 158 healthcare workers without, after 1 and 2 doses of vaccine, respectively. Moreover, geometric mean titers and relative fold changes (FC) were calculated. RESULTS: Both previously infected and not infected to SARS-CoV-2 subjects developed significant immune responses to SARS-CoV-2 after the administration of 1 and 2 doses of vaccine, respectively. Anti-S antibody responses to the first dose of vaccine were significantly higher in previously SARS-CoV-2-infected subjects in comparison to titers of not infected subjects after the first as well as the second dose of vaccine. Fold changes for subjects previously infected to SARS-CoV-2 was very modest, given the high basal antibody titer, as well as the upper limit of 2500.0 BAU/mL imposed by the Roche methods. Conversely, for naive subjects, mean fold change following the first dose was low ([Formula: see text] =1.6), reaching 3.8 FC in 72 subjects (45.6%) following the second dose. CONCLUSIONS: The results showed that, as early as the first dose, SARS-CoV-2-infected individuals developed a remarkable and statistically significant immune response in comparison to those who did not contract the virus previously, suggesting the possibility of administering only one dose in previously SARS-CoV-2-infected subjects. FC for previously infected subjects should not be taken into account for the generally high pre-vaccination values. Conversely, FC for not infected subjects, after the second dose, were = 3.8 in > 45.0% of vaccinees, and </= 3.1 in 19.0%, the latter showing a potential susceptibility to further SARS-CoV-2 infection.

Cavic, M., et al. (2021). "Exploring the real-world effect of the SARS-CoV-2 pandemic on the molecular diagnostics for cancer patients and high-risk individuals." Expert Rev Mol Diagn **21**(1): 101-107.

Background: The SARS-CoV-2 pandemic introduced a global distraction effect in cancer patients' care. The aim of this study was to explore the effect of the pandemic on the largest molecular diagnostics center for cancer patients and high-risk individuals in Serbia.Research design and methods: EGFR, KRAS/NRAS, BRAF, and BRCA1/2 mutation testing were performed by qPCR and NGS. NGS was used for panel testing of hereditary breast/ovarian cancer and cancers associated with Lynch syndrome. The analytical output during the state of emergency (SoE) was compared to the period

before and after the outbreak using one-way ANOVA. Statistical significance was set at $p < 0.05$.Results: A 38% reduction in the number of analysis was detected during the SoE. After the SoE, a 19% reduction was noted compared to SoE and 50% compared to the period before the SoE ($p = 0.038$). Three of the 48 scheduled appointments for pretest genetic counseling were carried out during the SoE, but the number of NGS tests increased by 50%.Conclusions: The SARS-CoV-2 pandemic had a profound negative effect on the diagnostic output of our centralized molecular diagnostics center. The only positive effect was shortening of waiting lists for hereditary cancer patients and high-risk individuals.

Chakravarty, D., et al. (2020). "Sex differences in SARS-CoV-2 infection rates and the potential link to prostate cancer." Commun Biol **3**(1): 374.

The recent outbreak of infections and the pandemic caused by SARS-CoV-2 represent one of the most severe threats to human health in more than a century. Emerging data from the United States and elsewhere suggest that the disease is more severe in men. Knowledge gained, and lessons learned, from studies of the biological interactions and molecular links that may explain the reasons for the greater severity of disease in men, and specifically in the age group at risk for prostate cancer, will lead to better management of COVID-19 in prostate cancer patients. Such information will be indispensable in the current and post-pandemic scenarios.

Chaudhari, S., et al. (2021). "Comorbidities and inflammation associated with ovarian cancer and its influence on SARS-CoV-2 infection." J Ovarian Res **14**(1): 39.

Coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide is a major public health concern. Cancer patients are considered a vulnerable population to SARS-CoV-2 infection and may develop several COVID-19 symptoms. The heightened immunocompromised state, prolonged chronic pro-inflammatory milieu coupled with comorbid conditions are shared in both disease conditions and may influence patient outcome. Although ovarian cancer (OC) and COVID-19 are diseases of entirely different primary organs, both diseases share similar molecular and cellular characteristics in their microenvironment suggesting a potential cooperativity leading to poor outcome. In COVID-19 related cases, hospitalizations and deaths worldwide are lower in women than in males; however, comorbidities associated with OC may increase the COVID-19 risk in women. The women at the age of 50-60 years are at greater risk of developing OC as well as SARS-CoV-2 infection. Increased levels of gonadotropin and androgen, dysregulated renin-angiotensin-aldosterone system (RAAS), hyper-coagulation and chronic inflammation are common conditions observed among OC and severe cases of COVID-19. The upregulation of common inflammatory cytokines and chemokines such as tumor necrosis factor alpha (TNF-alpha), interleukin (IL)-1beta, IL-2, IL-6, IL-10, interferon-gamma-inducible protein 10 (IP-10), granulocyte colony-stimulating factor (G-CSF), monocyte chemoattractant protein-1 (MCP-1), macrophage colony-stimulating factor (M-CSF), among others in the sera of COVID-19 and OC subjects suggests potentially similar mechanism(s) involved in the hyper-inflammatory condition observed in both disease states. Thus, it is conceivable that the pathogenesis of OC may significantly contribute to the potential infection by SARS-CoV-2. Our understanding of the influence and mechanisms of SARS-CoV-2 infection on OC is at an early stage and in this article, we review the underlying pathogenesis presented by various comorbidities of OC and correlate their influence on SARS-CoV-2 infection.

Chen, H., et al. (2020). "Differences in terms of presentation and outcomes between patients with lung cancer as opposed to other solid organ cancer after infection with SARS-CoV-2: protocol for a systematic review." BMJ Open **10**(11): e041790.

INTRODUCTION: Scholars believe that COVID-19 can be particularly lethal for patients with cancer. Some studies found that COVID-19 appears to be more lethal in patients with lung cancer than in other cancer patients. In order to take appropriate measures to balance a delay in lung cancer treatment against the risk for a potential COVID-19 exposure, we first need to know whether patients with lung cancer have special risks. We aim to conduct a systematic review and meta-analysis to examine differences in terms of presentation and outcomes between patients with lung cancer as opposed to other solid organ cancer after infection with SARS-CoV-2. METHODS AND ANALYSIS: A comprehensive search of published original research studies will be performed in Embase, MEDLINE, Web of Science, WangFangData, CQVIP, COMPENDEX and CNKI. The medRxiv preprint server will also be searched for applicable studies (grey literature). Original research studies will be included if they include patients with: (A) laboratory-confirmed SARS-CoV-2 infection and (B) confirmed solid cancer, and (C) measurable clinical presentation or outcome, such as mortality rate, intensive care unit admission rate, incidence of pneumonia. One author will conduct the electronic database searches, two authors will independently screen studies, two will extract data and two will assess study quality. If I(2) exceeds 60% for the pooled analysis, we will explore sources of heterogeneity in subgroups of studies. We will use fixed-effect, random-effects or mixed-effects models to estimate the relative risk or OR. If the data

reporting allows, a subgroup analysis between non-small cell lung cancer and small cell lung cancer patients will be performed. ETHICS AND DISSEMINATION: The proposed study will not collect individual-level data and, therefore, does not require ethical approval. We will submit our findings to a peer-reviewed scientific journal and will disseminate results through presentations at international scientific conferences. PROSPERO REGISTRATION NUMBER: CRD42020190118.

Chow, K., et al. (2021). "Risk of Healthcare-Associated Transmission of SARS-CoV-2 in Hospitalized Cancer Patients." Clin Infect Dis.

BACKGROUND: There is limited information on the risk of hospital-acquired COVID-19 among high-risk hospitalized patients after exposure to an infected patient or healthcare worker (HCW) in a non-outbreak setting. METHODS: This study was conducted at a tertiary care cancer center in New York City from March 10, 2020, until February 28, 2021. In early April 2020, the study institution implemented universal SARS-CoV-2 testing at admission and retesting every three days through the hospital stay. Contact tracing records were reviewed for all exposures to SARS-CoV-2 positive patients and HCWs. RESULTS: From March 10, 2020, to February 28, 2021, 11,348 unique patients who were SARS-CoV-2 PCR negative at the time of admission underwent 31,662 post-admission tests during their hospitalization, and 112 tested positive (0.98%). Among these, 49 patients housed in semi-private rooms during admission resulted in 74 close contacts and 14 secondary infections within 14 days, for an overall attack rate of 18.9%. Among those exposed to a roommate undergoing an aerosol-generating procedure (AGP), the attack rate was 35.7%. WGS corroborated transmission in 6/8 evaluated pairs. In addition, three transmission events occurred in 214 patients with significant exposure to 105 COVID-19 positive healthcare workers (1.4%). CONCLUSION: The overall risk of hospital-acquired COVID-19 is low for hospitalized cancer patients, even during periods of high community prevalence. However, shared occupancy with an unrecognized case is associated with a high secondary attack rate in exposed roommates.

Ciniselli, C. M., et al. (2021). "SARS-CoV-2 Serology Monitoring of a Cancer Center Staff in the Pandemic Most Infected Italian Region." Cancers (Basel) **13**(5).

Since the beginning of the COVID-19 outbreak, Cancer Centers adopted specific procedures both to protect patients and to monitor the possible spread of SARS-CoV-2 among healthcare personnel (HCP). In April 2020 at Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, one of the three oncologic hubs in Lombardy where the Health Regional Authorities referred all the cancer patients of the region, we implemented a prospective longitudinal study aimed at monitoring the serological response to SARS-Cov-2 in HCP. One hundred and ten HCP answered a questionnaire and were screened by nasopharyngeal swabs as well as for IgM/IgG levels; seropositive HCPs were further screened every 40-45 days using SARS-CoV-2-specific serology. We identified a fraction of HCP with long-term anti-SARS-CoV-2 antibody responses, though negative for viral RNA, and thus probably able to safely approach fragile cancer patients. Monitoring asymptomatic HCP might provide useful information to organize the healthcare service in a Cancer Center, while waiting for the effectiveness of the active immunization by SARS-CoV-2 vaccines, which will provide protection from infection.

Collaborative, C. O. (2020). "Outcomes from elective colorectal cancer surgery during the SARS-CoV-2 pandemic." Colorectal Dis.

AIM: This study aimed to describe the change in surgical practice and the impact of SARS-CoV-2 on mortality after surgical resection of colorectal cancer during the initial phases of the SARS-CoV-2 pandemic. METHOD: This was an international cohort study of patients undergoing elective resection of colon or rectal cancer without preoperative suspicion of SARS-CoV-2. Centres entered data from their first recorded case of COVID-19 until 19 April 2020. The primary outcome was 30-day mortality. Secondary outcomes included anastomotic leak, postoperative SARS-CoV-2 and a comparison with prepandemic European Society of Coloproctology cohort data. RESULTS: From 2073 patients in 40 countries, 1.3% (27/2073) had a defunctioning stoma and 3.0% (63/2073) had an end stoma instead of an anastomosis only. Thirty-day mortality was 1.8% (38/2073), the incidence of postoperative SARS-CoV-2 was 3.8% (78/2073) and the anastomotic leak rate was 4.9% (86/1738). Mortality was lowest in patients without a leak or SARS-CoV-2 (14/1601, 0.9%) and highest in patients with both a leak and SARS-CoV-2 (5/13, 38.5%). Mortality was independently associated with anastomotic leak (adjusted odds ratio 6.01, 95% confidence interval 2.58-14.06), postoperative SARS-CoV-2 (16.90, 7.86-36.38), male sex (2.46, 1.01-5.93), age >70 years (2.87, 1.32-6.20) and advanced cancer stage (3.43, 1.16-10.21). Compared with prepandemic data, there were fewer anastomotic leaks (4.9% versus 7.7%) and an overall shorter length of stay (6 versus 7 days) but higher mortality (1.7% versus 1.1%). CONCLUSION: Surgeons need to further mitigate against both SARS-CoV-2 and anastomotic leak when offering surgery during current and future COVID-19 waves based on patient, operative and organizational risks.

Consoli, F., et al. (2020). "New models of care and multidimensional solutions for oncological patients in the post-acute SARS-COV-2 period: a "Second Phase" also for cancer patients." Eur Rev Med Pharmacol Sci **24**(21): 11445-11454.

In Italy, SARS-CoV-2 outbreak registered a high transmission and disease rates. During the acute phase, oncologists provided to re-organize services and prioritize treatments, in order to limit viral spread and to protect cancer patients. The progressive reduction of the number of infections has prompted Italian government to gradually loosen the national confinement measures and to start the "Second phase" of measures to contain the pandemic. The issue on how to organize cancer care during this post-acute SARS-CoV-2 phase appears crucial and a reassessment of healthcare services is needed requiring new models of care for oncological patients. In order to address major challenges in cancer setting during post-acute SARS-CoV-2 phase, this work offers multidimensional solutions aimed to provide a new way to take care of cancer patients.

Corso, M. C. M., et al. (2021). "SARS-CoV-2 in children with cancer in Brazil: Results of a multicenter national registry." Pediatr Blood Cancer **68**(12): e29223.

BACKGROUND: Strategies to mitigate the impact of COVID-19 in special populations are complex and challenging. Few studies have addressed the impact of COVID-19 on pediatric patients with cancer in low- and middle-income countries. METHODS: Multicenter observational cohort study with prospective records and retrospective analyses starting in April 2020 in 21 pediatric oncology centers distributed throughout Brazil. PARTICIPANTS: Patients under 18 years of age who are infected by the SARS-CoV-2 virus (confirmed diagnosis through reverse transcriptase-polymerase chain reaction [RT-PCR]) while under treatment at pediatric oncology centers. The variables of interest included clinical symptoms, diagnostic and therapeutic measures. The repercussions of SARS-CoV-2 infection on cancer treatment and general prognosis were monitored. RESULTS: One hundred seventy-nine patients were included (median age 6 [4-13] years, 58% male). Of these, 55.9% had acute leukemia and 34.1% had solid tumors. The presence of SARS-CoV-2 was diagnosed by RT-PCR. Various laboratory markers were analyzed, but showed no correlation with outcome. Children with low or high BMI for age had lower overall survival (71.4% and 82.6%, respectively) than those with age-appropriate BMI (92.7%) ($p = .007$). The severity of presentation at diagnosis was significantly associated with outcome ($p < .001$). Overall mortality in the presence of infection was 12.3% ($n = 22$). CONCLUSION: In children with cancer and COVID-19, lower BMI was associated with worse prognosis. The mortality in this group of patients (12.3%) was significantly higher than that described in the pediatric population overall (approximately 1%).

Corti, C., et al. (2021). "SARS-CoV-2 vaccines for cancer patients: a call to action." Eur J Cancer **148**: 316-327.

Coronavirus disease 2019 (COVID-19) has affected more than 96 million people worldwide, leading the World Health Organization (WHO) to declare a pandemic in March 2020. Although an optimal medical treatment of COVID-19 remains uncertain, an unprecedented global effort to develop an effective vaccine hopes to restore pre-pandemic conditions. Since cancer patients as a group have been shown to be at a higher risk of severe COVID-19, the development of safe and effective vaccines is crucial. However, cancer patients may be underrepresented in ongoing phase 3 randomised clinical trials investigating COVID-19 vaccines. Therefore, we encourage stakeholders to provide real-time data about the characteristics of recruited participants, including clearly identifiable subgroups, like cancer patients, with sample sizes large enough to determine safety and efficacy. Moreover, we envisage a prompt implementation of suitable registries for pharmacovigilance reporting, in order to monitor the effects of COVID-19 vaccines and immunisation rates in patients with cancer. That said, data extrapolation from other vaccine trials (e.g. anti-influenza virus) showed a favourable safety and efficacy profile for cancer patients. On the basis of the evidence discussed, we believe that the benefits of the vaccination outweigh the risks. Consequently, healthcare authorities should prioritise vaccinations for cancer patients, with the time-point of administration agreed on a case-by-case basis. In this regard, the American Society of Clinical Oncology and the European Society of Medical Oncology are advocating for cancer patients a high priority status, in the hope of attenuating the consequences of the pandemic in this particularly vulnerable population.

Cui, Y., et al. (2021). "Comprehensive landscape of the renin-angiotensin system in Pan-cancer: a potential downstream mediated mechanism of SARS-CoV-2." Int J Biol Sci **17**(14): 3795-3817.

Background: SARS-CoV-2, the cause of the worldwide COVID-19 pandemic, utilizes the mechanism of binding to ACE2 (a crucial component of the renin-angiotensin system [RAS]), subsequently mediating a secondary imbalance of the RAS family and leading to severe injury to the host. However, very few studies have been conducted to reveal the mechanism behind the effect of SARS-CoV-2 on tumors. Methods: Demographic data extracted from 33 cancer types and over 10,000 samples were employed to determine the comprehensive landscape of the RAS. Expression distribution, pretranscriptional and posttranscriptional regulation

and posttranslational modifications (PTMs) as well as genomic alterations, DNA methylation and m6A modification were analyzed in both tissue and cell lines. The clinical phenotype, prognostic value and significance of the RAS during immune infiltration were identified. Results: Low expression of AGTR1 was common in tumors compared to normal tissues, while very low expression of AGTR2 and MAS1 was detected in both tissues and cell lines. Differential expression patterns of ACE in ovarian serous cystadenocarcinoma (OV) and kidney renal clear cell carcinoma (KIRC) were correlated with ubiquitin modification involving E3 ligases. Genomic alterations of the RAS family were infrequent across TCGA pan-cancer program, and ACE had the highest alteration frequency compared with other members. Low expression of AGTR1 may result from hypermethylation in the promoter. Downregulation of RAS family was linked to higher clinical stage and worse survival (as measured by disease-specific survival [DSS], overall survival [OS] or progression-free interval [PFI]), especially for ACE2 and AGTR1 in KIRC. ACE-AGTR1, a classical axis of the RAS family related to immune infiltration, was positively correlated with M2-type macrophages, cancer-associated fibroblasts (CAFs) and immune checkpoint genes in most cancers. Conclusion: ACE, ACE2, AGT and AGTR1 were differentially expressed in 33 types of cancers. PTM of RAS family was found to rely on ubiquitination. ACE2 and AGTR1 might serve as independent prognostic factors for LGG and KIRC. SARS-CoV-2 might modify the tumor microenvironment by regulating the RAS family, thus affecting the biological processes of cancer.

Dai, M., et al. (2020). "Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak." Cancer Discov **10**(6): 783-791.

The novel COVID-19 outbreak has affected more than 200 countries and territories as of March 2020. Given that patients with cancer are generally more vulnerable to infections, systematic analysis of diverse cohorts of patients with cancer affected by COVID-19 is needed. We performed a multicenter study including 105 patients with cancer and 536 age-matched noncancer patients confirmed with COVID-19. Our results showed COVID-19 patients with cancer had higher risks in all severe outcomes. Patients with hematologic cancer, lung cancer, or with metastatic cancer (stage IV) had the highest frequency of severe events. Patients with nonmetastatic cancer experienced similar frequencies of severe conditions to those observed in patients without cancer. Patients who received surgery had higher risks of having severe events, whereas patients who underwent only radiotherapy did not demonstrate significant differences in severe events when compared with patients without cancer. These findings indicate that patients with cancer appear more vulnerable to SARS-CoV-2 outbreak. SIGNIFICANCE: Because this is the first large cohort study on this topic, our report will provide much-needed information that will benefit patients with cancer globally. As such, we believe it is extremely important that our study be disseminated widely to alert clinicians and patients.This article is highlighted in the In This Issue feature, p. 747.

Dai, Y. J., et al. (2020). "Comprehensive analysis of two potential novel SARS-CoV-2 entries, TMPRSS2 and IFITM3, in healthy individuals and cancer patients." Int J Biol Sci **16**(15): 3028-3036.

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, with acute respiratory failure as the most significant symptom, has led to a global pandemic. Angiotensin-converting enzyme 2 (ACE2) is considered as the most important receptor of SARS-CoV-2 and wildly expressed in human tissues. Whereas, the extremely low expression of ACE2 in lung could hardly interpret the severe symptom of pneumonia in COVID-19 patients. Here we profiled two SARS-CoV-2 infection related genes, the transmembrane serine protease 2 (TMPRSS2) and the interferon-inducible transmembrane protein 3 (IFITM3), in human tissues and organs. Consistent with the expression and distribution of ACE2, TMPRSS2 was also highly expressed in digestive, urinary and reproductive systems, but low expressed in lung. Notably, the anti-virus protein IFITM3 also expressed much lower in lung than other tissues, which might be related to the severe lung symptoms of COVID-19. In addition, the low expression of IFITM3 in immune cells suggested that SARS-CoV-2 might attack lymphocytes and induce the cytokine release syndrome (CRS). Furthermore, cancer patients were considered as more susceptible to SARS-CoV-2 infection. Our data supposed that fourteen types of tumors might have different susceptibility to the virus according to ACE2, TMPRSS2 and IFITM3 expression patterns. Interestingly the prognosis of six types of cancers including breast carcinoma (BRCA), lung adenocarcinoma (LUAD), uterine corpus endometrial carcinoma (UCEC), renal clear cell carcinoma (KIRC), prostate adenocarcinoma (PRAD), and hepatocellular carcinoma (LIHC) were closely related to these gene expressions. Our study explored the expression and distribution profiles of two potential novel molecules that might participate in SARS-CoV-2 infection and involved in immunity, which may provide a functional basis for preventing infection of SARS-CoV-2.

Dettorre, G. M., et al. (2021). "Systemic pro-inflammatory response identifies patients with cancer with adverse outcomes from SARS-CoV-2 infection: the OnCovid Inflammatory Score." J Immunother Cancer **9**(3).

BACKGROUND: Patients with cancer are particularly susceptible to SARS-CoV-2 infection. The systemic inflammatory response is a pathogenic mechanism shared by cancer progression and COVID-19. We investigated systemic inflammation as a driver of severity and mortality from COVID-19, evaluating the prognostic role of commonly used inflammatory indices in SARS-CoV-2-infected patients with cancer accrued to the OnCovid study. METHODS: In a multicenter cohort of SARS-CoV-2-infected patients with cancer in Europe, we evaluated dynamic changes in neutrophil:lymphocyte ratio (NLR); platelet:lymphocyte ratio (PLR); Prognostic Nutritional Index (PNI), renamed the OnCovid Inflammatory Score (OIS); modified Glasgow Prognostic Score (mGPS); and Prognostic Index (PI) in relation to oncological and COVID-19 infection features, testing their prognostic potential in independent training (n=529) and validation (n=542) sets. RESULTS: We evaluated 1071 eligible patients, of which 625 (58.3%) were men, and 420 were patients with malignancy in advanced stage (39.2%), most commonly genitourinary (n=216, 20.2%). 844 (78.8%) had >/=1 comorbidity and 754 (70.4%) had >/=1 COVID-19 complication. NLR, OIS, and mGPS worsened at COVID-19 diagnosis compared with pre-COVID-19 measurement ($p<0.01$), recovering in survivors to pre-COVID-19 levels. Patients in poorer risk categories for each index except the PLR exhibited higher mortality rates ($p<0.001$) and shorter median overall survival in the training and validation sets ($p<0.01$). Multivariable analyses revealed the OIS to be most independently predictive of survival (validation set HR 2.48, 95% CI 1.47 to 4.20, p=0.001; adjusted concordance index score 0.611). CONCLUSIONS: Systemic inflammation is a validated prognostic domain in SARS-CoV-2-infected patients with cancer and can be used as a bedside predictor of adverse outcome. Lymphocytopenia and hypoalbuminemia as computed by the OIS are independently predictive of severe COVID-19, supporting their use for risk stratification. Reversal of the COVID-19-induced proinflammatory state is a putative therapeutic strategy in patients with cancer.

