# Cancer and Alternative Treatment Literatures

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**Abstract:** Alternative cancer treatments are alternative or complementary treatments for cancer including diet and exercise, chemicals, herbs, devices, and manual procedures. Some treatments that have been proposed in the past have been found in clinical trials to be useless or unsafe. Some of these obsolete or disproven treatments continue to be promoted, sold, and used. A distinction is typically made between complementary treatments which do not disrupt conventional medical treatment, and alternative treatments which may replace conventional treatment. Alternative cancer treatments are typically contrasted with experimental cancer treatments – which are treatments for which experimental testing is underway – and with complementary treatments, which are non-invasive practices used alongside other treatment. Since the 1940s, medical science has developed chemotherapy, radiation therapy, adjuvant therapy and the newer targeted therapies, as well as refined surgical techniques for removing cancer. Before the development of these modern, evidence-based treatments, 90% of cancer patients died within five years. This Article introduces recent reports as references in the related studies.
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**Key words:** cancer; alternative; life; medicine; stem cell; treatment

## 1. Introduction

Alternative cancer treatments are alternative or complementary treatments for cancer including diet and exercise, chemicals, herbs, devices, and manual procedures. Some treatments that have been proposed in the past have been found in clinical trials to be useless or unsafe. Some of these obsolete or disproven treatments continue to be promoted, sold, and used. A distinction is typically made between complementary treatments which do not disrupt conventional medical treatment, and alternative treatments which may replace conventional treatment. Alternative cancer treatments are typically contrasted with experimental cancer treatments – which are treatments for which experimental testing is underway – and with complementary treatments, which are non-invasive practices used alongside other treatment. Since the 1940s, medical science has developed chemotherapy, radiation therapy, adjuvant therapy and the newer targeted therapies, as well as refined surgical techniques for removing cancer. Before the development of these modern, evidence-based treatments, 90% of cancer patients died within five years.

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

Ahn, J. C., R. Biswas, et al. "Synergistic effect of radachlorin mediated photodynamic therapy on propolis induced apoptosis in AMC-HN-4 cell lines via caspase dependent pathway." Photodiagnosis Photodyn Ther. 2013 Sep;10(3):236-43. doi: 10.1016/j.pdpdt.2013.01.005. Epub 2013 Mar 30.

BACKGROUND: Photodynamic therapy (PDT) is alternative method for treating malignant tumors based on the principle of photodynamic damage to tumor cells through a photochemical reaction. Because of its localized effect, photodynamic therapy has become a very popular alternative treatment for cancer. PDT in combination with other drugs has been reported to have synergistic effects on various chemotherapeutic drugs. Thus for this synergistic effect of photodynamic therapy in combination with various chemotherapeutic drugs has gained the major interests to the scientists in recent days. Studies have been carried out to treat various ailments like cancer with this combination therapy. However, PDT in combination with biologically active natural product has not yet been studied in detail. One of the natural products which have been used as a folk medicine for many centuries is propolis. It is a resinous hive product collected from various plant materials by honeybees. It is reported to exhibit several biological activities. METHODS: In this study, we focused on the effect of propolis and radachlorin-mediated PDT on human head and neck cancer cells AMC-HN-4. After the administration of propolis and radachlorin followed by laser irradiation, the viability of AMC-HN-4 cells was analyzed using MTT assay. The cells were also stained with Hoechst 33342 and propidium iodide (PI) for morphological observations. For more detailed evaluation and observation, flowcytometric analysis and western blotting were also carried out after congruent treatment process.

RESULTS: From the result it was found that the proliferation of AMC-HN-4 cells was inhibited by propolis. The inhibition of cell proliferation was increased when the cells were treated in combination. The rate of cell death was also increased in combination. The expressions of different proteins related to apoptosis were also regulated significantly.

Aloysius, H. and L. Hu "Targeted Prodrug Approaches for Hormone Refractory Prostate Cancer." Med Res Rev. 2014 Dec 22. doi: 10.1002/med.21333.

Due to the propensity of relapse and resistance with prolonged androgen deprivation therapy (ADT), there is a growing interest in developing non-hormonal therapeutic approaches as alternative treatment modalities for hormone refractory prostate cancer (HRPC). Although the standard treatment for HRPC consists of a combination of ADT with taxanes and anthracyclines, the clinical use of chemotherapeutics is limited by systemic toxicity stemming from nondiscriminatory drug exposure to normal tissues. In order to improve the tumor selectivity of chemotherapeutics, various targeted prodrug approaches have been explored. Antibody-directed enzyme prodrug therapy (ADEPT) and gene-directed enzyme prodrug therapy (GDEPT) strategies leverage tumor-specific antigens and transcription factors for the specific delivery of cytotoxic anticancer agents using various prodrug-activating enzymes. In prostate cancer, overexpression of tumor-specific proteases such as prostate-specific antigen (PSA) and prostate-specific membrane antigen (PSMA) is being exploited for selective activation of anticancer prodrugs designed to be activated through proteolysis by these prostate cancer-specific enzymes. PSMA- and PSA-activated prodrugs typically comprise an engineered high-specificity protease peptide substrate coupled to a potent cytotoxic agent via a linker for rapid release of cytotoxic species in the vicinity of prostate cancer cells following proteolytic cleavage. Over the past two decades, various such prodrugs have been developed and they were effective at inhibiting prostate tumor growth in rodent models; several of these prodrug approaches have been advanced to clinical trials and may be developed into effective therapies for HRPC.

Al-Salahi, O. S., C. Kit-Lam, et al. "Anti-angiogenic quassinoid-rich fraction from Eurycoma longifolia modulates endothelial cell function." Microvasc Res. 2013 Nov;90:30-9. doi: 10.1016/j.mvr.2013.07.007. Epub 2013 Jul 27.

Targeting angiogenesis could be an excellent strategy to combat angiogenesis-dependent pathophysiological conditions such as cancer, rheumatoid arthritis, obesity, systemic lupus erythematosus, psoriasis, proliferative retinopathy and atherosclerosis. Recently a number of clinical investigations are being undertaken to assess the potential therapeutic application of various anti-angiogenic agents. Many of these angiogenesis inhibitors are directed against the functions of endothelial cells, which are considered as the building blocks of blood vessels. Similarly, roots of a traditional medicinal plant, Eurycoma longifolia, can be used as an alternative treatment to prevent and treat the angiogenesis-related diseases. In the present study, antiangiogenic potential of partially purified quassinoid-rich fraction (TAF273) of E. longifolia root extract was evaluated using ex vivo and in vivo angiogenesis models and the anti-angiogenic efficacy of TAF273 was investigated in human umbilical vein endothelial cells (HUVEC). TAF273 caused significant suppression in sprouting of microvessels in rat aorta with IC50 11.5mug/ml. TAF273 (50mug/ml) showed remarkable inhibition (63.13%) of neovascularization in chorioallantoic membrane of chick embryo. Tumor histology also revealed marked reduction in extent of vascularization. In vitro, TAF273 significantly inhibited the major angiogenesis steps such as proliferation, migration and differentiation of HUVECs. Phytochemical analysis revealed high content of quassinoids in TAF273. Specially, HPLC characterization showed that TAF273 is enriched with eurycomanone, 13alpha(21)-epoxyeurycomanone and eurycomanol. These results demonstrated that the antiangiogenic activity of TAF273 may be due to its inhibitory effect on endothelial cell proliferation, differentiation and migration which could be attributed to the high content of quassinoids in E. longifolia.

Amedei, A., E. Niccolai, et al. "Pancreatic cancer: role of the immune system in cancer progression and vaccine-based immunotherapy." Hum Vaccin Immunother. 2014;10(11):3354-68. doi: 10.4161/hv.34392.

Pancreatic cancer (PC) is the 5th leading cause of cancer related death in the developed world with more than 260,000 deaths annually worldwide and with a dismal 5-year survival. Surgery is the only potential hope of cure for PC, but, unfortunately, only 20% PC patients is resectable at the time of diagnosis. Therapeutic research efforts have mainly focused on improvements in radio/ chemo treatments and to date, there are only a few chemotherapeutic agents that have shown to be effective against PC, including gemcitabine with or without abraxane as well as a combination of 5-FU, leucovorin, oxaliplatin and irinotecan (the so-called FOLFIRINOX regimen). The survival of patients treated with these regimens is marginal and hence we are in urgent need of novel

therapeutic approaches to treat pancreatic cancer. The success of immunotherapeutic strategies in other cancers and various evidences that pancreatic adenocarcinoma elicits antitumor immune responses, suggest that immunotherapies can be a promising alternative treatment modality for this deadly disease. PC immunotherapy treatments include passive immunotherapeutic approaches, such as the use of effector cells generated in vitro, and active immunotherapeutic strategies, which goal is to stimulate an antitumor response in vivo, by means of vaccination.

Andreotti, C., J. C. Root, et al. "Cancer, coping, and cognition: a model for the role of stress reactivity in cancer-related cognitive decline." Psychooncology. 2014 Oct 6. doi: 10.1002/pon.3683.

BACKGROUND: Cognitive decline and accompanying neurological changes associated with non-CNS cancer diagnosis and treatment have been increasingly identified in a subset of patients. Initially believed to be because of neurotoxic effects of chemotherapy exposure, observation of cognitive decline in patients not treated with chemotherapy, cancer-diagnosed individuals prior to treatment, and patients receiving alternative treatment modalities (surgery, endocrine therapy, and radiation) has led to the investigation of additional potential etiologies and moderating factors. Stressful experiences have long been posited as a contributor to these cognitive changes. Through reciprocal connectivity with peripheral systems, the brain maintains a dynamic circuitry to adapt to stress (allostasis). However, overuse of this system leads to dysregulation and contributes to pathophysiology (allostatic load). At this time, little research has been conducted to systematically examine the role of allostatic load in cancer-related cognitive dysfunction. METHODS AND RESULTS: Here, we integrate theories of stress biology, neuropsychology, and coping and propose a model through which individuals with a high level of allostatic load at diagnosis may be particularly vulnerable to the neurocognitive effects of cancer.

