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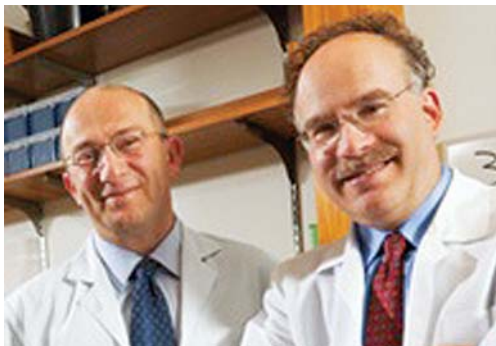
Supported by educational grants from Genentech and sanofi-aventis U.S.

The concept of tumor-cell dissemination was born more than a century ago. The use of molecular tools has resulted in explanations of how single tumor cells were both the descendants of a known primary tumor and the potential precursors of subsequent metastasis.

A Promising New Prognostic Marker Garner Attention

■ BOSTON — ACCORDING TO ITS developers, Daniel Haber, MD, PhD, director of the MGH Cancer Center and Mehmet Toner, PhD, director of the MGH BioMEMS Resource Center, a novel prognostic technology being called a “liquid biopsy,” may be a highly effective way to guide individualized treatment for cancer patients and offer better screening alternatives than mammogram and colonoscopy.

The test uses a microchip that resembles a lab slide covered in 78,000 tiny bristle-like posts, which are coated with antibodies that bind to tumor cells. According to the developers, when the patient’s blood is forced across the chip, cells ping off the posts like balls in a pinball machine. The cancer cells that adhere are nuclear stained, making them glow so researchers can capture them for study.



Daniel Haber, MD, PhD and Mehmet Toner, PhD

The test is the most promising of several dozen that companies and universities are developing to capture circulating tumor cells. The only test currently on the market to detect CTCs — CellSearch — records a cell count, but does not capture whole cells that can be analyzed in order to make more effective treatment decisions.

Four major US cancer centers will soon begin testing the technology: Massachusetts General, Memorial Sloan-Kettering Cancer Center in New York City, the University of Texas M. D. Anderson Cancer Center in Houston, and the Dana-Farber Cancer Institute in Boston. They are one of the “dream teams” sharing a \$15 million grant from the *Stand Up to Cancer* telethon run by the American Association for Cancer Research (AACR).

According to Dr. Toner, it will take them at least 5 years to test the new method before it will be out on the market. He added that the method is a significant one, “because of its potential to turn cancer into a chronic disease, which makes it easier for them to monitor their patients individually and to respond with treatment to the genetic makeup of their cancer.” ♦

Study Finds Lower Risk for Esophageal Cancer for Patients With GERD

■ ANN ARBOR — ACCORDING TO research from University of Michigan gastroenterologists, the risk of esophageal cancer among patients who suffer from gastroesophageal reflux disease (GERD) is not as high as previously thought. Some estimates say up to 25% of people in the US suffer from GERD.

In a statement, study author, Joel Rubenstein, MD, MSc, said, “Since GERD is incredibly common, many people may be worried about their increased risk for developing cancer due to GERD. This study helps put that risk into perspective and may help physicians decide when screening to prevent cancer is needed.”

GERD is characterized by symptoms that result from repeated exposure of stomach acid to the lining of the esophagus. It occurs when the lower esophageal sphincter does not seal off the esophagus from the stomach. Heartburn and regurgitation are the most common symptoms.

The research recently published in the *American Journal of Gastroenterology* found:

- Women with GERD likely have a low rate of esophageal adenocarcinoma, similar to the rate of breast cancer in men;
- The rate of esophageal adenocarcinoma in white men who are 60 years old with weekly GERD is just one third of their rate of colorectal cancer or 34.6 per 100,000 patients per year;
- The rate of esophageal adenocarcinoma in younger white men with GERD is less than one third of their incidence of colorectal cancer.

