THE CANCER LETTER

Vol. 35 No. 22
June 5, 2009

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

ASCO Annual Meeting:

PARP Inhibitors Show Promise Against Breast Cancer In Small Phase II Studies

By Kirsten Boyd Goldberg

A new class of drugs called PARP inhibitors demonstrated promising results in small studies in breast cancer, but generated a large amount of excitement among cancer specialists gathered at the annual meeting of the American Society of Clinical Oncology in Orlando, Fla., earlier this week.

The excitement is due to the ability of PARP inhibitors to block two pathways by which cancer cells can repair themselves following chemotherapy and radiotherapy. PARP, short for poly (ADP-ribose) polymerase, is an enzyme used by cancer cells to repair DNA damage, including the damage inflicted by cytotoxic therapy.

Inhibiting PARP may enhance the cytotoxicity of DNA-damaging agents

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Avastin For Adjuvant Treatment Of Colon Cancer Showed Benefit At One Year, But Failed Overall

By Paul Goldberg

The first trial of Avastin (bevacizumab) for colon cancer in the adjuvant setting showed a statistically significant improvement in disease-free survival for the first year, which corresponded with the duration of the therapy.

Though the National Surgical Adjuvant Breast & Bowel Program trial C-08 failed to meet its primary endpoint, the investigators say that a statistically significant advantage seen during the first year of the trial provides a rationale for long-term administration of the agent.

"During the administration of bevacizumab, these curves separate in favor of bevacizumab," said Norman Wolmark, chairman of NSABP. "Following bevacizumab treatment, these curves come together. The formal test for interaction between the effect of bevacizumab and time is highly statistically significant with a p-value of 0.001."

Wolmark presented the findings at the plenary session of the meeting of the American Society of Clinical Oncology.

Disagreeing with Wolmark, Lee Ellis, professor of surgical oncology and cancer biology at M.D. Anderson Cancer Center, said the small potential gains, high cost and unknown toxicities associated with long-term use don't justify this use of Avastin.

"Is a 3 to 5 percent improvement in disease-free survival clinically meaningful?" said Ellis, relying on his calculation of potential benefit. "Is

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PARP: "A Field That's Going To Explode In A Year Or Two"

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and may reverse tumor cell resistance to chemotherapy and radiotherapy. PARP inhibitors also selectively kill cells deficient in BRCA1 and 2, thus blocking a second pathway for cell repair.

PARP inhibition is considered sufficiently unfamiliar to oncologists that a special scientific discussion preceded the presentation of clinical results in the ASCO plenary session.

The discussant, Merrill Egorin, professor of medicine and pharmacology at University of Pittsburgh, said many questions about PARP inhibitors need to be resolved in clinical studies, including dose and frequency of use, whether they should be administered orally or intravenously, the timing of PARP inhibitor dosing relative to cytotoxic therapy dosing, and how long to continue the PARP inhibitor.

"Also, is there a role for chronic use of PARP inhibitors as chemopreventive agents in patients with BRCA mutations?" Egorin said. "These are only some of the questions to consider. I think this is a field that's going to explode within the next year or two, and I hope it's something we are prepared for."

Furthest along in clinical development is a PARP inhibitor called BSI-201, by BiPar Sciences. Sanofi-Aventis purchased BiPar Sciences in April for $500 million.

In a plenary session presentation at ASCO, results of a randomized phase II study demonstrated that women with metastatic triple-negative breast cancer who received BSI-201, in combination with conventional chemotherapy, lived significantly longer and experienced significantly better progression-free survival than women who received standard chemotherapy alone.

Triple-negative breast cancer is considered particularly difficult to treat because it lacks receptors for estrogen, progesterone, and human epidermal growth receptor 2 (HER2), which are targeted by widely-available drugs.

Triple-negative tumors often overexpress the epidermal growth factor receptor (EGFR) 1 and usually are high grade. These cancers account for about 15 to 20 percent of all breast cancer diagnosed and have a high risk of relapse in the first few years after diagnosis.

In the study, clinical benefit rate (defined by complete and partial responses and stable disease of at least six months), response rate, progression-free survival, and overall survival were compared among 116 women with metastatic triple-negative breast cancer who were randomly assigned to receive a standard chemotherapy treatment of gemcitabine (1,000 mg/m^2) and carboplatin (AUC=2) plus BSI-201, or standard treatment alone.

Eligible subjects had measurable disease and had received no more than two prior cytotoxic regimens. Chemotherapy was given on days 1 and 8, and BSI-201 (5.6 mg/kg iv biweekly) on days 1, 4, 8, and 11 every 21 days.

Results were as follows:

—Approximately 62 percent of patients receiving BSI-201 showed clinical benefit, compared with 21 percent in the chemotherapy only group (p=0.0002).

—Overall response rate to treatment with the drug combination containing BSI-201 was 48 percent in the group receiving BSI-201, compared to 16 percent in the group receiving standard chemotherapy alone (p=0.002).

—Median overall survival for women who received BSI-201 was 9.2 months compared with 5.7 months for the control group (p<0.0001).

—Median progression-free survival for the BSI-201 group was 6.9 months compared with 3.3 months (p=0.0005).

Patients assigned to receive chemotherapy without BSI-201 were allowed to receive BSI-201 at the time of disease progression.

"The results of this study provide early evidence that BSI-201 is a promising treatment for women with

THE CANCER LETTER

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Editorial: 202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
Letters to the Editor may be sent to the above address.

Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
General Information: www.cancerletter.com

Subscription $385 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.
Founded Dec. 21, 1973, by Jerry D. Boyd.

triple-negative breast cancer, an aggressive form of the disease for which we need new, more effective therapies," said Joyce O'Shaughnessy, co-director of the Breast Cancer Research Program at Baylor-Charles A. Sammons Cancer Center in Dallas, Texas.

The incidence of side effects was similar between the two groups. BSI-201 itself was well-tolerated and did not contribute any new side effects nor add to the known side effects of gemcitabine and carboplatin.

The most common severe (grades 3 and 4) side effects included neutropenia (25/57 in patients treated with GC and BSI-201; 31/59 patients treated with GC alone), thrombocytopenia and anemia. No febrile neutropenia was observed in patients receiving BSI-201 combined with chemotherapy.

"The promising safety and efficacy data from this phase II study justify further investigation of BSI-201 in a phase III study," O'Shaughnessy said. "The planned phase III study of gemcitabine plus carboplatin with or without BSI-201 in metastatic triple-negative breast cancer patients will open in late June. Patients randomized to chemotherapy alone will have the option to crossover to receive BSI-201 with chemotherapy at disease progression."

Barry Sherman, executive vice president of development for BiPar Sciences, said the phase III trial will be very similar in design to the phase II trial and will seek to randomized a little over 400 patients. O'Shaughnessy will be the lead investigator for the trial, which will involve about 60 or more centers, both within community oncology networks such as US Oncology as well as academic sites largely based in the U.S.

"The phase II trial randomized very rapidly and we expect, given the excitement around the result of the phase II study that phase III will enroll quickly," Sherman said.

BSI-201 was he work of Ernest Kun, an emeritus professor at University of California, San Francisco, who has had a longstanding interest in PARP inhibition. A firm that Kun founded licensed the molecule to BiPar in 2005.