Di Cosimo, S., et al. (2021). "Baseline Characteristics and Outcomes of Cancer Patients Infected with SARS-CoV-2 in the Lombardy Region, Italy (AIOM-L CORONA): A Multicenter, Observational, Ambispective, Cohort Study." Cancers (Basel) **13**(6).

Cancer patients may be at high risk of infection and poor outcomes related to SARS-CoV-2. Analyzing their prognosis, examining the effects of baseline characteristics and systemic anti-cancer active therapy (SACT) are critical to their management through the evolving COVID-19 pandemic. The AIOM-L CORONA was a multicenter, observational, ambispective, cohort study, with the intended participation of 26 centers in the Lombardy region (Italy). A total of 231 cases were included between March and September 2020. The median age was 68 years; 151 patients (62.2%) were receiving SACT, mostly chemotherapy. During a median follow-up of 138 days (range 12-218), 93 events occurred. Age >/=60 years, metastatic dissemination, dyspnea, desaturation, and interstitial pneumonia were all independent mortality predictors. Overall SACT had a neutral effect (Odds Ratio [OR] 0.83, 95%Confidence Interval [95%CI] 0.32-2.15); however, metastatic patients receiving SACT were less likely to die as compared to untreated counterparts, after adjusting for other confounding variables (OR 0.23, 95%CI 0.11-0.51, $p < 0.001$). Among cancer patients infected by SARS-CoV-2, those with metastases were most at risk of death, especially in the absence of SACT. During the ongoing pandemic, these vulnerable patients should avoid exposure to SARS-CoV-2, while treatment adjustments and prioritizing vaccination are being considered according to international recommendations.

Di Marzo, F., et al. (2020). "SARS-CoV-2 pandemic: implications in the management of patients with colorectal cancer." New Microbiol **43**(4): 156-160.

The SARS-CoV-2 pandemic has already reached 3,207,248 patients with more than 225,000 deaths all over the world. Colorectal cancer is the third most diagnosed cancer worldwide, and the healthcare system is struggling to manage daily activities for elective cancer surgery. This review integrates clinical, microbiological, architectural and surgical aspects to develop indications on strategies to manage colorectal cancer patients and ensure safety during the pandemic. Telephone or virtual clinics must be encouraged and phone follow-up should be implemented. Indications for surgery must be rigorous, balancing the advantage of early surgical treatment and risks of treatment delay. To decrease the occupancy rate of intensive care unit beds, elective surgical treatment should be delayed until local endemic control, according to stage of disease. Patients with SARS-CoV-2 infection should be treated only after clinical recovery, two consecutive negative oropharyngeal swabs and, if available, a negative stool sample. Before any elective oncologic procedure, a multidisciplinary oncologic team including an anaesthesiologist and an infectious disease specialist must assess every patient to evaluate the risk of infection and its impact on perioperative morbidity, mortality and oncologic prognosis. The hospital should organise to manage all elective oncologic patients in an 'infection-free' area or refer them to a non-SARS-CoV-2 hospital.

Dong, S., et al. (2020). "Expert Consensus for Treating Cancer Patients During the Pandemic of SARS-CoV-2." Front Oncol **10**: 1555.

The sudden pandemic of SARS-Cov-2 (also known as novel coronavirus disease 2019, COVID-19) poses a severe threat to hundreds of millions of lives in the world. The complete cure of the virus largely relies on the immune system, which becomes particularly a challenge for the cancer subjects, whose immunity is generally compromised. However, in a constant evolving situation, the clinical data on the prevalence of SARS-Cov-2 for cancer patients is still limited. On top of a wide range of medical references and interim guidelines including CDC, NCI, ASCO, ESMO, NCCN, AACR, ESMO, and the National Health Commission of China, etc., we formed into a guideline based on our experience in our specialized cancer hospital in Wuhan, the originally endemic center of the virus. Furthermore, we formulated an expert consensus which was developed by all contributors from different disciplines after fully discussion based on our understanding and analysis of limited information of COVID-19. The consensus highlighted a multidisciplinary team diagnostic model with assessment of the balance between risks and benefits prior to treatment, individualizing satisfaction of patients' medical needs, and acceptability in ethics and patients' socio-economic conditions.

Drozgyik, A., et al. (2021). "Complex oncologic therapy for loco-regionally advanced breast cancer associated with long-lasting SARS-CoV-2 PCR-positivity." Orv Hetil **162**(16): 611-614.

Osszefoglalo. A COVID-19 mortalitasat a sulyos tarsbetegsegek, kozottuk bizonyos daganatos betegsegek is novelik. Immunszuppresszív hatasuk miatt felmerulhet a citotoxikus kezelesek rizikonovelo hatasa is. Ugyanakkor az onkologiai terapia megszakitasa vagy halasztasa, kulonosen az agresszivebb, kiterjedtebb es fiatalkorban jelentkezo daganatok eseteben ronthatja a korjoslatot. Egy 39 eves nobeteg esetet ismertetjuk. A jarvany soran keslekedve felismert, lokoregionalisan kiterjedt emlodaganat miatt primer szisztemas kemoterapiaban reszesult. A kezeles 5. ciklusa soran enyhe leguti tunetek kapcsan, az onkologiai ambulancian SARS-CoV-2-fertozese igazolodott. Kemoterapias kezeleset felfuggesztettuk. A diagnozistol szamitott 3. napon tunetmentesse valt, am SARS-CoV-2-PCR-pozitivitasa meg a 43. napon is fennallt. A 19. napon hormongatlo kezelest inditottunk. Az 51. napon mastectomia es axillaris block dissectio tortent. A 82. napon a megszakitott kemoterapiat a hormongatlo kezeles leallitasat kovetoen G-CSF-profilaxis mellett ujrainditottuk. A kezeles soran fertozeses szovodmenyt nem eszleltunk. Kemoterapia es mutet SARS-CoV-2-fertozott, tunetmentes daganatos betegnel szovodmenymentesen vegezheto elhuzodo virologiai pozitivitas eseten, felszabadito vizsgalat nelkul is. A daganatos betegek koronavirus-fertozese eseten az onkologiai protokolltol torteno elteres egyenre szabott optimalizalasaval es a multidiszciplinaris team szorosabb egyuttmukodesevel az infektologiai es az onkologiai kockazat egyuttes alacsonyan tartasa is megvalosithato. Orv Hetil. 2021; 162(16): 611-614. Summary. Mortality of COVID-19 is increased when certain co-morbidities, among others advanced malignancies are present. Deleterious effect of cytotoxic therapy, related to its immunosuppressive effect, may also be hypothesised. However, postponing or cancelling oncologic treatment, especially in younger patients with advanced and more aggressive tumors may worsen the prognosis. The case of a 39-year-old female patient is presented, who was diagnosed with loco-regionally advanced breast cancer during the pandemic. Primary systemic chemotherapy was started. The patient presented with acute respiratory tract symptoms during the fifth cycle and subsequently SARS-CoV-2 infection was diagnosed. Chemotherapy was cancelled. Symptoms resolved in three days after diagnosis. SARS-CoV-2 PCR remained positive up to day 43. Antihormonal therapy was introduced on day 19 and she underwent mastectomy with axillary lymph node dissection on day 51. Chemotherapy was reset postoperatively on day 82 with prophylactic G-CSF protection. No adverse event was observed throughout the treatment. Cytotoxic chemotherapy and surgery can be successfully delivered in breast cancer patients with prolonged asymptomatic SARS-CoV-2 PCR positivity, even without negative swab result. Individual optimisation of the therapy may require deviations from standard protocols. Closer multidisciplinary cooperation may contribute to the minimisation of both oncologic and infectious risks. Orv Hetil. 2021; 162(16): 611-614.

Elaiw, A. M. and A. D. Al Agha (2021). "Global dynamics of SARS-CoV-2/cancer model with immune responses." Appl Math Comput **408**: 126364.

The world is going through a critical period due to a new respiratory disease called coronavirus disease 2019 (COVID-19). This disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Mathematical modeling is one of the most important tools that can speed up finding a drug or vaccine for COVID-19. COVID-19 can lead to death especially for patients having chronic diseases such as cancer, AIDS, etc. We construct a new within-host SARS-CoV-2/cancer model. The model describes the interactions between six compartments: nutrient, healthy epithelial cells, cancer cells, SARS-CoV-2 virus particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies. We verify the nonnegativity and boundedness of its solutions. We outline all possible equilibrium points of the proposed model. We prove the global stability of equilibria by constructing proper Lyapunov functions. We do some numerical simulations to

visualize the obtained results. According to our model, lymphopenia in COVID-19 cancer patients may worsen the outcomes of the infection and lead to death. Understanding dysfunctions in immune responses during COVID-19 infection in cancer patients could have implications for the development of treatments for this high-risk group.

Esperanca-Martins, M., et al. (2021). "Humoral Immune Response of SARS-CoV-2-Infected Patients with Cancer: Influencing Factors and Mechanisms." Oncologist **26**(9): e1619-e1632.

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected patients with cancer show worse outcomes compared with patients without cancer. The humoral immune response (HIR) of patients with cancer against SARS-CoV-2 is not well characterized. To better understand it, we conducted a serological study of hospitalized patients with cancer infected with SARS-CoV-2. MATERIALS AND METHODS: This was a unicentric, retrospective study enrolling adult patients with SARS-CoV-2 admitted to a central hospital from March 15 to June 17, 2020, whose serum samples were quantified for anti-SARS-CoV-2 receptor-binding domain or spike protein IgM, IgG, and IgA antibodies. The aims of the study were to assess the HIR to SARS-CoV-2; correlate it with different cancer types, stages, and treatments; clarify the interplay between the HIR and clinical outcomes of patients with cancer; and compare the HIR of SARS-CoV-2-infected patients with and without cancer. RESULTS: We included 72 SARS-CoV-2-positive subjects (19 with cancer, 53 controls). About 90% of controls revealed a robust serological response. Among patients with cancer, a strong response was verified in 57.9%, with 42.1% showing a persistently weak response. Treatment with chemotherapy within 14 days before positivity was the only factor statistically shown to be associated with persistently weak serological responses among patients with cancer. No significant differences in outcomes were observed between patients with strong and weak responses. All IgG, IgM, IgA, and total Ig antibody titers were significantly lower in patients with cancer compared with those without. CONCLUSION: A significant portion of patients with cancer develop a proper HIR. Recent chemotherapy treatment may be associated with weak serological responses among patients with cancer. Patients with cancer have a weaker SARS-CoV-2 antibody response compared with those without cancer. IMPLICATIONS FOR PRACTICE: These results place the spotlight on patients with cancer, particularly those actively treated with chemotherapy. These patients may potentially be more vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, so it is important to provide oncologists further theoretical support (with concrete examples and respective mechanistic correlations) for the decision of starting, maintaining, or stopping antineoplastic treatments (particularly chemotherapy) not only on noninfected but also on infected patients with cancer in accordance with cancer type, stage and prognosis, treatment agents, treatment setting, and SARS-CoV-2 infection risks.

Fares, A. F., et al. (2021). "Systematic SARS-CoV-2-testing for asymptomatic cancer patients treated at a public healthcare tertiary centre in Brazil." Ecancermedicalscience **15**: 1269.

Background: The coronavirus disease (COVID-19) pandemic has had enormous consequences in Brazil and worldwide. Patients with cancer affected by COVID-19 are at a higher risk of developing complications and worse outcomes compared to the non-cancer population, particularly the ones on active systemic treatment. Considering the COVID-19's high transmissibility in asymptomatic and pre-symptomatic patients, we sought to determine the prevalence of COVID-19 infection in patients with solid cancers receiving systemic therapy in a Brazilian public health hospital. Furthermore, we studied whether socio-economic status was associated with prevalence. Methods: Consecutive asymptomatic patients undergoing treatment for solid tumours at the chemotherapy and infusion centre of Hospital de Base were enrolled. Patients were prospectively tested for severe acute respiratory syndrome coronavirus 2 RNA real-time polymerase chain reaction with nasal and oropharyngeal swabs immediately prior to treatment. A socio-economic survey was carried out prior to testing. Demographic and socio-economic characteristics were summarised in means, medians and proportions. Results: From 6 to 13 October 2020, 148 asymptomatic patients were identified. Of those, 41 were excluded, leaving 107 eligible patients. The mean age of the population was 58 years (SD +/- 12.6); 54% were female and 90% were self-identified as White. The most common cancer sites were gastrointestinal tract (36%) and breast (25%). Most patients had a metastatic disease (59%) and were on anticancer treatment involving chemotherapy (95%). Regarding socio-economic status, 46% of our population had either primary school or illiterate as their highest educational level. In terms of monthly income, 92% had a personal income inferior to U$380 and 88% a household income inferior to U$585. Of the 107 patients tested, only 1 (0.9%) was positive for COVID-19. This is a 48-year-old man living in an urban area, with primary school educational level and a monthly personal income inferior to U$390. Conclusion: Despite a high prevalence of COVID-19 in Brazil, our cohort demonstrated a low prevalence of COVID-19 (0.9%) amongst asymptomatic patients with cancer. We hypothesise that patients with cancer, independent of their socio-economic status, are aware of the

increased risk of developing a severe disease and are adherent to physical distancing, masking and hygiene measures.

Farolfi, A., et al. (2021). "Lung uptake detected by (68)Ga-PSMA-11 PET/CT in prostate cancer patients with SARS-CoV-2: a case series." Am J Nucl Med Mol Imaging **11**(4): 300-306.

Coronavirus disease 2019 (COVID-19) pathology is associated with neoangiogenesis and interstitial pneumonia. (68)Ga-PSMA-11-PET/CT is able to image in vivo PSMA (Prostate-Specific Membrane Antigen) expression on both prostate cancer (PCa) cells and neovasculature endothelial cells. The aim of the case series was to explore pulmonary PSMA expression not related to cancer in patients with PCa and concomitant COVID-19. In this retrospective, multicenter case series, patients who underwent (68)Ga-PSMA-11-PET/CT for PCa and concomitant proven COVID-19 infection were analyzed. Patients were stratified according to (68)Ga-PSMA-11 intensity of uptake in the lung (SUVmax). Low uptake: < blood pool; mild-to-moderate uptake: > blood pool and < liver; intense uptake: > liver. Potential correlation between pulmonary (68)Ga-PSMA-11 uptake not related to PCa and CT patterns typical for COVID-19 was assessed. Nine patients were included, all of them presenting abnormal (68)Ga-PSMA-11 uptake, at different grades: 2/9 low, 6/9 mild-to-moderate, 1/9 high. Uptake distribution was generally bilateral, peripheral and posterior, positively matching with ground-glass CT alterations in 7/9 (78%) patients, while mismatch was observed in 2/9 (22%). 1/9 patients presented PCa lung metastases at (68)Ga-PSMA-11. (68)Ga-PSMA-11-PET/CT detected increased PSMA uptake within the lung, not related to PCa, matching with CT typical COVID-19 patterns in almost all patients. Further studies are needed to evaluate the role of (68)Ga-PSMA-11 PET in COVID-19 patients and the potential role of PSMA overexpression as a biomarker for neoangiogenesis, in both oncological and infective disorders.

Fendler, A., et al. (2021). "Functional antibody and T-cell immunity following SARS-CoV-2 infection, including by variants of concern, in patients with cancer: the CAPTURE study." Res Sq.

Patients with cancer have higher COVID-19 morbidity and mortality. Here we present the prospective CAPTURE study (NCT03226886) integrating longitudinal immune profiling with clinical annotation. Of 357 patients with cancer, 118 were SARS-CoV-2-positive, 94 were symptomatic and 2 patients died of COVID-19. In this cohort, 83% patients had S1-reactive antibodies, 82% had neutralizing antibodies against WT, whereas neutralizing antibody titers (NAbT) against the Alpha, Beta, and Delta variants were substantially reduced. Whereas S1-reactive antibody levels decreased in 13% of patients, NAbT remained stable up to 329 days. Patients also had detectable SARS-CoV-2-specific T cells and CD4+ responses correlating with S1-reactive antibody levels, although patients with hematological malignancies had impaired immune responses that were disease and treatment-specific, but presented compensatory cellular responses, further supported by clinical. Overall, these findings advance the understanding of the nature and duration of immune response to SARS-CoV-2 in patients with cancer.

Fenioux, C., et al. (2021). "[Differences of characteristics and outcomes between cancer patients and patients with no active cancer hospitalised for a SARS-CoV-2 infection]." Bull Cancer **108**(6): 581-588.

BACKGROUND: Patients with solid cancer or haematologic malignancies have been considered to be more susceptible to SARS-CoV-2 infection and to more often develop severe complications. We aimed to compare the differences in clinical features and outcomes of COVID-19 patients with and without cancer. METHODS: This was a prospective observational cohort study of consecutive adult patients hospitalised in a COVID-19 unit at Pitie-Salpetriere Hospital, Paris, France (NCT04320017). RESULTS: Among the 262 patients hospitalised in a medical ward during the pandemics with a confirmed COVID-19 diagnosis, 62 patients had cancer. Clinical presentation, comorbidities, and outcomes were similar between cancer and non-cancer patients. However, cancer patients were more likely to have been contaminated while being hospitalised. CONCLUSIONS: Oncologic and non-oncologic patients hospitalised for COVID-19 shared similar outcomes in terms of death, admission in intensive care, or thrombosis/bleeding. They should benefit from the same therapeutic strategy as the general population during the COVID-19 pandemic.

Ferrari, A., et al. (2021). "Prolonged SARS-CoV-2-RNA Detection from Nasopharyngeal Swabs in an Oncologic Patient: What Impact on Cancer Treatment?" Curr Oncol **28**(1): 847-852.

The pandemic of SARS-CoV-2 is a serious global challenge affecting millions of people worldwide. Cancer patients are at risk for infection exposure and serious complications. A prompt diagnosis of SARS-CoV-2 infection is crucial for the timely adoption of isolation measures and the appropriate management of cancer treatments. In lung cancer patients the symptoms of infection 19 may resemble those exhibited by the underlying oncologic condition, possibly leading to diagnostic overlap and delays. Moreover, cancer patients might display a prolonged positivity of nasopharyngeal RT-PCR assays for SARS-CoV-2, causing long interruptions or delay of cancer treatments. However,

the association between the positivity of RT-PCR assays and the patient's infectivity remains uncertain. We describe the case of a patient with non-small cell lung cancer, and a severe ab extrinseco compression of the trachea, whose palliative radiotherapy was delayed because of the prolonged positivity of nasopharyngeal swabs for SARS-CoV-2. The patient did not show clinical symptoms suggestive of active infection, but the persistent positivity of RT-PCR assays imposed the continuation of isolation measures and the delay of radiotherapy for over two months. Finally, the negative result of SARS-CoV-2 viral culture allowed us to verify the absence of viral activity and to rule out the infectivity of the patient, who could finally continue her cancer treatment.

Fong, D., et al. (2021). "Evaluating the longitudinal effectiveness of preventive measures against COVID-19 and seroprevalence of IgG antibodies to SARS-CoV-2 in cancer outpatients and healthcare workers." Wien Klin Wochenschr **133**(7-8): 359-363.

BACKGROUND: It has been assumed that cancer patients, especially those undergoing chemotherapy, are at increased risk for infection and severe illness from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) compared to the general population. After the first alert message from the local healthcare service, a series of drastic measures were taken at our outpatient clinic to contain the spread of coronavirus disease 2019 (COVID-19). METHODS: In this retrospective study, all consecutive cancer outpatients completed a baseline SARS-CoV2 test via real-time polymerase chain reaction (RT-PCR) from 15 March to 26 May 2020. In the later phase, after the peak of the pandemic, patients as well as healthcare workers were tested for anti-SARS-CoV2 IgG antibodies. RESULTS: Between 15 March and 26 May 2020, 0.78% (N= 5/640) cancer patients tested positive for SARS-CoV2 by RT-PCR. Between 22 June and 17 July 2020, anti-SARS-CoV2 IgG antibodies were detected in 2 out of 250 (0.8%) cancer patients and 2 out of 36 (5.5%) healthcare workers. In only 1 out of 4 cancer patients with confirmed COVID-19 infection, could SARS-CoV2 antibodies be detected. CONCLUSION: Our findings suggest that the majority of our patients and healthcare workers had not been infected with SARS-CoV2 and rapidly implemented measures were effective. Maintenance of preventive measures should be continued until vaccines or specific treatments are available.

Foote, M. B., et al. (2021). "Association of Antineoplastic Therapy With Decreased SARS-CoV-2 Infection Rates in Patients With Cancer." JAMA Oncol **7**(11): 1686-1691.

Importance: Novel therapies for SARS-CoV-2 infection are urgently needed. Antineoplastic compounds that target cellular machinery used by SARS-CoV-2 for entry and replication, including angiotensin-converting enzyme 2 (ACE2), may disrupt SARS-CoV-2 activity. Objectives: To determine whether patients with cancer treated with potential ACE2-lowering antineoplastic compounds exhibit lower SARS-CoV-2 infection rates. Design, Setting, and Participants: We used the Library of Integrated Network-Based Cellular Signatures database to identify antineoplastic compounds associated with decreased ACE2 gene expression across cell lines. We then evaluated a retrospective cohort of 1701 patients who were undergoing antineoplastic therapy at Memorial Sloan Kettering Cancer Center in New York, New York, during the COVID-19 pandemic to determine if treatment with an ACE2-lowering antineoplastic was associated with a decreased odds ratio (OR) of SARS-CoV-2 infection. Patients included in the analysis underwent active treatment for cancer and received a SARS-CoV-2 test between March 10 and May 28, 2020. Main Outcome and Measure: The association between potential ACE2-lowering antineoplastic treatment and a positive SARS-CoV-2 test. Results: In the cohort of 1701 patients, SARS-CoV-2 infection rates were determined for 949 (55.8%) female and 752 (44.2%) male patients (mean [SD] age, 63.1 [13.1] years) with diverse cancers receiving antineoplastic therapy. In silico analysis of gene expression signatures after drug treatment identified 91 compounds associated with downregulation of ACE2 across cell lines. Of the total cohort, 215 (12.6%) patients were treated with 8 of these compounds, including 3 mTOR/PI3K inhibitors and 2 antimetabolites. In a multivariable analysis of patients who received an ACE2-lowering antineoplastic adjusting for confounders, 15 of 215 (7.0%) patients had a positive SARS-CoV-2 test compared with 191 of 1486 (12.9%) patients who received other antineoplastic therapies (OR, 0.53; 95% CI, 0.29-0.88). Findings were confirmed in additional sensitivity analyses including cancer type, steroid use, and a propensity-matched subcohort. Gemcitabine treatment was associated with reduced SARS-CoV-2 infection (OR, 0.42; 95% CI, 0.17-0.87). Conclusions and Relevance: In this cohort study, in silico analysis of drug-associated gene expression signatures identified potential ACE2-lowering antineoplastic compounds, including mTOR/PI3K inhibitors and antimetabolites. Patients who received these compounds exhibited statistically significantly lower rates of SARS-CoV-2 infection compared with patients given other antineoplastics. Further evaluation of the biological and clinical anti-SARS-CoV-2 properties of identified antineoplastic compounds is warranted.

