

University of Chicago Cancer Research Center

In the News: Our Members in the Media

The University of Chicago Cancer Research Center (UCCRC) publishes this newsletter periodically to provide its members, University of Chicago Cancer Research Foundation members, and other associates with informative articles or press releases regarding cancer and research by our members. If you wish to include a media story in the next issue, please e-mail us at pbutera@medicine.bsd.uchicago.edu.

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ASCO Expert Corner: The 2009 ASCO Annual Meeting

Cancer.net
June 5, 2009

More than 30,000 medical professionals who treat people with cancer are meeting at the American Society of Clinical Oncology's (ASCO's) Annual Meeting May 29 to June 2 in Orlando, Florida, where nearly 4,000 new research studies are being featured. What should patients know about this meeting? To find out, Cancer.Net talked with Richard L. Schilsky, MD.

Q: What is the purpose of the ASCO Annual Meeting?

A: The primary purpose of the Annual Meeting is to provide a forum and opportunity for oncology specialists to exchange the latest information on cancer research, treatment, prevention, and survivorship. Through formal education sessions, presentation of original research, and informal meetings and networking, attendees of the Annual Meeting learn of the latest advances that directly affect the care of their patients.

Q: What makes it unique?

A: The ASCO Annual Meeting is the largest gathering of cancer specialists anywhere in the world. It brings together medical, surgical, and radiation oncologists from around the globe, as well as clinical and laboratory researchers, trainees, and established leaders in the field to learn about, discuss, and debate the latest findings.

Q: The theme of the Annual Meeting is "Personalizing Cancer Care." What does that mean and why was it chosen?

A: "Personalizing Cancer Care" reflects both the way oncologists deliver care to their patients and the scientific direction of contemporary cancer research. Each person with cancer is unique in the course of their illness, tolerance of treatment, and in how they are affected by and deal with

their diagnosis. Oncologists must consider the unique needs of each person in crafting a treatment and survivorship plan. Modern science has now begun to provide many tools to help tailor treatment programs to the specific features and needs of each person. By understanding the molecular characteristics of the tumor and the genetic makeup of the patient, oncologists can now design treatment programs that will be as effective as possible with fewer side effects. Cancer treatment is no longer "one size fits all," but now blends modern molecular biology with good old-fashioned caring to create a truly personalized approach to cancer care.

Q: Where can people learn more about the research studies presented at the meeting?

A: Cancer.Net is the premiere resource for all of the breaking research news coming from ASCO's Annual Meeting. Read patient-friendly summaries of important research studies that spell out what each study means for patients, what questions to ask the doctor, and where to find more information on Cancer.Net. Check back for more cancer news at www.cancer.net/ascoannualmeeting and listen to daily podcasts from leading oncologists that explain more about the research advances.

Q: How are patient advocates involved in the Annual Meeting?

A: ASCO's mission includes serving the educational needs of the patient advocate community. At this year's Meeting, approximately 300 patient advocates are in attendance, representing about 100 patient advocacy organizations. Twenty patient advocacy organizations are exhibiting in the ASCO-sponsored Patient Advocacy Booth in the Exhibit Hall. There are also about 40 additional patient advo-



Richard L. Schilsky, MD

cacy organizations exhibiting at the Annual Meeting. Individual patient advocates (not exhibiting at the Meeting and who meet certain criteria) are able to apply for a special discounted registration rate. For patient advocates who aren't able to attend the Meeting, ASCO offers a discounted subscription to the Virtual Meeting. With a Virtual Meeting subscription to the ASCO 2009 Annual Meeting, subscribers will be able to view audio and slides of presentations made at the Meeting. Visit www.asco.org/vm for more information.

Richard Schilsky, MD, is Professor of Medicine at the University of Chicago and Chairman of the Cancer and Leukemia Group B, a national cooperative group sponsored by the National Cancer Institute. Dr. Schilsky is the 2008-2009 ASCO President.

Detection of Nodal Involvement, Adjuvant Treatments for Rectal Cancer Debated

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June 1, 2009

The roles of preoperative treatment, local excision, and postoperative chemotherapy following neoadjuvant chemoradiotherapy for patients with rectal cancer were discussed at a recent Education Session, "Controversial Issues in the Management of Rectal Cancer." Speakers noted that neither the use of neoadjuvant therapy nor the extent of downstaging alter the standard of care — adjuvant chemotherapy — for patients with stage II and stage III rectal cancer.

