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ASCO RELEASES STUDIES FROM UPCOMING ANNUAL MEETING

– Important Advances in Treatment for Aggressive Cancers and Supportive Care–

Alexandria, Va. – The American Society of Clinical Oncology (ASCO) today highlighted five studies in a press briefing from among more than 4,500 abstracts publicly posted online at abstract.asco.org in advance of ASCO's 47th Annual Meeting.

Plenary, late-breaking and other major studies will be released in on-site press conferences at the Annual Meeting to be held June 1-5, 2012, at McCormick Place in Chicago, Ill. The meeting, which will feature the theme *Collaborating to Conquer Cancer*, is expected to draw approximately 30,000 cancer specialists from around the world.

"Nearly 50 years into the era of modern oncology, we can clearly see the fruits of our research investments," said Michael Link, MD, President of ASCO. "Findings to be presented at ASCO's Annual Meeting are part of the latest chapter in the history of progress against cancer. Today's studies demonstrate improvements in precision medicine that identify and exploit cancer's genetic weak spots to halt tumor growth and in some cases eradicate disease. Other studies give us valuable new tools and information to lessen the short- and long-term side effects of cancer treatment for our patients."

Studies highlighted in today's press briefing include:

- **In early study, crizotinib induces strong, long-lasting responses in aggressive pediatric cancers:** Phase I study reports that crizotinib (Xalkori) – an oral drug that targets genetic abnormalities in the *ALK* gene – stalled tumor growth and, in some cases, eliminated all signs of cancer in select children with neuroblastoma, anaplastic large cell lymphoma or inflammatory myofibroblastic tumors, cancers commonly driven by *ALK* gene abnormalities.
- **Combination of two molecularly targeted oral drugs show promise for advanced melanoma with *BRAF* mutations**: Results from an early-phase trial show that combination therapy with two investigational targeted drugs – the *BRAF* inhibitor dabrafenib and the *MEK* inhibitor trametinib – causes tumor regression and with a lower level of skin side effects than published studies of the current standard single-agent *BRAF*-targeted therapy, vemurafenib (Zelboraf), have shown.

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- **Anti-psychotic medicine effective in treating severe chemotherapy-related nausea:** A Phase III trial shows olanzapine (Zyprexa), an anti-psychotic medication, is superior to current standard treatment for breakthrough chemotherapy-induced nausea and vomiting. These results address an important unmet need for patients who experience such side effects, despite routine preventive treatment.
- **Adding abiraterone to standard hormone therapy eliminates cancer in some men with earlier-stage, aggressive prostate cancer:** A randomized Phase II study shows that six months of neo-adjuvant (pre-surgical) treatment with the targeted drug abiraterone (Zytiga) and hormonal therapy eliminated or nearly eliminated cancer in one-third of men with localized high-risk prostate cancer (which has spread throughout the prostate and is likely to spread further). Abiraterone is currently approved for men with advanced prostate cancer, following chemotherapy.
- **Survey highlights need for greater physician education, communication about late effects of common chemotherapy drugs:** A large survey finds that many primary care providers and some oncologists are not fully aware of major long-term side effects of four chemotherapy drugs that are widely used to treat breast and colorectal cancers, two of the most common forms of cancer.

Annual Meeting Media Resource Center: http://www.asco.org/AMpresskit

Additional Resources for Reporters and Patients:

- **ASCO's CancerProgress.Net** offers a detailed, interactive timeline of advances against 14 of the most common cancers. The site also includes simple, interactive charts on cancer survival, mortality, and incidence, along with downloadable timelines, historical commentary and other reporting resources.
- **Cancer.Net,** ASCO's award-winning patient website, provides comprehensive, oncologist-approved information on more than 120 cancer types, together with expert information on cancer treatments, managing side effects and coping with a cancer diagnosis. **This year Cancer.Net celebrates 10 years of helping patients**. When the site first launched in 2002, there were detailed sections on 22 different types of cancer. Now, Cancer.Net continues to lead the way in content, design, and interactivity, providing patients, their families and friends with timely and authoritative information.

Relevant Links From Cancer.Net, the oncologist-approved cancer information website from the American Society of Clinical Oncology:

- Cancer in Children
- Guide to Melanoma
- Guide to Neuroblastoma
- Guide to Childhood Non-Hodgkin Lymphoma
- Guide to Prostate Cancer
- Understanding Targeted Treatments
- Targeted Therapies for Melanoma
- Clinical Trials
- Managing Side Effects
- Side Effects of Chemotherapy
- Cancer.Net Video: Managing Side Effects of Chemotherapy, with Lynn Schuchter, MD
- Nausea and Vomiting
- What to Know: ASCO's Guideline on Preventing Vomiting Caused by Cancer Treatment
- Cancer Survivorship

- Late Effects
- ASCO Cancer Treatment Summaries
- Keeping a Personal Medical Record

Oral Abstract Session: Pediatric Oncology I
Saturday, June 2, 2012, 1:15 – 1:30 PM CDT
Room: S504

Study Author: Yael Mosse, MD
The Children's Hospital of Philadelphia
Philadelphia, PA

Crizotinib Induces Strong Responses in Three Pediatric Cancers Driven by *ALK* Gene Abnormalities

(Summary Includes Updated Data from the Abstract)

A Phase I study has shown that the targeted drug crizotinib (Xalkori) stalled tumor growth and, in some cases, eradicated all signs of cancer in select children with aggressive forms of neuroblastoma, anaplastic large cell lymphoma (ALCL) or inflammatory myofibroblastic tumors (IMT).