Fuereder, T., et al. (2020). "SARS-CoV-2 seroprevalence in oncology healthcare professionals and patients with cancer at a tertiary care centre during the COVID-19 pandemic." ESMO Open **5**(5): e000889.

BACKGROUND: During the COVID-19 outbreak, healthcare professionals (HCP) are at the frontline of clinical management and at increased risk for infection. The SARS-CoV-2 seroprevalence of oncological HCP and their patients has significant implications for oncological care. METHODS: HCP and patients with cancer at the Division of Oncology, Medical University of Vienna were included between 21 March and 4 June and tested for total antibodies against SARS-CoV-2 employing the Roche Elecsys Anti-SARS-CoV-2 immunoassay. Reactive samples were confirmed or disproved by the Abbott SARS-CoV-2 IgG test. Additionally, a structured questionnaire regarding basic demographic parameters, travel history and COVID-19-associated symptoms had to be completed by HCP. RESULTS: 146 subjects (62 HCP and 84 patients with cancer) were enrolled. In the oncological HCP cohort, 20 (32.3%) subjects were medical oncologists, 28 (45.2%) nurses at our ward and 14 (22.6%) fulfil other functions such as study coordinators. In the patient cohort, most individuals are on active anticancer treatment (96.4%). 26% of the HCP and 6% of the patients had symptoms potentially associated with COVID-19 since the end of February 2020. However, only in 2 (3.2%) HCP and in 3 (3.6%) patients, anti-SARS-Cov-2 total antibodies were detected. The second assay for anti-SARS-Cov-2 IgG antibodies confirmed the positive result in all HCP and in 2 (2.4%) patients, suggesting an initial assay's unspecific reaction in one case. In individuals with a confirmed test result, an active COVID-19 infection was documented by a positive SARS-CoV-2 RNA PCR test. CONCLUSION: Specific anti-SARS-CoV-2 antibodies were found solely in persons after a documented SARS-CoV-2 viral infection, thus supporting the test methods' high sensitivity and specificity. The low prevalence of anti-SARS-CoV-2 antibodies in our cohorts indicates a lack of immunity against SARS-CoV-2. It highlights the need for continued strict safety measures to prevent uncontrolled viral spread among oncological HCPs and patients with cancer.

Gambichler, T., et al. (2020). "Cancer and Immune Checkpoint Inhibitor Treatment in the Era of SARS-CoV-2 Infection." Cancers (Basel) **12**(11).

Whether cancer patients receiving immune checkpoint inhibitors (ICI) are at an increased risk of severe infection and mortality during the corona pandemic is a hotly debated topic that will continue to evolve. Here, we summarize and discuss current studies regarding COVID-19 and anti-cancer treatment with an emphasis on ICI. Importantly, several lines of evidence suggest that patients currently treated with ICI do not display an increased vulnerability to infection with SARS-CoV-2. Data regarding morbidity and mortality associated with COVID-19 in cancer patients receiving ICI are less clear and often conflicting. Although mostly based on experimental data, it is possible that ICI can promote the exacerbated immune response associated with adverse outcome in COVID-19 patients. On the other hand, mounting evidence suggests that ICI might even be useful in the treatment of viral infections by preventing or ameliorating T cell exhaustion. In this context, the right timing of treatment might be essential. Nevertheless, some cancer patients treated with ICI experience autoimmune-related side effects that require the use of immunosuppressive therapies, which in turn may promote a severe course of infection with SARS-CoV-2. Although there is clear evidence that withholding ICI will have more serious consequences, further studies are urgently needed in to better evaluate the effects of ICI in patients with COVID-19 and the use of ICI during the corona pandemic in general.

Gao, Y., et al. (2021). "Developing Acid-Responsive Glyco-Nanoplatform Based Vaccines for Enhanced Cytotoxic T-lymphocyte Responses Against Cancer and SARS-CoV-2." Adv Funct Mater: 2105059.

Cytotoxic T-lymphocytes (CTLs) are central for eliciting protective immunity against malignancies and infectious diseases. Here, for the first time, partially oxidized acetalated dextran nanoparticles (Ox-AcDEX NPs) with an average diameter of 100 nm are fabricated as a general platform for vaccine delivery. To develop effective anticancer vaccines, Ox-AcDEX NPs are conjugated with a representative CTL peptide epitope (CTLp) from human mucin-1 (MUC1) with the sequence of TSAPDTRPAP (referred to as Mp1) and an immune-enhancing adjuvant R837 (referred to as R) via imine bond formation affording AcDEX-(imine)-Mp1-R NPs. Administration of AcDEX-(imine)-Mp1-R NPs results in robust and long-lasting anti-MUC1 CTL immune responses, which provides mice with superior protection from the tumor. To verify its universality, this nanoplatform is also exploited to deliver epitopes from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to prevent coronavirus disease 2019 (COVID-19). By conjugating Ox-AcDEX NPs with the potential CTL epitope of SARS-CoV-2 (referred to as Sp) and R837, AcDEX-(imine)-Sp-R NPs are fabricated for anti-SARS-CoV-2 vaccine candidates. Several epitopes potentially contributing to the induction of potent and protective anti-SARS-CoV-2 CTL responses are examined and discussed. Collectively, these findings shed light on the universal use of Ox-AcDEX NPs to deliver both tumor-associated and virus-associated epitopes.

Garcia Rodriguez, J., et al. (2021). "Changes in the ambulatory care of prostate cancer patients during the SARS-CoV-2 pandemic. Literature review and contribution of our group in telematic care." Actas Urol Esp (Engl Ed) **45**(8): 530-536.

INTRODUCTION AND OBJECTIVE: The COVID-19 pandemic has brought about changes in the management of urology patients, especially those with prostate cancer. The aim of this work is to show the changes in the ambulatory care practices by individualized telematic care for each patient profile. MATERIALS AND METHODS: Articles published from March 2020 to January 2021 were reviewed. We selected those that provided the highest levels of evidence regarding risk in different aspects: screening, diagnosis, treatment and follow-up of prostate cancer. RESULTS: We developed a classification system based on priorities, at different stages of the disease (screening, diagnosis, treatment and follow-up) to which the type of care given, in-person or telephone visits, was adapted. We established 4 options, as follows: in priority A or low, care will be given by telephone in all cases; in priority B or intermediate, if patients are considered subsidiary of an in-person visit after telephone consultation, they will be scheduled within 3 months; in priority C or high, patients will be seen in person within a margin from 1 to 3 months and in priority D or very high, patients must always be seen in person within a margin of up to 48h and considered very preferential. CONCLUSIONS: Telematic care in prostate cancer offers an opportunity to develop new performance and follow-up protocols, which should be thoroughly analyzed in future studies, in order to create a safe environment and guarantee oncologic outcomes for patients.

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Introduction and objective: The COVID-19 pandemic has brought about changes in the management of urology patients, especially those with prostate cancer.The aim of this work is to show the changes in the ambulatory care practices by individualized telematic care for each patient profile. Materials and methods: Articles published from March 2020 to January 2021 were reviewed. We selected those that provided the highest levels of evidence regarding risk in different aspects: screening, diagnosis, treatment and follow-up of prostate cancer. Results: We developed a classification system based on priorities, at different stages of the disease (screening, diagnosis, treatment and follow-up) to which the type of care given, in-person or telephone visits, was adapted. We established 4 options, as follows: in priority A or low, care will be given by telephone in all cases; in priority B or intermediate, if patients are considered subsidiary of an in-person visit after telephone consultation, they will be scheduled within 3 months; in priority C or high, patients will be seen in person within a margin from 1 to 3 months and in priority D or very high, patients must always be seen in person within a margin of up to 48 hours and considered very preferential. Conclusions: Telematic care in prostate cancer offers an opportunity to develop new performance and follow-up protocols, which should be thoroughly analyzed in future studies, in order to create a safe environment and guarantee oncologic outcomes for patients.

Garde-Noguera, J., et al. (2020). "Impact of SARS-CoV-2 Infection on Patients with Cancer: Retrospective and Transversal Studies in Spanish Population." Cancers (Basel) **12**(12).

BACKGROUND: Studies of patients with cancer affected by coronavirus disease 2019 (COVID-19) are needed to assess the impact of the disease in this sensitive population, and the influence of different cancer treatments on the COVID-19 infection and seroconversion. MATERIAL AND METHODS: We performed a retrospective analysis of all patients hospitalized with RT-PCR positive for COVID-19 in our region to assess the prevalence of cancer patients and describe their characteristics and evolution (Cohort 1). Concurrently, a transversal study was carried out in patients on active systemic cancer treatment for symptomatology and seroprevalence (IgG/IgM by ELISA-method) against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Cohort 2). RESULTS: A total of 215 patients (Cohort 1) were admitted to hospital with a confirmed COVID-19 infection between February 28 and April 30, 2020, and 17 died (7.9%). A medical record of cancer was noted in 43 cases (20%), 6 of them required Intensive care unit ICU attention (14%), and 7 died (16%). There were thirty-six patients (83%) who tested IgG/IgM positive for SARS-CoV-2. Patients on immunosuppressive therapies presented a lower ratio of seroconversion (40% vs. 8%; $p = 0.02$). In Cohort 2, 166 patients were included in a symptoms-survey and tested for SARS-CoV-2. Any type of potential COVID-19-related symptom was referred up to 67.4% of patients (85.9% vs. 48.2% vs. 73.9%, for patients on chemotherapy, immunotherapy and targeted therapies respectively, $p < 0.05$). The seroprevalence ratio was 1.8% for the whole cohort with no significant differences by patient or treatment characteristics. CONCLUSION: Patients with cancer present higher risks for hospital needs for COVID-19 infection. The lack of SARS-CoV-2 seroconversion may be a concern for patients on immunosuppressive therapies. Patients receiving systematic therapies relayed a high rate of potentially COVID-19-related symptoms, particularly those receiving chemotherapy. However, the seroconversion rate remains low and in the range of general population.

Glasbey, J. C., et al. (2021). "Elective Cancer Surgery in COVID-19-Free Surgical Pathways During the SARS-CoV-2 Pandemic: An

International, Multicenter, Comparative Cohort Study." J Clin Oncol **39**(1): 66-78.

PURPOSE: As cancer surgery restarts after the first COVID-19 wave, health care providers urgently require data to determine where elective surgery is best performed. This study aimed to determine whether COVID-19-free surgical pathways were associated with lower postoperative pulmonary complication rates compared with hospitals with no defined pathway. PATIENTS AND METHODS: This international, multicenter cohort study included patients who underwent elective surgery for 10 solid cancer types without preoperative suspicion of SARS-CoV-2. Participating hospitals included patients from local emergence of SARS-CoV-2 until April 19, 2020. At the time of surgery, hospitals were defined as having a COVID-19-free surgical pathway (complete segregation of the operating theater, critical care, and inpatient ward areas) or no defined pathway (incomplete or no segregation, areas shared with patients with COVID-19). The primary outcome was 30-day postoperative pulmonary complications (pneumonia, acute respiratory distress syndrome, unexpected ventilation). RESULTS: Of 9,171 patients from 447 hospitals in 55 countries, 2,481 were operated on in COVID-19-free surgical pathways. Patients who underwent surgery within COVID-19-free surgical pathways were younger with fewer comorbidities than those in hospitals with no defined pathway but with similar proportions of major surgery. After adjustment, pulmonary complication rates were lower with COVID-19-free surgical pathways (2.2% v 4.9%; adjusted odds ratio [aOR], 0.62; 95% CI, 0.44 to 0.86). This was consistent in sensitivity analyses for low-risk patients (American Society of Anesthesiologists grade 1/2), propensity score-matched models, and patients with negative SARS-CoV-2 preoperative tests. The postoperative SARS-CoV-2 infection rate was also lower in COVID-19-free surgical pathways (2.1% v 3.6%; aOR, 0.53; 95% CI, 0.36 to 0.76). CONCLUSION: Within available resources, dedicated COVID-19-free surgical pathways should be established to provide safe elective cancer surgery during current and before future SARS-CoV-2 outbreaks.

Goshen-Lago, T., et al. (2021). "Serologic Status and Toxic Effects of the SARS-CoV-2 BNT162b2 Vaccine in Patients Undergoing Treatment for Cancer." JAMA Oncol **7**(10): 1507-1513.

Importance: The efficacy and safety profile of SARS-CoV-2 vaccines have been acquired from phase 3 studies; however, patients with cancer were not represented in these trials. Owing to the recommendation to prioritize high-risk populations for vaccination, further data are warranted. Objective: To evaluate the use and safety of the BNT162b2 vaccine in patients undergoing treatment for cancer. Design, Setting, and Participants: In January 2021, mass SARS-CoV-2 vaccination of high-risk populations, including patients with cancer, was initiated in Israel. This cohort study prospectively enrolled and followed up patients with cancer and healthy participants between January 15 and March 14, 2021. The study was conducted at the Division of Oncology of Rambam Health Care Campus, the major tertiary (referral) medical center of northern Israel. Participants included 232 patients with cancer who were receiving active treatment after the first and second doses of the BNT162b2 vaccine and 261 healthy, age-matched health care workers who served as controls. Exposures: Serum samples were collected after each vaccine dose and in cases of seronegativity. Questionnaires regarding sociodemographic characteristics and adverse reactions were administered at serum collection. A regulatory agencies-approved assay was used to assess IgG at all time points. Patients' electronic medical records were reviewed for documentation of COVID-19 infection and results of blood cell counts, liver enzyme levels, and imaging studies. Main Outcomes and Measures: Seroconversion rate after the first and second doses of the BNT162b2 vaccine and documented COVID-19 infection. Results: Of the 232 patients undergoing treatment for cancer, 132 were men (57%); mean (SD) age was 66 (12.09) years. After the first dose of BNT162b2 vaccine, 29% (n = 25) patients were seropositive compared with 84% (n = 220) of the controls (P < .001). After the second dose, the seropositive rate reached 86% (n = 187) in the patients. Testing rate ratios per 1000 person-days after the first dose were 12.5 (95% CI, 3.4-45.7) for the patients and 48.5 (95% CI, 37.2-63.2) for the controls. Patients undergoing chemotherapy showed reduced immunogenicity (odds ratio, 0.41; 95% CI, 0.17-0.98). In seronegative patients, the rate of documented absolute leukopenia reached 39%. No COVID-19 cases were documented throughout the study period; however, 2 cases in the patient cohort were noted immediately after the first dose. Reported adverse events were similar to data in former trials comprising mostly healthy individuals. Conclusions and Relevance: In this cohort study, the SARS-CoV-2 BNT162b2 vaccine appeared to be safe and achieve satisfactory serologic status in patients with cancer. There was a pronounced lag in antibody production compared with the rate in noncancer controls; however, seroconversion occurred in most patients after the second dose. Future real-world data are warranted to determine the long-term efficacy of the vaccine with regard to type of anticancer treatment.

Gupta, I., et al. (2020). "SARS-CoV-2 Infection and Lung Cancer: Potential Therapeutic Modalities." Cancers (Basel) **12**(8).

Human coronaviruses, especially SARS-CoV-2, are emerging pandemic infectious diseases

with high morbidity and mortality in certain group of patients. In general, SARS-CoV-2 causes symptoms ranging from the common cold to severe conditions accompanied by lung injury, acute respiratory distress syndrome in addition to other organs' destruction. The main impact upon SARS-CoV-2 infection is damage to alveolar and acute respiratory failure. Thus, lung cancer patients are identified as a particularly high-risk group for SARS-CoV-2 infection and its complications. On the other hand, it has been reported that SARS-CoV-2 spike (S) protein binds to angiotensin-converting enzyme 2 (ACE-2), that promotes cellular entry of this virus in concert with host proteases, principally transmembrane serine protease 2 (TMPRSS2). Today, there are no vaccines and/or effective drugs against the SARS-CoV-2 coronavirus. Thus, manipulation of key entry genes of this virus especially in lung cancer patients could be one of the best approaches to manage SARS-CoV-2 infection in this group of patients. We herein provide a comprehensive and up-to-date overview of the role of ACE-2 and TMPRSS2 genes, as key entry elements as well as therapeutic targets for SARS-CoV-2 infection, which can help to better understand the applications and capacities of various remedial approaches for infected individuals, especially those with lung cancer.

Haque, R. and L. Chen (2021). "SARS-CoV-2 Testing, Positivity Rates, and Healthcare Outcomes in a Cohort of 22,481 Breast Cancer Survivors." JCO Clin Cancer Inform **5**: 168-175.

PURPOSE: As health inequities during the pandemic have been magnified, we evaluated how use of SARS-CoV-2 testing differed by race or ethnicity in a large cohort of breast cancer survivors and examined the correlates of testing positive. METHODS: We conducted a retrospective cohort study of 22,481 adult breast cancer survivors who were active members of a large California integrated healthcare plan in 2020. We collected data on their breast cancer diagnosis, comorbidity, and demographic characteristics. We examined SARS-CoV-2 testing utilization between March 2020 and September 2020 by race or ethnicity, comorbidity, and other patient characteristics. We also examined the correlates of a having a positive SARS-CoV-2 test result. We conducted bivariable and multivariable logistic regression to identify correlates of testing utilization and test positivity. RESULTS: Of these 22,481 women, 3,288 (14.6%) underwent SARS-CoV-2 testing. The cohort included 51.8% women of color. Of the 3,288 tested, 264 (8.0%) women had a positive test result. In multivariable analyses, Latinx survivors were more likely (adjusted odds ratio [OR], 1.23; 95% CI, 1.12 to 1.34) to undergo testing than White survivors; however, Asian or Pacific Islander survivors were 16% less likely to get tested (adjusted OR, 0.84; 95% CI, 0.75 to 0.94). Compared to White survivors, Latinx survivors were 3.5 times (adjusted OR, 3.47; 95% CI, 2.52 to 4.77) and Asian or Pacific Islander or Other survivors were 2.2-fold (adjusted OR, 2.23; 95% CI, 1.49 to 3.34) more likely to test positive. Being overweight (adjusted OR, 1.83; 95% CI, 1.24 to 2.72) or obese (adjusted OR, 2.04; 95% CI, 1.39 to 2.98) were also strongly associated with SARS-CoV-2 positivity. CONCLUSION: Even in an integrated healthcare system, Asian or Pacific Islander patients were less likely to undergo SARS-CoV-2 testing than White survivors, but more likely to test positive. Additionally, Latinx ethnicity and high body mass index were strongly correlated with a greater odds of SARS-CoV-2 test positivity.

Haradaa, G., et al. (2020). "SARS-CoV-2 testing for asymptomatic adult cancer patients before initiating systemic treatments: a systematic review." Ecancermedicalscience **14**: 1100.

Introduction: Cancer patients may have a higher risk of severe events and unfavourable outcomes in the setting of COVID-19. This review addresses the question of whether to test asymptomatic cancer patients before initiating systemic cancer treatments. Methods: This systematic review was conducted based on the PRISMA framework. Pubmed, Embase, Web of Science and Cochrane Central Register of Controlled Trials were systematically searched, as well as guidelines from international institutions involved in cancer care and COVID-19 research. Studies published in English, from 1 December 2019 to 27 May 2020 were considered eligible. We included studies which mentioned testing strategies for SARS-CoV-2 of asymptomatic cancer patients before starting immunosuppressive treatments. Results: We identified 1,163 studies and 4 guidelines through the literature search. A total of 18 articles were considered eligible and were included in the final analysis. Two articles were cohort studies, and the remaining were expert consensuses and published guidelines. The most common recommendation among the studies in this systematic review was to test asymptomatic patients for SARS-CoV-2 prior to treatment. Conclusion: There is a lack of studies which directly address COVID-19 testing of asymptomatic patients before treatment. Our systematic review showed that most of the published data favours routine test for SARS-CoV-2 before initiating systemic treatment but failed to identify a good level of evidence to support these recommendations. Based upon this review, we proposed local recommendations at our centre. Each institution should consider the pros and cons of testing asymptomatic patients, evaluating accessibility to testing resources and local epidemiology.

Hempel, L., et al. (2021). "Rare SARS-CoV-2 antibody development in cancer patients." Semin Oncol **48**(2): 160-165.

SARS-CoV-2 antibody development and immunity will be crucial for the further course of the pandemic. Until now, it has been assumed that patients who are infected with SARS-CoV-2 will develop antibodies as has been the case with other coronaviruses, like MERS-CoV and SARS-CoV. In the present study, we analyzed the development of antibodies in 77 patients with an oncologic diagnosis 26 days after positive RT-qPCR testing for SARS-CoV2. RT-qPCR and anti-SARS-CoV2-antibody methods from BGI (MGIEasy Magnetic Beads Virus DNA/RNA Extraction Kit) and Roche (Elecsys Anti-SARS-CoV-2 immunoassay) were used, respectively, according to the manufacturers' specifications. Surprisingly, antibody development was detected in only 6 of 77 individuals with a confirmed history of COVID-19. Despite multiple testing, the remaining patients did not show measurable antibody concentrations in subsequent tests. These results undermine the previous hypothesis that SARS-CoV2 infections are regularly associated with antibody development and cast doubt on the provided immunity to COVID-19. Understanding the adaptive and humoral response to SARS-CoV2 will play a key role in vaccine development and gaining further knowledge on the pathogenesis.

Hempel, L., et al. (2020). "SARS-CoV-2 infections in cancer outpatients-Most infected patients are asymptomatic carriers without impact on chemotherapy." Cancer Med **9**(21): 8020-8028.

Oncologic patients are regarded as the population most at risk of developing a severe course of COVID-19 due to the fact that malignant diseases and chemotherapy often weaken the immune system. In the face of the ongoing SARS-CoV-2 pandemic, how particular patients deal with this infection remains an important question. In the period between the 15 and 26 April 2020, a total of 1227 patients were tested in one of seven oncologic outpatient clinics for SARS-CoV-2, regardless of symptoms, employing RT-qPCR. Of 1227 patients, 78 (6.4%) were tested positive of SARS-CoV-2. Only one of the patients who tested positive developed a severe form of COVID-19 with pneumonia (CURB-65 score of 2), and two patients showed mild symptoms. Fourteen of 75 asymptomatic but positively tested patients received chemotherapy or chemo-immunotherapy according to their regular therapy algorithm (+/-4 weeks of SARS-CoV-2 test), and 48 of 78 (61.5%) positive-tested patients received glucocorticoids as co-medication. None of the asymptomatic infected patients showed unexpected complications due to the SARS-CoV-2 infection during the cancer treatment. These data clearly contrast the view that patients with an oncologic disease are particularly vulnerable to SARS-CoV-2 and suggest that compromising therapies could be continued or started despite the ongoing pandemic. Moreover the relatively low appearance of symptoms due to COVID-19 among patients on chemotherapy and other immunosuppressive co-medication like glucocorticoids indicate that suppressing the response capacity of the immune system reduces disease severity.

Howell, M. C., et al. (2021). "SARS-CoV-2-Induced Gut Microbiome Dysbiosis: Implications for Colorectal Cancer." Cancers (Basel) **13**(11).

The emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), in December 2019 led to a worldwide pandemic with over 170 million confirmed infections and over 3.5 million deaths (as of May 2021). Early studies have shown higher mortality rates from SARS-CoV-2 infection in cancer patients than individuals without cancer. Herein, we review the evidence that the gut microbiota plays a crucial role in health and has been linked to the development of colorectal cancer (CRC). Investigations have shown that SARS-CoV-2 infection causes changes to the gut microbiota, including an overall decline in microbial diversity, enrichment of opportunistic pathogens such as Fusobacterium nucleatum bacteremia, and depletion of beneficial commensals, such as the butyrate-producing bacteria. Further, these changes lead to increased colonic inflammation, which leads to gut barrier disruption, expression of genes governing CRC tumorigenesis, and tumor immunosuppression, thus further exacerbating CRC progression. Additionally, a long-lasting impact of SARS-CoV-2 on gut dysbiosis might result in a greater possibility of new CRC diagnosis or aggravating the condition in those already afflicted. Herein, we review the evidence relating to the current understanding of how infection with SARS-CoV-2 impacts the gut microbiota and the effects this will have on CRC carcinogenesis and progression.

Hu, S., et al. (2021). "In silico analysis identifies neuropilin-1 as a potential therapeutic target for SARS-Cov-2 infected lung cancer patients." Aging (Albany NY) **13**(12): 15770-15784.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), and is highly contagious and pathogenic. TMPRSS2 and Neuropilin-1, the key components that facilitate SARS-CoV-2 infection, are potential targets for treatment of COVID-19. Here we performed a comprehensive analysis on NRP1 and TMPRSS2 in lung to provide information for treating comorbidity of COVID-19 with lung cancer. NRP1 is widely expressed across all the human tissues while TMPRSS2 is expressed in a restricted pattern. High level of NRP1 associates with worse prognosis in multiple cancers, while high level

of TMPRSS2 is associated with better survival of Lung Adenocarcinoma (LUAD). Moreover, NRP1 positively correlates with the oncogenic Cancer Associated Fibroblast (CAF), macrophage and endothelial cells infiltration, negatively correlates with infiltration of CD8(+) T cell, the tumor killer cell in Lung Squamous cell carcinoma (LUSC). TMPRSS2 shows negative correlation with the oncogenic events in LUAD. RNA-seq data show that NRP1 level is slightly decreased in peripheral blood of ICU admitted COVID-19 patients, unaltered in lung, while TMPRSS2 level is significantly decreased in lung of COVID-19 patients. Our analysis suggests NRP1 as a potential therapeutic target, while sets an alert on targeting TMPRSS2 for treating comorbidity of COVID-19 and lung cancers.

Ilikci Sagkan, R. and D. F. Akin-Bali (2020). "Structural variations and expression profiles of the SARS-CoV-2 host invasion genes in lung cancer." J Med Virol **92**(11): 2637-2647.

Recent days have seen growing evidence of cancer's susceptibility to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and of the effect of genomic differences on the virus' entrance genes in lung cancer. Genetic confirmation of the hypotheses regarding gene expression and mutation pattern of target genes, including angiotensin-converting enzyme-2 (ACE2), transmembrane serine protease 2 (TMPRSS2), basigin (CD147/BSG) and paired basic amino acid cleaving enzyme (FURIN/PCSK3), as well as correlation analysis, was done in relation to lung adenocarcinoma (LUAD) and lung squamous carcinoma (LUSC) using in silico analysis. Not only were gene expression and mutation patterns detected, but also there were correlation and survival analysis between ACE2 and other target genes expression levels. The total genetic anomaly carrying rate of target genes, including ACE2, TMPRSS2, CD147/BSG, and FURIN/PCSK3, was determined as 8.1% and 21 mutations were detected, with 7 of these mutations having pathogenic features. p.H34N on the RBD binding residues for SARS-CoV-2 was determined in our LUAD patient group. According to gene expression analysis results, though the TMPRSS2 level was statistically significantly decreased in the LUSC patient group compared to healthy control, the ACE2 level was determined to be high in LUAD and LUSC groups. There were no meaningful differences in the expression of CD147 and FURIN genes. The challenge for today is building the assessment of genomic susceptibility to COVID-19 in lung cancer, requiring detailed experimental laboratory studies, in addition to in silico analyses, as a way of assessing the mechanism of novel virus invasion that can be used in the development of effective SARS-CoV-2 therapy.

Isgro, M. A., et al. (2021). "Immunotherapy may protect cancer patients from SARS-CoV-2 infection: a single-center retrospective analysis." J Transl Med **19**(1): 132.

Coronavirus disease 2019 (COVID-19) global pandemic has created unique challenges to healthcare systems throughout the world. Ensuring subjects' safety is mandatory especially in oncology, in consideration of cancer patients' particular frailty. We examined the proportion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgM and/or IgG positive subjects in three different groups from Istituto Nazionale Tumori - IRCCS "Fondazione G. Pascale" in Naples (Campania region, Italy): cancer patients treated with Innovative Immunotherapy (Immune Checkpoint Inhibitors, ICIs), cancer patients undergoing standard Chemotherapies (CHTs) and healthcare providers. 9 out of 287 (3.1%) ICIs patients resulted positive, with a significant lower percentage in respect to CHTs patients (39 positive subjects out of 598, 6.5%) ($p = 0.04$). There was no statistically significant difference between ICIs cohort and healthcare providers, 48 out of 1050 resulting positive (4.6%). Performing a Propensity Score Matching based on gender and tumor stage, the effect of treatment on seropositivity was analyzed through a regression logistic model and the ICIs treatment resulted to be the only protective factor significantly ($p = 0.03$) associated with positivity (odds ratio-OR: 0.41; 95% confidence interval-CI 0.18-0.91). According to these preliminary data, ICIs would appear to be a protective factor against the onset of COVID-19 infection.

Ivanyi, P., et al. (2021). "Protective measures for patients with advanced cancer during the Sars-CoV-2 pandemic: Quo vadis?" Clin Exp Metastasis **38**(3): 257-261.

Cancer patients represent a vulnerable cohort during the Sars-CoV-2 pandemic. Oncological societies have generated a plethora of recommendations, but precise instructions about routine oncological procedures remain scarce. Here, we report on local COVID-19 protection measures established in an interdisciplinary approach at a tertiary care center during the first wave of the pandemia in Germany. Following these measures, no additional morbidity or mortality during oncological procedures was observed, and no nosocomial infections were registered. However, Validation of our measures is outstanding and regional SARS-CoV-2 prevalence was low. However, specific oncological measures might be important to ensure optimal oncological results, especially for advanced cancer stages during this and future pandemia. In the future, communication about these measures might be crucial to a cancer patient s assigned network to reduce the danger of excess mortality within the second wave of the COVID-19 pandemic.

Jach, R., et al. (2020). "Possible deferral of diagnostic and therapeutic procedures for patients with abnormal screening tests results in cervical cancer secondary prevention in current SARS-CoV-2 pandemic Interim guidelines of the Polish Society of Gynecologists and Obstetricians and the Polish Society of Colposcopy and Cervical Pathophysiology." Ginekol Pol **91**(7): 428-431.

The Polish Society of Gynecologists and Obstetricians and Polish Society of Colposcopy and Cervical Pathophysiology Interim Guidelines goal at aiding gynecologists in providing a cervical cancer prevention care during the evolving SARS-CoV-2 pan-demic. Presented guidelines were developed on a review of limited data and updated when new relevant publications were revealed. Timing for deferrals of diagnostic-therapeutic procedures were mostly covered in the guidelines. Also, a support for the existing Polish recommendations on abnormal screening results in a subject of minor and major screening abnor-malities terminology were given. The guidelines are obligatory for the specified COVID-19 pandemic period only and they might be changed depending on the new available evidence.

Jach, R., et al. (2021). "Cervical cancer screening in Poland in current SARS-CoV-2 pandemic: Interim guidelines of the Polish Society of Gynecologists and Obstetricians and the Polish Society of Colposcopy and Cervical Pathophysiology - a summary January 2021." Ginekol Pol **92**(2): 165-173.

The Polish Society of Colposcopy and Cervical Pathophysiology (PTKiPSM) together with the Polish Society of Gynecologists and Obstetricians (PTGiP) issued a final summary of interim guidelines for secondary cervical cancer prevention during the SARS-CoV-2 pandemic based on the analysis of the latest directional publications and the authors' own experiences. The aim of the summary is to facilitate the implementation of the most effective possible screening of cervical precancerous lesions and cervical cancer due to temporary significant limitation of screening as a consequence of the ongoing epidemiological threat. These final guidelines are taking into account the 2020 call of the World Health Organization (WHO) for global epidemiological elimination of cervical cancer. The guidelines supplement the interim guidelines of PTKiPSM and PTGiP announced in March 2020 on the possible deferral of diagnostic and therapeutic procedures in patients with abnormal screening tests results in secondary prevention of cervical cancer in current pandemic.

Jiang, Y., et al. (2021). "The potential role of abnormal angiotensin-converting enzyme 2 expression correlated with immune infiltration after SARS-CoV-2 infection in the prognosis of breast cancer." Aging (Albany NY) **13**(17): 20886-20895.

The potential role of abnormal ACE2 expression after SARS-CoV-2 infection in the prognosis of breast cancer is still ambiguous. In this study, we analyzed ACE2 changes in breast cancer and studied the correlation between ACE2 and the prognosis and further analyzed the relationship between immune infiltration and the prognosis of different breast cancer subtypes. Finally, we inferred the prognosis of breast cancer patients after SARS-CoV-2 infection. We found that ACE2 expression decreased significantly in breast cancer, except for basal-like subtype. Decreased ACE2 expression level was correlated with abnormal immune infiltration and poorer prognosis of luminal B breast cancer (RFS: HR 0.76, 95%CI=0.63-0.92, p=0.005; DMFS: HR 0.70, 95%CI=0.49-1.00, p=0.046). The expression of ACE2 was strongly positively correlated with the immune infiltration level of CD8(+) T cell (r=0.184, p<0.001), CD4(+) T cell (r=0.104, p=0.02) and neutrophils (r=0.101, p=0.02). ACE2 expression level in the luminal subtype was positively correlated with CD8A and CD8B markers in CD8+ T cells, and CEACAM3, S100A12 in neutrophils. In conclusion, breast tumor tissues might undergo a further decrease in the expression level of ACE2 after SARS-CoV-2 infection, which could contribute to further deterioration of immune infiltration and worsen the prognosis of luminal B breast cancer after SARS-CoV-2 infection.

Kamarajah, S. K., et al. (2020). "The influence of the SARS-CoV-2 pandemic on esophagogastric cancer services: an international survey of esophagogastric surgeons." Dis Esophagus.

BACKGROUND: Several guidelines to guide clinical practice among esophagogastric surgeons during the COVID-19 pandemic were produced. However, none provide reflection of current service provision. This international survey aimed to clarify the changes observed in esophageal and gastric cancer management and surgery during the COVID-19 pandemic. METHODS: An online survey covering key areas for esophagogastric cancer services, including staging investigations and oncological and surgical therapy before and during (at two separate time-points-24th March 2020 and 18th April 2020) the COVID-19 pandemic were developed. RESULTS: A total of 234 respondents from 225 centers and 49 countries spanning six continents completed the first round of the online survey, of which 79% (n = 184) completed round 2. There was variation in the availability of staging investigations ranging from 26.5% for endoscopic ultrasound to 62.8% for spiral computed tomography scan. Definitive chemoradiotherapy was offered in 14.8% (adenocarcinoma) and 47.0% (squamous cell carcinoma) of respondents and significantly increased by almost three-fold and two-fold, respectively, in both round 1 and 2. There were uncertainty and heterogeneity surrounding

prioritization of patients undergoing cancer resections. Of the surgeons symptomatic with COVID-19, only 40.2% (33/82) had routine access to COVID-19 polymerase chain reaction testing for staff. Of those who had testing available (n = 33), only 12.1% (4/33) had tested positive. CONCLUSIONS: These data highlight management challenges and several practice variations in caring for patients with esophagogastric cancers. Therefore, there is a need for clear consistent guidelines to be in place in the event of a further pandemic to ensure a standardized level of oncological care for patients with esophagogastric cancers.

Kaur, H., et al. (2021). "Impact of Underlying Comorbidities on Mortality in SARS-COV-2 Infected Cancer Patients: A Systematic Review and Meta-Analysis." Asian Pac J Cancer Prev **22**(5): 1333-1349.

BACKGROUND: The evidence has shown that SARS CoV-2 infected patients with comorbidities are more likely to have severe disease sequel and mortality. In SARS-CoV-2 infected cancer patients risks associated with other underlying comorbidities might vary from those in non-cancer SARS CoV-2 infected patients. The relative impact of different underlying health conditions among patients with cancer and SARS CoV-2 infection remains yet to be explored. This systematic review aims to explore the prevalence of comorbidities among cancer patients with SARS CoV-2 infection and their impact on mortality. METHODS: Online databases PubMed, Embase, Scopus and Web of science were searched for articles published between 9th July 2019 to July 8th 2020.Studies of cancer patients (>18 years) with diagnosis of SARS CoV-2 infection, published in English were included. A random-effects modelling for the meta-analyses was applied to assess the pooled prevalence and odds ratio for mortality due to comorbidities in SARS CoV-2 infected cancer patients. RESULTS: Total 31studies with 4086 SARS-CoV-2 infectedcancer patientsmet the inclusion criteria. Most prevalent co-morbidities in cancer patients with SARS CoV-2 infection were hypertension [42.3% (95%CI:37.5-47.0)], diabetes [17.8% (95% CI: 15.3-20.4)] and cardiovascular diseases [16.7% (95%CI:12.9-20.4)].The risk of mortality (pOR) was significantly higher in individuals with hypertension[1.6(95%CI 1.24-2.00)], cardiovascular diseases [2.2 (95%CI 1.49- 3.27)], chronic obstructive pulmonary diseases [1.4(95% CI 1.05-2.00)] and diabetes [1.35(95%CI 1.06-1.73)]. CONCLUSION: Our results indicates that the mortality in SARS-CoV-2 infected cancer patients is affected by preexisting non-cancer comorbidities. By identifying the comorbidities predictive for mortality, clinicians can better stratify the risk of cancer patients presenting with SARS-COV-2, on their initial contact with health services.
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Khusid, J. A., et al. (2021). "Cancer, Mortality, and Acute Kidney Injury among Hospitalized Patients with SARS-CoV-2 Infection." Asian Pac J Cancer Prev **22**(2): 517-522.

BACKGROUND: To evaluate Coronavirus Disease 2019-(COVID19) patients treated within our academic medical system to determine if history of malignancy, both in general and specifically in genitourinary oncology patients, is associated with adverse clinical outcomes, including acute kidney injury (AKI) and mortality. METHODS: We conducted a retrospective cohort study among patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a multi-hospital, academic medical institution in New York City. Outcomes included mortality, intensive care unit (ICU) admission and AKI among hospitalized patients. We also evaluated risk of hospitalization among all patients with SARS-CoV-2 infection. Multilevel logistic regression models were used for analysis. RESULTS: We identified 6,893 patients who met inclusion criteria, of which 4,018 were hospitalized. Among hospitalized patients 374 (9%) had a history of cancer, 281 (7%) experienced AKI, and 1,045 (26%) died. In adjusted analyses, patients with a history of cancer had 1.33 (95% CI = 1.05, 1.69) times the odds of death compared to those without cancer and this appeared to be driven by lung cancer (odds ratio (OR) = 2.44, 95% CI= 1.05, 4.39). Patients with a history of genitourinary cancer were not at higher risk of mortality compared to those without cancer (OR=0.99, 95% CI= 0.61, 1.62). History of cancer was not associated with ICU admission or AKI in overall and subgroup analyses. CONCLUSIONS: Patients with a history of cancer who are hospitalized with SARS-CoV-2 infection are not at greater risk for AKI, though they are at higher risk for mortality as compared to patients without a history of cancer. The increased risk in mortality appears driven by patients with pulmonary neoplasms. Patients with a history of genitourinary malignancies do not appear to be at higher risk for AKI or for mortality compared to the general population.

Klein, E. A., et al. (2021). "Androgen Deprivation Therapy in Men with Prostate Cancer Does Not Affect Risk of Infection with SARS-CoV-2." J Urol **205**(2): 441-443.

PURPOSE: TMPRSS2 is a host co-receptor for cell entry of SARS-CoV-2. A prior report suggested that use of androgen deprivation therapy, which downregulates TMPRSS2, may protect men with prostate cancer from infection. MATERIALS AND METHODS: This is a cohort study of a prospective registry of all patients tested for SARS-CoV-2 between March 12 and June 10, 2020 with complete followup until disease recovery or death. The main exposure examined was the use of

androgen deprivation therapy, and the outcome measures were the rate of SARS-CoV-2 positivity and disease severity as a function of androgen deprivation therapy use. RESULTS: The study cohort consisted of 1,779 men with prostate cancer from a total tested population of 74,787, of whom 4,885 (6.5%) were positive for SARS-CoV-2. Of those with prostate cancer 102 (5.7%) were SARS-CoV-2 positive and 304 (17.1%) were on androgen deprivation therapy. Among those on androgen deprivation therapy 5.6% were positive as compared to 5.8% not on androgen deprivation therapy. Men on androgen deprivation therapy were slightly older (75.5 vs 73.8 years, p=0.009), more likely to have smoked (68.1% vs 59.3%, p=0.005) and more likely to report taking steroids (43.8% vs 23.3%, p <0.001). Other factors known to increase risk of infection and disease severity were equally distributed (asthma, diabetes mellitus, hypertension, coronary artery disease, heart failure and immune suppressive disease). Multivariable analysis did not indicate a difference in infection risk for those with prostate cancer on androgen deprivation therapy (OR 0.93, 95% CI 0.54-1.61, p=0.8). CONCLUSIONS: Androgen deprivation therapy does not appear to be protective against SARS-CoV-2 infection.

Kothari, A. N., et al. (2021). "Surgical Outcomes in Cancer Patients Undergoing Elective Surgery After Recovering from Mild-to-Moderate SARS-CoV-2 Infection." Ann Surg Oncol **28**(13): 8046-8053.

BACKGROUND: An increasing number of patients with cancer diagnoses and prior SARS-CoV-2 infection will require surgical treatment. The objective of this study was to determine whether a history of SARS-CoV-2 infection increases the risk of adverse postoperative events following surgery in patients with cancer. METHODS: This was a propensity-matched cohort study from April 6, 2020 to October 31, 2020 at the UT MD Anderson Cancer Center. Cancer patients were identified who underwent elective surgery after recovering from SARS-CoV-2 infection and matched to controls based on patient, disease, and surgical factors. Primary study outcome was a composite of the following adverse postoperative events that occurred within 30 days of surgery: death, unplanned readmission, pneumonia, cardiac injury, or thromboembolic event. RESULTS: A total of 5682 patients were included for study, and 114 (2.0%) had a prior SARS-CoV-2 infection. The average time from infection to surgery was 52 (range 20-202) days. Compared with matched controls, there was no difference in the rate of adverse postoperative outcome (14.3% vs. 13.4%, p = 1.0). Patients with a SARS-CoV-2-related inpatient admission before surgery had increased odds of postoperative complication (adjusted odds ratio [aOR] 7.4 [1.6-34.3], p = 0.01). CONCLUSIONS: A minimal wait time of 20 days after recovering from minimally symptomatic SARS-CoV-2 infection appears to be safe for cancer patients undergoing low-risk elective surgery. Patients with SARS-CoV-2 infections requiring inpatient treatment were at increased risk for adverse events after surgery. Additional wait time may be required in those with more severe infections.

Kvale, R., et al. (2021). "Does a history of cardiovascular disease or cancer affect mortality after SARS-CoV-2 infection?" Tidsskr Nor Laegeforen **140**(2).

BACKGROUND: Cardiovascular disease and cancer have been described as possible risk factors for COVID-19 mortality. The purpose of this study was to investigate whether a history of cardiovascular disease or cancer affects the risk of dying after a COVID-19 diagnosis in Norway. MATERIAL AND METHOD: Data were compiled from the Norwegian Surveillance System for Communicable Diseases, the Norwegian Cardiovascular Disease Registry and the Cancer Registry of Norway. Univariable and multivariable regression models were used to calculate both relative and absolute risk. RESULTS: In the first half of 2020, 8 809 people tested positive for SARS-CoV-2 and 260 COVID-19-associated deaths were registered. Increasing age, male sex (relative risk (RR): 1.5; confidence interval (CI): 1.2-2.0), prior stroke (RR: 1.5; CI: 1.0-2.1) and cancer with distant metastasis at the time of diagnosis (RR: 3.0; CI: 1.1-8.2) were independent risk factors for death after a diagnosis of COVID-19. After adjusting for age and sex, myocardial infarction, atrial fibrillation, heart failure, hypertension, and non-metastatic cancer were no longer statistically significant risk factors for death. INTERPRETATION: The leading risk factor for death among individuals who tested positive for SARS-CoV-2 was age. Male sex, and a previous diagnosis of stroke or cancer with distant metastasis were also associated with an increased risk of death after a COVID-19 diagnosis.

Ladoire, S., et al. (2021). "Seroprevalence of SARS-CoV-2 among the staff and patients of a French cancer centre after first lockdown: The canSEROcov study." Eur J Cancer **148**: 359-370.

BACKGROUND: In view of the potential gravity of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection for patients with cancer, epidemiological data are vital to assess virus circulation among patients and staff of cancer centres. We performed a prospective study to investigate seroprevalence of SARS-CoV-2 antibodies among staff and patients with cancer at a large cancer centre, at the end of the period of first national lockdown in France and to determine factors associated with the risk of SARS-CoV-2 infection. METHODS: After the first lockdown, all medical and non-medical staff, as well as all patients attending the medical oncology department were

invited to undergo serological testing for SARS-CoV-2 between 11 May and 30 June 2020. All participants were also invited to complete a questionnaire collecting data about their living and working conditions, and for patients, medical management during lockdown. FINDINGS: A total of 1,674 subjects (663 staff members, 1011 patients) were included. Seroprevalence was low in both staff (1.8%) and patients (1.7%), despite more features of high risk for severe forms among patients. None of the risk factors tested in our analysis (working or living conditions, comorbidities, management characteristics during lockdown) was found to be statistically associated with seroprevalence in either staff or patients. There was no significant difference in the proportion of symptomatic and asymptomatic subjects between staff and patients. Only fever, loss of smell, and loss of taste were significantly more frequent among seropositive patients, in both staff and patients. INTERPRETATION: We report very low seroprevalence of antibodies against SARS-CoV-2 in the staff (caregiving and non-caregiving) and patients of a large cancer care centre in which strict hygiene, personal protection, and social distancing measures were implemented.

Lasagna, A., et al. (2021). "A snapshot of the immunogenicity, efficacy and safety of a full course of BNT162b2 anti-SARS-CoV-2 vaccine in cancer patients treated with PD-1/PD-L1 inhibitors: a longitudinal cohort study." ESMO Open **6**(5): 100272.

