



**Research**

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## PANCREATIC CANCER: NEWS & UPDATES

September 2010

### **BIOLOGY OF CANCER**

#### **PTEN Loss Accelerates KrasG12D-Induced Pancreatic Cancer Development**

<http://cancerres.aacrjournals.org/content/70/18/7114.abstract>

Conducted by a team of researchers, including Dr. David Dawson, 2008 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award recipient, this study examined the role of PTEN/PI3K/AKT signaling in KrasG12D-induced PDAC development. KRAS mutations are found in approximately 90% of human pancreatic ductal adenocarcinomas (PDAC). However, mice genetically engineered to express KrasG12D from its endogenous locus develop PDACs only after a prolonged latency, indicating that other genetic events or pathway alterations are necessary for PDAC progression. The PTEN-controlled phosphatidylinositol 3-kinase (PI3K)/AKT signaling axis is dysregulated in later stages of PDAC. In the current project, the researchers crossed Pten conditional knockout mice (Ptenlox/lox) to mice with conditional activation of KrasG12D. The resulting compound heterozygous mutant mice showed significantly accelerated development of acinar-to-ductal metaplasia (ADM), malignant pancreatic intraepithelial neoplasia (mPanIN), and PDAC within a year. Moreover, all mice with KrasG12D activation and Pten homozygous deletion succumbed to cancer by 3 weeks of age. Their data support a dosage-dependent role for PTEN, and the resulting dysregulation of the PI3K/AKT signaling axis, in both PDAC initiation and progression; and shed additional light on the signaling mechanisms that lead to the development of ADM and subsequent mPanIN and pancreatic cancer.

#### **DNA Trick May Be Clue to Cancer Cells' Eternal Life**

<http://www.medicalnewstoday.com/articles/200653.php>

Cancer Research UK scientists have uncovered a new strategy that could be used by cancer cells to side step the body's normal safety checks and become immortal, according to a study published in *Nature*. The strategy involves cells topping up their biological clock by making copies of spare DNA found elsewhere in the genome to replace the protective caps, called telomeres, which are usually found at the ends of chromosomes. In most cells of the body, telomeres shorten each time the cell divides. Once a critical length is reached, it triggers the cell to die, acting like an in-built timer to ensure that the cell can't live past its pre-programmed expiration date. However, in approximately 85% of cases, cancer cells manage to get around this safety check by reactivating telomerase - an enzyme that can rebuild the telomeres by creating new DNA repeats. This finding adds to scientists understanding of how cancer cells become immortal.

#### **MIT Researchers Discover an Unexpected Twist in Cancer Metabolism**

<http://www.acor.org/news/display.html?id=9841>

Researchers at MIT and Harvard University report a previously unknown element of cancer cells' peculiar metabolism. They found cells can trigger an alternative biochemical pathway that speeds up their metabolism and diverts the byproducts to construct new cells. This finding could help scientists design drugs that block cancer-cell metabolism, essentially starving them of the materials they need to grow and spread.

#### **First Molecule Blocks Key Component of Cancer Genes' On-Off Switch**

[http://www.eurekalert.org/pub\\_releases/2010-09/dci-rcf092410.php](http://www.eurekalert.org/pub_releases/2010-09/dci-rcf092410.php)

In the quest to arrest the growth and spread of tumors, there have been many attempts to get cancer genes to ignore their internal instruction manual. A team led by Dana-Farber Cancer Institute scientists has created the first molecule able to prevent cancer genes from "hearing" those instructions, stifling the cancer process at its root. The study demonstrates that proteins issuing stop and start commands to a cancer gene, known as epigenetic "reader" proteins, can be targeted for future cancer therapies.

### **Improvement in Prediction of Blood Clots in Cancer Patients**

<http://www.acor.org/news/display.html?id=9825>

The association of cancer and blood clots is a common concern. Venous thromboembolism (VTE) is the formation of blood clots in the veins and develops in up to 20% of cancer patients. VTEs are one of the leading causes of death in this patient population. Cancer patients commonly present with laboratory abnormalities of clotting marker underlying a subclinical hypercoagulable condition. Researchers report there is now an enhanced risk model to predict a cancer patients' chance of developing blood clots.

### **Protein Key to Growth of Pancreatic Cancer**

[http://www.eurekalert.org/pub\\_releases/2010-09/qmuo-pkt092710.php](http://www.eurekalert.org/pub_releases/2010-09/qmuo-pkt092710.php)

Researchers found a protein that could provide a target to develop new treatments for the disease or enable earlier diagnosis. Nearly three quarters of pancreatic cancer tumors had high levels of a protein known as P110γ. In laboratory experiments, when production of this protein was blocked, the cancer cells stopped growing. Researchers postulate P110γ is needed for pancreatic cancer cells to grow and likely plays a critical role in the progression of the disease, making it a potential target for developing new treatments.

