PANCREATIC CANCER: NEWS & UPDATES

March 2010

First Use of Innovative Irreversible Electroporation "IRE" on Pancreatic Tumor
http://www.medicalnewstoday.com/articles/181307.php
A new procedure for treating pancreatic and liver cancers using electrical fields to poke holes in tumors was used for the first time anywhere to fight pancreatic cancer at Stony Brook University Medical Center by Kevin Watkins, M.D., Chief of the Upper Gastrointestinal and General Oncologic Surgery Group. The procedure, performed in December 2009, is called Innovative Irreversible Electroporation (IRE) and is a minimally invasive surgical technique (also referred to as a "NanoKnife®") that selectively kills the cancer by using electrical fields to generate pores in tumor cells. The first patient had her six-week follow-up PET scan and the initial report showed no activity, making her a radiographic complete response at this time.

Researchers Confirm Role of Common Stomach Bacteria in Pancreatic Cancer
http://www.infectioncontroltoday.com/hotnews/stomach-bacteria-and-pancreatic-cancer.html
Yale University researchers have discovered that colonization by the common stomach bacteria Helicobacter pylori in people with non-O blood types is associated with a nearly three-fold increased risk of pancreatic cancer. Seven years ago, a research team from the Yale Cancer Center Prevention and Control Research Program proposed that colonization by Helicobacter pylori increased the risk of pancreatic cancer by boosting stomach acidity as well as the pancreatic response to neutralize the acidity. Over the intervening years, support for this relationship was generated by a large population-based, case-control study of pancreatic cancer in Connecticut.

Experts Call for Further Research into the Relationship between Insulin Therapy and Cancer
http://www.acor.org/news/display.html?id=9338
The benefits of using insulin to treat diabetes far outweigh the risks, but a review just published online by the International Journal of Clinical Practice suggests that commonly used diabetes therapies may differ when it comes to their influence on cancer risk. The research showed that people with type 2 diabetes may face an increased risk of cancer and that their cancer may be modified by treatment choices, noting metformin may provide a protective effect, while insulin and/or certain insulin analogues may promote tumor growth. Researchers report that diabetes appears to be associated with an intrinsic increase in cancer incidence. For example, a number of meta-analyses show that people with diabetes had an 80+% higher risk of developing pancreatic cancer (36 studies covering more than 9,000 patients). The excess risk of pancreatic cancer was highest in patients who only had diabetes for a short time, suggesting that cancer could cause diabetes; however, the incidence of this cancer in people with a long history of diabetes suggests there may also be an intrinsic cancer risk from diabetes. The authors note that the current evidence is far from clear-cut and further research is needed to examine the risks and mechanisms that appear to link insulin with tumor growth.

Diabetes May Elevate Risk of Cancer Surgery
http://www.medpagetoday.com/Endocrinology/Diabetes/19264
http://www.hemonctoday.com/article.aspx?rid=62615
Pre-existing diabetes may substantially boost postoperative mortality risk in cancer patients, according to Johns Hopkins researchers. Cancer patients were 51% to 85% more likely to die after surgical resection if they had preexisting diabetes. This extra risk appeared across a range of cancer types (including pancreatic cancer) and surgical cancer treatments. Diabetes patients have a well-documented predisposition to infection.

New Research Reveals Mechanism by Which TNFerade™ Suppresses Metastases
http://www.genvec.com/download/press/2010%2003.03%20TNFerade%20Mechanism%20Paper.pdf
GenVec announced the publication of new preclinical research revealing mechanisms by which TNFerade™ suppresses cancer metastases through activation of the immune system. This preclinical

data may help explain the encouraging results seen with TNFerade in the clinical setting. GenVec is currently conducting a phase III trial of TNFerade with 5FU and radiation therapy for the first-line treatment of unresectable locally advanced pancreatic cancer. The second interim analysis of this trial will take place during the second quarter of this year.

New Dimensions in the Analysis of the Immune Response to Cancer
http://www.newswise.com/articles/new-dimensions-in-the-analysis-of-the-immune-response-to-cancer
Cancer researchers have taken a major step forward toward what is planned to be the most comprehensive analysis of the body's antibody response to human cancer, an enterprise that has been termed "cancer seromics." Sera from patients with ovarian cancer and pancreas cancer were used to screen the protein arrays and a large number of antibodies with reactivity to individual proteins were identified and ranked in terms of frequency and strength. As the analysis of the full range of human cancers progresses, a public database of the human antibodies response to human cancer will be constructed and available for investigators around the world to use and compare results. This massive effort to identify and validate the complete library of antigenic targets for cancer immunotherapy is made possible by the availability of arrays containing more than 8,000 different human proteins on a glass chip. The two human cancers that were selected for the initial analysis (ovarian cancer and pancreas cancer) are usually found at a late, incurable stage. Consequently, there is a great need to develop early detection systems and antibody responses to the emerging tumor in these cancers.

Study Finds Cancer Mortality has Declined Since Initiation of 'War on Cancer'
http://www.acor.org/news/display.html?id=9360
A new American Cancer Society study finds progress in reducing cancer death rates is evident whether measured against baseline rates in 1970 or in 1990. The study finds a downturn in cancer death rates since 1990 results mostly from reductions in tobacco use, increased screening allowing early detection of several cancers, and modest to large improvements in treatment for specific cancers.

