ASCO® DAILY NEWS

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THE OFFICIAL DAILY NEWS SOURCE OF THE ASCO ANNUAL MEETING

Dr. Mark Kris Receives Society's First Humanitarian Award

The ASCO Humanitarian Award honors an oncologist who personifies ASCO's mission and values by going above and beyond the call of duty in providing outstanding patient care through innovative means or exceptional service and leadership in voluntary, uncompensated endeavors in the United States or abroad. This award is unique in that nominations were accepted from visitors to Cancer.Net, ASCO's patient-information website, as well as from ASCO members. The award was presented during yesterday's Opening Session.

In both his professional capacities and his personal time, Mark G. Kris, MD, of Memorial Sloan-Kettering Cancer Center, has exhibited a level of dedication and compassion that has touched the lives of countless individuals. According to his colleagues at Memorial Sloan-Kettering Cancer Center, Dr. Kris has been a pioneer in the advancement of lung cancer research and treatment. In addition to his contributions in developing new treatment approaches, he has demonstrated exemplary patient care, even making house calls when a visit to the hospital would be too taxing.

Mark G. Kris, MD

Dr. Kris has participated in two full marathons and half-marathons to benefit patients with cancer through Fred's Team (which raises funds for cancer research at Memorial Sloan-Kettering Cancer Center) as well as all seven "Run as One" races sponsored by The Thomas Labreque Foundation supporting lung cancer awareness and research.

"It's very gratifying to give patients with lung cancer and their families a place where they can celebrate their successes and meet other families that are going through the illness," Dr. Kris said in an interview with *ASCO Daily News*. "Seeing families rally around a member who is fighting the disease is even better than crossing the finish line in the marathon."

He has also served on the medical advisory boards of two non-profit organizations: Uniting Against Lung Cancer and Cancer*Care*. Through Cancer*Care* he has spoken to thousands of patients with cancer and their care-givers through educational telephone conferences.

Efforts Outside of Oncology

However, the effects of Dr. Kris' work are not limited to cancer care. He has spent much of his free time assisting with humanitarian efforts in poverty- and disaster-stricken areas in the United States, as well as overseas. Since 2000 he has assisted Habitat for Humanity in New York City, building new homes and renovating older homes for individuals and families in need. In 2004 and 2005, he traveled to Siquirres, Costa Rica — a rural area with limited economic opportunities — to help youth there build a basketball court and a church.

After Hurricane Katrina, Dr. Kris traveled to Biloxi, Mississippi, to rebuild damaged homes. He also made approximately six trips between 2006 and 2009 to Dulac, Louisiana, a town deep in the Louisiana bayou that had been devastated by Hurricane Rita in 2005 and Hurricane Ike in 2009, where many live below the poverty line. Dr. Kris helped the community rebuild homes there.

When Walton, New York was flooded in 2006, Dr. Kris helped clean water-damaged basements and raised funds to supply furnaces to homeowners. After the earthquake in Haiti, he traveled to the small town of Furcy, where he led efforts to rebuild a school, assisted in the construction of new buildings, worked in a health clinic, formed a scholarship to build additional schools, and acquired seeds for local residents to plant new crops.

"There's a tremendous need for others to get involved," Dr. Kris said of his disaster-relief work. "There is a need for all kinds of skills, from drivers to cooks to good listeners. Right after Hurricane Katrina, people had to tell their stories — you just had to find time to listen. All you need is a plane ticket and a set of ears."

Service to Science

Dr. Kris, a medical oncologist, currently serves as Chief of the Thoracic Oncology

See Humanitarian Award, Page 15B

INSIDE THIS SECTION

Increase in Cancer Survivors Demands Dedicated Survivorship Care Plans

Confusion among oncologists and primary care physicians over provision of follow-up care leads to many survivors feeling "lost in transition"

The number of cancer survivors in the United States has steadily increased throughout the past few decades due to advances in cancer screening, treatment, and supportive care. This figure is expected to continue to rise with the aging of the population. The most recent estimate indicates that the number of cancer survivors in the United States was more than 11.7 million in 2007, according to data from nine Surveillance, Epidemiology, and End Results programs (SEER).[1] Cancer is a curable disease for some but, more often, a chronic disease that people live with for many years after treatment. However, the question of who will care for these survivors and the late or long-term adverse effects of their disease is of growing concern among members of the health care community. Fridays' Education Session, "Survivorship Care: Whose Job Is It?", examined recent survivorship data and trends, as well as some of the attitudes and beliefs among oncologists and primary care physicians facing the growing challenge of caring for this population.

In 2005, the Institute of Medicine published a report *From Cancer Patient to Cancer Survivor: Lost in Transition*. The report suggested that the current system of care was failing many cancer survivors who were getting "lost in transition" as they moved from active treatment to the recovery or survivorship phase of their care, with all of its unique medical and psychosocial follow-up needs.

Julie H. Rowland, PhD, Director of the National Cancer Institute's Office of Cancer Survivorship, who served as chair of the session, echoed this concern in an interview with *ASCO Daily News*.

"What many survivors tell us happens is that after definitive treatment ends, they fall into an abyss. It is not clear to them who should be following them, where they should

See Survivorship Care Plans, Page 6B

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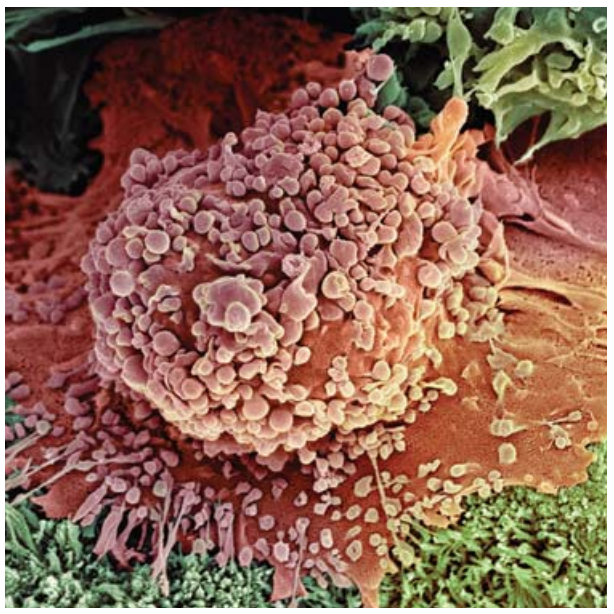

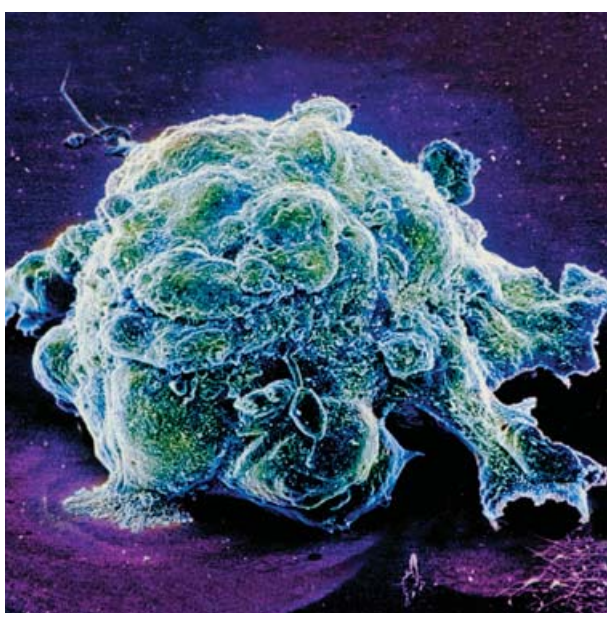

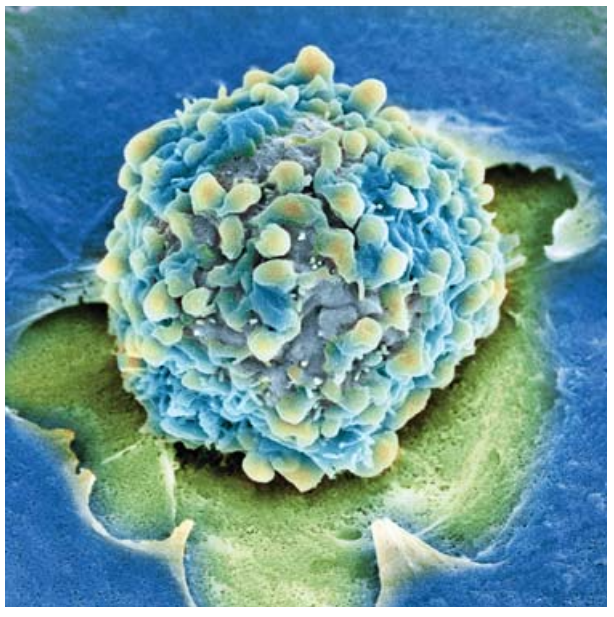

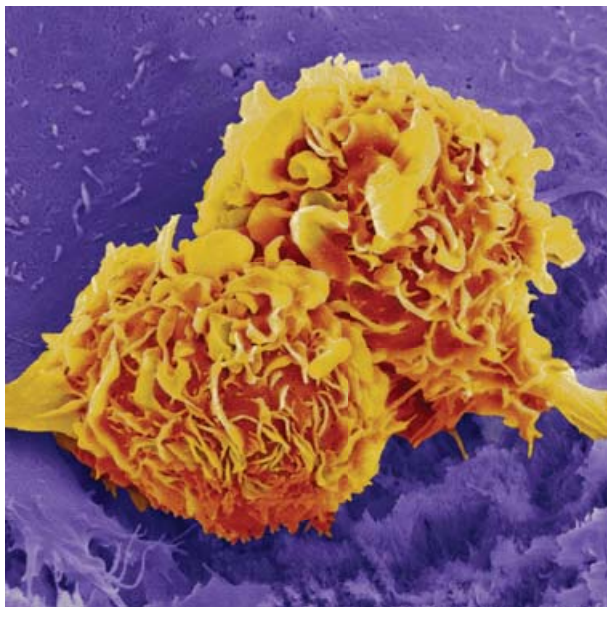

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Pediatric Oncology Award Presented for Research in Novel Approaches to Pediatric Tumors

Researcher focuses on pathways that drive tumor growth in pediatric sarcomas and the effect they have on existing and potential future therapies

Lee J. Helman, MD, of the National Cancer Institute (NCI) has been awarded the 2011 Pediatric Oncology Award. Dr. Helman accepted the award and gave his lecture, "Pathways to New Targets for Pediatric Sarcomas," during a Special Session yesterday.

Dr. Helman's research focuses on the basic biology of pediatric sarcomas, such as rhabdomyosarcoma, Ewing's sarcoma, and osteosarcoma in the laboratory, and he uses the insights gained in clinical trials of novel therapies.

"My colleagues and I are working on three main areas," said Dr. Helman in an interview with *ASCO Daily News*. "We continue to work on IGF signaling, trying to identify mechanisms of acquired resistance and to identify patients who are likely to respond to IGF-1 receptor antibodies. We also are using shRNA screening to identify new targets in rhabdomyosarcoma, and we are developing inhibitors of EWS-FLI-1 in Ewing's sarcoma."


Lee J. Helman, MD

Throughout his career, Dr. Helman has made many important contributions to understanding the role IGF signaling in pediatric tumors, including identifying IGF-2 as an important growth and survival factor in rhabdomyosarcoma, demonstrating that IGF-1R was necessary for EWS-FLI-1-transforming activity, and identifying the loss of imprinting of IGF-2 in rhabdomyosarcoma and Ewing's sarcoma. He also identified ezrin as a key regulator of metastases in osteosarcoma.

When asked about the goals he has for his research, Dr. Helman said that he would like to improve pediatric sarcoma therapy "by developing effective novel therapies that target critical pathways that drive growth of these tumors, and by rationally combining these approaches with both standard and other novel treatments."

Combining Research and Patient Care

Despite the important strides he has made in the field of pediatric oncology, Dr. Helman hasn't always known that he wanted to embark on an oncology research career. As an undergraduate at George Washington University, Dr. Helman realized his call to medicine, but it wasn't until he was attending the University of Maryland School of Medicine that he solidified his career path.

"In medical school I became really interested in research because I saw its impact,"

See Pediatric Oncology Award, Page 14B

Pediatric Oncology Sessions by Day

Today, June 5

Pediatric Oncology General Poster Session
(8:00 AM – 12:00 PM, Hall A,
South Building

Pediatric Oncology Poster Discussion Session (Posters: 8:00 AM – 12:00 PM, Hall A, South Building; Discussion: 11:30 AM – 12:30 PM, S504, South Building)

Plenary Session
1:00 PM – 4:00 PM, Hall B1, North Building
Plenary Session includes two pediatric oncology abstracts. See the Annual Meeting Program *for exact presentation times.*

Abstract #1: Comparison of high-dose methotrexate (HD-MTX) with Capizzi methotrexate plus asparaginase (C-MTX/ASNase) in children and young adults with high-risk acute lymphoblastic leukemia (HR-ALL): A report from the Children's Oncology Group Study AALL0232.
E. C. Larsen

Abstract #2: Busulphan-melphalan as a myeloablative therapy (MAT) for high-risk neuroblastoma: Results from the HR-NBL1/SIOPEN trial.
R. L. Ladenstein

Clinical Science Symposium: Anti-angiogenic Therapies and Biomarkers in Pediatric Cancer
4:30 PM – 6:00 PM, S504, South Building

Monday, June 6

Oral Abstract Session:
Pediatric Oncology II
8:00 AM – 11:00 AM, S504, South Building

Advances in Risk Stratification, Biology, and Treatment of Neuroblastoma
11:30 AM – 12:45 PM, S504,
South Building

Challenges in Treating Children, Adolescents, and Adults with Benign and Malignant Vascular Tumors
1:15 PM – 2:30 PM, S504,
South Building

Update on the Treatment of Adolescents and Young Adults with Acute Lymphocytic Leukemia (M17) — Ticketed Session
3:00 PM – 4:15 PM, E451a,
East Building

To Transplant or Not to Transplant? Current Controversies in Transplantation for Pediatric Acute Leukemias
4:45 PM – 6:00 PM, S504,
South Building

To Keep Them from Injustice: Reflections on Care of the Unauthorized Immigrant with Cancer

EXPERT EDITORIAL

Paul R. Helft, MD

You see in your office for an initial visit a 45-year-old Spanish-speaking man with newly-diagnosed metastatic pancreatic cancer. His work up included a computed tomography scan and needle biopsy of a liver lesion, which were performed at a county public-access hospital with which you are not affiliated. In the course of your encounter with the patient and his wife, he informs you that he immigrated to this country from the Mexican State of Oaxaca nearly 9 years ago and that he has worked in a meat packing facility since that time. He entered the United States without documentation and obtained working papers illegally. In your state, the patient cannot obtain access to Medicaid without proof of citizenship and his employer does not provide health insurance. As you begin to discuss his diagnosis, prognosis, and options for treatment, you struggle with how to provide the patient with medical treatments you would ordinarily provide without forethought.


Paul R. Helft, MD

The situation presented in this vignette is now common in many locations across the United States. Estimates from 2010 suggest that more than 11 million unauthorized immigrants reside in the United States.[1] The United States federal government, state governments, and individual health care institutions have all wrestled with this issue in ways that have not led to satisfactory resolution for anyone.[2] I do not know of any systematic assessments of the attitudes of oncology professionals regarding this emotionally charged issue. However, in many informal conversations with colleagues around the country, I know that many have struggled with how to fulfill their perceived obligations in such situations. Some — in States such as Texas — face such issues every day. Because of current realities in medical economics and reimbursement policy, there simply isn't enough profit margin in most practices realistically to offer free care to everyone who needs it. I cannot offer any easy, neat, or roundly satisfying answers to the difficult questions raised by the challenge of providing cancer care to unauthorized persons who come to us with a cancer diagnosis. I offer instead some thoughts in which I attempt to clarify why it is we feel so much obligation to do so, and whether the reasons behind this sense of obligation point us toward a consistent stance we should have toward the problem.

Justice for All or for Each Individual?

As stated in the Oath of Hippocrates (as translated by Steven Miles, MD), "I will use regimens for the benefit of the ill in accordance with my ability and my judgment, but from what is to their harm or injustice I will keep them.… Into as many houses as I may enter, I will go for the benefit of the ill.…"[3] This excerpt holds an important clue about how the foundations of our ethical framework compel us to feel obligations toward this group of patients. I do not intend to imply that the words contained in the Oath of Hippocrates are in any way a definitive statement of Western or any other medical ethics; however, this mysterious document has endured for more than 2,400 years and, still, some version of the Oath is recited by medical students around the United States at the time of their graduations as doctors of medicine.[4] I quote the passages here because the words raise two very important issues.

The first is the striking use of the word "injustice." Although we immediately feel at home with the first part of this sentence, which concerns our overall obligations to advocate for what ethicists call "beneficence," the second construct, which asserts that one of our central obligations is to protect our patients from injustice, is less acutely obvious. Yet the unauthorized immigrant with cancer who seeks treatment from us seems exactly like all of our patients with cancer: having cancer in and of itself seems unjust, and living in a world where treatments that may help the disease but to which one does not have easy access is a double injustice. We know this and are frustrated by our inability to administer the treatments without obstacles. The second part of the quotation above is even less obvious, but has always provided me with a key to understanding what I hear in the Oath. The Oath tells us that our patients are the ones into whose houses we go to

> **I agree that our obligation is to advocate for justice for all of our patients. That we do not achieve justice for all of our patients does not mean that we fail them.**
>
> — Paul R. Helft, MD

See Reflections on Care, Page 8B

In Advanced Renal Cell Carcinoma...

Indication

VOTRIENT is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

Important Safety Information

WARNING: HEPATOTOXICITY
Severe and fatal hepatotoxicity has been observed in clinical studies. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended. See "Warnings and Precautions," Section 5.1, in complete Prescribing Information.

Hepatic Effects: Patients with pre-existing hepatic impairment should use VOTRIENT with caution. Treatment with VOTRIENT is not recommended in patients with severe hepatic impairment. Increases in serum transaminase levels (ALT, AST) and bilirubin were observed. Severe and fatal hepatotoxicity has occurred. Transaminase elevations occur early in the course of treatment (92.5% of all transaminase elevations of any grade occurred in the first 18 weeks). Before the initiation of treatment and regularly during treatment, **monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended**.

QT Prolongation and Torsades de Pointes: Prolonged QT intervals and arrhythmias, including torsades de pointes, have been observed with VOTRIENT. Use with caution in patients at higher risk of developing QT interval prolongation, in patients taking antiarrhythmics or other medications that may prolong QT interval, and those with relevant pre-existing cardiac disease. Baseline and periodic monitoring of electrocardiograms and maintenance of electrolytes within the normal range should be performed.

Hemorrhagic Events: Fatal hemorrhagic events have been reported (all grades [16%] and Grades 3 to 5 [2%]). VOTRIENT has not been studied in patients who have a history of hemoptysis, cerebral, or clinically significant gastrointestinal hemorrhage in the past 6 months and should not be used in those patients.

Arterial Thrombotic Events: Arterial thrombotic events have been observed and can be fatal. In clinical RCC studies of VOTRIENT, myocardial infarction, angina, ischemic stroke, and transient ischemic attack (all grades [3%] and Grades 3 to 5 [2%]) were observed. Use with caution in patients who are at increased risk for these events.

Gastrointestinal Perforation and Fistula: Gastrointestinal perforation or fistula has occurred. Fatal perforation events have occurred. Use with caution in patients at risk for gastrointestinal perforation or fistula. Monitor for symptoms of gastrointestinal perforation or fistula.

Hypertension: Hypertension has been observed. Hypertension was observed in 47% of patients with RCC treated with VOTRIENT. Hypertension occurs early in the course of treatment (88% occurred in the first 18 weeks). Blood pressure should be well-controlled prior to initiating VOTRIENT. Monitor for hypertension and treat as needed. If hypertension persists despite antihypertensive therapy, the dose of VOTRIENT may be reduced or discontinued as appropriate.

Move Forward With VOTRIENT

In a phase 3, randomized, double-blind, placebo-controlled trial, VOTRIENT provided significant improvement in progression-free survival (PFS) in both treatment-naïve and cytokine-pretreated patients with advanced RCC[1,2]

All patients
9.2 months
(95% CI, 7.4-12.9)
overall median PFS with VOTRIENT (n=290) vs **4.2 months** (95% CI, 2.8-4.2) with placebo (n=145) (*P*<0.001)[2,3]

Treatment-naïve patients
11.1 months
(95% CI, 7.4-14.8)
median PFS with VOTRIENT (n=155) vs **2.8 months** (95% CI, 1.9-5.6) with placebo (n=78) (*P*<0.001)[2,3]

Cytokine-pretreated patients
7.4 months
(95% CI, 5.6-12.9)
median PFS with VOTRIENT (n=135) vs **4.2 months** (95% CI, 2.8-5.6) with placebo (n=67) (*P*<0.001)[2,3]

NCCN Guidelines Category 1 recommendation[4]

- First-line therapy for relapsed or Stage IV unresectable RCC of predominant clear cell histology

Proven safety profile[1,2]

- Most common adverse events observed with VOTRIENT (>20%) were diarrhea, hypertension, hair color changes (depigmentation), nausea, anorexia, and vomiting
  - — Grade 3/4 fatigue occurred in 2% of patients; all grades, 19%
  - — Grade 3/4 asthenia occurred in 3% of patients; all grades, 14%

Most common laboratory abnormalities were ALT and AST increases[1]

- Grade 3 ALT increases occurred in 10% of patients; grade 4, 2%
- In clinical trials, 92.5% of all transaminase elevations of any grade occurred in the first 18 weeks of treatment with VOTRIENT
- Monitor serum liver tests before initiation of treatment with VOTRIENT and at least once every 4 weeks for at least the first 4 months of treatment or as clinically indicated. Periodic monitoring should then continue after this time period

Once-daily oral dosing[1]

- The recommended dosage of VOTRIENT is 800 mg once daily without food (at least 1 hour before or 2 hours after a meal)
- Dose modifications, interruptions, and discontinuations may be required in patients with hepatic impairment, drug interactions, and following adverse events
- Forty-two percent of patients on VOTRIENT required a dose interruption; 36% of patients on VOTRIENT were dose-reduced

VOTRIENT is a multitargeted tyrosine kinase inhibitor that is indicated for the treatment of patients with advanced RCC.

Votrient™
pazopanib tablets (200 mg)

Wound Healing: VOTRIENT may impair wound healing. Temporary interruption of therapy with VOTRIENT is recommended in patients undergoing surgical procedures. VOTRIENT should be discontinued in patients with wound dehiscence.