"Apart from the [phase II] results, which I think speak for themselves, there are a couple of things that we did here that are important to point out," Sherman said. "We targeted a particular group of patients based on biological markers. I think it reinforces the notion that being able to do that gives you a leg up in terms of potential positive outcome.

"The other thing we did in drug development terms was to do a randomized, controlled trial early in the development process so that we were able to quickly and convincingly show this kind of a result," Sherman said.

The market for a drug for triple-negative breast cancer is roughly equal to the market for Herceptin, a $2-billion drug, Sherman said. BiPar has ongoing trials of BSI-201 in other types of cancer that rely heavily on PARP, including ovarian, endometrial, and glioblastoma. The company plans to start a trial in squamous cell lung cancer later this year, Sherman said.

"It is too early to say with certainty that this is a major advance, but the arrows all point that way: a defined subgroup (triple-negative breast cancer), compelling preclinical biology (the DNA damage repair deficits seen in TNBC), a small randomized phase II trial, but with some of the more compelling results we've seen in quite some time," said George Sledge Jr., professor of pathology and laboratory medicine at the Indiana University Melvin and Bren Simon Cancer Center.

"I look forward to the phase III trial results, which given the rapidity with which this disease progresses, should become available in a fairly short while after accrual closes," Sledge said.

"Also worth mentioning is that there is now a race on, with multiple companies with drugs in development as PARP inhibitors," Sledge said.

The company is referring inquiries about the planned phase III study to its website at www.biparsciences.com.

Olaparib, AstraZeneca's PARP Inhibitor

A second phase II study tested the PARP inhibitor olaparib, under development by AstraZeneca, as a single agent in BRCA-deficient breast cancer.

The study reported that more than a third of women with BRCA1 or BRCA2 mutations and advanced breast cancer that persisted despite prior treatment experienced tumor shrinkage after receiving olaparib. This study is the first to evaluate olaparib when used alone in women with BRCA-deficient breast cancer.

"The findings of our study provide very promising evidence that the potent PARP inhibitor olaparib may be useful for treating BRCA-deficient breast cancers," said lead author Andrew Tutt, director of the Breakthrough Breast Cancer Research Unit at Kings College in London. "However, this drug is in a very early stage of development, and additional clinical trials are necessary to determine the best way to use olaparib in women with BRCA-deficient breast cancer. We are actively discussing the design of future PARP inhibitor studies for women with BRCA1 and BRCA2 mutations."

A prior phase II study showed that some women with BRCA-deficient ovarian cancers responded to olaparib. A phase I trial identified 400 mg bd as the maximum tolerated dose with an initial signal of efficacy in BRCA-deficient ovarian cancers (ASCO 2008; abst 5510).

In this study, Tutt and his colleagues examined the response rate to olaparib (as evidenced by tumor shrinkage) in 54 women with breast cancer that was deficient in BRCA1 or BRCA2 and that persisted despite several rounds of standard chemotherapy.

Two seqential patient cohorts received continuous oral olaparib in 28-day cycles initially at 400 mg bd (27 patients), and subsequently at 100 mg bd (27 patients).

Forty percent of the patients responded to olaparib (9/24) at the higher of the two doses used in the study.

Olaparib was well tolerated, with the most common side effects being mild fatigue, nausea and vomiting.

Additional studies of PARP inhibitors are underway in several tumor types, including ovarian, colorectal, and pancreatic cancers, and malignant gliomas.

No Need For Frequent CA125 Tests?

In a study presented at the ASCO plenary session that could result in change in the treatment of recurrent ovarian cancer, European researchers found that treating relapse early based on CA125 blood levels alone does not improve overall survival, compared with delaying treatment until symptoms arise.

Women who have undergone treatment for ovarian cancer may have their CA125 levels tested as often as every three months for several years after initial treatment.

"Women who've completed ovarian cancer treatment often worry about a relapse, and they undergo frequent blood tests for CA125 in the hope of catching it early," said lead author Gordon Rustin, professor of oncology at Mount Vernon Cancer Center in Hertfordshire, U.K. The study was conducted by the MRC/NCRI and EORTC Gynae Cancer Intergroups.

"We thought that delaying chemotherapy might make overall quality of life worse, due to the symptoms of ovarian cancer, but this was not seen in women on this trial," Rustin said. "Since there is no benefit from early chemotherapy, patients may choose to avoid the inconvenience and anxiety associated with frequent retesting for CA125 levels as well as unnecessary early initiation of treatment for relapse."

In this study, investigators compared overall survival between 265 women with ovarian cancer in remission after initial chemotherapy who began second-line chemotherapy after experiencing a rise in CA125, and 264 women with rising CA125 whose treatment was delayed until symptoms of relapse appeared (such as pelvic pain or bloating).

Even though the early treatment group started second-line chemotherapy an average five months before the delayed treatment group, overall survival was the same between both groups: 41 months since completion of first-line chemotherapy.

Thus, women can safely delay treatment until symptoms develop, Rustin said.

"If early intervention for women with ovarian cancer doesn't improve survival, but affects quality of life, then why are we doing it?" said discussant Beth Karlan, director of the Women's Cancer Research Institute at the Samuel Oschin Comprehensive Cancer Institute, and professor of obstetrics and gynecology at the Geffen School of Medicine at University of California, Los Angeles.

It may be difficult to encourage physicians and patients to give up the long-standing practice of frequent CA125 tests, because it has become so ingrained in the clinical practice, Karlan said.

"It seems intuitive that initiating chemotherapy with smallest tumor burden would provide the most benefit—but it doesn't," Karlan said. Most ovarian cancer is diagnosed when it is metastatic, and even with the most meticulous surgery to remove the tumor, clones often develop into chemotherapy-resistant disease.

"I'd even go so far to say repeated treatment does more harm than good," Karlan said.

Intensive CA125 monitoring accelerates the reduction of patients' global health scores, causes patients to spend more time in treatment, and experience more anxiety and toxicities, she said.

"It may hasten the patient's demise in some cases," Karlan said.

Vaccine Prolongs DFS for Lymphoma

Also featured in the ASCO plenary session, an eight-year randomized, controlled phase III clinical study found that a patient-specific therapeutic vaccine, BiovaxID, significantly prolongs disease-free survival in follicular non-Hodgkin's lymphoma.

The study found that patients who received the vaccine experienced a median disease-free survival of approximately 44 months compared to approximately 30 months for those who received a control vaccine—an increase of 47 percent.

BiovaxID is individually manufactured from a

tissue biopsy obtained from a patient's own tumor. The vaccine targets a unique protein (idiotype) expressed by cancerous B cells in follicular lymphoma and spares normal, healthy B cells that do not express the tumor idiotype.

The final vaccine is administered as a subcutaneous injection along with granulocyte-monocyte colony stimulating factor and keyhole limpet hemocyanin, which together enhance the potency of the immune response induced by BiovaxID. A previous phase II study demonstrated that patients receiving the BiovaxID vaccine develop a highly-specific immune response against tumor cells.

"With this vaccine, we've now moved into an era where we can safely use a patient's immune system to effectively fight follicular lymphoma and enhance the response to conventional chemotherapy," said Stephen Schuster, associate professor at the University of Pennsylvania School of Medicine and the study's lead author. "Because this vaccine uniquely recruits the patient's immune system to seek and destroy only tumor B cells, this approach may be applicable to the treatment of other B-cell lymphomas."

