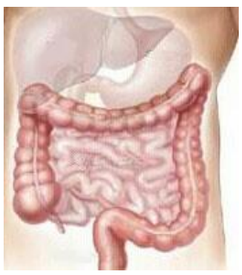
COLORECTAL CANCER RESEARCH UPDATES

Month Ending August 19, 2016



The following colorectal cancer research update extends from June 10th, – August 19th, 2016 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Cobimetinib/Atezolizumab Combo Achieves Response in Advanced Colorectal Cancer (Jun 7/16)

Results from a phase Ib dose escalation and cohort expansion trial demonstrate that the combination of cobimetinib (Cotellic) and atezolizumab (Tecentriq) is safe and clinically active among patients with advanced colorectal cancer (CRC) and led to higher clinical response rates among patients with microsatellite stable (MSS) colorectal cancer than either drug alone. Atezolizumab is an engineered antibody that inhibits PD-L1 binding to its receptors PD-1 and B7.1. This drug has demonstrated monotherapy activity in various human tumour types, but has not demonstrated significant response rates among microsatellite stable (MSS) CRC cases. Cobimetinib is a MEK inhibitor that results in increased expression of MHC I on tumour cells, increased intratumoral T-cell infiltration and increased anti-PDL1 activity. Among a cohort of 23 patients, the observed response rate (ORR) was 17% and the 6-month overall survival (OS) was 72%. These results suggest that cobimetinib may sensitize tumours to atezolizumab by promoting CD8 T-cell accumulation and increasing expression of MHC I on tumour cells, thereby enabling the body's immune system to more effectively infiltrate the cancerous cells. Among patients, the median number of prior systemic therapies was 3, with all patients having received prior oxaliplatin and irinotecan, and 52% having received prior adjuvant therapy. The most common adverse events were diarrhea (69.6%), fatigue (52.2%), dermatitis acneiform (43.5%), rash (34.8%), maculopapular rash (26.1%), nausea (26.1%) and pruritis (26.1%). The total incidence of serious treatment-related adverse events (grade 3) was 34.8%, with no patients experiencing grade 4 or grade 5 adverse events. Four patients experienced partial reductions in tumour size reduction from baseline, among which three were mismatch-repair proficient and one had unknown microsatellite instability status and thus was not evaluable. Among the 23 patients, the median progression-free survival (PFS) and median OS did not change. The 6-month PFS declined slightly to 35% and the 6-month OS declined to 72%. Results from this trial suggest further investigation of cobimetinib and atezolizumab combined therapy among **MSS** colorectal cancer patients as results are insufficient to support any change in standard practice.

http://www.targetedonc.com/conference/asco-immune-2016/cobimetinibatezolizumab-combo-achieves-response-in-advanced-colorectal-cancer

http://meetinglibrary.asco.org/content/171295-176

2. Merck (MRK) reveals data from ongoing studies on Keytruda (Jun 6/16)

Updated findings from a phase II study on Keytuda (pembrolizumab) in the treatment of patients with advanced cancers deficient for DNA mismatch repair (MMR-D) were presented by Merck at the annual meeting of the American Society of Clinical Oncology (ASCO). At a dose of 10mg/kg every two weeks, the study examined the clinical activity of Keytruda among patients with previously treated progressive metastatic disease with or without MMR deficiency. Among MMR-deficient advanced non-colorectal cancers, the overall response rate (ORR) was 53% and **57% among patients with MMR-deficient advanced colorectal** cancer (CRC). It was observed that patients with MMR-proficient advanced CRC did not respond to therapy. Keytruda's safety profile remained consistent with observations from previous studies. Two concomitant phase II studies (KEYNOTE-164 and KEYNOTE-158) are also examining Keytruda among patients with previously treated, locally advanced unresectable or metastatic (Stage IV) MMR-deficient or microsatellite instability-high (MSI-H) CRC, as well as in patients with advanced tumours classified as MSI-H (not including colorectal carcinoma). Merck also revealed data from three different Keytruda studies: MASTERKEY-265 (phase 1b), KEYNOTE-022 and KEYNOTE-029. MASTERKEY examined the safety, efficacy and tolerability of Keytruda in combination with Imlygic (talimogene laherparepvec) among patients with previously untreated and unresectable advanced melanoma, demonstrating that the drug combination resulted in an overall response rate (ORR) of 57.1%. The KEYNOTE-022 study (phase I/II) examined Keytruda in combination with Tafinlar (dabrafenib) and Mekinist (trametinib) among patients with advanced melanoma. KEYNOTE-029 (phase I/II) examined Keytruda in combination with low-dose Yervoy (ipilimumab) among patients with advanced melanoma, demonstrating an ORR of 57%.

http://www.nasdaq.com/article/merck-mrk-reveals-data-from-ongoing-studies-on-keytruda-cm631242

3. Pill may increase survival after colon cancer (Jun 10/16)

A study from the Biotechnology Centre in Oslo and the Norwegian Centre for Molecular Medicine demonstrates that aspirin may be used to reduce the mortality risk among colon cancer patients by 15-25%. Given that aspirin is a cheap drug that is not associated with many adverse effects, such findings present potential benefits to patients diagnosed with colon cancer. The study examined over 23,000 individuals from the Norwegian Cancer Registry and the Norwegian Prescription Database, being the first study to show a clear response regarding the effect of aspirin among colon cancer patients treated post-diagnosis. While aspirin has demonstrated a preventative effect on carcinogenesis (development of cancer) in the intestine, its use in cancer prevention among a healthy population has been contested due to its association with brain haemorrhages and gastric ulcers among a minority of healthy individuals. Due to the immune system's ability to summon anti-tumour immunity only after exposure to cancer cells and because prostaglandin has an inhibitory effect on this anti-tumour immunity, the study's hypothesis suggested that aspirin's effects were greater only after someone was diagnosed with cancer. This suggests that aspirin's effects may be more

important in preventing cancer relapse in the patient – an important factor in the cost-benefit analysis given that the risk of relapse is much higher than the risk of initial onset of cancer.