Arozarena, I., I. Goicoechea, et al. "Differential chemosensitivity to antifolate drugs between RAS and BRAF melanoma cells." Mol Cancer. 2014 Jun 19;13:154. doi: 10.1186/1476-4598-13-154.

BACKGROUND: The importance of the genetic background of cancer cells for the individual susceptibility to cancer treatments is increasingly apparent. In melanoma, the existence of a BRAF mutation is a main predictor for successful BRAF-targeted therapy. However, despite initial successes with these therapies, patients relapse within a year and have to move on to other therapies. Moreover, patients harbouring a wild type BRAF gene (including 25% with NRAS mutations) still require alternative treatment such as chemotherapy. Multiple genetic parameters have been associated with response to chemotherapy, but despite their high frequency in melanoma nothing is known about the impact of BRAF or NRAS mutations on the response to chemotherapeutic agents. METHODS: Using cell proliferation and DNA methylation assays, FACS analysis and quantitative-RT-PCR we have characterised the response of a panel of NRAS and BRAF mutant melanoma cell lines to various chemotherapy drugs, amongst them dacarbazine (DTIC) and temozolomide (TMZ) and DNA synthesis inhibitors. RESULTS: Although both, DTIC and TMZ act as alkylating agents through the same intermediate, NRAS and BRAF mutant cells responded differentially only to DTIC. Further analysis revealed that the growth-inhibitory effects mediated by DTIC were rather due to interference with nucleotide salvaging, and that NRAS mutant melanoma cells exhibit higher activity of the nucleotide synthesis enzymes IMPDH and TK1. Importantly, the enhanced ability of RAS mutant cells to use nucleotide salvaging resulted in resistance to DHFR inhibitors.

Authier, A., K. J. Farrand, et al. "Enhanced immunosuppression by therapy-exposed glioblastoma multiforme tumor cells." Int J Cancer. 2015 Jun 1;136(11):2566-78. doi: 10.1002/ijc.29309. Epub 2014 Nov 12.

Glioblastoma multiforme (GBM) is a highly malignant brain tumor with an extremely short time to relapse following standard treatment. Since recurrent GBM is often resistant to subsequent radiotherapy and chemotherapy, immunotherapy has been proposed as an alternative treatment option. Although it is well established that GBM induces immune suppression, it is currently unclear what impact prior conventional therapy has on the ability of GBM cells to modulate the immune environment. In this study, we investigated the interaction between immune cells and glioma cells that had been exposed to chemotherapy or irradiation in vitro. We demonstrate that treated glioma cells are more immunosuppressive than untreated cells and form tumors at a faster rate in vivo in an animal model. Cultured supernatant from in vitro-treated primary human GBM cells were also shown to increase suppression, which was independent of accessory suppressor cells or T regulatory cell generation, and could act directly on CD4(+) and CD8(+) T cell proliferation. While a number of key immunosuppressive cytokines were overexpressed in the treated cells, including IL-10, IL-6 and GM-CSF, suppression could be alleviated in a number of treated GBM lines by inhibition of prostaglandin E2.

Berking, C., A. Hauschild, et al. "Basal cell carcinoma-treatments for the commonest skin cancer." Dtsch Arztebl Int. 2014 May 30;111(22):389-95. doi: 10.3238/arztebl.2014.0389.

BACKGROUND: With an incidence of 70 to over 800 new cases per 100 000 persons per year, basal cell carcinoma (BCC) is a very common disease, accounting for about 80% of all cases of non-melanoma skin cancer. It very rarely metastasizes. A variety of treatments are available for the different subtypes and stages of BCC. METHOD: This review is based on pertinent literature retrieved by a selective search in the Medline database, as well as the American Cancer Society guidelines on BCC and the German guidelines on BCC and skin cancer prevention. RESULTS: The gold standard of treatment is surgical excision with histological control of excision margins, which has a 5-year recurrence rate of less than 3% on the face. For superficial BCC, approved medications such as imiquimod (total remission rate, 82-90%) and topical 5-fluorouracil (80%) are available, as is photodynamic therapy (71-87%). Other ablative methods (laser, cryosurgery) are applicable in some cases. Radiotherapy is an alternative treatment for invasive, inoperable BCC, with 5-year tumor control rates of 89-96%. Recently, drugs that inhibit an intracellular signaling pathway have become available for the treatment of locally advanced or metastatic BCC. Phase I and II clinical trials revealed that vismodegib was associated with objective response rates of 30-55% and tumor control rates of 80-90%. This drug was approved on the basis of a non-randomized trial with no control arm. It has side effects ranging from muscle cramps (71%) and hair loss (65%) to taste disturbances (55%) and birth defects. CONCLUSION: The established, standard treatments are generally highly effective. Vismodegib is a newly approved treatment option for locally advanced BCC that is not amenable to either surgery or radiotherapy.

Bratus, A. S., E. Fimmel, et al. "On assessing quality of therapy in non-linear distributed mathematical models for brain tumor growth dynamics." Math Biosci. 2014 Feb;248:88-96. doi: 10.1016/j.mbs.2013.12.007. Epub 2013 Dec 31.

In this paper a mathematical model for glioma therapy based on the Gompertzian law of cell growth is presented. In the common case the model is considered with non-linear spatially varying diffusion depending on a parameter. The case of the linear spatially-varying diffusion arose as a special case for a particular value of the parameter. Effectiveness of the medicine is described in terms of a therapy function. At any given moment the amount of the applied chemotherapeutic agent is regulated by a control function with a bounded maximum. Additionally, the total quantity of chemotherapeutic agent which can be used during the treatment process is bounded. The main goal of the work is to compare the quality of the optimal strategy of treatment with the quality of another one, proposed by the authors and called the alternative strategy. As the criterion of the quality of the treatment, the amount of the cancer cells at the end of the therapy is chosen.

Cox, J. A. and T. A. Swanson "Current modalities of accelerated partial breast irradiation." Nat Rev Clin Oncol. 2013 Jun;10(6):344-56. doi: 10.1038/nrclinonc.2013.65. Epub 2013 Apr 30.

The benefits of adjuvant whole-breast irradiation (WBI) after breast-conserving surgery are well established and WBI is a standard of care. In selected patients with early stage breast cancer, accelerated partial breast irradiation (APBI) has emerged as an alternative treatment option to WBI. Early trials of APBI have demonstrated an excellent local control rate and an associated good-to-excellent cosmetic outcome. APBI can reduce both the treatment volume and overall treatment time of adjuvant radiation therapy, which potentially overcomes logistical barriers associated with WBI that have previously prevented eligible women from pursuing breast-conserving therapy. Likewise, the addition of new modalities for APBI delivery has increased the number of patients who might be eligible for this adjuvant treatment-in the setting of breast-conserving surgery-despite the limited availability of long-term data on APBI outcomes compared to historical WBI outcomes.

de Brum Vieira, P., R. B. Giordani, et al. "Natural and synthetic compound anti-Trichomonas vaginalis: an update review." Parasitol Res. 2015 Apr;114(4):1249-61. doi: 10.1007/s00436-015-4340-3. Epub 2015 Feb 18.

Trichomonas vaginalis is a flagellate protozoan that causes trichomonosis, a sexually transmitted disease of worldwide importance. However, the infection has long received much less attention than other parasitic and sexually transmitted diseases. This negligence leads to poor diagnosis and underestimated prevalence values, and consequently, it has been associated to increasing acquisition and transmission of HIV, pregnancy outcomes, infertility, pelvic inflammatory disease, and cervical and prostate cancer. In view of increased resistance to drugs belonging to the nitroimidazole class, new treatment alternatives are urgently needed. Natural products provide an immeasurable wealth of active molecules, and a great number of new drugs have been originated

from these compounds. In addition, new synthetic products or derivatives from old drugs also provide an alternative to treat trichomonosis. Albeit many studies have been performed with natural products against T. vaginalis, none of them progressed to clinical trials. Overall, inadequate financial investments are made, and no alternative treatment for trichomonosis has been discovered; meanwhile, hundreds of thousands of people will remain infected and suffering the serious consequences of this nonviral STD.

Ehrlich, D., B. Wang, et al. "Intratumoral anti-HuD immunotoxin therapy for small cell lung cancer and neuroblastoma." J Hematol Oncol. 2014 Dec 19;7(1):91.

BackgroundMost patients with small cell lung cancer (SCLC) or neuroblastoma (NB) already show clinically detectable metastases at diagnosis and have an extremely poor prognosis even when treated with combined modalities. The HuD-antigen is a neuronal RNA-binding protein that is expressed in 100% of SCLC tumor cells and over 50% of neuroblastoma cells. The correlation between high titers of circulating anti-HuD antibodies in patients and spontaneous tumor remission suggests that the HuD-antigen might be a potential molecular target for immunotherapy.MethodsWe have constructed a new antibody-toxin compound (called BW-2) by assembling a mouse anti-human-HuD monoclonal antibody onto streptavidin/saporin complexes.

Eichler, K., S. Jakobi, et al. "Transarterial chemoembolisation (TACE) with gemcitabine: phase II study in patients with liver metastases of breast cancer." Eur J Radiol. 2013 Dec;82(12):e816-22. doi: 10.1016/j.ejrad.2013.08.046. Epub 2013 Sep 1.

OBJECTIVE: Evaluation of the efficacy and tolerability of transarterial chemoembolization with gemcitabine in patients with inoperable liver metastases of breast cancer. MATERIALS AND METHODS: Open-label, prospective non-randomized single-center study design; patients had previous chemotherapy including anthracyclines and/or taxanes in the metastatic setting, adequate bone marrow reserve, sufficient liver/renal function, no centralnervous system metastases, Karnovsky-performance-status >70%, and life expectancy >12 weeks. Forty-three patients were enrolled (median 58 years, range 48-71). A suspension of gemcitabine 1.200mg/m(2), 2-10 ml/m(2) of Lipiodol, and 5 ml of a degradable starch microsphere (Embocept) suspension, were administered intra-arterially up to 3 times with a 4-weaks-interval. Dose-limiting toxicit is defined as grade 4 thrombocytopenia, neutropenia, or nonhematologic toxicity>grade 3. Tumor response was evaluated by magnetic resonance (MRI) and computed tomography (CT) imaging. RESULTS: All patients tolerated the treatment well; with no dose limiting toxicities. Imaging follow-up according to the RECIST-criteria (Response Evaluation Criteria in Solid Tumors) revealed a partial response in 3 patients, stable disease in 16 patients and progression in 22 patients.