The study achieved its primary endpoint of prolonging disease-free survival in patients vaccinated with BiovaxID after achieving a complete response to chemotherapy. In the study, 177 patients with follicular lymphoma who had achieved a complete response to PACE (prednisone, doxorubicin, cyclophosphamide and etoposide) chemotherapy were randomized to the BiovaxID vaccine arm (vaccine plus KLH/GMCSF) or to the control arm (KLH/GM-CSF alone).

Investigators analyzed the cohort of 117 patients who, as per study protocol requirements, maintained a complete response to chemotherapy for at least six months and received active (76 patients) or control (41 patients) vaccine. After a median follow-up of 4.71 years (56.6 months, range: 12.6 - 89.3 months), the median disease-free survival in the BiovaxID arm was 44.2 months compared with 30.6 months in the control arm, which is a statistically significant difference.

BiovaxID demonstrated a favorable safety profile and was very well-tolerated by patients. Further studies are planned to examine the role of BiovaxID in patients with other B-cell lymphomas and as maintenance therapy in patients with follicular lymphoma.

ASCO Annual Meeting:

Future Of Avastin In Adjuvant Colon Cancer Rests On AVANT

(Continued from page 1)

this enough of an improvement to justify the toxicity, the inconvenience, the cost?"

The future of Avastin in the adjuvant treatment of colon cancer is likely to be determined by the Roche-sponsored AVANT trial, a 3,450-patient study that is expected to report results within six months to a year.

"It is our sincere hope that the data from the AVANT trial will refute the observations from the NSABP protocol C-08," Wolmark said. "Alas, we suspect that the AVANT trial will simply confirm the results of NSABP C-08 showing a transient benefit for bevacizumab for as long as it is given—but hope springs eternal."

If this proves to be the case and AVANT shows that a benefit of adjuvant Avastin persists for the duration of care, further studies of the agent in this indication would no longer be justifiable, Ellis said.

"If AVANT is not outright positive, I do not think we should conduct trials with long-term anti-VEGF therapy in the adjuvant setting," Ellius said. "There was no increase in the cure rate with the addition of bevacizumab, so we have to assume that bevacizumab must be continued indefinitely in order to provide some benefit. We should not administer a potent drug like bevacizumab forever in a population where nearly all the patients will not benefit from the drug."

However, Ellis said, trials in other adjuvant settings should not be affected by findings in adjuvant colorectal cancer.

In his colorfully delivered presentation, Wolmark disputed the notion that C-08 trial was negative. "Well, nobody likes to fail," Wolmark said. "So just how badly did we fail? Did we fail abominably, or did we fail with distinction, *cum laude*, with the hope of redemption?"

Wolmark said the hope of redemption emanates from the interim analysis of DFS done at one year.

"The one-year time point is particularly interesting in that this corresponds to the duration that the bevacizumab was given," he said. "It also corresponds to an interim analysis that was pre-planned for NSABP protocol C-08.

"There was a robust benefit in favor of bevacizumab during the one year that it was given, a hazard ratio of 0.6, a 40 percent diminution in event rate, a p-value with lots of zeros after the decimal place, and those statisticians who had the opportunity to see this surely

got an endorphin rush, because we all know that zeros give statisticians a major endorphin rush, particularly if those zeros occur after the decimal place."

The p-value was 0.0004.

"But, alas, ladies and gentlemen, like so many things in life, we had peaked and didn't know it, because from this point on, this dramatic benefit became progressively more attenuated with time," Wolmark said. "Ironically, it was not until the final analysis was completed that the differences became non-statistically significant."

Ellis said it is plausible that the C-08 data suggests that Avastin may act as a cytostatic agent in this setting.

"What if long-term anti-VEGF therapy is necessary to prolong disease-free survival?" Ellis said. "How long do we give this therapy? Is it three years? If we give it for any period of time less than for the rest of the patient's life, then we can't use DFS as a primary endpoint, because once you stop the bevacizumab, the curves could converge again, so you must use overall survival as an endpoint. And I am not sure we could ever answer the question of how long we should give this therapy."

Wolmark's talk was easily the most colorful of all talks at the plenary session. Consider his disclosure of conflicts of interest:

"Of course, we start with the obligatory slide, where we disclose our iniquitous transgressions over the past year in the hope that it would afford me a certain relief and unburdening and expiation, and yet that just doesn't seem to be happening! Perhaps had I received payment for my services on these advisory boards, I would have a greater sense of spiritual equanimity."

Translation: Wolmark is an unpaid member of Genentech and Sanofi-Aventis advisory boards.

ASCO Certification Program Emphasizes Quality Of Care

The American Society of Clinical Oncology announced the Quality Oncology Practice Initiative Certification Program, a new program to certify oncology practices that achieve rigorous standards for high-quality cancer care.

"Increasingly, oncology practices are being asked by payors, patients, and others to attest to the quality of care they provide," said incoming ASCO President Douglas Blayney. "ASCO QOPI Certification will demonstrate a practice's commitment to delivering high-quality cancer care."

QOPI is a voluntary, self-assessment program launched by ASCO in 2006 to help hematology-oncology and medical oncology practices assess the quality of care they provide to patients. Through the QOPI program, practices abstract data from patients' medical charts twice a year and enter this information into a secure database. Currently, nearly 500 oncology practices are enrolled in the program.

ASCO analyzes this data for adherence to more than 80 evidence-based and consensus quality measures and provides feedback reports to participating practices to help them identify areas for improvement. Individual practices are also able to compare their performance to aggregate data from other practices across the country. Based on these data, doctors can focus on specific areas for quality improvement.

A study published in the Journal of Clinical Oncology documents the experience of the University of Michigan Comprehensive Cancer Center with the QOPI program. While the study authors determined that the Center was in compliance with the majority of quality measures, the QOPI data showed that use of chemotherapy within two weeks of death was significantly higher than other practices. After this data was presented to the cancer center faculty, use of chemotherapy at the end of life declined from 50 percent to 20 percent.

"It is rewarding to see that through the QOPI program we found areas where we could make striking, rapid improvements in the already high quality of care we were delivering," said Blayney.

The QOPI Certification Program will be available to all practices that meet specific performance requirements and that pass a new site assessment . Practices that participate in the fall 2009 QOPI data collection process will be the first eligible to receive certification in early 2010.

"The QOPI Certification Program puts oncologists at the forefront of defining the highest level of clinical care for people with cancer. We hope that health plans will recognize the QOPI measures, and use QOPI as a best practices model for their own quality initiatives."

* * *

ASCO and The ASCO Cancer Foundation honored 13 community oncology practices for their efforts to improve care through increasing and enhancing patient participation in cancer clinical trials.

The Community Oncology Research Grant and the Clinical Trials Participation Awards were presented May 31, at ASCO's annual meeting.

Practicing oncologists are essential to the clinical

trial infrastructure in the U.S.—about half of the patients who participate in cooperative group trials run by NCI join through community-based practices.

The Community Oncology Research Grants, supported by The Astellas USA Foundation, are designed to help practicing oncologists enhance their clinical trials programs, based on the ASCO Statement on Minimum Standards and Exemplary Attributes of Clinical Trial Sites. Each of this year's three award-winning practices will receive a one-year grant of $30,000.