### **Molecule 968 Binds Glutaminase and Starves Cancer Cells**

<http://www.pressoffice.cornell.edu/releases/release.cfm?r=49779>

<http://www.news.cornell.edu/stories/Sept10/CerioneStudy.html>

A molecule called 968 can starve cancer cells and the tumors they produce, according to Cornell University researchers. The key to this research is the amino acid glutamine. Researchers have long believed that starving cancer cells of glutamine, which cancer cells require in larger quantities than normal cells, would help fight some cancers. Now, a molecule has been discovered that does the job: Dubbed 968, this proof of concept molecule binds to the enzyme glutaminase to inhibit cancer growth by blocking the cancer cells' utilization of glutamine. The finding could lead to a new class of drugs, capable of halting cancer progression without harming normal cell growth.

### **ETIOLOGY**

#### **Metabolic Factors and the Risk of Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20826833>

The association between factors in metabolic syndrome and the risk of pancreatic cancer was examined using data from the Metabolic Syndrome and Cancer Project. This project collects data on body mass index, blood pressure, and blood levels of glucose, cholesterol, and triglycerides. Of the participants followed, 862 were diagnosed with pancreatic cancer. Analysis showed mid-blood pressure and glucose in men, and body mass index, mid-BP, and glucose in women, were risk factors for pancreatic cancer.

#### **Energy Balance, Host-Related Factors, and Cancer Progression**

<http://jco.ascopubs.org/content/28/26/4058.abstract>

Obesity is associated with an increased risk and worsened prognosis for many types of cancer, but the mechanisms underlying the obesity–cancer progression link are poorly understood. Several energy balance–related host factors are known to influence tumor progression and/or treatment responsiveness, and these have been implicated as key contributors to the complex effects of obesity on cancer outcome. These host factors include leptin, adiponectin, steroid hormones, reactive oxygen species associated with inflammation, insulin, insulin-like growth factor–1, and sirtuins. Each of these host factors is considered in this article in the context of energy balance and cancer progression.

#### **Environmental Factors Cannot be Ruled out for Cancer Rates in Port Clinton, Ohio**

<http://www.portclintonnewsheald.com/article/20100915/NEWS01/9150304>

In August 2010, Port Clinton's high rate of pancreatic, lung and bronchial cancer was attributed to smoking per an investigation conducted by the state's department of health. Now, the Center for Health, Environment and Justice released their assessment of the Ohio report and has concluded that environmental factors cannot be ruled out without further investigation. The Center noted Port Clinton resides in Ottawa County, which has the second lowest rate of smoking in the state of Ohio, and advised further study to identify the possible cause(s) for the increased cancer rates in this city.

#### **Heart Damage Seen in Mice with Cancer-Related Disease**

<http://www.cancercompass.com/cancer-news/article/34203.htm>

It was believed that cancer-related muscle wasting disease called cachexia didn't damage the heart. Ohio State University researchers report that cachexia can cause serious damage to the heart, reducing heart function and changing heart muscle structure. Cachexia is most common in patients with colon cancer and other gastrointestinal tumors, like pancreatic cancer. Researchers noted that the fatigue and weakness of cachexia have been attributed to skeletal muscle wasting; however, Ohio researchers' study results support that insufficient heart performance might also be responsible for fatigue symptoms, leading to less exercise and more severe muscle wasting and perpetuating the cycle that contributes to the complications of cancer cachexia.

### **ABO Blood Group and Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20833034>

Several studies have shown an association between ABO blood type and various malignancies, including pancreatic cancer. Researchers studied this association using data from a tumor registry. Information was retrieved for 15,359 cancer patients with defined ABO blood types. Results showed a significantly lower frequency of blood type O in patients with exocrine pancreatic cancer compared to patients with other forms of cancer. There was no association for endocrine pancreatic cancer or for cancer originating in other organs. The researchers concluded that the association between ABO blood group and pancreatic cancer is limited to exocrine pancreas malignancy.

### **Educational Level and Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20829145>

Studies examining the relationship between socioeconomic status and pancreatic cancer incidence have been inconclusive. This study prospectively investigated to what extent pancreatic cancer incidence varies according to educational level within the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Within the source population of 407,944 individuals at baseline, the crude difference in risk of pancreatic cancer according to level of education was small and not statistically significant.

### **DETECTION, DIAGNOSIS AND PROGNOSIS**

#### **Pancreatic Cancer Screening in a Prospective Cohort of High-Risk Patients: A Comprehensive Strategy of Imaging and Genetics**

<http://www.ncbi.nlm.nih.gov/pubmed/20876795>

Researchers questioned if screening to identify curable neoplasms is effective when offered to patients at high-risk of pancreatic cancer. Fifty-one high-risk patients were enrolled into a screening program. Of these patients, 31 underwent EUS and 33 MRI. Overall, 6 (12%) of the 51 patients had neoplastic lesions in the pancreas and 9 (18%) had neoplasms in any location. Pancreatic cancer screening for high-risk patients with a comprehensive strategy of imaging and genetics is effective and identifies curable neoplasms that can be resected. Ongoing study will better define who will benefit from screening and what screening strategy will be most effective.

#### **Pancreatic Intraepithelial Neoplasia - Can We Detect Early Pancreatic Cancer?**

<http://www.ncbi.nlm.nih.gov/pubmed/20875068>

Pancreatic adenocarcinoma develops through stepwise progression from precursor lesions. Detection and treatment of these precursor lesions would allow curative treatment. Three precursor lesions for PDAC have been identified: mucinous cystic neoplasms (MCNs), intraductal papillary mucinous neoplasms (IPMNs), and pancreatic intraepithelial neoplasia (PanIN). Currently, screening focuses upon high-risk individuals only.

