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ASCO RELEASES STUDIES FROM UPCOMING ANNUAL MEETING

-- Important Advances in Targeted Therapies, Screening, and Quality of Life --

Alexandria, Va. – The American Society of Clinical Oncology (ASCO) today highlighted six studies in a press briefing from among more than 4,000 abstracts publicly posted online at www.abstract.asco.org in advance of ASCO's 46th Annual Meeting. An additional 14 plenary, late-breaking and other major studies will be released at the Annual Meeting and highlighted in on-site press conferences.

The meeting, which is expected to draw approximately 30,000 cancer specialists, will be held June 4-June 8, 2010, at McCormick Place in Chicago, Ill. The theme of this year's meeting is "Advancing Quality Through Innovation."

"Our growing understanding of cancer's complex behavior is being translated into better, more targeted drugs against a variety of tumors," said Douglas W. Blayney, MD, President of ASCO, professor of internal medicine at the University of Michigan Medical School and medical director of the Comprehensive Cancer Center at the University of Michigan. "These studies show that investment in cancer research pays off. We're developing more personalized approaches to treating patients of all ages and across all cancer types, we're learning how to use current treatments more effectively, and we're identifying new ways to help patients live long, healthy lives following treatment."

"Clinical trials are essential to continued progress against cancer. Yet, the nation's federally funded clinical trial system is at a breaking point," said George W. Sledge Jr, MD, ASCO President-Elect, Ballve-Lantero Professor of Oncology and professor of pathology and laboratory medicine at the Indiana University School of Medicine. "ASCO has called for a doubling of support for federally funded clinical cancer research within the next five years. We've made impressive strides against this disease, and it's vital that the nation put more resources into these programs to continue the momentum.

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Studies highlighted in today's press briefing include:

- *Heart problems in childhood cancer survivors tied to specific gene and drug dose:* Survivors of childhood cancer who carry particular variants of a drug-metabolizing gene (*CBR*) and who received low doses of anthracycline chemotherapy were much more likely to develop heart disease than those without these forms of the gene who received low doses. The finding may help develop a more personalized approach to chemotherapy treatment in children.

- *Promising New Ovarian Cancer Screening Strategy Developed for Post-Menopausal Women at Average Risk:* A promising new screening approach for post-menopausal women at average risk of ovarian cancer is feasible and produces very few false-positive results. The method uses a mathematical model combining trends in CA-125 blood test results and a patient's age, followed by transvaginal ultrasound and referral to a gynecologic oncologist, if necessary.

- *Yoga Improves Sleep and Quality of Life, Lessens Fatigue for Cancer Survivors:* Sleep problems and fatigue are among the most common side effects experienced by cancer survivors. A four-week yoga program involving breathing, meditation, postures and other techniques helped cancer survivors sleep better, reduced fatigue and the use of sleep aids, and improved their quality of life.

- *Older Women with Early-Stage Breast Cancer May Skip Radiation Therapy:* Long-term follow-up from a randomized trial finds that women age 70 or older with early-stage breast cancer who undergo lumpectomy and receive tamoxifen can safely forego radiation therapy without significantly affecting their survival.

- *Maintenance Therapy with Rituximab Halves Risk of Lymphoma Recurrence:* The Phase III international PRIMA trial has found that two years of rituximab (Rituxan) "maintenance" therapy reduced the risk of follicular lymphoma recurrence by 50 percent in patients who responded to initial chemotherapy.

- *Lenalidomide Maintenance Therapy Slows Myeloma Progression:* Results from an interim analysis of a Phase III trial showed that maintenance therapy with lenalidomide (Revlimid) slowed disease progression by 54 percent among patients with multiple myeloma who had prior high-dose chemotherapy and an autologous stem cell transplant.

Oral Abstract Session: Pediatric Oncology II
Monday, June 7, 2010, 9:30-9:45 AM CDT
Room S504

Study Author: Smita Bhatia, MD, MPH
City of Hope National Medical Center
Duarte, CA

Heart Problems in Childhood Cancer Survivors Tied to Specific Gene and Drug Dose

[Note: This summary contains updated data not in the abstract]

A Children's Oncology Group study has shown that survivors of childhood cancer who carry particular variants of the *CBR* gene and who received low doses of anthracycline chemotherapy were much more likely to develop heart disease than those without this form of the gene who received low doses.