Crizotinib targets genetic abnormalities in the *ALK* gene, which are common in these pediatric cancers. If these promising early-phase findings are borne out in larger trials, crizotinib could become only the second effective molecularly targeted therapy for pediatric cancers. *ALK* abnormalities are present in 80 to 95 percent of ALCL cases, half of IMTs and 10 to 15 percent of aggressive neuroblastomas. Crizotinib was recently approved to treat adult *ALK*-driven lung cancers, about 5 percent of cases.

"It's remarkable that this targeted oral medication provided such a substantial benefit in these children with highly aggressive cancers, most of whom had already undergone every available therapy," said Yael Mosse, MD, assistant professor of pediatrics at the Children's Hospital of Philadelphia and the University of Pennsylvania. "Now that we know more about the drivers of some pediatric cancers, we can target those changes and treat patients in a much smarter, and potentially safer, way."

The study included 70 children whose cancer had progressed despite all standard therapies. When possible, patients' cancers were tested for *ALK* abnormalities, though this was not required for enrollment. Patients received one of six different doses of crizotinib – administered orally, twice a day – and remained on the drug as long as it was well-tolerated, which was the case in the vast majority of patients. By disease, researchers found:

- ***ALCL***: 88 percent (7/8) of patients experienced a complete response, having no detectable disease. Responses have been long-lasting, with patients remaining on treatment with no progression for as long as 18 months.
- ***IMTs***: Seven patients with this rare disease were enrolled onto this trial. The majority have experienced substantial benefit, ranging from tumor shrinkage to complete tumor regression. Such responses have lasted for up to two years, with all patients still receiving therapy; these findings are important because no other available anticancer therapies are effective in this disease.
- ***Neuroblastoma:*** Overall, two of 27 patients had a complete response, and eight have had no disease progression (stable disease). Of patients with a proven *ALK* abnormality, two of eight patients experienced a complete response. These responders have remained on therapy for between 9 months to more than two years without progression – a notable finding given that most heavily pre-treated neuroblastoma patients on a Phase I trial experience cancer progression in 1 to 2 months.

Researchers also observed that neuroblastoma patients treated with higher doses of crizotinib – which in some cases were twice the approved adult dose – experienced demonstrable responses. This may explain why some neuroblastoma patients with proven *ALK* abnormalities did not respond to crizotinib, since they had received lower doses of the drug than the responders.

Abstract 9500

Efficacy of crizotinib in children with relapsed/refractory ALK-driven tumors including anaplastic large cell lymphoma and neuroblastoma: A Children's Oncology Group phase I consortium study.

Authors: Yael P. Mosse, Frank M. Balis, Megan S Lim, Julie Laliberte, Stephan D Voss, Elizabeth Fox, Rochelle Bagatell, Brenda Weigel, Peter C. Adamson, Ashish M Ingle, Charlotte H Ahern, Susan Blaney; The Children's Hospital of Philadelphia, Philadelphia, PA; C S Mott Children's Hospital, Ann Arbor, MI; Children's Hospital of Boston, Boston, MA; Children's Hospital of Philadelphia, Philadelphia, PA; University of Minnesota, Minneapolis, MN; Children's Oncology Group, Arcadia, CA; Baylor College of Medicine, Houston, TX; Texas Children's Cancer Center, Houston, TX

Background: Genetic aberrations in the *anaplastic lymphoma kinase (ALK)* gene are found in anaplastic large cell lymphoma (ALCL), neuroblastoma (NB) and other tumors. Crizotinib, a small molecule inhibitor of ALK and c-Met, is active in non-small cell lung cancers (NSCLC) harboring an ALK translocation. We performed a phase 1 dose-escalation and pharmacokinetic (PK) trial of crizotinib in patients (pts) with refractory solid tumors and ALCL.

Methods: Crizotinib was administered bid without interruption in 28 day cycles using the rolling-six design. Six dose levels (100, 130, 165, 215, 280, 365 mg/m^2/dose) have been evaluated (A1). Pts with confirmed ALK fusion proteins, mutations or amplification (A2) could enroll at one dose level lower than part A1 and those with NB could enroll on a separate stratum (A3). PK studies were performed on day 1 and at steady state (SS). ALK genomic status in tumor tissue was evaluated and qPCR was used to measure *NPM-ALK* fusion transcript in bone marrow and blood samples of ALCL pts.