Hypothyroidism: Hypothyroidism was reported as an adverse reaction in 26/586 (4%). Monitoring of thyroid function tests is recommended.

Proteinuria: Monitor urine protein. Proteinuria was reported in 44/586 (8%) (Grade 3, 5/586 [<1%] and Grade 4, 1/586 [<1%]). Baseline and periodic urinalysis during treatment is recommended. Discontinue for Grade 4 proteinuria.

Pregnancy Category D: VOTRIENT can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant while taking VOTRIENT.

Drug Interactions: CYP3A4 Inhibitors (eg, ketoconazole, ritonavir, clarithromycin): Avoid use of strong inhibitors. Consider dose reduction of VOTRIENT when administered with strong CYP3A4 inhibitors.

CYP3A4 Inducers (such as rifampin): Consider an alternate concomitant medication with no or minimal enzyme induction potential or avoid VOTRIENT.

CYP Substrates: Concomitant use of VOTRIENT with agents with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6, or CYP2C8 is not recommended.

Adverse Reactions: The most common adverse reactions (>20%) for VOTRIENT versus placebo were diarrhea (52% vs. 9%), hypertension (40% vs. 10%), hair color changes (depigmentation) (38% vs. 3%), nausea (26% vs. 9%), anorexia (22% vs. 10%), and vomiting (21% vs. 8%).

Laboratory abnormalities occurring in >10% of patients and more commonly (≥5%) in the VOTRIENT arm versus placebo included increases in ALT (53% vs. 22%), AST (53% vs. 19%), glucose (41% vs. 33%), and total bilirubin (36% vs. 10%); decreases in phosphorus (34% vs. 11%), sodium (31% vs. 24%), magnesium (26% vs. 14%), and glucose (17% vs. 3%); leukopenia (37% vs. 6%), neutropenia (34% vs. 6%), thrombocytopenia (32% vs. 5%), and lymphocytopenia (31% vs. 24%).

VOTRIENT has been associated with cardiac dysfunction (such as a decrease in ejection fraction and congestive heart failure) in patients with various cancer types, including RCC. In the overall safety population for RCC (N=586), cardiac dysfunction was observed in 4/586 patients (<1%).

Please see Brief Summary of Prescribing Information on adjacent pages.

References: 1. VOTRIENT Prescribing Information. Research Triangle Park, NC: GlaxoSmith-Kline; 2010. **2.** Sternberg CN, et al. *J Clin Oncol*. 2010;28(6):1061–1068. **3.** Data on file, GlaxoSmithKline. **4.** Referenced with permission from ©National Comprehensive Cancer Network, Inc 2010. All Rights Reserved. NCCN Guidelines™: Kidney Cancer, V.1.2011. NCCN.org Accessed January 12, 2011. NCCN® and NCCN GUIDELINES™ are trademarks owned by the National Comprehensive Cancer Network, Inc.

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Oncology

Survivorship Care Plans

Continued from Page 1B

go for care, or how their care will be coordinated," Dr. Rowland said. "Recent survivorship trends are raising awareness of what survivor care should be like once their active treatment ends and, importantly, who should be responsible for this care."

In fact, the recent SEER data indicated that as of January 2007, approximately 64.8% of cancer survivors were still alive 5 or more years after diagnosis; 59.5% of survivors were older than age 65.

Providing Care

Although this is considered a "high-end" problem resulting from more effective cancer care, Dr. Rowland acknowledged that the increase in long-term cancer survivors represents an important challenge for the oncology field.

"It should be of great interest to practicing oncologists that a majority of their patients are going to become survivors," she told *ASCO Daily News*. "From a very practical point of view, if oncologists are going to continue to see new patients, they cannot keep following all of the other patients that they have cared for. They are faced with the dilemma of deciding how much post-treatment care they want to provide or are effectively able to deliver."

Survivorship care includes monitoring for persistent or chronic health problems associated with cancer treatment, such as pain, depression, fatigue, sexual dysfunction, or sleep problems. Psychosocial problems also must be addressed.

"In addition, these individuals must be monitored for recurrence of the primary cancer or development of a secondary cancer," Dr. Rowland said. "Survivors are also at risk for a number of comorbid diseases such as cardiac failure, hypertension, osteoporosis, diabetes, and functional impairment. Some of these disorders might represent premorbid conditions that were exacerbated by their cancer treatment, and others may be the direct consequence of these treatments."

To begin to address the care of these survivors, the Institute of Medicine recommended in its report that all cancer survivors be given a comprehensive care summary and a follow-up plan once active treatment is finished to facilitate the smooth transition of patients within the health care system. However, a shortage of manpower among oncologists and a lack of training among primary care physicians (PCPs) have made coordination of such transitions difficult.

Whose Job Is It?

In early 2009, the National Cancer Institute launched a national survey to identify perceptions, knowledge, and practices of primary care physicians and oncologists regarding caring for cancer survivors. The Survey of Physician Attitudes Regarding the Care of Cancer Survivors (SPARCCS) consisted of two surveys, one administered to 1,100 primary care physicians and another to 1,100 oncologists.

Paul Han, MD, MA, MPH, of Maine Medical Research Institute, discussed the early findings from this study in an interview with *ASCO Daily News*. Complete data from the Survey of Physician Attitudes Regarding the Care of Cancer Survivors (SPARCCS, Abstract 9006)

was presented yesterday by Katherine S. Virgo, PhD, during Clinical Science Symposium, "Survivorship: Care Plans, Quality of Care, and Barriers to Care."

"We wanted to examine the attitudes, knowledge and practices of PCPs and oncologists regarding the care of cancer survivors," Dr. Han said. "We focused on breast and colon cancer survivors, and we looked at things like how physicians perceived their roles and responsibilities in the care of cancer survivors vis-à-vis one another. [We also looked at] how much confidence they have in one another's skills and the knowledge that is required to take care of this group of patients."

According to Dr. Han, PCPs were asked about their confidence in their knowledge of care of patients with breast and colon cancer, follow-up surveillance of these patients, and the long-term and late effects of cancer treatment in these patients.

"In general, we found that PCPs had low confidence in their knowledge of these areas," Dr. Han said. In addition, PCPs rated their skills for caring for cancer survivors as low, and oncologists agreed.

"This data could have implications considering that many groups have argued that we should move toward a system of shared care between PCPs and oncologists, with PCPs demonstrating greater responsibility for cancer survivor care," Dr. Han said.

Other interesting findings were noted.

- Neither PCPs nor oncologists selected a PCP-led model as the ideal model for survivorship care.
- Although oncologists said that they provided treatment summaries or care plans to PCPs a majority of the time, PCPs reported a low frequency of receiving them a minority of the time.
- Oncologists reported frequent communication with other physicians to clarify their respective roles in follow-up care for cancer survivors; however, PCPs' perception was that this communication occurred infrequently.
- Oncologists and PCPs endorsed overuse of many cancer surveillance tests, although this overuse was greater among PCPs.

"There is an increase in the number of cancer survivors, but there is a limited capacity of the oncology workforce to support and follow these individuals," Dr. Han said. "We need to explore models where there is greater sharing of care with PCPs; yet these findings show that PCPs have very low confidence, and oncologists also rate PCPs' skills and knowledge very low. It suggests that we have a long way to go before physicians are comfortable with proposed shared-care models."

Potential improvements include provision of guidance to PCPs about recommended care practices through the use of treatment summaries, care plans, and other mechanisms, and improved communication between oncologists and PCPs about their respective roles and responsibilities. ●

References

1. Centers for Disease Control and Prevention (CDC). Cancer Survivors — United States, 2007. *MMWR Morb Mortal Wkly Rep*. 2011;60(9):269-272.

Table 1. Adverse Reactions Occurring in ≥10% of Patients who Received VOTRIENT

	VOTRIENT (N = 290)			Placebo (N = 145)		
Adverse Reactions	All Grades[a] %	Grade 3 %	Grade 4 %	All Grades[a] %	Grade 3 %	Grade 4 %
Diarrhea	52	3	<1	9	<1	0
Hypertension	40	4	0	10	<1	0
Hair color changes	38	<1	0	3	0	0
Nausea	26	<1	0	9	0	0
Anorexia	22	2	0	10	<1	0
Vomiting	21	2	<1	8	2	0
Fatigue	19	2	0	8	1	1
Asthenia	14	3	0	8	0	0
Abdominal pain	11	2	0	1	0	0
Headache	10	0	0	5	0	0

[a] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.

Other adverse reactions observed more commonly in patients treated with VOTRIENT than placebo and that occurred in <10% (any grade) were alopecia (8% versus <1%), chest pain (5% versus 1%), dysgeusia (altered taste) (8% versus <1%), dyspepsia (5% versus <1%), facial edema (1% versus 0%), palmar-plantar erythrodysesthesia (hand-foot syndrome) (6% versus <1%), proteinuria (9% versus 0%), rash (8% versus 3%), skin depigmentation (3% versus 0%), and weight decreased (9% versus 3%).

Table 2. Selected Laboratory Abnormalities Occurring in >10% of Patients who Received VOTRIENT and More Commonly (≥5%) in Patients who Received VOTRIENT Versus Placebo

	VOTRIENT (N = 290)			Placebo (N = 145)		
Parameters	All Grades[a] %	Grade 3 %	Grade 4 %	All Grades[a] %	Grade 3 %	Grade 4 %
Hematologic						
Leukopenia	37	0	0	6	0	0
Neutropenia	34	1	<1	6	0	0
Thrombocytopenia	32	<1	<1	5	0	<1
Lymphocytopenia	31	4	<1	24	1	0
Chemistry						
ALT increased	53	10	2	22	1	0
AST increased	53	7	<1	19	<1	0
Glucose increased	41	<1	0	33	1	0
Total bilirubin increased	36	3	<1	10	1	<1
Phosphorus decreased	34	4	0	11	0	0
Sodium decreased	31	4	1	24	4	0
Magnesium decreased	26	<1	1	14	0	0
Glucose decreased	17	0	<1	3	0	0

[a] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.

Hepatic Toxicity: In a controlled clinical study with VOTRIENT for the treatment of RCC, ALT >3 X ULN was reported in 18% and 3% of the VOTRIENT and placebo groups, respectively. ALT >10 X ULN was reported in 4% of patients who received VOTRIENT and in <1% of patients who received placebo. Concurrent elevation in ALT >3 X ULN and bilirubin >2 X ULN in the absence of significant alkaline phosphatase >3 X ULN occurred in 5/290 (2%) of patients on VOTRIENT and 2/145 (1%) on placebo. *[See Dosage and Administration (2.2) and Warnings and Precautions (5.1).]* Hypertension: In a controlled clinical study with VOTRIENT for the treatment of RCC, 115/290 patients (40%) receiving VOTRIENT compared with 15/145 patients (10%) on placebo experienced hypertension. Grade 3 hypertension was reported in 13/290 patients (4%) receiving VOTRIENT compared with 1/145 patients (<1%) on placebo. The majority of cases of hypertension were manageable with anti-hypertensive agents or dose reductions with 2/290 patients (<1%) permanently discontinuing treatment with VOTRIENT because of hypertension. In the overall safety population for RCC (N = 586), one patient had hypertensive crisis on VOTRIENT. [*See Warnings and Precautions (5.2).*] QT Prolongation and Torsades de Pointes: In a controlled clinical study with VOTRIENT, QT prolongation (≥500 msec) was identified on routine electrocardiogram monitoring in 3/290 (1%) of patients treated with VOTRIENT compared with no patients on placebo. Torsades de pointes was reported in 2/586 (<1%) patients treated with VOTRIENT in the RCC studies. *[See Warnings and Precautions (5.3).]* Arterial Thrombotic Events: In a controlled clinical study with VOTRIENT, the incidences of arterial thrombotic events such as myocardial infarction/ischemia [5/290 (2%)], cerebral vascular accident [1/290 (<1%)], and transient ischemic attack [4/290 (1%)] were higher in patients treated with VOTRIENT compared to the placebo arm (0/145 for each event). *[See Warnings and Precautions (5.4).]* Hemorrhagic Events: In a controlled clinical study with VOTRIENT, 37/290 patients (13%) treated with VOTRIENT and 7/145 patients (5%) on placebo experienced at least 1 hemorrhagic event. The most common hemorrhagic events in the patients treated with VOTRIENT were hematuria (4%), epistaxis (2%), hemoptysis (2%), and rectal hemorrhage (1%). Nine (9/37) patients treated with VOTRIENT who had hemorrhagic events experienced serious events including pulmonary, gastrointestinal, and genitourinary hemorrhage. Four (4/290) (1%) patients treated with VOTRIENT died from hemorrhage compared with no (0/145) (0%) patients on placebo. *[See Warnings and Precautions (5.5).]* In the overall safety population in RCC (N = 586), cerebral/intracranial hemorrhage was observed in 2/586 (<1%) patients treated with VOTRIENT. Hypothyroidism: In a controlled clinical study with VOTRIENT, more patients had a shift from thyroid stimulating hormone (TSH) within the normal range at baseline to above the normal range at any post-baseline visit in VOTRIENT compared with the placebo arm (27% compared with 5%, respectively). Hypothyroidism was reported as an adverse reaction in 19 patients (7%) treated with VOTRIENT and no patients (0%) in the placebo arm. *[See Warnings and Precautions (5.7).]* Diarrhea: Diarrhea occurred frequently and was predominantly mild to moderate in severity. Patients should be advised how to manage mild diarrhea and to notify their healthcare provider if moderate to severe diarrhea occurs so appropriate management can be implemented to minimize its impact. Proteinuria: In the controlled clinical study with VOTRIENT, proteinuria has been reported as an adverse reaction in 27 patients (9%) treated with VOTRIENT. In 2 patients, proteinuria led to discontinuation of treatment with VOTRIENT. Lipase Elevations: In a single-arm clinical study, increases in lipase values were observed for 48/181 patients (27%). Elevations in lipase as an adverse reaction were reported for 10 patients (4%) and were Grade 3 for 6 patients and Grade 4 for 1 patient. In clinical RCC studies of VOTRIENT, clinical pancreatitis was observed in 4/586 patients (<1%). Cardiac Dysfunction: Pazopanib has been associated with cardiac dysfunction (such as a decrease in ejection fraction and congestive heart failure) in patients with various cancer types, including RCC. In the overall safety population for RCC (N = 586), cardiac dysfunction was observed in 4/586 patients (<1%).

7 DRUG INTERACTIONS

7.1 Drugs That Inhibit or Induce Cytochrome P450 3A4 Enzymes: In vitro studies suggested that the oxidative metabolism of pazopanib in human liver microsomes is mediated primarily by CYP3A4, with minor contributions from CYP1A2 and CYP2C8. Therefore, inhibitors and inducers of CYP3A4 may alter the metabolism of pazopanib. CYP3A4 Inhibitors: Coadministration of pazopanib with strong inhibitors of CYP3A4 (e.g., ketoconazole, ritonavir, clarithromycin) may increase pazopanib concentrations. A dose reduction for VOTRIENT should be considered when it must be coadministered with strong CYP3A4 inhibitors *[see Dosage and Administration (2.2)]*. Grapefruit juice should be avoided as it inhibits CYP3A4 activity and may also increase plasma concentrations of pazopanib. CYP3A4 Inducers: CYP3A4 inducers such as rifampin may decrease plasma pazopanib concentrations. VOTRIENT should not be used if chronic use of strong CYP3A4 inducers can not be avoided *[see Dosage and Administration (2.2)]*. **7.2 Effects of Pazopanib on CYP Substrates:** Results from drug-drug interaction studies conducted in cancer patients suggest that pazopanib is a weak inhibitor of CYP3A4, CYP2C8, and CYP2D6 in vivo, but had no effect on CYP1A2, CYP2C9, or CYP2C19 *[see Clinical Pharmacology (12.3) of full prescribing information]*. Concomitant use of VOTRIENT with agents with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6, or CYP2C8 is not recommended. Coadministration may result in inhibition of the metabolism of these products and create the potential for serious adverse events. *[See Clinical Pharmacology (12.3) of full prescribing information.]*

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Pregnancy Category D *[see Warnings and Precautions (5.10)]*. VOTRIENT can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of VOTRIENT in pregnant women. In pre-clinical studies in rats and rabbits, pazopanib was teratogenic, embryotoxic, fetotoxic, and abortifacient. Administration of pazopanib to pregnant rats during organogenesis at a dose level of ≥3 mg/kg/day (approximately 0.1 times the human clinical exposure based on AUC) resulted in teratogenic effects including cardiovascular malformations (retroesophageal subclavian artery, missing innominate artery, changes in the aortic arch) and incomplete or absent ossification. In addition, there was

Reflections on Care

Continued from Page 3B

care for the sick. It does not compel us to care for and treat the population at large, or any particular group of patients for that matter. It implies that our patients are those we encounter individually. In ancient times — and occasionally in ours — such encounters happened in patients' homes. But unauthorized immigrants with cancer, just like patients who are citizens, come into our homes — our hospitals, clinics, and offices. They are then no longer the population at large but rather they seem to us just like all of our other patients, like human beings afflicted with illness who need help, care, treatment, and relief from suffering. The most profound sense of obligation we feel as physicians — no matter our personal political beliefs — stem from these two dimensions of our ethic: we want to help the sick directly in front of us.

All of this stands in contradistinction to the views derivable from policy or public health ethics. The framework for policy or public health points of view conceives of groups of patients and attempts to align available resources in ways that maximize benefits for populations. As such, these useful analytical systems deal with statistical patients. As oncology professionals, the patients who come to us for care are individuals, not statistics; therefore, efforts to place the burden of gatekeeping for cancer treatments or, to use the politically-charged term, "rationing," on those of us who care for actual patients, runs counter to our worldview as clinicians. Most of us could live in a system that rationed treatments based on, for example, cost-effectiveness, as long as the rules applied to everyone and were imposed on us by policy, statute, or regulation. Then the voting public would have decided, and the burden of decision making would not be left to those of us whose sense of obligation is generally more aligned with individual patients as I have outlined previously.

I have tried to establish thus far in this editorial that the sense of duty to care for every individual patient who comes to us for care stems from very deep, foundational views of our obligations as oncology professionals interested in the welfare of patients with cancer of all kinds. However, current economic, governmental, and regulatory realities make it impossible to offer every treatment to every patient irrespective of ability to pay. I think it is very important to recognize that, as much as we may feel for the suffering patients who come to us, the limitations of circumstance they face are not of our making. Having no access to resources is an example of such an unfortunate circumstance. This is troublesome and in some global sense unjust. We would like to fix it, but it is not our fault. I believe that those who might ascribe to us an ethical obligation to treat every patient we encounter at all costs, even if it would harm our ability to deliver care more broadly, mistakenly characterize our real obligations. In this way, discussions about human rights to health care (as much as I may admire them) cannot realistically address the real-world problem of the sick patient in our office who has an expensive disease such as cancer.[5] I agree that our obligation is to advocate for justice for all of our patients. That we do not achieve justice for all of our patients does not mean that we fail them. Moreover, we cannot realistically be expected to achieve it to the detriment of our overall practices or to the other patients for whom we care.

For the patient described in this editorial, this might mean accepting the fact that, although many patients with health insurance might choose to be treated with chemotherapy for advanced pancreatic cancer, overall it is likely to add little to his survival or quality of life. So donating the costs of such treatments does not do much to further this patient's outcome (or to keep him from injustice). His circumstances — the inability to pay for chemotherapy out of pocket or obtain insurance coverage for it — make such treatments even less cost-effective. Our deepest obligations might be fulfilled in other ways. Continuing to care for this patient through office visits, prescriptions for medicines important to palliative care, and emotional support can all be provided relatively cheaply by comparison, and to me would represent a pathway for fulfilling our ethical obligation to care for such a patient irrespective of his ability to pay. ●

About the Author: *Dr. Helft is an Associate Professor of Medicine at the Indiana University School of Medicine and the Indiana University Melvin and Bren Simon Cancer Center. He also is the Director of the Charles Warren Fairbanks Center for Medical Ethics at Indiana University Health. He has been an ASCO member for 11 years.*

References

1. See *Unauthorized Immigrant Population: National and State Trends, 2010*. Pew Hispanic Center. Available at http://pewhispanic.org/files/reports/133.pdf. Accessed March 3, 2011.
2. See Sarah Kershaw. U.S. Rule Limits Emergency Care for Immigrants. *New York Times*. September 22, 2007. Available at http://www.nytimes.com/2007/09/22/washington/22emergency.html?hp. Accessed March 3, 2011.
3. Steven H. Miles. The Hippocratic Oath and the Ethics of Medicine. Oxford University Press. New York, New York. 2004.
4. Orr RD, Pang N, Pellegrino ED, Siegler M. Use of the Hippocratic oath: a review of twentieth century practices and a content analysis of oaths administered in medical schools in the US and Canada in 1993. *J Clin Ethics*. Winter 1997;8:377-388.
5. Eleanor D. Kinney. The International Human Right to Health: What Does This Mean for Our Nation and World? *Indiana Law Review*, Vol. 34, P. 1457, 2001.

NOW ENROLLING

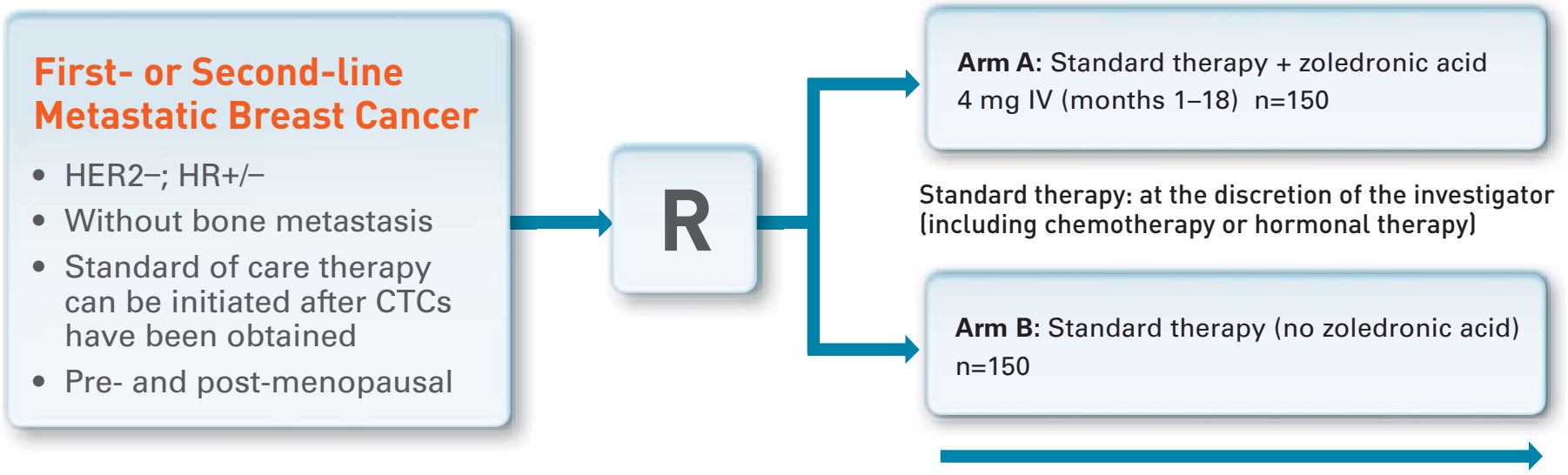
Z-ACT 1

Effect of Zoledronic Acid as Anti-Cancer Treatment in Metastatic Breast Cancer Patients

Study Description

A multicenter, open-label, randomized trial to evaluate the potential anti-cancer effects of zoledronic acid and circulating tumor cell (CTC) measurements in patients with HER2-negative metastatic breast cancer (MBC) without bone metastasis. (Clinical Trial Protocol CZOL446EUS147)

Study Design



Primary Endpoint

Progression-free survival (PFS)

Secondary Endpoint

- Proportion of patients with CTCs ≥5 per 7.5 mL of peripheral blood at 1, 2, 4 and 6 months
- Time to progression (TTP)
- Time to development of bone metastasis
- Overall survival (OS)
- Changes from baseline in urinary NTX and its correlation with CTCs
- Change from baseline in Functional Assessment of Cancer Therapy-Bone Pain total score

For more information:

- Call Novartis Oncology at 1-800-340-6843
- Contact your local Novartis Medical Science Liaison (MSL)

Zoledronic acid has not been approved by the FDA for this indication and this information has been approved for scientific exchange only.