S. J. Bains, M. Mahic, T. A. Myklebust, M. C. Smastuen, S. Yaqub, L. M. Dorum, B. A. Bjornbeth, B. Moller, K. W. Brudvik, K. Tasken. Aspirin As Secondary Prevention in Patients With Colorectal Cancer: An Unselected Population-Based Study. *Journal of Clinical Oncology*, **2016.**

https://www.sciencedaily.com/releases/2016/06/160610095040.htm

4. Biomarker identifies mCRC patients likely to respond to Cetuximab (Jun 20/16)

Findings from a study identify a variant of FCGR2A as a biomarker that can indicate which metastatic colorectal cancer (mCRC) patients will benefit from cetuximab (also known as erbitux) treatment. Cetuximab is a monoclonal antibody that targets epidermal growth factor receptor (EGFR). It was observed that patients with mCRC with H alleles of FCGR2A treated with cetuximab had significantly increased overall and progression-free survival compared to patients with R alleles (H/R or R/R) treated with the drug. Findings suggest that patients with the R/R genotype can avoid cetuximab, a drug that demonstrates limited effectiveness in their tumour regression. Instead, such patients may be promptly redirected to try other treatments. Such findings are an expansion of previous studies that have identified polymorphisms of BRAF and KRAS genes as predictive tumour biomarkers of cetuximab treatment efficacy. In the future, it is hoped that more biomarkers and therapy refinements will be discovered in order to create a panel of tests to best identify a patient's drug therapy and sequence and further streamline the practice of personalized oncology.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-mcrc-biomarker-cetuximab-response-treatment/article/504318/

5. Rare mutations in bowel (colorectal) cancer may identify patients with a better prognosis (Jul 19/16)

A recent study has demonstrated a correlation between a rare mutation in colorectal cancers (CRC) and improved prognosis, suggesting that such patients may not need chemotherapy post-surgery. The study examined patients for the presence of a mutation in a gene that is necessary for the accurate copying of DNA during cell division – DNA polymerase epsilon (POLE). Patients with this mutation have tumours that contain a far greater number of mutations compared to other CRCs, a feature which may explain the heightened immune response targeted against them. Despite the potential advantage of the POLE mutation, it is uncommon and occurs in only 1-2% of all CRC cases. This, however, still means that 6,000-12,000 patients each year in Europe and the US may be affected. It was observed that CRCs with POLE mutations were significantly less likely to recur, and the association was particularly strong in cases diagnosed at an early stage during which time the benefits of chemotherapy are modest. Due to the fact that most patients included in the study had already received some form of chemotherapy, the study was unable to distinguish whether or not the improved prognosis was due to POLE mutations alone or a combination of the mutations with chemotherapy. The high number of mutations also makes these cancers interesting from an immunotherapy perspective, given that very high number of mutations may make such tumours more susceptible to drug targeting. Further research is necessary to confirm results before they may be implemented into clinical practice.

http://medicalxpress.com/news/2016-07-rare-mutations-bowel-cancer-patients.html

6. Mismatch repair deficiency an ideal marker to initiate precision care in CRC (Jul 19/16)

Researchers from the University of Texas MD Anderson Cancer Center have demonstrated that **DNA mismatch repair deficiency (dMMR) rectal cancer**, which accounts for 15% of colorectal cancers (CRCs), has excellent pathologic response and prognosis under the current treatment options. Research into the genetic basis of CRC has been helping to improve patient outcomes by identifying patients that belong to specific subsets, thereby streamlining their treatment path as early on as possible. University of Texas researchers conducted a retrospective analysis from 62 patients with dMMR rectal cancer who were treated over a 20-year period. The most common tumour mutations were observed in the MSH2 (53%) and MSH6 (23%) genes. The 5-year rectal cancer-specific survival was observed to be 100% for stage I and II patients, 85.1% for stage III patients, and 60% for stage IV patients. Neoadjuvant chemoradiation (fluoropyrimidine-based) resulted in complete pathologic response of 27.6%. A better understanding of the hereditary nature of such mutations can help better predict how patients will do in the long term and to choose the best treatment options. Such genetic understanding of the disease thus enables a patient as well as their at-risk family members known to carry the mutations to be followed and enrolled in early surveillance testing to detect lesions as early as possible.

de Rosa N, Rodriguez-Bigas M A, Chang GJ, et al. DNA mismatch repair deficiency in rectal cancer: benchmarking its impact on prognosis, neoadjuvant response prediction, and clinical cancer genetics [published online July 18, 2016]. J Clin Oncol. doi:10.1200/JCO.2016.66.6826.

http://www.ajmc.com/newsroom/mismatch-repair-deficiency-an-ideal-marker-to-initiate-precision-care-in-crc

7. Liver-directed therapies crucial in metastatic colorectal cancer (Jul 25/16)

Poor diagnosis among patients with metastatic colorectal cancer (mCRC) has long been associated with unresectable liver metastases. Increased research into liver-directed treatment options until surgery becomes possible as well as surgery alternatives among nonresectable patients are directed towards

slowing down progression, which is the most aggressive part of mCRC that leads to the patient progressing and eventually succumbing to the disease. A recent study examined ways to "reset the clock" on the liver, thereby improving chances for survival in mCRC patients with liver metastases. In the study, patients unable to undergo immediate resection of the liver were examined using computed tomography (CT) to monitor resectability following chemotherapy "conversion" regimens. The study treated patients with unresectable liver metastases or with a minimum of 5 metastases with cetuximab in combination with either FOLFOX-6 or FOLFIRI. Patients were monitored using CT scan every 2 months to observe whether the metastases had been "converted" to being resectable. 32% of patients were eligible for surgery at baseline, compared to 60% of patients eligible post-chemotherapy treatment. The **FOLFOX-6** treatment group experienced a **68%** objective response rate (ORR) compared to 57% ORR in the FOLFIRI group.