Session Chair Bruce D. Minsky, MD, of the University of Chicago, said the benefit of postoperative radiotherapy for patients with T3N0 tumors who have undergone a total mesorectal excision is clear, provided there are at least 12 negative lymph nodes. "There is a 3-4 percent increase in local control, but the benefits do not outweigh the risks," he said.

However, when preoperative radiotherapy is examined, as it was in studies that Dr. Minsky reviewed, there was improved local control but conflicting methodologies. A potential problem is the significant overtreatment of patients with preoperative chemotherapy, he said. Discussing a study presented at the ASCO 2008 Annual Meeting by Guillem et al, Dr. Minsky noted that as many as 40 percent of patients who underwent surgery alone had node-positive disease at the time of surgery, and 22 percent of patients who had preoperative chemotherapy had positive nodes. These patients then require postoperative treatment that, when compared with preoperative treatment, offers inferior local control, higher toxicity, and inferior functional results.

The risk of positive nodes is not dependent on the distance of the tumor from the anal verge.

"Regardless of where the tumor is located in the rectum, the chances of a positive node are the same," Dr. Minsky said. His recommendation was that all patients be treated with preoperative chemotherapy. "Although we may be overtreating them, if we send them to surgery and they need postoperative treatment, the results are inferior."

Philip Paty, MD, of Memorial Sloan-Kettering Cancer Center, noted that local excision of T1 rectal tumors is actually a biopsy and, with more screening, more polyps and small nodular cancers are located and excised. The subsequent presence of positive lymph nodes and metastasis following local excision leads to new questions about the procedure's long-term efficacy. In one study, he noted



Bruce Minsky, MD

that nearly one-third of patients who had local excision also had positive nodes. "The inability to accurately detect regional lymph node metastases is the major barrier to individualizing treatment approaches for patients with localized rectal cancer," he said. The greatest predictor, he noted, was the depth of the tumor's invasion into submucosal tissue.

Dr. Paty also noted that local excision may offer inferior oncologic results for those patients whose disease progresses as a result of metastasis. "Local excision is inferior cancer treatment compared with more radical surgery because it yields incomplete staging and a risk of incomplete local resection," he said. Better imaging and neoadjuvant therapy may expand the number of patients for whom this is an

adequate treatment.

Carmen Joseph Allegra, MD, of the University of Florida, reviewed the studies that led to the 1990 National Institutes of Health Consensus statement, which indicated that for rectal cancer, adjuvant therapy combining chemotherapy and radiation therapy improves local control and survival for patients with stage II and III disease.

However, Dr. Allegra noted, "This was based on a study that was woefully underpowered by today's standards and used chemotherapy combinations we don't use." Subsequent pooled analyses indicated that adding chemotherapy improved patient survival, but a 2006 European Organization for Research and Treatment of Cancer (EORTC) study called that conclusion into question with its finding that chemotherapy — whether administered preoperatively or postoperatively — had no significant effect on survival.

Many factors, however, diminished the power of the EORTC study. Of those patients who underwent resection, 28 percent assigned to receive adjuvant chemotherapy never received it, and half of the patients assigned to postoperative chemotherapy received 2 months of preoperative chemotherapy. In addition, fewer than half of the study patients had node-positive disease compared with 70 percent in prior studies [that showed] a benefit for adjuvant chemotherapy. "Patients with node-positive disease have a worse prognosis relative to those with node-negative disease," noted Dr. Allegra.

Given that there is now a preponderance of evidence strongly favoring the use of chemotherapy for patients with stage II and III rectal cancer, questions remain as to which regimens and dosages are optimal. Much of the available data, Dr. Allegra said, indicates that the available fluorouracil regimens are almost equally efficacious, but the addition of oxaliplatin does confer a benefit, according to results from the Adjuvant Treatment of Colon Cancer (MOSAIC) trial. Agents such as bevacizumab and cetuximab are being investigated for the treatment of patients with colon cancer, and some results are becoming available.

ASCO.org June 1, 2009

Even in the era of targeted therapies, treatment of gastrointestinal tumors is challenging. Discussions during ASCO's recent Clinical Science Symposium "Looking into the Crystal Ball: Up and Coming Agents for Treating Upper Gastrointestinal Cancers" focused on why this is so, whether some of the targeted agents on the horizon hold promise, and how patients who may benefit from these agents can be identified.