Dr. Rubenstein, an investigator with the Department of Veterans Affairs Center for Clinical Management Research in Ann Arbor and Assistant Professor in the University of Michigan’s Department of Internal Medicine, concluded that, “Screening for esophageal adenocarcinoma should not be performed in men younger than age 50 or in women because of the



Joel Rubenstein, MD, MSc

very low incidences of the cancer, regardless of the frequency of GERD symptoms. However, in white men with weekly GERD over the age of 60, the incidence of esophageal adenocarcinoma is substantial and may warrant screening.” ♦

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Study Finds Racial Disparity in HCC Survival

■ ANN ARBOR, MI — A NEW STUDY reported in a recent issue of the Archives of Surgery, found that mortality rates among patients with early-stage hepatocellular carcinoma (HCC) were nearly 25% higher in blacks than whites.

Using the Surveillance, Epidemiology and End Results (SEER) Program, the researchers studied survival data on 13,244 stage I or II HCC patients to assess racial/ethnic differences in overall and treatment-related survival. Base- and treatment-stratified models were included in the analyses.

In the base survival model, black and hispanic patients seemed more likely to die of HCC when compared with white patients, whereas Asians were at lower risk. After adjusting for treatment type received, black patients had a 12% increased rate of death when compared with white patients. Hispanic and white patients had similar mortality after stratification, and Asian patients had a 16% lower death rate. Interestingly, black and Hispanic patients were both less likely to receive invasive therapies compared with white, Asian, or other groups.

Overall, 5-year survival rates were 17.9%. When analyzed by racial/ethnic group, survival rates were highest for Asian patients (22%), followed by white patients (18.2%), other groups (17.1%), and Hispanics (15.2%). The 5-year survival was lowest for black patients, at 12.2%.

Richard D. Schulick, MD, a professor of surgery, oncology, gynecology and obstetrics, and biomedical engineering at the Johns Hopkins University

School of Medicine, Baltimore, Maryland, was invited to comment on the paper. In a statement, Dr. Schulick said, "This is alarming, because stage I and II disease is typically treated with good outcomes. If only 32.8% of patients received invasive therapy for early stage HCC, then this study points to a clear underuse of therapy for patients who are likely to receive the most benefit."

He added that there are many limitations associated with the use of large databases that cannot capture all relevant



Richard D. Schulick, MD

factors, such as tumor characteristics, comorbidities of patients, or details of the treatments given to the patients.

The study authors concluded, "The issue of health-related racial/ethnic disparities is complicated, but improving access to care is one step. Further research regarding the heterogeneity of treatment effects is needed. Persistent racial/ethnic disparities in survival even after adjusting for the effects of treatment are of particular concern and may be related to the quality of health care delivered. This variation may require a comprehensive evaluation of centers where minorities receive care to standardize and improve the structure and process of cancer care delivery." ♦



The Eighth Annual Gastrointestinal (GI) Cancers Symposium

JANUARY 20–22, 2011, THE MOSCONE WEST BUILDING, SAN FRANCISCO, CA: The 3-day symposium will highlight important advances in research and emerging therapies for gastrointestinal cancers with a variety of sessions designed for a multidisciplinary audience. The meeting has 32 oral abstract presentations: 8 esophagus and stomach presentations; 11 pancreas, small bowel & hepatobiliary tract; and 13 colon and rectum presentations.

GIST Protein That Drives Survival Identified

A study of genetically modified mice lacking the gene for ETV1 showed they have far fewer of the gastrointestinal cells that are prone to a specific type of tumor. The finding suggests that ETV1 is a survival factor for GISTs.

■ NEW YORK — SINCE THE INTRODUCTION of imatinib (Gleevec), survival rates for patients with gastrointestinal stromal tumors (GISTs) have increased substantially and recurrence has fallen by approximately two thirds. But over time, many patients develop resistance to the drug.

Now, researchers at Rockefeller University and Memorial Sloan-Kettering Cancer Center have identified a molecule that acts as a survival factor for gastrointestinal tumors, a finding that may lead to next-generation therapies that address the drug-resistance issues associated with long-term use of imatinib. By analyzing patient tumor samples stored at MSKCC,

the researchers found that the protein ETV1 is expressed in all GISTs at significantly greater levels than in any other type of tumor.