Adjunctive procedures may also be performed in interventional radiology treatment to help stimulate the regeneration of compromised livers to reduce the change of liver failure post-surgery. Portal vein embolization (PVE) is a common adjunct liver-directed procedure, which may also be used as a surgical resection alternative. The procedure increases portal blood flow to liver remnants in order to increase patient resectability. Similar survival rates have been achieved among patients receiving PVE and resectable patients who do not require the adjunct procedure. Similarly, radiofrequency ablation demonstrated the same clinical outcomes as surgical resection in liver metastases. In recurrent disease, solitary lesions can be altered and eliminated via radiofrequency ablation, a procedure that may be considered a potential equivalent or alterative to surgical resection. The EORTC CLOCC trial investigated the use of radiofrequency ablation in a first-line setting by combining radiofrequency ablation with systemic therapy against standard therapy alone in patients with liver metastases. Progression-free survival (PFS) among patients in the radiofrequency ablation group was 16.82 months, compared to 9.92 months for the control group. 8-year PFS was 22.3% and 2.0% for the radiofrequency group and control group, respectively.

With unresectable liver metastases, liver-directed therapies can still be beneficial. Selective internal radiation therapy (SIRT) can be a useful method to induce cytoreduction among such patients. In the SIRFLOX phase III trial, SIRT was combined with chemotherapy as a first-line therapy. The PFS for the SIRT group for any site did not demonstrate any significant difference, but did show a 7.9 month improvement in median PFS among sites in the liver – an unsurprising observation given that SIRT is a liver-directed therapy. FOLFOX + bevacizumab demonstrated a median PFS of 12.6 months in the liver, whereas the SIRT group had a median **PFS of 20.5 months**. A 31% reduction in the risk of disease progression within the liver was also observed in the investigational SIRT group. Researchers emphasize that SIRT therapy alters the biology of mCRC within the liver by creating a heightened response.

http://www.targetedonc.com/publications/targeted-therapy-news/2016/july-2016/liverdirected-therapies-crucial-in-metastatic-colorectal-cancer

8. Adjuvant therapy improves survival in stage II colon cancer, study confirms (Jul 29/16)

Findings from a large retrospective study of stage II colon cancer patients reveal that adjuvant therapy improves survival irrespective of treatment regimen, patient age or high-risk pathologic risk features. While adjuvant chemotherapy is known to be beneficial in treating advanced colon cancer, its role among stage II cancer patients is limited to cases that are considered high-risk and likely to recur post-surgery. Through a review of health information from over 150,000 patients with stage II colon cancer, it was found that patients who received adjuvant postoperative chemotherapy experienced increased survival across all subgroups of patients including low-risk patients. Such observations are important to future research on the possible use of adjuvant chemotherapy in the treatment for **stage II colon cancer**.

Casadaban L, Rauscher G, Akilu M, et al. Adjuvant chemotherapy is associated with improved survival in patients with stage II colon cancer. Cancer. 2016 Jul 15. doi: 10.1002/cncr.30181. [Epub ahead of print]

http://www.oncologynurseadvisor.com/colorectal-cancer/adjuvant-therapy-improves-survival-in-stage-ii-colon-cancer/article/512670/

RADIATION THERAPIES/INTERVENTIONAL

9. Patients with colorectal cancer liver metastases had significantly greater depth of tumour response to SIR-spheres (R) Y-90 resin microspheres, new SIRFLOX analysis shows (Jul 1/16)

The recently published SIRFLOX study suggests that patients with recently diagnosed liver-dominant metastatic colorectal cancer (mCRC) who underwent first-line therapy combining mFOLFOX6 with SIR-Spheres Y-90 resin microspheres experienced a deeper response to treatment in the liver compared to those who received chemotherapy alone. The Depth of Response (DpR) analysis demonstrated a significantly greater DpR (75.0% vs. 67.8% mean reduction in liver tumour burden) among patients receiving the SIR-Spheres Y-90 resin microspheres with chemotherapy. Patients also demonstrated a statistically significant two-month longer time to DpR or maximal tumour shrinkage (266 vs. 206 days) compared to the control group. It was observed that patients with greater baseline liver tumour burden, representing over half the patients in the SIRFLOX study, experienced 20% greater DpR and over three-month longer time to DpR compared to those treated in the control group. Patients with a smaller liver tumour burden on study entry

were more than 6 times more likely to experience a complete response or regression of all liver tumours post-SIR-spheres Y-90 resin microspheres treatment compared to the chemotherapy only group. Results demonstrated no significant difference in progression-free survival (PFS) at any site in the patients receiving the combined treatment, an unsurprising outcome giving that the SIR-Spheres Y-90 resin microspheres are a liver-directed therapy and have no impact on metastases found outside the liver. A significantly prolonged PFS in the liver was reported, however, from a median of 12.6 months for chemotherapy alone patients to 20.5 months for patients receiving the chemo-radiotherapy. This resulted in a 31% reduction in the risk of progression in the liver. Overall survival data will be gathered from SIRFLOX alongside data from a similarly designed study FOXFIRE being conducted in the UK and the FOXFIRE Global international study. The combined survival data are expected to be released in 2017.