Foley, O. W., J. A. Rauh-Hain, et al. "Trends in the treatment of uterine leiomyosarcoma in the medicare population." Int J Gynecol Cancer. 2015 Mar;25(3):453-8. doi: 10.1097/IGC.0000000000000372.

OBJECTIVE: Uterine leiomyosarcoma (LMS) is a relatively rare malignancy that is associated with a poor prognosis. The rarity of LMS has led to a lack of consensus regarding appropriate treatment. The goal of this study was to identify the role that chemotherapy and radiotherapy have played in the treatment of uterine LMS in the United States as well as the effectiveness of adjuvant treatment. MATERIALS/METHODS: We used the SEER (Surveillance, Epidemiology, and End Results)-Medicare database to gather information on uterine LMS patients older than the age of 66 years diagnosed between 1992 and 2009. Basic demographic and clinical characteristics were collected. A logistic regression model analysis was performed to determine predictors of treatment. Cox proportional hazards models were used to identify clinical parameters and treatment strategies associated with survival differences. RESULTS: Our final study group included 230 patients. We found that the rate of use of chemotherapy and radiotherapy in the treatment of patients with uterine LMS increased over the period investigated. However, we identified no significant survival advantage associated with either mode of therapy. The strongest predictor of survival was stage at diagnosis. The logistic regression model analysis revealed that age at diagnosis, treatment year, stage, and underlying health status were all independent predictors of chemotherapy.

Fukuhara, H., M. Yagi, et al. "Long-term administration of single-agent carboplatin (AUC 4) for advanced testicular seminoma safely achieved complete response in an 80-year-old man with chronic heart failure: A case report." Can Urol Assoc J. 2014 Nov;8(11-12):E931-3. doi: 10.5489/cuaj.2089.

Carboplatin is often used instead of cisplatin as an alternative treatment for advanced testicular cancer. However, the safety, optimal dose, and optimal duration of this agent are unclear in patients with cardiac complications. We report the safety and effectiveness of long-term single-agent carboplatin for the treatment of testicular cancer in a patient with

chronic heart failure (CHF). An 80-year-old man was referred to our institution for evaluation of painless swelling of the left scrotum. Computed tomography revealed lung metastases. Left radical inguinal orchiectomy was performed, and pathologic examination revealed a pure seminoma. Because he had CHF, there was high possibility of onset of acute heart failure secondary to fluid administration. Thus, single-agent carboplatin (AUC 4) was selected for therapy. A complete response was achieved after 8 of 13 cycles, and no serious adverse events occurred, including cardiac problems. Neither recurrence nor metastasis was detected during the 6-month follow-up. Low-dose, long-term carboplatin is likely effective for patients who are unfit for cisplatin administration because of comorbidities, especially CHF.

Gamerith, G., T. Auer, et al. "Increase in antibody-dependent cellular cytotoxicity (ADCC) in a patient with advanced colorectal carcinoma carrying a KRAS mutation under lenalidomide therapy." Cancer Biol Ther. 2014 Mar 1;15(3):266-70. doi: 10.4161/cbt.27327. Epub 2013 Dec 18.

The failure of EGFR inhibitors in colorectal tumors with KRAS mutations requires the development of alternative treatment strategies for this patient subgroup. Among the hallmarks of cancer the disturbed immunosurveillance and cancer immune evasion have become emerging targets for cancer therapy. Due to their pleiotropic functions immunomodulatory drugs (IMiDs) are interesting agents for combination therapies in solid tumors. However, their possible contribution and a way of monitoring their biological effects have yet to be revealed. In a heavily pretreated patient with advanced colorectal cancer carrying mutations in APC and KRAS genes, we show an early metabolic response and enhanced NK cell activity to monotherapy with lenalidomide. After subsequent lenalidomide/cetuximab combination treatment, the patient had progressive disease. At the same time a reduced performance status, complicated by febrile neutropenia, occurred, as well as a slight increase in metabolic activity. Concordantly NK cell activity dropped back to baseline.

Genzini, T., H. M. Noujaim, et al. "Renal autotransplantation to treat renal artery aneurysm: case report." Sao Paulo Med J. 2014;132(5):307-10. Epub 2014 Jul 29.

CONTEXT: Renal artery aneurysm (RAA) is uncommon and usually asymptomatic, but complications like rupture or thromboembolism of the aneurysm can occur, with consequent renal infarction. Most of the clinical findings are found incidentally through imaging examinations, in investigating other diseases. Renal autotransplantation (RAT) is an alternative treatment for complex RAA, with satisfactory results described in the literature. CASE REPORT: The patient was a 48-year-old man with a history of systemic arterial hypertension, thrombocytopenia and advanced hepatosplenic schistosomiasis. He complained of right lumbar pain, which was investigated through imaging examinations (computed tomography and angiotomography). These revealed right RAA of 2.5 cm in diameter. Evaluation by the vascular surgery team found that this was untreatable using endovascular methods. The treatment performed was open right nephrectomy with kidney preservation in solution, followed by aneurysmectomy, suturing of the injured artery and kidney reimplantation in the right iliac fossa with anastomosis of the iliac vessels and ureter. The durations of the surgery and kidney ischemia were 385 and 140 minutes, respectively. The patient was discharged on the 20th postoperative day, with creatinine concentration of 1.4 mg/dL, urea 41 mg/dL, urine volume 1400 mL/24 h and ascites treated with diuretics. CONCLUSION: RAT is indicated basically in three situations: extracorporeal reconstruction of complex aneurysms of the renal pedicle, extensive ureteral injury, and conservative kidney cancer surgery in patients with a single kidney. This study presents a case of a patient with advanced liver disease and RAA that was untreatable using endovascular methods and was successfully treated using RAT.

Gomez-Veiga, F., S. Martinez-Breijo, et al. "Focal therapy for prostate cancer. Alternative treatment." Actas Urol Esp. 2014 Sep;38(7):465-75. doi: 10.1016/j.acuro.2013.12.006. Epub 2014 Mar 4.

CONTEXT: The great controversy surrounding the treatment of localized prostate cancer is related with its possibilities of radical treatment or active surveillance. The objective of this paper is to analyze the rationale selection among current focal therapy modalities regarding tumor and patient selection. EVIDENCE ACQUISITION: Current articles about advantages and disadvantages on the treatment of localized prostate cancer as well as information about focal therapy regarding tumour selection, characteristics and indications cited in MEDLINE search were reviewed. SUMMARY OF EVIDENCE: Focal therapy standardized criteria must be: low risk tumors, PSA<10-15, Gleason score </= 6, and unilateral presentation all supported by image-guided biopsy and nuclear magnetic resonance (NMR). There are doubts about the suitability of focal therapy in cases of bilateralism or in those with Gleason score 3+4 or PSA>15.

Grzywacz, A., M. Dziuk, et al. "[Refractory hypercalcemia in patient with lung cancer]." Pol Merkur Lekarski. 2014 Apr;36(214):261-4.

Hypercalcemia is a common complication of malignancy which recognition is usually delayed. Severe hypercalcemia can lead to death. Mechanisms of hypercalcemia of malignancy include excessive production of parathyroid hormone related protein (PTHrP), local osteolysis, absorptive hypercalcemia due to overproduction of calcitriol and ectopic parathormone (PTH) production. Volume expansion with normal saline solution, loop diuretics and intravenous bisphosphonates are mainstays of therapy for hypercalcemia. As an adjunctive therapy calcitonin and corticosteroids are used. In refractory cases gallium nitrate and denosumab can be an option. In patients with severe acute kidney disease hemodialysis with a low-calcium bath is an alternative treatment. In this paper we present a case of severe, refractory hypercalcemia in 53-years old patient with squamous cell carcinoma of the lung and multiple metastases to bones. Despite intensive treatment, that included also intravenous bisphosphonates, patient relapsed on therapy and didn't respond to subsequent doses. Patient received subcutaneous denosumab with good hypocalcemic effect. In this paper we present pathogenesis and treatment of hypercalcemia, including advantages and limitations of denosumab.

Hahn, T., P. L. McCarthy, et al. "Simplified validated prognostic model for progression-free survival after autologous transplantation for hodgkin lymphoma." Biol Blood Marrow Transplant. 2013 Dec;19(12):1740-4. doi: 10.1016/j.bbmt.2013.09.018. Epub 2013 Oct 3.

Hodgkin lymphoma (HL) prognostic models based on factors measured at time of autologous hematopoietic cell transplantation (AHCT) are limited by small sample sizes. Models based on information at diagnosis are often not uniformly collected or available at transplantation. We propose an easily implementable prognostic model for progression-free survival (PFS) post-AHCT based on factors available at transplantation in a large international cohort of HL patients. The outcomes of 728 AHCT recipients for relapsed/refractory HL were studied. Patients were randomly selected for model development (n = 337) and validation (n = 391). The multivariate model identified 4 major adverse risk factors at the time of AHCT with the following relative weights: Karnofsky performance score <90 and chemotherapy resistance at AHCT were each assigned 1 point, whereas at least 3 chemotherapy regimens pre-AHCT and extranodal disease at AHCT were each assigned 2 points. Based on the total score summed for the 4 adverse risk factors, 3 risk groups were identified: low (score = 0), intermediate (score = 1 to 3), or high (score = 4 to 6). The 4-year PFS for the low- (n = 176), intermediate- (n = 261), and high- (n = 283) risk groups were 71% (95% confidence interval [CI], 63% to 78%), 60% (95% CI, 53% to 66%), and 42% (95% CI, 36% to 49%), respectively. The prognostic model was validated in an independent cohort. The Center for International Blood and Marrow Transplant Research model is based on factors easily available at the time of AHCT and discriminates patients with favorable post-AHCT outcomes as well as an intermediate-risk group. This model should assist in the prospective evaluation of alternative treatment strategies.