Disease Cause Is Pinpointed With Genome
http://www.nytimes.com/2010/03/11/health/research/11gene.html?ref=research
Two research teams have independently decoded the entire genome of patients to find the exact genetic cause of their disease. Geneticists said the new research showed it was now possible to sequence the entire genome of a patient at reasonable cost and with sufficient accuracy to be of practical use to medical researchers. Diseases like cancer are thought to be caused by mutations in several genes, and finding the causes was the principal goal of the $3 billion human genome project. Medical geneticists have invested heavily over the last eight years in an alluring shortcut, but the shortcut was based on a premise that is turning out to be incorrect. Scientists thought the mutations that caused common diseases would themselves be common; however, common diseases are surprisingly caused by rare, not common, mutations. In the last few months, researchers have begun to conclude that a new approach is needed, one based on decoding the entire genome of patients.

The Heart: An Unintended Victim of Some Targeted Cancer Therapies
http://www.cancer.gov/ncicancerbulletin/030910/page6
Heart failure is among the most common "cardiotoxicities" associated with certain cancer treatments, in particular the class of chemotherapy drugs known as anthracyclines. As the use of targeted therapies becomes more widespread, there is mounting scrutiny of their cardiac effects, which can include heart failure, fatal rhythm disturbances, blood clots, and hypertension.

Doctors, Patients Should Weigh Risks vs. Rewards of Medical Imaging
http://www.cancercompass.com/cancer-news/article/33036.htm
As physicians find new ways to use diagnostic imaging to discover and deal with disease, concern is growing about Americans' increased exposure to potentially cancer-causing radiation. Annual radiation doses from medical imaging have soared sevenfold since the early 1980s, according to a report last year from the National Council on Radiation Protection and Measurements. Meanwhile, as many as 14,500 people a year may end up dying of radiation-induced cancers caused by CT scans, new research suggests. Scrutiny is focusing primarily on more than 70 million CT scans performed in the US every year, up from 3 million in the early 1980s. CT scans shower patients with far more of it than other diagnostic tests. For example, a routine head CT produces the same dose as 400 dental X-rays, while the dose from a chest CT equals to more than 100 X-rays. With the exception of mammography, patients' exposure to radiation from diagnostic imaging exams isn't regulated.

Going for Gold with a Novel Interventional Radiology Treatment for Pancreatic Cancer
http://www.prnewswire.com/news-releases/going-for-gold-with-a-novel-interventional-radiology-treatment-for-pancreatic-cancer-87781397.html
http://www.sirweb.org/news/newsPDF/70_pancreatic_final.pdf
An experimental treatment for pancreatic cancer involving the injection of gold nanoparticles coated with a cancer-killing agent into the tumor was presented at the recent Annual Scientific Meeting of the Society of Interventional Radiology. Researchers created gold particles 13 nanometers in diameter (a row of 8,000 particles is shorter than the width of a human hair) and then using a technique called image-guided "nanoembolization," they inserted a catheter into an artery near the groin and threaded through blood vessels to the pancreas. The nanoparticles bearing the therapeutic agent are injected directly into the tumor, breaching the scar tissue that can be a barrier to treatment by intravenous injection. The nanoembolization technique resulted in a 55-fold increase in the concentration of the nanoparticles in the tumor compared to venous delivery, noting this technique may avoid some of the side effects of chemotherapy, such as vomiting and hair loss. More studies are needed to show safety and effectiveness before the new treatment is ready for human patients.

Nanoparticles Switch Off Cancer Genes in Human Tumors
http://www.medicalnewstoday.com/articles/183633.php
http://www.nlm.nih.gov/medlineplus/news/fullstory_96670.html
US scientists have successfully completed a study where they showed targeted nanoparticles injected directly into a patient's bloodstream navigated into tumors, delivered double-stranded small interfering RNAs and turned off a gene that drives cancer growth. The results are from a Phase 1 clinical trial that began treating patients with nanoparticles in May 2008. A UCLA statement describes the study as the first to prove that a targeted nanoparticle can be used as an experimental therapeutic in human cancer tumors. It demonstrates the "feasibility of using both nanoparticles and RNA interference-based therapeutics in patients".

Pancreatic Cancer Study Reveals Mechanism Initiating Disease in Mice
http://www.sciencedaily.com/releases/2010/03/100312091407.htm
Scientists at the University of California, San Francisco have discovered how Kras is able to hijack mouse cells damaged by acute pancreatitis and progress becoming pancreatic cancer cells. They report the finding suggests one way in which the mutated gene Kras, found in nearly all cases of pancreatic cancer, exacts its toll in humans. It also strengthens evidence that chronic pancreatitis may be a risk factor in the development of pancreatic cancer.

Stunning Recovery Gives Hope for Advanced Pancreatic Cancer Patient
http://au.news.yahoo.com/thewest/a/-/breaking/6952388/stunning-recovery-gives-hope-for-cancer/
A metastatic pancreatic cancer patient living in Australia had a stunning response following treatment with Abraxane plus standard chemotherapy. Within three months of therapy, the patient's tumor shrunk by 65% and by five months it shrunk by 85%. Abraxane is currently in a phase III US trial looking at Abraxane plus gemcitabine in metastatic pancreatic cancer patients.