http://finance.yahoo.com/news/patients-colorectal-cancer-liver-metastases-073000196.html

SCREENING

10. Stent in colorectal cancer reduces need for stoma (Jun 10/16)

Researchers have suggested that using a stent to unblock the colon in **left-sided colorectal cancer** patients prior to surgery may significantly reduce the number of patients requiring a stoma. Approximately 20% of colorectal cancer cases present as an emergency, with 80% of such patients experiencing colonic obstruction. Emergency surgery to unblock such obstructions often results in the need for a stoma and colostomy bag. Recent research has demonstrated that using a stent may reduce the need for a stoma among patients by about 25%. It was observed that stenting followed by surgery 1 to 4 weeks later showed no impact on 1-month or 1-year postoperative mortality, critical care utilization or on quality of life. Although stenting followed by surgery requires two procedures to be done, the approach may still be cost-effective compared to emergency surgery if it is able to reduce the patient's stay in the hospital. Furthermore, stoma care and appliances are very expensive, and by avoiding the need for stomas altogether presents a cost-effective advantage.

http://www.medscape.com/viewarticle/864622

11. Genetic testing in colorectal cancer a roadmap for treatment (Jun 2016)

Patients with multiple family members with certain gastrointestinal cancers, cancer syndromes or a history of genetic abnormalities are often referred for genetic testing even if they have no symptoms or signs of illness. As personalized cancer medicine becomes more refined, patients can be genetically analyzed in order to best select their treatment course and better predict clinical outcomes. In colorectal cancer (CRC), the most common hereditary form is Lynch syndrome which accounts for approximately 2-3% of all CRCs. For patients diagnosed with Lynch syndrome, surveillance colonoscopy is commonly advised according to American Gastroenterological Association guidelines. Aspirin as cancer prevention in patients with Lynch syndrome has been more controversial, and remains a conditional recommendation due to insufficient evidence behind the potential risks and benefits of taking aspirin in the long-term. While patients with Lynch syndrome have a 50-80% lifetime risk of developing CRC, less than 10% of families with Lynch syndrome are even aware of their diagnosis. This confirms that many high-risk family members are not referred for genetic counselling frequently enough and do not have a good understanding of screening recommendations based on their hereditary condition.

For cases of Lynch syndrome with CRC that necessitate surgery, the standard operation is colectomy with an ileorectal anastomosis which involves removing a large portion of the colon to prevent the very likely occurrence of a second CRC in the future. Oncologists try to balance the significant risk of a second cancer with any concerns for functional symptoms post-surgery – some studies demonstrate that patients who undergo subtotal colectomy are more likely to have functional complications, whereas in other studies resection extent does not show a differential impact on quality of life. It has been observed that for people 50 and younger at the highest risk of Lynch syndrome, only 23% were undergoing Lynch syndrome screening by microsatellite instability (MSI) tumour analysis, while preoperative tumour testing to help guide germline testing and surgical resection extent was only available in 16.9% of cases. Abnormal MSI testing that prompts germline genetic testing to look for specific mutations can help guide patient-physician decisions with respect to the extent of colonic resection.

Given the increase in CRC incidence among individuals below the age of 50, genetic testing may be used to identify such patients before they are diagnosed with the disease. With improvements in next-generation gene sequencing, the ability to test for number genetic conditions at the same time is heightened. Within this approach, more patients with mutations are being captured that various traditional targeted testing based methods would have missed. With a multi-gene testing focus, however, genetic changes that are not necessarily clinically significant are more likely to be found. Thus the importance of appropriate counselling and proper interpretation of results of genetic testing is essential.

http://www.healio.com/gastroenterology/oncology/news/print/healio-gastroenterology/%7B791f7999-eded-4a23-9fbc-0802e09a88df%7D/genetic-testing-in-colorectal-cancer-a-roadmap-for-treatment?page=3

12. Blood test may predict colon cancer's return (Jul 7/16)

Researchers suggest that a blood test that detects DNA shed from colon cancers may be used to help predict cancer relapse. Despite the imperfection of such tests, also known as “liquid biopsies”, researchers have shown that when tumour DNA is found circulating in the blood, cancer recurrence is more likely. Stage II colon tumours generally have not undergone metastases, which makes it difficult to predict which patients would benefit from postoperative chemotherapy. The researchers’ study followed 230 patients with stage II colon cancer treated for four years. More than 1,000 blood samples were collected pre- and post-surgery, and genetic analysis of tumour samples were analyzed. Cancer-related mutations in blood samples were monitored through DNA testing, and CT scans were used to examine the body every six months for 2 years post-surgery. Among the 230 patients, 20 demonstrated cancer-linked DNA fragments in their blood. Of the 20, six received additional chemotherapy and 50% of these patients experienced a cancer recurrence. Of the 14 patients who did not undergo additional chemotherapy, 79% developed tumour recurrence. Another 14 patients experienced cancer recurrences, despite non-detection of cancer-linked DNA through their blood testing, emphasizing the imperfect nature of the liquid biopsy testing. Thus further research into more sensitive methods to predict patients’ risk for cancer recurrence is necessary, though cost presents itself as an issue: according to the study’s researchers, these blood tests could cost hundreds or thousands of dollars and insurance coverage is still uncertain.

http://www.webmd.com/colorectal-cancer/news/20160707/researchers-get-closer-to-test-predicting-colon-cancers-return?page=2