Holyoake, T. L. and G. V. Helgason "Do we need more drugs for chronic myeloid leukemia?" Immunol Rev. 2015 Jan;263(1):106-23. doi: 10.1111/imr.12234.

The introduction of protein tyrosine kinase inhibitors (TKIs) in 1998 transformed the management of chronic myeloid leukemia (CML), leading to significantly reduced mortality and improved 5 year survival rates. However, the CML community is faced with several clinical issues that need to be addressed. Ten to 15% of CML patients are diagnosed in advanced phase, and small numbers of chronic phase (CP) cases experience disease progression each year during treatment. For these patients, TKIs induce only transient responses and alternative treatment strategies are urgently required. Depending on choice of first line TKI, approximately 30% of CML CP cases show suboptimal responses, due to a combination of poor compliance, drug intolerance, and drug resistance, with approximately 50% of TKI-resistance caused by kinase domain mutations and the remainder due to unknown mechanisms. Finally, the chance of successful treatment discontinuation is on the order of only 10-20% related to disease persistence. Disease persistence is a poorly understood phenomenon; all CML patients have functional Philadelphia positive (Ph+) stem and progenitor cells in their bone marrows and continue to express BCR-ABL1 by DNA PCR, even when in very deep remission and following treatment discontinuation. What controls the maintenance of these persisting cells, whether it is necessary to fully eradicate the malignant clone to achieve cure, and how that might be approached therapeutically are open questions.

Ibrahim, N., N. Mohamed, et al. "Update on statins: hope for osteoporotic fracture healing treatment." Curr Drug Targets. 2013 Dec;14(13):1524-32.

Fracture healing is a process of recovering injured bone tissue forms and functions. Osteoporosis can delay the healing process, which contributes to personal suffering and loss of activities. Osteoporosis patients tend to lose bone mass at the metaphyseal

region which require treatment to increase bone mass. Postmenopausal osteoporosis is the most common osteoporosis that occurs in women which subsequently resulted in fractures even under slight trauma. Estrogen Replacement Therapy (ERT), the recommended therapy for postmenopausal osteoporosis, is associated with higher risk of breast cancer, ovarian cancer and cardiovascular diseases. As osteoporotic fractures are becoming a public health issue, alternative treatment is now being thoroughly explored. The potential agent is statins, the HMG-CoA reductase inhibitor which is widely used for hypercholesterolemia treatment. Statins have been found to increase bone mass by stimulation of Bone morphogenetic protein-2 (BMP-2) expression and Vascular Endothelial Growth Factor (VEGF) production. However, these bone forming effects were achieved at very high systemic doses. Therefore, studies on locally applied statins are required to further explore the ability of statins to stimulate bone formation at acceptable doses for better fracture healing. This review highlights the animal and clinical studies on fracture healing promotions by statins and the mechanisms involved.

Ikeda, S. "[Economic evaluation of targeted cancer therapy]." Gan To Kagaku Ryoho. 2013 Aug;40(8):967-70.

Medical technology, especially cancer therapy, has been recognized as having a major role both in improving health care and in increasing costs. Economic evaluation is considered the basis for resource allocation because it allows decision makers to consider the relative value of alternative uses of available resources. Analytical techniques used for economic evaluation in the healthcare sector are designed to compare alternative treatment strategies in terms of cost and outcome. There are 4 types of economic evaluation: cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis. The difference between these techniques relates to the way in which the outcomes are measured. Cost-utility analysis reflects value for money in terms of a single type of health outcome, such as quality-adjusted life year(QALY). This approach incorporates both an increase in survival time(extra life years)and changes in the quality of life(with or without increased survival)into 1 measure. An increase in the quality of life is expressed as a utility value on a scale of 0(dead)to 1 (perfect quality of life). The incremental cost-effectiveness ratio(ICER)in this case is expressed as the incremental cost to gain an extra QALY. The main attraction of cost-utility analysis is its ability to compare different interventions for different diseases, and this type of economic evaluation is widely used for targeted cancer therapy.

Jeon, H. W., S. H. Choi, et al. "Single incision thoracoscopic left lower lobe superior segmentectomy for non-small cell lung cancer." Korean J Thorac Cardiovasc Surg. 2014 Apr;47(2):185-8. doi: 10.5090/kjtcs.2014.47.2.185. Epub 2014 Apr 10.

Lobectomy with mediastinal node dissection has been standard treatment for non-small cell lung cancer (NSCLC). Nowadays, video-assisted thoracoscopic surgery (VATS) is gaining acceptance as an alternative treatment option, given the quality-of-life benefits that it confers. For the VATS procedure, most surgeons create two or three ports with a utility incision of 3 to 5 cm. However, with acquired skill and instrumentation advances, single-incision thoracoscopic surgery has emerged over time. Here, we report the case of an 86-year-old female with NSCLC treated by single-incision segmentectomy.

Jiang, G., Z. Li, et al. "Computed tomography-guided iodine-125 interstitial implantation as an alternative treatment option for lung cancer." Indian J Cancer. 2015 Feb;51 Suppl 2:e9-e12. doi: 10.4103/0019-509X.151999.

PURPOSE: The aim was to evaluate the safety, feasibility and efficacy of computed tomography (CT)-guided percutaneous interstitial brachytherapy using radioactive iodine-125 ( 125 I) seeds for the treatment of lung cancer. MATERIALS AND METHODS: Included in this study were 45 male and 35 female patients aged 52-85 years (mean 72-year) who were diagnosed with lung cancer. Of the 80 cases of lung cancer, 38 were pathologically confirmed as squamous cell carcinoma, 29 as adenocarcinoma, 2 as small cell lung cancer, and 11 as metastatic lung cancer. Percutaneous interstitial implantation of radioactive 125 I seeds was performed under CT guidance. The treatment planning system was used to reconstruct three-dimensional images of the tumor to determine the quantity and distribution of 125 I seeds to be implanted. Under CT guidance, 125 I seeds were embedded into the tumor, with the matched peripheral dose set at 100-130 Gy. Follow-up CT scan was done in 2-month to explore the treatment efficacy. RESULTS: The procedure was successful in all patients. No major procedure-associated death occurred. The duration of follow-up was 6-month. Complete response (CR) was seen in 38 cases (47.5%), partial response (PR) in 27 cases (33.75%), stable disease (SD) in 10 cases (12.5%), and progressive disease in 5 cases (6.25%), with a local control rate (CR + PR + SD) of 93.75%. The 2-, 4- and 6-month overall response rate (CR + PR) was 78%, 83% and 81%, respectively. CONCLUSION:

Implantation of CT-guided 125 I seeds is a safe and effective alternative option for the treatment of lung cancer.

Juliachs, M., A. Vidal, et al. "Effectivity of pazopanib treatment in orthotopic models of human testicular germ cell tumors." BMC Cancer. 2013 Aug 10;13:382. doi: 10.1186/1471-2407-13-382.

BACKGROUND: Cisplatin (CDDP) resistance in testicular germ cell tumors (GCTs) is still a clinical challenge, and one associated with poor prognosis. The purpose of this work was to test pazopanib, an anti-tumoral and anti-angiogenic multikinase inhibitor, and its combination with lapatinib (an anti-ErbB inhibitor) in mouse orthotopic models of human testicular GCTs. METHODS: We used two different models of human testicular GCTs orthotopically grown in nude mice; a CDDP-sensitive choriocarcinoma (TGT38) and a new orthotopic model generated from a metastatic GCT refractory to first-line CDDP chemotherapy (TGT44). Nude mice implanted with these orthotopic tumors were treated with the inhibitors and the effect on tumoral growth and angiogenesis was evaluated. RESULTS: TGT44 refractory tumor had an immunohistochemical profile similar to the original metastasis, with characteristics of yolk sac tumor. TGT44 did not respond when treated with cisplatin. In contrast, pazopanib had an anti-angiogenic effect and anti-tumor efficacy in this model. Pazopanib in combination with lapatinib in TGT38, an orthotopic model of choriocarcinoma had an additive effect blocking tumor growth. CONCLUSIONS: We present pazopanib as a possible agent for the alternative treatment of CDDP-sensitive and CDDP-refractory GCT patients, alone or in combination with anti-ErbB therapies.

Karsono, A. H., O. M. Tandrasasmita, et al. "Molecular effects of bioactive fraction of Curcuma mangga (DLBS4847) as a downregulator of 5alpha-reductase activity pathways in prostatic epithelial cells." Cancer Manag Res. 2014 Jun 6;6:267-78. doi: 10.2147/CMAR.S61111. eCollection 2014.

DLBS4847 is a standardized bioactive fraction of Curcuma mangga. In this study, we used prostate cancer (PC)-3 as the cell line to study the effects of DLBS4847 on prostatic cell viability, as well as related molecular changes associated with the decreased cell number. The observation revealed that DLBS4847 inhibited the growth of PC3 cells through downregulation of the 5alpha-reductase (5AR) pathway. At the transcription level, 5AR1 and androgen-receptor gene expressions were downregulated in a dose-dependent manner. Furthermore, 5AR-1 and dihydrotestosterone expression were also downregulated at the protein level. A microarray study was also performed to see the effects of DLBS4847 on differential gene expressions in prostate cancer 3 cells. Among others, DLBS4847 downregulated genes related to prostate growth and hypertrophy. Our results suggested that DLBS4847 could potentially become an alternative treatment for prostate disorders, such as benign prostatic hyperplasia. In this regard, DLBS4847 exerts its growth inhibition partially through downregulation of the 5AR pathway.

Kouloulias, V., S. Triantopoulou, et al. "Combined chemoradiotherapy with local microwave hyperthermia for treatment of T3N0 laryngeal carcinoma: a retrospective study with long-term follow-up." Acta Otorhinolaryngol Ital. 2014 Jun;34(3):167-73.