The Media Downplays the Failings of Cancer Treatments
http://www.medpagetoday.com/PublicHealthPolicy/HealthPolicy/19040
http://www.hemonctoday.com/article.aspx?rid=62003
University of Pennsylvania researchers report that media coverage may paint an overly optimistic picture of cancer and cancer outcomes. A study published in *Archives of Internal Medicine* states the media frequently discusses aggressive treatment and survival but rarely discusses treatment failure, adverse events, end-of-life, or death and does not reflect the fact that approximately half of all U.S. patients with cancer die of their illness or of related complications. The results suggested that if patients knew only what was reported in these articles, they would have a distorted view of the risks and benefits of cancer treatment and little notion of palliative end-of-life options.

National Comprehensive Cancer Network (NCCN) Panel: Straight Talk with Compassion Urged for End-of-Life Cancer Care
http://www.medscape.com/viewarticle/718426?sssdmh=dm1.601268&src=nlconfnews&spon=7&uac=61043SJ
Although telling patients that they have cancer and/or that the end is near is difficult, it should be handled

in an informative, compassionate, individualized manner, according to a mainstage roundtable discussion at the National Comprehensive Cancer Network (NCCN) 15th Annual Conference.

War on Cancer: Some Progress but No Victory (includes 3-minute audioclip)
http://www.medpagetoday.com/PublicHealthPolicy/HealthPolicy/19046
Cancer is currently the second leading cause of death in the US, and is far more complex than scientists had predicted in 1971 when then president Richard Nixon declared “War on Cancer." Cancer not only comprises more than 100 different anatomical and histological subtypes, but also exists in multiple molecular variants, with different prognoses and clinical features. Over time, it has become clear that there will be no single "silver bullet" to win the war on cancer. While progress has been made in cancers such as breast, colorectal, and prostate, the prognosis for most cancers is excellent if they are localized when diagnosed. Metastases remain a critical problem, as do certain highly lethal cancers like pancreas, liver, ovary, lung, brain, that remain refractory to current therapies.

MD Anderson News: Disabling Skp2 Gene Helps Shut Down Cancer Growth
http://mdanderson.bm23.com/public/
http://www.eurekalert.org/pub_releases/2010-03/uotm-dsg031510.php
Increased understanding of the Skp2 gene and its relation to cellular senescence may lead to the development of novel agents that can suppress tumor development in cancer. Skp2 is involved in promoting cell cycle regulation, cell proliferation, cell growth and the formation of tumors; it is over expressed in a variety of human cancers. Researchers found that inactivating Skp2 after oncogenes are overexpressed stifles cancer growth by causing senescence - the irreversible loss of a cell's ability to divide and grow. Harnessing the power of cellular senescence to push rapidly dividing cells into a dormant state might provide another way to prevent or control cancer.

Harvard Researchers Report New Attack on Cancer Forces Cells to Grow Old and Die
http://www.nlm.nih.gov/medlineplus/news/fullstory_96535.html
Instead of killing off cancer cells with toxic drugs, scientists have discovered a molecular pathway that forces them to grow old and die. Cancer cells spread and grow because they can divide indefinitely, but a study in mice showed that blocking a cancer-causing gene called Skp2 forced cancer cells to go through senescence. Harvard researchers report that if you block Skp2 in cancer cells, this process is triggered. Takeda Pharmaceutical’s drug MLN4924 is already in early-stage clinical trials and appears to have the power to do just that. The finding may offer a new strategy for fighting cancer.

Chemotherapy Plus Synthetic Compound Provides Potent Anti-Tumor Effect in Pancreatic Cancers
http://www.utsouthwestern.edu/utsw/cda/dept353744/files/581359.html
http://www.eurekalert.org/pub_releases/2010-03/usmc-cps032210.php
http://www.ncbi.nlm.nih.gov/pubmed/20332237
UT Southwestern Medical Center found human pancreatic cancer cells dramatically regress when treated with chemotherapy in combination with a synthetic compound that mimics the action of a naturally occurring "death-promoting" protein found in cells. The study was conducted in mice and reported that the findings could lead to more effective therapies for pancreatic cancer and possibly other cancers.

FDA Approves Orphan Drug Status for Pancreatic Cancer Vaccine
http://www.medscape.com/viewarticle/718748?src=mpnews&spon=7&uac=61043SJ
The US Food and Drug Administration approved orphan drug status for the therapeutic vaccine GVAX to treat pancreatic cancer. The pancreatic cancer vaccine is composed of tumor cells that are genetically engineered to produce granulocyte macrophage colony-stimulating factor, which is a crucial growth and activation factor for antigen-presenting cells that play a vital role in the initiation of systemic immune response. Ongoing trials at Johns Hopkins are evaluating the safety and benefit of adding pancreatic cancer vaccine to other anticancer agents alone or with other drugs.

Research at the University of Kent Leads Towards New Cancer Treatment that Could Have Particular Benefit for Pancreatic Cancer
http://www.medicalnewstoday.com/articles/183601.php
Research conducted and patented by Dr. Mark Howard at the University of Kent's School of Biosciences has led to the development of a new technique that will deliver cancer treatments directly to certain tumors. One of the cancers this could have particular benefit in targeting is pancreatic cancer. The

technique involves cancer-targeting peptides binding to a protein complex found in high levels on many tumor cells but absent in most normal tissues. By seeking out this protein and binding to it, the peptides can deliver cancer treatments directly to the site with increased precision and reduced side effects.

Early Termination of Clinical Trials May Overestimate Treatment Effects
http://www.clinicaspace.com/news_story.aspx?NewsEntityId=174822
http://www.medscape.com/viewarticle/719011
Early termination of clinical trials may overestimate treatment effects, according to the results of a systematic review and meta-regression analysis reported in *Journal of the American Medical Association*. According to study authors multiple problems may emerge when investigators terminate a trial earlier than planned, especially when the decision to terminate the trial is based on the finding of an apparently beneficial treatment effect. Bias may arise because large random fluctuations of the estimated treatment effect can occur, particularly early in the progress of a trial.