BACKGROUND: Very few cancer patients were enrolled in coronavirus disease-2019 vaccine studies. In order to address this gap of knowledge, real-world studies are mandatory. The aim of this study was to assess both humoral and cellular response after a messenger RNA vaccination schedule. PATIENTS AND METHODS: Eighty-eight consecutive cancer patients treated with programmed cell death protein 1/programmed death-ligand 1 inhibitors were enrolled from the beginning of the vaccination campaign for frail patients. Blood samples for humoral and cell-mediated immune response evaluation were obtained before vaccination (T0), before the second administration (T1) and 21 days after the second dose (T2). The primary endpoint was the evaluation of the percentage of participants showing a significant increase in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific T cells, measured by an enzyme-linked immunospot assay, after the second dose of BNT162b2 vaccine. The proportion of patients who reached the primary endpoint is computed together with its exact binomial 95% confidence interval. RESULTS: In SARS-CoV-2-naive subjects, spike-specific T-cell response was almost undetectable at T0 [median 0.0 interferon-gamma (IFN-gamma) spot forming units (SFU)/million peripheral blood mononuclear cell (PBMC) interquartile range (IQR) 0-7.5] and significantly increased at T1 and T2 (median 15.0 IFN-gamma SFU/million PBMC, 25th-75th 0-40 versus 90 IFN-gamma SFU/million PBMC, 25th-75th 32.5-224, respectively) ($P < 0.001$). Focusing on naive and experienced SARS-CoV-2 subjects, no differences were reported both in terms of CD4- and CD8-specific T-cell response, suggesting that BNT162b2 is able to elicit both adaptive responses after complete vaccination schedule, regardless of previous SARS-CoV-2 exposure. The level of SARS-CoV-2 neutralizing antibodies was low at T1 in SARS-CoV-2-naive subjects [median 1 : 5 (IQR 1 : 5-1 : 20)] but reached a significantly higher median of 1 : 80 (25th-75th 1 : 20-1 : 160) at T2 ($P < 0.0001$). Moreover, no COVID-19 cases were documented throughout the period of study. CONCLUSIONS: Our data have demonstrated that the administration of a full course of BNT162b2 vaccine elicited a sustained immune response against SARS-CoV-2 regardless of the type of cancer and/or the type of immune checkpoint inhibitors.

Li, H., et al. (2020). "Genomic, epigenomic, and immune subtype analysis of CTSL/B and SARS-CoV-2 receptor ACE2 in pan-cancer." Aging (Albany NY) **12**(22): 22370-22389.

SARS-coronavirus 2 (SARS-CoV-2) has been spreading widely and posing an international challenge for both healthcare and society. At present, cancer has been identified as an individual risk factor for COVID-19. Angiotensin converting enzyme 2 (ACE2) and Cathepsin L/Cathepsin B (CTSL/B), which act as the receptor and entry-associated proteases of SARS-CoV-2 respectively, are pivotal for SARS-CoV-2 infection. To investigate the possible SARS-CoV-2 infection risk of pan-cancer, we analyzed the genetic alterations, RNA expression, DNA methylation, and the association with immune subtypes of ACE2 and CTSL/B with the prognosis in pan-cancer. Results showed the upregulation of CTSL/B and ACE2 in Pancreatic adenocarcinoma (PAAD) and Stomach adenocarcinoma (STAD) and demonstrated a positive correlation between copy number alteration (CNA) and gene expression for CTSB in PAAD and STAD. Hypomethylation and a negative correlation of gene expression and methylation for CTSB were detected in PAAD. In addition, ACE2 and CTSL/B are overexpressed in the IFN-gamma immune subtype of ovarian serous Cystadenocarcinoma (OV), Cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), and Bladder urothelial carcinoma (BLCA). Our study presents a bioinformatics assessment for the potential risk of SARS-CoV-2 infection in pan-cancer.

Li, P., et al. (2021). "Effect of antitumor therapy on cancer patients infected by SARS-CoV-2: A

systematic review and meta-analysis." Cancer Med **10**(5): 1644-1655.

BACKGROUND: Cancer patients are at a high risk of being infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and are more likely to develop severe illness and have higher mortality once infected. In the COVID-19 pandemic, it is urgent to understand the effects of antitumor therapy on the prognosis of patients with COVID-19. METHODS: A systematic literature search was conducted in PubMed, Cochrane Library, Embase, MedRxiv, and Chinese National Knowledge Infrastructure (CNKI) until 21 June 2020. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were evaluated using a random effects model to analyze the effects of antitumor therapies on COVID-19 patients. RESULTS: For cancer patients with COVID-19, the death events related to antitumor treatment were higher than those with no antitumor treatment (OR = 1.55; 95% CI 1.07-2.25; p = 0.021). Compared with patients in the survival group, the non-survival group showed no significant differences in patients who received antitumor therapy. Compared with patients in the non-severe group, the severe group was more likely to receive antitumor therapy (OR = 1.50; 95% CI 1.02-2.19; p = 0.037) and there was a significant difference. The incidence of severe events was higher in the subgroup of chemotherapy (OR = 1.73; 95% CI 1.09-2.73). CONCLUSION: The synthesized evidence suggests that cancer patients with COVID-19 who received antitumor treatment shortly before symptom onset are more likely to experience severe symptoms and have high mortality. Receiving chemotherapy is an unfavorable factor for the prognosis of cancer patients with COVID-19.

Locantore, P., et al. (2021). "Lenvatinib treatment for thyroid cancer in COVID era: safety in a patient with lung metastases and SARS-CoV-2 infection." Anticancer Drugs **32**(10): 1116-1117.

During the coronavirus disease 2019 (COVID-19) pandemic, clinicians are required to manage patient care for pre-existing conditions. Currently, there are no clear indications regarding the management of lenvatinib-treated patients for radioiodine-refractory thyroid cancer and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. A 74-year-old male patient was treated with lenvatinib since March 2019, with disease recurrence in the thyroid bed and bilateral multiple lung metastases. The patient partially responded to treatment, with reduction in lung metastases. In September 2019, the patient tested positive for SARS-CoV-2 and isolated at home. Initially asymptomatic, the patient developed mild symptoms. Lenvatinib treatment continued with daily monitoring of vital signs. After telemedicine consultation of patient's clinical condition, severity of symptoms was low. He tested negative for SARS-CoV-2 21 days after testing positive. The patient received the full course of lenvatinib treatment. This is the first reported case of a lenvatinib-treated patient who developed COVID-19 and could continue treatment. Despite concerns over COVID-19, clinicians should not overlook treatment of pre-existing diseases or discontinue treatment, particularly for cancer. Clinicians should evaluate a patient's history and clinical presentation, monitoring the patient to reduce the development of complications in high-risk settings, avoiding treatment discontinuation.

Lovly, C. M., et al. (2020). "Rapidly fatal pneumonitis from immunotherapy and concurrent SARS-CoV-2 infection in a patient with newly diagnosed lung cancer." medRxiv.

Immune checkpoint inhibitors (ICIs) are used for the treatment of numerous cancers, but risks associated with ICI-therapy during the COVID-19 pandemic are poorly understood. We report a case of acute lung injury in a lung cancer patient initially treated for ICI-pneumonitis and later found to have concurrent SARS-CoV-2 infection. Post-mortem analyses revealed diffuse alveolar damage in both the acute and organizing phases, with a predominantly CD68+ inflammatory infiltrate. Serum was positive for anti-SARS-CoV-2 IgG, suggesting that viral infection predated administration of ICI-therapy and may have contributed to a more fulminant clinical presentation. These data suggest the need for routine SARS-CoV-2 testing in cancer patients, where clinical and radiographic evaluations may be non-specific.

Lundon, D. J., et al. (2020). "A Decision Aide for the Risk Stratification of GU Cancer Patients at Risk of SARS-CoV-2 Infection, COVID-19 Related Hospitalization, Intubation, and Mortality." J Clin Med **9**(9).

Treatment decisions for both early and advanced genitourinary (GU) malignancies take into account the risk of dying from the malignancy as well as the risk of death due to other causes such as other co-morbidities. COVID-19 is a new additional and immediate risk to a patient's morbidity and mortality and there is a need for an accurate assessment as to the potential impact on of this syndrome on GU cancer patients. The aim of this work was to develop a risk tool to identify GU cancer patients at risk of diagnosis, hospitalization, intubation, and mortality from COVID-19. A retrospective case showed a series of GU cancer patients screened for COVID-19 across the Mount Sinai Health System (MSHS). Four hundred eighty-four had a GU malignancy and 149 tested positive for SARS-CoV-2. Demographic and clinical variables of >38,000 patients were available in the institutional database and were utilized to develop decision aides to predict a positive SARS-CoV-2 test,

as well as COVID-19-related hospitalization, intubation, and death. A risk tool was developed using a combination of machine learning methods and utilized BMI, temperature, heart rate, respiratory rate, blood pressure, and oxygen saturation. The risk tool for predicting a diagnosis of SARS-CoV-2 had an AUC of 0.83, predicting hospitalization for management of COVID-19 had an AUC of 0.95, predicting patients requiring intubation had an AUC of 0.97, and for predicting COVID-19-related death, the risk tool had an AUC of 0.79. The models had an acceptable calibration and provided a superior net benefit over other common strategies across the entire range of threshold probabilities.

Mandala, M., et al. (2021). "SARS-CoV-2 infection and adverse events in patients with cancer receiving immune checkpoint inhibitors: an observational prospective study." J Immunother Cancer **9**(2).

BACKGROUND: In ambulatory patients with cancer with asymptomatic or pauci-symptomatic SARS-CoV-2 infection, the safety of targeted therapies (TTs), chemotherapy (CT) or immune checkpoint inhibitors (ICIs) therapy is still unknown. MATERIAL AND METHODS: From the start of the first epidemic wave of SARS-CoV-2 in Bergamo, Italy, we have prospectively screened all consecutive outpatients who presented for treatment to the Oncology Division of the Papa Giovanni XXIII Hospital, Bergamo for SARS-CoV-2 antigen expression. We identified patients treated with ICIs and compared these to patients with the same cancer subtypes treated with TTs or CT. RESULTS: Between March 5 and May 18, 293 consecutive patients (49% melanoma, 34% non-small cell lung cancer, 9% renal cell carcinoma, 8% other) were included in this study: 159 (54%), 50 (17%) and 84 (29%) received ICIs, CT or TTs, respectively. Overall 89 patients (30.0%) were SARS-CoV-2 positive. Mortality of SARS-CoV-2-positive patients was statistically significantly higher compared with SARS-CoV-2 negative patients (8/89 vs 3/204, respectively, Fisher's exact test p=0.004). All deaths were due to COVID-19. Serious adverse events (SAEs) were more frequent in SARS-CoV-2-positive patients compared with SARS-CoV-2-negative cases (Cochran-Mantel-Haenszel (CMH) test p=0.0008). The incidence of SAEs in SARS-CoV-2 positive compared with SARS-CoV-2 negative patients was similar in ICI and CT patients (17.3% and 3.7% for positive and negative patients in ICIs and 15.4% and 2.7% in CT, Breslow-Day test p=0.891). No COVID-19-related SAEs were observed in the TTs patients. CONCLUSIONS: The incidence of SAEs was higher for SARS-CoV-2-positive patients treated with ICIs and CT, mostly in advanced disease. No SAEs were observed in patients treated with TTs. SAEs were COVID-19 related rather than treatment related. Treatment with ICIs does not appear to significantly increase risk of SAEs compared with CT. This information should be considered when determining treatment options for patients.

Marra, A., et al. (2021). "Seroconversion in patients with cancer and oncology health care workers infected by SARS-CoV-2." Ann Oncol **32**(1): 113-119.

BACKGROUND: Patients with cancer have high risk for severe complications and poor outcome to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related disease [coronavirus disease 2019 (COVID-19)]. Almost all subjects with COVID-19 develop anti-SARS-CoV-2 immunoglobulin G (IgG) within 3 weeks after infection. No data are available on the seroconversion rates of cancer patients and COVID-19. PATIENTS AND METHODS: We conducted a multicenter, observational, prospective study that enrolled (i) patients and oncology health professionals with SARS-CoV-2 infection confirmed by real-time RT-PCR assays on nasal/pharyngeal swab specimens; (ii) patients and oncology health professionals with clinical or radiological suspicious of infection by SARS-CoV-2; and (iii) patients with cancer who are considered at high risk for infection and eligible for active therapy and/or major surgery. All enrolled subjects were tested with the 2019-nCoV IgG/IgM Rapid Test Cassette, which is a qualitative membrane-based immunoassay for the detection of IgG and IgM antibodies to SARS-CoV-2. The aim of the study was to evaluate anti-SARS-CoV-2 seroconversion rate in patients with cancer and oncology health care professionals with confirmed or clinically suspected COVID-19. RESULTS: From 30 March 2020 to 11 May 2020, 166 subjects were enrolled in the study. Among them, cancer patients and health workers were 61 (36.7%) and 105 (63.3%), respectively. Overall, 86 subjects (51.8%) had confirmed SARS-CoV-2 diagnosis by RT-PCR testing on nasopharyngeal swab specimen, and 60 (36.2%) had a clinical suspicious of COVID-19. Median time from symptom onset (for cases not confirmed by RT-PCR) or RT-PCR confirmation to serum antibody test was 17 days (interquartile range 26). In the population with confirmed RT-PCR, 83.8% of cases were IgG positive. No difference in IgG positivity was observed between cancer patients and health workers (87.9% versus 80.5%; P = 0.39). CONCLUSIONS: Our data indicate that SARS-CoV-2-specific IgG antibody detection do not differ between cancer patients and healthy subjects.

Marschner, S., et al. (2020). "SARS-CoV-2 prevalence in an asymptomatic cancer cohort - results and consequences for clinical routine." Radiat Oncol **15**(1): 165.

BACKGROUND: Starting in December 2019, the current pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2) confronts the world with an unprecedented challenge. With no vaccine or drug being currently available to control the pandemic spread, prevention and PCR (Polymerase chain reaction) testing becomes a crucial pillar of medical systems. Aim of the present study was to report on the first results of the measures taken in a large German Department of Radiation Oncology, including PCR testing of asymptomatic cancer patients. METHODS: Pandemic-adapted hygiene regulations and prevention measures for patients and staff were implemented. A visiting ban on both wards was implemented from the beginning and medical staff and patients were required to wear face masks at all times. The waiting rooms were rearranged to ensure distance between patients of at least 1.5 m. Clinical follow up was mainly done by telephone and all patients had to complete a questionnaire regarding symptoms and contacts with COVID-19 patients before entering our department. Educational documents were created for patients to raise awareness of symptoms and avoidance strategies for interactions with other people. Indications for therapy and fractionation schemes were adapted when possible. In a subsequent step, all new asymptomatic patients were tested via nasopharyngeal swab at our screening station shortly before their simulation CT. RESULTS: All these measures and implementations have been well accepted semiquantitatively measured by the consent received from patients and staff. Regarding the PCR testing, only 1 out of 139 asymptomatic patients of our cohort so far tested positive for SARS-CoV-2, reflecting a prevalence of 0.72% in this cancer patient population. Up to this point no staff members was tested positive. The start of the treatment for the PCR-positive patient was deferred for 2 weeks. CONCLUSION: Due to the pandemic-adapted implementations, our department seems well prepared during this crisis. The initial screening helps to identify asymptomatic COVID-19 patients in order to protect other patients and our staff from infection and the observed PCR prevalence is in line with comparable studies. A regular PCR testing (e.g. twice a week) of all patients and staff would in principle be desirable but is limited due to testing capacities at present.

Matuschek, C., et al. (2020). "Measures of infection prevention and incidence of SARS-CoV-2 infections in cancer patients undergoing radiotherapy in Germany, Austria and Switzerland." Strahlenther Onkol **196**(12): 1068-1079.

PURPOSE: COVID-19 infection has manifested as a major threat to both patients and healthcare providers around the world. Radiation oncology institutions (ROI) deliver a major component of cancer treatment, with protocols that might span over several weeks, with the result of increasing susceptibility to COVID-19 infection and presenting with a more severe clinical course when compared with the general population. The aim of this manuscript is to investigate the impact of ROI protocols and performance on daily practice in the high-risk cancer patients during this pandemic. METHODS: We addressed the incidence of positive COVID-19 cases in both patients and health care workers (HCW), in addition to the protective measures adopted in ROIs in Germany, Austria and Switzerland using a specific questionnaire. RESULTS: The results of the questionnaire showed that a noteworthy number of ROIs were able to complete treatment in SARS-CoV2 positive cancer patients, with only a short interruption. The ROIs reported a significant decrease in patient volume that was not impacted by the circumambient disease incidence, the type of ROI or the occurrence of positive cases. Of the ROIs 16.5% also reported infected HCWs. About half of the ROIs (50.5%) adopted a screening program for patients whereas only 23.3% also screened their HCWs. The range of protective measures included the creation of working groups, instituting home office work and protection with face masks. Regarding the therapeutic options offered, curative procedures were performed with either unchanged or moderately decreased schedules, whereas palliative or benign radiotherapy procedures were more often shortened. Most ROIs postponed or cancelled radiation treatment for benign indications (88.1%). The occurrence of SARS-CoV2 infections did not affect the treatment options for curative procedures. Non-university-based ROIs seemed to be more willing to change their treatment options for curative and palliative cases than university-based ROIs. CONCLUSION: Most ROIs reported a deep impact of SARS-CoV2 infections on their work routine. Modification and prioritization of treatment regimens and the application of protective measures preserved a well-functioning radiation oncology service and patient care.

McKay, S. C., et al. (2021). "Impact of SARS-CoV-2 pandemic on pancreatic cancer services and treatment pathways: United Kingdom experience." HPB (Oxford) **23**(11): 1656-1665.

INTRODUCTION: The SARS-CoV-2 pandemic presented healthcare providers with an extreme challenge to provide cancer services. The impact upon the diagnostic and treatment capacity to treat pancreatic cancer is unclear. This study aimed to identify national variation in treatment pathways during the pandemic. METHODS: A survey was distributed to all United Kingdom pancreatic specialist centres, to assess diagnostic, therapeutic and interventional services availability, and alterations in treatment pathways. A repeating methodology enabled assessment over time as the pandemic evolved. RESULTS: Responses were received from all 29 centres. Over the first six weeks of the pandemic, less than a quarter of centres had

normal availability of diagnostic pathways and a fifth of centres had no capacity whatsoever to undertake surgery. As the pandemic progressed services have gradually improved though most centres remain constrained to some degree. One third of centres changed their standard resectable pathway from surgery-first to neoadjuvant chemotherapy. Elderly patients, and those with COPD were less likely to be offered treatment during the pandemic. CONCLUSION: The COVID-19 pandemic has affected the capacity of the NHS to provide diagnostic and staging investigations for pancreatic cancer. The impact of revised treatment pathways has yet to be realised.

Meti, N., et al. (2021). "SARS-CoV-2 Testing for Asymptomatic Patients with Cancer Prior and during Treatment: A Single Centre Experience." Curr Oncol **28**(1): 278-282.

Patients with cancer are more vulnerable to severe COVID-19. As a result, routine SARS-CoV-2 testing of asymptomatic patients with cancer is recommended prior to treatment. However, there is limited evidence of its clinical usefulness. The objective of this study is to evaluate the value of routine testing of asymptomatic patients with cancer. Asymptomatic patients with cancer attending Odette Cancer Centre (Toronto, ON, Canada) were tested for SARS-CoV-2 prior to and during treatment cycles. Results were compared to positivity rates of SARS-CoV-2 locally and provincially. All 890 asymptomatic patients tested negative. Positivity rates in the province were 1.5%, in hospital were 1.0%, and among OCC's symptomatic cancer patients were 0% over the study period. Given our findings and the low SARS-CoV-2 community positivity rates, we recommend a dynamic testing model of asymptomatic patients that triggers testing during increasing community positivity rates of SARS-CoV-2.

Mukkada, S., et al. (2021). "Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study." Lancet Oncol **22**(10): 1416-1426.

BACKGROUND: Previous studies have shown that children and adolescents with COVID-19 generally have mild disease. Children and adolescents with cancer, however, can have severe disease when infected with respiratory viruses. In this study, we aimed to understand the clinical course and outcomes of SARS-CoV-2 infection in children and adolescents with cancer. METHODS: We did a cohort study with data from 131 institutions in 45 countries. We created the Global Registry of COVID-19 in Childhood Cancer to capture de-identified data pertaining to laboratory-confirmed SARS-CoV-2 infections in children and adolescents (<19 years) with cancer or having received a haematopoietic stem-cell transplantation. There were no centre-specific exclusion criteria. The registry was disseminated through professional networks through email and conferences and health-care providers were invited to submit all qualifying cases. Data for demographics, oncological diagnosis, clinical course, and cancer therapy details were collected. Primary outcomes were disease severity and modification to cancer-directed therapy. The registry remains open to data collection. FINDINGS: Of 1520 submitted episodes, 1500 patients were included in the study between April 15, 2020, and Feb 1, 2021. 1319 patients had complete 30-day follow-up. 259 (19.9%) of 1301 patients had a severe or critical infection, and 50 (3.8%) of 1319 died with the cause attributed to COVID-19 infection. Modifications to cancer-directed therapy occurred in 609 (55.8%) of 1092 patients receiving active oncological treatment. Multivariable analysis revealed several factors associated with severe or critical illness, including World Bank low-income or lower-middle-income (odds ratio [OR] 5.8 [95% CI 3.8-8.8]; p<0.0001) and upper-middle-income (1.6 [1.2-2.2]; p=0.0024) country status; age 15-18 years (1.6 [1.1-2.2]; p=0.013); absolute lymphocyte count of 300 or less cells per mm(3) (2.5 [1.8-3.4]; p<0.0001), absolute neutrophil count of 500 or less cells per mm(3) (1.8 [1.3-2.4]; p=0.0001), and intensive treatment (1.8 [1.3-2.3]; p=0.0005). Factors associated with treatment modification included upper-middle-income country status (OR 0.5 [95% CI 0.3-0.7]; p=0.0004), primary diagnosis of other haematological malignancies (0.5 [0.3-0.8]; p=0.0088), the presence of one of more COVID-19 symptoms at the time of presentation (1.8 [1.3-2.4]; p=0.0002), and the presence of one or more comorbidities (1.6 [1.1-2.3]; p=0.020). INTERPRETATION: In this global cohort of children and adolescents with cancer and COVID-19, severe and critical illness occurred in one fifth of patients and deaths occurred in a higher proportion than is reported in the literature in the general paediatric population. Additionally, we found that variables associated with treatment modification were not the same as those associated with greater disease severity. These data could inform clinical practice guidelines and raise awareness globally that children and adolescents with cancer are at high-risk of developing severe COVID-19 illness. FUNDING: American Lebanese Syrian Associated Charities and the National Cancer Institute.

Noveron, N. R., et al. (2021). "SARS-CoV-2 positivity rates in asymptomatic workers at a cancer referral center in Mexico City: A prospective observational study in the context of adapting hospitals back to regular practice." Am J Infect Control **49**(12): 1469-1473.

