

San Antonio Breast Cancer Symposium:
**Multi-Gene Assay Predicts Recurrence
In Newly Diagnosed Breast Cancer**

The National Surgical Adjuvant Breast and Bowel Project and Genomic Health Inc. said their large, prospective trial met its defined endpoints and validated that Genomic Health's breast cancer assay can accurately and precisely quantify the likelihood of breast cancer recurrence in a large segment of newly diagnosed breast cancer patients.

The study also showed that the "recurrence score" determined by the assay provides a level of correlation to breast cancer recurrence and performance that exceeds standard measures, such as patient age, tumor size and tumor grade.

These results, which were presented at the annual San Antonio Breast
(Continued to page 2)

Colorectal Cancer:
**FOLFOX 4 Should Be First-Line Therapy
For Advanced Disease, NCCTG Finds**

The results of a five-year study of 795 patients show that the combination of chemotherapy drugs known as FOLFOX 4 outperforms the standard chemotherapy treatment for advanced colorectal cancer.

The study found that patients who received FOLFOX 4—a regimen that includes the recently approved drug oxaliplatin (Eloxatin) combined with 5-Fluorouracil (5-FU) and leucovorin—lived an average of 19.5 months after beginning treatment. This compared to 14.8 months for patients who received the standard IFL treatment, which uses the chemotherapy drugs irinotecan (Camptosar, CPT-11) with 5-FU and leucovorin.

Participants who received FOLFOX 4 also had fewer serious side effects often associated with chemotherapy, including fewer infections, less diarrhea and vomiting and did not as frequently experience severe hair loss.

The phase-3 clinical study was sponsored by the U.S. National Cancer Institute and conducted by the North Central Cancer Treatment Group, based at Mayo Clinic. Results of the study were published online Dec. 9 by the Journal of Clinical Oncology.

"This is the greatest increase in survival time recorded to date with a new treatment used by patients enrolled in a large randomized study of colorectal cancer in the United States," said Richard Goldberg, the lead researcher on the study and formerly a medical oncologist at Mayo Clinic.

(Continued to page 5)

© Copyright 2003
The Cancer Letter Inc.
All rights reserved.

Breast Cancer:
Surgery Alone
Inadequate For DCIS
... Page 3

Femara QOL Same
As Placebo
... Page 3

Larynx Cancer:
RTOG Study Finds
Chemo+Radiation
Preserves Voice
... Page 5

Melanoma:
Low-Dose IFN Found
Ineffective In Trial
... Page 6

Brain Tumors:
NeoPharm To Begin
Phase III Trial Of Agent
Against Glioblastoma
... Page 7

Prostate Cancer:
Elderly Men Say
Physicians Push PSA
... Page 7

NCI-Approved Trials
... Page 8

PO Box 9905
Washington DC 20016
Telephone 202-362-1809

"Recurrence Score" Becomes A New Prognostic Factor

(Continued from page 1)

Cancer Symposium earlier this month, are the first large-scale, multi-center validation of a multi-gene assay. It is also the first time that such a study has been conducted using thin sections from standard diagnostic pathology specimens (fixed paraffin-embedded tissue) that are routinely available.

"We are excited about the results of this trial, which represent a practical advance in breast cancer diagnosis because the assay uses tumor tissue that is routinely obtained and stored for every patient," said Norman Wolmark, chairman of the NSABP and the Department of Human Oncology at Allegheny General Hospital in Pittsburgh. "Based on our studies, the recurrence score becomes as important a prognostic measure for this group of node-negative patients as nodal status is for all patients."

Using NSABP's extensive patient database, the cooperative group and Genomic Health designed a blinded, prospective validation using surgical tissue samples from 668 patients, who were node-negative, ER-positive and tamoxifen-treated. These tissue samples were from patients who enrolled in the NSABP B-14 clinical trial from 1982-1988 and whose outcomes have been tracked over time by NSABP sites. Using RNA analysis of tumor tissues, the study evaluated Genomic Health's breast cancer assay to

determine the likelihood of breast cancer recurrence as defined by a recurrence score from 0-100. The recurrence score was able to accurately assign patients into high and low risk groups ($p < 0.00001$), and when the recurrence score was examined together with age and tumor size in a multivariate analysis only recurrence score remained a significant predictor of patient outcome ($p < 0.00001$).