They are: Billings Clinic Cancer Center (Billings, Mont.), Marion L. Shepard Cancer Center (Washington, N.C.); and Nebraska Cancer Specialists (Omaha, Neb.)

The Clinical Trials Participation Awards, supported by a grant from the Coalition of Cancer Cooperative Groups, enable ASCO to recognize eight practices and provide travel grants to attend the annual meeting. The award winners were selected based on a number of factors, including their patient accrual rates and accrual of minority and under-represented populations and innovative techniques in overcoming barriers to participation in clinical trials.

The 2009 honorees: Nebraska Cancer Specialists, Omaha; University of Hawaii Cancer Research Center of Hawaii; Doctors Hospital of Laredo (Tex.); Iowa Oncology Research Association CCOP; Comprehensive Cancer Centers of Nevada (Las Vegas); Wilshire Oncology Medical Group Inc. (La Verne, Calif.); Yakima Valley Memorial Hospital/North Star (Yakima, Wash.); and Helen DeVos Children's Hospital (Grand Rapids, Mich.).

* * *

ASCO Cancer Foundation awarded more than $6.1 million to support clinical and translational research designed to improve cancer prevention, treatment and care.

Merrill Egorin, University of Pittsburgh Cancer Institute, received the Translational Research Professorship, an award of $500,000 over five years to support continued efforts to bring advances in basic sciences into the clinical arena. Egorin also will serve as a mentor for other translational researchers.

Shanu Modi and **Ingo Mellinghoff**, both of Memorial Sloan-Kettering Cancer Center, received Advanced Clinical Research Awards. Each will receive a three-year award totaling $450,000 to support original research currently not funded.

Career Development Awards, a three-year grant totaling $200,000 to establish an independent clinical cancer research program, was presented to: **Don Benson**, Ohio State University; **Jaishri Blakeley**, Johns Hopkins University; **Daniel Cho**, Beth Israel Deaconess Medical Center; **Daniel Costa**, Beth Israel Deaconess Medical Center; **David Gerber**, University of Texas, Southwestern Medical Center; **Margaret Kasner**, Thomas Jefferson University; **Rebecca Leboeuf**, Memorial Sloan-Kettering Cancer Center; **Richard Lee**, Massachusetts General Hospital Cancer Center; **Deric Park**, University of Pittsburgh; **Mary Sehl**, University of California, Los Angeles; and **Brian Wolpin**, Dana-Farber Cancer Institute.

Young Investigator Awards were presented to 48 physicians.

In Brief:

Geneticists Copeland, Jenkins Elected To National Academy

NEAL COPELAND and **NANCY JENKINS**, Singapore-based cancer geneticists previously with NCI, were elected into the National Academy of Sciences. Copeland, executive director of the Institute of Molecular and Cell Biology of Singapore's Agency for Science, Technology and Research, was elected to NAS this year. NAS elected Jenkins, deputy director of IMCB's Genetics and Genomics Division, in 2008. Their membership takes effect this year.

Copeland and Jenkins, who have co-authored over 750 papers and been cited over 30,000 times, have worked together for 30 years since they met as postdoctoral follows in Harvard Medical School. Prior to joining IMCB in 2006, Copeland headed NCI's molecular genetics of oncogenesis section and was director of the mouse cancer genetics program, while Jenkins headed the molecular genetics of development section.

Since joining A*STAR, they have set up IMCB's cancer genetics laboratory and have been working on new ways of analyzing the cancer genome, by characterizing the genetic changes required to promote or sustain tumor formation.

In their research to induce different types of human cancer in mice, their IMCB group has recently discovered ways of manipulating the genetic structure of "Sleeping Beauty," a mutagenic transposon, a sequence of DNA that can move around to different positions within the genome of a single cell. In moving around, a transposon can cause mutations and change the amount of DNA in the genome.

Copeland and Jenkins' group plans to use another whimsically named transposon, "PiggyBac," to model cancer in mice and potentially zebrafish. With these

cancer models, as well as recent advancements in cloning and sequencing technologies, they hope to better understand and devise more effective treatment strategies for various forms of cancer.

ONCOLOGY NURSING SOCIETY announced its 2009–2010 Board of Directors at its 34th Annual Congress in San Antonio, Tex.

Brenda Nevidjon continues her two-year term as president. She is a clinical professor and director of the nursing & healthcare leadership specialty at Duke University School of Nursing.

Newly-elected officers include president-elect **Carlton Brown**, assistant professor in the University of Delaware's School of Nursing. Brown will serve one year as president-elect, and he will take office as ONS president in 2010. He has been an ONS member for more than 17 years.

Beginning her first year in office is newly-elected treasurer **Colleen Corish**, clinical director, oncology & professional services at Medical University Hospital Authority in Charleston, S.C.

Amy Strauss Tranin, solution consultant at Cerner Corporation in Kansas City, Mo., continues as board secretary.

Newly-elected ONS directors-at-large are **Laura Fennimore**, director of organizational development, nursing education and research at the University of Pittsburgh Medical Center, Presbyterian Hospital, and **Michele Gaguski**, oncology clinical specialist at Ocean Medical Center in Brick, N.J.

ONS directors-at-large continuing their terms are **Barbara Holmes Gobel**, oncology clinical nurse specialist at Northwestern Memorial Hospital in Chicago; **Joanne Itano**, associate professor of nursing and director, academic affairs at the University of Hawaii; **Susan Schneider**, associate professor, director oncology nursing specialty at Duke University School of Nursing; and **Virginia Martin**, clinical director, ambulatory care services at Fox Chase Cancer Center.

Funding Opportunities:

NIH Funding Announcements

Notice of Intent to Publish a Request for Applications for the Cancer Intervention and Surveillance Modeling Network CISNET (U01) (NOT-CA-09-028) http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-028.html

Extension of the Expiration Date for PAR-07-344, Innovations in Biomedical Computational Science and Technology (R01) (NOT-GM-09-021) http://grants.nih.gov/grants/guide/notice-files/NOT-GM-09-021.html

Extension of the Expiration Date for PAR-06-411, Exploratory Innovations in Biomedical Computational Science and Technology (R21) (NOT-GM-09-022) http://grants.nih.gov/grants/guide/notice-files/NOT-GM-09-022.html

Extension of the Expiration Date for PAR-07-160, Innovations in Biomedical Computational Science and Technology Initiative (SBIR [R43/R44]) (NOT-GM-09-023) http://grants.nih.gov/grants/guide/notice-files/NOT-GM-09-023.html

Extension of the Expiration Date for PAR-07-161, Innovations in Biomedical Computational Science and Technology Initiative (STTR [R41/R42]) (NOT-GM-09-024) http://grants.nih.gov/grants/guide/notice-files/NOT-GM-09-024.html

RFAs Available

Centers of Cancer Nanotechnology Excellence (CCNEs)(U54) (RFA-CA-09-012) Application Receipt Date: Oct. 14. http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-012.html

Cancer Nanotechnology Platform Partnerships (U01) (RFA-CA-09-013)

Application Receipt Date: Oct. 14 http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-013.html

Pilot-Scale Libraries (PSL) for High-Throughput Screening (P41) (RFA-RM-09-007) NIH Roadmap Initiatives, Application Receipt Date: Oct. 1 http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-007.html

Program Announcements

Mechanisms, Measurement, and Management of Pain in Aging: from Molecular to Clinical (R01) (PA-09-193) http://grants.nih.gov/grants/guide/pa-files/PA-09-193.html

Mechanisms, Measurement, and Management of Pain in Aging: from Molecular to Clinical (R21) (PA-09-194) http://grants.nih.gov/grants/guide/pa-files/PA-09-194.html

Mechanisms, Measurement, and Management of Pain in Aging: from Molecular to Clinical (R03) (PA-09-195) http://grants.nih.gov/grants/guide/pa-files/PA-09-195.html

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THE CANCER LETTER

Vol. 24 No. 5
May 2009

Business & Regulatory Report

FDA Approvals and Applications

ODAC Recommends Accelerated Approval Of Arzerra For Refractory Leukemia

The FDA Oncologic Drugs Advisory Committee voted 10 to 3 to recommend accelerated approval for Arzerra (ofatumumab) for patients with chronic lymphocytic leukemia whose disease is refractory to fludarabine and alemtuzumab.