BACKGROUND: Healthcare workers are at increased risk of SARS-CoV-2 infection. The positivity rates in hospitals that do not receive

patients with COVID-19, such as the National Cancer Institute (INCan) in Mexico, and the associated factors are unknown. OBJECTIVE: To assess the incidence and factors associated with SARS-CoV-2 infection in health workers at INCan. METHODS: A cohort study of 531 workers who were followed for 6 months. RT-PCR analysis of saliva and nasopharyngeal swab samples were used in the baseline and to confirm cases during follow-up The incidence rate ratio was calculated according to the measured characteristics and the associated factors were calculated using logistic regression models. RESULTS: Out of 531 workers, 9.6% tested positive for SARS-CoV-2, Being male (RR: 2.07, 95% CI: 1.1-3.8, P = .02), performing administrative tasks (RR: 1.99, 95% CI: 1.0-3.9, P = .04), and having relatives also working at INCan (RR: 3.7, 95% CI: 1.4-9.5, P < .01) were associated with higher positivity rates. DISCUSSION: Incidence of positive cases in health workers were similar to that reported in non-COVID hospitals from other countries. CONCLUSIONS: Even though active surveillance helped to detect a significant number of asymptomatic infections, it is still necessary to reinforce preventive measures in non-medical staff to prevent nosocomial transmission.

Obispo, B., et al. (2021). "Prevalence of thrombosis in patients with cancer and SARS-CoV-2 infection." Med Clin (Barc).

BACKGROUND: Covid-19 infection and cancer are associated with an increased risk of thrombotic events. The aim of our study is to analyze the cumulative incidence of thrombosis in oncological patients with Covid-19 and detect differences with the non-cancer Covid-19 population. METHODS: We retrospectively reviewed 1127 medical records of all admitted patients to ward of the Hospital Universitario Infanta Leonor (Madrid, Spain), including 86 patients with active cancer between March 5th, 2020 to May 3rd, 2020. We analyzed cumulative incidence of thrombosis and risk factors associated to the cancer patient's cohort. RESULTS: We diagnosed 10 thrombotic events in 8 oncological patients with a cumulative incidence of 9.3%. A statistically significant association was found regarding thrombosis and history of obesity (p=0.009). No differences related to cumulative incidence of thrombosis between both groups were detected (9.8% vs 5.80%) in our hospital (p=0.25). CONCLUSION: No significant differences were observed in the cumulative incidence of thrombosis in the two study groups. The thrombotic effect of Covid-19 is not as evident in cancer patients and does not seem to be added to its prothrombotic activity.

Odeleye, E., et al. (2021). "Successful Implementation of Routine SARS-CoV-2 Screening in Children With Cancer and Their Parents During the Pandemic in the United Kingdom." J Pediatr Hematol Oncol **43**(7): e1046-e1047.

Ottaiano, A., et al. (2021). "Unexpected tumor reduction in metastatic colorectal cancer patients during SARS-Cov-2 infection." Ther Adv Med Oncol **13**: 17588359211011455.

Herein, we describe three patients affected by metastatic colorectal cancer (mCRC) experiencing infection by severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) and reduction of disease burden during coronavirus disease 2019 (COVID-19) course. Insights into tumor-associated angiotensin-converting enzyme (ACE)-2 expression and lymphocyte function suggest a correlation between host/SARS-Cov-2 infection and tumor burden reduction. This may shed new light into (a) the infection mechanism of SARS-CoV-2 virus and (b) the multiple aspects of a composite antiviral immune response with potential paradoxical and unexpected applications.

Pala, L., et al. (2020). "Data of Italian Cancer Centers from two regions with high incidence of SARS CoV-2 infection provide evidence for the successful management of patients with locally advanced and metastatic melanoma treated with immunotherapy in the era of COVID-19." Semin Oncol **47**(5): 302-304.

BACKGROUND: Patients with cancer are presumed to have a higher risk to contract SARS-CoV-2 infection, because of their immunosuppressed status. The impact and course of COVID-19 infection in cancer patients receiving immunotherapy remains unknown. OBJECTIVES: To evaluate the safety of the management of patients with advanced melanoma treated with immunotherapy in 2 Cancer Centers located in areas of Italy with a high incidence of COVID-19 infections. METHODS: We retrospectively analyzed data from January 1 to April 30, 2020 on patients with locally advanced and metastatic melanoma receiving immunotherapy at either Istituto Europeo di Oncologia or Citta della Salute e della Scienza University Hospital. RESULTS: One-hundred and sixty-nine patients with stage III and IV melanoma were treated with an immunotherapy regimen at either Istituto Europeo di Oncologia or Citta della Salute e della Scienza University Hospital. One-hundred and four patients continued treatment without interruption or delay, while 49 patients had a treatment delay. The main reasons for treatment delay were older age (median age of the group of patients with or without treatment-delay, respectively 60 and 69 years, P value <0.001) and/or presence of comorbidities (percentage of patients with at least one comorbidity respectively 81% and 62%, in patients with or without treatment delay, P value=0.001). One-hundred and twelve patients had at least 1 thoracic CT scan performed and radiological findings

suspicious for COVID-19 were observed in only 7 cases (4%). Fifteen patients (9%) developed symptoms potentially related to COVID-19; nasopharyngeal swabs were collected in 9 patients and only 1 was positive for SARS-CoV-2. CONCLUSIONS: The incidence of symptomatic COVID-19 infection observed in our cohort of patients with advanced malignant melanoma treated with immunotherapy appears meaningfully lower as compared with that reported in the overall population in Italy as well as in patients affected by solid tumors. We conclude that in patients with locally advanced and metastatic melanoma, immunotherapy can be safely continued without delay in the majority of cases, reserving precautionary delay only for the most frail patients.

Pinato, D. J., et al. (2020). "Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients." Cancer Discov.

The SARS-Cov-2 pandemic significantly impacted on oncology practice across the globe. There is uncertainty as to the contribution of patients' demographics and oncological features on severity and mortality from Covid-19 and little guidance as to the role of anti-cancer and anti-Covid-19 therapy in this population. In a multi-center study of 890 cancer patients with confirmed Covid-19 we demonstrated a worsening gradient of mortality from breast cancer to haematological malignancies and showed that male gender, older age, and number of co-morbidities identifies a subset of patients with significantly worse mortality rates from Covid-19. Provision of chemotherapy, targeted therapy and immunotherapy did not worsen mortality. Exposure to antimalarials was associated with improved mortality rates independent of baseline prognostic factors. This study highlights the clinical utility of demographic factors for individualized risk-stratification of patients and support further research into emerging anti-Covid-19 therapeutics in SARS-Cov-2 infected cancer patients.

Pinto, C., et al. (2020). "SARS-CoV-2 Positive Hospitalized Cancer Patients during the Italian Outbreak: The Cohort Study in Reggio Emilia." Biology (Basel) **9**(8).

In the coronavirus disease (COVID-19) pandemic, cancer patients could be a high-risk group due to their immunosuppressed status; therefore, data on cancer patients must be available in order to consider the most adequate strategy of care. We carried out a cohort study on the risk of hospitalization for COVID-19, oncological history, and outcomes on COVID-19 infected cancer patients admitted to the Hospital of Reggio Emilia. Between 1 February and 3 April 2020, a total of 1226 COVID-19 infected patients were hospitalized. The number of cancer patients hospitalized with COVID-19 infection was 138 (11.3%). The median age was slightly higher in patients with cancers than in those without (76.5 vs. 73.0). The risk of intensive care unit (ICU) admission (10.1% vs. 6.7%; RR 1.23, 95% Confidence Interval (CI) 0.63-2.41) and risk of death (34.1% vs. 26.0%; RR 1.07, 95% CI 0.61-1.71) were similar in cancer and non-cancer patients. In the cancer patients group, 89/138 (64.5%) patients had a time interval >5 years between the diagnosis of the tumor and hospitalization. Male gender, age > 74 years, metastatic disease, bladder cancer, and cardiovascular disease were associated with mortality risk in cancer patients. In the Reggio Emilia Study, the incidence of hospitalization for COVID-19 in people with previous diagnosis of cancer is similar to that in the general population (standardized incidence ratio 98; 95% CI 73-131), and it does not appear to have a more severe course or a higher mortality rate than patients without cancer. The phase II of the COVID-19 epidemic in cancer patients needs a strategy to reduce the likelihood of infection and identify the vulnerable population, both in patients with active antineoplastic treatment and in survivors with frequently different coexisting medical conditions.

Purcaru, O. S., et al. (2021). "The Interference between SARS-CoV-2 and Tyrosine Kinase Receptor Signaling in Cancer." Int J Mol Sci **22**(9).

Cancer and viruses have a long history that has evolved over many decades. Much information about the interplay between viruses and cell proliferation and metabolism has come from the history of clinical cases of patients infected with virus-induced cancer. In addition, information from viruses used to treat some types of cancer is valuable. Now, since the global coronavirus pandemic erupted almost a year ago, the scientific community has invested countless time and resources to slow down the infection rate and diminish the number of casualties produced by this highly infectious pathogen. A large percentage of cancer cases diagnosed are strongly related to dysregulations of the tyrosine kinase receptor (TKR) family and its downstream signaling pathways. As such, many therapeutic agents have been developed to strategically target these structures in order to hinder certain mechanisms pertaining to the phenotypic characteristics of cancer cells such as division, invasion or metastatic potential. Interestingly, several authors have pointed out that a correlation between coronaviruses such as the SARS-CoV-1 and -2 or MERS viruses and dysregulations of signaling pathways activated by TKRs can be established. This information may help to accelerate the repurposing of clinically developed anti-TKR cancer drugs in COVID-19 management. Because the need for treatment is critical, drug repurposing may be an advantageous choice in the search for new and efficient therapeutic compounds. This approach would be advantageous from a financial point of

view as well, given that the resources used for research and development would no longer be required and can be potentially redirected towards other key projects. This review aims to provide an overview of how SARS-CoV-2 interacts with different TKRs and their respective downstream signaling pathway and how several therapeutic agents targeted against these receptors can interfere with the viral infection. Additionally, this review aims to identify if SARS-CoV-2 can be repurposed to be a potential viral vector against different cancer types.

Quagliariello, V., et al. (2020). "SARS-CoV-2 Infection and Cardioncology: From Cardiometabolic Risk Factors to Outcomes in Cancer Patients." Cancers (Basel) **12**(11).

The coronavirus disease-2019 (COVID-19) is a highly transmissible viral illness caused by SARS-CoV-2, which has been defined by the World Health Organization as a pandemic, considering its remarkable transmission speed worldwide. SARS-CoV-2 interacts with angiotensin-converting enzyme 2 and TMPRSS2, which is a serine protease both expressed in lungs, the gastro-intestinal tract, and cardiac myocytes. Patients with COVID-19 experienced adverse cardiac events (hypertension, venous thromboembolism, arrhythmia, myocardial injury, fulminant myocarditis), and patients with previous cardiovascular disease have a higher risk of death. Cancer patients are extremely vulnerable with a high risk of viral infection and more negative prognosis than healthy people, and the magnitude of effects depends on the type of cancer, recent chemotherapy, radiotherapy, or surgery and other concomitant comorbidities (diabetes, cardiovascular diseases, metabolic syndrome). Patients with active cancer or those treated with cardiotoxic therapies may have heart damages exacerbated by SARS-CoV-2 infection than non-cancer patients. We highlight the cardiovascular side effects of COVID-19 focusing on the main outcomes in cancer patients in updated perspective and retrospective studies. We focus on the main cardio-metabolic risk factors in non-cancer and cancer patients and provide recommendations aimed to reduce cardiovascular events, morbidity, and mortality.

Ravaioli, S., et al. (2020). "ACE2 and TMPRSS2 Potential Involvement in Genetic Susceptibility to SARS-COV-2 in Cancer Patients." Cell Transplant **29**: 963689720968749.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic. One open question is whether genetics could influence the severity of symptoms. Considering the limited data on cancer patients, we analyzed public data repositories limited to investigate angiotensin-converting enzyme 2 (ACE2) and the transmembrane serine protease 2 (TMPRSS2) expressions and genetic variants to identify the basis of individual susceptibility to SARS-CoV-2.Gene expression and variant data were retrieved from Tissue Cancer Genome Atlas, Genotype-Tissue Expression, and gnomAD. Differences in gene expression were tested with Mann-Whitney U-test. Allele frequencies of germline variants were explored in different ethnicities, with a special focus on ACE2 variants located in the binding site to SARS-CoV-2 spike protein.The analysis of ACE2 and TMPRSS2 expressions in healthy tissues showed a higher expression in the age class 20 to 59 years (false discovery rate [FDR] < 0.0001) regardless of gender. ACE2 and TMPRSS2 were more expressed in tumors from males than females (both FDR < 0.0001) and, opposite to the regulation in tissues from healthy individuals, more expressed in elderly patients (FDR = 0.005; FDR < 0.0001, respectively). ACE2 and TMPRSS2 expressions were higher in cancers of elderly patients compared with healthy individuals (FDR < 0.0001). Variants were present at low frequency (range 0% to 3%) and among those with the highest frequency, the variant S19P belongs to the SARS-CoV-2 spike protein binding site and it was exclusively present in Africans with a frequency of 0.2%.The mechanisms of ACE2 and TMPRSS2 regulation could be targeted for preventive and therapeutic purposes in the whole population and especially in cancer patients.Further studies are needed to show a direct correlation of ACE2 and TMPRSS2 expressions in cancer patients and the incidence of COVID-19.

Reale, M. L., et al. (2020). "SARS-CoV-2 Infection in Cancer Patients: A Picture of an Italian Onco-Covid Unit." Front Oncol **10**: 1722.

Background: The world, and Italy on the front lines, has experienced a major medical emergency due to the novel coronavirus outbreak. Cancer patients are one of the potentially most vulnerable cohorts of people, but data about their management are still few. Patients and Methods: In this monocentric retrospective study we included all SARS-CoV-2 oncological patients accepted, between March 27th and April 19th 2020, at the Onco-COVID Unit at San Luigi Gonzaga Hospital, one of the few Italian oncological-COVID wards. Data were obtained from medical records. Results: Eighteen cancer patients with COVID-19 were included. The mean (+/-SD) age of patients was 67 +/- 14 years, 89% were men. Seven (39%) developed infection in communities and 11 (61%) during hospitalization. Lung cancer was the most frequent type of cancer (10, 56%). Seven patients (39%) were symptomatic for COVID-19 at the time of diagnosis and symptoms began 2 (+/-2) days before. The most common were shortness of breath and diarrhea. Fever was present in 5 patients (28%). Among the 11 asymptomatic patients, 8 (73%) became symptomatic during the hospitalization (mean time of symptoms

onset 4 days +/-4). Six patients (33%) were on active anti-tumor treatment: 2 (33%) received anti-tumor therapy within 2 weeks before the infection diagnosis and 2 (33%) continued oncological treatment after SARS-CoV-2 positivity. Eight (44%) patients died within a mean of 12 days (+/-8) from the infection diagnosis. Conclusions: Our series confirms the high mortality among cancer patients with COVID-19. The presence of asymptomatic cases evidences that typical symptoms and fever are not the only parameters to suspect the infection. The Onco-Covid unit suggests the importance of a tailored and holistic approach, even in this difficult situation.

Ricciardiello, L., et al. (2021). "Impact of SARS-CoV-2 Pandemic on Colorectal Cancer Screening Delay: Effect on Stage Shift and Increased Mortality." Clin Gastroenterol Hepatol **19**(7): 1410-1417 e1419.

BACKGROUND & AIMS: The SARS-CoV-2 pandemic had a sudden, dramatic impact on healthcare. In Italy, since the beginning of the pandemic, colorectal cancer (CRC) screening programs have been forcefully suspended. We aimed to evaluate whether screening procedure delays can affect the outcomes of CRC screening. METHODS: We built a procedural model considering delays in the time to colonoscopy and estimating the effect on mortality due to up-stage migration of patients. The number of expected CRC cases was computed by using the data of the Italian screened population. Estimates of the effects of delay to colonoscopy on CRC stage, and of stage on mortality were assessed by a meta-analytic approach. RESULTS: With a delay of 0-3 months, 74% of CRC is expected to be stage I-II, while with a delay of 4-6 months there would be a 2%-increase for stage I-II and a concomitant decrease for stage III-IV (P = .068). Compared to baseline (0-3 months), moderate (7-12 months) and long (> 12 months) delays would lead to a significant increase in advanced CRC (from 26% to 29% and 33%, respectively; P = .008 and P < .001, respectively). We estimated a significant increase in the total number of deaths (+12.0%) when moving from a 0-3-months to a >12-month delay (P = .005), and a significant change in mortality distribution by stage when comparing the baseline with the >12-months (P < .001). CONCLUSIONS: Screening delays beyond 4-6 months would significantly increase advanced CRC cases, and also mortality if lasting beyond 12 months. Our data highlight the need to reorganize efforts against high-impact diseases such as CRC, considering possible future waves of SARS-CoV-2 or other pandemics.

Romano, E., et al. (2021). "Implications of mRNA-based SARS-CoV-2 vaccination for cancer patients." J Immunother Cancer **9**(6).

SARS-CoV-2 infection and the resulting COVID-19 have afflicted millions of people in an ongoing worldwide pandemic. Safe and effective vaccination is needed urgently to protect not only the general population but also vulnerable subjects such as patients with cancer. Currently approved mRNA-based SARS-CoV-2 vaccines seem suitable for patients with cancer based on their mode of action, efficacy, and favorable safety profile reported in the general population. Here, we provide an overview of mRNA-based vaccines including their safety and efficacy. Extrapolating from insights gained from a different preventable viral infection, we review existing data on immunity against influenza A and B vaccines in patients with cancer. Finally, we discuss COVID-19 vaccination in light of the challenges specific to patients with cancer, such as factors that may hinder protective SARS-CoV-2 immune responses in the context of compromised immunity and the use of immune-suppressive or immune-modulating drugs.

Sacconi, A., et al. (2020). "TMPRSS2, a SARS-CoV-2 internalization protease is downregulated in head and neck cancer patients." J Exp Clin Cancer Res **39**(1): 200.

BACKGROUND: SARS-coronavirus-2 enters host cells through binding of the Spike protein to ACE2 receptor and subsequent S priming by the TMPRSS2 protease. We aim to assess differences in both ACE2 and TMPRSS2 expression in normal tissues from oral cavity, pharynx, larynx and lung tissues as well as neoplastic tissues from the same areas. METHODS: The study has been conducted using the TCGA and the Regina Elena Institute databases and validated by experimental model in HNSCC cells. We also included data from one COVID19 patient who went under surgery for HNSCC. RESULTS: TMPRSS2 expression in HNSCC was significantly reduced compared to the normal tissues. It was more evident in women than in men, in TP53 mutated versus wild TP53 tumors, in HPV negative patients compared to HPV positive counterparts. Functionally, we modeled the multivariate effect of TP53, HPV, and other inherent variables on TMPRSS2. All variables had a statistically significant independent effect on TMPRSS2. In particular, in tumor tissues, HPV negative, TP53 mutated status and elevated TP53-dependent Myc-target genes were associated with low TMPRSS2 expression. The further analysis of both TCGA and our institutional HNSCC datasets identified a signature anti-correlated to TMPRSS2. As proof-of-principle we also validated the anti-correlation between microRNAs and TMPRSS2 expression in a SARS-CoV-2 positive HNSCC patient tissues Finally, we did not find TMPRSS2 promoter methylation. CONCLUSIONS: Collectively, these findings suggest that tumoral tissues, herein exemplified by HNSCC and lung cancers might be more resistant to SARS-CoV-2 infection due to reduced expression of TMPRSS2.

These observations may help to better assess the frailty of SARS-CoV-2 positive cancer patients.

Samad, A., et al. (2020). "Identification of angiotensin-converting enzyme 2 (ACE2) protein as the potential biomarker in SARS-CoV-2 infection-related lung cancer using computational analyses." Genomics **112**(6): 4912-4923.

COVID-19 is a pandemic that began to spread worldwide caused by SARS-CoV-2. Lung cancer patients are more susceptible to SARS-CoV-2 infection. The SARS-CoV-2 enters into the host by the ACE2 receptor. Thus, ACE2 is the key to understand the mechanism of SARS-CoV-2 infection. However, the lack of knowledge about the biomarker of COVID-19 warrants the development of ACE2 biomarkers. The analysis of ACE2 expression in lung cancer was performed using The Cancer Genome Atlas (TCGA). Therefore, we investigated the prognosis, clinical characteristics, and mutational analysis of lung cancer. We also analyzed the shared proteins between the COVID-19 and lung cancer, protein-protein interactions, gene-miRNAs, gene-transcription factors (TFs), and the signaling pathway. Finally, we compared the mRNA expression of ACE2 and its co-expressed proteins using the TCGA. The up-regulation of ACE2 in lung adenocarcinoma (LUAD) and lung squamous carcinoma (LUSC) was found irrespective of gender and age. We found the low survival rate in high expression of ACE2 in lung cancer patients and 16 mutational positions. The functional assessment of targeted 12,671, 3107, and 29 positive genes were found in COVID-19 disease, LUAD, and LUSC, respectively. Then, we identified eight common genes that interact with 20 genes, 219 miRNAs, and 16 TFs. The common genes performed the mRNA expression in lung cancer, which proved the ACE2 is the best potential biomarker compared to co-expressed genes. This study uncovers the relationship between COVID-19 disease and lung cancer. We identified ACE2 and also its co-expressed proteins are the potential biomarker and therapy as the current COVID-19 disease and lung cancer.

Sari Motlagh, R., et al. (2021). "Association between SARS-CoV-2 infection and disease severity among prostate cancer patients on androgen deprivation therapy: a systematic review and meta-analysis." World J Urol.

PURPOSE: Androgen-regulated enzymes such as the angiotensin-converting enzyme 2 (ACE2) and the transmembrane serine protease 2 (TMPRSS2) are involved in the SARS-CoV-2 infection process. The expression of TMPRSS2 and its fusion gene, which are increased in the epithelium of the human prostate gland during prostate carcinogenesis, are regulated by androgens. Our goal was to assess the risk of the SARS-CoV-2 infection and the severity of the disease in PCa patients treated with androgen deprivation therapy (ADT). METHODS: We conducted a systematic review and meta-analysis according to PRISMA guidelines. We queried PubMed and Web of Science databases on 1 July 2021. We used random- and/or fixed-effects meta-analytic models in the presence or absence of heterogeneity according to Cochrane's Q test and I(2) statistic, respectively. RESULTS: Six retrospective studies (n = 50,220 patients) were selected after considering inclusion and exclusion criteria for qualitative evidence synthesis. Four retrospective studies were included to assess the SARS-CoV-2 infection risk in PCa patients under ADT vs. no ADT and the summarized risk ratio (RR) was 0.8 (95% confidence intervals (CI) 0.44-1.47). Five retrospective studies were included to assess the severity of coronavirus disease 2019 (COVID-19) in PCa patients under ADT versus no ADT and the summarized RR was 1.23 (95% CI 0.9-1.68). CONCLUSION: We found a non-significant association between the risk of SARS-CoV-2 infection and COVID-19 severity in PCa patients treated with ADT. However, our results suggest that during the COVID-19 pandemic PCa patients can safely undergo ADT as a cancer therapy without worsening COVID-19 risk and trajectory.

Scarlattei, M., et al. (2020). "Unknown SARS-CoV-2 pneumonia detected by PET/CT in patients with cancer." Tumori **106**(4): 325-332.