"The results of this trial demonstrate a major advance in molecular pathology by showing that the performance of this genomic assay exceeds the standard measures of patient age, tumor size and tumor grade, characteristics that clinicians have used to predict prognosis for the better part of a century," said Soonmyung Paik, director, Division of Pathology, NSABP. "Even more important is the fact that we can perform this assay in a reproducible and accurate manner using routinely available diagnostic biopsy tissue, unlike other genome based assays which require special handling, such as snap freezing in liquid nitrogen. We believe our findings will provide critical information for this substantial group of patients."

The NSABP trial studied a specific population of breast cancer patients, those who were node-negative, hormone-receptor-positive and tamoxifen-treated. This is a substantial breast cancer patient population, making up approximately 70 percent of the newly diagnosed node-negative patients each year.

Genomic Health's breast cancer assay used in the trial is the first gene panel to be validated in a large-scale, multi-center, prospective validation study. The study showed that using multiple genes is more powerful than using single genes and will provide more consistent and reliable information for physicians and patients. The gene panel includes genes related to the estrogen receptor, HER2, proliferation and invasion as well as several other important categories.

"These validated, pivotal findings provide physicians and patients with quantifiable information that we believe will greatly improve treatment planning," said Steven Shak, chief medical officer of Genomic Health, of Redwood City, Calif. The company plans to make its assay available in early 2004 as a clinical laboratory service under the name *OncotypeDX*.

"The results of our trial with NSABP mark the beginning of a new era in individualized medicine by demonstrating for the first time the practical application of genomic research to the development of validated molecular diagnostics in the treatment

THE CLINICAL CANCER LETTER

Member,
Newsletter and Electronic
Publishers Association

World Wide Web: [http://
www.cancerletter.com](http://www.cancerletter.com)

Publisher: Kirsten Boyd Goldberg

Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 **Fax:** 202-318-4030

PO Box 9905, Washington DC 20016

E-mail: news@cancerletter.com

Customer Service: 800-513-7042

PO Box 40724, Nashville TN 37204-0724

THE CLINICAL CANCER LETTER (ISSN 164-985X). Published monthly, subscription \$99 per year, by The Cancer Letter Inc. All rights reserved. None of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, mechanical, photocopying, facsimile, or otherwise) without prior written permission of the publisher. Violators risk criminal penalties and \$100,000 damages.

of cancer,” said Randy Scott, chairman and CEO of Genomic Health and co-founder of Incyte. Genomic Health has begun to expand the study of the *OncotypeDX* service in other cancer patient populations related to disease recurrence and is also studying the responsiveness of individual tumors to chemotherapy and specific targeted therapies.

Surgery Without Radiation Found Inadequate for DCIS

A study by researchers at Dana-Farber Cancer Institute and Brigham and Women’s Hospital has found that women who chose not to receive radiation therapy following surgery for ductal carcinoma in situ experienced recurrences at a surprisingly high rate. This suggests that surgery alone is inadequate in treating these small, very early breast cancers.

The research, presented at the San Antonio Breast Cancer Symposium earlier this month, is the first prospective study to evaluate the hypothesis that DCIS can be treated by removing it along with a wide margin of healthy tissue on all sides. If surgery alone proved to be effective, women with DCIS could be spared the inconvenience of daily radiation treatments and their slight worsening of the breast’s appearance, and the treatment costs would be lower.

At least one previous study had indicated that women who had wide excision of their DCIS and skipped radiation therapy had no higher risk of a recurrence DCIS than those who received it.

“This was a good hypothesis, but it certainly didn’t work out in our study,” said Jay Harris, chief of radiation oncology at Dana-Farber and the study’s senior author. “The recurrence rate was surprise. We were all much more optimistic about not doing radiation.”

The study began in 1994 enrolling patients at the time of treatment for DCIS and monitoring them for recurrences. To qualify, patients were required to have a DCIS lesion less than an inch across.

The research was headed by Julia Wong, a radiation oncologist at Dana-Farber and Brigham and Women’s in Boston, who presented the work at the San Antonio conference.

As the study progressed toward its intended goal of treating 200 patients, the rate of recurrence (both repeated DCIS lesions and more-serious invasive cancers) rose to a level that had been previously agreed on as grounds to halt the study, and no new patients were enrolled as of July 2002.