Results: 70 pts were enrolled, 57 fully evaluable for toxicity , [median (range) age 9.9 yrs (1.1–21.3)]: 29 on A1, 18 on A2, and 10 on A3. In A1, 2/7 pts developed DLT (grade 3 dizziness, grade 5 intra-tumoral hemorrhage) at 215 mg/m^2 and 1/6 pts developed DLT (grade 4 liver enzyme elevation) at 365 mg/m^2. In A2, 1 grade 4 DLT (neutropenia) occurred at 165 mg/m^2; in A3, no DLTs occurred. Mean (±SD) C_{ave} (=$AUC_{0\text{-}12h}$/12h) of crizotinib at SS was 466±114 ng/mL at 215 mg/m^2/dose (n=5), 443±121 ng/mL at 280 mg/m^2/dose (n=8), and 720±230 ng/mL at 365mg/m^2/dose (n=4). Response data for pts with ALCL (six at 165 mg/m^2, two at 280 mg/m^2) approved for release by the Data Safety Monitoring Committee demonstrates 7/8 (88%) complete response (CR) rate to date. RT-PCR data for 6 of these pts at 57 time points was obtained and will be described. In addition, 2 pts with NB have had CRs, one with a documented ALK mutation. One patient with an inflammatory myofibroblastic tumor and one with NSCLC had PRs.

Conclusions: Inhibition of ALK in pediatric pts with ALK-driven tumors occurs with minimal toxicity and is associated with objective anti-tumor activity.

Disclosures: Yael P. Mosse, MD, Research Funding, Pfizer

Oral Abstract Session: Mutated Melanoma: The Role for MEK Inhibitors
Monday, June 4, 2012, 3:30 – 3:45 PM CDT
Room: E354a

Study Author: Jeffrey Weber, MD, PhD
H. Lee Moffitt Cancer Center
Tampa, FL

Combining Two Targeted Drugs Shows Encouraging Activity, Fewer Toxicities for Advanced Melanoma Patients

Results from an expanded Phase IB trial show that combination therapy with two investigational targeted drugs – the *BRAF* inhibitor dabrafenib and the *MEK* inhibitor trametinib – stalls cancer progression and with a lower level of skin side effects than published studies of the current standard single-agent *BRAF*-targeted therapy, vemurafenib (Zelboraf), have shown. The analysis included patients with advanced melanoma who had a V600 *BRAF* mutation and who had no previous *BRAF*-targeted treatment.

Approximately half of all melanomas harbor a V600E mutation in the *BRAF* gene; in those patients, the nearby *MEK* pathway is also highly active. While the approval of vemurafenib last year represented a major research achievement, most patients eventually develop resistance to the drug. It is hoped that simultaneously targeting the two active pathways – *BRAF* and *MEK* – will provoke a stronger anti-cancer response and prevent, or further delay, treatment resistance.

"It's fascinating to find such promising effects with this combination regimen. Not only are the two drugs causing shrinkage of the cancer, but we're seeing that a second anti-cancer therapy may actually suppress the side effects of the first," said Jeffrey Weber, MD, PhD, a senior member at H. Lee Moffitt Cancer Center and director of the Donald A. Adam Comprehensive Melanoma Research Center.

While the overall trial included 125 patients who received varying doses of dabrafenib and trametinib, the current analysis focuses on a sub-group of 77 patients who received no prior *BRAF*-targeted therapy (other prior therapies, such as chemotherapy, were permitted), and thus had no prior resistance to *BRAF*-targeted therapy. Among these 77 patients, median progression-free survival was 7.4 months, which is comparable to what was observed in past single-agent vemurafenib studies. Survival data is expected later this year.

Skin lesions are a well-known side effect of vemurafenib therapy, occurring in up to one-quarter of patients. In this trial, such toxicities were far less common: just 2 percent of the 125 patients in the overall trial developed squamous cell carcinomas and another two percent developed actinic keratoses (small pre-malignant lesions). Additional common, but manageable, side effects included fever, fatigue and dehydration.

Abstract 8510
Updated safety and efficacy results from a phase I/II study of the oral BRAF inhibitor dabrafenib (GSK2118436) combined with the oral MEK 1/2 inhibitor trametinib (GSK1120212) in patients with BRAFi-naive metastatic melanoma.
Authors: Jeffrey S. Weber, Keith T. Flaherty, Jeffrey R. Infante, Gerald Steven Falchook, Richard Kefford, Adil Daud, Omid Hamid, Rene Gonzalez, Ragini Reiney Kudchadkar, Donald P. Lawrence, Howard A. Burris III, Georgina V. Long, Alain Patrick Algazi, Karl D Lewis, Kevin B. Kim, Igor Puzanov, Peng Sun, Shonda M Little, Kiran Patel, Jeffrey Alan Sosman; Comprehensive Melanoma Research Center, H. Lee Moffitt Cancer Center, Tampa, FL; Massachusetts General Hospital, Boston, MA; Sarah Cannon Research Institute/Tennessee Oncology, PLLC, Nashville, TN; Department of Investigational Cancer Therapeutics (Phase I Program), University of Texas M. D. Anderson Cancer Center, Houston, TX; Melanoma Institute Australia, Westmead Institute for Cancer Research and Westmead Hospital, The University of Sydney, Sydney, Australia; University of California, San Francisco, San Francisco, CA; Department of Medical Oncology, The Angeles Clinic and Research Institute, Los Angeles, CA; Department of Medicine, University of Colorado, Aurora, CO; Comprehensive Melanoma Research