The committee met in Orlando, in conjunction with the annual meeting of the American Society of clinical Oncology.

The agent is sponsored by **GlaxoSmithKline** (NYSE: GSK) and

(Continued to page 2)

Clinical Trials

AlphaVax Completes Enrollment Of Early Trial Of CEA Cancer Immunotherapy

AlphaVax of Research Triangle, N.C., announced the completion of enrollment in a phase I/II CEA cancer immunotherapy study being conducted by the Duke University Comprehensive Cancer Center.

The phase I/II study is an open-label, dose-escalation study to evaluate the safety and immunogenicity of carcinoembryonic antigen (CEA(6D))-expressing virus-like replicon particle immunotherapy in patients with advanced or metastatic CEA-expressing malignancies.

CEA is tumor protein found on many types of cancer including colorectal, pancreatic, gastric, breast, ovarian, and lung.

The phase I study consists of a dose escalation at three dosage levels of CEA-expressing VRP and the phase II component has additional patients at the maximally tolerated dose. CEA-expressing VRP were administered by intramuscular injection every three weeks for a minimum of four immunizations, with additional doses in patients without progressive disease every three months.

Results from the trial are expected to be released later this year, the company said. The study is funded by NCI.

The Avon Foundation of New York and the **Dr. Susan Love Research Foundation** of Los Angeles said their joint venture, the Love/Avon Army of Women, (www.armyofwomen.org) will be supported by AARP, the nonprofit membership organization for people 50-plus.

The Army of Women is currently recruiting one million women who are interested in taking part in the research studies that will help scientists

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FDA Task Force To Study Agency's Transparency

(Continued from page 1)

Genmab A/S (Copenhagen: GEN).

"While current initial treatments for CLL can provide prolonged remissions, some patients will progress rapidly and relapse, which highlights the need for new therapies," said Debasish Roychowdhury, senior vice president and head, medicines development, GlaxoSmithKline Oncology.

The committee made its decision based on an interim analysis of a pivotal trial that was presented at the American Society of Hematology 2008 annual meeting and will be presented at the American Society of Clinical Oncology 2009 annual meeting.

FDA announced the formation of a task force to develop recommendations for enhancing the transparency of the agency's operations and decision-making process.

The task force will hold a public meeting June 24 to solicit recommendations on how the agency can make more available, useful and understandable information on its activities and decisions.

"Our administration is committed to making government open and transparent," HHS Secretary Kathleen Sebelius said in a statement. "The Transparency Task Force will give the American people a seat at the table and make the FDA more open and accountable."

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Business & Regulatory Report is a supplement to The Cancer Letter. ISSN 1053-9611.

The agency also will seek public input through a docket that will be open until Aug. 7. The FDA is also exploring additional electronic means for the public to provide comments and feedback on this topic. A second public meeting in the fall of 2009 is anticipated.

"President Obama has pledged to strengthen our democracy by creating an unprecedented level of openness and public participation in government, and the FDA looks forward to participating in this process," said FDA Commissioner Margaret Hamburg. "I have asked the Transparency Task Force to deliver recommendations to me for ways to make more information available and foster better understanding of decision-making."

The task force will be chaired by Principal Deputy Commissioner Joshua Sharfstein and will include center directors, the associate commissioner for regulatory affairs, chief scientist, and the chief counsel.

According to the agency, the task force will:

* Seek public input on issues related to transparency;

* Recommend ways that the agency can better explain its operations compatible with the appropriate protection of confidential information;

* Identify information the FDA should provide about specific agency operations and activities, including enforcement actions and product approvals;

* Identify problems and barriers, both internal and external, to providing useful and understandable information about FDA activities and decision-making to the public;

* Identify appropriate tools and new technologies for informing the public;

* Recommend changes to the FDA's current operations, including internal policies and guidance, to improve the agency's ability to provide information to the public in a timely and effective manner;

* Recommend legislative or regulatory changes, if appropriate, to improve the FDA's ability to provide information to the public; and

* Submit a written report to the commissioner on the Transparency Task Force's findings and recommendations.

Additional information is posted at www.fda.gov/AboutFDA/WhatWeDo/FDATransparencyTaskForce/default.htm

Amgen Inc. an **FDA** have agreed on at least one element of a "pharmacovigilance program" for Aranesp (darbepoietin) that includes a new study in patients with chemotherapy induced anemia following treatment for

non-small cell lung cancer.

The study will evaluate the effect of Aranesp on overall survival.

The company said it has not yet finalized a "risk evaluation and mitigation strategy," or REMS, for erythropoietic stimulating agents in the treatment of chemotherapy induced anemia.

A description of the trial is posted at www.clinicaltrials.gov/ct2/show/NCT00858364?term=darbepoetin&recr=Open&rank=8

A.P. Pharma Inc. (Nasdaq: APPA) of Redwood City, Calif., said it has submitted a New Drug Application for its lead product, APF530, to FDA.

APF530 is being developed for the prevention of chemotherapy-induced nausea and vomiting (CINV) and is a long-acting formulation of granisetron that utilizes the Company's proprietary Biochronomer drug delivery system.

"The submission of this NDA marks a significant milestone for the APF530 program, our Biochronomer drug delivery technology and A.P. Pharma as a company," said Ronald Prentki, A.P. Pharma's president and CEO.

"Our number-one priority has been to assemble and submit a complete and high-quality NDA. We thank our regulatory, CMC, clinical and e-filing experts for their tireless efforts and look forward to a timely review by the FDA."

"The favorable efficacy and safety demonstrated in the APF530 Phase 3 clinical program provides a strong foundation for our submission," stated Mr. Prentki. "We believe APF530, which maintains therapeutic drug levels for five days, will be a 'long acting' agent offering important advantages over anti-emetics currently used in the prevention of CINV, and would provide a particular benefit to those many patients suffering with delayed onset nausea and vomiting."

Arno Therapeutics, Inc. of Parsippany, NJ, said FDA has accepted the company's Investigational New Drug application for the use of AR-12, a potentially first-in-class, orally available, PDK1 inhibitor that blocks the PI3K/Akt pathway and induces the endoplasmic reticulum stress pathway.

Acceptance of the IND permits Arno to initiate a Phase I clinical trial in adults with advanced or recurrent solid tumors or lymphoma for which no standard therapy is available.

Arno expects the phase I clinical trial to begin during the second half of 2009 and will be designed to assess the safety and early evidence of activity of AR-12.