The patients were accrued from Dana-Farber, Brigham and Women’s Hospital, Beth Israel Deaconess Medical Center, and Massachusetts General Hospital. Among the 157 patients who had been followed for an average of about three-and-one-half years, 13 had recurrences in the same breast that had previously been treated. Nine patients were diagnosed with a second DCIS lesion, and four had invasive breast cancer. None of the patients had experienced spreading to the lymph nodes or beyond, and were treated with standard therapy.

QOL With Femara Comparable To Placebo, Analysis Finds

Quality of life for postmenopausal women who took Femara after five years of tamoxifen was comparable to that of patients taking placebo, according to data presented at the San Antonio Breast Cancer Symposium.

Quality of life included patients’ ability to engage in activities of everyday living, including work and recreation, subjective evaluation of mood and emotion and occurrence of adverse events as measured by the SF-36 Health Survey, a general health status questionnaire.

The international breast cancer trial of nearly 5,200 women is the first study designed to examine the effectiveness of an aromatase inhibitor, Femara, in the extended adjuvant setting, the period following five years of post-surgery tamoxifen treatment.

The study was coordinated by the National Cancer Institute of Canada Clinical Trials Group. The interim data were published in the Nov. 6 issue of *The New England Journal of Medicine* (**The Clinical Cancer Letter**, October 2003).

At a median follow-up of 2.4 years, the Femara group showed a 43% reduction in risk of overall recurrence compared with placebo ($P=0.00008$) as well as a significant reduction (46%) in contralateral disease. The estimated absolute improvement in disease free survival at four years was 6% for postmenopausal patients taking Femara compared with placebo (93% Femara vs. 87% placebo).

According to the interim analysis, no difference in cholesterol levels have been seen between study arms, nor have there been any differences in patient-reported cardiovascular events.

Hot flashes, arthralgia, and myalgia were more common in those receiving Femara than placebo ($P<0.05$). Vaginal bleeding was more common in

those taking placebo ($P < 0.05$).

The number of women reporting a new bone fracture to date is 77/2166 (3.6%) in the Femara group, compared with 63/2157 (2.9%) in the placebo group ($P = 0.24$). The authors noted a trend to more newly diagnosed osteoporosis in women taking Femara (124/2166 [5.7%]) vs. placebo (97/2157 [4.5%]) ($P = 0.07$).

The most commonly reported adverse events for Femara vs. tamoxifen were bone pain (22% vs. 21%), hot flashes (19% vs. 16%), back pain (18% vs. 19%), nausea (17% vs. 17%), dyspnea or labored breathing (18% vs. 17%), arthralgia (16% vs. 15%), fatigue (13% vs. 13%), coughing (13% vs. 13%), constipation (10% vs. 11%), chest pain (6% vs. 6%) and headache (8% vs. 6%). The incidence of peripheral thromboembolic events, cardiovascular events, and cerebrovascular events was 3-4% in each treatment arm.

A second phase III adjuvant study with Femara is being conducted by the Breast International Group (BIG 1-98) in collaboration with Novartis. This study has four treatment arms comparing five years of Femara, five years of tamoxifen, two years of Femara followed by three of tamoxifen, and two years of tamoxifen followed by three years of Femara. Recruitment in the BIG 1-98 trial was recently closed, with more than 8,000 women enrolled.

EMEND Improved Emesis In Men And Women, Trials Find

A post-hoc analysis of two phase III trials for EMEND (aprepitant) presented at the San Antonio Breast Cancer Symposium showed that treatment with EMEND in combination with a 5-HT₃ receptor antagonist and a corticosteroid significantly improved emetic control in both genders and was generally well tolerated compared to a 5-HT₃ receptor antagonist and a corticosteroid alone.

Although women generally experience more nausea and vomiting after undergoing chemotherapy, women have not responded as well as men have to antiemetic therapies in large, randomized studies using highly emetogenic chemotherapy.

The analysis showed that EMEND in combination with standard antiemetics provided similar efficacy for both women and men, in both the acute (day one) and delayed (days two through five) phases of nausea and vomiting.

“In this analysis, with the addition of EMEND,

we saw equal protection from nausea and vomiting in both women and men,” said Richard Gralla, president, Multinational Association of Supportive Care in Cancer. “This is the first study to demonstrate equal protection from nausea and vomiting in both genders.”