INTRODUCTION: In January 2020, the coronavirus disease 2019 (COVID-19) outbreak in Italy necessitated rigorous application of more restrictive safety procedures in the management and treatment of patients with cancer to ensure patient and staff protection. Identification of respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was a challenge during the pandemic owing to a large number of asymptomatic or mildly symptomatic patients. METHODS: We report 5 patients with unknown SARS-CoV-2 infection undergoing positron emission tomography (PET)/computed tomography (CT) with radiopharmaceuticals targeting different tumor processes: (18)F-FDG, (18)F-choline (FCH), and (68)Ga-PSMA. RESULTS: In all patients, PET/CT showed increased tracer uptake in the lungs corresponding to CT findings of SARS-CoV-2 pneumonia. Quantitative assessment of tracer uptake showed more elevated values for the glucose analogue (18)F-FDG (mean SUVmax 5.4) than for the other tracers (mean SUVmax 3.5). CONCLUSIONS: Our findings suggest that PET/CT is a sensitive modality to hypothesize SARS-CoV-2 pneumonia in patients with cancer, even when asymptomatic. More data are needed to verify the correlation among immune response to SARS-CoV-2 infection, clinical evolution, and PET results. Under the strict safety measures implemented at the PET center, the number of potentially SARS-CoV-2-

positive patients undergoing PET/CT was very low (1.6%), and no staff member has been diagnosed with infection as of April 30, 2020.

Serraino, D., et al. (2021). "Prevalence, determinants, and outcomes of SARS-COV-2 infection among cancer patients. A population-based study in northern Italy." Cancer Med **10**(21): 7781-7792.

BACKGROUND: It is well established that cancer patients infected with SARS-CoV-2 are at particularly elevated risk of adverse outcomes, but the comparison of SARS-CoV-2 infection risk between cancer patients and cancer-free individuals has been poorly investigated on a population-basis. METHODS: A population-based study was thus conducted in Friuli Venezia Giulia region, northeastern Italy, to estimate prevalence and determinants of SARS-CoV-2 infection among cancer patients, as compared to cancer-free individuals, and to evaluate adverse outcomes of SARS-CoV-2 infection. The study included 263,042 individuals tested for SARS-CoV-2 in February-December 2020 with cancer history retrieved through the regional cancer registry. Odds ratios (ORs) of SARS-CoV-2 positivity, with corresponding 95% confidence intervals (CIs), were calculated using multivariable logistic regression models, adjusted for sex and age. Hazard ratios (HRs) adjusted for sex and age for intensive care unit (ICU) admission and all-cause death were estimated using Cox models. RESULTS: Among 26,394 cancer patients tested for SARS-CoV-2, the prevalence of infection was 11.7% versus 16.2% among 236,648 cancer-free individuals, with a corresponding OR = 0.59 (95% CI: 0.57-0.62). The prevalence was much higher (29% in both groups) during the second pandemic wave (October-December 2020). Among cancer patients, age >/=80 years and cancer diagnosis >/=13 months before SARS-CoV-2 testing were the major risk factors of infection. Among 3098 infected cancer patients, the fatality rate was 17.4% versus 15.8% among 23,296 negative ones (HR = 1.63, 95% CI: 1.49-1.78), and versus 5.0% among 38,268 infected cancer-free individuals (HR = 1.23, 95% CI: 1.12-1.36). No significant differences emerged when considering ICU admission risk. CONCLUSION: Albeit cancer patients reported reduced SARS-CoV-2 infection risk, those infected showed higher mortality than uninfected ones and infected cancer-free population. Study findings claim for continuing to protect cancer patients from SARS-CoV-2, without reducing the level of oncologic care.

Seth, G., et al. (2020). "SARS-CoV-2 Infection in Cancer Patients: Effects on Disease Outcomes and Patient Prognosis." Cancers (Basel) **12**(11).

The severity of coronavirus disease 2019 (COVID-19) symptoms and outcomes vary immensely among patients. Predicting disease progression and managing disease symptoms is even more challenging in cancer patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cancer therapies, including chemotherapy, radiotherapy, and immunotherapy, often suppress the immune system, rendering cancer patients more susceptible to SARS-CoV-2 infection and the development of severe complications. However, data on the effects of immunosuppression on COVID-19 outcomes in cancer patients remain limited. Further investigations are warranted to better understand the implications of SARS-CoV-2 infection in cancer patients, particularly those that are immunocompromised. In this review, we outline the current knowledge of the effects of SARS-CoV-2 infection in cancer patients.

Shah, M. R., et al. (2021). "SARS-CoV-2 nosocomial infection: Real-world results of environmental surface testing from a large tertiary cancer center." Cancer **127**(11): 1926-1932.

BACKGROUND: Despite consensus guidelines, concern about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission has dissuaded patients with cancer from seeking medical care. Studies have shown that contaminated surfaces may contain viable virus for up to 72 hours in laboratory settings. The purpose of this study was to investigate contamination of SARS-CoV-2 on commonly used environmental surfaces in a tertiary cancer care center. METHODS: This study evaluated the incidence of SARS-CoV-2 viral RNA in high-touch outpatient and inpatient cancer center spaces. Surfaces were tested over a 2-week period after patient or staff exposure but before scheduled disinfection services according to the World Health Organization protocols for coronavirus disease 2019 (COVID-19) surface sampling. Samples were analyzed via reverse transcriptase-polymerase chain reaction for the presence of SARS-CoV-2 RNA. RESULTS: Two hundred four environmental samples were obtained from inpatient and outpatient oncology clinics and infusion suites, and they were categorized as 1) public areas, 2) staff areas, or 3) medical equipment. One hundred thirty surfaces from 2 outpatient hematology and oncology clinics and 36 surfaces from an inpatient leukemia/lymphoma/chimeric antigen receptor T-cell unit were examined, and all 166 samples were negative for SARS-CoV-2. One of 38 samples (2.6%) from COVID-19+ inpatient units was positive. Altogether, the positive test rate for SARS-CoV-2 RNA across all surfaces was 0.5% (1 of 204). CONCLUSIONS: This prospective, systematic quality assurance investigation of real-world environmental surfaces, performed in inpatient and outpatient hematology/oncology units, revealed overall negligible detection of SARS-CoV-2 RNA when strict mitigation strategies against COVID-19 transmission were instituted. LAY SUMMARY: The potential risks of nosocomial infection with severe

acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have deterred patients with cancer from seeking timely care despite consensus guidelines. This study has found negligible rates of environmental contamination with SARS-CoV-2 across a multitude of commonly used surfaces in outpatient and inpatient hematology/oncology settings with adherence to strict infection control protocols.

Shaimoldina, A. and Y. Q. Xie (2020). "Challenges of SARS-CoV-2 prevention in flights, suggested solutions with potential on-site diagnosis resembling cancer biomarkers and urgency of travel medicine." Eur Rev Med Pharmacol Sci **24**(23): 12589-12592.

OBJECTIVE: The current pandemic makes the international flights facing multiple challenges including infection during flights. Here the objective is to analyze the infection trend of flights from a regional data set and discuss the solutions for diagnosis and travel medicine. MATERIALS AND METHODS: The public data was applied for trend analysis and new solutions were provided based on the current diagnosis information and resembling cancer diagnosis. RESULTS: Flights infection has decreased since the large-scale cease of flights. Challenges of prevention of SARS-CoV-2 infection in flights exist due to testing accuracy, asymptomatic and many other factors including people gathering. To avoid the pandemic worsen, the solutions are provided for new coming flight resumes. Hotel, mandatory PPE, airport diagnosis, rapid imaging/biomarker diagnosis by advanced high-technology and emergency-travel medicine department are suggested as solutions. CONCLUSIONS: SARS-CoV-2 prevention in flights needs multiple solutions by potential on-site diagnosis and urgent establishment of a travel medicine unit at airport.

Singh, M. K., et al. (2021). "Associated pathogenesis of bladder cancer and SARS-CoV-2 infection: a treatment strategy." Virusdisease: 1-3.

Coronavirus disease 19 (Covid-19) is a pandemic that affects every human on Earth. Mortality rates are greater in people with both cancer and Covid-19. In comparison, patients with non-Muscle-Invasive Bladder Cancer (NMIBC) had reduced susceptibility to moderate Covid-19 mortality. The treatment and clinical management of NMIBC are consistent with BCG-mediated intravesical adjuvant therapy as a protective function against tumors. BCG vaccination exhibits a non-specific protective role against respiratory infections. This non-specific effect of BCG is partially mediated by innate immune memory due to epigenetic changes in innate and adaptive immune system cells induced by the microbe. This editorial suggests that regularly test repurposed drugs include anti-cancer drugs till the proper antiviral drugs or vaccines will be developed.

Siqueira, J. D., et al. (2020). "SARS-CoV-2 genomic and quasispecies analyses in cancer patients reveal relaxed intrahost virus evolution." bioRxiv.

Numerous factors have been identified to influence susceptibility to SARS-CoV-2 infection and disease severity. Cancer patients are more prone to clinically evolve to more severe COVID-19 conditions, but the determinants of such a more severe outcome remain largely unknown. We have determined the full-length SARS-CoV-2 genomic sequences of cancer patients and healthcare workers (HCW; non-cancer controls) by deep sequencing and investigated the within-host viral quasispecies of each infection, quantifying intrahost genetic diversity. Naso- and oropharyngeal SARS-CoV-2 (+) swabs from 57 cancer patients and 14 healthcare workers (HCW) from the Brazilian Cancer Institute were collected in April-May 2020. Complete genome amplification using ARTIC network V3 multiplex primers was performed followed by next-generation sequencing. Assemblies were conducted in Geneious R11, where consensus sequences were extracted and intrahost single nucleotide variants (iSNVs) were identified. Maximum likelihood phylogenetic analysis was performed using PhyMLv.3.0 and lineages were classified using Pangolin and CoV-GLUE. Phylogenetic analysis showed that all but one strain belonged to clade B1.1. Four genetically linked mutations known as the globally dominant SARS-CoV-2 haplotype (C241T, C3037T, C14408T and A23403G) were found in the majority of consensus sequences. SNV signatures of previously characterized Brazilian genomes were also observed in most samples. Another 85 SNVs were found at a lower frequency (1.4-19.7%). Cancer patients displayed a significantly higher intrahost viral genetic diversity compared to HCW ($p = 0.009$). Intrahost genetic diversity in cancer patients was independent of SARS-CoV-2 Ct values, and was not associated with disease severity, use of corticosteroids, or use of antivirals, characteristics that could influence viral diversity. Such a feature may explain, at least in part, the more adverse outcomes to which cancer/COVID-19 patients experience. Author Summary: Cancer patients are more prone to clinically evolve to more severe COVID-19 conditions, but the determinants of such a more severe outcome remain largely unknown. In this study, phylogenetic and variation analysis of SARS-CoV-2 genomes from cancer patients and non-cancer healthcare workers at the Brazilian National Cancer Institute were characterized by deep sequencing. Viral genomes showed signatures characteristic of Brazilian viruses, consistent with the hypothesis of local, community transmission rather than virus importation from abroad. Despite most genomes in patients and healthcare workers

belonging to the same lineage, intrahost variability was higher in cancer patients when compared to non-cancer counterparts. The intrahost genomic diversity analysis presented in our study highlights the relaxed evolution of SARS-CoV-2 in a vulnerable population of cancer patients. The high number of minor variations can result in the selection of immune escape variants, resistance to potential drugs, and/or increased pathogenicity. The impact of this higher intrahost variability over time warrants further investigation.

Siqueira, J. D., et al. (2021). "SARS-CoV-2 genomic analyses in cancer patients reveal elevated intrahost genetic diversity." Virus Evol **7**(1): veab013.

Numerous factors have been identified to influence susceptibility to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and disease severity. Cancer patients are more prone to clinically evolve to more severe COVID-19 conditions, but the determinants of such a more severe outcome remain largely unknown. We have determined the full-length SARS-CoV-2 genomic sequences of cancer patients and healthcare workers (non-cancer controls) by deep sequencing and investigated the within-host viral population of each infection, quantifying intrahost genetic diversity. Naso- and oropharyngeal SARS-CoV-2(+) swabs from 57 cancer patients and 14 healthcare workers from the Brazilian National Cancer Institute were collected in April to May 2020. Complete genome amplification using ARTIC network V3 multiplex primers was performed followed by next-generation sequencing. Assemblies were conducted in Geneious R11, where consensus sequences were extracted and intrahost single nucleotide variants were identified. Maximum likelihood phylogenetic analysis was performed using PhyMLv.3.0 and lineages were classified using Pangolin and CoV-GLUE. Phylogenetic analysis showed that all but one strain belonged to clade B1.1. Four genetically linked mutations known as the globally dominant SARS-CoV-2 haplotype (C241T, C3037T, C14408T and A23403G) were found in the majority of consensus sequences. SNV signatures of previously characterized Brazilian genomes were also observed in most samples. Another 85 SNVs were found at a lower frequency (1.4%-19.7%) among the consensus sequences. Cancer patients displayed a significantly higher intrahost viral genetic diversity compared to healthcare workers. This difference was independent of SARS-CoV-2 Ct values obtained at the diagnostic tests, which did not differ between the two groups. The most common nucleotide changes of intrahost SNVs in both groups were consistent with APOBEC and ADAR activities. Intrahost genetic diversity in cancer patients was not associated with disease severity, use of corticosteroids, or use of antivirals, characteristics that could influence viral diversity. Moreover, the presence of metastasis, either in general or specifically in the lung, was not associated with intrahost diversity among cancer patients. Cancer patients carried significantly higher numbers of minor variants compared to non-cancer counterparts. Further studies on SARS-CoV-2 diversity in especially vulnerable patients will shed light onto the understanding of the basis of COVID-19 different outcomes in humans.

Song, C., et al. (2021). "An online tool for predicting the prognosis of cancer patients with SARS-CoV-2 infection: a multi-center study." J Cancer Res Clin Oncol **147**(4): 1247-1257.

PURPOSE: During the 2019 coronavirus disease (COVID-19) pandemic, oncologists face new challenges, and they need to adjust their cancer management strategies as soon as possible to reduce the risk of SARS-CoV-2 infection and tumor recurrence. However, data on cancer patients with SARS-CoV-2 infection remains scarce. METHODS: We conducted a retrospective study on 223 cancer patients with SARS-CoV-2 from 26 hospitals in Hubei, China. An individualized nomogram was constructed based on multivariate Cox analysis. Considering the convenience of the nomogram application, an online tool was also created. The predictive performance and clinical application of nomogram were verified by C-index, calibration curve and decision curve analysis (DCA). RESULTS: Among cancer patients with SARS-CoV-2, there were significant differences in clinical characteristics between survivors and non-survivors, and compared with patients with solid tumors including lung cancer, patients with hematological malignancies had a worse prognosis. Male, dyspnea, elevated PCT, increased heart rate, elevated D-dimers, and decreased platelets were risk factors for these patients.

Song, S. H., et al. (2020). "Clinical characteristics of four cancer patients with SARS-CoV-2 infection in Wuhan, China." Infect Dis Poverty **9**(1): 82.

BACKGROUND: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to the outbreak of pneumonia in Wuhan. The virus is highly infectious. Patients with cancer might be susceptible to the viral infection because of the immunosuppressive state cause by therapies on tumors. CASE PRESENTATION: We present the clinical features of four cancer patients who were infected with SARS-CoV-2 in late January of 2020 in our hospital. Cases 1 and 3 were diagnosed as mild and common type of coronavirus disease 2019 (COVID-2019) and survived from the viral infection. They acquired SARS-CoV-2 infection during their staying in hospital under radiotherapy and surgery of the tumors. Cases 2 and 4 suffered from severe type of COVID-19, and Case 2 was dead owning to the advanced age, uncontrolled chronic B cell lymphocytic leukemia and many other underlying

diseases. The immunosuppressive state induced by liver transplantation and anti-rejection therapy might contribute to the severity of COVID-19 in Case 4, who suffered from hepatitis B related hepatocellular carcinoma. However, Case 4 was recovered from COVID-19 after a combination therapy against virus, bacteria and fungi, and also respiratory support. Nearly all patients showed a decrease in lymphocytes including total CD3(+) T cells, B cells, and natural killer cells after infection of the virus. CONCLUSIONS: The severity of COVID-19 might be influenced by immune system state and underlying diseases in cancer patients. And the treatment of SARS-CoV-2 infection in cancer patients is challenged by the immunosuppressive state of these patients under chemotherapy or surgery.

Soosaipillai, G., et al. (2021). "Specialist palliative and end-of-life care for patients with cancer and SARS-CoV-2 infection: a European perspective." Ther Adv Med Oncol **13**: 17588359211042224.

Background: Specialist palliative care team (SPCT) involvement has been shown to improve symptom control and end-of-life care for patients with cancer, but little is known as to how these have been impacted by the COVID-19 pandemic. Here, we report SPCT involvement during the first wave of the pandemic and compare outcomes for patients with cancer who received and did not receive SPCT input from multiple European cancer centres. Methods: From the OnCovid repository (N = 1318), we analysed cancer patients aged 18 diagnosed with COVID-19 between 26 February and 22 June 2020 who had complete specialist palliative care team data (SPCT+ referred; SPCT- not referred). Results: Of 555 eligible patients, 317 were male (57.1%), with a median age of 70 years (IQR 20). At COVID-19 diagnosis, 44.7% were on anti-cancer therapy and 53.3% had 1 co-morbidity. Two hundred and six patients received SPCT input for symptom control (80.1%), psychological support (54.4%) and/or advance care planning (51%). SPCT+ patients had more 'Do not attempt cardio-pulmonary resuscitation' orders completed prior to (12.6% versus 3.7%) and during admission (50% versus 22.1%, $p < 0.001$), with more SPCT+ patients deemed suitable for treatment escalation (50% versus 22.1%, $p < 0.001$). SPCT involvement was associated with higher discharge rates from hospital for end-of-life care (9.7% versus 0%, $p < 0.001$). End-of-life anticipatory prescribing was higher in SPCT+ patients, with opioids (96.3% versus 47.1%) and benzodiazepines (82.9% versus 41.2%) being used frequently for symptom control.

Stewart, C. A., et al. (2021). "Lung cancer models reveal SARS-CoV-2-induced EMT contributes to COVID-19 pathophysiology." bioRxiv.

COVID-19 is an infectious disease caused by SARS-CoV-2, which enters host cells via the cell surface proteins ACE2 and TMPRSS2. Using a variety of normal and malignant models and tissues from the aerodigestive and respiratory tracts, we investigated the expression and regulation of ACE2 and TMPRSS2. We find that ACE2 expression is restricted to a select population of highly epithelial cells. Notably, infection with SARS-CoV-2 in cancer cell lines, bronchial organoids, and patient nasal epithelium, induces metabolic and transcriptional changes consistent with epithelial to mesenchymal transition (EMT), including upregulation of ZEB1 and AXL, resulting in an increased EMT score. Additionally, a transcriptional loss of genes associated with tight junction function occurs with SARS-CoV-2 infection. The SARS-CoV-2 receptor, ACE2, is repressed by EMT via TGFbeta, ZEB1 overexpression and onset of EGFR TKI inhibitor resistance. This suggests a novel model of SARS-CoV-2 pathogenesis in which infected cells shift toward an increasingly mesenchymal state, associated with a loss of tight junction components with acute respiratory distress syndrome-protective effects. AXL-inhibition and ZEB1-reduction, as with bemcentinib, offers a potential strategy to reverse this effect. These observations highlight the utility of aerodigestive and, especially, lung cancer model systems in exploring the pathogenesis of SARS-CoV-2 and other respiratory viruses, and offer important insights into the potential mechanisms underlying the morbidity and mortality of COVID-19 in healthy patients and cancer patients alike.

Stingi, A. and L. Cirillo (2021). "SARS-CoV-2 infection and cancer: Evidence for and against a role of SARS-CoV-2 in cancer onset." Bioessays **43**(8): e2000289.

Despite huge efforts towards understanding the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pathogenesis, little is known about the long-term consequences of the disease. Here, we critically review existing literature about oncogenesis as a potential long-term effect of SARS-CoV-2 infection. Like other viral infections, SARS-CoV-2 may promote cancer onset by inhibiting tumor suppressor genes. We conclude that, although unlikely, such hypothesis cannot be excluded a priori and we delineate an experimental approach to address it. Also see the video abstract here: https://youtu.be/TBUTDSLR7vY.

Sun, L., et al. (2021). "SARS-CoV-2 Seropositivity and Seroconversion in Patients Undergoing Active Cancer-Directed Therapy." JCO Oncol Pract: OP2100113.

PURPOSE: Multiple studies have demonstrated the negative impact of cancer care delays during the COVID-19 pandemic, and transmission mitigation techniques are imperative for

continued cancer care delivery. We aimed to gauge the effectiveness of these measures at the University of Pennsylvania. METHODS: We conducted a longitudinal study of SARS-CoV-2 antibody seropositivity and seroconversion in patients presenting to infusion centers for cancer-directed therapy between May 21, 2020, and October 8, 2020. Participants completed questionnaires and had up to five serial blood collections. RESULTS: Of 124 enrolled patients, only two (1.6%) had detectable SARS-CoV-2 antibodies on initial blood draw, and no initially seronegative patients developed newly detectable antibodies on subsequent blood draw(s), corresponding to a seroconversion rate of 0% (95% CI, 0.0 TO 4.1%) over 14.8 person-years of follow up, with a median of 13 health care visits per patient. CONCLUSION: These results suggest that patients with cancer receiving in-person care at a facility with aggressive mitigation efforts have an extremely low likelihood of COVID-19 infection.

Sun, L., et al. (2021). "SARS-CoV-2 seropositivity and seroconversion in patients undergoing active cancer-directed therapy." medRxiv.

Multiple studies have demonstrated the negative impact of cancer care delays during the COVID-19 pandemic, and transmission mitigation techniques are imperative for continued cancer care delivery. To gauge the effectiveness of these measures at the University of Pennsylvania, we conducted a longitudinal study of SARS-CoV-2 antibody seropositivity and seroconversion in patients presenting to infusion centers for cancer-directed therapy between 5/21/2020 and 10/8/2020. Participants completed questionnaires and had up to five serial blood collections. Of 124 enrolled patients, only two (1.6%) had detectable SARS-CoV-2 antibodies on initial blood draw, and no initially seronegative patients developed newly detectable antibodies on subsequent blood draw(s), corresponding to a seroconversion rate of 0% (95%CI 0.0-4.1%) over 14.8 person-years of follow up, with a median of 13 healthcare visits per patient. These results suggest that cancer patients receiving in-person care at a facility with aggressive mitigation efforts have an extremely low likelihood of COVID-19 infection.

Szabados, B., et al. (2020). "Clinical Characteristics and Outcome for Four SARS-CoV-2-infected Cancer Patients Treated with Immune Checkpoint Inhibitors." Eur Urol **78**(2): 276-280.