Delcath Systems Inc. (NASDAQ: DCTH) of New York said FDA has granted its application for orphan-drug designation for the drug melphalan for the treatment of patients with neuroendocrine tumors.

Delcath is enrolling patients in a phase II clinical trial testing its proprietary drug delivery system, known as the Delcath Percutaneous Hepatic Perfusion System, with ultra-high doses of the drug melphalan for the treatment of neuroendocrine tumors metastatic to the liver.

The trial is treating patients with pancreatic islet-cell and carcinoid tumors at NCI.

Orphan drug designation, when granted by the FDA's Office of Orphan Products Development, allows for up to seven years of marketing exclusivity after gaining FDA approval, as well as clinical study incentives, study design assistance, waivers of certain FDA user fees, and potential tax credits.

Genentech Inc. of South San Francisco said FDA has granted accelerated approval of Avastin (bevacizumab) for glioblastoma with progressive disease following prior therapy.

The effectiveness of Avastin in this aggressive form of brain cancer is based on an improvement in objective response rate. Currently, no data are available from randomized controlled trials demonstrating an improvement in disease-related symptoms or increased survival with Avastin in glioblastoma.

The indication for Avastin was granted under the FDA's accelerated approval program that allows provisional approval of medicines for cancer or other life-threatening diseases.

"People with this type of brain cancer have had no new treatments in more than a decade," said Timothy Cloughesy, director, Neuro-Oncology Program of the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles. "After so many years with little progress in this field, Avastin was associated with a durable tumor response and doctors now have a new medicine to offer patients."

The accelerated approval is based on independently reviewed data from an open-label, multicenter, non-comparative phase II study that included 167 patients with glioblastoma that had progressed following initial treatment with temozolomide and radiation. Patients were randomized into two arms: Avastin alone or Avastin in combination with irinotecan.

A primary endpoint of the study was objective response rate. Response was assessed by magnetic resonance imaging (MRI) and measured using World Health Organization radiographic criteria along with decreased or stable corticosteroid use.

MRI does not necessarily distinguish between the tumor, swelling (edema), or tissue death (necrosis) caused by prior radiation therapy.

According to an FDA analysis of the study, tumor responses were observed in 26 percent (95% confidence interval: 17.0%, 36.1%) of the 85 patients treated with Avastin alone, and the median duration of response in these patients was 4.2 months (95% confidence interval: 3.0 months, 5.7 months).

The efficacy of Avastin in glioblastoma that has progressed following prior therapy is supported by another study that used the same response assessment criteria as AVF3708g.

In this single-arm study, 56 patients were treated with Avastin alone. Responses were observed in 20 percent of patients (95% confidence interval: 10.9%, 31.3%), and the median duration of response was 3.9 months (95% confidence interval: 2.4 months, 17.4 months).

FDA has approved an Investigational New Drug application by **Nerviano Medical Sciences** of Italy to begin a phase I study with its selective PLK-1 small molecule inhibitor for the treatment of cancer. PLK-1 is a mitotic kinase required for the proliferation of cancer cells.

This new compound is orally bioavailable, highly efficient and well tolerated in preclinical models of cancer after repeated dosing. The inhibitor adds another promising candidate to the pipeline of innovative cell cycle targets with different mechanisms of action in clinical development which have been discovered and developed by NMS.

These include inhibitors of CDK, Aurora and CDC-7. An IND for an inhibitor of CDC-7 was approved by the FDA in January this year and the first patients were treated with the compound in April.

NMS CDK and Aurora inhibitors are in phase I and II clinical development, respectively, and are starting to show promising activity in specific patient populations.

Nerviano Medical Sciences is the largest pharmaceutical R&D facility in Italy and one of the largest oncology-focused, integrated discovery and development companies in Europe. The company has already finalized partnerships with major companies, including Pfizer Inc., Bristol-Myers Squibb Co., Genentech Inc. as well as with several biotech companies and academic institutions.

Palladia (toceranib phosphate), the first drug developed specifically for the treatment of cancer in dogs, was approved by FDA.

Palladia is approved to treat canine cutaneous (skin-based) mast cell tumors, a type of cancer responsible for about 1 out of 5 cases of canine skin tumors. The drug is approved to treat the tumors with or without regional lymph node involvement.

Palladia is manufactured by **Pfizer Animal Health Inc.**

The agent is a tyrosine kinase inhibitor and works in two ways: by killing tumor cells and by cutting off the blood supply to the tumor. In a clinical trial, Palladia showed a statistically significant difference in tumor shrinkage when compared with placebo.

All cancer drugs now used in veterinary medicine originally were developed for use in humans and are not approved for use in animals. Cancer treatments used in animals are used in an "extra-label" manner as allowed by the Animal Medicinal Drug Use Clarification Act of 1994.

"This cancer drug approval for dogs is an important step forward for veterinary medicine," said Bernadette Dunham, director of FDA's Center for Veterinary Medicine. "Prior to this approval, veterinarians had to rely on human oncology drugs, without knowledge of how safe or effective they would be for dogs. Today's approval offers dog owners, in consultation with their veterinarian, an option for treatment of their dog's cancer."

While canine mast cell tumors often appear small and insignificant, they can be a very serious form of cancer in dogs. Some mast cell tumors are easily removed without the development of any further problems, while others can lead to life threatening disease.

Clinical Trials:

Bayer, Onyx Begin Phase III Of Nexavar In NSCLC

(Continued from page 1)

learn what causes breast cancer and how to prevent it. To date, the Army of Women has signed on more than 270,000 women and issued five calls-to-action for research studies.

Bayer HealthCare Pharmaceuticals Inc.

of Wayne, N.J., and **Onyx Pharmaceuticals Inc.** (NASDAQ: ONXX) of Emeryville, Calif. have begun enrolling patients in an international phase III trial to evaluate Nexavar (sorafenib) tablets in non-squamous non-small cell lung cancer patients who have failed two or three previous treatments.

"Nexavar has proven efficacy in liver cancer and kidney cancer and we are committed to researching Nexavar in a variety of other solid tumors," said Dimitris Voliotis, vice president, Nexavar Clinical Development, Bayer HealthCare Pharmaceuticals. "Based on the results of a signal generating Phase 2 study, Bayer and Onyx initiated this phase III trial to evaluate Nexavar in non-small cell lung cancer."

The MISSION (Monotherapy admInistration of Sorafenib in patientS wIth nOn-small cell luNg cancer) trial, is an international multicenter study that will enroll approximately 850 patients with advanced relapsed or refractory non-squamous NSCLC who have failed two or three previous treatments.

Patients will be randomized to receive either Nexavar as single agent or placebo. In both treatment arms, best supportive care will be provided. The primary endpoint of this trial is overall survival, and secondary endpoints include progression-free survival and overall response rate. The safety and tolerability of the two treatment groups will also be compared.

The study will be conducted at more than 120 sites in North America, South America, Europe, Africa and the Asia-Pacific region, including Japan.

Oncolytics Biotech Inc. (TSX:ONC, NASDAQ: ONCY) of Calgary has completed patient enrolment in a multicenter phase II trial to evaluate the intravenous administration of REOLYSIN in patients with various sarcomas that have metastasized to the lung.

A total of 52 patients have been enrolled in the trial.