Discussing a presentation by Rachna T. Shroff, MD, of M.D. Anderson Cancer Center, on the value of single nucleotide polymorphisms (SNPs) of the insulin growth factor (IGF) signaling pathway (Abstract 4500), Manuel Hidalgo, MD, PhD, of Johns Hopkins University, indicated that although there are several prognostic factors for pancreatic cancer, there are no known markers that can predict response to IGF1 receptor (IGF1R) treatments. He suggested that SNPs in IGF1R and the insulin receptor substrate 1 (IRS1) that were associated with better survival of patients with locally advanced pancreatic cancer may help identify patients who will likely derive benefit from therapy with

agents that target the IGFR pathway. However, he indicated that it was important to determine SNPs in tumor samples, as they are known to affect serum levels of proteins associated with IGF1 signaling.

Lee M. Ellis, MD, of M.D. Anderson Cancer Center, highlighted potential lessons from a study presented by Minaxi P. Jhaver, MD, of Memorial Sloan-Kettering Cancer Center, in which foretinib was ineffective at treating metastatic gastroesophageal cancer (Abstract 4502). According to Dr. Ellis, it was important to match a target with a disease because cancers are dependent on (or "addicted to") a few genes for both maintenance and survival. "Since foretinib was used as a single agent, this trial was betting on c-Met as being an oncogene-addicted target," he said. But c-Met is just one of many tyrosine kinase receptors in upper gastrointestinal cancers. In addition, c-Met amplification was seen in three of 59 evaluable patients and was present at a lower-than-expected frequency.

Several challenges must be recognized as oncologists move forward. "Although it is convenient to group [patients with gastroesophageal cancer] for logistic reasons, tumors in

these patients are molecularly and clinically distinct," Dr. Ellis said. "By adding tumor subtypes, one loses the ability to enrich for the tumor target." In addition, evaluating single-agent targeted therapies in phase II trials in hard-to-treat cancers is not recommended even if one drug hits multiple targets. "Adding the apoptotic hit with chemotherapy is still necessary," Dr. Ellis concluded.

Metastatic pancreatic cancer also is a disease for which targeted agents have shown little success. A phase Ib study presented by Hedy L. Kindler, MD, of the University of Chicago, using conatumumab (AMG 655) showed better promise for future investigations in treating this disease (Abstract 4501). Conatumumab targets the death receptor 5 (DR5) in cells and induces apoptosis. In this study, conatumumab was used in combination with standard gemcitabine therapy in 13 patients with metastatic pancreatic cancer. Discussant David A. Tuveson, MD, PhD, of Cancer Research UK, contended that, based on an overall survival of 11 months and a progression-free survival of 5.3 months, the combination should be further evaluated in a phase II trial. 

Androgen Deprivation Linked to Diabetes, Prostate Cancer

HealthDay News June 10, 2009


Researchers have found that androgen deprivation therapy (ADT) is associated with a higher risk of diabetes and fragility fractures in men with prostate cancer, according to a study published online June 8 in the *Journal of Clinical Oncology*. In a related study in the same issue, pretreatment prostate specific antigen (PSA) dynamics do not add predictive value for prostate cancer outcomes.

In the first study, Shabbir M.H. Alibhai, MD, from the University Health Network in Toronto, and colleagues examined whether ADT was associated with adverse outcomes in 19,079 men with prostate cancer and the same number of matched men who did not receive ADT. After a mean follow-up of 6.47 years, they found that ADT was associated with a higher risk of diabetes mellitus (hazard ratio, 1.16)

and fragility fracture (hazard ratio, 1.65), but not acute myocardial infarction or sudden cardiac death.

In the second study, Matthew Frank O'Brien and colleagues from Memorial Sloan-Kettering Cancer Center in New York City investigated whether pretreatment PSA dynamics were associated with outcomes among 2,938 men undergoing prostate cancer treatment. They found that neither pretreatment PSA velocity or doubling time had much predictive accuracy for recurrence or metastasis over PSA alone, stage, and grade.

"The most novel finding is the increase in well-characterized incident diabetes in those men undergoing ADT," William Dale, MD, from the University of Chicago, writes in an accompanying editorial. "This convincingly supports the conclusion that ADT contributes to the development of diabetes mellitus and that providers should test

for underlying hyperglycemia in men being considered for ADT or in men currently receiving ADT who have not been diagnosed with diabetes mellitus." 



William Dale, MD, PhD

New Immune Therapies Finally Working Against Cancer

Associated Press
May 31, 2009

First there was surgery, then chemotherapy and radiation. Now, doctors have overcome 30 years of false starts and found success with a fourth way to fight cancer: using the body's natural defender, the immune system.

The approach is called a cancer vaccine, although it treats the disease rather than prevents it. At a recent cancer conference, researchers said one such vaccine kept a common form of lymphoma from worsening for more than a year. That's huge in this field, where progress is glacial and success with a new treatment is often measured in weeks or even days.