NOVARTIS ONCOLOGY

ZOM-1015358

April 2011

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Practice Consolidation Models for Community Practices, Institutions of All Sizes to Form Effective Multispecialty Groups

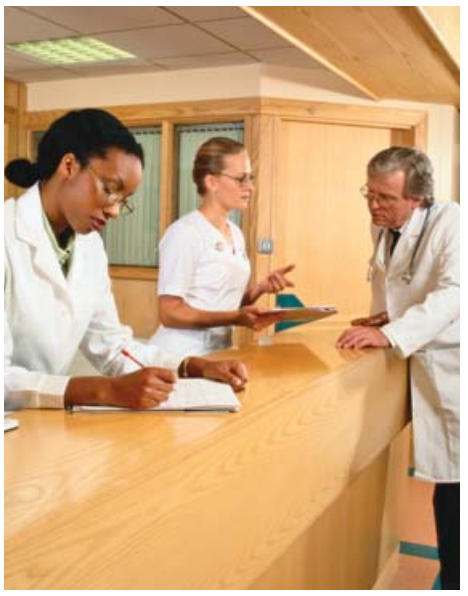
In a hotly competitive marketplace with large integrated systems of care devouring market share, how will the typical oncology practice — whether it's a community-based single specialty practice, a hospital- or university-affiliated practice, or a regional multispecialty group — survive in the coming years?

Three prominent ASCO leaders will address that question in the Educational Session, "Oncology Practice Models: Strategies to Overcome Competitive Disadvantages," to be held this morning, 8:00 AM – 9:15 AM, Room E353, East Building.

Harvey D. Bichkoff, MPH, Chief Executive Officer at Pacific Specialty Care, Inc., will discuss successful practice model strategies for community-based single-specialty practices.

"In our market we have a large prepaid health system in Kaiser Permanente that is growing in market share, and a large hospital in Sutter Medical Center that is acquiring practices and expanding," Bichkoff told *ASCO Daily News* in an interview. "We are a moderate-sized medical oncology practice, and we want to maintain our autonomy and continue to provide high-quality care while meeting the challenges of healthcare reform."

Mr. Bichkoff said California Cancer Care has begun to consolidate with other similar specialty practices to form a multispecialty group while also collaborating with a local freestanding hospital to help diversify revenue streams. Mr. Bichkoff will present data from the Kantar Health Research Group about trends in small and large oncology practice models. These include:



- Twenty percent of practices today are comprised of one or two oncologists, down from 33% in 2006. Mr. Bichkoff said that practices of this size have difficulty recruiting management and have diminished clout with payers and drug wholesalers. These practices may be forced to merge or exit the market entirely; practices that close their doors typically join a local hospital.
- Seventy percent of practices have three to 10 medical oncologists. These practices can leverage infrastructure and fixed costs, recruit and retain savvy business management, and can leverage their size for better contracts. They also are better positioned to invest in electronic medical records, thereby improving patient compliance and office efficiency.

Consolidation of Clinical and Ancillary Services

R. Steven Paulson, MD, President and Chairman of the Board for Texas Oncology, will discuss successful practice models for a regional multispecialty groups. Dr. Paulson will emphasize the need for such groups to aggregate ancillary and clinical services within the practice to create a "one-stop shopping" experience for the patient and a competitive advantage for the practice.

"If you can create a center of excellence by bringing together critical physician groups, a practice can create an advantage for themselves," Dr. Paulson told *ASCO Daily News*. "For instance, if you have a prostate cancer practice, you must have urologists as well as oncologists in the same practice. By aggregating clinical and ancillary services you can provide everything from diagnosis to radiation to resolution of disease under one roof. The patient has one place to go and has a much less stressful and more cohesive, integrated plan of care."

According to Dr. Paulson, payers will favor the larger, integrated practice because they can contract with one entity.

Denis B. Hammond, MD, of New Hampshire Oncology/Hematology, in Manchester, New Hampshire, will discuss practice models for the hospital or university-affiliated practice.

Dr. Hammond told *ASCO Daily News* that in 2004, in response to increasing competitive pressure in the New England area, his practice began discussions with the

See Practice Consolidation, Page 17B

Rapid-learning Model: The Future is Now for Oncologists and Their Patients

Use of health information technology to consolidate data sets will allow for higher-quality patient care and an ever-growing foundation of knowledge for oncologists

EXPERT EDITORIAL

Amy P. Abernethy, MD

Rapid-learning health care has received considerable attention as a national model that, when implemented, will conjoin the processes of research discovery and patient care while also ensuring innovation, quality, safety, and value in the healthcare system.[1-3] In a rapid-learning system, data generated through both patient care and clinical research feed into an ever-growing databank or set of coordinated databases. The system "learns" through several mechanisms: the routine collection of data in a planned and strategic manner, iterative analysis of captured data, generation of evidence and translation of results through analysis of both retrospective and prospective data, incorporation of new insights into clinical care, evaluation of outcomes of changes in clinical practice, and generation of new hypotheses for investigation.[4] Examples of possible insights gained through this model include:

- knowledge and understanding of the clinical effectiveness of treatments for patients frequently excluded from clinical trials (e.g., the advanced elderly or individuals with multiple comorbidities),
- knowledge and understanding of how the sequencing and timing of antineoplastic treatments affect real-world trajectories of cancer care,
- identification of unexpected associations that predict treatment response or symptoms,
- improvement in healthcare delivery systems, and
- embedding of clinically relevant information into the process of basic discovery.

In 2007, the Institute of Medicine (IOM) Roundtable on Evidence-based Medicine formally convened leading authorities to describe the vision of "The Learning Healthcare System" and present recommendations for next steps.[1] In October 2009, the IOM's National Cancer Policy Forum conducted a follow-up workshop, "A Rapid Learning System for Cancer Care."[5] These high-level forums spawned collaborative discussion, serving as a catalyst for widespread motivation to redesign the health care system using a rapid-learning paradigm. First steps in this endeavor have been to develop infrastructure for data interoperability and management and to consider methods for leveraging longstanding national investments in registries, clinical trials infrastructure, and quality monitoring processes for cancer. Funding has been secured for the development, implementation, refinement, and examination of the effect of prototype rapid-learning models in specific disciplines, diseases, and populations. In addition, the development of new healthcare models has been aligned with opportunities in the Affordable Care Act of 2010 to use rapid learning to facilitate health care redesign. With respect to the first (infrastructure development), the Cancer Biomedical Informatics Grid® (caBIG®) has made significant strides in defining data elements, creating tools, and establishing standards that will support a nationwide data foundation for rapid learning.

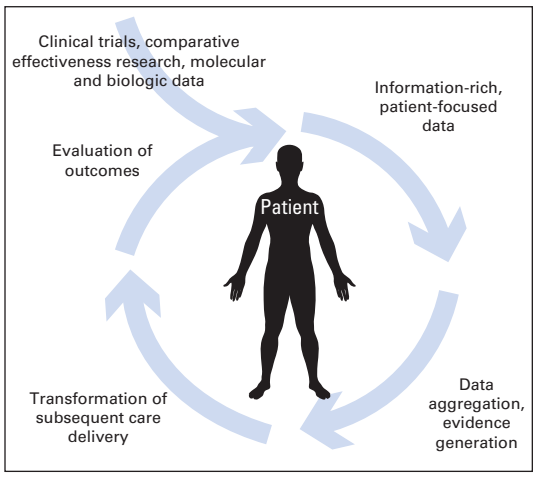
Amy P. Abernethy, MD

Paving the Way in Oncology

Cancer has been suggested as a first disease in which to test a rapid-learning model because its severity, threat to life, costliness, intrinsic and consistent strong patient engagement, and population-wide effects.[6] A sense of urgency surrounds the need for better comparative effectiveness data, particularly in oncology where the pace at which new cancer treatments emerge outstrips the rate of evidence review and dissemination, where many investigational therapies exist alongside U.S. Food and Drug Administration (FDA)-approved therapies, and where off-label prescribing constitutes a major and important proportion of all pharmaceutical treatments delivered. In cancer research, the concepts of continuous investigation, discovery, and evidence implementation are already well accepted. Patient-reported outcomes (PRO), a core feature of rapid-learning models under development, have been well studied in this field; patient-centeredness has been articulated as a priority for cancer care.[4,7]

Redesign of oncology in a rapid-learning model would entail a restructuring of the existing systems of research and care, seamlessly coordinating these distinct spheres. A rapid-learning system simultaneously generates and is driven by data (i.e., uses the results of retrospective analyses and prospective studies), hence it contains continuous feedback/evaluation loops that could improve accountability throughout the system. Quality of care (i.e., the extent to which care is evidence- and/or guideline-based, exhibits continuity over time and across settings, and incorporates longitudinal monitoring of outcomes) will improve with the greater access to data and transparency afforded by the rapid-learning system. Supported by health information technology and by secure, trustworthy, information systems, a rapid-learning model will facilitate improved communications between clinicians, researchers, patients, administrators, and other stakeholders. Its use of health information technology for data collection and for bidirectional communication will open numerous opportunities for patient education.

Progress is already being made on the ground in implementing and testing components of a rapid-learning system. At Duke, as a proof of concept and to test what rapid-learning health care looks like on the frontline, we systematically built the fundamental components of a patient-centered, informatics-enabled, rapid-learning system based on PROs such as symptoms and functional status. We adapted an information technology-based system for collecting PRO data electronically (ePRO) at the point of care for use in support of both clinical and research purposes, and we demonstrated the system's feasibility and acceptability in the academic oncology setting.[8] We found ePRO data collected electronically to be equivalent to data collected using traditional paper questionnaires.[9] We then used this ePRO system as the hub of an institutional data ecosystem which links patient-reported, clinical, administrative, financial, genomic, and other datasets in Duke's enterprise data warehouse.[4] The system is designed for interoperability with national datasets such as caBIG®, Surveillance, Epidemiology and End Results (SEER) data, and the Medicare 5% dataset. We have used the system to identify underattended areas of patient need,[10] automate triaging in the clinic, and evaluate a new psychosocial intervention.[11-13] In a current American Reinvestment and Recovery Act Grand Opportunities grant, we are using the ePRO system as a central facilitator of large-scale data linkage to support comparative effectiveness research in breast and lung cancer; this project includes development of an informatics-enabled data registry and biorepository that allows rapid assessment of outcomes differentiated by biomarker. In the meantime, standardized ePRO collection is advancing various goals integral to quality cancer care and research; for example, a contract from the National Cancer Institute has funded development of an ePRO version of the Common Toxicity Criteria for Adverse Event reporting.



Effects of Rapid-learning Health Care on the Practicing Oncologist

The following scenario depicts a near-term reality.

Gertrude Q, a 67-year-old patient with metastatic breast cancer, visits Dr. Smith in July. Her clinical note is generated from an amalgamation of codified data elements, each discretely documented by Dr. Smith using data standards that ensure interoperability across data systems. Recognizing the complexity of care and the importance of the narrative to shape its vivid picture, only those parts of the note that must be codified flow into categorical fields. Dr. Smith provides text comments that supplement the coded data and provide important contextual information for the discrete data. A report joins the discrete coded information and text information into an informative clinical synopsis for Dr. Smith's use in Gertrude's subsequent visits. Data security controls ensure that privacy is maintained; only appropriate clinical, research, administrative, and regulatory personnel can access Gertrude's personal health data.

Using a digital interface in the clinic waiting room, Gertrude completes a series of breast cancer-specific electronic questionnaires to report her symptoms during the past week. This patient-reported information is automatically imported into the codified clinic note, and Dr. Smith reviews the report before entering Gertrude's room, prepared to discuss changes and her principal concerns. As she waits, Gertrude watches tailored video modules that are matched to the symptoms she has indicated as well as her age, disease, and gender. Dr. Smith uses clinical decision support software that is automatically tailored to Gertrude's personal health history to choose the best first-line chemotherapy program for her newly diagnosed metastatic disease; treatment choice is made in real-time reflective of the most up-to-date information available in the databases. After the visit, Dr. Smith updates the clinical note with Gertrude's new clinical notes, interpretation, and plan. When Dr. Smith next sees Gertrude, relevant information from July's note automatically populates the August note.

All codified information from Gertrude's visits enter an ever-growing database available to researchers, quality improvement staff, and the Centers for Medicare and Medicaid Services; it is stored for future analyses, data needs, and quality assessment. Quality assessment results and outcomes data are available to clinicians making treatment decisions for future patients. The data system can generate various continuously updated reports, from patient-level graphs of Gertrude's fatigue as associated with her chemotherapy, to health system-level summaries designed to help optimize patient care and satisfaction, to evaluation of cancer treatment outcomes by stage of disease and patient characteristics. Dashboards and clinical decision support tools assist the various users in navigating the system, as well as in accessing and understanding appropriate data. Other clinicians treating patients with similar characteristics can query across the data system to understand the effectiveness of available treatments, optimal treatment sequence, and influence of comorbid illness on outcomes. Researchers can aggregate Gertrude's clinical data with those of appropriate patients to create a research sample, through which they can explore disease history, treatment patterns, and outcomes at the population level. Meanwhile, bench scientists working with Gertrude's banked tumor specimens have a fully annotated clinical record to enhance discovery and to ensure that basic science research is maximally clinically relevant. When Gertrude returns to see Dr. Smith, her information is updated and the databases continue to grow.

Hence, in this rapid-learning system, the care of the individual patient at hand is informed by all similar patients who came before her, and data regarding her care and outcomes are reinvested into continuously

See Rapid-learning Model, Page 15B

Celgene is now joining the battle against metastatic breast cancer

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Abraxane®
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(albumin-bound)

ABRAXANE for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

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ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

IMPORTANT SAFETY INFORMATION

WARNING

ABRAXANE for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) should be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

ABRAXANE therapy should not be administered to patients with metastatic breast cancer who have baseline neutrophil counts of less than 1,500 cells/mm^3. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE.

Note: An albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.

ADDITIONAL WARNINGS

- The use of ABRAXANE has not been studied in patients with renal dysfunction. In the randomized controlled trial, patients were excluded for baseline serum bilirubin >1.5 mg/dL or baseline serum creatinine >2 mg/dL

Pregnancy-Teratogenic Effects: Pregnancy Category D

- ABRAXANE can cause fetal harm when administered to a pregnant woman
- If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus
- Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with ABRAXANE

Use in Males:

- Men should be advised to not father a child while receiving treatment with ABRAXANE

Albumin (human):

- ABRAXANE contains albumin (human), a derivative of human blood

PRECAUTIONS

Drug Interactions:

- No drug interaction studies have been conducted with ABRAXANE
- Caution should be exercised when administering ABRAXANE concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4

Hematology:

- ABRAXANE therapy should not be administered to patients with baseline neutrophil counts of less than 1,500 cells/mm^3
- It is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE
- Patients should not be retreated with subsequent cycles of ABRAXANE until neutrophils recover to a level >1,500 cells/mm^3 and platelets recover to >100,000 cells/mm^3
- In the case of severe neutropenia (<500 cells/mm^3 for 7 days or more) during a course of ABRAXANE therapy, a dose reduction for subsequent courses of therapy is recommended

Nervous System:

- Sensory neuropathy occurs frequently with ABRAXANE
- The occurrence of grade 1 or 2 sensory neuropathy does not generally require dose modification
- If grade 3 sensory neuropathy develops, treatment should be withheld until resolution to grade 1 or 2 followed by a dose reduction for all subsequent courses of ABRAXANE

Hepatic Impairment:

- Because the exposure and toxicity of paclitaxel can be increased with hepatic impairment, administration of ABRAXANE in patients with hepatic impairment should be performed with caution
- The starting dose should be reduced for patients with moderate and severe hepatic impairment

Injection Site Reaction:

- Injection site reactions occur infrequently with ABRAXANE and were mild in the randomized clinical trial
- Given the possibility of extravasation, it is advisable to closely monitor the infusion site for possible infiltration during drug administration

Nursing Mothers:

- It is not known whether paclitaxel is excreted in human milk
- Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, it is recommended that nursing be discontinued when receiving ABRAXANE therapy

Ability to Drive and Use Machines:

- Adverse events such as fatigue, lethargy, and malaise may affect the ability to drive and use machines

ADVERSE EVENTS

- Severe cardiovascular events possibly related to single-agent ABRAXANE occurred in approximately 3% of patients in the randomized trial
- These events included chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary emboli, and hypertension
- Cases of cerebrovascular attacks (strokes) and transient ischemic attacks have been reported rarely
- During postmarketing surveillance, rare reports of congestive heart failure and left ventricular dysfunction were observed, primarily among individuals with underlying cardiac history or prior exposure to cardiotoxic drugs

In the randomized metastatic breast cancer study, the most important adverse events included alopecia (90%), neutropenia (all cases 80%; severe 9%), sensory neuropathy (any symptoms 71%; severe 10%), asthenia (any 47%; severe 8%), myalgia/arthralgia (any 44%; severe 8%), anemia (all 33%; severe 1%), nausea (any 30%; severe 3%), diarrhea (any 27%; severe <1%), infections (24%), vomiting (any 18%; severe 4%), and mucositis (any 7%; severe <1%).

Other adverse reactions have included ocular/visual disturbances (any 13%; severe 1%), renal dysfunction (any 11%; severe 1%), fluid retention (any 10%; severe 0%), hepatic dysfunction (elevations in bilirubin 7%, alkaline phosphatase 36%, AST [SGOT] 39%), hypersensitivity reactions (any 4%; severe 0%), cardiovascular reactions (severe 3%), thrombocytopenia (any 2%; severe <1%), and injection site reactions (<1%). In clinical trials and during postmarketing surveillance, dehydration was common and pyrexia was very common. Rare occurrences of severe hypersensitivity reactions have also been reported during postmarketing surveillance.

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

Pediatric Oncology Award

Continued from Page 3B

said Dr. Helman. "Then during my residency, I decided a career in oncology would allow me to combine research and patient care."

Dr. Helman trained in internal medicine at Barnes Hospital of Washington University. He then began his career at the NCI, where he completed his fellowship and postdoctoral training in the Molecular Genetics Section in the Pediatric Oncology Branch.

"Just as I was about to leave [NCI after my postdoctoral training], I was given an opportunity to develop an independent lab," said Dr. Helman. "This is when I made my decision to study pediatric sarcomas because I saw an opportunity for new discovery, and because I really enjoyed caring for these patients — often adolescents and young adults."

Dr. Helman was appointed Head of the Molecular Oncology Section, Pediatric Oncology Branch of NCI in 1993 and then served as Chief of the Pediatric Oncology Branch from 1997 to 2007. In 2007, he was appointed Scientific Director for Clinical Research in the Center for Cancer Research at NCI, where he currently serves. Dr. Helman also is a part-time Professor of Pediatrics and of Oncology at Johns Hopkins University.

"Since I have had the opportunity to serve as Scientific Director for Clinical Research at NCI, I have been able to work toward defining and prioritizing the focus of the NCI intramural clinical research program while being able to maintain my own laboratory research, something of which I am very proud," said Dr. Helman.

Dr. Helman credits much of his success in pediatric oncology research to his first research mentor Mark Israel, MD, now of the Norris Cotton Cancer Center at Dartmouth-Hitchcock. Dr. Israel was Dr. Helman's laboratory chief during his postdoctoral training at the NCI.

"I can't overemphasize how important [Dr. Israel's] teaching and guidance was to my future success," said Dr. Helman. "I have had the good fortune to remain good friends with [Dr. Israel] over the years, and this relationship has also helped shape my own dedication to mentor junior faculty over the years."

In addition to his positions at NCI and Johns Hopkins, Dr. Helman has been an ASCO member for more than 20 years. He has served the Society in many ways including as a current member of the *Journal of Clinical Oncology* Editorial Board, as a past member of the Board of Directors, and as past chair of the Bylaws Committee. He is a member of the Board of Directors of and Clinical Advisor to The Children's Inn at the National Institutes of Health. Dr. Helman is a past member of the Board of Governors of the Clinical Center at the National Institutes of Health, and he was a founding member of the Connective Tissue Oncology Society.

"This (award) is a wonderful acknowledgement by my peers that my work is considered valuable to the field," said Dr. Helman. "All science is by nature collaborative, so this honor also goes to my colleagues and many postdoctoral fellows and students." ●

Rapid-learning Model

Continued from Page 11B

aggregating datasets to inform the care of similar patients in the future.