Release of 1999-2006 United States Cancer Statistics: Incidence and Mortality Web-Based Report
http://apps.nccd.cdc.gov/uscs/
This report includes the official federal statistics on cancer incidence from registries that have high-quality data and cancer mortality statistics for each year between 1999 and 2006 and 2002–2006 combined. The report is produced by the Centers for Disease Control and Prevention (CDC) and the National Cancer Institute (NCI), in collaboration with the North American Association of Central Cancer Registries (NAACCR). This year's report features information on more than one million invasive cancer cases diagnosed during 2006 among residents of 48 states, six metropolitan areas, and the District of Columbia—geographic areas in which about 96% of the US population reside.

Where Cancer Treatment Takes Place May Influence Outcome
http://www.nlm.nih.gov/medlineplus/news/fullstory_96681.html
When Caucasian and African American cancer patients receive similar care at specialized cancer centers, there is no significant difference in cancer death rates, a US study has found. The finding suggests that *where* patients receive care may partly account for previous findings of racial disparities in cancer deaths.

Fatigue: Is it Normal or Pathological and How Can We Best Treat It?
http://www.cancer.gov/ncicancerbulletin/032310/page5
Despite years of scientific study of cancer-related fatigue (CRF), questions related to its definition, measurement, underlying mechanisms, and effective interventions remain unanswered. Yet the high prevalence of CRF and its negative effects on quality-of-life outcomes make it a critical problem for cancer patients and survivors. CRF is a difficult symptom to understand because fatigue can be caused by both disease and treatment. Because people without cancer can experience fatigue, the line between fatigue as a normal occurrence and fatigue as a pathological symptom is blurred. Researchers are examining the underlying biology, which will help researchers develop new therapies for CRF.

Training Providers and Patients to Talk About End-of-Life Care
http://www.cancer.gov/ncicancerbulletin/032310/page8
It has been widely documented that most doctors and patients do not want to talk about death and dying. Failing to discuss transitions of care, from active cancer treatment to end-of-life care once treatment options are exhausted, can leave doctors unsure of what a patient truly wants at the end of his or her life. An article recently published in *Cancer,* based on findings from the NCI-funded study, reported that most doctors would not initiate discussions about end-of-life care options with terminally ill patients who still felt well. Instead doctors waited for symptoms or until there were no more cancer treatments to offer. Physicians who did not feel confident in the realm of end-of-life discussions were less likely to initiate them, until the last minute.

Treatment Resistance in Some Cancer Cells May be Reversible
http://www.eurekalert.org/pub_releases/2010-04/mgh-tri033010.php
http://www.nlm.nih.gov/medlineplus/news/fullstory_97123.html
The ability of cancer cells to resist treatment with either targeted drug therapies or traditional chemotherapy may, in some cases, result from a transient state of reversible drug "tolerance." When cells within a tumor that had responded to treatment resume uncontrolled growth, drug therapy is typically stopped. However, there have been many reports indicating that some tumors can regain sensitivity to

the previously ineffective treatment after a "drug holiday." Researchers at Massachusetts General Hospital examined cell lines and saw a small number of tumor cells survived exposure to concentrations of a drug 100 times greater than levels that killed the vast majority of the cells. When these drug-tolerant cells were placed in an environment without the drug, their offspring eventually regained sensitivity to the drug.

New York University Scientists Find Therapeutic Target to Stop Cancer Metastases
http://www.eurekalert.org/pub_releases/2010-03/foas-sst033110.php
Scientists have uncovered what could be a very important clue in answering one of the most perplexing questions about cancer: why does it spread to the liver more than any other organ? In a new research report, scientists from New York University describe experimental results suggesting that the immune system may be the reason, and targeting immune suppressive cells in the livers in patients with early cancer can have great benefit.

Clinical Trial Test Helps Measure Effectiveness of Treatment for Patients with Metastatic Cancer
http://www.medicalnewstoday.com/articles/184240.php
Roswell Park Cancer Institute researchers are studying how a new test called CellSearch could be used with standard radiographic methods to monitor treatment results in patients with locally advanced or metastatic gallbladder or biliary duct cancers. The goal of the study is to see if CellSearch could predict patient response to therapy earlier than traditional measures, which would enable patients to be spared the expense and unpleasant side effects of continuing with an ineffective treatment course. CellSearch is the first automated, FDA-approved system for detecting and counting circulating tumor cells (CTC) in the blood of patients with metastatic breast, prostate and colon cancer. It requires less than two teaspoons of blood and is sensitive enough to detect a single CTC in that small sample. Used in conjunction with imaging, the results can help guide treatment decisions.