Center, Moffitt Cancer Center, Tampa, FL; Department of Medicine, University of Colorado Cancer Center, Aurora, CO; Department of Melanoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; Department of Hematology and Oncology, Vanderbilt University Medical Center, Nashville, TN; GlaxoSmithKline, Collegeville, PA
Background: In preclinical models, the BRAFi/MEKi combination has demonstrated enhanced activity against BRAF-mutant cancer cells compared with either drug alone, delayed emergence of BRAFi resistance, and prevented BRAFi-related proliferative skin lesions. A 3-part study investigating the dabrafenib/trametinib combination was conducted in patients (pts) with V600 *BRAF* mutant solid tumors. Interim data from the study were previously reported (Infante, ASCO 2011); updated safety and efficacy data are presented.
Methods: In Part 2, 125 pts with V600 *BRAF* mutant solid tumors enrolled, including 77 melanoma pts with no prior BRAFi, and measurable disease according to RECIST 1.1. Pts were treated on 4 escalating dose levels of dabrafenib/trametinib (mg BID/mg QD): 75/1, 150/1, 150/1.5, 150/2. Demographic and efficacy data for the 77 melanoma pts with no prior BRAFi and safety data for all 125 Part 2 pts are reported.
Results: Among 77 melanoma pts, median age was 52 years, 61% male, 57% ECOG PS of 0, 91% V600E, 65% M1c stage, 26% prior brain metastases, and 52% LDH > ULN. Confirmed ORR was 56% (95% CI: 44.1%-67.2%) with 4 CR, 39 PR, 29 SD and, 3 PD. Confirmed response rate for each dose level, respectively, was 67% (n=6), 64% (n=22), 48% (n=25), and 54% (n=24). Median PFS (months) for each dose level, respectively, was: 8.7, 8.3, 5.5; PFS is not mature for 150/2. Overall PFS was 7.4 (95% CI: 5.5-9.2). Among the 125 pts, there were 2 grade (G) 5 adverse events (AEs), pneumonia and hyponatraemia. The most common G3/4 AEs were pyrexia (n=6, 5%), fatigue (n=6, 5%) and dehydration (n=6, 5%). Skin toxicity ≥ G2 occurred in 17 (14%) pts. Cutaneous squamous cell carcinoma occurred in 3 (2%) pts and actinic keratoses in 2 (2%).
Conclusions: The combination of dabrafenib/trametinib has an acceptable safety profile, with a lower incidence of MEKi-related rash and BRAFi-induced hyperproliferative skin lesions compared with the single agents. The clinical activity of dabrafenib/trametinib observed in pts with V600 *BRAF* mutant metastatic melanoma is encouraging and will be investigated further in a phase III trial.
Disclosures: Jeffrey S. Weber, MD, PhD, Consultant or Advisory Role with GlaxoSmithKline, Honoraria from GlaxoSmithKline, Research Funding from GlaxoSmithKline; Keith T. Flaherty, MD, , Consultant or Advisory Role with GlaxoSmithKline; Gerald Steven Falchook, MD, MS, Research Funding from GlaxoSmithKline, Other Renumeration from GlaxoSmithKline; Richard Kefford, MD, PhD, FRACP with GlaxoSmithKline; Omid Hamid, MD, Honoraria from Bristol-Myers Squibb, Research Funding from Bristol-Myers Squibb; Rene Gonzalez, MD, Consultant or Advisory Role with GlaxoSmithKline, Honoraria from GlaxoSmithKline, Research Funding from GlaxoSmithKline; Georgina V. Long, MBBS, PhD, FRACP, Consultant or Advisory Role with GlaxoSmithKline, Other Renumeration from GlaxoSmithKline; Alain Patrick Algazi, MD, Research Funding from GlaxoSmithKline; Karl D Lewis, MD, Research Funding from GlaxoSmithKline; Kevin B. Kim, MD, Research Funding from GlaxoSmithKline; Igor Puzanov, MD, Consultant or Advisory Role with GlaxoSmithKline; Peng Sun, PhD, Employment/Leadership Position with GlaxoSmithKline, Stock Ownership with GlaxoSmithKline; Shonda M Little, MPH, Employment/Leadership Position with GlaxoSmithKline, Stock Ownership with GlaxoSmithKline; Kiran Patel, MD, MBA, Employment/Leadership Position with GlaxoSmithKline, Stock Ownership with GlaxoSmithKline; Jeffrey Alan Sosman, MD, Consultant or Advisory Role with GlaxoSmithKline, Research Funding from GlaxoSmithKline.