Using RNA interference, in which small RNAs are deployed to prevent gene expression, they blocked ETV1 in GIST cell lines. The result was a decrease in cell division and an increase in cell death, findings that indicated that GISTs require ETV1 for growth and survival. According to the researchers, about 5% of GISTs are KIT negative by immunohistochemistry. Because all GISTs express ETV1, we now have a very good biomarker for diagnosing GISTs. ♦

Plant Offers Insights Into Peutz-Jeghers Syndrome

■ LEIDEN, THE NETHERLANDS — From studying a plant, Dutch scientists recently gained new insights into Peutz-Jeghers Syndrome, the hereditary disorder in which people develop intestinal polyps that eventually turn into malignant tumors.

Principle investigator, Professor Maikel Peppelenbosch of Cell Biology at the Erasmus Medical Center in Rotterdam said

in a statement, "With experiments on these plants we now have a better understanding of how cancer cells react in the human body. Cancer cells that sense they are getting too much food will rapidly multiply. By imitating this process in plants and studying what happens to the plant cells we have learned a great deal about the development of Peutz-Jeghers Syndrome." ♦



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Current Advances in Biologic Therapy in Colorectal and Pancreatic Cancer: Part III

UPDATE ON BIOLOGIC THERAPY IN PANCREATIC CANCER

PHILADELPHIA, PA — THIS report on pancreatic cancer, delivered by Philip A. Philip, MD, PhD, Professor of Medicine and Oncology, Karmanos Cancer Institute, Detroit, concludes *GIORO's* coverage of a special session on Biologic Therapy held at ISGIO's 2010 meeting.

Dr. Philip started his presentation by elucidating the grim clinical realities of pancreatic cancer. "Most of the patients we see have advanced disease, and about 10% of patients come to us with end-stage disease, where nothing can be done. Depending on the circumstance, some end-stage patients are put on protocols, but they die within a few weeks of starting treatment."

Status of Cytotoxic Therapy

"Gemcitabine is the drug we use in advanced disease. I do not use the term "gold standard," because it can't really be considered a standard, with a median survival still being 6 months or less, with less than 20% of the patients surviving at 1 year," noted Dr. Philip.

He continued, "In terms of cytotoxic combinations in average patient populations, we haven't really seen a benefit in adding another cytotoxic drug. But subsets of patients with good performance status and low tumor volume may benefit from combinations with platinum, such as cisplatin or oxaliplatin; or fluoropyrimidines like 5-FU or capecitabine."

Dr. Philip noted that the only targeted agent to show some benefit is

erlotinib, which was combined with gemcitabine in a phase III trial published in *JCO* by Moore et al. [Figure 3-1] "In this study, there was an improvement in survival and performance-free survival, but as you can see from the data, improvement was marginal, and we question its clinical benefit in this disease," said Dr. Philip.

He alluded to three phase III trials that all failed and then posited why angiogenesis treatment has shown so little benefit in this group of patients. "Possibly because of the extreme hypovascularity of the disease and the presence of the dense stroma that may impede the diffusion of drugs into the tumor cells and microenvironment." Therefore, the stromal compartment has become an increasingly important area in trying to deal with this disease.

cancer cells," commented Dr. Philip.

Another Promising Pathway

"The other interesting pathway is the hedgehog-signaling pathway, which is a potential target in pancreas cancer," said Dr. Philip. He explained that there are a number of drugs, including GDC-0449 that are targeting this pathway. "In this case it is Smoothed (SMO) and in that way, you may really be able to arrest tumor growth and also work on angiogenesis," he added.