Pancreatic Adenocarcinoma Exerts Systemic Effects on the Peripheral Blood Myeloid and Plasmacytoid Dendritic Cells: An Indicator of Disease Severity?
http://www.ncbi.nlm.nih.gov/pubmed/20214814
http://www.biomedcentral.com/content/pdf/1471-2407-10-87.pdf
Dendritic cells isolated from solid tumors display functional abnormalities and dendritic cell impairment has emerged as one mechanism for tumor evasion from the control of the immune system. Researchers examined the systemic influence pancreatic adenocarcinoma exerted on levels of peripheral blood dendritic cells and inflammatory mediators in comparison to the effects exerted by other pancreatic tumors, chronic pancreatitis, and age-matched controls. They found that solid pancreatic tumors, including pancreatic adenocarcinoma, systemically affect blood dendritic cells. The impairments do not seem to be tumor-specific, since similar results were obtained in subjects with chronic pancreatitis. Furthermore, they found that pancreatic adenocarcinoma patients with a survival over 2 years had significant higher levels of blood dendritic cells compared to patients with less than a year survival. Their findings reveal that the preservation of the blood dendritic cells in pancreatic adenocarcinoma patients seems to benefit their ability to control the disease and survival.

Advanced Pancreatic Carcinoma: Current Treatment and Future Challenges
http://www.nature.com/nrclinonc/journal/v7/n3/pdf/nrclinonc.2009.236.pdf
Drs. Anastasios Stathis and Malcolm J. Moore review the current management of advanced pancreatic cancer, new treatment strategies and future directions in drug development.

Abstracts

Epidemiologic Evidence on Coffee and Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20358464
Coffee consumption is a major and frequent dietary exposure in diverse cultures around the globe. A substantial body of epidemiologic evidence relates the consumption of coffee to cancer of various sites. However, there is no comprehensive, up-to-date overview of the overall knowledge base. The authors reviewed and summarized the data, noting there appears to be a strong and consistent protective association for colorectal cancer. No association appears to exist with breast, pancreatic, kidney, ovarian, prostate, or gastric cancer.

Phase II Study of S-1 in Patients with Gemcitabine-Resistant Advanced Pancreatic Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20352216
The study sought to assess the efficacy and safety of S-1 in patients with gemcitabine-resistant advanced pancreatic cancer who had received first-line gemcitabine chemotherapy. Twenty-one patients received S-1 orally twice daily for 28 days, followed by 14 days of rest. Treatment was repeated every six weeks until disease progression. Second-line chemotherapy with S-1 had acceptable toxicity and resulted in a relatively high disease control rate in patients with gemcitabine-resistant advanced pancreatic cancer. S-1 may be a feasible treatment option for this patient population.

Risk of Pancreatic Cancer by Alcohol Dose, Duration, and Pattern of Consumption, Including Binge Drinking: A Population-Based Study
http://www.ncbi.nlm.nih.gov/pubmed/20349126
Alcohol consumption is postulated to be a risk factor for pancreatic cancer but clarification of degree of risk related to consumption characteristics is lacking. This study examined the association between alcohol consumption and pancreatic cancer in a population-based case-control study in the San Francisco Bay Area. Depending on dose, duration, and pattern of drinking, odd ratios were increased 1.5- to 6-fold among men but not women. Most notable were effects for history of binge drinking, including increased number of drinks per day and increased years of binge drinking. Results from this analysis provide support for heavy alcohol consumption (including binge drinking) as a risk factor for pancreatic cancer in men.

The Relative Influence of Diet and Serum Concentrations of Organochlorine Compounds on K-ras mutations in exocrine pancreatic cancer
http://www.ncbi.nlm.nih.gov/pubmed/20350743
The study examined the relationship between food intake and serum concentrations of OCs (organochloriine compounds) in pancreatic cancer patients and the relative influence of food and OCs on the frequency of K-ras mutations in these patients. Dairy products were a source of OCs. The association between dairy products and K-ras mutations was not independent of OCs. By contrast, the association between OCs and K-ras was not confounded by dairy products. OCs may be more likely to contribute to the occurrence of K-ras mutations than nutrients contained in dairy products.

Stereotactic Body Radiotherapy in the Treatment of Advanced Adenocarcinoma of the Pancreas
http://www.ncbi.nlm.nih.gov/pubmed/20308870
The aim of the study was to assess the feasibility and safety of stereotactic body radiotherapy (SBRT) in 71 advanced pancreatic cancer patients. Forty patients (56%) had locally unresectable disease, 11 patients (16%) had local recurrence following surgical resection, eight patients (11%) had metastatic disease, and 12 patients (17%) received adjuvant SBRT for positive margins. The median OS was 10.3 months, with 6 month/1 year OS rates of 65.3%/41%, respectively. SBRT is feasible, with minimal grade >/=3 toxicity.

Phase I Trial of Gemcitabine Dose Escalation with Concurrent Radiotherapy for Patients with Locally Advanced Pancreatic Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20332663
The study evaluated the safety, efficacy, DLT, and maximum tolerated dose of gemcitabine with concurrent radiotherapy in patients with unresectable locally advanced pancreatic cancer. Of the 12 patients, there were 11 sustained responses of which two underwent surgery after re-evaluation. Weekly gemcitabine with concurrent radiation therapy in patients with locally advanced pancreatic cancer was well tolerated.

Dasatinib Inhibits the Development of Metastases in a Mouse Model of Pancreatic Ductal Adenocarcinoma
http://www.ncbi.nlm.nih.gov/pubmed/20303350
The aim of this study was to assess the importance of Src in human PDAC and to use a genetically engineered mouse model of PDAC to determine the effects of dasatinib on PDAC progression. Researchers report that there was no survival advantage in the dasatinib treated animals due to continued growth of the primary tumor.