Preliminary data suggest that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is associated with higher mortality among cancer patients, particularly in those on systemic therapy. It is unclear whether this applies to patients receiving immune checkpoint inhibitors (ICIs). In this case series, 74 patients from a single institution with genitourinary (GU) cancer on ICI were followed up during a 12-wk period. During this period, 11 patients (15%) developed symptoms consistent with coronavirus disease 2019 (COVID-19) and four (5%) tested positive. Two patients had metastatic urothelial cancer (treated with atezolizumab) and two had metastatic renal cancer (treated with ipilimumab and nivolumab). All had additional risk factors associated with COVID-19 mortality and two received steroids within 1 mo of infection. Two patients developed symptoms requiring hospitalisation. All four are alive 32-45 d after their first symptoms and 28-38 d after testing positive. These patients all had multiple risk factors associated with severe COVID-19. These data suggest that the higher risk of COVID-19 death associated with systemic therapy in cancer may not apply to patients on ICIs. Assessment of COVID-19 severity in these patients can be complicated by the underlying cancer and its treatment.

Taborska, P., et al. (2021). "CD4(+) T Cells of Prostate Cancer Patients Have Decreased Immune Responses to Antigens Derived From SARS-CoV-2 Spike Glycoprotein." Front Immunol **12**: 629102.

The adaptive immune response to severe acute respiratory coronavirus 2 (SARS-CoV-2) is important for vaccine development and in the recovery from coronavirus disease 2019 (COVID-19). Men and cancer patients have been reported to be at higher risks of contracting the virus and developing the more severe forms of COVID-19. Prostate cancer (PCa) may be associated with both of these risks. We show that CD4(+) T cells of SARS-CoV-2-unexposed patients with hormone-refractory (HR) metastatic PCa had decreased CD4(+) T cell immune responses to antigens from SARS-CoV-2 spike glycoprotein but not from the spiked glycoprotein of the 'common cold'-associated human coronavirus 229E (HCoV-229E) as compared with healthy male volunteers who responded comparably to both HCoV-229E- and SARS-CoV-2-derived antigens. Moreover, the HCoV-229E spike glycoprotein antigen-elicited CD4(+) T cell immune responses cross-reacted with the SARS-CoV-2 spiked glycoprotein antigens. PCa patients may have impaired responses to the vaccination, and the cross-reactivity can mediate antibody-dependent enhancement (ADE) of COVID-19. These findings highlight the potential for increased vulnerability of PCa patients to COVID-19.

Terpos, E., et al. (2021). "Low titers of SARS-CoV-2 neutralizing antibodies after first vaccination dose in cancer patients receiving checkpoint inhibitors." J Hematol Oncol **14**(1): 86.

Vaccination for SARS-CoV-2 provides significant protection against the infection in the general population. However, only limited data exist for patients with cancer under systemic therapy. Based on this, our site has initiated a study evaluating

safety and efficacy of SARS-CoV-2 vaccination in patients with solid and hematological malignancies under several systemic therapies. The initial results of the cohort of 59 patients receiving Immune Checkpoint Inhibitors are presented here. Despite no new safety issues have been noticed, the levels of SARS-CoV-2 neutralizing antibodies are significantly lower in comparison to matched healthy volunteers up to day 22 post the first dose. These results should be taken into consideration for the patients under treatment.

Theodoropoulos, G., et al. (2021). "Perspective on the treatment of non-small cell lung cancer in the context of potential SARS-CoV-2 infection during the pandemic." J Curr Sci Technol **11**(1).

SARS-CoV-2 infections are rising at an alarming rate and various aspects of this pandemic must be quickly and adequately addressed in order to enhance effective healthcare delivery and protect at risk populations such as cancer patients. Preventing Covid-19 infection must be a top system wide priority to avoid mortality, and considerable financial and disease burden. Most cancer patients, and in particular those with tumors resistant to chemotherapy are particularly vulnerable to infection. In this review, we connect potential viral infection of patients with lung tumors that have somewhat quiescence the immune response in the tumor microenvironment and categorize target molecules in metabolism that may be used to identify at risk patients leading to more effective treatment regimens; keeping continuity of therapy and disease prevention during a very tumultuous period of time surrounding the pandemic.

von Lilienfeld-Toal, M., et al. (2021). "[Vaccination against SARS-CoV-2 in cancer patients]." Onkologe (Berl): 1-6.

Patients with cancer are at an increased risk to suffer severe coronavirus disease 2019 (COVID-19). Therefore, specific preventative measures including COVID-19 vaccines are especially important. Both anticancer therapies and the underlying malignancy itself can lead to significant immunosuppression posing a particular challenge for vaccination strategies in these patients. At the moment, four COVID-19 vaccines are European Medicines Agency (EMA) approved in Germany: two mRNA and two viral vector-based vaccines. All four vaccines show excellent protection against severe COVID-19. Their mechanism of action relies on the induction of the production of virus-specific proteins by human cells and the following activation of a specific adaptive immune response. Vaccination against COVID-19 has been prioritized for cancer patients and medical personnel in Germany. Regarding timing of vaccination, vaccination prior to initiation of anticancer therapy seems ideal in newly diagnosed disease. However, due to the significant risk of severe COVID-19 in cancer patients, vaccination is also strongly recommended for patients already undergoing anticancer therapy. In these patients, immune response might be reduced. In two particular patient cohorts, namely stem cell transplant recipients and patients treated with Bcell depleting agents, an interval of several months following therapy is recommended because otherwise the response to vaccination will most likely be severely reduced. Preliminary data suggest only low rates of seroconversion following a single shot of vaccine in cancer patients. Therefore, on the long run, repeat vaccination regimens might be preferable in cancer patients.

von Lilienfeld-Toal, M., et al. (2020). "Frequently asked questions regarding SARS-CoV-2 in cancer patients-recommendations for clinicians caring for patients with malignant diseases." Leukemia **34**(6): 1487-1494.

Since early 2020, the SARS-CoV-2 pandemic has a massive impact on health care systems worldwide. Patients with malignant diseases are assumed to be at increased risk for a worse outcome of SARS-CoV-2 infection, and therefore, guidance regarding prevention and management of the infection as well as safe administration of cancer-therapy is required. Here, we provide recommendations for the management of patients with malignant disease in the times of COVID-19. These recommendations were prepared by an international panel of experts and then consented by the EHA Scientific Working Group on Infection in Hematology. The primary aim is to enable clinicians to provide optimal cancer care as safely as possible, since the most important protection for patients with malignant disease is the best-possible control of the underlying disease.

Wang, H. and J. Yang (2021). "Colorectal Cancer that Highly Express Both ACE2 and TMPRSS2, Suggesting Severe Symptoms to SARS-CoV-2 Infection." Pathol Oncol Res **27**: 612969.

The epidemic of the novel, pathogenic SARS-coronavirus 2 (SARS-CoV-2) in the world pose a global health emergency. Cancer has been identified as a risk factor for the novel Coronavirus disease 2019 (COVID-19). The ACE2 and TMPRSS2 have been implicated in SARS-CoV-2 infection for mediating viral entry into the host cell. However, a systematic analysis of aberrant expression of ACE2 and TMPRSS2 was not yet reported in multiple human cancers. Here, we analyzed gene expression of ACE2 and TMPRSS2 across 31 types of tumors. Notably, overexpression of ACE2 and TMPRSS2 have been observed in colorectal cancer including colon adenocarcinoma (COAD), and rectum adenocarcinoma (READ). In addition, the colorectal tumors with upregulated gene expressing presented with decreased DNA

methylation levels. DNA methylation might be one of the reasons for abnormal expression of ACE2 and TMPRSS2. Conclusively, colorectal cancer was the only cancer with the upregulated expression of ACE2 and TMPRSS2. More care of colorectal cancer patients is needed in multiple cancers affected by the COVID-19 outbreak.

Wang, J., et al. (2021). "Prognostic and immunological value of ATP6AP1 in breast cancer: implications for SARS-CoV-2." Aging (Albany NY) **13**(13): 16904-16921.

Abnormal ATPase H+ Transporting Accessory Protein 1 (ATP6AP1) expression may promote carcinogenesis. We investigated the association of ATP6AP1 with breast cancer (BC) and COVID-19. The Oncomine, Gene Expression Profiling Interactive Analysis, Human Protein Atlas and Kaplan-Meier plotter databases were used to evaluate the expression and prognostic value of ATP6AP1 in BC. ATP6AP1 was upregulated in BC tissues, and higher ATP6AP1 expression was associated with poorer outcomes. Data from the Tumor Immune Estimation Resource, Tumor-Immune System Interaction Database and Kaplan-Meier plotter indicated that ATP6AP1 expression correlated with immune infiltration, and that its prognostic effects in BC depended on tumor-infiltrating immune cell subtype levels. Multiple databases were used to evaluate the association of ATP6AP1 with clinicopathological factors, assess the mutation and methylation of ATP6AP1, and analyze gene co-expression and enrichment. The ATP6AP1 promoter was hypomethylated in BC tissues and differentially methylated between different disease stages and subtypes. Data from the Gene Expression Omnibus indicated that ATP6AP1 levels in certain cell types were reduced after SARS-CoV-2 infections. Ultimately, higher ATP6AP1 expression was associated with a poorer prognosis and with higher or lower infiltration of particular immune cells in BC. BC patients may be particularly susceptible to SARS-CoV-2 infections, which may alter their prognoses.

Wang, J., et al. (2020). "Cancer patients in SARS-CoV-2 infection: a single-center experience from Wuhan." J Cancer **11**(21): 6243-6247.

Background: The Coronavirus disease 2019 (COVID-19) global pandemic has posed unprecedented challenges to the health-care systems all over the world. Among the booming literatures about COVID-19, there is yet a paucity of study addressing the association between COVID-19 and cancer, which is a rare comorbidity of COVID-19, as well as consensus for treatment of cancer in this pandemic. Methods: In this retrospective, single-center cohort study, information of all inpatient cases with laboratory-confirmed COVID-19 who had treatment outcome were collected from the designated departments in Zhongnan Hospital of Wuhan University, Wuhan, China on March 10, 2020. Demographic data, clinical information, and treatment outcomes were extracted from electronic medical records. Severe events were defined as admission to intensive care unit (ICU), the use of mechanical ventilation, or death. Result: A total of 716 patients with laboratory-confirmed COVID-19 infection were identified. Among them, a total of 12 cases (1.7%, 95% CI: 0.7%-2.6%) had history of cancer with 4 cases (33%) experienced severe events. Compared with cases without cancer, patients with cancer have higher risks of severe events (33% vs 7.7%, p=0.012) and deaths (25% vs 3.6%, p=0.009). Multivariable logistic regression model showed that cancer was independently associated with increased odds of severe events after adjusting for other risk factors (OR 6.51, 95% CI 1.72-24.64; p=0.006). Among COVID-19 patients with cancer, we found that patients older than 60 years (75%), with other comorbidities (50%), or experiencing anticancer treatment in past month (42.9%) had a numerically higher incidence of severe events. Conclusion: Cancer is a rare comorbidity of patients with COVID-19; however, it cannot be overemphasized due to its poorer outcomes. We propose that personalized treatment recommendation for cancer patients should be addressed during COVID-19 pandemic, along with meticulous personal protective protocols for them to mitigate the risk of SARS-CoV-2 infection.

Wang, Q., et al. (2021). "High Expression of ACE2 and TMPRSS2 at the Resection Margin Makes Lung Cancer Survivors Susceptible to SARS-CoV-2 With Unfavorable Prognosis." Front Oncol **11**: 644575.

Background: Coronavirus disease 2019 (COVID-19) has rapidly spread worldwide. Systematic analysis of lung cancer survivors at molecular and clinical levels is warranted to understand the disease course and clinical characteristics. Methods: A single-center, retrospective cohort study was conducted in 65 patients with COVID-19 from Wuhan Huoshenshan Hospital, of which 13 patients were diagnosed with lung cancer. The study was conducted from February 4 to April 11, 2020. Results: During the course of treatment, lung cancer survivors infected with severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) had shorter median time from symptom onset to hospitalization (P = 0.016) and longer clinical symptom remission time (P = 0.020) than non-cancer individuals. No differences were observed among indicators such as time from symptom onset to hospitalization and symptom remission time between medium-term and short-term survivors. The expression of ACE2 (P = 0.013) and TMPRSS2 (P <0.001) was elevated in lung cancer survivors as compared with that in non-cancer individuals. Conclusions: ACE2 and TMPRSS2

levels were higher at resection margins of lung cancer survivors than those in normal tissues of non-cancerous individuals and may serve as factors responsible for the high susceptibility to COVID-19 among lung cancer survivors. Lung cancer patients diagnosed with COVID-19, including medium-term survivors, have worse outcomes than the general population.

Weisel, K. C., et al. (2020). "Implications of SARS-CoV-2 Infection and COVID-19 Crisis on Clinical Cancer Care: Report of the University Cancer Center Hamburg." Oncol Res Treat **43**(6): 307-313.

With the outbreak of the COVID-19 pandemia, routine clinical work was immediately, deeply, and sustainably impacted in Germany and worldwide. The infrastructure of almost all hospitals is currently redirected to provide a maximum of intensive care resources, including the necessary staff. In parallel, routine as well as emergency clinical care for all patients in need has to be secured. This challenge becomes particularly evident in cancer care. In order to maintain adequate oncological care at all levels of provision and to conduct especially curative and intensive treatments with a maximum of safety, continuous adaption of the oncology care system has to be ensured. Intensive communication with colleagues and patients is needed as is consequent expert networking and continuous reflection of the own developed strategies. In parallel, it is of high importance to actively avoid cessation of innovation in order not to endanger the continuous improvement in prognosis of cancer patients. This includes sustained conduction of clinical trials as well as ongoing translational research. Here, we describe measures taken at the University Cancer Center Hamburg (UCCH) - a recognized comprehensive oncology center of excellence - during the COVID-19 crisis. We aim to provide support and potential perspectives to generate a discussion basis on how to maintain high-end cancer care during such a crisis and how to conduct patients safely into the future.

Westblade, L. F., et al. (2020). "SARS-CoV-2 Viral Load Predicts Mortality in Patients with and without Cancer Who Are Hospitalized with COVID-19." Cancer Cell **38**(5): 661-671 e662.

Patients with cancer may be at increased risk of severe coronavirus disease 2019 (COVID-19), but the role of viral load on this risk is unknown. We measured SARS-CoV-2 viral load using cycle threshold (CT) values from reverse-transcription polymerase chain reaction assays applied to nasopharyngeal swab specimens in 100 patients with cancer and 2,914 without cancer who were admitted to three New York City hospitals. Overall, the in-hospital mortality rate was 38.8% among patients with a high viral load, 24.1% among patients with a medium viral load, and 15.3% among patients with a low viral load ($p < 0.001$). Similar findings were observed in patients with cancer (high, 45.2% mortality; medium, 28.0%; low, 12.1%; $p = 0.008$). Patients with hematologic malignancies had higher median viral loads (CT = 25.0) than patients without cancer (CT = 29.2; $p = 0.0039$). SARS-CoV-2 viral load results may offer vital prognostic information for patients with and without cancer who are hospitalized with COVID-19.

Yarza, R., et al. (2020). "SARS-CoV-2 infection in cancer patients undergoing active treatment: analysis of clinical features and predictive factors for severe respiratory failure and death." Eur J Cancer **135**: 242-250.

AIM: Previous studies have suggested a more frequent and severe course of novel coronavirus SARS-CoV-2 infection in cancer patients undergoing active oncologic treatment. Our aim was to describe the characteristics of the disease in this population and to determine predictive factors for poor outcome in terms of severe respiratory distress (acute respiratory distress syndrome [ARDS]) or death. PATIENTS AND METHODS: Patients consecutively admitted for SARS-CoV-2 infection were prospectively collected, and retrospective statistical analysis was performed. Univariate and multivariate analyses were performed to assess potential factors for poor outcomes defined as ARDS or death. RESULTS: Sixty-three patients were analysed, and 34 of them developed respiratory failure (70% as ARDS). Lymphocytes/mm3 (412 versus 686; $p = 0.001$), serum albumin (2.84 versus 3.1); lactate dehydrogenase (LDH) (670 versus 359; $p < 0.001$) and C-reactive protein (CRP) levels (25.8 versus 9.9; $p < 0.001$) discriminate those that developed respiratory failure. Mortality rate was 25%, significantly higher among ARDS, neutropenic patients ($p = 0.01$) and in those with bilateral infiltrates (44% versus 0%; $p < 0.001$). Multivariate logistic analyses model confirmed the predictive value of severe neutropenia (odds ratio [OR] 16.54; 95% confidence interval [CI] 1.43-190.9, p 0.025), bilateral infiltrates (OR 32.83, CI 95% 3.51-307, p 0.002) and tumour lung involvement (OR 4.34, CI 95% 1.2-14.95, p 0.02). CONCLUSION: Cancer patients under active treatment admitted for SARS-CoV-2 infection have worse outcomes in terms of mortality and respiratory failure rates compared with COVID-19 global population. Lymphopenia, LDH, CRP and albumin discriminate illness severity, whereas neutropenia, bilateral infiltrates and tumour pulmonary involvement are predictive of higher mortality.

Yildirim, O. A., et al. (2021). "Depression and anxiety in cancer patients before and during the SARS-CoV-2 pandemic: association with treatment delays." Qual Life Res **30**(7): 1903-1912.

PURPOSE: Pandemics can be associated with anxiety and depression in cancer patients who are undergoing treatment. In the present study, we aimed to perform a comparative evaluation of the conditions of cancer patients before and during the severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) pandemic using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) to detect the impact of the pandemic on treatment delays that are associated with anxiety and depression in cancer patients. In addition, the effect of public transport use on treatment delays was examined. METHODS: BDI and BAI were administered to 595 breast, ovarian, colon and gastric cancer patients before and during the pandemic. The questionnaires were administered by the physician blindly, who was unaware of the delay of the patients. The number of days by which the patients delayed their treatment due to the fear of contamination were recorded retrospectively. Correlation analyses were performed between the obtained scores and treatment delays. RESULTS: The depression and anxiety levels in cancer patients were found to increase during the pandemic ($p = 0.000$), and this increase was positively correlated with the disruption of their treatment ($p = 0.000$, $r = 0.81$). Depression and anxiety levels and treatment delays were higher in elderly patients ($p = 0.021$). Depression and anxiety were more pronounced in female patients ($p = 0.000$). Moreover, treatment delays were more common in patients who had to use public transportation ($p = 0.038$). CONCLUSION: SARS-CoV-2 pandemic may increase anxiety and depression in cancer patients. This can cause patients to experience treatment delays due to concerns about becoming infected. At this point, if necessary, assistance should be obtained from psychiatric and public health experts.

Yin, J., et al. (2020). "Association of Cigarette Smoking, COPD, and Lung Cancer With Expression of SARS-CoV-2 Entry Genes in Human Airway Epithelial Cells." Front Med (Lausanne) **7**: 619453.

SARS-CoV-2 enters into human airway epithelial cells via membrane fusion or endocytosis, and this process is dependent on ACE2, TMPRSS2, and cathepsin L. In this study, we examined the expression profiles of the three SARS-CoV-2 entry genes in primary human airway epithelial cells isolated from smokers, non-smokers, patients with chronic obstructive pulmonary disease or lung cancer. An exhaustive search of the GEO database was performed to identify eligible data on 1st June 2020. In total, 46 GEO datasets comprising transcriptomic data of 3,053 samples were identified as eligible data for further analysis. All meta-analysis were performed using RStudio. Standardized mean difference was utilized to assess the effect size of a factor on the expression of targeted genes and 95% confidence intervals (CIs) were calculated. This study revealed that (i) cigarette smoking is associated with an increased expression of ACE2 and TMPRSS2 and a decreased expression of cathepsin L; (ii) significant alternations in expression of ACE2, TMPRSS2, and cathepsin L were observed between current smokers and former smokers, but not between former smokers and never smokers; (iii) when compared with healthy controls with identical smoking status, patients with COPD or lung cancer showed negligible changes in expression of ACE2, TMPRSS2, and cathepsin L. Therefore, this study implicates cigarette smoking might contribute to the development of COVID-19 by affecting the expression of SARS-CoV-2 entry genes, while smoking cessation could be effective to reduce the potential risk.

Zagouri, F., et al. (2021). "SARS-CoV-2 neutralizing antibodies after first vaccination dose in breast cancer patients receiving CDK4/6 inhibitors." Breast **60**: 58-61.

Undoubtedly, the development of COVID-19 vaccines displays a critical step towards ending this devastating pandemic, considering their protective benefits in the general population. Yet, data regarding their efficacy and safety in cancer patients are limited. Herein we provide the initial analysis of immune responses after the first dose of vaccination in 21 breast cancer patients receiving cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors. The levels of neutralizing antibodies post vaccination were similar to the matched healthy controls, whereas no safety issues have been raised. Further exploration is needed to reduce the uncertainty of SARS-CoV-2 immunity among cancer patients under treatment.

Zambelli, A., et al. (2021). "Prevalence and Clinical Impact of SARS-CoV-2 Silent Carriers Among Actively Treated Patients with Cancer During the COVID-19 Pandemic." Oncologist **26**(4): 341-347.

INTRODUCTION: In Europe, the SARS-CoV-2 pandemic had its first epicenter in Italy. Despite a significant mortality rate, the severity of most cases of COVID-19 infection ranges from asymptomatic to mildly symptomatic, and silent infection affects a still-unknown proportion of the general population. No information is available on the prevalence and clinical impact of SARS-CoV-2 silent infection among patients with cancer receiving anticancer treatment during the pandemic. MATERIALS AND METHODS: From April 1, 2020, to the end of the same month, 560 consecutive patients with cancer, asymptomatic for COVID-19 and on anticancer treatment at Papa Giovanni XXIII Hospital in Bergamo, were evaluated and tested for SARS-CoV-2. We implemented a two-step diagnostics, including the rapid serological immunoassay for anti-SARS-CoV-2 immunoglobulin (Ig) G/IgM and the nasopharyngeal swab reverse

transcriptase-polymerase chain reaction (RT-PCR) test in case of seropositivity to identify SARS-CoV-2 silent carriers. RESULTS: In 560 patients, 172 (31%) resulted positive for anti-SARS-CoV-2 IgM/IgG antibodies, regardless of different type of cancer, stage, and treatment. The Ig-seropositive patients were then tested with RT-PCR nasopharyngeal swabs, and 38% proved to be SARS-CoV-2 silent carriers. At an early follow-up, in the 97 SARS-CoV-2-seropositive/RT-PCR-negative patients who continued their anticancer therapies, only one developed symptomatic COVID-19 illness. CONCLUSION: Among patients with cancer, the two-step diagnostics is feasible and effective for SARS-CoV-2 silent carriers detection and might support optimal cancer treatment strategies at both the individual and the population level. The early safety profile of the different anticancer therapies, in patients previously exposed to SARS-CoV-2, supports the recommendation to continue the active treatment, at least in cases of RT-PCR-negative patients. IMPLICATIONS FOR PRACTICE: This is the first study evaluating the prevalence and clinical impact of SARS-CoV-2 silent infection in actively treated patients with cancer, during the epidemic peak in one of the worst areas of the COVID-19 pandemic. Lacking national and international recommendations for the detection of asymptomatic SARS-CoV-2 infection, a pragmatic and effective two-step diagnostics was implemented to ascertain SARS-CoV-2 silent carriers. In this series, consisting of consecutive and unselected patients with cancer, the prevalence of both SARS-CoV-2-seropositive patients and silent carriers is substantial (31% and 10%, respectively). The early safety profile of the different anticancer therapies, in patients previously exposed to SARS-CoV-2, supports the recommendation to continue the active treatment, at least in case of RT-PCR-negative patients.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

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