Oral Abstract Session: Patient and Survivor Care Poster Session
Saturday, June 2, 2012, 8:00 AM – 12:00 PM CDT
Room: S Hall A2

Study Author: Rudolph M. Navari, MD, PhD
Indiana University School of Medicine
South Bend, IN

Olanzapine, an Anti-Psychotic, Controls Breakthrough Chemotherapy-Induced Nausea and Vomiting

A Phase III trial in cancer patients with chemotherapy-induced nausea and vomiting (CINV) that does not respond to conventional treatments provides the first conclusive evidence that olanzapine (Zyprexa), an anti-psychotic medication, is effective in controlling these sometimes debilitating side effects of cancer therapy.

Overall, CINV affects about 50 to 60 percent of patients taking certain types of chemotherapy. While these side effects can usually be controlled with available medications, a significant minority of patients, about 30 to 40 percent, experience "breakthrough" CINV, which is defined as nausea and vomiting that persists despite preventive treatment recommended by ASCO or other guidelines.

The double-blind, randomized controlled trial compared olanzapine to metoclopramide, a drug often prescribed for breakthrough CINV although research has not been conducted to confirm its effectiveness for that purpose. Patients who received olanzapine did significantly better than the patients who received metoclopramide.

"This is the first time that breakthrough CINV has been studied in a systematic way," said Rudolph M. Navari, MD, PhD, lead author of the study and professor of medicine, associate dean and clinical director of the Harper Cancer Institute, Indiana University School of Medicine-South Bend. "This study suggests that olanzapine will be very useful in these patients who feel very sick and sometimes come to the clinic, hospital or emergency room. As a result, patients will feel better."

Breakthrough CINV can lower the quality of life for cancer patients and can even necessitate reductions in their chemotherapy doses, possibly limiting the effectiveness of treatment. The study enrolled patients receiving highly emetogenic (causing nausea and vomiting) chemotherapy drugs, including cisplatin, doxorubicin and cyclophosphamide.

In the study, 205 patients who had never received chemotherapy were first given standard guideline-recommended drugs to prevent CINV prior to starting their chemotherapy. While these drugs prevented CINV in most of the patients, 80 patients developed breakthrough CINV. These patients were then randomized to receive either daily oral olanzapine or daily oral metoclopramide for three days. They were followed for 72 hours, through phone calls from study nurses, and were asked to fill out a diary.

During the 72-hour observation period, 71 percent (30 of 42) of those receiving olanzapine had no vomiting, compared to 32 percent (12 of 38) of those receiving metoclopramide. Sixty-seven percent (28 of 42) of the patients taking olanzapine experienced no nausea, compared with 24 percent (9 of 38) of those taking metoclopramide.

While olanzapine, approved by FDA for treatment of psychosis, is known to cause a variety of side effects when taken daily for six months or longer, the short-term use in this study did not lead to any significant toxicities. Breakthrough CINV generally develops between the second to fourth days after

chemotherapy treatment, so it would not be necessary to take olanzapine for longer than three days, Dr. Navari said. Olanzapine is relatively inexpensive and is taken orally.

Abstract 9064

The use of olanzapine versus metoclopramide for the treatment of breakthrough chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy.

Authors: Rudolph M. Navari, Cindy K Nagy, Sarah E Gray; Indiana University School of Medicine South Bend, South Bend, IN; University of Notre Dame, Notre Dame, IN

Background: Olanzapine (OLN) has been shown to be a safe and effective agent for the prevention of CINV. OLN may also be an effective rescue medication for patients who develop breakthrough CINV despite having received guideline directed CINV prophylaxis.

Methods: A double blind, randomized phase III trial was performed for the treatment of breakthrough CINV in chemotherapy naïve patients receiving highly emetogenic chemotherapy (HEC) (cisplatin, >70 mg/m^2, or doxorubicin, >50 mg/m^2 and cyclophosphamide, > 600mg/m^2) comparing OLN to Metoclopramide (METO). Patients who developed breakthrough emesis or nausea despite prophylactic dexamethasone (12 mg IV), palonosetron (0.25 mg IV), and fosaprepitant (150 mg IV) pre chemotherapy and dexamethasone (8 mg p.o. daily, days 2-4) post chemotherapy were randomized to receive OLN, 10 mg orally daily for three days or METO, 10 mg orally TID for three days. Patients were monitored for emesis and nausea for the 72 hours after taking OLN or METO. Eighty patients (median age 56 yrs, range 38-79; 43 females; ECOG PS 0,1) consented to the protocol and all were evaluable.