#### **Marker Expression in Circulating Cancer Cells of Pancreatic Cancer Patients**

<http://www.ncbi.nlm.nih.gov/pubmed/20869080>

The detection of pancreatic cancer cells in the peripheral circulation could be used to diagnose early pancreatic cancer, which would otherwise not be detected by current imaging methods. The expression levels of h-TERT, CK20, CEA, and C-MET were detected in a model of circulating micrometastasis in pancreatic cancer that were enriched using immune-magnetic separation of the circulating cancer cells. The expression of these genes was measured in the circulating cancer cells of pancreatic cancer patients. The expression rate in pancreatic cancer patients was compared at different stages to screen for the indicator with highest sensitivity and specificity for the detection of circulating pancreatic cancer cells. The researchers concluded that the positive expression of C-MET, h-TERT, CK20, and CEA in the circulation of pancreatic patients could be used as an indicator for circulating cancer cells.

### **University of North Carolina- Chapel Hill Granted \$2.3M to Use Nanotechnology against Pancreatic Cancers**

<http://www.newswise.com/articles/unc-scientists-receive-grant-to-develop-nanotechnology-for-pancreatic-cancer-diagnosis-and-treatment>

UNC researchers received a five-year \$2.3 million grant from the National Cancer Institute's Nanotechnology Platform Partnerships to use nanotechnology to address the need for early diagnosis and the development of more effective treatments for pancreatic cancer.

### **Tiny Tools Aren't Toys - Enzyme-Based Machinery Could have Medical Applications**

[http://www.sciencenews.org/view/generic/id/63745/title/Tiny\\_tools\\_aren%E2%80%99t\\_toys](http://www.sciencenews.org/view/generic/id/63745/title/Tiny_tools_aren%E2%80%99t_toys)

Researchers have created millimeter-sized metal tools that contort on command, clamping shut or popping open in response to specific chemical cues. The smart devices may one day be used to biopsy an organ, prop open an artery or deliver drugs to a target site. Rather than use batteries or electrical wires as the power source, the tiny metal tools are powered by biologically friendly polymers that breakdown in the presence of enzymes.

### **New Biomarkers Discovered for Pancreatic Cancer and Mesothelioma**

[http://www.eurekalert.org/pub\\_releases/2010-09/aafc-nbd092110.php](http://www.eurekalert.org/pub_releases/2010-09/aafc-nbd092110.php)

<http://www.reuters.com/article/idUSN284519420100928?type=marketsNews>

Results of an ongoing study presented at the 4<sup>th</sup> AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development indicate that researchers believe they have identified biomarkers and protein signatures with high accuracy for early stage detection of pancreatic cancer and mesothelioma. Moreover, they found high specificity, meaning few people without the disease will be incorrectly diagnosed. Validation studies are underway.

### **Thrombotic Complications of Pancreatic Cancer: Classical Knowledge Revisited**

<http://content.karger.com/produktedb/produkte.asp?doi=319413>

This paper reviews the association between deep vein thrombosis and pancreatic cancer. Pancreatic cancer is among the most common malignancies associated with thrombosis, due to the fact that cancer may induce the activation of the coagulation. There are genetic factors linked to this association. It has also been speculated that deep vein thrombosis or pulmonary embolism could represent a warning sign for a latent cancer. The practical question posed regarding this association is whether doctors should recommend searching for pancreatic and other cancers in all patients with thrombosis.

### **EUS-Guided FNA of Local Recurrence of Pancreatic Cancer after Surgical Resection**

<http://www.ncbi.nlm.nih.gov/pubmed/20869713>

While EUS-guided FNA (EUS-FNA) is a test used for the preoperative diagnosis of pancreatic cancer, its use for diagnosing local tumor recurrence after surgical resection has not been described. This study aimed to determine the sensitivity of EUS-FNA for this indication. Of 17 patients who underwent EUS after resection for suspected local recurrence of pancreatic cancer, recurrence was located in the head in 14 patients, the body in 1, and the tail in 2. EUS-FNA is sensitive for the diagnosis of retroperitoneal recurrence of pancreatic cancer after surgical resection.

### **Positive Reimbursement Coverage Issued for RedPath's PathFinderTG<sup>®</sup> Technology for Pancreatic Cancer, Cysts, and Masses**

<http://www.businesswire.com/news/home/20100927005231/en/Positive-Reimbursement-Coverage-Issued-RedPath%E2%80%99s-PathFinderTG%C2%AE-Technology>

RedPath Integrated Pathology, Inc., a cancer molecular diagnostics company announced that Highmark Medicare Services the contractor that administers Medicare programs for providers in Pennsylvania, New Jersey, Maryland, Delaware and the District of Columbia, has issued a positive Local Coverage Decision for the company's PathFinderTG<sup>®</sup> Technology for pancreatic cancer, cysts, and masses. PathFinderTG<sup>®</sup> Technology<sup>®</sup> will be covered as a "reasonable and necessary" service for the analysis of pancreatic cysts and masses when traditional diagnostic evaluations are inconclusive.