OTHER

13. Rates of colorectal cancer are increasing in younger patients, despite an overall decline (Jun 8/16)

Despite a decline in the overall rate of colorectal cancer (CRC) in recent years, an increase in the cases of young-onset CRC has continued to puzzle researchers. While a great deal of attention has been directed towards increasing awareness and screening among individuals 50 and older, a study reveals that much more attention needs to be directed towards individuals under the age of 50, a subset not normally considered at risk for the disease. The study demonstrated that the rate of CRC among the under 50 age group is rising, and that individuals were diagnosed with the disease at a younger age with a higher percentage being diagnosed at later stages of cancer (stage 3 or 4). Researchers examined health records from more than 1 million patients with CRC over 10 years. It was found that the number of CRC cases decreased by 2.5% in patients 50 and older and increased by 11.4% among patients below the age of 50. Furthermore, young-onset cases were more prevalent among non-white patients than late-onset cases (22.1% vs. 16.0%). The younger group also experienced a higher incidence of more advanced cancer than the older group. Despite such evidence that CRC is increasing among people below the age of 50, it is still important to note that the majority of CRC cases still affect patients 50 and older. This study suggests that *clinicians should lower the threshold for colonoscopy* and be more conscious of detecting symptoms in younger patients.

Sutton E, Bellini G, Lee D, et al. An update on young-onset colorectal cancer, an NCDB analysis. Presentation at: Digestive Disease Week 2016; May 22-24, 2016; San Diego, CA.

http://www.oncologynurseadvisor.com/colorectal-cancer/rates-of-colorectal-cancer-are-increasing-in-younger-patients-despite-an-overall-decline/article/501868/

14. Letting Go: No reduction in aggressive care for advanced cancer (Jun 9/16)

A recent study demonstrates that despite being well-known to be harmful to patients and their families, aggressive care is still administered to 75% of patients with incurable metastatic cancer. The researchers suggest that physicians have an important responsibility to thoroughly discuss the goals of treatment with their patients (including how these goals may change throughout the disease course) given that toward the very end of life aggressive treatment is likely to cause a great deal of side effects but be unlikely to significantly extend a patient’s life. The American Society of Clinical Oncology (ASCO) issued a strong recommendation against the use of cancer treatments in late metastatic disease, suggesting instead a shift to palliative care. The recent study examined over 28,000 patients with various cancer types from the HealthCare Integrated Research Database. Among the 28,000 patients, approximately 75% received care that could be considered “aggressive”. Furthermore, between 25-30% of patients received chemotherapy in the last month of life, with the same number of patients having received invasive procedures. Some researchers believe that the use of aggressive therapies toward the end of life include physicians’ desire to help patients when a cancer is progressing, and an inability to realize when a patient truly is approaching the end of life. Other researchers believe that many oncologists feel pressure to offer hope to patients, and feel compelled to do something even if there is no evidence that such a procedure will be helpful. Pressure from patients’ family members to try anything to save their loved ones’ lives also encourages more aggressive treatments to be tried. The study stresses the need for more discussion between patient and physician, closely observing treatment effectiveness and how treatment goals may change through time. Understanding how aggressive care and palliative care can complement one another could also help in maximizing patient quality of life as palliative care specialists can aid in monitoring and caring for patients’ treatment side effects and clarify discussions along the cancer journey. Furthermore, more studies on how aggressive cancer care

affects quality of life is much needed, where outcomes data such as progressive-free survival can be linked to more meaningful outcomes for patients, such as the ability to achieve personal life goals.

http://www.medscape.com/viewarticle/864558

15. Less than 3% of IBD patients develop colorectal cancer after colectomy (Jun 16/16)

According to results from a systematic review and meta-analysis, the prevalence and incidence of colorectal cancer (CRC) among patients with inflammatory bowel disease (IBD) is less than 3% after colectomy and less than 1% after ileal pouch-anal anastomosis. Colectomy substantially minimizes the risk of developing colorectal neoplasia. It has been observed, however, that neoplasia of the residual rectum or ileoanal pouch is still a possibility and linked to a poor prognosis. The most significant risk factor for CRC post-colectomy was a history of CRC, while additional risk factors for rectal pouch neoplasia were IBD duration and a diagnosis of ulcerative colitis vs. Crohn's disease. Such findings are promising in the development of more personalized post-surgical surveillance strategies, and emphasize the need for persistent vigilance in monitoring this patient subset for dysplasia and cancer, particularly those with CRC history and long IBD duration.

http://www.healio.com/gastroenterology/inflammatory-bowel-disease/news/online/%7B7745db26-e729-4cb7-909d-5bee292ff97f%7D/less-than-3-of-ibd-patients-develop-colorectal-cancer-after-colectomy

16. Hong Kong researchers identify new high-risk group for colorectal cancer (Jun 21/16)

Findings from a study from 2010 to 2014 reveals that siblings of patients with advanced adenomas (polyps with a higher chance of becoming malignant) were six times more likely to develop such adenomas compared to siblings of unaffected people. In the study, researchers used colonoscopies to evaluate 600 individuals aged 52-64 and compared 200 asymptomatic siblings of patients with advanced adenomas against 400 age and sex-matched siblings of subjects with normal colonoscopies and no family history of the disease. If an advanced adenoma was not removed, it was found to increase a person's risk of developing colorectal cancer (CRC) after 5 years by 2-3%, increasing to 10% after 10 years. Such findings are promising in helping to identify high-risk individuals before they develop the disease. The removal of intestinal adenomas is crucial given that colorectal cancers tend to evolve from such growths over time. Siblings of individuals with advanced adenomas were strongly advised to undergo colonoscopy for early detection and removal in order to minimize their CRC risk. Since the presence of advanced adenomas often does not present any notable symptoms such as pain, the early detection through colonoscopy is important to avoid catching the disease in a stage too late for effective treatment.