Results: During the 72 hour observation period, 30 of 42 (71%) patients receiving OLN had no emesis compared to 12 of 38 (32%) patients with no emesis for patients receiving METO ($p<0.01$). Patients without nausea (0, scale 0-10, M.D. Anderson Symptom Inventory) during the 72 hour observation period was: OLN: 67% (28 of 42); METO 24% (9 of 38) ($p<0.01$). There were no Grade 3 or 4 toxicities.

Conclusions: OLN was significantly better than METO in the control of breakthrough emesis and nausea in patients receiving HEC.

Disclosures: Nothing to disclose

Oral Abstract Session: New Paradigms for Hormone Therapy in Prostate Cancer
Saturday, June 2, 2012, 9:10 – 9:20 AM CDT
Room: E Arie Crown Theater

Study Author: Mary-Ellen Taplin, MD
Dana-Farber Cancer Institute
Boston, MA

Adding Abiraterone to Hormonal Therapy Before Surgery Can Eliminate Tumor in the Prostate in Some Men with High-Risk Prostate Cancer

A randomized Phase II study shows that six months of treatment with the targeted drug abiraterone (Zytiga), in addition to standard hormonal therapy before surgical removal of the prostate, eliminated or nearly eliminated cancer in one-third of men with localized high-risk prostate cancer. The study marks the first time that abiraterone ─ a drug used to treat more advanced prostate cancer ─ has been explored for the treatment of earlier-stages of prostate cancer, including in the neoadjuvant (pre-surgical) setting.

Localized high-risk disease is generally defined as prostate cancer in men with a PSA level above 20, high-grade disease (a Gleason score of 8 or more), and stage T3 disease (indicating the tumor has spread throughout the prostate). Men with this stage of disease tend to have a poor prognosis, often experiencing cancer spread to other parts of the body despite aggressive treatment with available therapies.

"For this proportion of patients with high-risk disease to have very little to no detectable cancer in the prostate after six months of therapy is dramatic," said Mary-Ellen Taplin, MD, Associate Professor of Medicine at Harvard Medical School and the Dana-Farber Cancer Institute and the study's lead author. "Our findings suggest that this combination therapy approach could improve outcomes for a substantial number of men, but larger, long-term trials are needed to confirm this approach."

Previous studies have shown that use of standard hormonal therapy alone, including treatment with leuprolide, before surgery had limited benefits for men with localized high-risk prostate cancer. This study evaluated the effect of adding abiraterone to leuprolide in two groups of men with this form of the disease: Group A included 27 men who received leuprolide hormonal therapy for 12 weeks followed by leuprolide plus abiraterone for another 12 weeks. The second group, Group B, included 29 men who received both abiraterone and leuprolide for the entire 24-week period. Prostate surgery was performed in all men after 24 weeks of therapy, and the tissue was examined for evidence of cancer.

Among men in Group B (24 weeks of abiraterone therapy), 34 percent had either complete elimination (3/29) or nearly complete elimination (7/29) of their cancer upon surgery. In Group A (12 weeks of abiraterone therapy), 15 percent of men had either complete elimination (1/27) or nearly complete elimination (3/27) of their cancer upon surgery. Therapy was well-tolerated by both groups.

Abiraterone works by blocking production of the male hormone testosterone and related metabolites that often fuel prostate cancer growth. The addition of abiraterone to traditional hormonal therapy, which restricts testosterone production in a different way, further shuts down the body's ability to produce the hormones that prostate cancer cells need to grow. The clinical benefit of intensive androgen deprivation therapy, either before or after prostatectomy, will need to be validated in prospective, randomized clinical trials, but these data suggest a benefit for some men.

Abstract 4521
Effect of neoadjuvant abiraterone acetate (AA) plus leuprolide acetate (LHRHa) on PSA, pathological complete response (pCR), and near pCR in localized high-risk prostate cancer (LHRPC): Results of a randomized phase II study.

Authors: Mary-Ellen Taplin, Robert B. Montgomery, Christopher Logothetis, Glenn J. Bubley, Jerome P. Richie, Bruce L. Dalkin, Martin G. Sanda, Massimo F. Loda, Lawrence D. True, Patricia Troncoso, Elizabeth M. Genega, Steven P. Balk, Peter Nelson, Wanling Xie, Christopher M. Haqq, Namphuong Tran, Cameron S. Liu, Thian San Kheoh, Arturo Molina, Philip Kantoff; Dana-Farber Cancer Institute, Boston, MA; University of Washington, Seattle, WA; University of Texas M. D. Anderson Cancer Center, Houston, TX; Beth Israel Deaconess Medical Center, Boston, MA; Brigham and Women's Hospital, Boston, MA; Fred Hutchinson Cancer Research Center, Seattle, WA; Genomic Systems, San Francisco, CA; Janssen Research & Development, Los Angeles, CA

Background: LHRPC is infrequently cured with prostatectomy (RP). To date neoadjuvant androgen deprivation therapy (ADT) has not improved outcomes and residual intra-prostatic androgens remain. AA lowers serum testosterone (T) and DHT to < 1 ng/dL and has improved survival in advanced PC.