The purpose of our study was to test the efficacy and toxicity of hyperthermia in conjunction with chemoradiotherapy for T3N0 laryngeal cancer. From 1997-2006, 25 patients diagnosed with T3N0 laryngeal carcinoma who denied laryngectomy were selected for this retrospective study. Patients received a total dose of 70 Gy (2 Gy per fraction, 5 days per week) in combination with 6 weekly sessions of hyperthermia, in addition to weekly cisplatin chemotherapy. The hyperthermia device was operated as a 433 MHz microwave heating with water loaded and water-cooled waveguides. The temperature was monitored subcutaneously in the skin under the aperture of the waveguide. The median follow-up was 60 months, while 23 of 25 patients (92%) presented complete response to treatment. The two patients that did not respond to thermoradiotherapy underwent total laryngectomy, and during follow-up were alive and free of disease. According to EORTC/RTOG criteria, toxicity was mild: three patients (12%) presented grade III, eight (32%) presented grade II and 14 (56%) presented grade I acute skin toxicity. Grade III laryngeal late toxicity (vocal cord malfunction due to severe oedema) was noted in two patients (8%) at 6-8 months post-thermo-chemoradiotherapy. Tmin was correlated (Spearman rho, $p < 0.05$) with response to treatment as well as with acute skin toxicity and laryngeal function. When a patient with T3N0 laryngeal carcinoma denies laryngectomy, an alternative treatment is combined thermo-chemoradiotherapy which seems to be effective and generally tolerable with radiation-induced skin toxicity and/or late side effects. A larger patient cohort is needed to confirm these results.

Lewis, V. O. "IL-11Ralpha: a novel target for the treatment of osteosarcoma." Adv Exp Med Biol. 2014;804:285-9. doi: 10.1007/978-3-319-04843-7_15.

Recent advances have shown that cell surface receptors are expressed differentially in normal and pathological conditions. Novel organ specific and disease specific proteins expressed on tumor vasculature have been identified by in vivo phage display technology and the diversity of the tumor-associated vasculature has provided the basis for the development of targeted therapeutics. Investigators recently screened a phage display library in a human cancer patient. An IL-11 mimic phage displaying the cyclic peptide CGRRAGGSC (single letter amino acid code) specifically bound to immobilized IL-11Ralpha. It has been demonstrated that the expression of the IL-11Ralpha is increased in several other types of tumors including osteosarcoma. The ability to selectively target the IL-11Ralpha may provide an alternative treatment of for a disease where new treatment options are truly needed.

Llorente, J. L., F. Lopez, et al. "Sinonasal carcinoma: clinical, pathological, genetic and therapeutic advances." Nat Rev Clin Oncol. 2014 Aug;11(8):460-72. doi: 10.1038/nrclinonc.2014.97. Epub 2014 Jun 17.

The sinonasal cavities represent an anatomical region affected by a variety of tumours with clinical, aetiological, pathological, and genetic features distinct from tumours at the main head and neck cancer localizations. Together, squamous-cell carcinoma and adenocarcinoma account for 80% of all sinonasal tumours, and are aetiologically associated with professional exposure to wood and leather dust particles and other industrial compounds, and therefore, are officially recognized as an occupational disease. Owing to their distinctive characteristics, sinonasal tumours should be considered as separate entities, not to be included in the miscellany of head and neck cancers. Sinonasal tumours are rare, with an annual incidence of approximately 1 case per 100,000 inhabitants worldwide, a fact that has hampered molecular-genetic studies of the tumorigenic pathways and the testing of alternative treatment strategies. Nevertheless, the clinical management of sinonasal cancer has improved owing to advances in imaging techniques, endoscopic surgical approaches, and radiotherapy. Genetic profiling and the development of in vitro cell lines and animal models currently form the basis for future targeted anticancer therapies. We review these advances in our understanding and treatment of sinonasal tumours.

Lopes-Ramos, C., A. Habr-Gama, et al. "Overexpression of miR-21-5p as a predictive marker for complete tumor regression to neoadjuvant chemoradiotherapy in rectal cancer patients." BMC Med Genomics. 2014 Dec 11;7(1):68.

BackgroundNeoadjuvant chemoradiotherapy (nCRT) followed by radical surgery is the preferred treatment strategy for locally advanced rectal cancer. However, complete tumor regression is observed in a significant proportion of patients after nCRT, making them ideal candidates for alternative treatment strategies to this considerably morbid procedure. Identification of such patients based on clinical findings (complete clinical response - cCR) is difficult mainly because it relies on subjective clinical and imaging studies. Our goal was to identify biomarkers capable of predicting complete response to nCRT.MethodsWe analyzed miRNA expression profile using deep sequencing in rectal tumor biopsies prior to nCRT. Differential expression was investigated by EdgeR for a training (n inverted question mark= inverted question mark27) and a validation (n inverted question mark= inverted question mark16) set of patients to identify miRNAs associated with treatment response (complete vs. incomplete). In vitro experiments with two cancer cell lines were also performed in order to evaluate the possible role of miRNAs on response to nCRT.ResultsWe found 4 miRNAs differentially expressed between complete and incomplete responders to nCRT. In addition, validation was performed using an independent group of patients and miR-21-5p was confirmed as being overexpressed in complete responders. Overall sensitivity and specificity of miR-21-5p expression in predicting complete response to nCRT was 78% and 86% respectively. Interestingly, in a subset of patients with cCR followed by early local recurrence, the expression level of miR-21-5p was considerably low, similarly to incomplete responders. We also found SATB1, a miR-21-5p target gene and known multidrug resistance gene, whose expression was inversely correlated with miR-21-5p expression. Finally, we performed functional experiments and showed that miR-21-5p and SATB1 may be directly involved with poor response to nCRT in rectal cancer patients.ConclusionsThis study suggests miR-21-5p as a promising predictive biomarker, which should aid in the selection of patients with cCR to nCRT that potentially could be spared from radical surgery.

Micali, G., F. Lacarrubba, et al. "Medical approaches to non-melanoma skin cancer." Expert Rev Anticancer Ther. 2013 Dec;13(12):1409-21. doi: 10.1586/14737140.2013.856759.

Medical therapy represents an alternative treatment approach that can be considered for some forms of non-melanoma skin cancer (NMSC). In selected cases, topical treatments are preferable to invasive procedures, especially in the case of multifocal lesions, unclear lesion edges, risk of

keloids, surgical risk factors and localization in some areas such as the face and decolletage, as the cosmetic outcomes are generally excellent. In the case of advanced and metastatic NMSC, molecularly targeted therapy represents a reasonably promising alternative to classical cytotoxic chemotherapy. Based on the existing literature and the authors' experience, this paper analyzes and discusses the mechanisms of action, formulations, official and off-label indications, efficacy, side effects and contraindications of medical treatments that are utilized in the treatment of NMSC, including 5-fluorouracil, imiquimod, diclofenac, ingenol mebutate, resiquimod, piroxicam, dobesilate, betulinic acid, vismodegib, cetuximab, gefitinib and cytotoxic chemotherapy.

Micali, G., F. Lacarrubba, et al. "Topical pharmacotherapy for skin cancer: part I. Pharmacology." J Am Acad Dermatol. 2014 Jun;70(6):965.e1-12; quiz 977-8. doi: 10.1016/j.jaad.2013.12.045.

Topical pharmacotherapy represents an effective alternative treatment for superficial skin cancer, primarily actinic keratoses and basal cell carcinomas. We provide an in-depth analysis of the pharmacologic aspects of available topical drugs for the treatment of primary skin tumors. In particular, we evaluate the mechanisms of action, formulations and indications, side effects, and contraindications of 5-fluorouracil, imiquimod, diclofenac, ingenol mebutate, and retinoids. Moreover, the characteristics of some investigational molecules (ie, resiquimod, piroxicam, dobesilate, and betulinic acid) are presented.

Miszczyk, L., A. Tukiendorf, et al. "Linac based radical radioablation of liver tumors." Technol Cancer Res Treat. 2013 Jun;12(3):225-32. doi: 10.7785/tcrt.2012.500311. Epub 2012 Dec 26.

Due to the low percentage of resectable liver tumors, new alternative treatment modalities are used. Among them, radioablation, that is, by using a limited number of high dose radiation. The aim of this study was to evaluate the effectiveness of liver tumor radioablation at 36 Gy delivered in three fractions. The analyzed material comprised of 65 liver tumors. In 61 cases, we irradiated metastases (20 rectal cancers) and in 4 primary liver tumors. Radioablation, was done using 6 and 20 MV photons with a fraction dose of 12 Gy once a week up to a total dose of 36 Gy. During the follow-up we measured tumor diameters, and for our statistics we used a classical linear regression and the Bayesian approach. Mild and moderate late toxicity was observed. We found a significant absolute and relative decrease in tumor size during the first 6 months from the whole analyzed group. In subgroups with adenocarcinomas, metastases of gastrointestinal tract (GI) cancers, metastases of cancers other than GI cancers, and in the subgroup in which 2D-2D kV system (IGRT) and respiratory gating was used. The percentage of tumors with local control (lack of "in field" progression) after 6 months was 89%. The obtained results permit us to conclude that gated SBRT of liver tumors is an effective and safe treatment modality resulting in a significant regression of liver tumors and that the highest degree of tumor size reduction can be expected for metastases of non-gastro intestinal tract cancers.

Munoz-Alvarez, K. A., J. Altomonte, et al. "PET Imaging of Oncolytic VSV Expressing the Mutant HSV-1 Thymidine Kinase Transgene in a Preclinical HCC Rat Model." Mol Ther. 2015 Jan 22. doi: 10.1038/mt.2015.12.