### **Estimating Prognosis and Palliation Based on Tumor Marker CA 19-9 and Quality of Life Indicators in Advanced Pancreatic Cancer Patients on Chemotherapy**

<http://www.ncbi.nlm.nih.gov/pubmed/20877359>

The study investigated the prognostic value of quality of life relative to tumor marker carbohydrate antigen (CA) 19-9, and the role of CA 19-9 in estimating palliation in patients with advanced pancreatic cancer receiving chemotherapy. Patients' CA 19-9 serum concentration was measured at baseline and every 3 weeks in a phase III trial. In advanced pancreatic cancer, pain and tiredness are independent prognostic factors for survival, although less prognostic than CA 19-9. Quality of life improves before best CA 19-9 response but the maximum CA 19-9 decrease has no impact on subsequent quality of life.

## **TREATMENT**

### **Combination DR5 Agonistic Monoclonal Antibody with Gemcitabine Targets Pancreatic Cancer Stem Cells and Results in Long-term Disease Control in Human Pancreatic Cancer Model**

<http://mct.aacrjournals.org/content/9/9/2582.short>

This article is co-authored by Dr. Zeshaan Rasheed, 2010 Tempur-Pedic Retailers – Pancreatic Cancer Action Network – AACR Pathway to Leadership Grant recipient. Pancreatic ductal adenocarcinoma (PDA) often recurs after initial treatment, resulting in patient death despite the use of chemotherapy or radiation therapy. PDA contains a subset of tumor-initiating cells, known as cancer stem cells (CSC), that are capable of extensive self renewal and may contribute to therapeutic resistance and metastasis. At present, conventional chemotherapy and radiotherapy are largely ineffective in depleting CSC pool, suggesting the need for novel therapies that specifically target the cancer-sustaining stem cells for tumor eradication and to improve the poor prognosis of PDA patients. In this study, death receptor 5 (DR5) is enriched in pancreatic CSCs compared with the bulk of the tumor cells. Treating a collection of freshly generated patient-derived PDA xenografts with gemcitabine, the first-line chemotherapeutic agent for PDA, is initially effective in reducing tumor size, but largely ineffective in diminishing the CSC populations, and eventually culminated in tumor relapse. However, a combination of tigatuzumab, a fully humanized DR5 agonist monoclonal antibody, with gemcitabine proved to be more efficacious by providing a double hit to kill both CSCs and bulk tumor cells. The combination therapy produced remarkable reduction in pancreatic CSCs, tumor remissions, and significant improvements in time to tumor progression in a model that is considered more difficult to treat. These data provide the rationale to explore the DR5-directed therapies in combination with chemotherapy as a therapeutic option to improve the current standard of care for pancreatic cancer patients.

### **NCI Grant Launches Nanotech Cancer Center**

<http://gazette.jhu.edu/2010/09/07/nci-grant-launches-nanotech-cancer-center/>

Faculty members associated with the Johns Hopkins Institute for NanoBioTechnology have received a \$13.6 million five-year grant from the National Cancer Institute to establish a Center of Cancer Nanotechnology Excellence. The new Johns Hopkins Center brings together a multidisciplinary team of scientists, engineers and physicians to develop nanotechnology-based diagnostic platforms and therapeutic strategies for comprehensive cancer care. Seventeen faculty members will be involved initially, with pilot projects adding more participants later. The Center will consist of four primary research projects, including one project led by Dr. Anirban Maitra, a 2004 Pancreatic Cancer Action Network – AACR Career Development Grant recipient, and associate professor of pathology and oncology at Johns Hopkins Kimmel Cancer Center. The project will focus on curcumin, a substance found in the traditional Indian spice turmeric. In preclinical studies, curcumin has demonstrated anti-cancer properties but, because of its physical size, it is not readily taken up into the bloodstream or into tissues. Engineered curcumin nanoparticles can more easily reach tumors arising in abdominal organs such as the pancreas. This team will try to determine whether nanocurcumin, combined with chemotherapeutic agents, could become a treatment for highly lethal cancers, such as pancreatic cancer.

### **University of Alabama Birmingham (UAB) Comprehensive Cancer Center Awarded \$11.5 Million Grant in Fight against Pancreatic Cancer**

<http://main.uab.edu/Sites/MediaRelations/articles/80795/>

The UAB Comprehensive Cancer Center, in collaboration with the University of Minnesota, won an \$11.5 million grant from the National Cancer Institute to explore groundbreaking pancreatic cancer research, prevention and treatment. The Specialized Program of Research Excellence (SPORE) in pancreatic cancer is designed to draw upon UAB and its partner's advances in genomic medicine and test new anti-cancer agents.

### **NCCN Clinical Practice Guidelines in Oncology on Pancreatic Adenocarcinoma**

<http://www.ncbi.nlm.nih.gov/pubmed/20876541>

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology are a statement of consensus of the panel regarding their views of currently accepted approaches to treatment. These guidelines only discuss tumors of the exocrine pancreas; neuroendocrine tumors are not included. The panel unanimously endorses participation in a clinical trial as the preferred option over standard or accepted therapy.