"We are extremely pleased to have had the opportunity to participate in this study," said Monica Mita, principal investigator at the **Institute of Drug Development, the Cancer Therapy & Research Center** at the University of Texas Health Science Center of San Antonio.

The primary statistical endpoint of the trial was met in late 2008. To meet the endpoint, at least three out of 52 patients had to experience stabilization of disease or better for more than six months. Of the 33 patients evaluable at that time, five had experienced stable disease for periods greater than six months, including one patient who had maintained stable disease for more than 16 months. An additional 10 patients had experienced stable disease for periods ranging from three to six cycles (cycle = 28 days). Updated results are scheduled to be presented May 30, 2009 at the American Society of Clinical Oncology (ASCO) Annual Meeting in Orlando, Florida.

The trial (REO 014) is a Phase 2, open-label, single agent study whose primary objective is to measure tumour responses and duration of response, and to describe any evidence of antitumour activity of intravenous, multiple dose REOLYSIN in patients with bone and soft tissue sarcomas metastatic to the lung. REOLYSIN is delivered intravenously to patients at a dose of 3x1010 TCID50 for five consecutive days, every 28 days.

Eligible patients had to have a bone or soft tissue sarcoma metastatic to the lung deemed by their physician to be unresponsive to or untreatable by standard therapies. These included patients with osteosarcoma, Ewing sarcoma family tumours, malignant fibrous histiocytoma, synovial sarcoma, fibrosarcoma and leiomyosarcoma.

The University of Pittsburgh Cancer Institute will be the primary site for a clinical trial of ABT-888 a drug previously proven in combination treatments to improve chemotherapy's effectiveness by lowering cancer cells' resistance to treatment.

This trial will, for the first time, examine ABT-888 as a single agent for patients with cancers related to BRCA 1 or 2 genetic mutations, which predispose patients to breast and ovarian cancers.

According to the study's principal investigator, Shannon Puhalla, assistant professor at the University of Pittsburgh School of Medicine and breast oncologist at Magee-Womens Cancer Program of UPMC Cancer Centers, ABT-888 targets the polymerase (PARP) family of enzymes responsible for a wide variety of cellular processes in cancer cells.

"Cancer cells have been shown to have increased levels of PARP, which we believe causes resistance to chemotherapies and other cancer treatments," said Dr. Puhalla. Tumor cells in patients with BRCA mutations are particularly reliant on the mechanism of DNA repair that is inhibited by the PARP, she explained.

In previous trials in which ABT-888 was used as combination treatment, it appeared to inhibit PARP, making cancer cells more sensitive to chemotherapy. "Our hope with this trial is that patients with BRCA mutations or certain other breast or ovarian cancers may respond to ABT-888 as a single agent," said Dr.

Puhalla.

"This drug is also intriguing because breast cancer patients with BRCA mutations who have exhausted all other therapeutic options may have another treatment to turn to," noted Merrill Egorin, professor of medicine and pharmacology at the University of Pittsburgh School of Medicine and study co-investigator. "Other trials also have suggested that ABT-888 may also have fewer side-effects than many other therapies."

The study will primarily be open to breast and ovarian cancer patients with a BRCA 1 or 2 genetic mutation, but patients with other subtypes of breast, ovarian or prostate cancer may be eligible.

The study is part of an NCI-funded initiative to develop new therapies to treat cancer more effectively. The program at UPCI is one of 15 in the country.

Early phase clinical trials are the first step for all new therapeutics, and they are designed to evaluate the safety and dosing of novel therapies that have shown promise in earlier animal and preclinical studies.

Rigel Pharmaceuticals Inc. (NASDAQ:RIGL) of South San Francisco said its oral Syk inhibitor, R788, is being evaluated in a phase II trial funded, designed and implemented by NCI.

The open-label, single arm clinical trial will include patients with advanced colorectal, thyroid, non-small cell lung, hepatocellular, head and neck, or renal cell cancers who have failed to respond to at least one line of therapy.

Enrolled patients will receive 200 mg of R788 twice a day and will be monitored to measure a variety of clinical responses as well as drug safety. Patients will continue to receive R788 in 28-day treatment cycles until disease progression, or patient or physician withdrawal occurs.

NCI will conduct the clinical trial, Rigel will supply study drug and will receive clinical data and trial results.

Rigel is conducting two phase IIb clinical trials with R788, known as TASKi2 and TASKi3, in patients with rheumatoid arthritis. Results from these trials are expected in July of this year.

In addition, the company has an ongoing phase 2 clinical trial of R788 in patients with peripheral T-cell lymphoma and reported favorable results from a phase 2 clinical trial of R788 in the treatment of patients with certain B-cell lymphomas in June 2008.

Deals and Collaborations:

ACR's Image Metrix Chosen To Provide Data Storage

American College of Radiology Image Metrix has been chosen by the Academy of Molecular Imaging to provide data and image storage infrastructure for a new study

to compare the effectiveness of conventional planar 99mTc-MDP bone imaging with 18F-sodium fluoride PET/CT (18F-NaF) at detecting bony metastases in patients with breast, prostate and non–small-cell lung cancers.

The protocol was developed in conjunction with FDA and the Centers for Medicare and Medicaid Services CMS and calls for data collection on more than five hundred patients at 13 sites nationwide.

"Just as early detection of cancer is important, early detection of any spread of a cancer is vitally important to determining the best and most timely treatment for patients. PET and PET/CT are serving an increasingly important role in this care. Each refinement in care can make a big difference in the success of treatment for additional patients. ACR Image Metrix is proud to serve such a significant role in this important trial as the selected CRO [Contract Research Organization]," said ACR Image Metrix Chief Scientific Officer Bruce Hillman, who worked with AMI investigators to develop the protocol for the research.

Cancer patients undergo more than 2 million planar 99mTc-MDP scans each year to determine whether cancer has spread from the organ of primary diagnosis to their bones. However, the test may miss some disease. 18F-NaF PET/CT bone scanning may have advantages over the conventional method in that it is often able to find smaller metastases and differentiate more accurately between cancerous and non-cancerous conditions.

"ACR Image Metrix is unique in the CRO landscape regarding its ability to assist in protocol development then transmit, archive, and retrieve imaging data for such important trials. We are proud of our ability to substantively contribute to advances in patient care by providing significant infrastructure for cutting edge medical research," said Michal Morales, General Manager of ACR Image Metrix.

ACR Image Metrix, located in the American College of Radiology Clinical Research Center in Philadelphia, PA, applies imaging techniques as a predictive and prognostic biomarker improving the efficiency for drug development programs. The world-class team of physicians and scientists at ACR Image

Metrix work with pharmaceutical, biotech and medical device companies to increase the efficiency of drug and device development programs by integrating the appropriate imaging modalities. ACR Image Metrix has years of experience and proven expertise in employing state-of-the-art technologies and provide a complete imaging CRO line of imaging services.

Advanced Cancer Therapeutics of Louisville, KY, announced that it has signed an exclusive license to develop and commercialize small molecule compound inhibitors of choline kinase, an enzyme discovered to be required for the survival of tumors by scientists at the **University of Louisville's James Graham Brown Cancer Center.**

Brown Cancer Center researchers Brian Clem, Sucheta Telang, Jason Chesney and John Trent recently found that removal of the gene for choline kinase caused a block in signals required for the survival of tumors.