Hepatocellular carcinoma (HCC) is the most predominant form of liver cancer and the third leading cause of cancer-related death worldwide. Due to the relative ineffectiveness of conventional HCC therapies, oncolytic viruses have emerged as novel alternative treatment agents. Our previous studies have demonstrated significant prolongation of survival in advanced HCC in rats after oncolytic vesicular stomatitis virus (VSV) treatment. In this study, we aimed to establish a reporter system to reliably and sensitively image VSV in a clinically relevant model of HCC for clinical translation. To this end, an orthotopic, unifocal HCC model in immune-competent Buffalo rats was employed to test a recombinant VSV vector encoding for an enhanced version of the herpes simplex virus 1 (HSV-1) thymidine kinase (sr39tk) reporter, which would allow the indirect detection of VSV via positron emission tomography (PET). The resulting data revealed specific tracer uptake in VSV-HSV1-sr39tk-treated tumors. Further characterization of the VSV-HSV1-sr39tk vector demonstrated its optimal detection time-point after application and its detection limit via PET. In conclusion, oncolytic VSV expressing the HSV1-sr39tk reporter gene allows for highly sensitive in vivo imaging via PET. Therefore, this imaging system may be directly translatable and beneficial in further clinical applications.Molecular Therapy (2015); doi:10.1038/mt.2015.12.

Myint, A. S. "Novel radiation techniques for rectal cancer." J Gastrointest Oncol. 2014 Jun;5(3):212-7. doi: 10.3978/j.issn.2078-6891.2014.031.

The concepts for management of rectal cancer have changed drastically over the past few years. Through national bowel cancer screening programmes in the Western countries and the increasing use of endoscopic procedures as diagnostic tool, there is increase in detection of rectal cancer in early stages. There is increase in ageing population

worldwide but more so in Western countries. In addition, there is realisation of harm from extirpative surgical procedures which are directed towards managing advanced rectal cancer in the past. Increase in cost of health care burden has also led the investigators to seek alternative treatment options which are effective, safe and cost effective. There are several modern radiation techniques which fits this bill and we need to be aware of newer novel radiation techniques to fulfil this gap.

Ohzeki, T., S. Fukasawa, et al. "Efficacy of traditional and alternative sunitinib treatment schedules in Japanese patients with metastatic renal cell carcinoma." Int J Urol. 2014 Oct;21(10):1065-8. doi: 10.1111/iju.12504. Epub 2014 Jun 15.

We report the adverse events and efficacy of traditional (4 weeks on 2 weeks off) and alternative sunitinib treatment schedules for Japanese patients with metastatic renal cell carcinoma. We retrospectively investigated 54 patients who received sunitinib for metastatic renal cell carcinoma between May 2006 and June 2012: 32 received a traditional treatment schedule and 22 received an alternative schedule. According to the Memorial Sloan-Kettering Cancer Center risk classification, five patients had favorable prognoses, 42 had intermediate prognoses and seven had poor prognoses. The mean observation periods were 16.3 and 20 months for the traditional and alternative schedule groups, respectively. Adverse events were significantly less common in the alternative schedule group, including most high-grade events. In the traditional and alternative schedule groups, median times to failure were 4.1 and 11.6 months (P = 0.040), median progression-free survival times were 4.1 and 11.3 months (P = 0.031), and median overall survival times were 12.0 and 32.1 months (P = 0.018), respectively. Each of these measures was better in the group of patients who received an alternative treatment schedule, suggesting that individualized changes to the sunitinib administration schedule can be effective.

Orza, A., D. Casciano, et al. "Nanomaterials for targeted drug delivery to cancer stem cells." Drug Metab Rev. 2014 May;46(2):191-206. doi: 10.3109/03602532.2014.900566. Epub 2014 Apr 4.

Recent developments in cancer biology have identified the existence of a sub-poplulation of cells - cancer stem cells (CSC) that are resistant to most traditional therapies (e.g. chemotherapy and radiotherapy) and have the ability to repair their damaged DNA. These findings have necessitated a break with traditional oncology management and encouraged new perspectives concerning cancer treatment. Understanding the functional biology of CSCs - especially the signaling pathways that are involved in their self-renewal mechanisms - is crucial for discovering new forms of treatment. In this review, we highlight current and future prospects for potential cancer therapies based on the use of nano-sized materials. Nanomaterials could revolutionize cancer management because of their distinctive features - unique surface chemistry, strong electronic, optic, and magnetic properties - that are found neither in bulk materials nor in single molecules. Based on these distinct properties, we believe that nanomaterials could be excellent candidates for use in CSC research in order to optimize cancer therapeutics. Moreover, we propose these nanomaterials for the inhibition of the self-renewal pathways of CSCs by focusing on the Hedgehog, Notch, and Wnt/beta-catenin self-renewal mechanisms. By introducing these methods for the detection, targeting, and destruction of CSCs, an efficient alternative treatment for the incurable disease of cancer could be provided.

Pezzolo, E., Y. Modena, et al. "Germ line polymorphisms as predictive markers for pre-surgical radiochemotherapy in locally advanced rectal cancer: a 5-year literature update and critical review." Eur J Clin Pharmacol. 2015 Mar 6.

PURPOSE: Locally advanced rectal cancer is currently treated with pre-surgical radiotherapy and chemotherapy. Approximately one-half of patients obtain a relevant shrinkage/disappearance of tumour, with major clinical advantages. The remaining patients, in contrast, show no benefit and possibly need alternative treatment. To provide the best therapeutic option for each individual patient, predictive markers have been widely researched. This review was undertaken to evaluate recent progress made in this field. METHODS: A systematic literature search was performed using PubMed and Scopus database, focused on germ line gene polymorphisms as biomarkers and response and toxicity as outcomes. Because an exhaustive previous review was available describing findings up to 2008, we restricted our analysis to the last 5 years. RESULTS: Ten original research articles were found, reporting promising results for some candidate genes in drug metabolism (TYMS, MTHFR), DNA repair (XRCC1, OGG1, CCND1) and inflammation (SOD2, TGFB1)/immunity (IL13) pathways, but with no firm conclusion. All the studies had small sample size and were defined as exploratory. This review highlights pivotal molecular, clinical, genetic and statistical issues in the investigation of genetic polymorphisms as outcome predictors for rectal cancer and offers suggestions for future development. CONCLUSIONS: What emerges is a clear need for new proposals, especially in view of the increasing evidence for tumour-host and gene-gene

interactions during anticancer treatment, together with stronger adherence to proper methodological requirements.

Philippe, Y., F. Espitalier, et al. "Partial laryngectomy as salvage surgery after radiotherapy: oncological and functional outcomes and impact on quality of life. A retrospective study of 20 cases." Eur Ann Otorhinolaryngol Head Neck Dis. 2014 Feb;131(1):15-9. doi: 10.1016/j.anorl.2012.11.008. Epub 2013 Oct 16.

The gold standard for the management of laryngeal squamous cell carcinoma in a previously irradiated patient is "salvage" total laryngectomy, but surgical management by partial laryngectomy can sometimes be proposed in selected patients. OBJECTIVES: This study was designed to review the functional and oncological outcomes of patients treated by open partial laryngectomy for recurrent squamous cell carcinoma after failure of radiotherapy or involving previously irradiated tissues and to define prognostic criteria for the selection of patients eligible for this treatment strategy. MATERIALS AND METHODS: In this retrospective study, 20 patients underwent partial laryngectomy between 2000 and 2011 for recurrence or second primary stage I or II laryngeal squamous cell carcinoma in an irradiated territory (11 vertical partial laryngectomies; 9 horizontal partial laryngectomies). RESULTS: The 3-year overall survival rate in patients with negative resection margins was 66%, with higher survival rates for tumours confined to the glottis, and the 2-year local control rate was 67%. Positive resection margins requiring total laryngectomy were observed in 20% of cases. The 3-year overall survival rate was 56% in these patients. Exclusive oral feeding was restored in 75% of patients after an average of 32 days. The tracheotomy tube was removed after an average of 18 days in 90% of patients.

Rettig, I., E. Koeneke, et al. "Selective inhibition of HDAC8 decreases neuroblastoma growth in vitro and in vivo and enhances retinoic acid-mediated differentiation." Cell Death Dis. 2015 Feb 19;6:e1657. doi: 10.1038/cddis.2015.24.

For differentiation-defective malignancies, compounds that modulate transcription, such as retinoic acid and histone deacetylase (HDAC) inhibitors, are of particular interest. HDAC inhibitors are currently under investigation for the treatment of a broad spectrum of cancer diseases. However, one clinical drawback is class-specific toxicity of unselective inhibitors, limiting their full anticancer potential. Selective targeting of individual HDAC isozymes in defined tumor entities may therefore be an attractive alternative treatment approach. We have previously identified HDAC family member 8 (HDAC8) as a novel target in childhood neuroblastoma. Using small-molecule inhibitors, we now demonstrate that selective inhibition of HDAC8 exhibits antineuroblastoma activity without toxicity in two xenograft mouse models of MYCN oncogene-amplified neuroblastoma. In contrast, the unselective HDAC inhibitor vorinostat was more toxic in the same models. HDAC8-selective inhibition induced cell cycle arrest and differentiation in vitro and in vivo. Upon combination with retinoic acid, differentiation was significantly enhanced, as demonstrated by elongated neurofilament-positive neurites and upregulation of NTRK1. Additionally, MYCN oncogene expression was downregulated in vitro and tumor cell growth was markedly reduced in vivo. Mechanistic studies suggest that cAMP-response element-binding protein (CREB) links HDAC8- and retinoic acid-mediated gene transcription. In conclusion, HDAC-selective targeting can be effective in tumors exhibiting HDAC isozyme-dependent tumor growth in vivo and can be combined with differentiation-inducing agents.

Ruixo, J. J., S. Doshi, et al. "Quantitative pharmacology of denosumab in patients with bone metastases from solid tumors." J Clin Pharmacol. 2015 Mar;55 Suppl 3:S85-92. doi: 10.1002/jcph.388.