### **Phase I/II Study of Gemcitabine-Based Chemotherapy Plus Curcumin for Patients with Gemcitabine-Resistant Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20859741>

Researchers evaluated the safety and feasibility of combination therapy using curcumin with gemcitabine-based chemotherapy in gemcitabine-resistant pancreatic cancer patients. Median survival time after initiation of curcumin was 161 days, and 1-year survival rate was 19%. Combination therapy using oral curcumin daily with gemcitabine-based chemotherapy was safe and feasible in patients with pancreatic cancer and warrants further investigation into its efficacy.

### **Phase II Trial of Single Agent Ipilimumab (Anti-CTLA-4) for Locally Advanced or Metastatic Pancreatic Adenocarcinoma**

<http://www.ncbi.nlm.nih.gov/pubmed/20842054>

This phase II trial evaluated the efficacy of Ipilimumab for advanced pancreatic cancer. Twenty-seven patients with locally advanced or metastatic pancreas adenocarcinoma and minimal comorbidities were enrolled. There were no responders by response evaluation criteria, and single agent Ipilimumab (at 3.0 mg) was ineffective for the treatment of advanced pancreas cancer. However, a significant delayed response in one subject of this trial suggests that immunotherapeutic approaches to pancreas cancer may deserve further exploration.

### **Adjuvant Chemotherapy Drugs Equal for Pancreatic Cancer (ESPAC-3 Trial)**

<http://www.acor.org/news/display.html?id=9818>

<http://www.medpagetoday.com/Oncology/Chemotherapy/22072>

The European Study Group for Pancreatic Cancer (ESPAC)-3 trial studied whether fluorouracil or gemcitabine was superior in overall survival as adjuvant treatment following resection of pancreatic cancer. This phase III randomized controlled trial was conducted in Europe, Australia, Japan and Canada. Over 1,000 pancreatic adenocarcinoma patients who had undergone cancer resection were randomized to receive fluorouracil plus folinic acid or gemcitabine once a week for three of every four weeks. Median survival was 23.0 months for patients treated with fluorouracil plus folinic acid and 23.6 months for those treated with gemcitabine. Compared with the use of fluorouracil plus folinic acid, gemcitabine did not result in improved overall survival in patients with completely resected pancreatic cancer. Dr. Eileen O'Reilly wrote an editorial about this study and noted that although gemcitabine is typically the preferred treatment because of its more favorable toxicity profile and survival trend in prior studies, for patients unable to tolerate gemcitabine, there is a valid alternative with fluorouracil and folinic acid.

### **Adjuvant Chemotherapy with Fluorouracil Plus Folinic Acid vs Gemcitabine following Pancreatic Cancer Resection: A Randomized Controlled Trial**

<http://www.ncbi.nlm.nih.gov/pubmed/2082343>

This study evaluated whether fluorouracil or gemcitabine is superior in terms of overall survival as adjuvant treatment following resection of pancreatic cancer. Patients received either fluorouracil plus folinic acid, followed by fluorouracil or gemcitabine for 6 months. There were no significant differences in either progression-free survival or global quality-of-life scores between the treatment groups.

### **Adjuvant Gemcitabine Alone Versus Gemcitabine-Based Chemoradiotherapy After Curative Resection for Pancreatic Cancer**

<http://jco.ascopubs.org/content/early/2010/09/13/JCO.2010.30.3446>

The role of adjuvant chemoradiotherapy (CRT) in resectable pancreatic cancer is still debated. This randomized phase II intergroup study explored the feasibility and tolerability of a gemcitabine based CRT regimen after R0 resection of pancreatic head cancer and concluded that adjuvant gemcitabine-based CRT is feasible, well-tolerated, and not deleterious. Adding this treatment to full-dose adjuvant gemcitabine after resection of pancreatic cancer should be evaluated in a phase III trial.

### **Is Prior Cholecystectomy Associated with Decreased Survival in Patients with Resectable Pancreatic Adenocarcinoma Following Pancreaticoduodenectomy?**

<http://www.ncbi.nlm.nih.gov/pubmed/20864079>

Pancreatic cancer patients who present with biliary symptoms may undergo cholecystectomy and thus delay cancer diagnosis. Researchers hypothesized that prior cholecystectomy leads to decreased overall survival in patients with pancreatic adenocarcinoma. Upon reviewing 365 patients with a diagnosis of resectable periampullary pancreatic adenocarcinoma the median survival was 14 months for patients with a history of cholecystectomy and 16 months for those without. Previous cholecystectomy was not a predictor of survival on Cox regression analysis.

### **Neoadjuvant Docetaxel-Based Chemoradiation for Resectable Adenocarcinoma of the Pancreas**

<http://www.ncbi.nlm.nih.gov/pubmed/20828979>

The study assessed the safety and efficacy of neoadjuvant chemoradiation docetaxel-based regimen in patients with resectable adenocarcinoma of the pancreatic head or body. Of 34 patients with resectable pancreatic adenocarcinoma, tumor progression was documented in 11 patients (32%), stable disease was documented in 20 patients (59%), and partial remission was documented in 3 patients (9%). Neoadjuvant docetaxel-based chemoradiation is well-tolerated, and resected patients had a prolonged survival time.