Rapid-learning health care offers a compelling vision. In this new paradigm, clinical care is data driven, customized to the individual, and patient centered in that it prioritizes symptoms and experiences important to patients. Continuous, clinically relevant research ensures that patient care is grounded in the latest evidence, is informed by outcomes (e.g., retrospective analyses of large aggregate datasets, individuals matched on patient characteristics) as well by results of prospective clinical trials, and leverages existing data including administrative and financial outcomes to optimize efficiency and value in the health care system. The linkage of data systems and the interoperability of data within them create a context for comprehensive consideration of diverse patient variables. This transdisciplinary, ultimately transinstitutional, approach will result in both new insights that can be pursued through subsequent research and in delivery of truly personalized medicine. ●

About the Author: *Dr. Abernethy is Associate Professor of Medicine with Tenure in the Department of Medicine, Division of Medical Oncology, at Duke University Medical Center. Her primary areas of focus are patient-centered comparative effectiveness research, clinical trials, melanoma, and palliative and supportive care.*

For more information about rapid-learning health care models and how they can be used to expedite guidelines development, see the Expert Editorial by Dr. Peter Paul Yu in yesterday's edition of ASCO Daily News*, section B.*

References

1. Institute of Medicine. *The Learning Healthcare System: Workshop Summary (IOM Roundtable on Evidence-Based Medicine)*. Washington, DC: National Academies Press; 2007.
2. Institute of Medicine. *Knowing What Works in Health Care: A Roadmap for the Nation*. Washington, DC: National Academies Press; 2008.
3. Etheredge LM. A rapid-learning health system. *Health Aff (Millwood)*. 2007; 26(2):w107-w118.
4. Abernethy AP, Ahmad A, Zafar SY, et al. Electronic patient-reported data capture as a foundation of rapid learning cancer care. *Med Care*. 2010;48(6 Suppl):S32-S38.
5. Abernethy AP, Etheredge LM, Ganz PA, et al. Rapid-learning system for cancer care. *J Clin Oncol*. 2010;28(27):4268-4274.
6. Etheredge LM. Medicare's future: cancer care. *Health Aff (Millwood)*. 2009;28(1):148-159.
7. Institute of Medicine. *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*. Washington, DC: National Academies Press; 2008.
8. Abernethy AP, Herndon JE, Wheeler JL, et al. Feasibility and Acceptability to Patients of a Longitudinal System for Evaluating Cancer-Related Symptoms and Quality of Life: Pilot Study of an e/Tablet Data-Collection System in Academic Oncology. *J Pain Symptom Manage*. 2009;37(6):1027-1038.
9. Abernethy AP, Herndon JE 2nd, Wheeler JL, et al. Improving health care efficiency and quality using tablet personal computers to collect research-quality, patient-reported data. *Health Serv Res*. 2008;43(6):1975-1991.
10. Reese JB, Keefe FJ, Herndon JEI, et al. Reduced sexual enjoyment, interest, and performance are a concern of GI and breast cancer patients. *Support Care Cancer*. 2008;16(6):654.
11. Abernethy AP, Staley T, Herndon JEI, et al. Pathfinders: A pilot study of an integrative psychosocial care program for cancer patients. *Support Care Cancer*. 2009;17(7):988.
12. Abernethy AP, Herndon JE 2nd, Coan A, et al. Phase 2 pilot study of Pathfinders: a psychosocial intervention for cancer patients. *Support Care Cancer*. 2010;18(7):893-898.
13. Smith SK, Herndon JE, Lyerly HK, et al. Brief Report: Correlates of quality of life-related outcomes in breast cancer patients participating in Pathfinders pilot. *Psychooncology*. 2010;doi: 10.1002/pon.1770.

Humanitarian Award

Continued from Page 1B

Service and the William and Joy Ruane Chair in Thoracic Oncology at Memorial Sloan-Kettering Cancer Center, where he has been on the staff since 1983. He also is a Professor of Medicine at Weill Cornell Medical College. He specializes in thoracic malignancies including lung cancer, thymoma, and cancer of unknown primary site. His research interests include targeted therapies for lung cancer, multimodality therapy, the development of new anticancer drugs, and symptom management with a focus on preventing emesis, the most dreaded side effect of cancer and cancer treatment. He will be making a presentation in the Lung Cancer Oral Session at the 2011 ASCO Annual Meeting on behalf of the Lung Cancer Mutation Consortium that is trying to make personalized care a reality for all Americans with lung adenocarcinoma.

Dr. Kris received his medical degree from Cornell University Medical College, completed residencies at the New York Hospital-Cornell Medical Center/Memorial Sloan-Kettering Cancer Center program, and performed his fellowship at Memorial Sloan-Kettering.

An ASCO member since 1983, Dr. Kris has served on and led numerous committees. He received an ASCO Statesman Award in 2010 in recognition of his service to the Society. ●

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Randomized

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*One of which must be a platinum-doublet therapy.

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SECONDARY ENDPOINTS

- Progression-free survival
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New *JOP* Thematic Issues Highlight EHR and Palliative Care

The *Journal of Oncology Practice* (*JOP*) provides oncologists and other oncology professionals with information and tools to enhance practice efficiency and promote a high standard for quality patient care. The *Journal* is an authoritative resource on clinical and administrative management for oncology professionals. Each issue of *JOP* includes peer-reviewed original research and articles on a variety of issues important to daily practice operations and to the care of patients. In the coming months, *JOP* will be releasing two special thematic issues.

Electronic Health Records (EHRs)

Several topics will be addressed in this thematic issue, to be published in July 2011.

- Positive and negative effects of EHRs in oncology practice
- Meaningful use of the Center for Medicare and Medicaid Services' (CMS) Electronic Health Records (EHR) Incentive Program
- Use of decision support in EHRs, as well as leveraging the ability of EHRs to generate and organize data
- Administrative burdens of implementing EHRs
- Financial implications and comparative costs

Overall, readers will be provided with a better understanding of the effect of EHRs on the culture of practice. Information on augmenting clinical-data repositories and EHR registries will also be featured.

JOP's EHR thematic issue will be guest edited by ASCO Health Information Technology Work Group members Robert Miller, MD, of Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, and Peter Yu, MD, of Palo Alto Medical Foundation. *(For more information on health information technology, specifically rapid-learning health care systems, see Dr. Yu's editorial in the Saturday issue of* ASCO Daily News, *Section B.)*

Palliative Care

This thematic issue will be published in November 2011 and will include information on six aspects of palliative care:

- acceptance of palliative care services by oncology professionals and the assessment of patient experience and satisfaction,
- integration of palliative care services in ambulatory settings,
- caregiver study outcomes of individuals who are in the care giving role,
- the effect of public policy and reimbursement on palliative care services, and
- measurement of outcomes and quality measures.

Overall, the issue will address the structural, logistical, operational, and financial challenges associated with palliative care, as well as the unique delivery mechanisms and programmatic structures for palliative care services. Readers will learn about phase III studies of palliative care interventions including symptom control, maintenance of function, nonpharmacologic interventions, and psychosocial support. *(For information about early identification and incorporation of palliative care throughout the cancer-care continuum, see the Expert Editorial by Jamie Von Roenn, MD, in the Saturday issue of* ASCO Daily News, *Section B. Also look for palliative-care focused articles on awards and grants, Education Sessions, and more in each day's Table of Contents.)*

For more information on *JOP's* special thematic issues, please visit jop.asco.org. ●

"Weight Matters": Education Session Addresses Associations between Weight and Cancer Outcomes

A growing body of evidence suggests that body weight affects health outcomes in a number of cancer types. Today's Education Session examining the relationships between body weight and cancer outcomes will be of interest to a wide variety of oncologists and other health care professionals who care for patients with cancer and survivors, according to the Chair of the Session.

"Weight matters for cancer survival, and it affects outcomes in several different types of cancer, including breast, colon, and prostate cancers," said Anne McTiernan, MD, PhD, of the Fred Hutchinson Cancer Research Center. Dr. McTiernan will chair the session, entitled "Weight of Evidence: Associations between Body Weight and Health Outcomes (Including Survival) in Cancer Populations," to be held today 9:45 AM – 11:00 AM, Room S406, South Building.

Dr. McTiernan will present an overview of the current evidence supporting body weight status, adiposity, and weight loss on cancer outcomes. "There is quite a bit of evidence emerging for the relationship between weight and outcomes in cancer, particularly for breast and prostate cancers," she told *ASCO Daily News*.

The session aims to identify the cancers in which overweight and obesity are linked to reduced disease-free and overall survival and to identify other health outcomes that are adversely affected by excess adiposity.

Exploring Biologic Mechanisms

Prof. Rudolf Kaaks, PhD, of the German Cancer Research Center in Heidelberg, Germany, will explore the biologic mechanisms by which weight status and weight loss affect cancer progression.

His presentation will review the mechanisms that have been implicated in increased risk of cancer incidence and survival in people who are overweight or obese. "The pathways most heavily studied are typically related to metabolism — metabolism of insulin and glucose, for instance, or metabolism of sex hormones," Dr. Kaaks said in an interview with *ASCO Daily News*. I will address whether such metabolic factors are associated with survival and what kinds of effects can be achieved by drugs that influence such pathways. This is the direction that research is driving," he continued.

For example, he said, a number of studies suggest that metformin, a drug that has been used for many years to lower blood glucose levels in patients with diabetes, may have an effect on cancer risk. "There is evidence that, among diabetics who use metformin as opposed to other forms of treatment, there is a reduced risk of developing cancer. Trials are also exploring whether metformin has preventive effects on recurrence or survival," Dr. Kaaks said.

Dr. Kaaks will discuss the "obesity paradox" often seen in patients with heart disease: obesity is a risk for heart failure, but those who are overweight have a better chance of survival. According to Dr. Kaaks, however, it is fairly clear that such a paradox does not exist in the cancer field because obesity is a risk factor for developing a tumor and also for poor survival. Dr. Kaaks's presentation will explore possible mechanisms that may explain why this is so.

Effect of Weight Loss on Outcomes

Cheryl L. Rock, PhD, RD, of the University of California, San Diego, School of Medicine, will present the design of a trial that is evaluating the effect of weight loss in cancer survivors.

The Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) trial is a vanguard randomized, controlled, prospective 4-year study with the primary endpoint of clinically significant sustained weight loss. The trial will enroll 800 breast cancer survivors who are overweight or obese at four clinical centers.

"In addition to the primary endpoint of clinically significant sustained weight loss, other endpoints include the effects of weight loss on psychosocial factors such as quality of life and fatigue, and on comorbidities such as osteoarthritis complaints, elevated blood sugar and blood pressure, and other factors that occur at higher levels in breast cancer survivors who are overweight," Dr. Rock said.

The trial is currently in the recruitment phase, so Dr. Rock's presentation will focus on its rationale, design, methods, and outcome measures.

According to Dr. Rock, if the researchers can show sustained weight loss and favorable effects of weight loss on psychosocial factors and comorbidities, it will be the first step toward a larger clinical trial that will address cancer outcomes.

"This is important because a woman who is obese at the time of diagnosis has a 78% greater likelihood of having a recurrence, all other factors being equal, compared with a woman who is not obese," she said. "So the question is, can we reduce the risk of recurrence and improve survival if we help these women who are overweight to lose weight after diagnosis?"

Women will be recruited into the study after they have completed their initial treatment for breast cancer, including chemotherapy, radiation therapy, and surgery. ●

Practice Consolidation

Continued from Page 10B

Dana-Farber Cancer Institute at Harvard University about developing a collaborative partnership.

In January 2005 the two parties signed a "memorandum of understanding" to develop joint programs together without a formal financial relationship and with the agreement that programs would not harm each party's competitive interests. In time both groups signed a provider services agreement, and in 2008 a second clinic was opened in nearby Londerry, New Hampshire, a bedroom community of Manchester.

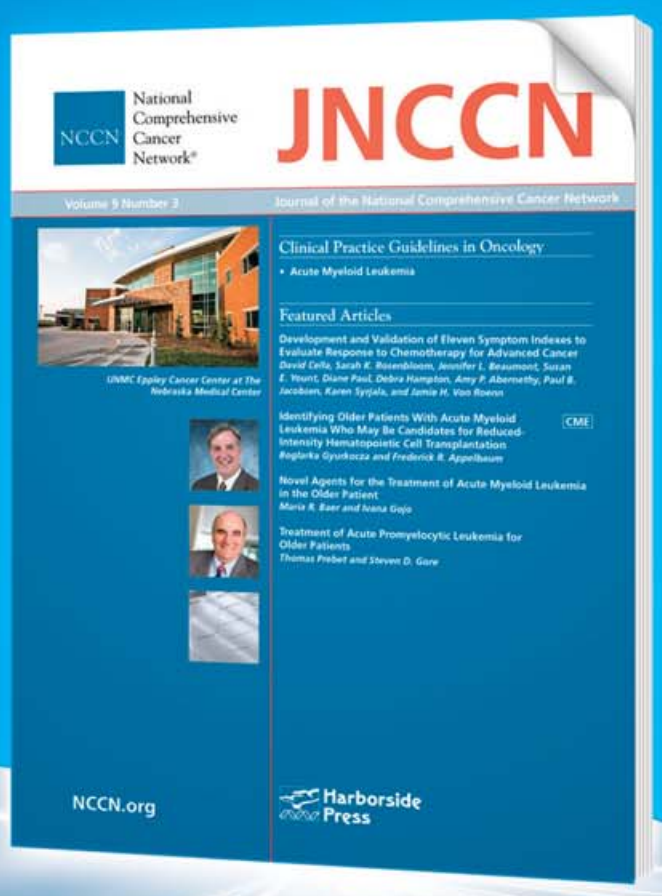
"Not only would the Dana-Farber Cancer Institute contract for our services, but it would work to enhance the quality of care in New Hampshire for patients with cancer," Dr. Hammond told *ASCO Daily News*.

> **"If you can create a center of excellence by bringing together critical physician groups, a practice can create an advantage for themselves."**
>
> — R. Steven Paulson, MD

Today, the volume of patients served by New Hampshire Oncology/Hematology, in partnership with the Dana-Farber Cancer Institute, has expanded dramatically; in the first quarter of 2009, the total number of clinic visits was 600. By the last quarter of 2010 the number had increased to 1,200. In addition, the number of new patients or consults per full-time employed physician went from 375 in 2009 to 450 in 2010.

Dr. Hammond said that collaboration of this sort with a large, well-established university institute depends on the size of the university partner. "The university needs to have a magnanimous desire to enhance your practice and to improve care in the community," he said. ●

A Network of Knowledge on Every Page



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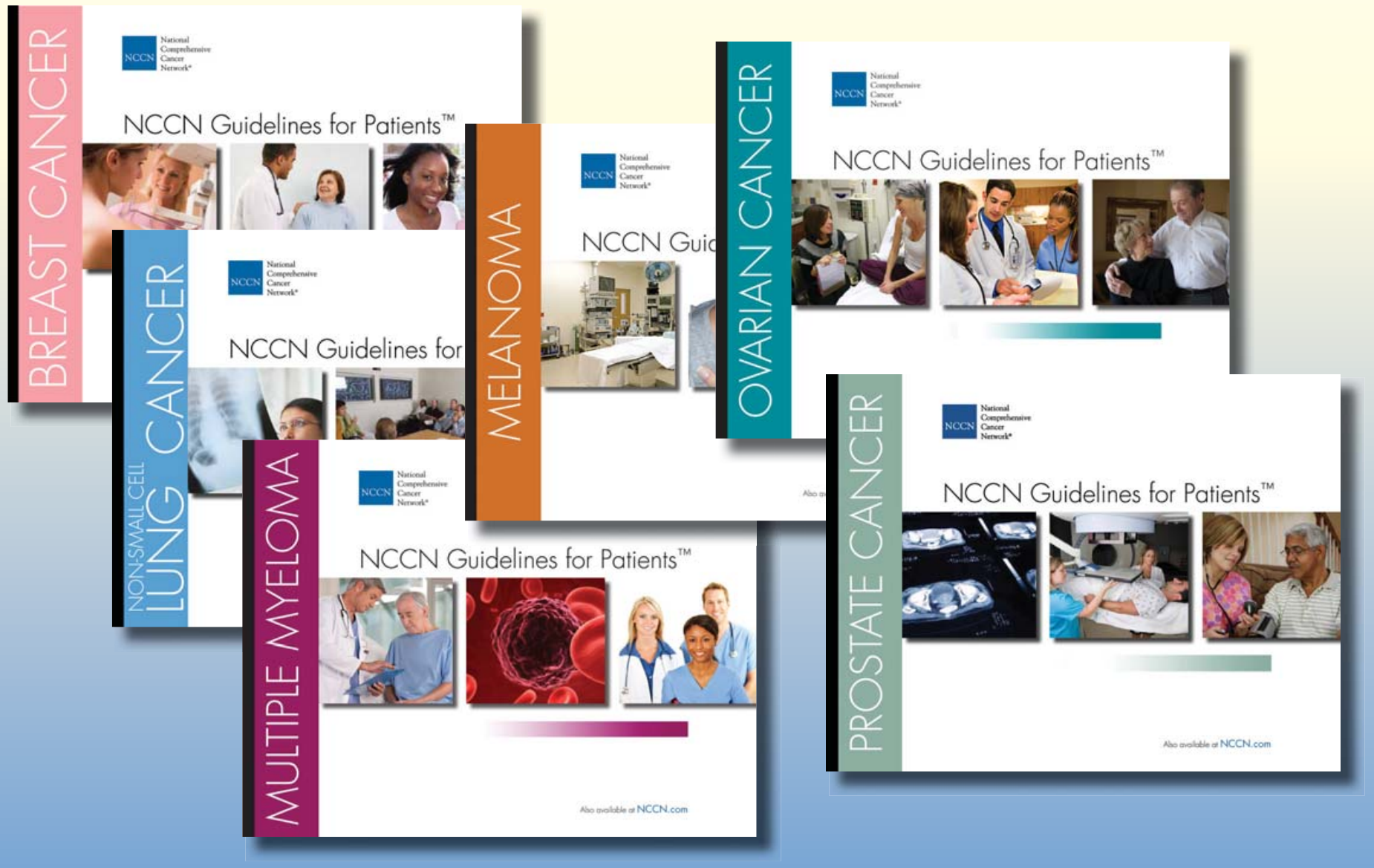

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2011 Gastrointestinal Cancers Symposium Makes Electronic, Environmental Advancements

With more than 2,800 in attendance, the 2011 Gastrointestinal Cancers Symposium was held January 20-22 at the Moscone West Building in San Francisco, California. The meeting program showcased advances in research and highlighted strategies for the treatment of patients with gastrointestinal cancers during a variety of sessions tailored for a multidisciplinary audience. The cosponsors for the 2011 Gastrointestinal Cancers Symposium were the American Gastroenterological Association Institute, the American Society of Clinical Oncology (ASCO), the American Society for Radiation Oncology, and the Society of Surgical Oncology.

Designed as a discussion-based meeting, the Symposium fostered dialogue among oncologists and other members of the cancer care community. More than 600 abstracts were presented in Oral Abstract, General, and Poster Sessions, and, new this year, attendees were able to submit questions electronically via Twitter, text message, or a website as part of "e-Q&A" during all Oral Abstract Sessions.

Other sessions included three Translational Research Sessions, which offered attendees cutting-edge details on the latest research in the field of gastrointestinal oncology on topics such as gastrointestinal stromal tumors, clinical trials, and genome sequencing. Another highlight was the evening Tumor Board Session, "How Should Histology Influence the Selection of Treatment in Esophageal Cancer?" that employed audience-response technology, allowing more time to be devoted to interactive learning. Four panelists served as faculty for the session, which was open to all attendees.

This year's Meet the Professor Sessions — during which experts discussed important research on a variety of topics — were very well attended, as was the Fellows, Residents, and Junior Faculty Networking Luncheon, which had record-breaking attendance. The 2011 Symposium's keynote lecture, "The Influence of Microsatellite Instability on Management of Colon Cancer," was delivered by Henry T. Lynch, MD, of Creighton University. Dr. Lynch's lecture focused on how predictive genetic testing, especially for Lynch syndrome, garners evidence of cancer-causing mutations, leading to highly targeted screening for early cancer detection and/or to definitive management.

"Lynch syndrome is quite common as it accounts for somewhere between 3% and 5% [of colorectal cancers], [which is] 61,000 cases estimated worldwide. In the United States, we have about 142,000 cases, and [more than] 7,000 [hereditary] cases," Dr. Lynch said during his Keynote lecture. "When you have a hereditary case, you really have a lot of material [in] your hands, and you can save lives. As everyone in the audience knows, colorectal cancer is truly a preventable disease."

Several electronic additions were made to this year's meeting, including the choice between receiving the *Gastrointestinal Cancers Symposium Proceedings* on USB or in print. In addition, Symposium attendees were able to access the entirety of *Proceedings* electronically at www.gicasym.org, allowing for a wider variety of format options.

As another technologic first for the Gastrointestinal Cancers Symposium, all attendees received Virtual Meeting access with their Symposium registration. Virtual Meeting, the largest online collection of oncology-related slides, audio, and video presentations, is a valuable resource for viewing presentations that an attendee may have missed and for reviewing crucial information after the Symposium's conclusion. Access the Virtual Meeting by going to gicasym.org.

The technologic aspects of the Symposium weren't the only changes to be seen this year. The GastrointestinaI Cancers Symposium cosponsors incorporated many eco-conscious initiatives in order to host an environmentally sensitive meeting. These changes included: encouraging attendees to bring tote bags to the Symposium in an effort to avoid waste and use fewer shipping resources;

See GI Cancers Symposium, Page 30B

Merit Awards and Save the Date Info

Merit Awards recognize the work of oncology fellows who are first authors on outstanding Gastrointestinal Cancers Symposium abstracts. These awards provide residents and fellows with the opportunity to present their research and interact with others in their field, as well as further promote clinical research by young scientists. GI Cancers Symposium Merit Award application materials must be submitted through the 2012 abstract submitter. Check www.gicasym.org for updates and application deadlines.

The following are the recipients of the 2011 Gastrointestinal Cancers Symposium Merit Awards:

Anasooya A. Abraham, MD
University of Minnesota
Pierre Bohanes, MD
University of Southern California Norris Comprehensive Cancer Center
Chiara Braconi, MD, PhD
The Ohio State University Medical Center
Jean Butte, MD
Memorial Sloan-Kettering Cancer Center
David Chang, MD
Garvan Institute of Medical Research
Giovanni Corso, MD
Translational Research Laboratory and ITT, University of Siena
Johan L. Dikken, MD
Leiden University Medical Center
Marjun Philip Duldulao, MD
City of Hope National Medical Center
Ryan C. Fields, MD
Memorial Sloan-Kettering Cancer Center
Mark D. Girgis, MD
University of California, Los Angeles
Christopher Hanyoung Lieu, MD
University of Texas M. D. Anderson Cancer Center
Joyce Ho, MD
City of Hope National Medical Center
Maria Ho, MD
British Columbia Cancer Agency
Edward Kim, MD
University of Michigan Comprehensive Cancer Center
Christopher Moran, MD
John Wayne Cancer Institute
Geraldine Perkins, MD
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Mayo Clinic
Akihiro Suzuki, MD
University of Texas M. D. Anderson Cancer Center
Federico Tozzi, MD
University of Texas M. D. Anderson Cancer Center
Richard Tuli, MD, PhD
The Johns Hopkins University School of Medicine
Rebecca Wiatrek, MD
City of Hope National Medical Center

The 2012 Gastrointestinal Cancers Symposium will be held January 19-21, 2012, at the Moscone Center in San Francisco, California.