Using computing technologies that Trent developed in Kentucky, they then screened millions of chemicals and identified one that turned off the enzyme. This lead chemical inhibitor of choline kinase caused the death of lung tumors in mice.

Gene Network Sciences Inc. of Cambridge, Mass., has entered into a research collaboration with **The University of Connecticut Health Center's Carole and Ray Neag Comprehensive Cancer Center** in which the parties will incorporate genetic, genomic and clinical data ("3-D Data") together into computer models of different cancers to be used to identify the best treatments for individual patients and to develop new drug treatments and diagnostics. Financial terms were not disclosed.

GNS and the Neag Comprehensive Cancer Center started collaboration as a result of a connection made last year between Carolyn Runowicz Director of the Neag Comprehensive Cancer Center and Tom Neyarapally, GNS senior vice president, corporate development.

The parties are also in the process of assembling a consortium in ovarian cancer with additional cancer centers that have yet to be named.

"With ever-increasing quantities of molecular and genetic data from cancer patients becoming available, we as clinicians are in great need of capabilities to optimally and rapidly utilize this information," Runowicz said in a statement. "We are excited to link up with GNS, which has created a unique supercomputer-driven technology platform to turn this information directly into simulation models, and ultimately better treatments, for cancer patients."

ImmunoVaccine Technologies Inc. of Halifax, a vaccine development company, has announced a collaboration agreement with the **National Research Council Institute for Biodiagnostics Atlantic**. This collaboration will develop new 3-D MRI technology to track the effect of IVT's DepoVax technology on reducing tumour growth.

In pre-clinical studies, IVT has shown that DepoVax vaccines can eradicate cancerous tumors. This new research involves labeling liposomes, suspended in the DepoVax formulation, with iron-oxide nanoparticles.

The 3-D MRI analysis will shed light on the activity of DepoVax in vivo, and allow the monitoring of tumor elimination in real time.

Ortho Biotech Oncology Research & Development, a unit of Centocor Research & Development, Inc., today announced that it has entered into a five-year Cooperative Research and Development Agreement with the National Cancer Institute, with Steven Rosenberg, chief, Surgery Branch, serving as the NCI principal investigator, to research and develop novel cell therapy technologies as potential treatments for a variety of cancers.

These adoptive immunotherapy technologies are designed to work by helping the immune system fight cancer. Adoptive immunotherapies have the potential to spare healthy tissue because they are designed to directly find and destroy cancerous tumor cells using a patient's own immune system T cells.

Rosenberg has been a pioneer in the field of adoptive immunotherapy of cancer for decades. His group developed Tumor Infiltrating Lymphocytes (TILs), T cells obtained from a patient's tumor, expanded and then re-administered to actively seek and destroy cancer cells. Remarkable responses to this therapy have been observed in patients with malignant melanoma, according to the NCI.

In recent years, Rosenberg's team pioneered a new technology in which T cells obtained from a patient's blood are genetically engineered to express receptors that give them specific immunity against cancer cells and then re-administered.

Researchers at Ortho Biotech Oncology Research & Development independently developed a different and proprietary adoptive immunotherapeutic approach that uses tumor antigens and other materials to stimulate T cells from a patient's blood to become Cytotoxic

T Lymphocytes (CTLs), which recognize and attack tumor cells.

Early clinical results show that this technology holds promise in melanoma patients and also has the potential to work in other types of cancers.

Under the CRADA, Rosenberg's lab will conduct a clinical trial in melanoma patients using Ortho Biotech Oncology Research & Development's proprietary technology. It is hoped that the technology will be effective in other types of cancer, as well.

The other part of the CRADA will focus on a collaborative effort on a T-Cell Receptor (TCR) research program.

"This public-private partnership represents an extraordinary opportunity to bring together complementary and substantial expertise and resources from two groups with the common goal of advancing a highly promising new modality of therapy for patients with cancer," said Jay Siegel, chief biotechnology officer of Johnson & Johnson's Pharmaceuticals and Medical Devices & Diagnostics businesses.

"Dr. Rosenberg and NCI have extensive experience in the development of immunotherapies for melanoma and other cancers, as well as a strong track record in conducting early phase clinical studies," said William Hait, senior vice president and worldwide head of oncology research and development, who with Siegel will direct the Ortho Biotech Oncology Research & Development team under the collaboration.

"We look forward to collaborating with NCI to optimize technologies and to begin testing of our immunotherapy technology in melanoma patients by the end of 2009, with the possibility of additional studies for other types of cancer and other technologies in years to come," Hait said.

Quest Diagnostics Inc. (NYSE: DGX), launched the EGFR Pathway test (KRAS with reflex to NRAS, BRAF), the first laboratory-developed test from a national commercial reference laboratory for comprehensively identifying, in a single reflex test offering, genetic mutations in the KRAS, NRAS and BRAF genes.

The test is designed to aid the identification of the roughly half of all metastatic colorectal cancer (mCRC) patients who, because of certain mutations of the epidermal growth factor receptor (EGFR) pathway, are believed to be unresponsive to anti-EGFR cancer therapies for mCRC.

While some commercial laboratory tests for predicting anti-EGFR response analyze certain mutations of the KRAS and BRAF genes, such as codons 12 and 13 of KRAS, the Quest Diagnostics test detects mutations in codons 12, 13 and 61 of both the KRAS and NRAS genes and mutations in exons 11, 12, and 15 of the BRAF gene, in a sequential reflex manner.

"Our EGFR Pathway test will provide physicians with the most comprehensive data available from a single test offering for identifying RAS and BRAF gene mutations in patients with mCRC who may be considered for anti-EGFR therapy. Given that research suggests these gene mutations may inhibit therapeutic response in many patients, our goal is to give physicians a personalized diagnostic tool that can help them determine more reliably whether or not to provide therapy with EGFR antagonists to the individual patient," said Maher Albitar, medical director and chief of Research and Development, Hematology and Oncology, Quest Diagnostics.

Anti-EGFR therapies are designed to impede cellular proliferation caused by activation of EGFR, but can trigger several side effects, including fatigue, skin rash, and nausea and vomiting. Up to 40 percent of patients with mCRC in the U.S. have mutations in the KRAS gene that render anti-EGFR therapy ineffective. In January, the American Society of Clinical Oncology produced a provisional clinical opinion (PCO) recommending that all patients with mCRC who are candidates for anti-EFGR therapy be tested for KRAS gene mutations (specifically in codons 12 and 13), and that anti-EFGR antibody therapy should not be administered if mutations are found.

However, fewer than 50 percent of patients with wild-type (normal) KRAS genes respond to anti-EGFR therapy, suggesting that additional mechanisms may affect response. Studies demonstrate that in patients with mCRC, about five percent may have mutations in the NRAS gene and eight percent may have mutations in the BRAF gene, and that mutations in these genes are associated with poor anti-EGFR treatment response.

In February, The New England Journal of Medicine published correspondence by Albitar and his colleagues at Quest Diagnostics regarding results of a study of 572 colon cancer samples that found that 11 percent of RAS mutations would have been missed if only codons 12 and 13 of the KRAS gene had been analyzed (as recommended by ASCO's PCO), and recommended RAS mutation testing include KRAS and NRAS encompassing codon 61 in addition to codons 12 and 13.

The company also launched laboratory tests for identifying mutations in the NRAS and BRAF genes.