### **NeoGemOx: Gemcitabine and Oxaliplatin as Neoadjuvant Treatment for Locally Advanced, Nonmetastasized Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20817204>

Results from a phase II study using gemcitabine-oxaliplatin neoadjuvant chemotherapy for patients with locally advanced unresectable pancreatic cancer shows that it was well tolerated and safe. There was substantive tumor regression in some locally advanced patients on this neoadjuvant regimen, offering the potential for curative resection. Researchers conclude additional studies using neoadjuvant GemOx should be conducted to evaluate the safety and efficacy of this combination.

### **First-Line Chemotherapy with Capecitabine and Temozolomide in Patients with Metastatic Pancreatic Endocrine Carcinomas**

<http://www.ncbi.nlm.nih.gov/pubmed/20824724>

Temozolomide is an active agent in metastatic pancreatic endocrine carcinomas. In-vitro data indicate that the combination of capecitabine and temozolomide is synergistic for induction of apoptosis in neuroendocrine tumor cell lines. The efficacy of capecitabine and temozolomide was retrospectively reviewed in metastatic pancreatic endocrine carcinoma patients. Results showed the two-year survival rate was 92%, and only 12% experienced grade 3 or 4 adverse events.

### **Preoperative 18[F]-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Predicts Early Recurrence After Pancreatic Cancer Resection**

<http://www.ncbi.nlm.nih.gov/pubmed/20862596>

An important step in deciding the treatment strategy for pancreatic cancer is to preoperatively predict the possibility of early recurrence. Researchers reviewed whether FDG-PET/CT before pancreatic cancer resection could predict tumor recurrence in the early postoperative period. The maximum standardized uptake (SUV(max)) values obtained by FDG-PET/CT were compared between two groups: patients with and without recurrence within the first 6 postoperative months. Results show preoperative SUV(max) was higher in the recurrence group during the early postoperative period, and a high SUV(max) was a risk factor for early postoperative recurrence.

### **Pancreaticoduodenectomy Can Be Performed Safely in Patients Aged 80 years and Older**

<http://www.ncbi.nlm.nih.gov/pubmed/20824366>

The outcomes after pancreaticoduodenectomy in patients 80 years and older were examined using retrospectively collected data from 1992 to 2009. Analysis showed there were no differences in overall complications, major complications, and mortality when comparing older (80 years and above) to younger (under age 80) patients. In a subset who underwent pancreaticoduodenectomy for ductal adenocarcinoma, older patients had a median survival time of 11.6 months compared to 18.1 months for younger patients. Researchers conclude age alone should not dissuade surgeons from offering resection to older patients.

### **Complications after Pancreatectomy for Neuroendocrine Tumors: A National Study**

<http://www.ncbi.nlm.nih.gov/pubmed/20599224>

Although resection of pancreatic neuroendocrine tumors (PNETs) has a demonstrated survival advantage, further evaluation of the overall morbidity of these procedures is needed. The study examined the outcome of major postoperative complications, including in-hospital mortality in all patients with a diagnosis of PNET who had undergone pancreatectomy. The study involved 463 patients. The overall composite postoperative complication rate was 29.6%. The majority of complications involved infections (11.1%), digestive complications (8.8%), or pulmonary compromise (7.3%). While in-hospital mortality rates were low for surgical resection of PNETs, there is a considerable overall postoperative complication rate associated with these procedures. Careful patient and surgery selection may be the key to a surgical treatment approach for PNETs that may optimize outcomes.

### **Redefining Mortality After Pancreatic Cancer Resection**

<http://www.ncbi.nlm.nih.gov/pubmed/20844977>

Distinct outcome measures such as in-hospital and 30-day mortality have been used to evaluate pancreatectomy results. Researchers posited that these measures could be compared using national data, providing more precision for evaluating published outcomes after pancreatectomy. Patients who underwent resection for pancreatic cancer were identified via SEER-Medicare database. Mortality was analyzed to evaluate risk of death at 60 days and at 2-years. Of 1,847 resected patients, 7.7% died within the first 30 days. Risk of death decreased significantly over the first 60 days; after 60 days, the risk did not decrease through 2 years, suggesting that mortality after pancreatectomy is not limited to early complication and late cancer phases.

### **Advances in Cancer Surgery: Natural Orifice Surgery (NOTES) for Oncological Diseases**

<http://www.ncbi.nlm.nih.gov/pubmed/20832296>

Natural orifice transluminal endoscopic surgery (NOTES) is a new concept that attempts to reduce the impact of surgery on the patient. In surgical oncology, several studies have already revealed that a minimally invasive approach provides at least the same, if not a better, long-term outcome. NOTES has become a clinical reality and today nearly every organ is accessible by a transluminal approach, in at least the experimental setting. Subsequent to published research, first clinical studies on NOTES in oncology were reported and the accuracy of transgastric peritoneoscopy for staging of pancreas cancer was shown to be similar to laparoscopy in humans. Although still somewhat controversial, the subject of natural orifice surgery in oncological disease indicates that current laboratory efforts to introduce NOTES into cancer surgery could be ready for cautious clinical investigations. The final determination of patient benefit will need well-constructed prospective study.