Oncologist-approved GI Patient Materials Available on Cancer.Net

Sharing research from the 2011 Gastrointestinal Cancers Symposium with your patients is simple with Cancer.Net, ASCO's patient information website. This resource features interactive, easy-to-find information in several formats, including videos with ASCO experts and podcasts, as well as weekly articles on special topics. Below are some of the oncologist-vetted patient materials available on Cancer.Net:

- To help patients understand what the latest findings mean for them, the *Gastrointestinal Cancer Advances: News from the 2011 Gastrointestinal Cancers Symposium* (www.cancer.net/canceradvances) newsletter highlights the most noteworthy studies in patient-friendly language. The newsletter also provides a list of suggested questions patients can ask their doctor as well as links to additional disease-specific resources on Cancer.Net.
- *ASCO Answers* fact sheets on colorectal, esophageal, liver, pancreatic, and stomach cancer, including a fact sheet on colorectal cancer in Spanish, are available to download at www.cancer.net/factsheets or to order at www.asco.org/store.
- Detailed Guides to Cancer are available on gastrointestinal cancers at www.cancer.net/cancer or in Spanish at www.cancer.net/espanol. In addition, a printed version of the Guide to Colorectal Cancer is available for order at www.asco.org/store.
- Patient-friendly versions of ASCO's clinical practice guidelines on tumor markers for gastrointestinal cancers and follow-up care for colorectal cancer are available at www.cancer.net/whattoknow.
- Videos with ASCO experts discussing what's new in colorectal cancer care and treatments can be viewed online at www.cancer.net/videos.
- Podcasts covering the recent research on gastrointestinal cancers from the ASCO Annual Meeting and Gastrointestinal Cancers Symposium can be found at www.cancer.net/podcasts.

Stop by ASCO Central (Booth #7004) in the Oncology Professional's Hall to pick up copies of these educational and promotional materials for your patients and to take a tour of Cancer.Net. You also can order free Cancer.Net promotional materials — including referral cards, leaflets, cancer information prescription pads, and posters for waiting rooms and resource centers — through the ASCO University Bookstore (www.cancer.net/ordermaterials). ●

Core

TRIAL CURRENTLY RECRUITING

A Randomized Phase II Trial for Newly Diagnosed Glioblastoma Patients: Cilengitide in subjects with newly diagnOsed glioblastoma multifoRme and unmethylated MGMT genE promoter

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MGMT: O^6-methylguanine–DNA methyltransferase; RT: radiotherapy; TMZ: temozolomide

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Learn More About the CORE trial

Please call 1-800-507-5284 or refer to ClinicalTrials.gov for more information (http://www.clinicaltrials.gov/ct2/show/NCT00813943)

The CORE study is in collaboration with the Canadian Brain Tumour Consortium (CBTC).

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ASCO Develops New Formats for Delivering, Updating Clinical Practice Guidelines

The ASCO Clinical Practice Guidelines program is using new vehicles for delivering the most up-to-date clinical guidance to practicing oncologists and for enhancing the quality of clinical oncology practice. Clinical practice guidelines are consistently among the most-downloaded items from the *Journal of Clinical Oncology* and the *Journal of Oncology Practice*.

Provisional Clinical Opinions

In 2011 ASCO expects to expand its portfolio of provisional clinical opinions (PCOs), which are issued in response to emerging information that has the potential to change the practice of oncology. PCOs offer timely clinical direction to the oncology community following the publication or presentation of potentially practice-changing data from major studies, and may serve in some cases as interim direction to the membership pending the development or updating of an ASCO clinical practice guideline.

The PCO on "Epidermal Growth Factor Receptor (EGFR) Mutation Testing for Patients with Advanced Non-small Cell Lung Cancer Considering First-line EGFR Tyrosine-kinase Inhibitor (TKI) Therapy" recommends that patients with non-small cell lung cancer who are being considered for first-line therapy with an EGFR TKI should have their tumor tested for EGFR mutations to determine appropriate therapy. The PCO was published ahead of print at jco.ascopubs.org. (*For more information on the ASCO PCO on EGFR mutation testing, see the related article in tomorrow's issue of* ASCO Daily News, *Section B.*)

PCOs in Development

The Clinical Practice Guideline Committee is involved in the creation of a PCO to be published this summer related to the appropriate timing and delivery of palliative care, in response to a study of palliative care and non-small cell lung cancer published in the *New England Journal of Medicine*. (*For more information on this landmark study, see the short article in Saturday's issue of* ASCO Daily News, *Section B.)*

Two PCOs debuted in 2010 and can be accessed at www.asco.org/guidlines.

- Testing for KRAS Gene Mutations in Patients with Metastatic Colorectal Carcinoma to Predict Response to Anti-Epidermal Growth Factor Receptor Monoclonal Antibody Therapy and
- Chronic Hepatitis B Virus Infection Screening in Patients Receiving Cytotoxic Chemotherapy for Treatment of Malignant Diseases

Focused Updates

Existing guidelines are reviewed and updated periodically, but new information about evolving standards of care and best practices is constantly emerging. In order to incorporate the latest discoveries into existing guidelines, ASCO will begin issuing focused updates. These focused updates offer new information on a single recommendation (or subset of recommendations) in advance of a scheduled guideline update, allowing for more timely incorporation of new evidence into clinical guidance.

The first focused update will be to the ASCO Guideline Update on Chemotherapy for Stage IV Non-Small Cell Lung Cancer regarding maintenance chemotherapy, and was published in order to address a U.S. Food and Drug Administration (FDA) indication for pemetrexed that was approved after the original guideline was issued. (*The recommendation on maintenance therapy in this guideline will be updated pending consideration of recently published relevant data on this and other agents. At the time this article was written, publication was expected to be in early to mid-summer.)*

Expert-consensus–based Guidelines

In the past, ASCO has issued primarily evidence-based guidelines, in which strong scientific data inform the recommendations of the guideline. However, there are many clinical scenarios in which scientific evidence does not clearly indicate appropriate treatment, yet oncologists still need guidance on how to best manage the disease and provide the highest level of care to patients.

In these cases, ASCO will begin to issue expert-consensus–based guidelines informed by both systematic literature review and recommendations by experts in the field. When a recommendation is supported by a high percentage of the expert contributors, it will be included in the ASCO-issued guidance.

In March, the Clinical Practice Guideline Committee began the process of creating an expert-consensus–based guideline in the area of optimal treatment for castration-resistant prostate cancer.

A Critical Component of Quality Care

Clinical practice guidelines and other ASCO-issued guidance are one leg, together with electronic health records (EHR) and the

See Clinical Practice Guidelines, Page 27B

Diabetes and Cancer: Education Session Examines Metformin's Prevention Potential

Diabetes may increase risk of malignancies, but evidence is mounting on metformin's anticancer effects

Evidence continues to accumulate on the associations between diabetes and increased risk of a number of cancer types. One of the most commonly prescribed medications for diabetes has shown substantial promise in cancer prevention. Today's Education Session "Diabetes and Anti-diabetic Drugs: Association with Cancer Risk and Potential for Primary and Secondary Prevention" will discuss the epidemiologic evidence of the diabetes–cancer link, as well as the preclinical and clinical progress toward understanding metformin's potential in cancer prevention. The session will be held today, 11:30 AM – 12:45 AM, Room S100a, South Building.

Pamela J. Goodwin, MD, MSc, FRCPC, of Mount Sinai Hospital in Toronto, will serve as Chair of the session. She will discuss the diabetes drug metformin and its potential as a cancer prevention and treatment agent. Metformin is a cheap and easily accessible drug around the world, highlighting the global potential if it proves to be effective at reducing cancer risk.

"Early results of observational and intervention studies suggest that metformin may enhance the efficacy of standard chemotherapy, or that it may actually alter the biologic growth rates of cancer cells by itself," Dr. Goodwin said in an interview with *ASCO Daily News*. She noted that there are pilot studies planned to look into metformin's effect on mammographic density, and her own group has already begun a large, randomized, international trial that will examine the effect of metformin on breast cancer outcomes. The study will eventually include 3,582 patients. A second study will examine the potential for metformin to enhance response to chemotherapy in metastatic breast cancer.

Epidemiologic Links

Lorraine Lipscombe, MD, MSc, FRCPC, of the University of Toronto, will discuss the epidemiologic evidence that links diabetes and cancer. A number of cancer types have been associated with diabetes, including malignancies of the breast, endometrium, pancreas, and colon. Dr. Lipscombe said that other tumor types have shown weaker associations with diabetes, but the effect does seem to be wide-ranging across many cancers.

"The risks are in the area of maybe a 20% increase up to a doubling of cancer risk," Dr. Lipscombe told *ASCO Daily News*. "For

example, for endometrial cancer, women with diabetes have double the risk of cancer, whereas for breast cancer it is about a 20% increase." There also is evidence that patients with diabetes who do develop cancer have a worse prognosis. It remains unclear why this is the case, because diabetes itself has been shown to shorten life spans and may not actually worsen the cancer directly.

There are a number of possible explanations for the increased cancer risk associated with diabetes. There may simply be a constellation of overlapping risk factors — obesity, lifestyle, genetic factors, and nutritional factors — for the two conditions. The specifics of diabetes also may play a role, with increased circulating glucose and/or insulin promoting the growth of tumor cells.

In addition, there is a possibility that certain drugs prescribed as treatments for diabetes could increase the risk of cancer or accelerate tumor development. For example, in recent years there was a suggestion that the insulin analog glargine was associated with an increased risk of cancer. Subsequent studies, however, have called that finding into question.

Preclinical Evidence on Metformin

Although some diabetes drugs could raise the risk of cancer, it is increasingly clear that metformin does just the opposite. Ann Thor, MD, of the University of Colorado School of Medicine, will discuss the preclinical and laboratory evidence explaining metformin's effect as a cancer prevention agent.

According to Dr. Thor, metformin's mechanism of action appears to differ in the different molecular subtypes of breast cancer. She said that metformin "is perhaps most effective in triple-negative breast cancer tumors, which is exciting because those are the tumors for which we have the least effective therapeutics, and those are the tumors with the worst outcomes." She added that, although breast cancer is among the more promising settings for metformin, there is evidence for efficacy in other tumor types as well.

Dr. Thor noted that metformin could reduce effects of resistance to chemotherapeutic agents such as trastuzumab and lapatinib. "The combination of metformin with these other agents has been proposed by some people as a possible treatment in patients with HER2-positive breast cancer," she said.

See Diabetes and Cancer, Page 32B

Optimal Antiemetic Control Requires Optimal Treatment

ASCO GUIDELINES

The next guideline readying for print in the *Journal of Clinical Oncology (JCO)* is an update to, "The American Society of Clinical Oncology Clinical Practice Guideline Update on Antiemetics in Oncology." This supportive care guideline was originally published in 1999 and updated once in 2006. The Steering Committee charged with overseeing this effort included Ethan M. Basch, MD, Paul J. Hesketh, MD, Mark G. Kris, MD, and Gary H. Lyman, MD, MPH, FRCP.

The antiemetics guideline is the most frequently downloaded guideline from among the ASCO guidelines repertoire. In fact, the guideline was among the top five most downloaded articles from *JCO* in 2010. Dr. Kris, of Memorial Sloan-Kettering Cancer Center stated in an interview with *ASCO Daily News* that of all side effects, nausea and vomiting are the leading concerns among patients starting cancer treatment.

"Being able to deliver state-of-the-art care to lessen or eliminate that problem is extraordinarily important," Dr. Kris said. "The guideline assures that the enormous research that been done on the prevention of emesis is translated into care. Of all the ASCO guidelines, this is the one that probably has the greatest immediacy to the whole community of patients who are facing cancer treatment."

The intended audience for this guideline is medical oncologists, radiation oncologists, oncology nurses, and oncology pharmacists. To update the recommendation, a systematic review of randomized, controlled trials was completed and includes patients treated with both radiation therapy and chemotherapy. The Update Committee considered data from the review to revise recommendations.

Tailoring Treatment Based on Emetic Risk

The guideline update includes two tables that differentiate emetic risk based on treatment and allow tailoring of antiemetic therapy. One table delineates risk according to radiation site, and the other defines emetic risk for single chemotherapy agents. Both emetic-risk tables have been revised over time to include information on new agents.[1] The Update Committee endorsed one revision to the chemotherapy-risk table, concerning the emetic risk of treatment with combined

anthracycline and cyclophosphamide, which is frequently used in the adjuvant setting for breast cancer.

The guideline also includes recommendations for patients who experience symptoms despite optimal prophylaxis, as well as for those who experience anticipatory nausea and emesis. The committee evaluated how likely patients were to experience nausea or vomiting and whether this likelihood met the defined threshold for highly emetic risk (90%); historical data from women who were treated with combination anthracycline and cyclophosphamide in the absence of antiemetics were considered.

In accordance with previous recommendations, members of the Update Committee described this combination as a highly emetic regimen, although each agent alone demonstrates only moderate risk for this treatment-related side effect. The current recommendation for patients who receive highly emetogenic chemotherapy is a combined three-drug antiemetic regimen of neurokinin 1 (NK-1) antagonist, a 5-HT_3 antagonist, and a corticosteroid — a recommendation initially developed in the 2006 update and supported by more recently published data.[2]

New Formulations of Existing Antiemetics

Since 2006, a new formulation of the oral NK-1 antagonist aprepitant has been approved by the U.S. Food and Drug Administration (FDA). Fosaprepitant, an intravenous formulation, is available, and data describing equivalence with aprepitant has been published. In contrast to the 3-day dosing schedule for aprepitant, fosaprepitant is delivered only once.[3]

A new formulation for the serotonin antagonist granisetron, previously available as intravenous and oral preparations, also was approved. A transdermal patch was recommended by the Update Committee for patients undergoing multiday chemotherapy and either moderate- or high-risk radiation therapy. The patch must be applied at least 24 hours before the start of treatment.

The Update Committee made some additional comments on patient treatment intended for consideration by clinicians who treat patients at risk of developing treatment-related nausea and vomiting. Suggestions include that patients be given a prescription for rescue therapy before they leave the office on the first day of treatment and that clinicians should ask patients about symptoms experienced throughout the entire course of treatment.

"This is an area of oncology treatment that has changed radically," Dr. Kris told *ASCO Daily News*. "Thirty years ago patients would be hospitalized for days just to support them through a period of severe nausea. Today, research has produced effective treatments that permit all care on an outpatient basis, allowing patients to get back to their normal activities with as little disruption as possible. With symptoms prevented, patients are more concerned with where to have lunch on the day of treatment than [they are with] side-effects, [which] is the way it should be." ●

References

1. Hesketh PJ, Kris MG, Grunberg SM, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. *J Clin Oncol*. 1997;15:103-109.
2. Hoshi E, Takahashi t, Takagi M, et al. Aprepitant prevents chemotherapy-induced nausea and vomiting in Japanese cancer patients receiving high-does cisplatin: a multicenter randomized, double-blind, placebo-controlled study (abstract P-20). Presented at the 20th Anniversary International MASCC/ISOO Symposium, St. Gallen, Switzerland, June 27-30, 2007.
3. Grunberg S, Chua D, Maru A, et al. Single-Dose Fosaprepitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting Associated With Cisplatin Therapy: Randomized, Double-Blind Study Protocol--EASE. *J Clin Oncol*. 2011, March 7. Epub ahead of print.

Clinical Practice Guidelines

Continued from Page 23B

Quality Oncology Practice Initiative (QOPI®; ASCO's oncologist-driven performance measurement program), of what Society leadership calls "the quality triangle."

Guidelines, QOPI, and EHR "are the corners, if you will, of quality. They all relate to one another and they all have to be designed with the other two pieces of the triangle in mind," ASCO CEO Allen S. Lichter, MD, said in an interview with *ASCO Daily News*. "In order to make QOPI more productive, you should be able to report information electronically. To do that, you have to design measures that are based, at least in part, on our guidelines and that can be abstracted from an EHR."

Over the next several years, legislation in the Patient Protection and Affordable Care Act will begin to reward practices that meet quality standards and penalize those that fall short or choose not to participate in quality measurement. In this environment, Dr. Lichter said, that there is concern about the fragmentation of quality reporting in oncology. "If every major insurer, health agency, and organization has a quality program, the physician in the field could be bedeviled with half a dozen or more quality programs with different reporting requirements and different measurements," he said. "Creating a very robust quality system through the quality triangle and through our new Quality Department, where all three components will sit together, is an important policy priority for ASCO." ●

Leadership Development Program Nurtures Aspiring Leaders in the Oncology Community

Mid-career oncologists interested in taking on a more visible role within ASCO have a unique opportunity to gain extensive exposure to the mission of ASCO, to leadership positions within the organization, and to the Society's role in improving cancer care and patient welfare by participating in the organization's formal Leadership Development Program. The year-long program is designed to set oncologists in the early phases of their career on the path to becoming future leaders within the Society.

A time commitment for travel and training is required for the Program, as participants must attend all of the program's meetings/activities held throughout the year, including the ASCO Annual Meeting. As part of this year-long commitment, participants will network with prominent Society leaders, participate in a leadership boot camp held at ASCO Headquarters, and gain firsthand knowledge about ASCO research activities.

Participants will also participate in an interactive learning project, allowing them to collaborate with both ASCO staff and volunteers. The projects will offer hands-on training that will further participants' leadership skills, as well as benefit the Society as a whole.

Participants in the 2010–2011 program will graduate during the 2011 ASCO Annual Meeting in Chicago. Upon completion of the program, graduates will have opportunities to take on roles within ASCO's Committees and Task Forces.

Although applications for the 2011–2012 Leadership Development Program are closed, visit ASCO.org for information about the application process for the 2012–2013 Program or send an e-mail to professionaldevelopment@asco.org.

Participants of the 2010-2011 Leadership Development Program acquire the leadership skills and practical knowledge needed to excel as modern oncology leaders. Participants collaborate with ASCO staff and volunteers in an interactive project, as well as in a leadership bootcamp.

Participant Perspectives

In an effort to relay firsthand experiences from the program, the 2010-2011 graduating class was asked to answer one of two questions. The questions and a sampling of responses are provided below; a complete panel of responses can be found at *ASCO Daily News* online.

Q With regard to the ASCO Leadership Development Program, how have you been stretched by the program and how has that affected your vision for the future of your career?

Marcia Brose, MD, PhD
2000 Young Investigator Award recipient

I learned valuable skills that expanded my vision for my career as a physician–scientist and leader in medical oncology. The training in leadership skills that formed a core of the program allowed me to understand how a large goal can be accomplished with a level of ease that I previously did not think possible. I learned how far-reaching ASCO's role is in developing policies for issues such as conflict of interest, and how those policies are developed with input from a great number of experts in many fields. Most importantly, I learned how to work effectively with a group of extremely talented individuals using ASCO's vast resources (including leadership and staff) to complete a project that was of great importance to all of us.

As a result of this experience, I will now approach large career challenges with excitement and confidence, not with dread or anxiety that I will overwhelmed by the task.

Melissa S. Dillmon, MD

The ASCO Leadership Development Program strives to teach its participants how to build a team and then lead that team to greatness. As participants in this program, we have been challenged to define a strategic issue and work together to reach a desired outcome. Many of us are at critical turning points in our early careers. My clinic is building a new cancer center, and I have used my leadership training to work with a radiation oncologist to redefine the vision of our cancer program. We are working through the same process our leadership development team has used to develop a strategy that will take our patients' experiences from good to great. I also have been personally challenged by the call of our mentors at ASCO to be assertive and to seek roles of leadership where my skills can be best used. I recently ran for a position on the Executive Board of my clinic, which is comprised of 200 providers. I am now the first woman to sit on that board since the clinic's creation in 1948. I see this program as a springboard for future leadership opportunities in my clinic and in the larger oncology community.

Q With regard to the ASCO Leadership Development Program, what is the single most important effect this experience has thus far had on you and your career?

Stephen Grobmyer, MD, FACS

The ASCO Leadership Development Program has uniquely provided with new insight about successfully handling the challenges associated with leading an initially unfamiliar and diverse group of individuals. I have learned that the most successful leaders prioritize the success of their team over personal success. Also, I have learned that many leaders don't listen enough; listening, however, is a very important part of leading others to success. There are recurring challenges in group leadership that one can learn to anticipate and solve for the ultimate benefit of a group or organization. The important skills of strategic planning, professional

See Leadership Development, Page 30B

2011–2012 Leadership Development Program Participants

Anne C. Chiang, MD, PhD
Connecticut Oncology and Hematology, LLP
2005 YIA recipient, 2007 CDA recipient

Cathy Eng, MD
University of Texas M. D. Anderson Cancer Center

Ralph J. Hauke, MD
Nebraska Cancer Specialists

Reshma Jagsi, MD
University of Michigan

Tari A. King, MD
Memorial Sloan-Kettering Cancer Center

Natasha B. Leighl, MD
Princess Margaret Hospital
2001 YIA recipient, 2002 CDA recipient

Bruno C. Medeiros, MD
Stanford Cancer Center
2007 YIA recipient

Wells A. Messersmith, MD
University of Colorado
2004 YIA recipient

Ann H. Partridge, MD
Dana-Farber Cancer Institute
2001 YIA recipient, 2003 CDA recipient, 2010 ICCG

Blase N. Polite, MD, MPH
University of Chicago
2008 CDA recipient

Karen L. Reckamp, MD
City of Hope
2004 YIA recipient

Lecia V. Sequist, MD, MPH
Massachusetts General Hospital

YIA, Young Investigator Award; CDA, Career Development Award; ICCG: Conquer Cancer Foundation Improving Cancer Care Grant, funded by Susan G. Komen for the Cure®. Both the YIA and CDA are funded by the Conquer Cancer Foundation (previously known as The ASCO Cancer Foundation®).

New Cardiac Comorbidity Boards on ASCO University®

ASCO University® is now offering a pilot series that focuses on cardiovascular disease and cancer treatment-related toxicities in patients. Each module in this online program features a patient case that is presented and discussed by expert faculty and an open discussion forum that facilitates continued interaction and dialogue between online participants and the faculty.