http://www.scmp.com/news/hong-kong/health-environment/article/1978568/hong-kong-researchers-identify-new-high-risk-group

NUTRITION/HEALTHY LIFESTYLE

17. Analysis shows whole grains cut cancer, heart disease deaths (Jun 15/16)

A new analysis of past studies demonstrates that people who consume plenty of whole grains are less likely to die from cardiovascular disease or cancer over long periods of follow-up. While the American Heart Association recommends that at least half of the grains we consume be in their whole form (e.g. oats, rye, barley, corn or brown rice), and that individuals should consume three or more servings of such grains per day, most American adults get less than one serving per day. Due to their high fibre content, whole grains minimize unhealthy blood fats and stimulate the body's insulin sensitivity, which helps to keep sugar levels under control. Results from 14 long-term studies of whole-grain consumption and mortality rate including a total of 786,076 people were analyzed, with 24,000 deaths from cardiovascular disease and more than 37,000 from cancer. Individuals who consumed the most whole grains were 16% less likely to die of any cause, 20% less likely to die from cardiovascular disease and 10% less likely to die of cancer compared to those who ate the least whole grains. For each additional 16g serving of whole grains, it was found that cardiovascular disease-related death risk decreased by 9% and cancer death risk by 5%, illustrating a linear association between whole-grain intake and mortality.

http://www.todayonline.com/daily-focus/health/analysis-shows-whole-grains-cut-cancer-heart-disease-deaths

18. Java lovers, rejoice: coffee doesn't post a cancer risk, WHO panel says (Jun 15/16)

The World Health Organization's cancer research agency concludes that regular coffee drinking **does not** pose a cancer risk and may even protect good health. In 1991, the World Health Organization's International Agency for Research on Cancer (IARC) listed coffee as a potential carcinogen, based on limited evidence that cancer was linked to increased risk of developing bladder cancer. Since the 1991 report, many epidemiological studies have shown that coffee does not have a carcinogenic effect. Researchers have reviewed over 500 studies on more than 20 types of cancers, concluding that coffee may actually protect against the risk of cancers of the liver and uterus. Furthermore, *coffee drinking has even been associated with a lowered risk of colorectal cancer.* Surprisingly, researchers have shown that very hot beverages may actually increase the risk of cancer. Epidemiological studies found that cancer of the esophagus is associated with drinking beverages at very hot temperatures but not with warm or cold beverages. The

researchers concluded that the cancer-causing effects were likely to occur with beverages consumed at temperatures of 150 degrees Fahrenheit or higher. So while coffee drinking may be protective of good health, don't drink it too hot!

http://www.scpr.org/news/2016/06/15/61690/java-lovers-rejoice-coffee-doesn-t-pose-a-cancer-r/

19. Avoid these 10 cancer causing food items (Jun 23/16)

Processed meat: a 2015 study conducted by the International Agency for Research on Cancer (IARC) classified processed meat as a category 1 cancer causing substance (most carcinogenic). The study suggests that a daily consumption of just 50g of processed meats like ham, bacon or hot dogs which undergo the process of smoking, salting, curing or fermenting can increase the risk of colorectal cancer by 18%. The chemicals sodium nitrite and sodium nitrate, both of which are found in such meats, are linked to a higher risk of developing cancer. Red meat has also been classified by the IARC as a probable carcinogen.

Microwave popcorn: the **bag** which microwave popcorn is wrapped in contained perfluorooctanoic acid (PFOA) which has been linked to infertility, cancer and other diseases. Furthermore, microwave popcorn's aroma enhancing chemical diacetyl has been linked to incidence of lung disease. Stick to popcorn kernels that you can pop the traditional way.

Refined white flour: this flour has zero nutritional value and has been bleached with chlorine gas. The high glycemic index causes sharp spikes in blood sugar levels which can lead to insulin resistance. This condition has been linked to the growth and spread of cancer cells. Whole grain flours provide far more nutritional value and a protective effect on good health.

Refined sugar: High glucose levels in the blood feed cells in the body, with cancer cells taking in sugar 10-12 times the rate of healthy cells. Furthermore, refined sugar acidifies the blood, thereby creating a more favourable environment to low-pH loving cancer cells. Excess sugar consumption also leads to obesity which has been linked to the incidence of numerous cancers. Less refined sweeteners such as honey, stevia or molasses provide sweetness while being lower on the glycemic index and providing various other nutrients and minerals.

Cured and salt preserved food: A diet rich in salt has been linked to increased risk of stomach cancer through its stimulation of the activity of the bacterium *Helicobactor pylori*, which is known to cause stomach ulcers and inflammation which may later progress into cancer. Cured foods are high in salt and often preserved using nitrites and/or nitrates which have also been linked to an increased risk of developing cancer.

Hydrogenated oils: The consumptions of hydrogenated oils (e.g. trans fats) has been linked to increased breast cancer incidence.

Farmed fish: Research has shown that farmed salmon contains polychlorinated biphenyls, which are carcinogenic. Furthermore, many farmed fish are treated with potentially carcinogenic pesticides and antibiotics.

Soda drinks: Sodas contain a high number of calories for zero nutritional value. Studies have revealed that only two sodas a week can increase the amount of insulin the pancreas produces, thereby doubling the risk of pancreatic cancer. Furthermore, the chemical responsible for various sodas' caramel colour, 4-methylimidazole, has been linked to an increased risk of developing cancer.

Genetically modified food: A French study found that rats fed on genetically modified corn developed mammary tumours and had severe liver and kidney damage. Eating naturally grown, preferably organic produce is emphasized whenever possible.

