

From the 40th Annual American Society of Clinical Oncology Meeting

Community physicians encouraged to consider high-priority phase III trials

A trio of high-priority cooperative group phase III clinical trials is currently enrolling patients and seeking the participation of community physicians. An overview of the three trials was presented at the 40th annual meeting of the American Society of Clinical Oncology.

“The Clinical Trials Cooperative Group [program] is really the prime engine for accomplishing the phase III treatment and prevention trials that NCI sponsors,” said session co-chair Jeffrey S. Abrams, MD, a senior

investigator at the National Cancer Institute. “The program now has more than 1,800 clinical trials treatment sites throughout the United States and provides patients across the country ready access to physicians involved in clinical research.”

Collaboration between the cooperative groups and the NCI has led to the development of the Cancer Trials Support Unit (CTSU). The CTSU provides a common informatics platform for all the adult cooperative group studies, Dr. Abrams noted, and has opened up many of the groups’

phase III trials to members of other cooperative groups. Now the CTSU is opening trials to the community oncologist who is not a member of an established cooperative group, as well.

“The CTSU mechanism is a good way to get into the system if you don’t have a significant track record in clinical research,” Dr. Abrams said. For more information on working with the CTSU and participating in clinical trials research, see *Washington Update* on page 189: “NCI extends clinical trials to community oncologists.”

Session co-chair Norman Wolmark,

MD, said that rising costs, over-regulation, and underfunding may discourage physicians from participating in clinical trials, but participation is critical for advancing clinical care. "The randomized prospective clinical trial represents the clinician's laboratory, the opportunity for us as clinicians to further the state of the art using the scientific method in an unbiased and disinterested way," commented Dr. Wolmark, who is chairman of the NSABP, based in Pittsburgh, PA. "It is an extremely powerful and effective tool."

The following studies are now open to participation by community physicians, whether these clinicians are affiliated or not with existing cooperative groups.

NSABP C-08

The National Surgical Adjuvant Breast and Bowel Project's C-08 trial will test the value of adding antiangiogenesis therapy with the anti-vascular endothelial growth factor (VEGF) antibody bevacizumab (Avastin) to standard chemotherapy for adjuvant therapy in colon cancer, said Carmen J. Allegra, MD, co-chairman of the NSABP Colorectal Committee and chief medical officer of the Network for Medical Communication and Research, in North Potomac, MD.

"It will include patients who have had potentially curative resection for their stage II and III colon cancer," Dr. Allegra said. To be eligible, patients must have had adenocarcinomas that were at least 12 cm from the anal verge, must have undergone resection 29–50 days before randomization, and must have adequate organ function and good performance status. Patients are not eligible if they have active bleeding, uncontrolled hypertension, or clinically significant peripheral neuropathy.

After stratification according to number of positive nodes, patients will be randomly assigned in equal numbers to treatment with modified FOLFOX6 (a regimen containing 5-

fluorouracil, leucovorin, and oxaliplatin [Eloxatin]) with or without bevacizumab, Dr. Allegra said. He noted that modified FOLFOX6 was selected as the control based on the efficacy results of the MOSAIC trial (which used the similar FOLFOX4 regimen) and this regimen's convenience and acceptable safety profile.

The primary endpoint will be disease-free survival, and the secondary endpoint will be overall survival. Target enrollment is set at 2,632 patients.

RTOG P-0014

The Radiation Therapy Oncology Group's P-0014 trial will compare immediate versus delayed chemotherapy in men receiving hormonal therapy (androgen blockade) for high-risk, hormone-naïve prostate cancer, said Kenneth J. Pienta, MD, the trial's protocol chairman and an oncologist at the University of Michigan Medical Center, Ann Arbor.

Eligibility criteria for the study include an initial Gleason score of 7 or higher (or 6 if there was capsular penetration or involvement of the seminal vesicles or lymph nodes) and a failure of local treatment, defined as a rising prostate-specific antigen (PSA) level of 2.0 ng/mL or higher with a doubling time of 32 weeks or less. "The rationale is that patients with a rising PSA after failing primary or salvage therapy are not currently curable, and the primary objective of this trial is to test if early chemotherapy done at the initiation of androgen blockade will improve survival," Dr. Pienta said. Patients are ineligible if they have metastatic disease or have had previous neoadjuvant or adjuvant hormonal therapy for more than 32 weeks.

Patients will be randomly assigned to receive hormonal therapy plus 4 cycles of immediate (concurrent) chemotherapy or to hormonal therapy with initiation of chemotherapy at the time of clinical failure. "The whole idea of this trial is that it is physician- and patient-friendly," Dr. Pienta said.

"The choice of hormonal therapy regimens is up to the physician—it can be monotherapy or complete androgen blockade. And there is a choice of multiple chemotherapy regimens."

The trial's primary endpoint is overall survival; secondary endpoints include biochemical control and time to clinical failure. The target enrollment is 1,050 patients.

CALGB 90206

"CALGB 90206 is a randomized phase III trial of interferon alfa monotherapy or interferon alfa and the anti-VEGF antibody bevacizumab in patients with advanced kidney cancer," said Brian I. Rini, MD, the trial's protocol chairman and an assistant professor of medicine at the University of California, San Francisco.

Eligibility criteria include metastatic or unresectable renal cancer of clear cell histology (with a clear cell component) and no previous systemic therapy. Patients are ineligible if they have significant bleeding or clotting risk factors, evidence or history of central nervous system metastases, or uncontrolled hypertension.

After stratification by nephrectomy status and number of risk factors, patients are randomized to receive interferon alfa-2b (Intron A) alone or in combination with bevacizumab. The trial's primary endpoint is overall survival, and its secondary endpoints include disease progression-free survival and objective response rate. Target enrollment is set at 700 patients.

"In terms of correlative science..., we are collecting plasma and urine samples at baseline and throughout therapy to look at the prognostic and/or predictive power of such assays as serum VEGF or basic FGF," Dr. Rini said. "In addition, all patients will have their archived renal tumors collected, and immuno-histochemical staining will be performed for relevant proteins, as well as gene expression analysis and other assays that may develop over time."