The multi-center, randomized, double-blind, placebo-controlled clinical trials evaluated 1,043 patients (435 female; 608 male) who were randomly assigned to one of two treatment groups: a control regimen or a regimen with EMEND. Patients were asked to record episodes of nausea and vomiting in a diary, and the primary endpoint was complete response (no emesis and no rescue therapy for nausea or vomiting).

In an analysis of the combined study data for each gender, the percentage of patients with overall complete response (days 1-5) was significantly higher in the group receiving the regimen including EMEND than in the control regimen group (66 percent versus 41 percent for women and 69 percent versus 53 percent for men). The rates of control in this analysis of complete response were nearly identical for men and women receiving the regimen with EMEND.

In separate comparisons for complete response on day 1 (acute emesis) and during days 2-5 (delayed emesis), similar superiority was observed with the regimen including EMEND in both genders (acute phase: 86 percent versus 66 percent for women and 87 percent versus 80 percent for men; delayed phase: 76 percent versus 47 percent for women and 77 percent versus 58 percent for men). In an analysis of each study separately, the trend of the treatment effect is the same in both Phase III studies.

The regimen with EMEND was generally well tolerated, with a side effect profile similar to the control group.

Biopsies Could Be Reduced By Computer-Aided-Detection

A clinical study suggests that use of computer-aided-detection technology in evaluating breast MRI exams could reduce the number of biopsies of breast lesions detected by MRI.

The study, by Connie Lehman of the University of Washington and Seattle Cancer Care Alliance, was presented earlier this month at the Radiological Society of North America's annual meeting in Chicago.

Lehman analyzed MRI-detected lesions using

the CADstream computer-aided-detection system. CADstream automates the processing of the 800 or more images produced by breast MRI, corrects for patient movement and analyzes the behavior of tissue over time with an IV-injected contrast agent (used in the identification of abnormal versus normal tissue). In the study, CADstream accurately identified significant enhancement (areas of possible concern) in all malignant lesions, while ruling out 12 of 24 benign lesions.

“If these results are validated by a larger study, the number of unnecessary biopsies of MR lesions could be reduced by half without a concomitant decrease in cancer detection,” said Lehman, Director of Breast Imaging at the University of Washington and the Seattle Cancer Care Alliance, an associate professor of radiology at University of Washington and an affiliate investigator of the Fred Hutchinson Cancer Research Center.

Colorectal Cancer: **Study Advocates FOLFOX 4 As First-Line Therapy**

(Continued from page 1)

Goldberg currently is associate director of the Lineberger Comprehensive Cancer Center at the University of North Carolina in Chapel Hill.

“A tingling sensation in the hands and feet that got better over time was the most commonly reported side effect of FOLFOX 4,” Goldberg said.

All of the participants in the study had been diagnosed with advanced colorectal cancer. They were randomly assigned to one of three groups that compared FOLFOX 4, IFL and IROX, another chemotherapy regimen for colorectal cancer treatment that includes the drugs oxaliplatin and irinotecan.

“Our goal was to compare the IFL and FOLFOX4 treatments, and the IFL and IROX treatments to determine overall survival, response rate, the length of time between when patients began their assigned treatments to when their cancer began to grow, and to establish the side effects associated with each treatment,” said Goldberg.

In addition to increased survival, the study found:

—45 percent of the patients treated with FOLFOX 4 responded with shrinkage of their cancer, compared to a 31 percent response rate for IFL and 34 percent for IROX.

—After beginning treatment, the average time

before the cancer was observed to spread or progress was 8.7 months for FOLFOX 4, 6.9 months for IFL and 6.5 months for IROX.

—One year after beginning treatment, 72 percent of patients receiving FOLFOX 4 were alive compared to 67 percent of patients in the IROX group and 59 percent of those receiving the IFL treatment.

“Based on these findings, we conclude that the FOLFOX 4 treatment should be considered as a first-line treatment over IFL and IROX for patients with advanced colorectal cancer,” Goldberg said.

The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B collaborated with NCCTG to conduct the study.

Larynx Cancer: **Chemo+Radiation Preserves Voice, RTOG Study Finds**

Results of a clinical trial by the Radiation Therapy Oncology Group confirm that simultaneous treatment with chemotherapy and radiation preserves the voice of patients with advanced larynx cancer without compromising survival rates.