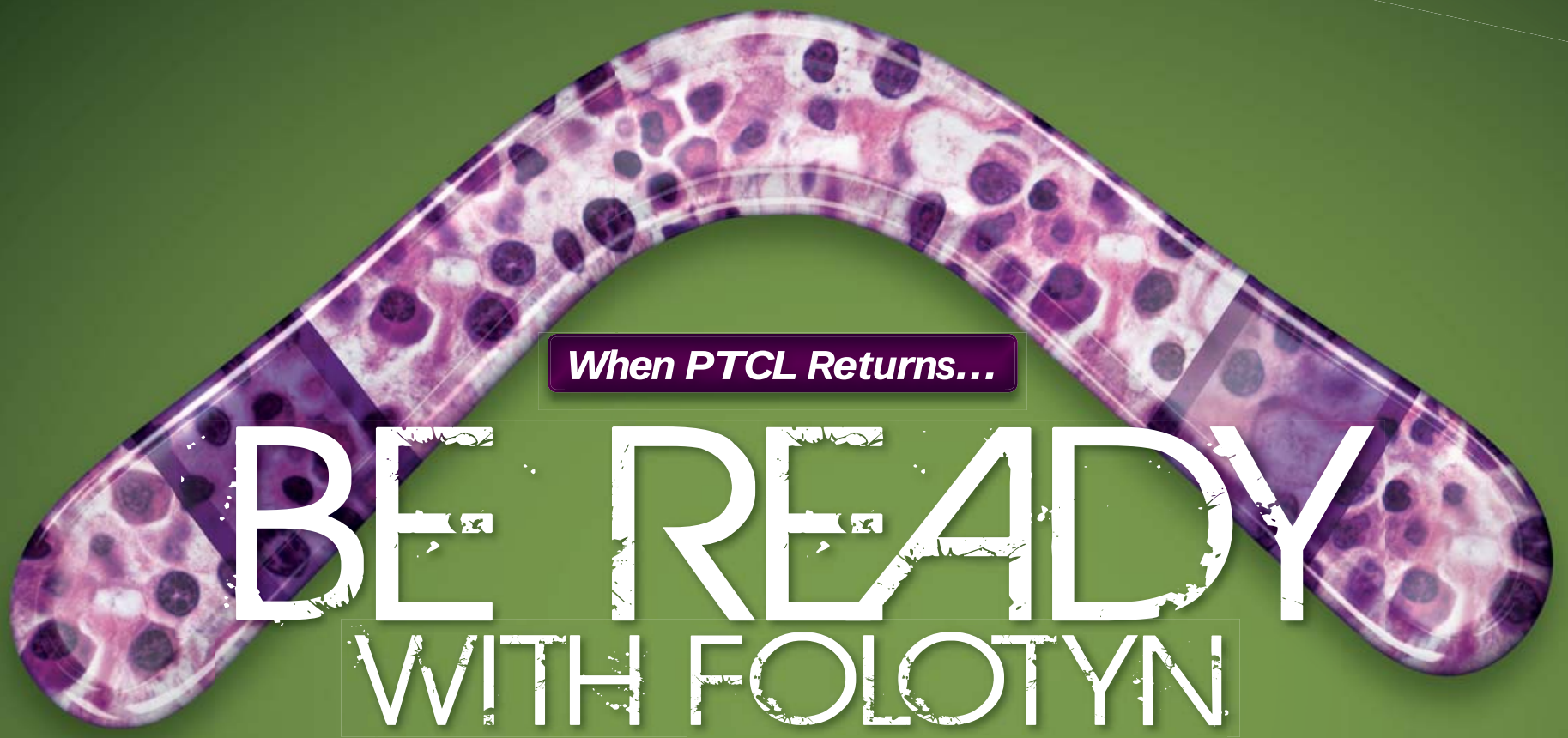
Planning Group members, Sandra Swain, MD, Director of the Washington Cancer Center in Washington, DC, and Richard Steingart, MD, FACC, FSGC, Chief of Cardiology Service at Memorial Sloan-Kettering Cancer Center in New York, collaborate to identify topic areas for each module and identify experts in cardiology and oncology to present the case discussion.

ASCO University®
Your online educational home for oncology

"This new series addresses some of the difficult cardiac issues that must be managed in our patients," Dr. Swain said.

Two case topics are currently available; the first deals with toxicities associated with trastuzumab and anthracycline therapy, and the second, just released in May 2011, focuses on hypertension and VEGF signaling pathway inhibitors. A third module will be released in the fall and will address issues related to treatment with tyrosine kinase inhibitors. All of this content may be found on ASCO University located at http://university.asco.org/cardiac. Demonstrations of content are available at the ASCO University portion of ASCO Central (Booth #7004) in the Oncology Professionals Hall. ●

The indication for FOLOTYN is based on overall response rate.
Clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated.



When PTCL Returns…

BE READY WITH FOLOTYN

(pralatrexate injection)

Demonstrated response in relapsed or refractory PTCL[1]

27% overall response rate (CR+CRu+PR) by central review (95% CI, 19–36)*

Of the responders, 66% responded within Cycle 1*

- *Median time to first response was 45 days (range=37-349 days)*

9.4-month median duration of response by central review (range=1–503 days)*

- *12% (95% CI, 7-20) of patients had responses lasting ≥14 weeks (range=98-503 days)*

Demonstrated response in PROPEL—the largest prospective single-arm, open-label clinical trial in PTCL

Important Safety Information

Warnings and Precautions

FOLOTYN may suppress bone marrow function, manifested by thrombocytopenia, neutropenia, and anemia. Monitor blood counts and omit or modify dose for hematologic toxicities.

Mucositis may occur. If ≥Grade 2 mucositis is observed, omit or modify dose. Patients should be instructed to take folic acid and receive vitamin B_{12} to potentially reduce treatment-related hematological toxicity and mucositis.

Fatal dermatologic reactions may occur. Dermatologic reactions may be progressive and increase in severity with further treatment. Patients with dermatologic reactions should be monitored closely, and if severe, FOLOTYN should be withheld or discontinued.

Tumor lysis syndrome may occur. Monitor patients and treat if needed.

FOLOTYN can cause fetal harm. Women should avoid becoming pregnant while being treated with FOLOTYN and pregnant women should be informed of the potential harm to the fetus.

Use caution and monitor patients when administering FOLOTYN to patients with moderate to severe renal function impairment.

Elevated liver function test abnormalities may occur and require monitoring. If liver function test abnormalities are ≥Grade 3, omit or modify dose.

Adverse Reactions

The most common adverse reactions were mucositis (70%), thrombocytopenia (41%), nausea (40%), and fatigue (36%).The most common serious adverse events are pyrexia, mucositis, sepsis, febrile neutropenia, dehydration, dyspnea, and thrombocytopenia.

Use in Specific Patient Populations

Nursing mothers should be advised to discontinue nursing or the drug, taking into consideration the importance of the drug to the mother.

Drug Interactions

Co-administration of drugs subject to renal clearance (e.g., probenecid, NSAIDs, and trimethoprim/sulfamethoxazole) may result in delayed renal clearance.

Please see FOLOTYN Full Prescribing Information.

*Per independent central review

Reference: 1. FOLOTYN Prescribing Information. Allos Therapeutics, Inc., 2011.

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Please see accompanying brief summary of Prescribing Information.

FOLOTYN® (pralatrexate injection)

www.FOLOTYN.com

Brief summary of Full Prescribing Information for FOLOTYN® (pralatrexate injection)—Please consult Full Prescribing Information.

INDICATIONS AND USAGE

FOLOTYN is indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). This indication is based on overall response rate. Clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated.

WARNINGS AND PRECAUTIONS

Bone Marrow Suppression

FOLOTYN can suppress bone marrow function, manifested by thrombocytopenia, neutropenia, and anemia. Dose modifications are based on ANC and platelet count prior to each dose.

Mucositis

Treatment with FOLOTYN may cause mucositis. If ≥Grade 2 mucositis is observed, omit dose and follow guidelines in Table 1.

Dermatologic Reactions

FOLOTYN has been associated with severe dermatologic reactions, which may result in death. These dermatologic reactions have been reported in clinical studies (14/663 patients [2.1%]) and post marketing experience, and have included skin exfoliation, ulceration, and toxic epidermal necrolysis (TEN). These reactions may be progressive and increase in severity with further treatment, and may involve skin and subcutaneous sites of known lymphoma. Patients with dermatologic reactions should be monitored closely, and if severe, FOLOTYN should be withheld or discontinued.

Tumor Lysis Syndrome

Tumor lysis syndrome has been reported in patients with lymphoma receiving FOLOTYN. Patients receiving FOLOTYN should be monitored closely and treated for complications.

Folic Acid and Vitamin B_{12} Supplementation

Patients should be instructed to take folic acid and receive vitamin B_{12} to potentially reduce treatment-related hematological toxicity and mucositis.

Pregnancy Category D

FOLOTYN can cause fetal harm when administered to a pregnant woman. FOLOTYN was embryotoxic and fetotoxic in rats and rabbits. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Decreased Renal Function

Although FOLOTYN has not been formally tested in patients with renal impairment, caution is advised when administering FOLOTYN to patients with moderate to severe impairment. Monitor patients for renal function and systemic toxicity due to increased drug exposure.

Elevated Liver Enzymes

Liver function test abnormalities have been observed after FOLOTYN administration. Persistent liver function test abnormalities may be indicators of liver toxicity and require dose modification. Monitor patients for liver function.

ADVERSE REACTIONS

The most common adverse reactions observed in patients with peripheral t-cell lymphoma (PTCL) treated with FOLOTYN were mucositis, thrombocytopenia, nausea, and fatigue.

Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The safety of FOLOTYN was evaluated in 111 PTCL patients in a single-arm clinical study in which patients received a starting dose of 30 mg/m^2 once weekly for 6 weeks in 7-week cycles. The median duration of treatment was 70 days (range 1-540 days).

Most Frequent Adverse Reactions

Table 4 summarizes the most frequent adverse reactions, regardless of causality, using the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI CTCAE, version 3.0).

Table 4 Adverse Reactions Occurring in PTCL Patients (Incidence ≥10% of patients)

	N=111					
	Total		Grade 3		Grade 4	
Preferred Term	**N**	**%**	**N**	**%**	**N**	**%**
Any Adverse Event	111	100	48	43	34	31
Mucositis[a]	78	70	19	17	4	4
Thrombocytopenia[b]	45	41	15	14	21	19[b]
Nausea	44	40	4	4	0	0
Fatigue	40	36	5	5	2	2
Anemia	38	34	17	15	2	2
Constipation	37	33	0	0	0	0
Pyrexia	36	32	1	1	1	1
Edema	33	30	1	1	0	0
Cough	31	28	1	1	0	0
Epistaxis	29	26	0	0	0	0
Vomiting	28	25	2	2	0	0
Neutropenia	27	24	14	13	8	7
Diarrhea	23	21	2	2	0	0
Dyspnea	21	19	8	7	0	0
Anorexia	17	15	3	3	0	0
Hypokalemia	17	15	4	4	1	1
Rash	17	15	0	0	0	0
Pruritus	16	14	2	2	0	0
Pharyngolaryngeal pain	15	14	1	1	0	0

[a] Stomatitis or mucosal inflammation of the gastrointestinal and genitourinary tracts

[b] Five patients with platelets <10,000/µL

[c] Alanine aminotransferase, aspartate aminotransferase, and transaminases increased

Serious Adverse Events

Forty-four percent of patients (n=49) experienced a serious adverse event while on study or within 30 days after their last dose of FOLOTYN. The most common serious adverse events (>3%), regardless of causality, were pyrexia, mucositis, sepsis, febrile neutropenia, dehydration, dyspnea, and thrombocytopenia. One death from cardiopulmonary arrest in a patient with mucositis and febrile neutropenia was reported in this trial. Deaths from mucositis, febrile neutropenia, sepsis, and pancytopenia occurred in 1.2% of patients treated on all FOLOTYN trials at doses ranging from 30 to 325 mg/m^2.

Discontinuations

Twenty-three percent of patients (n=25) discontinued treatment with FOLOTYN due to adverse reactions. The adverse reactions reported most frequently as the reason for discontinuation of treatment were mucositis (6%, n=7) and thrombocytopenia (5%, n=5).

Dose Modifications

The target dose of FOLOTYN was 30 mg/m^2 once weekly for 6 weeks in 7-week cycles. The majority of patients (69%, n=77) remained at the target dose for the duration of treatment. Overall, 85% of scheduled doses were administered.

Post Marketing Experience

Toxic epidermal necrolysis has been identified during post approval use of FOLOTYN. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure (*see Warnings and Precautions*).

DRUG INTERACTIONS

In vitro studies indicate that pralatrexate is not a substrate, inhibitor, or inducer of CYP450 isoenzymes and has low potential for drug-drug interactions at CYP450 isoenzymes. No formal clinical assessments of pharmacokinetic drug-drug interactions between FOLOTYN and other drugs have been conducted. The effect of co-administration of the uricosuric drug probenecid on pralatrexate pharmacokinetics was investigated in a Phase 1 clinical study. Co-administration of increasing doses of probenecid resulted in delayed clearance of pralatrexate and a commensurate increase in exposure.

Due to the contribution of renal excretion (approximately 34%) to the overall clearance of pralatrexate, concomitant administration of drugs that are subject to substantial renal clearance (eg, NSAIDs, trimethoprim/sulfamethoxazole) may result in delayed clearance of pralatrexate.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category D (*see Warnings and Precautions*).

FOLOTYN can cause fetal harm when administered to a pregnant woman. Pralatrexate was embryotoxic and fetotoxic in rats at IV doses of 0.06 mg/kg/day (0.36 mg/m^2/day or about 1.2% of the clinical dose on a mg/m^2 basis) given on gestation days 7 through 20. Treatment with pralatrexate caused a dose-dependent decrease in fetal viability manifested as an increase in late, early, and total resorptions. There was also a dose-dependent increase in post-implantation loss. In rabbits, IV doses of 0.03 mg/kg/day (0.36 mg/m^2/day) or greater given on gestation days 8 through 21 also caused abortion and fetal lethality. This toxicity manifested as early and total resorptions, post-implantation loss, and a decrease in the total number of live fetuses. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Nursing Mothers

It is not known whether pralatrexate is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from this drug, a decision should be made whether to discontinue nursing or to discontinue FOLOTYN, taking into account the importance of FOLOTYN to the mother.

Pediatric Use

Pediatric patients were not included in clinical studies with FOLOTYN. The safety and effectiveness of FOLOTYN in pediatric patients have not been established.

Geriatric Use

In the PTCL efficacy study, 36% of patients (n=40) were 65 years of age and over. No overall differences in efficacy and safety were observed in patients based on age (<65 years compared with ≥65 years).

No dosage adjustment is required in elderly patients with normal renal function.

Hepatic Impairment

Formal studies have not been performed with FOLOTYN in patients with hepatic impairment. Patients with the following laboratory values were excluded from the pralatrexate lymphoma clinical trials: total bilirubin >1.5 mg/dL; aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >2.5 × upper limit of normal (ULN); and AST or ALT >5 × ULN if documented hepatic involvement with lymphoma.

Renal Impairment

See Warnings and Precautions.

OVERDOSAGE

No specific information is available on the treatment of overdosage of FOLOTYN. If an overdose occurs, general supportive measures should be instituted as deemed necessary by the treating physician. Based on FOLOTYN'S mechanism of action the prompt administration of leucovorin should be considered.

PATIENT COUNSELING INFORMATION

See FDA-approved Patient Package Insert.

Patients should be instructed to read the Patient Package Insert carefully.

DOSAGE AND ADMINISTRATION

FOLOTYN should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

Peripheral T-cell Lymphoma

The recommended dose of FOLOTYN is 30 mg/m^2 administered as an intravenous (IV) push over 3-5 minutes via the side port of a free-flowing 0.9% Sodium Chloride Injection, USP IV line once weekly for 6 weeks in 7-week cycles until progressive disease or unacceptable toxicity.

Vitamin Supplementation

Patients should take low-dose (1.0-1.25 mg) oral folic acid on a daily basis. Folic acid should be initiated during the 10-day period preceding the first dose of FOLOTYN, and dosing should continue during the full course of therapy and for 30 days after the last dose of FOLOTYN. Patients should also receive a vitamin B_{12} (1 mg) intramuscular injection no more than 10 weeks prior to the first dose of FOLOTYN and every 8-10 weeks thereafter. Subsequent vitamin B_{12} injections may be given the same day as treatment with FOLOTYN (*see Warnings and Precautions*).

Monitoring and Dose Modifications

Management of severe or intolerable adverse reactions may require dose omission, reduction, or interruption of FOLOTYN therapy.

Monitoring

Complete blood cell counts and severity of mucositis should be monitored weekly. Serum chemistry tests, including renal and hepatic function, should be performed prior to the start of the first and fourth dose of a given cycle.

Dose Modification Recommendations

Prior to administering any dose of FOLOTYN:

- Mucositis should be ≤Grade 1.
- Platelet count should be ≥100,000/µL for first dose and ≥50,000/µL for all subsequent doses.
- Absolute neutrophil count (ANC) should be ≥1,000/µL.

Doses may be omitted or reduced based on patient tolerance. Omitted doses will not be made up at the end of the cycle; once a dose reduction occurs for toxicity, do not re-escalate. For dose modifications and omissions, use the guidelines in Tables 1, 2, and 3.

Table 1 FOLOTYN Dose Modifications for Mucositis

Mucositis Grade[a] on Day of Treatment	Action	Dose upon Recovery to ≤Grade 1
Grade 2	Omit dose	Continue prior dose
Grade 2 recurrence	Omit dose	20 mg/m^2
Grade 3	Omit dose	20 mg/m^2
Grade 4	Stop therapy	

[a] Per National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI CTCAE, Version 3.0)

Table 2 FOLOTYN Dose Modifications for Hematologic Toxicities

Blood Count on Day of Treatment	Duration of Toxicity	Action	Dose upon Restart
Platelet <50,000/µL	1 week	Omit dose	Continue prior dose
	2 weeks	Omit dose	20 mg/m^2
	3 weeks	Stop therapy	
ANC 500-1,000/µL and no fever	1 week	Omit dose	Continue prior dose
ANC 500-1,000/µL with fever or ANC <500/µL	1 week	Omit dose, give G-CSF or GM-CSF support	Continue prior dose with G-CSF or GM-CSF support
	2 weeks or recurrence	Omit dose, give G-CSF or GM-CSF support	20 mg/m^2 with G-CSF or GM-CSF support
	3 weeks or 2nd recurrence	Stop therapy	

Table 3 FOLOTYN Dose Modifications for All Other Treatment-related Toxicities

Toxicity Grade[a] on Day of Treatment	Action	Dose upon Recovery to ≤Grade 2
Grade 3	Omit dose	20 mg/m^2
Grade 4	Stop therapy	

[a] Per National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI CTCAE, Version 3.0)

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U.S. Patent: 6,028,071 and 7,622,470
Rev.3: January 2011

Leadership Development

Continued from Page 28B

relationship building, conflict resolution, and consensus building learned in the course are ones that I am certain will be useful throughout the remainder of my professional career in oncology. I look forward to seeking out leadership opportunities in the future to apply skills learned in the course to broaden the effect of my efforts aimed at high-quality clinical care, education, and research in oncology.

Edward S. Kim, MD

2002 Young Investigator Award recipient

The ASCO Leadership Development Program has allowed me the opportunity to become more personally involved with a large comprehensive organization. I was involved as an active member prior to my involvement in the program; however, I now feel closer to the workings of ASCO and feel more personally involved with helping to support and define the future of ASCO. The personal interactions with my colleagues from other institutions also have been great experiences.

A. Craig Lockhart, MD

In most situations we volunteer for leadership assignments where we believe we can constructively contribute based on prior experience. In the Leadership Development Program we were assigned a project that was outside of our areas of expertise and that required immersion within an unfamiliar topic. We had to become facile with the issues surrounding our assignment, do background research to understand the unanswered questions, and be familiar with the complexities of the assignment including interactions with a related ASCO committee. The skills are not unlike those required for grant proposal writing. The experience of developing a grant proposal is personal, however, and the results of the outcome will have personal and individual affects. Conversely, the Leadership Development Program project had the potential to affect the Society and possibly the profession as a whole, therefore, a level of global sensitivity was required.

During the process, I have come to appreciate the scope of ASCO both nationally and internationally as a first-class organization with interests in many areas that I had not appreciated prior to this, including public policy, treatment guidelines that affect professional reimbursement, and the organization's excursions into new media. My experience within this program has galvanized my interest in professional leadership and broadened my leadership goals. ●

GI Cancers Symposium

Continued from Page 21B

distributing lanyards made from 100% bamboo, which is a renewable and sustainable natural resource; providing water coolers in instead of distributing bottled water; and reducing paper waste by making Symposium evaluations available online only.