### **Image-Guided Stereotactic Radiosurgery for Locally Advanced Pancreatic Adenocarcinoma**

<http://www.ncbi.nlm.nih.gov/pubmed/20839073>

Real-time image-guided stereotactic radiosurgery (SRS) has made it possible to treat locally advanced unresectable pancreatic adenocarcinoma. Of 85 patients with locally advanced or recurrent pancreatic adenocarcinoma, tumor control (complete, partial, and stable disease) was observed in 78 patients for the duration of 3-36 months, with median of 8 months. Pain relief was noted in the majority of patients lasting for 18-24 weeks. Most of the patients died of distant disease progression while their primary tumor was controlled. Overall, median survival from diagnosis was 18.6 months and from SRS it was 8.65 months. SRS for unresectable pancreatic carcinoma can be delivered with minimal morbidity and a local tumor control rate of 91.7%. Survival is comparable or better than the reported results for advanced pancreatic cancer, specifically for the group of previously untreated patients with unresectable tumors. Development of distant metastases remains a significant factor.

### **Metformin Still Hot Topic in Cancer Prevention**

<http://www.medpagetoday.com/MeetingCoverage/EASD/22426>

Metformin may be the shining star rising out of the recent rediscovery of the connection between type-2 diabetes and cancer. This old drug could well perform a new trick for cancer prevention and even treatment. It is still too early to suggest that cancer patients should take metformin based on largely epidemiologic and mechanistic studies. But if a diabetes patient has cancer and metformin is an option for glycemic control, then it might be worth considering when choosing among antidiabetic agents.

### **Targeted Therapy Triggers Complex Mechanism of Resistance**

<http://www.acor.org/news/display.html?id=9852>



In order for targeted therapies against cancer to be effective, scientists need to understand upfront what related proteins in a signaling "network" makes a cancer cell resistant to a drug and selectively target them as well. Investigators report how cancer cells activate a network of pro-growth proteins that can bypass a molecule being therapeutically targeted. The researchers specifically found that many different genes were involved in rescuing cancer cells from treatment by different FDA-approved drugs that are designed to shut down the epidermal growth factor receptor – a major driver of cancer and a target of many new therapies.

### **'Synthetic Lethality' Strategy Improves Molecularly Targeted Cancer Therapy**

<http://www.medicalnewstoday.com/articles/202088.php>

Molecularly targeted therapies can reduce tumors rapidly. However, not all tumors respond to the drugs, and even those that do often develop resistance over time. Looking for a way to combat the problem of resistance, researchers at Fox Chase Cancer Center hypothesized that hitting already weakened cancer cells with a second targeted agent could kill them - but only if it was the right second agent. They report that knocking out one or the other target doesn't have a major effect, but knocking out both increases tumor cell death.

### **Role of Vitamin and Mineral Supplementation and Aspirin Use in Cancer Survivors**

<http://jco.ascopubs.org/content/28/26/4081.abstract>

Multivitamins and multi-minerals are widely used in the United States, but their efficacy and potential for harm in individuals who have cancer have received relatively little study. The use of vitamins and minerals by patients with cancer has unique implications because of their potential direct effects on existing cancers, effects on factors that may influence carcinogenesis, such as immunity, and interactions with treatment. Some evidence suggests that vitamin D at higher than standard doses may improve cancer-specific and overall survival for several cancer sites. Besides vitamin D, there is little evidence that nutritional supplements lower the risk of recurrence or improve survival from cancer, although some benefits may be possible in specific subgroups. Some data suggest that higher than standard doses of some vitamins or minerals could even enhance carcinogenesis or worsen survival in patients with cancer. The potential beneficial or adverse effects of dietary supplements and aspirin in survivors of cancer warrant further study.

### **Curing Cancer - What Treatable Tumors can Teach us About Improving the Odds in the Deadliest Cases**

<http://www.newsweek.com/2010/09/07/what-we-can-learn-from-curable-cancers.html>

The recognition that different tumors are powered by, and even addicted to, specific mutations is triggering a revolutionary change in how cancers are classified and treated. Treatment will not be based on the organ where the cancer originated, such as the pancreas or lung, but on the driver mutation that is the cancer's Achilles' heel. Genotyping is not routinely done in clinical trials testing experimental drugs. As a result, some claim cancer research has been a decade of missteps keeping effective therapies from reaching the market.

### **Current and Emerging Therapies for the Treatment of Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2939765/?tool=pubmed>

This article reviews the therapeutic options for the treatment of various stages of pancreatic cancer. Research in chemotherapy for metastatic disease has made only modest progress and the standard of care remains the purine analog gemcitabine. For resectable pancreatic cancer, presumed micrometastases provide the rationale for adjuvant chemotherapy and chemoradiation (CRT) to supplement surgical management. Numerous randomized control trials, none definitive, of adjuvant chemotherapy and CRT have been conducted and are summarized in this review, along with recent developments in how unresectable disease can be subcategorized according to the potential for eventual curative resection. This review also discusses palliative care and some avenues of research that show early promise.