The findings, published in the Nov. 27 issue of the New England Journal of Medicine, are compelling enough to have the combination treatment become the standard of care for such patients, the study’s authors report.

“Chemotherapy and radiation together are recommended for advanced laryngeal cancer patients who are otherwise in good health and want to preserve their voice,” said Arlene Forastiere, professor of oncology and otolaryngology at the Johns Hopkins Kimmel Cancer Center. “For patients who have other significant medical problems or little support at home, we would recommend radiation alone. In all cases, patients should be followed closely during treatment by a head and neck surgeon, so that surgery can be performed if there is residual or recurrent cancer after treatment.”

Experience with combined treatment has reduced the need for complete removal of the larynx from 100 percent to about 15 percent, Forastiere said. Removing the larynx leaves patients unable to speak with their natural voice and typically use speaking aids such as an electronic device. Other previously-studied treatment options included radiation therapy alone or several cycles of chemotherapy followed by radiation. Studies from a decade ago showed that the

survival rate of patients treated with chemotherapy followed by radiation was just as good as those receiving surgery.

“RTOG clinical trial research is once again determining the standard of care for cancer patients, said Walter Curran Jr., RTOG chairman and clinical director of the Kimmel Cancer Center at Thomas Jefferson University. “Our 30 years experience in head and neck cancer research has put us at the forefront of multi-modality oncology research.”

This new study of 547 patients entered on RTOG 9111 shows that giving chemotherapy and radiation together instead of sequentially is more effective in preserving the voice box. Patients who received chemotherapy and radiation together still had their voice box after two years 88 percent of the time as compared to 75 percent for those who received chemotherapy followed by radiation and 70 percent for patients who received radiation alone. For each of these three treatment options, overall survival was similar at about 75 percent after two years.

“Giving chemotherapy with radiation at the same time makes cancer cells more susceptible to radiation, so effectively more tumor cells are destroyed,” Forastiere said.

The study was coordinated by the RTOG, with participation from its member institutions and members of the Southwest Oncology Group and the Eastern Cooperative Oncology Group.

Melanoma: **Low-Dose IFN Not Effective Against Melanoma, Study Finds**

A study examining the use of low-dose interferon following surgery in patients with high-risk melanoma showed no significant difference in recurrence-free or overall survival compared to patients receiving no further treatment.

After more than a decade of conflicting studies on adjuvant interferon use, researchers stressed that patients and their physicians should know the facts about interferon before pursuing treatment options for high-risk melanoma.

The results of the phase III study were published online in the *Journal of Clinical Oncology* on Dec. 9.

“Our study found no clear advantage of low-dose interferon therapy following surgery in high-risk melanoma patients,” said Barry Hancock, professor in the Academic Unit of Clinical Oncology at the University of Sheffield in the United Kingdom and

lead author of the study.

According to Hancock, the trial was initiated after a series of studies on adjuvant interferon produced conflicting results and, in turn, conflicting interpretations of these results in both Europe and the U.S. In Europe, prolonged duration of low-dose interferon is often considered standard therapy, while in the U.S., high-dose interferon is more commonly administered.

However, despite studies showing high-dose interferon to be effective in extending disease-free survival, there has been widespread concern, even in the U.S., among physicians and patients who believe the treatment to be ineffective or too toxic. As a result, researchers wanted to see whether prolonged, low doses of the drug would be effective in extending survival, without the harmful side effects of high-dose interferon.

Of the 674 patients enrolled in this trial, 338 received interferon following surgery, and 336 received no follow up treatment. After five years, 63% of patients in both groups experienced disease recurrence (211 IFN vs. 215 control), and 46% of patients in both groups died (151 IFN vs. 156 control). Five-year overall and recurrence-free survival was the same in both groups, estimated to be 44% and 32%, respectively.

The analysis found no clear difference in overall or recurrence-free survival when patients were compared by disease stage, age, and gender. As researchers expected, low-dose interferon was relatively well tolerated, with patients noting fatigue and mood disturbance as the primary side effects.

“The debate on adjuvant interferon in high-risk melanoma continues,” Hancock said. “After many years of clinical research, there is good evidence that high-dose interferon improves recurrence-free survival, but no clear evidence of the benefit to overall survival. Physicians and patients should be armed with all the facts so that they can make informed decisions regarding treatment.”