Denosumab (XGEVA(R)) is a recombinant, fully human IgG2 monoclonal antibody directed against the receptor activator of nuclear factor kappa-B ligand (RANKL) that prevents differentiation of osteoclast precursors into mature osteoclasts and acceleration of bone resorption, resulting in the inhibition of osteoclast activation. Denosumab is indicated for the prevention of skeletal-related events (SREs) in adult patients with bone metastases from solid tumors at the dose of 120 mg administered subcutaneously (SC) every 4 weeks. This review is focused on describing its target-mediated disposition and direct inhibitory effect on bone resorption, as well as the modeling and simulation techniques used to integrate the PKPD information collected during clinical development of denosumab. In addition, this review further discusses the clinical relevance of patient covariate effects on denosumab systemic exposure, target engagement and downstream pharmacodynamics biomarkers, and the rationale for dosing regimen selection for Phase 3 studies. Phase 3 clinical studies demonstrated that denosumab was superior to zoledronic acid in inhibiting bone resorption and, consequently, delaying the time to first SRE by a median of 8.2 months in patients with bone metastases from solid tumors. Thus, denosumab may be considered a better alternative treatment than

zoledronic acid for the prevention of SRE in patients with bone metastases from solid tumors.

Sackmann-Sala, L., A. Chiche, et al. "Prolactin-induced prostate tumorigenesis links sustained Stat5 signaling with the amplification of basal/stem cells and emergence of putative luminal progenitors." Am J Pathol. 2014 Nov;184(11):3105-19. doi: 10.1016/j.ajpath.2014.07.020. Epub 2014 Sep 3.

Current androgen ablation therapies for prostate cancer are initially successful, but the frequent development of castration resistance urges the generation of alternative therapies and represents an important health concern. Prolactin/signal transducer and activator of transcription 5 (STAT5) signaling is emerging as a putative target for alternative treatment for prostate cancer. However, mechanistic data for its role in development or progression of prostate tumors are scarce. In vivo mouse studies found that local prolactin induced the amplification of prostate epithelial basal/stem cells. Because these cells are proposed cells of origin for prostate cancer and disease recurrence, we looked further into this amplification. Our results indicated that sustained Stat5 activation was associated with the occurrence of abnormal basal/stem cell clusters in prostate epithelium of prostate-specific prolactin-transgenic mice. Analysis of epithelial areas containing these clusters found high proliferation, Stat5 activation, and expression of stem cell antigen 1. Furthermore, enhanced prolactin signaling also led to amplification of a luminal cell population that was positive for stem cell antigen 1. These cells may originate from amplified basal/stem cells and might represent important progenitors for tumor development in prostate epithelium. These data provide a deeper understanding of the initial stages of prostate tumorigenesis induced by prolactin to help determine whether this hormone or its downstream messengers could be useful targets for prostate cancer treatment in the future.

Samarghandian, S. and A. Borji "Anticarcinogenic effect of saffron (Crocus sativus L.) and its ingredients." Pharmacognosy Res. 2014 Apr;6(2):99-107. doi: 10.4103/0974-8490.128963.

Conventional and newly emerging treatment procedures such as chemotherapy, catalytic therapy, photodynamic therapy and radiotherapy have not succeeded in reversing the outcome of cancer diseases to any drastic extent, which has led researchers to investigate alternative treatment options. The extensive repertoire of traditional medicinal knowledge systems from various parts of the world are being re-investigated for their healing properties Crocus sativus L., commonly known as saffron, is the raw material for one of the most expensive spice in the world, and it has been used in folk medicine for centuries. Chemical analysis has shown the presence of more than 150 components in saffron stigmas. The more powerful components of saffron are crocin, crocetin and safranal. Studies in animal models and with cultured human malignant cell lines have demonstrated antitumor and cancer preventive activities of saffron and its main ingredients, possible mechanisms for these activities are discussed. More direct evidence of anticancer effectiveness of saffron as chemo-preventive agent may come from trials that use actual reduction of cancer incidence as the primary endpoint. This review discusses recent literature data and our results on the cancer chemopreventive activities of saffron and its main ingredients.

Samat, N., P. J. Tan, et al. "Prioritization of natural extracts by LC-MS-PCA for the identification of new photosensitizers for photodynamic therapy." Anal Chem. 2014 Feb 4;86(3):1324-31. doi: 10.1021/ac403709a. Epub 2014 Jan 13.

Photodynamic therapy (PDT) is an alternative treatment for cancer that involves administration of a photosensitive drug or photosensitizer that localizes at the tumor tissue followed by in situ excitation at an appropriate wavelength of light. Tumour tissues are then killed by cytotoxic reactive oxygen species generated by the photosensitizer. Targeted excitation and photokilling of affected tissues is achieved through focal light irradiation, thereby minimizing systemic side effects to the normal healthy tissues. Currently, there are only a small number of photosensitizers that are in the clinic and many of these share the same structural core based on cyclic tetrapyrroles. This paper describes how metabolic tools are utilized to prioritize natural extracts to search for structurally new photosensitizers from Malaysian biodiversity. As proof of concept, we analyzed 278 photocytotoxic extracts using a hyphenated technique of liquid chromatography-mass spectrometry coupled with principal component analysis (LC-MS-PCA) and prioritized 27 extracts that potentially contained new photosensitizers for chemical dereplication using an in-house UPLC-PDA-MS-Photocytotoxic assay platform. This led to the identification of 2 new photosensitizers with cyclic tetrapyrrolic structures, thereby demonstrating the feasibility of the metabolic approach.

Sczesni, K. C., R. Wiebringhaus, et al. "Mechanical thrombectomy - an alternative treatment option in a patient with acute ischemic stroke and multiple contraindications for systemic thrombolysis: a case report." J Med Case Rep. 2013 Nov 7;7:256. doi: 10.1186/1752-1947-7-256.

INTRODUCTION: Acute ischemic stroke is a common cause of disability and death in developed countries. Standard therapy for patients who present within 4.5 hours from the onset of symptoms is intravenous thrombolysis if contraindications such as oral anticoagulation, cancer or recent surgery are ruled out. Apart from that, mechanical recanalization is a new treatment option for patients with occlusion of major cerebral arteries as a cause of ischemic stroke. CASE PRESENTATION: In this case report we describe a 55-year-old Caucasian man with a right hemispheric ischemic syndrome who presented in time but who had multiple contraindications against systemic thrombolysis. He was then treated with mechanical recanalization and recovered. On discharge from the hospital he had only a slight left-sided facial paresis and discrete impairment of motion smoothness in his left hand. CONCLUSION: We conclude that multimodal imaging should be performed in all patients with an acute onset of neurological symptoms suspicious of ischemic stroke, even if they have contraindications against an intravenous thrombolytic treatment.

Shaitelman, S. F., A. J. Khan, et al. "Shortened radiation therapy schedules for early-stage breast cancer: a review of hypofractionated whole-breast irradiation and accelerated partial breast irradiation." Breast J. 2014 Mar-Apr;20(2):131-46. doi: 10.1111/tbj.12232. Epub 2014 Jan 31.

Breast-conserving therapy consisting of segmental mastectomy followed by whole-breast irradiation (WBI) has become widely accepted as an alternative to mastectomy as a treatment for women with early-stage breast cancer. WBI is typically delivered over the course of 5-6 weeks to the whole breast. Hypofractionated whole-breast irradiation and accelerated partial breast irradiation have developed as alternative radiation techniques for select patients with favorable early-stage breast cancer. These radiation regimens allow for greater patient convenience and the potential for decreased health care costs. We review here the scientific rationale behind delivering a shorter course of radiation therapy using these distinct treatment regimens in this setting as well as an overview of the published data and pending trials comparing these alternative treatment regimens to WBI.

Shioya, M., T. Nishimura, et al. "[Two cases of successful sorafenib retreatment with the addition of steroid therapy following sorafenib-induced erythema multiforme in two patients with hepatocellular carcinoma]." Nihon Shokakibyo Gakkai Zasshi. 2014 Jul;111(7):1424-32.

Erythema multiforme (EM) is a known side effect of sorafenib therapy in cancer patients; at onset, the causative medication should be permanently discontinued. Here we report two cases of hepatocellular carcinoma (HCC) that developed sorafenib-induced EM. In both cases, retreatment with sorafenib combined with steroid therapy achieved effective tumor control without EM recurrence. The first patient was a 72-year-old woman who showed a dramatic response to sorafenib retreatment, with complete remission after 8 months of therapy. There was no rash recurrence after the steroid dose was gradually tapered and stopped. The second patient was a 69-year-old man who responded to sorafenib and exhibited stable disease, with no recurrence of the rash after the steroid dose was tapered. However, mild hand-foot syndrome persisted throughout sorafenib therapy. Although sorafenib should be discontinued if EM occurs, if there is no suitable alternative treatment, retreatment may be considered with steroid cover in patients with unresectable HCC.

Sunar, U. "Monitoring photodynamic therapy of head and neck malignancies with optical spectroscopies." World J Clin Cases. 2013 Jun 16;1(3):96-105. doi: 10.12998/wjcc.v1.i3.96.

In recent years there has been significant developments in photosensitizers (PSs), light sources and light delivery systems that have allowed decreasing the treatment time and skin phototoxicity resulting in more frequent use of photodynamic therapy (PDT) in the clinical settings. Compared to standard treatment approaches such as chemo-radiation and surgery, PDT has much reduced morbidity for head and neck malignancies and is becoming an alternative treatment option. It can be used as an adjunct therapy to other treatment modalities without any additive cumulative side effects. Surface illumination can be an option for pre-malignant and early-stage malignancies while interstitial treatment is for debulking of thick tumors in the head and neck region. PDT can achieve equivalent or greater efficacy in treating head and neck malignancies, suggesting that it may be considered as a first line therapy in the future. Despite progressive development, clinical PDT needs improvement in several topics for wider acceptance including standardization of protocols that involve the same administrated light and PS doses and establishing quantitative tools for PDT dosimetry planning and response monitoring. Quantitative measures such as optical parameters, PS concentration, tissue oxygenation and blood flow are essential for accurate PDT dosimetry as well as PDT response monitoring and assessing therapy outcome. Unlike conventional imaging modalities like magnetic resonance imaging,

novel optical imaging techniques can quantify PDT-related parameters without any contrast agent administration and enable real-time assessment during PDT for providing fast feedback to clinicians. Ongoing developments in optical imaging offer the promise of optimization of PDT protocols with improved outcomes.