Philip A. Philip, MD, PhD

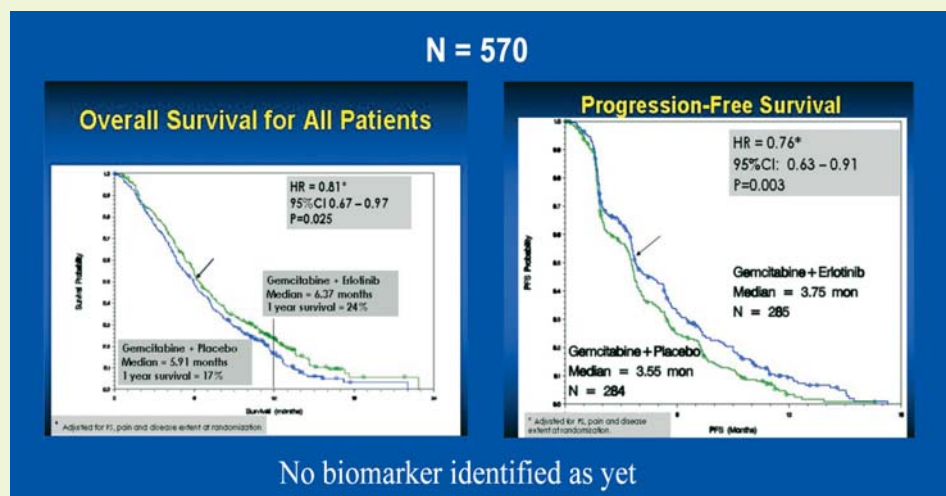


Fig 3-1: Erlotinib plus gemcitabine. Moore et al: *J Clin Oncol*, 2007.

Targeting the Stroma

Dr. Philip examined data based on a phase I/II study by Von Hoff's group and other preclinical studies showing that nab-paclitaxel can target the stroma. Nab-paclitaxel in combination with gemcitabine has gone into phase III study. "It is currently accruing, requiring more than 600 patients. We'll see the results probably within the next 12 months. This is a treatment that may be considered an early step in trying to attack the stroma in pancreas

Dr. Philip continued, looking at a highly publicized trial using a different hedgehog pathway inhibitor. "In pre-clinical studies using tumor models, IPI-926 plus gemcitabine has shown evidence of at least added activity," said Dr. Philip, continuing his discussion with a look at several other interesting pathways and early preclinical (continued on page 4)

Gene Mutation Might Confer Greater Susceptibility To Recessively Inherited Gastrointestinal Cancers

MONTREAL — ACCORDING TO research recently published in the *New England Journal of Medicine*, a single mutation in the BUB1B gene appears to result in greater susceptibility to recessively inherited gastrointestinal cancers.

Thomas Rio Frio, PhD, and colleagues of the McGill University Health Centre in Montreal, genetically analyzed a patient who experienced adenomatous polyps and subsequent multiple primary invasive gastrointestinal adenocarcinomas 20 years after he was diagnosed with adenocarcinoma of the ampulla of Vater, at age 34.

The researchers identified a germ-line homozygous intronic mutation in the BUB1B gene that resulted in a splice site favored over the preferentially used site.

In a statement, the authors concluded, "Our findings expand the phenotype associated with BUB1B mutations and the mosaic variegated aneuploidy syndrome to include common adult-onset cancers and provide evidence for the interdependency of the APC protein (encoded by the adenomatous polyposis coli gene) and the BUBR1 protein (encoded by BUB1B) in humans." ♦

ISGIO IMPRESSIONS



MICHEL DUCREUX, MD

Institut Gustave-Roussy, Villejuif, France
ISGIO is interesting to learn about current practice in the US — difficult to do at a huge meeting such as ASCO. Here you see clinical practice. You learn interactively how actual patients are managed by Japanese, US, and European experts. It shows that it is impossible to do GI oncology without a multidisciplinary approach.

In the News

CMS Launches First Phase of "Physician Compare" Website

WASHINGTON, DC—The Centers for Medicare & Medicaid Services (CMS) enhanced its Physician Directory tool with a feature called Physician Compare, which provides information about physicians and the services they provide. The new tool, which was required by the Affordable Care Act (ACA) of 2010, expands the doctor-specific information into the suite of informational tools for Medicare beneficiaries and other consumers.

In a statement, CMS administrator, Donald Berwick, MD, said, "The new Physician Compare tool begins to fill an important gap by providing more information about physicians. This paves the way for consumers to have similar information about their physicians as they have for nursing homes, home health agencies, and health and drug plans."