In light of these findings, two accompanying editorials appearing in *JCO* discuss the debate over adjuvant-interferon trials for patients with resected high-risk melanoma. The authors note that although the study did not find low-dose interferon to be a promising treatment for high-risk melanoma, it does provide insight into the available treatment options and implications for the design of future clinical trials.

“This study confirms that optimal care for patients with high-risk melanoma is still not clear,”

said Lynn Schuchter, associate professor of medicine at the Abramson Cancer Center of the University of Pennsylvania and author of the accompanying editorial. "As a result, treatment decisions will require the integration of existing evidence, judgment of experienced clinicians, and informed input from patients. Continued participation by physicians and patients in well-designed randomized clinical trials will facilitate continued progress in the treatment of melanoma."

Brain Tumors: **NeoPharm To Begin Phase III Trial For Glioblastoma**

NeoPharm Inc. said it is preparing to begin a pivotal phase III clinical trial for IL13-PE38QQR for the treatment of glioblastoma multiforme.

IL13-PE38QQR has received orphan drug designation in Europe and the U.S., and fast track drug development program status from the U.S. Food and Drug Administration.

NeoPharm licensed the agent from the National Cancer Institute and the FDA, and is developing the agent under a Cooperative Research and Development Agreement in collaboration with the laboratory of Raj Puri, at FDA Center for Biologics Evaluation and Research.

IL13-PE38QQR is under investigation in four phase I/II clinical trials in patients with recurrent malignant glioma. The first study is being conducted through the NCI Clinical Trial Evaluation Program-funded New Approaches to Brain Tumor Therapy (NABTT) Consortium. Johns Hopkins University Medical Center is the coordinating site for NABTT.

Results from 21 patients enrolled in this trial were presented as a poster discussion at the Society for Neuro-Oncology, held in Keystone, Colo., last month. The patients were all diagnosed with recurrent supratentorial malignant glioma. IL13-PE38QQR is administered by CED, a novel technique using positive pressure infusion to distribute therapeutic agents within brain tumors and in areas at risk for tumor spread. Two infusions are planned eight weeks apart without planned tumor resection. Patients are dosed with IL13-PE38QQR via two, intra-tumoral catheters at 200 microliters/catheter/hour for 96 hours (total 38.4 mL). The IL13-PE38QQR concentration is being increased in individual cohorts to determine the maximum tolerated dose. Six patients received IL-13PE38QQR at 0.125 micrograms/mL followed by

three patients at each dose level of 0.25, 0.50, 1.0, 2.0 and 4.0 micrograms/mL. Intratumoral infusion of the drug appears to be well tolerated. Similar adverse events occurred across all cohorts, with most being neurological or related to neurosurgical site. Tumor response, either microscopic or radiologic, has been observed in some patients. Although this trial was not designed to determine efficacy, extended patient survival has also been observed.

The second study involves several institutions including the University of California San Francisco, M.D. Andersen Cancer Center, Memorial Sloan-Kettering Cancer Center, and Yale University. Primary objectives include determination of the dose of IL13-PE38QQR that produce tumor cell death, referred to as the histologically effective concentration and the corresponding drug toxicities following IL13-PE38QQR infusion into the tumor and areas adjacent to the tumor. A total of 29 patients have been treated to date in this study.

In Stage 1, patients receive drug intratumorally before (escalating concentrations) and peritumorally after (0.25 micrograms/mL, fixed) tumor resection. On Day 8 of Stage 1, en bloc tumor resection is performed to assess HEC and 2-3 peritumoral catheters are placed adjacent to the resection site in areas where residual tumor cells may be present. In Stage 2, the pre-resection infusion is eliminated and post-resection drug concentrations are escalated.

In Stage 1, 15 patients were treated at escalating pre-resection concentrations (0.25, 0.50, 1.0, and 2.0 micrograms/mL). Histopathological (microscopic) analysis revealed early tumor necrosis in most patients receiving concentrations of 0.5 micrograms/mL and higher. Five specimens had necrosis topographically related to the catheter in an ovoid zone extending up to 2.5 cm. All patients were able to complete the post-resection infusion at 0.25 micrograms/mL.