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Experimental vaccines against three other cancers — prostate, the deadly skin disease melanoma and an often fatal childhood tumor called neuroblastoma — also gave positive results in late-stage testing in recent weeks, after decades of struggles in the lab.

"I don't know what we did differently to make the breakthrough," said Dr. Len Lichtenfeld of the American Cancer Society.

Instead of a single "A-Ha!" moment, there have been many "ah, so" discoveries about the immune system that now seem to be paying off, said Dr. John Niederhuber, Director of the National Cancer Institute.

It's way too soon to declare victory. No one knows how long the benefits will last, whether people will need "boosters" to keep their disease in check, or whether vaccines will ever be a cure. Many vaccines must be custom-made for each patient. How practical will that be, and what will it cost? Those are all good questions — but there are no answers yet, said Richard Schilsky, MD, a University of Chicago cancer specialist who is President of the American Society of Clinical Oncology.

Several vaccine studies were reported over the weekend at the oncology group's annual meeting in Florida.

A big problem has been getting the immune system to "see" cancer as a threat, said Dr. Patrick Hwu, melanoma Chief at the University of Texas M.D. Anderson Cancer Center.

Viruses like the flu or polio are easily spotted by the immune system because they look different from human cells.

"But cancer comes from our own cells. And so it's more like guerrilla warfare — the immune system has trouble distinguishing the normal cells from the cancer cells," he said.

To help it do that, many cancer vaccines take a substance from a cancer cell's surface and attach it to something the immune system already recognizes as foreign — in the lymphoma vaccine's case, a shellfish protein. "It's a mimic to what you're trying to kill, a training device to train the immune system to kill something," Hwu explained.

To make the attack as strong as possible, doctors add a substance to put the immune system on high alert.

Dr. Stephen Schuster of the University of Pennsylvania School of Medicine led a study testing BiovaxID, an experimental vaccine against follicular lymphoma developed by the National Cancer Institute. Rights to it are now held by Biovest International Inc. of Worcester, Mass., and some of his co-researchers have financial ties to the company.

To be in the study, patients had to have achieved a remission for at least six months with standard chemo. This often occurs with this type of lymphoma, but the disease usually comes back.

Researchers gave 41 patients the shellfish protein and an immune booster; 76 other patients were given those plus the vaccine. After nearly five years of followup, the average time until the cancer worsened was 44 months in the vaccine group and 30 months in the others.

Big gains also were seen with a neuroblastoma vaccine developed by the cancer institute. In a study of 226 patients, 86 percent of vaccine recipients were still alive after two years versus 75 percent of others not given the vaccine. Results were released by the oncology society two weeks ago.

The benefits from a melanoma vaccine developed by the cancer institute were more modest. It extended the time until patients relapsed — three months versus one and a half for

those not given the vaccine.

Hilde Stapleton, 53, of suburban Houston, is one of the lucky ones it helped. Still, she found what many other vaccine recipients have learned: The vaccine had few side effects, but the immune system boosters were "like the worst case of flu you've ever had," she said.

The prostate cancer vaccine, Provenge, is the farthest along. Its maker, Seattle-based Dendreon Corp., is seeking federal Food and Drug Administration approval for its use. A study last month found that it extended survival by four months in men with very advanced disease.

Doctors unconnected with these experiments are cautiously optimistic.

"We've raised so many false hopes in the past," said Lichtenfeld of the Cancer Society. "What's different this time is we have the science reports to back up improvements."



EDITOR'S NOTES:

This issue of "In the News" highlights the important contributions our members are making in all phases of cancer research and outreach.

On page 1, Richard L. Schilsky, MD, University of Chicago Professor of Medicine, and President of ASCO, discusses the ASCO Annual Meeting which took place May 29—June 2, 2009, in Orlando, Florida.

On page 2, Bruce Minsky, MD, discusses the effectiveness of various treatment options for patients with rectal cancer.

On page 3, a study about pancreatic cancer presented at the ASCO Annual Meeting by University of Chicago researcher Hedy L. Kindler, MD, is discussed. Also on page 3, William Dale, MD, PhD, Chief of Geriatric & Palliative Medicine, is quoted in an article discussing a study on prostate cancer.

On page 4, Richard L. Schilsky, MD, is quoted about new immune therapies, such as vaccines, to fight cancer.

Richard L. Schilsky, MD, recently reviewed the latest approach to cancer treatment on WTTW public television. To view this video, please go to: <http://www.wttw.com/main.taf?p=42,8,8&vid=060909d>.