Physician Compare also shows consumers whether the practice reported certain data to CMS through the Physician Quality Reporting System, formerly known as the Physician Quality Reporting Initiative (PQRI). Currently, the PQRI reporting system is a voluntary reporting program that rewards physicians and other eligible healthcare professionals for reporting data on quality measures related to services furnished to Medicare beneficiaries. ♦

(continued on page 4)



Donald Berwick, MD

In the News... (continued)

New Health Care Rules to Take Effect

WASHINGTON, DC — IMPORTANT changes to US health-insurance rules are anticipated as new provisions related to last year's massive health care bill take effect. The new rules are designed to help those caught in Medicare's "doughnut hole," offer seniors more preventative care, and limit how much of their customers' money health-insurance companies can

keep for overhead and profit.

Another provision starts closing the "doughnut hole" for seniors on Medicare Part D. Now, beneficiaries with drug costs that surpass \$2,840 within a year must pay full price for all drugs until their annual drug costs reach \$4,550. The new rule offers a 50% discount on brand-name medicines for those who fall in that gap.

A rule giving seniors free screenings

for cancer and other diseases is on the horizon. Nearly all Medicare beneficiaries will be able to receive for free all "preventive services" screenings given an A or B rating by the U.S. Preventive Services Task Force. That could include mammograms, colorectal cancer screening, bone mass measurement, and nutritional counseling.

The new rules also include a mandate that requires that insurers spend at least

80% of premiums on their customers. The companies must either spend this money to pay insurance claims or use it for activities that improve customers' health. For policies that are sold to large groups instead of small companies and individuals, the number is even higher: 85%. Previously, there were no federal restrictions on insurance companies' spending. ❖

Current Advances in Biologic Therapy in Colorectal and Pancreatic Cancer (cont'd from page 3)

work that have the possibility of leading to phase III trials.

Conclusion

"I want to finish with a study looking at FOLFIRINOX vs. gemcitabine as first-line treatment for metastatic pancreatic adenocarcinoma that was presented at ASCO 2010. It was not biologic, but it has a lot of impact on how we look at treating this disease," said Dr. Philip. The trial showed that overall survival with FOLFIRINOX improved by over 4 months. This is a major improvement over gemcitabine that we haven't seen any time before," stressed Dr. Philip.

Of particular importance, according to Dr. Philip is that a number of trials would be launched in this study trying to confirm FOLFIRINOX in the US population. "And there's also a move to use FOLFIRINOX in early disease in the adjuvant and neoadjuvant setting," he said.

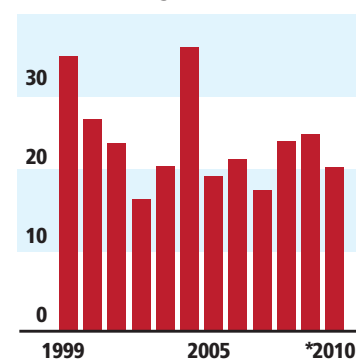
"We need better understanding of the complex biology in this disease and future studies must consider biomarker-driven patient selection and the use of a multi targeted approach, which is always a challenge when working with various pharmaceutical companies," concluded Dr. Philip. ❖

2010 Was a Down Year for Drug Approvals, 2011 Might Follow Suit

WASHINGTON, DC — BASED ON statistics presented by Center for Drug Evaluation & Research Director Janet Woodcock during the recent FDA/CMS Summit for Biopharma Executives, the number of applications for approval of new molecules dropped sharply in 2010. As of November 15, FDA has received only 17 new molecular entity (NME) applications, about half the total received in 2009. Since the number of NME approvals typically tracks a year behind the number of NME filings, that is a sign of a relatively sparse crop of new drugs in 2011. That comes on the heels of a down year in 2010, when FDA cleared 22 NMEs and novel ther-

apeutic biologics, reversing a nicely increasing trend in 2008 and 2009. ❖

Slow Years
New drugs approved by the Food and Drug Administration



*Unofficial Source: FDA

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Abstracts must be written in English and begin with a concise **Title** followed by a list of all **Authors** and their respective **Affiliations**. The body of the abstract should not exceed 500 words and must contain the following labeled sections:

- **Background**, including a statement of the hypothesis or research question;
- **Methods**, an explanation of the study design and experimental methods used;
- **Results**, a summary of the major findings; and

ISGIO invites all participants to submit abstracts describing original work to the 2011 Conference Organizing Committee.

- **Conclusions**, a summary of the overall findings and implications of the results

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