Tachihara, M., K. Kobayashi, et al. "Successful crizotinib rechallenge after crizotinib-induced interstitial lung disease." Jpn J Clin Oncol. 2014 Aug;44(8):762-4. doi: 10.1093/jjco/hyu074. Epub 2014 May 28.

We report the case of a 70-year-old Japanese male diagnosed with advanced lung adenocarcinoma harboring the echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase fusion gene. As soon as crizotinib was administered, tumor shrank immediately. On Day 25, he developed interstitial lung disease. Bronchoalveolar lavage fluid analysis demonstrated elevated lymphocytes fractionation. A drug lymphocyte stimulating test for crizotinib with the bronchoalveolar lavage lymphocytes was negative. Crizotinib administration was discontinued, but a life-threatening flare of tumor growth occurred. Since there was no alternative treatment for the lung cancer, we restarted crizotinib in combination with prednisolone. The patient experienced neither disease progression nor recurrence of interstitial lung disease at 6 months. In cases in which no alternate treatment is known, crizotinib retreatment combined with steroid therapy after crizotinib-induced interstitial lung disease could be considered after a careful consideration of the potential risks and benefits.

Ullah, M. F., S. H. Bhat, et al. "Pharmacological Intervention through Dietary Nutraceuticals in Gastrointestinal Neoplasia." Crit Rev Food Sci Nutr. 2014 Nov 3:0.

Abstract Neoplastic conditions associated with gastrointestinal (GI) tract are common worldwide with colorectal cancer alone accounting for the third leading rate of cancer incidence. Other GI malignancies such as esophageal carcinoma have shown an increasing trend in the last few years. The poor survival statistics of these fatal cancer diseases highlight the need for multiple alternative treatment options along with effective prophylactic strategies. Worldwide geographical variation in cancer incidence indicates a correlation between dietary habits and cancer risk. Epidemiological studies have suggested that populations with high intake of certain dietary agents in their regular meals have lower cancer rates. Thus an impressive embodiment of evidence supports the concept that dietary factors are key modulators of cancer including those of GI origin. Preclinical studies on animal models of carcinogenesis have reflected the pharmacological significance of certain dietary agents called as nutraceuticals in the chemoprevention of GI neoplasia. These include stilbenes (from red grapes and red wine), isoflavones (from soy), carotenoids (from tomatoes), curcuminoids (from spice turmeric), catechins (from green tea) and various other small plant metabolites (from fruits, vegetables and cereals). Pleiotropic action mechanisms have been reported for these diet-derived chemopreventive agents to retard, block or reverse carcinogenesis.

Vaeteewoottacharn, K., W. Seubwai, et al. "Potential targeted therapy for liver fluke associated cholangiocarcinoma." J Hepatobiliary Pancreat Sci. 2014 Jun;21(6):362-70. doi: 10.1002/jhbp.65. Epub 2014 Jan 10.

Biliary tree cancer or cholangiocarcinoma (CCA) is an unusual subtype of liver cancer with exceptionally poor prognosis. Lack of specific symptoms and availability of early diagnostic markers account for late diagnosis of CCA. Surgical treatment is a gold standard choice but few patients are candidates and local recurrence after surgery is high. Benefit of systemic chemotherapy is limited; hence, better treatment options are required. The differences in etiology, anatomical positions and pathology make it difficult to generalize all CCA subtypes for a single treatment regimen. Herein, we review the uniqueness of molecular profiling identified by multiple approaches, for example, serial analysis of gene expression, exome sequencing, transcriptomics/proteomics profiles, protein kinase profile, etc., that provide the opportunity for treatment of liver fluke-associated CCA. Anti-inflammatory, immunomodulator/immunosuppressor, epidermal growth factor receptor or platelet-derived growth factor receptor inhibitors, multi-targeted tyrosine kinase inhibitor, IL6 antagonist, nuclear factor-kappaB inhibitor, histone modulator, proteasome inhibitor as well as specific inhibitors suggested from various study approaches, such as MetAP2 inhibitor, 1,25(OH)2 D3 and cyclosporine A are suggested in this review for the treatments of this specific CCA subtype. This might provide an alternative treatment option for CCA patients; however, clinical trials in this specific CCA group are required.

Varol, U., I. Yildiz, et al. "Anticancer therapy for breast cancer patients with skin metastases refractory to conventional treatments." Asian Pac J Cancer Prev. 2014;15(4):1885-7.

Skin metastases of breast cancer are usually late events in the course of tumor progression and signify a poor prognosis. They may remain as a

therapeutic challenge especially after failure of standard treatments. Topical interventions, together with or without radiotherapy, may only palliate the symptoms temporarily. However, there may be alternative treatment modalities for unresectable breast cancer skin metastases resistant to chemotherapy and radiotherapy. There are various genetic alterations in tumors and therapeutic potential of expression patterns for factors like epidermal growth factor receptor may have important clinical implications in case of disease refractory to the conventional treatments. Here, we clarified the therapeutic options and genetic alterations in skin metastatic breast cancer patients refractory to standard chemotherapeutics.

von Schwarzenberg, K., T. Lajtos, et al. "V-ATPase inhibition overcomes trastuzumab resistance in breast cancer." Mol Oncol. 2014 Feb;8(1):9-19. doi: 10.1016/j.molonc.2013.08.011. Epub 2013 Sep 5.

The HER2 oncogene targeting drug trastuzumab shows remarkable efficacy in patients overexpressing HER2. However acquired or primary resistance develops in most of the treated patients why alternative treatment strategies are strongly needed. As endosomal sorting and recycling are crucial steps for HER2 activity and the vacuolar H(+)-ATPase (V-ATPase) is an important regulator of endocytotic trafficking, we proposed that targeting V-ATPase opens a new therapeutic strategy against trastuzumab-resistant tumor cells in vitro and in vivo. V-ATPase inhibition with archazolid, a novel inhibitor of myxobacterial origin, results in growth inhibition, apoptosis and impaired HER2 pro-survival signaling of the trastuzumab-resistant cell line JIMT-1. This is accompanied by a decreased expression on the plasma membrane and accumulation of HER2 in the cytosol, where it colocalizes with endosomes, lysosomes and autophagosomes. Importantly, microscopic analysis of JIMT-1 xenograft tumor tissue of archazolid treated mice confirms the defect in HER2-recycling which leads to reduced tumor growth. These results suggest that V-ATPase inhibition by archazolid induces apoptosis and inhibits growth of trastuzumab-resistant tumor cells by retaining HER2 in dysfunctional vesicles of the recycling pathway and consequently abrogates HER2-signaling in vitro as well as in vivo. V-ATPase inhibition is thus suggested as a promising strategy for treatment of trastuzumab-resistant tumors.

Yano, T., K. Hatogai, et al. "Photodynamic therapy for esophageal cancer." Ann Transl Med. 2014 Mar;2(3):29. doi: 10.3978/j.issn.2305-5839.2014.03.01.

Photodynamic therapy (PDT) is a treatment that uses a photosensitizing drug that is administered to the patient, localized to a tumor, and then activated with a laser to induce a photochemical reaction to destroy the cell. PDT using porfimer sodium followed by excimer dye laser irradiation is approved as a curative treatment for superficial esophageal cancer in Japan. While endoscopic submucosal dissection (ESD) is currently more popular for esophageal cancer, there is evidence to support PDT as an alternative treatment and as a salvage treatment for local failure after chemoradiotherapy (CRT). A photosensitizing agent has also been developed that requires a shorter sun shade period after administration, and studies are currently underway to establish an esophageal cancer indication for this next-generation PDT in Japan.

Younan, P., J. Kowalski, et al. "Genetic modification of hematopoietic stem cells as a therapy for HIV/AIDS." Viruses. 2013 Nov 28;5(12):2946-62. doi: 10.3390/v5122946.

The combination of genetic modification and hematopoietic stem cell (HSC) transplantation may provide the necessary means to develop an alternative treatment option to conventional antiretroviral therapy. As HSCs give rise to all hematopoietic cell types susceptible to HIV infection, modification of HSCs is an ideal strategy for the development of infection-resistant immune cell populations. Although promising results have been obtained in multiple animal models, additional evidence is needed to convincingly demonstrate the feasibility of this approach as a treatment of HIV-1 infected patients. Here, we review the potential of HSC transplantation and the recently identified limitations of this approach. Using the Berlin Patient as a model for a functional cure, we contrast the confines of autologous versus allogeneic transplantation. Finally, we suggest that although autologous, gene-modified HSC-transplantation may significantly reduce plasma viremia, reaching the lower detection limits currently obtainable through daily HAART will remain a challenging endeavor that will require innovative combinatorial therapies.

Yulyana, Y., I. A. Ho, et al. "Paracrine Factors of Human Fetal MSCs Inhibit Liver Cancer Growth Through Reduced Activation of IGF-1R/PI3K/Akt Signaling." Mol Ther. 2015 Jan 26. doi: 10.1038/mt.2015.13.

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death in the world. The multikinase inhibitor sorafenib only demonstrated marginal improvement in overall survival for advanced disease prompted the search for alternative treatment options. Human mesenchymal stem cells (MSCs) have the ability to home to tumor cells. However, its functional roles on the tumor microenvironment remain controversial. Herein, we showed that conditioned media derived from human

fetal MSC (CM-hfMSCs) expressed high level of the insulin growth factor binding proteins IGFBPs and can sequester free insulin-like growth factors (IGFs) to inhibit HCC cell proliferation. The inhibitory effect of IGFBPs on IGF signaling was further evident from the reduction of activated IGF-1R and PI3K/Akt, leading eventually to the induction of cell cycle arrest. We also demonstrated that CM-hfMSCs could enhance the therapeutic efficacy of sorafenib and sunitinib. To the best of our knowledge, this is the first report to show that CM-hfMSCs has a tumor-specific, antiproliferative effect that is not observed with normal human hepatocyte cells and patient-derived matched normal tissues. Our results thus suggest that CM-hfMSCs can provide a useful tool to design alternative/adjuvant treatment strategies for HCC, especially in related function to potentiate the effects of chemotherapeutic drugs.Molecular Therapy (2015); doi:10.1038/mt.2015.13.

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