Thymidylate Synthase (TYMS) Enhancer Region Genotype-Directed Phase II Trial of Oral Capecitabine for 2nd Line Treatment of Advanced Pancreatic Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20306339
The primary aim of this study was to characterize the six-month overall survival and toxicity associated with second-line capecitabine treatment of advanced pancreatic cancer patients harboring the TYMS *2/*2 allele. Eighty patients with stage IV pancreatic cancer were screened for the *2/*2 TYMS allele; those with the *2/*2 TYMS polymorphism were treated with capecitabine. Sixteen of the 80 screened patients tested positive for *2/*2 TYMS variant and four out of the 16 eligible patients were treated in the study. The study was terminated early due to poor accrual and increased toxicity. The presence of the *2/*2 TYMS genotype in all of the screened patients trended toward a decreased overall survival. It appears capecitabine therapy in pancreatic cancer patients harboring the TYMS *2/*2 variant may be associated with increased non-hematologic toxicity.

ABC Transporters as Molecular Effectors of Pancreatic Oncogenic Pathways: The Hedgehog-GLI Model
http://www.ncbi.nlm.nih.gov/pubmed/20333482
Chemoresistance is the main cause of disease progression and mortality among patients diagnosed from pancreatic adenocarcinoma. One of the better known mechanisms of drug resistance in cancer is related to ATP-binding cassette (ABC) transporters, highly expressed in solid tumors and cancer stem cells. These cancer stem cells are thought to be responsible for tumor maintenance, progression, and relapse of the disease due, in part, to an exhibition of multiple resistance mechanisms to chemotherapy and radiation. This study suggests a potential role of hedgehog-GLI pathway in pancreatic cancer chemoresistance, based on ABC transporters' overexpression.

Availability and Integration of Palliative Care at US Cancer Centers
http://jama.ama-assn.org/cgi/content/short/303/11/1054?home
http://mdanderson.bm23.com/public/?q=preview_message&fn=Link&t=1&ssid=6781&id=en75n7rpizhor0o0ncb5r3qgdwfqs&id2=b5fwqiqc1w8p6mucd4ervpau4agkk&subscriber_id=afhopbiydnopexrxurhbqpbbpbbubbg&messageversion_id=basvhmtqzhcemevdyhrfqtiemujabif&delivery_id=bvyrli
A study from the MD Anderson Cancer Center reports that although US cancer centers provide patients and their families with palliative care, the depth, range and integration of programs and services widely vary. Despite the many advances in cancer research, palliative care continues to play a vital role in the continuum of cancer care. Lead author Dr. David Hui added that although palliative care is most effective when incorporated early in oncology care, their study showed that patients and their families were referred to palliative care often too late when the full value of palliative care may not be realized.

Efficacy and Safety of Capecitabine in Combination with Docetaxel and Mitomycin C in Pre-Treated Pancreatic, Gallbladder, and Bile Duct Carcinoma
http://www.ncbi.nlm.nih.gov/pubmed/20224968
Twenty-eight pre-treated patients with a median age of 59 suffering from pancreatic, gallbladder, intra- or extrahepatic bile duct carcinoma were included in the study. Six patients achieved partial and seven patients minor remissions, while six patients had stable disease adding to a tumor control rate of 68%. In all, the DocMitoCape regimen exhibited a favorable safety profile and a high rate of tumor stabilizations in patients with pre-treated gallbladder, bile duct and pancreatic carcinoma. The study authors note that it might be considered after failure of standard regimens in these types of cancer.

Unresectable Locally Advanced Pancreatic Cancer: A Multimodal Treatment Using Neoadjuvant Chemoradiotherapy (Gemcitabine Plus Stereotactic Radiosurgery) and Subsequent Surgical Exploration
http://www.ncbi.nlm.nih.gov/pubmed/20224860
The study was a prospective, nonrandomized study of patients with locally advanced pancreatic cancer (LAPC) to assess the effect of stereotactic body radiotherapy (SBRT) on local response, pain control, and quality of life (QOL). Twenty-three patients with histologically confirmed LAPC underwent SBRT and received gemcitabine chemotherapy. No grade 2 or higher acute or late toxicity was observed. The overall local response ratio was 82.6%. SBRT showed a good short-term efficacy in controlling both pain and QOL. The SBRT method is a promising treatment for LAPC. Local control rates, even compared to historical data from conventional radiotherapy, can be achieved with minimal toxicity.

Chemotherapy with 5-Fluorouracil, Cisplatin and Streptozocin for Neuroendocrine Tumors
http://www.ncbi.nlm.nih.gov/pubmed/20234360
The role of chemotherapy for neuroendocrine tumors remains controversial and there is no standard regimen. Researchers report the outcome for a consecutive series of chemonaive patients with metastatic or locally advanced neuroendocrine tumors treated with a combination of 5-fluorouracil, cisplatin and streptozocin administered three weekly for up to six cycles. In the 79 patients assessable for response, treatment was associated with an overall response rate of 33%. Stable disease occurred in a further 51%, with progression in 16%. The median time to progression was 9.1 months and median overall survival was 31.5 months. This is an effective regimen for neuroendocrine tumors with an acceptable toxicity profile.

Efficacy of Radionuclide Treatment DOTATATE Y-90 in Patients with Progressive Metastatic Gastroenteropancreatic Neuroendocrine Carcinomas (GEP-NETs): A Phase II Study
http://annonc.oxfordjournals.org/content/early/2009/10/15/annonc.mdp372.abstract
This study evaluated the clinical and radiological effectiveness of DOTATATE Y-90 in patients with extensive progressive gastroenteropancreatic neuroendocrine carcinomas (GEP-NETs). Sixty patients with histologically proven GEP-NETs were treated with DOTATATE Y-90. Clinical responses were assessed 6 weeks after completing therapy and then after each of the 3- to 6-month intervals. The radiological response was classified according to RECIST criteria. DOTATATE Y-90 therapy is effective and relatively safe in patients with GEP-NET. Standard doses of DOTATATE Y-90 result in a relatively low risk of myelotoxicity. However, due to ongoing risk of renal toxicity, careful monitoring of the kidney is recommended.