Methods: We conducted a neoadjuvant, phase II trial of AA/LHRHa in LHRPC. The primary aim was to evaluate intra-prostatic T/DHT with LHRHa vs LHRHa/AA. We report secondary endpoints of PSA, pCR and near pCR ([≤ 5mm residual tumor]) and safety. Eligibility: ≥ 3 positive biopsies and either Gleason ≥ 7 (4+3), T3, PSA ≥ 20 ng/mL or PSA velocity > 2 ng/mL/year. For the first 12 wks men were randomized to LHRHa or LHRHa/AA/prednisone (P) 5mg qd. After 12 wks, a prostate biopsy was done to measure T/DHT. Men received 12 more wks of LHRHa/AA/P followed by RP.

Results: 58 men enrolled: 28 to initial LHRHa and 30 to initial AA/LHRHa. 2 withdrew prior to RP (1/group). Median age was 58 (50-75). pCR/near pCR was 14/56 (25%). Grade 3 AEs included elevated AST/ALT 5/58 (9%) and hypokalemia 3/58 (5%). No grade 4 mineralocorticoid-related AEs were observed.

Conclusions: Neoadjuvant ADT with AA was well tolerated in LHRPC. PSA (<0.2) declines were high and achieved earlier on AA/LHRHa compared to LHRHa. The pCR/near pCR rates were higher for 24 wks AA (34%) than 12 wks AA (15%). No new safety signals were seen with AA used with P 5 mg. These results support further evaluation of aggressive ADT as neoadjuvant/adjuvant therapy for LHRPC.

Baseline	**12 wks AA/24 wks LHRHa n= 28**	**24 wks AA/24 wks LHRHa n=30**
Gleason: 7/8/9/10	8/10/10/0	9/7/11/3
PSA (median)	10.6	6.8
PSA: < 10/10-20/≥ 20	12/9/7	20/6/4
Elevated PSA velocity	6	3
Stage T3	8	6
Results	**n=27**	**n=29**
PSA: wk 4/8/12/16/20/24	4.34/1.35/1.06/0.20/0.09/0.06	0.65/0.17/0.10/0.09/0.06/0.05
12 wk nadir PSA ≤ 0.2	1/27 (4%)	26/29 (90%) p<0.0001
24 wk nadir PSA ≤ 0.2	23/27 (85%)	25/29 (86%) p=0.9131
pCR	1/27 (4%)	3/29 (10%) p=0.3349
Near pCR (tumor ≤ 5mm)	3/27 (11%)	7/29 (24%) p=0.2034
Total pCR/near pCR	4/27 (15%)	10/29 (34%) p=0.0894
pT3	16/27	14/29
Positive nodes	3/27 (11%)	7/29 (24%)
Positive margins	5/27 (19%)	5/29 (17%)

Disclosures: Mary-Ellen Taplin, MD, Consultant or Advisory Role with Johnson & Johnson, Honoraria from Johnson & Johnson, Research Funding from Johnson & Johnson; Robert B. Montgomery, MD, Research Funding from Cougar Biotechnology and Johnson & Johnson; Christopher Logothetis, MD, Consultant or Advisory Role with Janssen Pharmaceutical and Johnson & Johnson, Honoraria from Johnson & Johnson, Research Funding from Johnson & Johnson; Steven P. Balk, MD, Consultant or Advisory Role with Johnson & Johnson; Peter Nelson, MD, Consultant or Advisory Role with Johnson & Johnson, Honoraria from Johnson & Johnson, Other Renumeration from Johnson & Johnson; Christopher M. Haqq, MD, Stock Ownership with Johnson & Johnson, Employment/Leadership Position with Janssen Pharmaceutical, Stock Ownership with Johnson & Johnson; Cameron S. Liu, PhD, Employment/Leadership Position with Janssen Pharmaceutical, Stock Ownership with Johnson & Johnson; Thian San Kheoh, PhD, Employment/Leadership Positon with Janssen Pharmaceutical, Stock Ownership with Johnson & Johnson; Arturo Molina, MD, Employment/Leadership Position with Janssen Pharmaceutical, Stock Ownership with Johnson & Johnson; Philip Kantoff, MD, Consultant or Advisory Role with Johnson & Johnson.

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Oral Abstract Session: Health Services Research
Saturday, June 2, 2012, 5:30 – 5:45 PM CDT
Room: S404

Study Author: Larissa Nekhlyudov, MD, MPH
Harvard Medical School
Boston, MA

Survey: Many Primary Care Providers Are Unaware of Long-Term Side Effects of Chemotherapy for Common Cancers

(Summary Includes Updated Data from the Abstract)

A large survey has shown that many primary care providers (PCPs) are not familiar with the long-term side effects of four chemotherapy drugs that are widely used to treat breast and colorectal cancers, two of the most common forms of cancer. The results highlight the need for improved communication between oncologists, cancer survivors and PCPs to improve the continuity of care after patients have completed their cancer therapy, and to monitor survivors for late effects of cancer and its treatment.