With confirmation of the HEC in Stage I, the pre-resection infusion was omitted and escalation of post-resection peritumoral infusion concentration began at 0.5 micrograms/ml in Stage 2. Nine patients completed Stage 2 to determine the maximum tolerated infusion concentration. All patients tolerated the peritumoral infusion and no dose limiting toxicities were observed for the six patients at 0.5 micrograms/mL. Two of three patients at 1.0 micrograms/mL developed symptomatic radiographic changes near the former catheter insertion location. As a result, 0.5 micrograms/mL was designated the MTIC post-resection. Enrollment of patients in Stage 3, to

examine escalation of the infusion duration, has completed. Stage 4 to assess deferred catheter placement post tumor resection is underway. Clinical follow-up has revealed overall patient survival from time of treatment to up to 125+ weeks (median 52 weeks). Survival was more prolonged in patients with optimal catheter placement.

A third study presented at SNO described preliminary data from a trial conducted at six sites including Tel Aviv Sourasky Medical Center and Chaim Sheba Medical Center in Israel, University Hospital Eppendorf and University Hospital Kiel in Germany, the Cleveland Clinic and the University of Colorado. This study is designed to determine the maximum tolerated dose in terms of infusion duration and drug concentration of IL13-PE38QQR delivered by CED via one or two intratumoral catheters in patients with recurrent or progressive malignant glioma prior to planned tumor resection. Twenty-two patients have been enrolled. Duration of infusion up to seven days and concentrations of 3.0 micrograms/mL appear to be safe and well tolerated. Evidence of tumor necrosis in some patients has also been observed, as well as extended patient survival.

A fourth clinical study being conducted at Duke University is assessing drug distribution in patients undergoing treatment with IL13-PE38QQR. This study utilizes a radioactive tracer to confirm drug distribution and parameters for CED of drug.

Prostate Cancer: **Elderly Men Say Physicians Are Recommending PSA Tests**

Physicians are frequently recommending prostate-specific antigen screening to men ages 75 and older, despite general agreement that routine prostate cancer screening of men in this age range has little benefit, according to a study by researchers at the Cancer Institute of New Jersey

A review of screening in a nationally representative sample of 7,889 men who participated in a 2000 National Health Interview Survey found that approximately 32.5% of men ages 75 or older reported that they had undergone a PSA screening test during the preceding 12 months, which on the national level would represent approximately 1.47 million U.S. men.

Among screened elderly men, 88.4% reported that their doctor first suggested screening and 66.5% reported having a discussion about the advantages

and disadvantages of the test with their doctor before the screening was performed.

The review, by Grace Lu-Yao, of CINJ and HealthStat in Princeton, N.J., Therese Stukel, of the Institute for Clinical Evaluative Sciences in Toronto, and Siu-Long Yao, also of CINJ, was published in the Dec. 3 issue of the Journal of the National Cancer Institute.

“It is somewhat surprising that so many physicians would suggest screening (or be perceived as suggesting screening) in elderly men when the benefits have not even been established among younger men,” the authors write. Screening a population that is unlikely to benefit may deplete health care resources, potentially harm the patient, and generate unnecessary anxiety.

NCI-Approved Protocols Listed

The National Cancer Institute’s Cancer Therapy Evaluation Program Approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase I

Phase I Study of Bevacizumab in Refractory Solid Tumors. COG Phase 1 Consortium, protocol ADVL0314, Adamson, Peter, phone 215-590-6359.

Phase II

Phase II Evaluation with Correlative Studies of Fenretinide as a Single Agent in the Treatment of Adult Patients with Recurrent Glioblastoma Multiforme. M.D. Anderson Cancer Center, protocol 5770, phone Puduvalli, Vinay Kumar, phone 713-745-0187.

Phase II Study of Triapine in Combination with Gemcitabine in Adenocarcinoma of the Biliary Ducts and Gall Bladder. New York Hospital-Cornell University Medical Center, protocol 6254, Wadler, Scott, phone 212-746-2844.

Phase II Trial of Gemcitabine, Carboplatin and PS-341 in the First-Line Treatment of Advanced Non-Small Cell Lung Cancer. Southwest Oncology Group, protocol S0339, Davies, Angela, phone 916-734-3772.

Pilot

Pilot Trial of Valproic Acid in Patients with Kaposi’s Sarcoma. AIDS-Associated Malignancies Clinical Trials Consortium, protocol AMC-038, Ambinder, Richard, phone 410-955-5617.