French fries: the crispiness of French fries and potato chips may be due to a chemical known as acrylamide, which is a known carcinogen. This chemical is also found in cigarette smoke.

https://in.style.yahoo.com/avoid-these-10-cancer-causing-food-items-182741751.html

20. Food's transit time through colon affects health of the digestive system (Jun 28/16)

Findings from a recent study demonstrate that the time it takes for food to travel through the gut, also known as transit time, impacts the amount of harmful waste products that are produced along the way. In particular, the study examined how food's transit time affects gut bacteria's role in activity and health of the digestive system by measuring the products of bacterial activity which end up in the urine. While intestinal bacteria prefer to digest dietary carbohydrates, they will begin to digests other nutrients such as proteins once the carbohydrate levels are depleted. Previous research has established correlations between bacterial protein degradation products produces in the intestinal tract and the development of diseases including colorectal cancer, chronic renal disease, and autism. The study demonstrates that the longer the transit time, the more harmful bacterial degradation products are produced. Conversely, a shorter transit time resulted in a higher amount of substances produced when the colon epithelial wall renews itself, suggesting a healthier intestinal

lining. While a diverse bacterial flora in the intestine is considered healthy, a high bacterial content in the stool is often linked to a longer transit time. Thus a diverse intestinal flora may not necessarily translate to a healthy digestive system if it is accompanied by a longer transit time. A diet rich in fibre and water can help minimize constipation and decrease transit time. Limiting meat intake may also help lower transit time as it is slow to digest. Furthermore, increasing physical activity has been shown to reduce the time it takes food to pass through the digestive tract.

http://www.news-medical.net/news/20160628/Foods-transit-time-through-colon-affects-health-of-digestive-system.aspx

21. How vitamin D reduces the risk of cancer (Jul 2/16)

In the body, vitamin D the "sunshine vitamin" is responsible for facilitating the absorption of calcium, iron, magnesium, phosphate and zinc. When exposed to the sun's rays, in particular ultraviolet B (UVB) rays, the human body is capable of producing the necessary amounts of vitamin D. Vitamin D stimulates the immune system, has anti-inflammatory effects, regulates various cellular pathways and supports neuromuscular functioning. Recent studies have demonstrated that vitamin D has an important role in the prevention and treatment of various forms of cancer. The 2016 PLOS ONE study reported that higher levels of vitamin D in the blood are linked to a reduced risk of cancer. It has been found that the lowest colon cancer diagnosis and death rates are found in states with the highest mean solar radiation. A 2011 study suggests that vitamin D may decrease colon cancer risk by improving differentiation and apoptosis (programmed cell death) and decreasing proliferation, invasiveness, metastatic potential and angiogenesis. The study also suggests that vitamin D is even more strongly associated with a reduction in rectal cancer risk. A 2014 study found that high plasma 25-hydroxyvitamin D is linked to a lower risk of colorectal cancer with high immune reaction, suggesting a role of vitamin D in cancer immune prevention via tumour-host interaction. Furthermore, high plasma vitamin D levels can improve the body's response to chemotherapy and targeted anticancer drugs in patients with advanced colon cancer. The best sources of vitamin D include: short periods of sun exposure without sunscreen (approximately **20-25 minutes of unprotected exposure**); fatty fish such as salmon, trout and mackerel; canned tuna and sardines; fortified milk; fortified orange juice; daily vitamin D supplements; egg yolks; fortified cereals; beef liver; and cod liver oil supplements.

http://www.herald.co.zw/how-vitamin-d-reduces-the-risk-of-cancer/

22. Breaking cancer news: high doses of vitamin C may cure colorectal cancer (Jul 2/16)

A 2015 study demonstrated that high doses of vitamin C may be used to cure colorectal cancer with KRAS or BRAF mutations. Results from the study demonstrated that when colorectal cancer cells were exposed to high doses of vitamin C, the cells increased their uptake of the oxidized form of the vitamin via the GLU1 glucose transporter. Increased uptake of oxidized vitamin C resulted in oxidative stress and increased accumulation of reactive oxygen compounds, leading to inactivation or inhibition of an important enzyme that cancer cells need in order to generate energy, eventually leading to cell death. The high dosage of vitamin C was also tested among Apc/Kras mutant mice, resulting in suppression of tumour growth. This suggests that vitamin C may be effective at killing cancer cells in vivo. KRAS mutations are commonly found in leukemia, colon cancer, pancreatic cancer and lung cancer, while over 30 mutations in the BRAF gene have been identified and commonly observed in thyroid carcinoma, colorectal cancer, melanoma and non-small-cell lung cancer.

http://www.foodconsumer.org/newsite/Nutrition/Vitamins/vitamin_c_may_cure_colorectal_cancer_0702160444.html

23. Oily fish may reduce risk of death from bowel cancer, study suggests (Jul 20/16)

A recent study suggests that consuming small amounts of oily fish on a daily basis can reduce the risk of colon cancer death by up to 70%. The omega-3 fatty acids found in fatty fish such as sardines and mackerel is believed to suppress tumour growth and inhibit blood supply to tumour cells. Importantly, the study revealed that **only small amounts of omega-3s** were necessary for the protective effect: while a normal serving of oily fish contains about 1.8g of omega-3, **only 0.3g a day** was sufficient to decrease the risk of death within 10 years of diagnosis by 41%. ***Colon cancer patients who increased their intake of omega-3s by 0.15g post-diagnosis were accompanied by a 70% lower risk of death***. Through an analysis of health records from 200,000 individuals from two large cohort studies monitoring diet and cancer prevalence, it was observed that regular intake of oily fish was especially beneficial to tall individuals (risk of death reduced by 85%), individuals with a BMI below 25 (90% risk reduction) and individuals who did not take a regular aspirin (88% risk reduction). The study examined individuals whose omega-3 intake was achieved by eating fish rather than taking supplements, so it remains unknown if the reduced risk would hold true for omega-3 supplements.