In 2012, the Gastrointestinal Cancers Symposium will be held January 19-21, 2012, once again at the Moscone Center West Building in San Francisco, California. The abstract submitter will be open in early August 2011 and will close at 11:59 PM October 4, 2011. For more information about the upcoming Symposium, visit gicasym.org. ●

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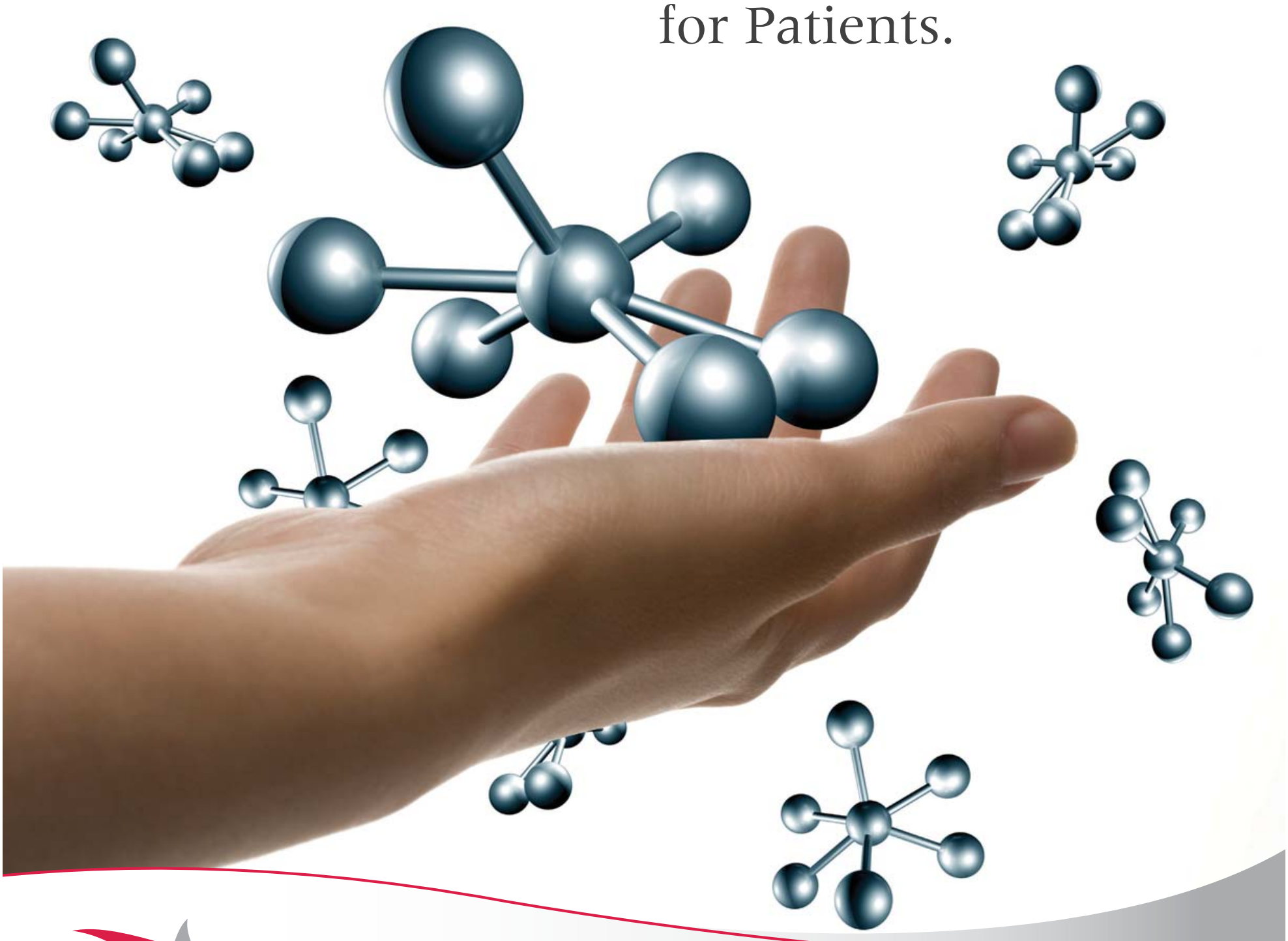

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A Decade of Change: Dr. Daniel Haller Reflects on *JCO* Editorship


Daniel G. Haller, MD, FACP

Daniel G. Haller, MD, has been at the forefront of the *Journal of Clinical Oncology (JCO)* since 2001, serving as Editor-in-Chief. With his service coming to a close, Dr. Haller will carry a legacy, alongside former *JCO* Editors-in-Chief Joseph R. Bertino, MD (1983-1987), and George P. Canellos, MD (1987-2001), of having facilitated the dissemination of high-quality research to thousands of readers across the world.

Dr. Haller's time as *JCO* Editor-in-Chief covered two 5-year terms — the maximum number of years of service for editors of ASCO journals, as stated in the ASCO bylaws. He was appointed by then ASCO President Joseph S. Bailes in early 2000. Dr. Haller assumed editorial oversight during a critical point in the history of the *Journal*. Having become an established, trusted commodity in the international oncology community, *JCO* faced the challenge of how to remain relevant and timely in a rapidly changing research and health care environment.

To that end, Dr. Haller oversaw a number of relevant changes to the *Journal*, including: a large surge in circulation and manuscript submissions; the move to ASCO self-publishing in 2003; the launch of the electronic manuscript submission system in 2004; an increase in frequency from 24 to 36 issues, including the launch of 12 Special Series issues in 2005; and an extensive redesign and enhancement project that included considerations for both the print and online versions of the *Journal*. Furthermore, during his tenure, *JCO*'s impact factor (which measures the frequency with which the "average article" in a journal has been cited) increased from 8.773 in 2001 to 17.793 in 2010 — with more than a four-point increase during the past 3 years.

In the interview that follows, Dr. Haller reflects on his 10 years of service with *JCO*.

Q What influenced your decision to want to take on a *JCO* leadership role?

I was Editor at *Annals of Internal Medicine* for 18 years and Editor-in-Chief of Physician Data Query (PDQ®), the National Cancer Institute's cancer information database, for 7 years.

I started at *JCO* in 1991. When [then *JCO* Editor-in-Chief] George Canellos was finishing his term, *JCO* was based in Boston and published by another society using a paper-based system. My mentor John H. Glick, MD, told me to apply for the *JCO* Editor-in-Chief position; I demurred a bit, but he pushed me very hard.

Q What does the role of *JCO* Editor-in-Chief mean for you?

I look at *JCO* Editor-in-Chief as a presidential appointment in that it is one of the great privileged roles within ASCO. I've enjoyed the role, people have been complimentary about my oversight, and I've managed to keep myself out of trouble.

Q What are some of your greatest accomplishments as *JCO* Editor-in-Chief?

The *Journal* has evolved; we are now our own publisher in both print and electronic formats. We can direct our own fate. It is a substantial income generator for ASCO and, after the Annual Meeting, *JCO* is the most visible tangible aspect of the Society. Users can read the *Journal* whenever and whenever is most convenient for them — *JCO* brings the latest information to them. It's like attending the Annual Meeting three times a month.

I've had the privilege of working with up to 30 Associate Editors, representing various subspecialties, and a tremendous staff. With the help of all of these folks, we're probably now the single most important oncology journal.

Q How does *JCO* stand out from other journals?

There are some general journals, such as *The Lancet* and the *Journal of American Medical Association (JAMA)*, with higher impact factors, but that's based on 5% of their papers being oncology papers. Conversely, *JCO* as an oncology journal represents 12% to 14% of all the oncology citations in the world's literature.

We continue to evolve. We're just starting. ●

Diabetes and Cancer

Continued from Page 25B

Generally, there are two potential ways that metformin might be an effective anticancer agent. One is by acting directly on AMP-kinase in the tumor cells, thereby slowing down or arresting cell growth. It also can act by slowing down gluconeogenesis in the liver, which lowers circulating glucose and insulin levels. With less circulating insulin, there would be less growth signaling in tumor cells even without a direct effect of metformin on the tumor itself.

Dr. Goodwin said that in her group's randomized trial of metformin's effects in breast cancer, the hypothesis is that the liver-mediated effect and not the direct tumor effect will prove the prominent driver of any reduction in cancer risk.

"Evidence is emerging that when metformin is used at doses that are safe clinically, it is working through the liver, the indirect insulin-mediated effect, and not the direct anti-AMP-kinase effect," Dr. Goodwin said. ●

SUTENT® (sunitinib malate) is indicated for the treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate.

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SUTENT: PROVEN EFFICACY IN IMATINIB-RESISTANT OR -INTOLERANT GIST

In the phase 3, randomized, multicenter trial comparing SUTENT with placebo in patients with imatinib-resistant or -intolerant GIST (N=312)...

SUTENT DEMONSTRATED A SIGNIFICANT 4-FOLD INCREASE IN TTP AND A 67% REDUCED RISK OF PROGRESSION

- 27.3 weeks (6.3 months) vs 6.4 weeks (1.5 months) for placebo (95% CI: 16.0, 32.1 and 4.4, 10.0, respectively; HR=0.33; 95% CI: 0.23, 0.47; *P*<.0001)

SUTENT REACHED A MEDIAN OS OF MORE THAN 16 MONTHS

- 72.7 weeks (16.8 months) vs 64.9 weeks (15.0 months) with placebo (HR=0.876; 95% CI: 0.679, 1.129)
- The majority of patients in the placebo arm (99/118) crossed over to SUTENT in the open-label treatment phase

SUTENT OFFERS AN ESTABLISHED SAFETY PROFILE

- The most common adverse reactions (ARs) occurring in ≥20% of patients with GIST and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (40% vs 27%), anorexia (33% vs 29%), skin discoloration (30% vs 23%), mucositis/stomatitis (29% vs 18%), asthenia (22% vs 11%), altered taste (21% vs 12%), and constipation (20% vs 14%)

SUTENT IS THE ONLY APPROVED AGENT FOLLOWING PROGRESSION ON IMATINIB

- Drug resistance can occur any time over the course of GIST treatment[1]
- When disease progression or intolerance to imatinib occurs, the current therapy may no longer be appropriate[1]
- The NCCN sarcoma guidelines for GIST include treatment with sunitinib after both limited and widespread disease progression in patients on imatinib[1]

NCCN=National Comprehensive Cancer Network; OS=overall survival; TTP=time to tumor progression.

Reference: 1. National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology™. Soft tissue sarcoma. V.1.2011. www.nccn.org. Accessed April 15, 2011.

Please see study description and brief summary, including boxed warning, on the following page.

Important safety information

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity may be severe, and deaths have been reported. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 drug-related hepatic adverse events and discontinued if there is no resolution.

Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant.

Left ventricular ejection fraction declines to below the lower limit of normal have occurred. Monitor patients for signs and symptoms of congestive heart failure (CHF) and, in the presence of clinical manifestations, discontinuation is recommended. Patients who presented with cardiac events, pulmonary embolism, or cerebrovascular events within the previous 12 months were excluded from clinical studies.

SUTENT has been shown to prolong QT interval in a dose-dependent manner, which may lead to an increased risk for ventricular arrhythmias including torsades de pointes, which has been seen in <0.1% of patients. Monitoring with on-treatment electrocardiograms and electrolytes should be considered.

Hypertension may occur. Monitor blood pressure and treat as needed.

Hemorrhagic events including tumor-related hemorrhage, some of which were fatal, have occurred. Perform serial complete blood counts (CBCs) and physical examinations.

Thyroid dysfunction may occur. Monitor thyroid function in patients with signs and/or symptoms of hypothyroidism or hyperthyroidism and treat per standard medical practice.

Adrenal hemorrhage was observed in animal studies. Monitor adrenal function in case of stress such as surgery, trauma, or severe infection.

CBCs and serum chemistries should be performed at the beginning of each treatment cycle.

Dose adjustments are recommended when administered with CYP3A4 inhibitors or inducers.

The most common grade 3/4 ARs (occurring in ≥4% of patients with GIST receiving SUTENT vs placebo) were asthenia (5% vs 3%), hand-foot syndrome (4% vs 3%), diarrhea (4% vs 0%), and hypertension (4% vs 0%).

The most common grade 3/4 lab abnormalities (occurring in ≥5% of patients with GIST receiving SUTENT vs placebo) included lipase (10% vs 7%), neutrophils (10% vs 0%), amylase (5% vs 3%), and platelets (5% vs 0%).

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The Proven Path

In the multicenter, double-blind, placebo-controlled study, 312 patients with imatinib-resistant or -intolerant GIST were randomized 2:1 to receive either SUTENT (50 mg once daily in cycles of 4 weeks on/2 weeks off) or placebo.

SUTENT® (SUNITINIB MALATE) CAPSULES, ORAL

Brief Summary of Prescribing Information

WARNING: HEPATOTOXICITY

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity may be severe, and deaths have been reported. *[See Warnings and Precautions]*

INDICATIONS AND USAGE: SUTENT is indicated for the treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate.

DOSAGE AND ADMINISTRATION

Recommended Dose. The recommended dose of SUTENT for GIST is one 50 mg oral dose taken once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off (Schedule 4/2). SUTENT may be taken with or without food.

Dose Modification. Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS

Hepatotoxicity. SUTENT has been associated with hepatotoxicity, which may result in liver failure or death. Liver failure has been observed in clinical trials (7/2281 [0.3%]) and post-marketing experience. Liver failure signs include jaundice, elevated transaminases and/or hyperbilirubinemia in conjunction with encephalopathy, coagulopathy, and/or renal failure. Monitor liver function tests (ALT, AST, bilirubin) before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 drug-related hepatic adverse events and discontinued if there is no resolution. Do not restart SUTENT if patients subsequently experience severe changes in liver function tests or have other signs and symptoms of liver failure.
Safety in patients with ALT or AST >2.5 x ULN or, if due to liver metastases, >5.0 x ULN has not been established.

Pregnancy/Pregnancy Category D. As angiogenesis is a critical component of embryonic and fetal development, inhibition of angiogenesis following administration of SUTENT should be expected to result in adverse effects on pregnancy. There are no adequate and well-controlled studies of SUTENT in pregnant women. If the drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with SUTENT.
Sunitinib was evaluated in pregnant rats (0.3, 1.5, 3.0, 5.0 mg/kg/day) and rabbits (0.5, 1, 5, 20 mg/kg/day) for effects on the embryo. Significant increases in the incidence of embryolethality and structural abnormalities were observed in rats at the dose of 5 mg/kg/day (approximately 5.5 times the systemic exposure [combined AUC of sunitinib + primary active metabolite] in patients administered the recommended daily doses [RDD]). Significantly increased embryolethality was observed in rabbits at 5 mg/kg/day while developmental effects were observed at ≥1 mg/kg/day (approximately 0.3 times the AUC in patients administered the RDD of 50 mg/day). Developmental effects consisted of fetal skeletal malformations of the ribs and vertebrae in rats. In rabbits, cleft lip was observed at 1 mg/kg/day and cleft lip and cleft palate were observed at 5 mg/kg/day (approximately 2.7 times the AUC in patients administered the RDD). Neither fetal loss nor malformations were observed in rats dosed at ≤3 mg/kg/day (approximately 2.3 times the AUC in patients administered the RDD).

Left Ventricular Dysfunction

In the presence of clinical manifestations of congestive heart failure (CHF), discontinuation of SUTENT is recommended. The dose of SUTENT should be interrupted and/or reduced in patients without clinical evidence of CHF but with an ejection fraction <50% and >20% below baseline. Cardiovascular events, including heart failure, myocardial disorders and cardiomyopathy, some of which were fatal, have been reported through post-marketing experience. More patients treated with SUTENT experienced decline in left ventricular ejection fraction (LVEF) than patients receiving either placebo or interferon-α (IFN-α). In the double-blind treatment phase of GIST Study A, 22/209 patients (11%) on SUTENT and 3/102 patients (3%) on placebo had treatment-emergent LVEF values below the lower limit of normal (LLN). Nine of 22 GIST patients on SUTENT with LVEF changes recovered without intervention. Five patients had documented LVEF recovery following intervention (dose reduction: one patient; addition of antihypertensive or diuretic medications: four patients). Six patients went off study without documented recovery. Additionally, three patients on SUTENT had Grade 3 reductions in left ventricular systolic function to LVEF <40%; two of these patients died without receiving further study drug. No GIST patients on placebo had Grade 3 decreased LVEF. In the double-blind treatment phase of GIST Study A, 1 patient on SUTENT and 1 patient on placebo died of diagnosed heart failure; 2 patients on SUTENT and 2 patients on placebo died of treatment-emergent cardiac arrest.
Patients who presented with cardiac events within 12 months prior to SUTENT administration, such as myocardial infarction (including severe/unstable angina), coronary/peripheral artery bypass graft, symptomatic CHF, cerebrovascular accident or transient ischemic attack, or pulmonary embolism were excluded from SUTENT clinical studies. It is unknown whether patients with these concomitant conditions may be at a higher risk of developing drug-related left ventricular dysfunction. Physicians are advised to weigh this risk against the potential benefits of the drug. **These patients should be carefully monitored for clinical signs and symptoms of CHF while receiving SUTENT. Baseline and periodic evaluations of LVEF should also be considered while these patients are receiving SUTENT. In patients without cardiac risk factors, a baseline evaluation of ejection fraction should be considered.**

QT Interval Prolongation and Torsade de Pointes. SUTENT has been shown to prolong the QT interval in a dose dependent manner, which may lead to an increased risk for ventricular arrhythmias including Torsade de Pointes. Torsade de Pointes has been observed in <0.1% of SUTENT-exposed patients.
SUTENT should be used with caution in patients with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. When using SUTENT, periodic monitoring with on-treatment electrocardiograms and electrolytes (magnesium, potassium) should be considered. Concomitant treatment with strong CYP3A4 inhibitors, which may increase sunitinib plasma concentrations, should be used with caution and dose reduction of SUTENT should be considered.

Hypertension. Patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In cases of severe hypertension, temporary suspension of SUTENT is recommended until hypertension is controlled.
While all-grade hypertension was similar in GIST patients on SUTENT compared to placebo, Grade 3 hypertension was reported in 9/202 GIST patients on SUTENT (4%), and none of the GIST patients on placebo. No Grade 4 hypertension was reported. No GIST patients discontinued treatment due to hypertension. Severe hypertension (>200 mmHg systolic or 110 mmHg diastolic) occurred in 8/202 GIST patients on SUTENT (4%) and 1/102 GIST patients on placebo (1%).

Hemorrhagic Events. Hemorrhagic events reported through post-marketing experience, some of which were fatal, have included GI, respiratory, tumor, urinary tract and brain hemorrhages. Bleeding events occurred in 37/202 patients (18%) receiving SUTENT in the double-blind treatment phase of GIST Study A, compared to 17/102 patients (17%) receiving placebo. Epistaxis was the most common hemorrhagic adverse event reported. Less common bleeding events in GIST or RCC patients included rectal, gingival, upper gastrointestinal, genital, and wound bleeding. In the double-blind treatment phase of GIST Study A, 14/202 patients (7%) receiving SUTENT and 9/102 patients (9%) on placebo had Grade 3 or 4 bleeding events. In addition, one patient in GIST Study A taking placebo had a fatal gastrointestinal bleeding event during Cycle 2.
Tumor-related hemorrhage has been observed in patients treated with SUTENT. These events may occur suddenly, and in the case of pulmonary tumors may present as severe and life-threatening hemoptysis or pulmonary hemorrhage. Fatal pulmonary hemorrhage occurred in 2 patients receiving SUTENT on a clinical trial of patients with metastatic non-small cell lung cancer (NSCLC). Both patients had squamous cell histology. SUTENT is not approved for use in patients with NSCLC. Treatment-emergent Grade 3 and 4 tumor hemorrhage occurred in 5/202 patients (3%) with GIST receiving SUTENT on Study A. Tumor hemorrhages were observed as early as Cycle 1 and as late as Cycle 6. One of these five patients received no further drug following tumor hemorrhage. None of the other four patients discontinued treatment or experienced dose delay due to tumor hemorrhage. No patients with GIST in the Study A placebo arm were observed to undergo intratumoral hemorrhage. Clinical assessment of these events should include serial complete blood counts (CBCs) and physical examinations. Serious, sometimes fatal gastrointestinal complications including gastrointestinal perforation have occurred rarely in patients with intra-abdominal malignancies treated with SUTENT.

Thyroid Dysfunction. Baseline laboratory measurement of thyroid function is recommended and patients with hypothyroidism or hyperthyroidism should be treated as per standard medical practice prior to the start of SUTENT treatment. All patients should be observed closely for signs and symptoms of thyroid dysfunction on SUTENT treatment. Patients with signs and/or symptoms suggestive of thyroid dysfunction should have laboratory monitoring of thyroid function performed and be treated as per standard medical practice.
Treatment-emergent acquired hypothyroidism was noted in eight GIST patients (4%) on SUTENT versus one (1%) on placebo.
Cases of hyperthyroidism, some followed by hypothyroidism, have been reported in clinical trials and through post-marketing experience.

Adrenal Function. Physicians prescribing SUTENT are advised to monitor for adrenal insufficiency in patients who experience stress such as surgery, trauma or severe infection. Adrenal toxicity was noted in non-clinical repeat dose studies of 14 days to 9 months in rats and monkeys at plasma exposures as low as 0.7 times the AUC observed in clinical studies. Histological changes of the adrenal gland were characterized as hemorrhage, necrosis, congestion, hypertrophy and inflammation. In clinical studies, CT/MRI obtained in 336 patients after exposure to one or more cycles of SUTENT demonstrated no evidence of adrenal hemorrhage or necrosis. ACTH stimulation testing was performed in approximately 400 patients across multiple clinical trials of SUTENT. Among patients with normal baseline ACTH stimulation testing, one patient developed consistently abnormal test results during treatment that are unexplained and may be related to treatment with SUTENT. Eleven additional patients with normal baseline testing had abnormalities in the final test performed, with peak cortisol levels of 12-16.4 mcg/dL (normal >18 mcg/dL) following stimulation. None of these patients were reported to have clinical evidence of adrenal insufficiency.

Laboratory Tests. CBCs with platelet count and serum chemistries including phosphate should be performed at the beginning of each treatment cycle for patients receiving treatment with SUTENT.

ADVERSE REACTIONS

The data described below reflect exposure to SUTENT in 577 patients who participated in the double-blind treatment phase of a placebo-controlled trial (n=202) for the treatment of GIST *[see Clinical Studies]* or an active-controlled trial (n=375) for the treatment of RCC *[see Clinical Studies]*. The patients received a starting oral dose of 50 mg daily on Schedule 4/2 in repeated cycles.
The most common adverse reactions (≥20%) in patients with GIST or RCC are fatigue, asthenia, fever, diarrhea, nausea, mucositis/stomatitis, vomiting, dyspepsia, abdominal pain, constipation, hypertension, peripheral edema, rash, hand-foot syndrome, skin discoloration, dry skin, hair color changes, altered taste, headache, back pain, arthralgia, extremity pain, cough, dyspnea, anorexia, and bleeding. The potentially serious adverse reactions of hepatotoxicity, left ventricular dysfunction, QT interval prolongation, hemorrhage, hypertension, thyroid dysfunction, and adrenal function are discussed in *Warnings and Precautions*. Other adverse reactions occurring in the GIST study are described below.
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse Reactions in GIST Study A. Median duration of blinded study treatment was two cycles for patients on SUTENT (mean 3.0, range 1-9) and one cycle (mean 1.8, range 1-6) for patients on placebo at the time of the interim analysis. Dose reductions occurred in 23 patients (11%) on SUTENT and none on placebo. Dose interruptions occurred in 59 patients (29%) on SUTENT and 31 patients (30%) on placebo. The rates of treatment-emergent, non-fatal adverse reactions resulting in permanent discontinuation were 7% and 6% in the SUTENT and placebo groups, respectively.
Most treatment-emergent adverse reactions in both study arms were Grade 1 or 2 in severity. Grade 3 or 4 treatment-emergent adverse reactions were reported in 56% versus 51% of patients on SUTENT versus placebo, respectively, in the double-blind treatment phase of the trial. The following table compares the incidence of common (≥10%) treatment-emergent adverse reactions for patients receiving SUTENT and reported more commonly in patients receiving SUTENT than in patients receiving placebo.