There are nearly 12 million cancer survivors in the U.S. today, up from three million in the 1970s. Once active cancer treatment ends, survivors are eventually seen more commonly in primary care settings for ongoing follow-up care.

Prior results from the survey ─ the Survey of Physician Attitudes Regarding the Care of Cancer Survivors (SPARCCS) ─ revealed that many PCPs feel they lack the general knowledge and confidence to care for people who have been treated for cancer. The new analysis specifically examines knowledge of the most common late effects of treatment, including heart function problems, nerve problems, premature menopause and second cancers.

SPARCCS surveyed 1,072 PCPs and 1,130 oncologists by mail in 2009. Doctors were asked to select which of five late effects of each of four widely used breast and colorectal cancer drugs ─ doxorubicin (Adriamycin), paclitaxel (Taxol), oxaliplatin (Eloxatin), and cyclophosphamide (Cytoxan) ─ they have observed most often in their practices or seen reported.

Researchers found that among PCPs surveyed, 55.1 percent identified heart dysfunction as a late effect of doxorubicin, 26.9 percent recognized peripheral neuropathy as being associated with paclitaxel, and 21.8 percent noted peripheral neuropathy as a late effect of oxaliplatin. For cyclophosphamide, the risk of premature menopause and second cancers was identified by 14.8 and 17.2 percent of PCPs, respectively. Most oncologists surveyed were able to correctly identify these same late effects, although there was also need for improvement among these specialists—knowledge of the late effects ranged from 62 to 97 percent for the four drugs.

"While we strongly encourage patients to be aware of the chemotherapy drugs they receive and their side effects, it is vitally important that oncologists relay this information to patients' primary care providers so their risks can be appropriately managed throughout their lives," said lead author Larissa Nekhlyudov, MD, MPH, Assistant Professor of Population Medicine at Harvard Medical School and internist at Harvard Vanguard Medical Associates. “At the same time, our findings underscore the need for ongoing education among all physicians who care for cancer survivors, including oncologists, about the potential late effects of treatment.”

Abstract 6008
Oncologists' and primary care providers' awareness of late effects of cancer treatment: Implications for survivorship care.

Authors: Larissa Nekhlyudov, Noreen Aziz, Catherine C. Lerro, Katherine S. Virgo; Harvard Medical School and Harvard Vanguard Medical Associates, Boston, MA; National Institute of Nursing Research, Bethesda, MD; American Cancer Society, Atlanta, GA
Background: There is a growing population of cancer survivors, many of whom may experience late or long-term effects (LEs) of treatment. The goal of our study was to describe and compare primary care providers' (PCP) and oncologists' awareness of LEs.
Methods: The Survey of Physician Attitudes Regarding the Care of Cancer Survivors was completed by a nationally representative sample of 1,072 PCPs and 1,130 oncologists (cooperation rate 65%). Respondents were asked to report for each of four standard chemotherapy drugs used to treat breast or colorectal cancer the five LEs they had observed and/or had seen reported in the literature. We described and compared the physicians' responses and, using separate multinomial logistic regression models, determined predictors of their ability to identify the main LEs for all agents, adjusting for physician demographics and practice characteristics.
Results: Almost all (95.3%) oncologists identified cardiac dysfunction as a LE of adriamycin, and peripheral neuropathy as LEs of both taxol (97.3%) and oxaliplatin (96.6%); while these LEs were identified by only 55.1%, 21.8% and 21.8% of PCPs, respectively. Most oncologists identified premature menopause (71.4%) and secondary malignancies (62.0%) as LEs of cytoxan, compared with only 14.8% and 17.2% of PCPs. Main LEs for all four chemotherapy drugs were identified by 65% (n=741) of oncologists and only 6% (n=60) of PCPs. In adjusted models, oncologists were more likely to identify the main LEs for all chemotherapy drugs if they spent 51-90% (OR 1.87, 95% CI 1.21-2.88) or >90% (OR 1.82, 95% CI 1.08-3.08) of their time on patient care, and less likely if they were not board certified (OR 0.58, 95% CI 0.37-0.89). African American PCPs were less likely to identify the main LEs for all chemotherapy drugs (OR 0.19, 95% CI 0.08-0.45).
Conclusions: Oncologists often identified the main LEs of cancer drugs while PCPs did not. While not surprising, these findings emphasize that in the transition of patients from oncology to primary care settings, PCPs should be informed about the LEs of cancer treatment so that they may be better prepared to recognize and address these among survivors in their post-treatment care.
Disclosures: Nothing to disclose

ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL NEWS COVERAGE.

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Click here to view the disclosures for the 2012 ASCO Annual Meeting News Planning Team.

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