http://www.telegraph.co.uk/science/2016/07/20/oily-fish-may-reduce-risk-of-death-from-bowel-cancer-study-sugge/

24. Overweight colorectal cancer patients could fare better (Jul 21/16)

While a higher body mass index (BMI) is associated with various health risks, findings from a recent study indicate that overweight patients who are diagnosed with colorectal cancer (CRC) may experience a better prognosis compared to individuals with a healthy weight. Controlling for socioeconomic, demographic, disease severity, prediagnosis BMI, smoking and other factors, it was found that patients in the high-

overweight category with a BMI of 28-30 at diagnosis had a 48% lower overall mortality risk and a 55% lower mortality risk related to CRC in comparison with patients with a low to normal BMI (18.5-23). It was observed, however, that underweight patients (BMI below 18.5) or obese patients (BMI > 35) at diagnosis experienced an elevated mortality risk. Further research is necessary to understand the underlying mechanisms of this cancer paradox. Researchers suggest that given the current body of evidence on cancer outcomes and obesity, the recommendations for an ideal weight range associated with best outcomes post-diagnosis may indeed be different from the ideal weight range to prevent cancer. Furthermore, researchers suggest that ideal weight recommendations may vary according to cancer site just as treatment differs by cancer type.

http://www.pharmacytimes.com/publications/issue/2016/july2016/overweight-colorectal-cancer-patients-could-fare-better

25. Herbal cure: turmeric can help fight colon cancer (Jul 26/16)

A new study from Belgium demonstrates that a compound in turmeric may help prevent and treat colon cancer. The study suggests that the combination of two plant compounds, curcumin (found in turmeric) and silymarin (found in milk thistle), can effectively prevent cancer cells from developing in the colon. While each compound was effective in preventing the spread of colon cancer cells when used separately, the combination of the two resulted in a synergistic effect in suppressing the development and spread of cancerous cells. The study demonstrated that colon cells treated with either plant compound alone showed low levels of apoptosis or programmed cell death, while treating the cells with curcumin followed by silymarin resulted in increased cell death, thereby demonstrating a stronger cancer-fighting effect. Such research is highly valuable given that phytochemical treatments may offer alternative therapy approaches to standard cancer treatment courses, thereby avoiding the high toxicity and side effects that often accompany chemotherapy.

http://www.healthnewsline.net/herbal-cure-turmeric-can-help-fight-colon-cancer/2535694/

26. Sleep disturbances worsen outcomes for colorectal cancer (Aug 8/16)

According to a recent study, patients with metastatic colorectal cancer (mCRC) who experience sleep difficulties and disturbances in their circadian rhythms have worse outcomes than other patients. Circadian rhythms synchronize cell functioning with the sleep-wake cycle, and growing research supports that disturbances to such biological rhythms puts individuals at higher risk for disease. A past study found that mCRC patients who experienced circadian disruptions had reduced median overall survival compared to patients who did not experience such disturbances (11.9 vs. 21.6 months). The current study examined the respective effect circadian rhythm disturbances and patient-reported sleep disturbances. Of the 237 patients, 54.9% had circadian disruptions, and 65.4% reported a sleep complaint. The majority of patients who reported either problem suffered from both. Patients who reported no sleep disturbances and had no circadian disturbances had a median overall survival of **28.3 months**, while patients suffering from both circadian disruptions and sleep disturbances had a median overall survival of **12 months**. Further research is needed to examine personalized behavioural interventions to improve sleep and circadian rhythms in mCRC patients, such as nighttime lighting changes, exercise regimens and improved sleep hygiene guidelines.

http://www.clinicaloncology.com/Colorectal-Cancer/Article/08-16/Sleep-Disturbances-Worsen-Outcomes-For-Colorectal-Cancer-Patients/37482

27. How brushing your teeth could prevent cancer: twice daily scrub reduces bacteria linked to bowel tumours (Aug 10/16)

A recent study suggests that regular teeth brushing can help prevent bowel cancer. It is believed that mouth bacteria that are responsible for gingivitis and bleeding gums can travel to the bowel via the blood where they can trigger carcinogenesis (development of cancer) and worsen existing tumours. Upon examination of tumour cells, *Fusobacterium* has been found to be hundreds of times more prevalent compared to normal cells. The study found that the bacterium has the potential to facilitate the transition of precancerous to cancerous growths in the colon, as well as supporting the growth of existing tumours. It was found that the bacteria contain a protein that enables them to stick to sugar molecules attached to benign growths (polyps) as well as cancerous growths in the colon. After attaching to the growths, the presence of the bacteria appears to promote their proliferation. These bacteria worsen gum disease by acting as an anchor on teeth and gums for other bacteria to attach to, thereby encouraging a film of all kinds of bacteria to grow and damage the gums and teeth. These bacteria have also been found to worsen ulcerative colitis, which is also a condition linked to colon cancer. Such bacteria have also been linked to heart disease and stroke, and more recently, to Alzheimer's disease where they trigger inflammation in the brain that results in the growth of plaques and the accumulation of protein masses which are characteristic of the condition. A 2012 study demonstrated that individuals with the highest levels of plaque on the surface of their teeth and gums experienced an 80% increased risk of premature death. Such studies suggest that proper oral hygiene has benefits which extend much further than aesthetics.

http://www.dailymail.co.uk/health/article-3733276/How-brushing-teeth-prevent-cancer-Twice-daily-scrub-reduces-bacteria-linked-bowel-tumours.html