Chitosan and Glyceryl Monooleate Nanostructures Containing Gemcitabine: Potential Delivery System for Pancreatic Cancer Treatment
http://www.ncbi.nlm.nih.gov/pubmed/20238190
The study looked at ways to enhance cellular accumulation of gemcitabine with chitosan/glyceryl monooleate (GMO) nanostructures, and to provide significant increase in cell death of human pancreatic cancer cells in vitro. The delivery system demonstrated a significant decrease in cell survival for gemcitabine nanostructures post-treatment when compared with a solution of gemcitabine alone. The nanostructure demonstrated increased effective treatment compared with gemcitabine treatment alone in an in vitro model of human pancreatic cancer.

Phase II Trial of Gemcitabine, Irinotecan, and Celecoxib in Patients with Advanced Pancreatic Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20216081
Cyclooxygenase-2 (COX-2) has been shown to be expressed in a variety of tumors including pancreatic cancer. The combination of gemcitabine and irinotecan is active in pancreatic cancer. This study examined the toxicity and response rate to the addition of the selective oral COX-2 inhibitor, celecoxib, to gemcitabine and irinotecan in patients with inoperable pancreatic cancer and found it to be an active therapy for this group. A marked reduction in CA19-9 was observed in all evaluable patients by cycle 2. Toxicity was tolerable and the majority of patients reported a decrease in pain and a significant improvement in quality of life.

External Beam Radiotherapy Plus 24-Hour Continuous Infusion of Gemcitabine in Unresectable Pancreatic Carcinoma: Long-Term Results of a Phase II Study
http://www.ncbi.nlm.nih.gov/pubmed/19427747
This study evaluated the efficacy of gemcitabine-based chemoradiation in patients with locally advanced pancreatic cancers. Forty patients were treated from 2000 to 2005; the majority had T4 tumor. Grade 3-4 acute toxicity was observed in 21 patients and 30 patients completed the treatment schedule. A clinical response was achieved in 12 patients (30%). With a median follow-up of 76 months, the 2-year local control was 39.6% and 2-year metastases-free survival was 29.7%. Two-year overall survival compared with the researcher's previous study on 5-fluorouracil-based CT-RT was significantly improved. Gemcitabine chemoradiation seems correlated with improved outcomes. Healthier patients who are likely to complete the treatment schedule may benefit most from this therapy.

Gemcitabine Therapy for Unresectable Pancreatic Cancer in Elderly Patients
http://www.ncbi.nlm.nih.gov/pubmed/20203443
The study evaluated the therapeutic effect of gemcitabine therapy in 153 unresectable pancreatic cancer patients, divided into younger patients (under 65), early-stage elderly patients (age 65-74) and advanced-stage elderly patients (age 75 and over). Among those patients who received only best supportive care (BSC), the most common reasons to be selected for BSC were family requests in the advanced-stage elderly patients, and poor general condition in the rest. Among the patients who received GEM therapy, there were no significant differences in response rate, or adverse events including the rate of dose reduction, postponement or cessation of GEM administration due to toxicity. Multivariate analysis using patient backgrounds and response to GEM therapy showed that CA 19-9 response and performance status did not change with age. GEM therapy for both early-stage and advanced-stage elderly UPC patients was as safe and useful as in younger patients.

Identifying Pancreatic Cancer Patients for Targeted Treatment: The Challenges and Limitations of the Current Selection Process and Vision for the Future
http://www.ncbi.nlm.nih.gov/pubmed/20201734
Recent preclinical data have demonstrated that pancreatic adenocarcinoma cells with defects in the Fanconi anemia/BRCA2 pathway are hypersensitive to interstrand crosslinking agents. This study highlights the challenge of treating pancreatic adenocarcinoma patients and selecting those eligible for targeted therapy. A new multidisciplinary approach for stratifying pancreatic cancer patients for promising targeted adjuvant therapy and familial risk counseling is proposed.

Chemoradiation in Pancreatic Adenocarcinoma: A Literature Review
http://www.ncbi.nlm.nih.gov/pubmed/20203172
Various strategies in the form of neoadjuvant and adjuvant treatment have been employed over the years to improve outcome, with limited success, in pancreatic cancer. Systemic chemotherapy remains the gold standard in the metastatic setting in good performance status patients, and adjuvant chemotherapy after resection of localized and locally advanced cancer has been found to improve outcome. The role of radiotherapy, however, remains controversial and is an area that merits further investigation. This article reviewed published literature on the use of chemoradiation as a modality in various stages of pancreatic adenocarcinoma and highlighted areas that future trials should target for a way forward in this malignancy.

Parenteral Nutrition Support for Patients with Pancreatic Cancer: Results of a Phase II Study
http://www.ncbi.nlm.nih.gov/pubmed/20214798
Cachexia is a common problem in patients with upper gastrointestinal cancer. In addition, most of these patients suffer from malabsorption and stenosis of the gastrointestinal tract due to their illness. Various methods of supplementary nutrition (enteral, parenteral) are practiced. The study examined the impact of additional parenteral nutrition (APN) in advanced pancreatic patients with progressive cachexia. Thirty-two patients suffering from progressive weight loss in spite of additional enteral nutritional support were eligible for the study. The study demonstrated a positive impact of APN on the assessed parameters, and at least a temporary benefit or stabilization of the nutritional status in the majority of the investigated patients.