Adverse Reactions Reported in Study A in at Least 10% of GIST Patients who Received SUTENT in the Double-Blind Treatment Phase and More Commonly Than in Patients Given Placebo*

	SUTENT (n=202)		Placebo (n=102)	
Adverse Reaction, n (%)	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Any		114 (56)		52 (51)
Gastrointestinal				
Diarrhea	81 (40)	9 (4)	27 (27)	0 (0)
Mucositis/stomatitis	58 (29)	2 (1)	18 (18)	2 (2)
Constipation	41 (20)	0 (0)	14 (14)	2 (2)
Cardiac				
Hypertension	31 (15)	9 (4)	11 (11)	0 (0)
Dermatology				
Skin discoloration	61 (30)	0 (0)	23 (23)	0 (0)
Rash	28 (14)	2 (1)	9 (9)	0 (0)
Hand-foot syndrome	28 (14)	9 (4)	10 (10)	3 (3)
Neurology				
Altered taste	42 (21)	0 (0)	12 (12)	0 (0)
Musculoskeletal				
Myalgia/limb pain	28 (14)	1 (1)	9 (9)	1 (1)
Metabolism/Nutrition				
Anorexia[a]	67 (33)	1 (1)	30 (29)	5 (5)
Asthenia	45 (22)	10 (5)	11 (11)	3 (3)

*Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0
[a]Includes decreased appetite

In the double-blind treatment phase of GIST Study A, oral pain other than mucositis/stomatitis occurred in 12 patients (6%) on SUTENT versus 3 (3%) on placebo. Hair color changes occurred in 15 patients (7%) on SUTENT versus 4 (4%) on placebo. Alopecia was observed in 10 patients (5%) on SUTENT versus 2 (2%) on placebo.

The following table provides common (≥10%) treatment-emergent laboratory abnormalities.

Laboratory Abnormalities Reported in Study A in at Least 10% of GIST Patients Who Received SUTENT or Placebo in the Double-Blind Treatment Phase*

	SUTENT (n=202)		Placebo (n=102)	
Laboratory Parameter, n (%)	**All Grades***	**Grade 3/4*[a]**	**All Grades***	**Grade 3/4*[b]**
Any		68 (34)		22 (22)
Gastrointestinal				
AST / ALT	78 (39)	3 (2)	23 (23)	1 (1)
Lipase	50 (25)	20 (10)	17 (17)	7 (7)
Alkaline phosphatase	48 (24)	7 (4)	21 (21)	4 (4)
Amylase	35 (17)	10 (5)	12 (12)	3 (3)
Total bilirubin	32 (16)	2 (1)	8 (8)	0 (0)
Indirect bilirubin	20 (10)	0 (0)	4 (4)	0 (0)
Cardiac				
Decreased LVEF	22 (11)	2 (1)	3 (3)	0 (0)
Renal/Metabolic				
Creatinine	25 (12)	1 (1)	7 (7)	0 (0)
Potassium decreased	24 (12)	1 (1)	4 (4)	0 (0)
Sodium increased	20 (10)	0 (0)	4 (4)	1 (1)
Hematology				
Neutrophils	107 (53)	20 (10)	4 (4)	0 (0)
Lymphocytes	76 (38)	0 (0)	16 (16)	0 (0)
Platelets	76 (38)	10 (5)	4 (4)	0 (0)
Hemoglobin	52 (26)	6 (3)	22 (22)	2 (2)

LVEF=Left ventricular ejection fraction

*Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0
[a]Grade 4 laboratory abnormalities in patients on SUTENT included alkaline phosphatase (1%), lipase (2%), creatinine (1%), potassium decreased (1%), neutrophils (2%), hemoglobin (2%), and platelets (1%).
[b]Grade 4 laboratory abnormalities in patients on placebo included amylase (1%), lipase (1%) and hemoglobin (2%).

After an interim analysis, the study was unblinded, and patients on the placebo arm were given the opportunity to receive open-label SUTENT treatment. For 241 patients randomized to the SUTENT arm, including 139 who received SUTENT in both the double-blind and open-label treatment phases, the median duration of SUTENT treatment was 6 cycles (mean 8.5, range 1 – 44). For the 255 patients who ultimately received open-label SUTENT treatment, median duration of study treatment was 6 cycles (mean 7.8, range 1 – 37) from the time of the unblinding. A total of 118 patients (46%) required dosing interruptions, and a total of 72 patients (28%) required dose reductions. The incidence of treatment-emergent adverse reactions resulting in permanent discontinuation was 20%. The most common Grade 3 or 4 treatment-related adverse reactions experienced by patients receiving SUTENT in the open-label treatment phase were fatigue (10%), hypertension (8%), asthenia (5%), diarrhea (5%), hand-foot syndrome (5%), nausea (4%), abdominal pain (3%), anorexia (3%), mucositis (2%), vomiting (2%), and hypothyroidism (2%).

Venous Thromboembolic Events. Seven patients (3%) on SUTENT and none on placebo in the double-blind treatment phase of GIST Study A experienced venous thromboembolic events; five of the seven were Grade 3 deep venous thrombosis (DVT), and two were Grade 1 or 2. Four of these seven GIST patients discontinued treatment following first observation of DVT.

Reversible Posterior Leukoencephalopathy Syndrome. There have been rare (<1%) reports of subjects presenting with seizures and radiological evidence of reversible posterior leukoencephalopathy syndrome (RPLS). None of these subjects had a fatal outcome to the event. Patients with seizures and signs/symptoms consistent with RPLS, such as hypertension, headache, decreased alertness, altered mental functioning, and visual loss, including cortical blindness should be controlled with medical management including control of hypertension. Temporary suspension of SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating physician.

Pancreatic and Hepatic Function. If symptoms of pancreatitis or hepatic failure are present, patients should have SUTENT discontinued. Hepatotoxicity was observed in patients receiving SUTENT *[see Boxed Warning and Warnings and Precautions]*.

Post-marketing Experience. The following adverse reactions have been identified during post-approval use of SUTENT. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Cases of serious infection (with or without neutropenia), in some cases with fatal outcome, have been reported. Cases of myopathy and/or rhabdomyolysis with or without acute renal failure, in some cases with fatal outcome, have been reported. Patients with signs or symptoms of muscle toxicity should be managed as per standard medical practice. Thrombotic microangiopathy has been reported in patients on SUTENT. Suspension of SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating physician. Cases of fatal hemorrhage associated with thrombocytopenia have been reported. Pulmonary embolism, in some cases with fatal outcome, has been reported. Cases of renal impairment and/or failure, in some cases with fatal outcome, have been reported. Cases of proteinuria and rare cases of nephrotic syndrome have been reported. Baseline urinalysis is recommended, and patients should be monitored for the development or worsening of proteinuria. The safety of continued SUTENT treatment in patients with moderate to severe proteinuria has not been systematically evaluated. Discontinue SUTENT in patients with nephrotic syndrome. Hypersensitivity reactions, including angioedema, have been reported. Cases of fistula formation, sometimes associated with tumor necrosis and/or regression, in some cases with fatal outcome, have been reported.

DRUG INTERACTIONS/CYP3A4 Inhibitors. Strong CYP3A4 inhibitors such as ketoconazole may **increase** sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme inhibition potential is recommended. Concurrent administration of SUTENT with the strong CYP3A4 inhibitor, ketoconazole, resulted in 49% and 51% increases in the combined (sunitinib + primary active metabolite) C_{max} and $AUC_{0-\infty}$ values, respectively, after a single dose of SUTENT in healthy volunteers. Co-administration of SUTENT with strong inhibitors of the CYP3A4 family (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) may increase sunitinib concentrations. Grapefruit may also increase plasma concentrations of sunitinib. A dose reduction for SUTENT should be considered when it must be co-administered with strong CYP3A4 inhibitors.

CYP3A4 Inducers. CYP3A4 inducers such as rifampin may **decrease** sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended. Concurrent administration of SUTENT with the strong CYP3A4 inducer, rifampin, resulted in a 23% and 46% reduction in the combined (sunitinib + primary active metabolite) C_{max} and $AUC_{0-\infty}$ values, respectively, after a single dose of SUTENT in healthy volunteers. Co-administration of SUTENT with inducers of the CYP3A4 family (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St. John's Wort) may decrease sunitinib concentrations. St. John's Wort may decrease sunitinib plasma concentrations unpredictably. Patients receiving SUTENT should not take St. John's Wort concomitantly. A dose increase for SUTENT should be considered when it must be co-administered with CYP3A4 inducers.

In Vitro Studies of CYP Inhibition and Induction. *In vitro* studies indicated that sunitinib does not induce or inhibit major CYP enzymes. The *in vitro* studies in human liver microsomes and hepatocytes of the activity of CYP isoforms CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4/5, and CYP4A9/11 indicated that sunitinib and its primary active metabolite are unlikely to have any clinically relevant drug-drug interactions with drugs that may be metabolized by these enzymes.

USE IN SPECIFIC POPULATIONS

Pregnancy. Pregnancy Category D *[see Warnings and Precautions]*.

Nursing Mothers. Sunitinib and its metabolites are excreted in rat milk. In lactating female rats administered 15 mg/kg, sunitinib and its metabolites were extensively excreted in milk at concentrations up to 12-fold higher than in plasma. It is not known whether sunitinib or its primary active metabolite are excreted in human milk. Because drugs are commonly excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug taking into account the importance of the drug to the mother *[see Nonclinical Toxicology]*.

Pediatric Use. The safety and efficacy of SUTENT in pediatric patients have not been established. Physeal dysplasia was observed in Cynomolgus monkeys with open growth plates treated for ≥ 3 months (3 month dosing 2, 6, 12 mg/kg/day; 8 cycles of dosing 0.3, 1.5, 6.0 mg/kg/day) with sunitinib at doses that were > 0.4 times the RDD based on systemic exposure (AUC). In developing rats treated continuously for 3 months (1.5, 5.0 and 15.0 mg/kg) or 5 cycles (0.3, 1.5, and 6.0 mg/kg/day), bone abnormalities consisted of thickening of the epiphyseal cartilage of the femur and an increase of fracture of the tibia at doses ≥ 5 mg/kg (approximately 10 times the RDD based on AUC). Additionally, caries of the teeth were observed in rats at >5 mg/kg. The incidence and severity of physeal dysplasia were dose-related and were reversible upon cessation of treatment however findings in the teeth were not. A no effect level was not observed in monkeys treated continuously for 3 months, but was 1.5 mg/kg/day when treated intermittently for 8 cycles. In rats the no effect level in bones was ≤ 2 mg/kg/day.

Geriatric Use. Of 825 GIST and RCC patients who received SUTENT on clinical studies, 277 (34%) were 65 and over. No overall differences in safety or effectiveness were observed between younger and older patients.

Hepatic Impairment. No dose adjustment is required when administering SUTENT to patients with Child-Pugh Class A or B hepatic impairment. Sunitinib and its primary metabolite are primarily metabolized by the liver. Systemic exposures after a single dose of SUTENT were similar in subjects with mild or moderate (Child-Pugh Class A and B) hepatic impairment compared to subjects with normal hepatic function. SUTENT was not studied in subjects with severe (Child-Pugh Class C) hepatic impairment. Studies in cancer patients have excluded patients with ALT or AST >2.5 x ULN or, if due to liver metastases, >5.0 x ULN.

OVERDOSAGE

Treatment of overdose with SUTENT should consist of general supportive measures. There is no specific antidote for overdosage with SUTENT. If indicated, elimination of unabsorbed drug should be achieved by emesis or gastric lavage. A few cases of accidental overdose have been reported; these cases were associated with adverse reactions consistent with the known safety profile of SUTENT, or without adverse reactions. A case of intentional overdose involving the ingestion of 1,500 mg of SUTENT in an attempted suicide was reported without adverse reaction. In non-clinical studies mortality was observed following as few as 5 daily doses of 500 mg/kg (3000 mg/m^2) in rats. At this dose, signs of toxicity included impaired muscle coordination, head shakes, hypoactivity, ocular discharge, piloerection and gastrointestinal distress. Mortality and similar signs of toxicity were observed at lower doses when administered for longer durations.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility. Although definitive carcinogenicity studies with sunitinib have not been completed, carcinoma and hyperplasia of the Brunner's gland of the duodenum have been observed at the highest dose tested in H2ras transgenic mice administered doses of 0, 10, 25, 75, or 200 mg/kg/day for 28 days. Sunitinib did not cause genetic damage when tested in *in vitro* assays (bacterial mutation [AMES Assay], human lymphocyte chromosome aberration) and an *in vivo* rat bone marrow micronucleus test. Effects on the female reproductive system were identified in a 3-month repeat dose monkey study (2, 6, 12 mg/kg/day), where ovarian changes (decreased follicular development) were noted at 12 mg/kg/day (approximately 5.1 times the AUC in patients administered the RDD), while uterine changes (endometrial atrophy) were noted at ≥2 mg/kg/day (approximately 0.4 times the AUC in patients administered the RDD). With the addition of vaginal atrophy, the uterine and ovarian effects were reproduced at 6 mg/kg/day in the 9-month monkey study (0.3, 1.5 and 6 mg/kg/day administered daily for 28 days followed by a 14 day respite; the 6 mg/kg dose produced a mean AUC that was approximately 0.8 times the AUC in patients administered the RDD). A no effect level was not identified in the 3 month study; 1.5 mg/kg/day represents a no effect level in monkeys administered sunitinib for 9 months.
Although fertility was not affected in rats, SUTENT may impair fertility in humans. In female rats, no fertility effects were observed at doses of ≤5.0 mg/kg/day [(0.5, 1.5, 5.0 mg/kg/day) administered for 21 days up to gestational day 7; the 5.0 mg/kg dose produced an AUC that was approximately 5 times the AUC in patients administered the RDD], however significant embryolethality was observed at the 5.0 mg/kg dose. No reproductive effects were observed in male rats dosed (1, 3 or 10 mg/kg/day) for 58 days prior to mating with untreated females. Fertility, copulation, conception indices, and sperm evaluation (morphology, concentration, and motility) were unaffected by sunitinib at doses ≤10 mg/kg/day (the 10 mg/kg/day dose produced a mean AUC that was approximately 25.8 times the AUC in patients administered the RDD).

PATIENT COUNSELING INFORMATION

Gastrointestinal Disorders. Gastrointestinal disorders such as diarrhea, nausea, stomatitis, dyspepsia, and vomiting were the most commonly reported gastrointestinal events occurring in patients who received SUTENT. Supportive care for gastrointestinal adverse events requiring treatment may include anti-emetic or anti-diarrheal medication.

Skin Effects. Skin discoloration possibly due to the drug color (yellow) occurred in approximately one third of patients. Patients should be advised that depigmentation of the hair or skin may occur during treatment with SUTENT. Other possible dermatologic effects may include dryness, thickness or cracking of skin, blister or rash on the palms of the hands and soles of the feet.

Other Common Events. Other commonly reported adverse events included fatigue, high blood pressure, bleeding, swelling, mouth pain/irritation and taste disturbance.

Concomitant Medications. Patients should be advised to inform their health care providers of all concomitant medications, including over-the-counter medications and dietary supplements *[see Drug Interactions]*.

Rx only

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ASCO Funds Projects Aimed at Understanding Health Care Disparities

Investigation of disparities in access to care, treatment, and outcomes is an often underfunded and overlooked area of research. ASCO continues efforts toward eliminating health care disparities, including funding substantial research in the area through a number of grant programs and partnerships.

In 2009 ASCO published a policy statement in the *Journal of Clinical Oncology* that emphasized the critical importance of racial and ethnic disparities in cancer care in the oncology community and society at large. The statement put forth ASCO's commitment to collaboration with a large and diverse community of stakeholders for the development of policies to guarantee equal access to health care, with special emphasis on the reduction of barriers to care related to insurance and to economic status. In conjunction with its focus on improving clinical trials across oncology, ASCO has a goal of developing mechanisms to increase participation of racially and ethnically diverse populations in cancer clinical trials and enhancing patient involvement in care. ASCO also will develop a comprehensive plan to increase awareness of racial and ethnic disparities in cancer care, execute a strategy to enhance the supply of minority physicians and to improve the training of the oncology workforce to meet the needs of racially and ethnically diverse patients, and increase prioritization of public and private research on cancer care disparities.

Progress through Funding

Among the grant programs that provide funding for health care disparity research is the Young Investigator Award (YIA), which dates back to 1984. Several YIA awards given in 2010 focus on health care disparities, including an ASCO Clinical Practice Committee-sponsored award given to Keerthi Gogineni, MD, of the University of Pennsylvania in Philadelphia. Dr. Gogineni's project involves examining the community and provider determinants of breast cancer stage at diagnosis, treatment, and mortality.

"Traditionally, it is well understood that if you have no insurance or you are poorly insured, you have worse outcomes. You present at a more advanced stage when you're diagnosed, and you get substandard care," Dr. Gogineni told *ASCO Daily News*. What is less understood, she said, is how "having a lot of folks who are uninsured in a given area affects the people in a community who do have insurance."

Previous work has indicated that in areas of high uninsurance, outcomes can be worse for the insured as well; this was shown for heart attacks[1] in California, and other data suggest that women were less likely to get mammograms[2] in areas with high uninsurance rates. Dr. Gogineni's project will also attempt to address the mechanism behind such disparities.

"One possibility is that if you have a community where providers are caring for high proportions of people who are uninsured, [providers] may compensate for reduced revenues by either providing fewer services or by relocating," Dr. Gogineni said. Also, it may be that areas with high uninsurance rates have higher workforce shortages — fewer breast imaging personnel, medical oncologists, or radiation facilities, for example — which would clearly affect both the uninsured and the insured in the area.

"[Identification of] a shared harm [would] provide support for the goal of implementing universal health insurance over the next 10 years; it makes sense in more terms than just the moral imperative," Dr. Gogineni said. It also could provide a guide in terms of which areas require focused efforts to increase the workforce and provide better care in general.

Another project, led by Victoria Blinder, MD, of Memorial Sloan-Kettering Cancer Center, is being funded by the 2010 Career Development Award through Susan G. Komen for the Cure®. Dr. Blinder's study will examine the return-to-work process following treatment and recovery from breast cancer in an ethnically diverse population.

According to the study's abstract, "Our study of employment, financial situation, and quality-of-life will lay the foundation for future investigation and for the development of ethnically sensitive interventions aimed at improving the [quality of life] of a significant proportion of the population, comprised of people who may be doubly marginalized due to their ethnic minority status and [to] their illness." *(For more on Dr. Blinder's study, see the sidebar below.)*

Veena Shankaran, MD, of Northwestern University, received a 2009 YIA and continues to look into another area related to health care disparities. Her study will identify the out-of-pocket costs associated with cancer care for Medicare-eligible patients; the economic effects of cancer, Dr. Shankaran has noted, can be particularly devastating in older patients.

"This research will improve our understanding of the financial challenges that face older patients [with cancer]," she wrote in her abstract. "Based on this information, future studies will focus on incorporating routine economic assessments into clinical trials and investigating potential mechanisms to alleviate financial burdens for [these] patients."

Another 2009 Young Investigator Award recipient, Mandira Ray, MD, of Brigham and Women's Hospital in Boston, is studying the role of race in clinical trial enrollment. She is using a paired patient and physician survey to examine the patient–physician encounter specifically at the point of clinical decision making.

If Dr. Ray's study can elucidate some of the reasons for the historical underrepresentation of minorities in cancer clinical trials, then trials in the future might use the results to eliminate that disparity.

Finally, 2009 YIA recipient Elizabeth Trice Loggers, MD, of the Seattle Cancer Care Alliance, is studying the role of acculturation in end-of-life care for Hispanic patients with advanced cancer.

According to Dr. Loggers' study abstract, "Results will provide novel evidence regarding the role of acculturation in end-of-life care for [these patients living] in America [and will]inform oncologists, palliative care providers, patients, and their caregivers, leading to more culturally competent care and the amelioration of end-of-life disparities."

ASCO will continue to fund efforts to understand and mitigate disparities in oncology care around the country in 2011 and beyond. ●

For more information about common-sense solutions to disparities in cancer care, see the Expert Editorial by Blase Polite, MD, in tomorrow's issue of ASCO Daily News, *Section B. More information about this year's Young Investigator Award (YIA) and Career Development Award (CDA) winners, see Section C of today's issue.*

References

1. 1. Daysal, Meltem. "Does Uninsurance Affect the Health Outcomes of the Insured? Evidence from Heart Attack Patients in California," University of Maryland Working Paper, 2009.
2. 2. Pagán JA, Asch DA, Brown CJ, et al. Lack of Community Insurance and Mammography Screening Rates Among Insured and Uninsured Women. *J Clin Oncol*. 2008;26(11):1865-1870.

Restoring the Rhythm of Life's Routine after Cancer Treatment

Victoria Blinder, MD, is working to ease the transition for women at work while addressing issues regarding disparities in care.

Life is different after cancer. Re-entry into everyday routine — work, relationships, tasks, and projects — can seem daunting. But life beckons. And an important element of survivorship that provides psychological and financial support is return to work.

Supported by a 2010 Career Development Award, funded by Susan G. Komen for the Cure®, Victoria Blinder, MD — a medical oncologist at Memorial Sloan-Kettering Cancer Center in New York City — seeks to discover why women of different ethnicities may sometimes have different return-to-work experiences after treatment for breast cancer.

The topic has been of interest to her since her fellowship at Weill Cornell Medical College, when Dr. Blinder collaborated with colleagues to conduct focus groups of ethnically diverse breast cancer survivors after anecdotal data suggested that Filipina nurses seemed to have a harder time returning to work. Later, she analyzed 3 years of longitudinal data from medically underserved Latina and Caucasian women in California who had been screened, diagnosed, and treated for breast cancer under the state's Medi-Cal public insurance program. These data revealed that fewer than half as many of the Latina women as Caucasian women had returned to work 18 months after diagnosis, and that differences in job type appeared to play an important role in this disparity.[1]

Martin J. Murphy, PhD, DMedSc, Chair of The Conquer Cancer Foundation Board of Directors, presenting Dr. Blinder her Career Development Award.

"There's a lot of data about return to work after breast cancer treatment, but there is very little literature on the specific experiences of women who may be of low income and may be members of socially marginalized, less acculturated groups," says Dr. Blinder. "Is it a matter of having very physical jobs that require upper-body strength? Is it because of language barriers or other factors that may prevent workers from advocating for themselves? Do employers need to be better educated?"

To find some answers, Dr. Blinder is developing a study that will explore the return-to-work experiences of 750 African-American, Caucasian, Korean, Latina, and Chinese breast cancer survivors through telephone interviews and online surveys conducted in their native languages.

"I always knew that I wanted to do something related to disparities, to try to help disenfranchised groups," says Dr. Blinder, who moved to New York City from Argentina with her parents at the age of five and was educated in the rich multicultural environment of the United Nations International School. "I was in a position where I could see how lucky I had been in terms of my experience as an immigrant, and I wanted to try to help people who hadn't had that good fortune. This kind of work is a way to do a lot of good for a lot of people."

**This article was originally published in the Conquer Cancer Foundation of ASCO Case For Support.*

Reference

1. Blinder VS, Patil S, Diamant A, et al. Employment status among low-income Caucasian and Latina breast cancer survivors. *J Clin Oncol*. 2009; 27(15S):Abstract 6612.

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