### **Recent Stress May Reduce Cancer Therapy Effectiveness**

<http://www.cancercompass.com/cancer-news/article/34300.htm>

While the following research was done in breast cancer cell cultures the findings are intriguing and it will be interesting if this can be replicated in other cancer types. Physical or mental stress one or two days before cancer treatment may reduce the effectiveness of the therapy, Ohio State researchers report. In a series of experiments using breast cancer cell cultures, researchers found that mental and physical stress

activates a stress-related protein that can trigger a chain reaction that enables cancer cells to survive cancer treatments. Investigators discovered that the presence of the heat shock factor-1 (HSF-1) protein could impair the process that kills cancer cells even after their DNA was damaged by radiation or chemotherapy.

### **\$93,000 Cancer Drug Renews Debate on Price of Life**

<http://www.msnbc.msn.com/id/39329909/ns/health-cancer/>

Many new drug treatments cost nearly \$100,000 a year, sparking debate about how much a few months more of life is worth. For the last decade, new cancer-fighting drugs have been topping \$5,000 a month. Only a few of these keep cancer in remission. For most, the drugs may buy a few months or years. Insurers usually pay if Medicare pays, but some people have lifetime caps and many are uninsured because of job layoffs. For example, Genentech's Tarceva for pancreatic cancer costs \$4,000/month and boosts median survival by 12 days. Pancreatic cancer patients who added Tarceva to standard chemotherapy lived nearly 6½ months, versus 6 months for those on chemotherapy alone, spending \$24,000 for those extra 12 days.

### **End-of-Life Talks May Have Different Ending for Blacks**

<http://www.medpagetoday.com/Geriatrics/GeneralGeriatrics/22455>

According to a study from the Dana-Farber Cancer Institute, the wishes expressed in discussions about end-of-life care do not necessarily translate into action for black patients. In a multi-institutional prospective study of more than 300 patients with advanced cancer, black patients tended to receive life-prolonging measures at the end of life -- even when they had do-not-resuscitate orders in place or stated a preference for comfort care only. White patients appeared to get more benefit from end-of-life discussions, receiving care largely in accordance with their stated preferences. This occurred despite the finding that just over one-third of patients in both groups talked about end-of-life care with their doctors. The likely non-patient factors playing a role include less continuity of care for black patients, leading to less readily available documentation of end-of-life preferences, or racial biases among clinicians about what care patients want. Either way, too few patients actually have end-of-life care discussions with their physician.

### **'Magic Mushrooms' Possible Treatment in End-Stage Cancer**

<http://www.medpagetoday.com/Psychiatry/GeneralPsychiatry/22042>

<http://www.acor.org/news/display.html?id=9811>

UCLA researchers report the active ingredient in "magic mushrooms," psilocybin, may be useful to treat the anxiety and stress associated with end-stage cancer. In a small placebo-controlled randomized trial, the drug was safe both physiologically and psychologically, and despite a low dose the drug appeared to have some beneficial effect on mood. Psilocybin is an hallucinogen with some effects similar to those of LSD, but its effects are less emotionally intense and less likely to cause panic reactions and paranoia.

### **Suicide in Patients with Pancreatic Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20824626>

Depression is highly prevalent in patients with pancreatic cancer and can result in suicide. The authors report suicide rates among patients with pancreatic cancer in the United States and identify factors associated with greater suicide rates. Among 36,221 patients followed for 22,145 person-years, the suicide rate was 135.4 per 100,000 person-years. The corresponding rate in the US population aged 65-74 years was 12.5. Results show male pancreatic adenocarcinoma patients have a risk of suicide nearly 11 times that of the general population. Patients who undergo an operative intervention are more likely to commit suicide, generally in the early postoperative period

### **Impact of Hospice Disenrollment on Healthcare Use and Medicare Expenditures for Patients with Cancer**

<http://www.ncbi.nlm.nih.gov/pubmed/20805463>

[http://www.cancer.gov/ncicancerbulletin/090710/page3?utm\\_source=feedburner&utm\\_medium=feed&utm\\_campaign=Feed%3A+ncicancerbulletin+%28NCI+Cancer+Bulletin%29#](http://www.cancer.gov/ncicancerbulletin/090710/page3?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+ncicancerbulletin+%28NCI+Cancer+Bulletin%29#)

Cancer patients are the largest diagnostic group of hospice users. However, 11% to 15% of hospice users disenroll from hospice, and little is known about their health care use and Medicare expenditures. Researchers used SEER data of cancer patients who used hospice between 1998 and 2002. Cancer patients who disenrolled from hospice were more likely to be hospitalized, admitted to the emergency department or placed in the intensive care unit, and die in the hospital. Patients who disenrolled from

hospice died a median of 24 days following disenrollment, suggesting that the reason for hospice disenrollment was not improved health. Hospice disenrollees incurred higher per-day Medicare expenditures than patients who remained with hospice until death. Hospice disenrollment is a marker for higher health care use and expenditures for care.

### **Death at Home Less Distressing for Cancer Patients and Families**

<http://www.acor.org/news/display.html?id=9837>

<http://www.cancercompass.com/cancer-news/article/34190.htm>

Cancer patients who die in the hospital or an intensive care unit have worse quality of life at the end-of-life, compared to patients who die at home with hospice services. Moreover, their caregivers are at higher risk for developing psychiatric illnesses during bereavement, according to a study by researchers at Dana-Farber Cancer Institute.