Intraoperative Radiotherapy for Resected Pancreatic Cancer: A Multi-Institutional Retrospective Analysis of 210 Patients
http://www.ncbi.nlm.nih.gov/pubmed/20207498
Researchers retrospectively analyzed the results of intraoperative radiotherapy (IORT) with or without external beam radiotherapy (EBRT) for resected pancreatic cancer. The records of 210 patients treated with gross complete resection and IORT with or without EBRT were reviewed. Patients treated with IORT and chemotherapy had a significantly more favorable overall survival than those treated with IORT alone. IORT yielded an excellent local control rate for resected pancreatic cancer with few frequencies of severe late toxicity. IORT combined with chemotherapy confers a survival benefit compared with that of IORT alone.

Chromogranin A-Biological Function and Clinical Utility in Neuro Endocrine Tumor Disease
http://www.ncbi.nlm.nih.gov/pubmed/20217257
Neuroendocrine tumors synthesize, store, and secrete peptides (e.g., chromogranin A (CgA) and amines). A critical issue is late diagnosis due to failure to identify symptoms or to establish the biochemical diagnosis. Researchers reviewed the utility of CgA measurement in neuroendocrine tumors

and described its biological role and the clinical value of its measurement. Both functioning and nonfunctioning pancreatic NETs have elevated values. CgA is more frequently elevated in well-differentiated tumors compared to poorly differentiated NETs. Effective treatment is often associated with decrease in CgA levels. Proton pump inhibitors falsely increase CgA, but levels normalize with therapy cessation. CgA is currently the best available biomarker for the diagnosis of NETs. It is critical to establish diagnosis and has some utility in predicting disease recurrence, outcome, and efficacy of therapy. Measurement of plasma CgA is mandatory for the effective diagnosis and management of NET disease.

Adjuvant Chemoradiotherapy After Pancreatic Resection for Invasive Carcinoma Associated With Intraductal Papillary Mucinous Neoplasm of the Pancreas
http://www.redjournal.org/article/S0360-3016(09)00463-5/abstract
One-third of Intraductal papillary mucinous neoplasms are associated with invasive carcinoma. This study examined the benefit of adjuvant chemoradiotherapy (CRT) for this cohort and reported that adjuvant CRT conferred a 57% decrease in the relative risk of mortality after pancreaticoduodenectomy for intraductal papillary mucinous neoplasms with an associated invasive component after adjusting for major confounders. Patients with lymph node metastases or positive margins appeared to particularly benefit from CRT after definitive surgery.

Phase II Study of Gemcitabine Chemotherapy Alone for Locally Advanced Pancreatic Carcinoma: JCOG0506
http://www.ncbi.nlm.nih.gov/pubmed/20185458?itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum&ordinalpos=6
Gemcitabine monotherapy demonstrated far better survival than historical data for chemoradiotherapy with 5-fluorouracil with mild toxicities. Gemcitabine could be considered as a standard treatment for locally advanced pancreatic cancer.

Chemotherapy: Gemcitabine Remains the Standard of Care for Pancreatic Cancer
http://www.nature.com/nrclinonc/journal/v7/n3/full/nrclinonc.2010.16.html
A phase III trial for advanced pancreatic cancer comparing gemcitabine with gemcitabine plus capecitabine demonstrated that combination chemotherapy provided no significant outcome advantage for patients. A marked change in treatment paradigm is essential if therapeutic interventions are to move beyond the persistently dismal outcome results for the majority of pancreatic cancer patients, as reflected in the past decade of clinical research.

Fixed-Dose-Rate Gemcitabine: A Viable First-Line Treatment Option for Advanced Pancreatic and Biliary Tract Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20189980?itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum&ordinalpos=3
Currently available evidence, including this updated analysis, supports the use of fixed-dose-rate gemcitabine as a first-line option in advanced pancreatic adenocarcinoma and biliary tract cancer patients, and prompts the continued evaluation of this approach in combination regimens.

Phase III Trial of Gemcitabine Plus Cisplatin Compared With Single-Agent Gemcitabine as First-Line Treatment in Advanced Pancreatic Cancer
http://jco.ascopubs.org/cgi/content/short/JCO.2009.25.4433v1?rss=1
Single-agent gemcitabine became standard first-line treatment for advanced pancreatic cancer after demonstration of superiority compared with fluorouracil. The Gruppo Italiano Pancreas 1 (GIP-1) conducted a randomized phase III trial aimed to compare gemcitabine plus cisplatin versus gemcitabine alone and found the addition of weekly cisplatin to gemcitabine failed to demonstrate any improvement as first-line treatment of advanced pancreatic cancer.

Palliative First-Line Treatment with Weekly High-Dose 5-Fluorouracil as 24h-Infusion and Gemcitabine in Metastatic Pancreatic Cancer
http://www.ncbi.nlm.nih.gov/pubmed/20190682?itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum&ordinalpos=2
The administration of gemcitabine and 5-FU as a 24h-infusion is feasible and offers good tumor control rate accompanied by tolerable toxicity. The subgroup of patients with a good performance status (ECOG 0) and tumor markers within the normal range benefit from the gemcitabine combination therapy.