This finding may guide a more personalized approach to preventing toxicities associated with anthracycline chemotherapy among a specific subset of children with cancer. Prior to treatment, oncologists may be able to screen patients for these specific gene variants, and based on these results, to choose non-cardiotoxic alternatives.

"Although we depend heavily on anthracyclines for treating children with cancer, we are fully aware of their toxic effects to the heart. We also know that some patients -- despite being exposed to higher doses -- don't develop heart problems, while others with little exposure have considerable cardiac damage," said senior author Smita Bhatia, MD, MPH, professor and chair of the department of population sciences at the City of Hope National Medical Center in Duarte, Calif. "Our results are a good example of how understanding a cancer patient's genetic makeup can help us better tailor individual therapies."

Nearly 80 percent of children treated for cancer survive, but many have health effects from treatment later in life. A major late effect of some chemotherapy drugs, such as commonly used anthracyclines, is cardiomyopathy, where the heart cannot pump efficiently. CBRs, or carbonyl reductases, are enzymes that help metabolize anthracyclines into substances that can damage the heart. Variants in two CBR-producing genes, *CBR1* and *CBR3*, are known to affect CBR activity. The researchers examined the potential effects of the *CBR1* and *CBR3* variants on cardiomyopathy risk.

In this case-control study, Dr. Bhatia and her colleagues compared 165 childhood cancer survivors who developed cardiomyopathy (the largest cohort of documented childhood cancer-related cardiomyopathy) and 323 cancer survivor controls with no heart disease. The participants were diagnosed between 1966 and 2008, with approximately 80 percent treated beginning after 1981. The children's median age at diagnosis was 7.5 years.

The researchers found that among those with cardiomyopathy who had been treated with high doses (greater than 250 mg/m^2) of anthracyclines, the *CBR* genes had little effect on heart disease risk, since the risk was already high because of the large dose of drug. But among those who developed cardiomyopathy and received low drug doses (less than 250 mg/m^2), both *CBR1* and *CBR3* variants increased the cardiomyopathy risk. Those carrying the *CBR1* variant had a 5.3-fold increased risk for cardiomyopathy compared to those carrying the low-risk variant; those with the *CBR3* variant had a 3.1-fold increased risk.

The researchers believe that at the lower doses, anthracycline cardiotoxicity is dependent on *CBR* gene metabolism, whereas at higher doses, toxicity is likely mediated by other mechanisms driven by high doses of unmetabolized anthracyclines.

Abstract 9512
Abstract Title: Anthracycline-related cardiomyopathy in childhood cancer survivors and association with polymorphisms in the carbonyl reductase genes: A Children's Oncology Group study.

Authors: J. G. Blanco, C. Sun, W. Landier, L. Chen, K. C. Oeffinger, M. M. Hudson, J. P. Neglia, A. K. Ritchey, M. V. Relling, S. Bhatia
Background: Anthracycline-related cardiomyopathy is a well-recognized dose-limiting complication. Inter-individual variability in risk exists, potentially due to genetic susceptibility. Carbonyl reductases (CBR) catalyze reduction of anthracyclines to cardiotoxic alcohol metabolites. Polymorphisms in *CBR3* V244M and *CBR1* G1096A impact CBR activity. We examined the role of functional polymorphisms in *CBR3 and CBR1* on risk of cardiomyopathy.
Methods: Using a case-control design, 165 cases with documented cardiomyopathy and 323 controls (cancer survivors with no cardiomyopathy; matched on primary diagnosis, follow-up, race/ethnicity) provided germline DNA. Therapeutic exposures were summarized. **Results:** Primary diagnoses included acute leukemia (164), lymphoma (111), sarcoma (120) and others (93); 51% were females; 77% whites; median age at cancer diagnosis: 7.5 years; time to cardiomyopathy: 7.1 years; median anthracycline dose – cases: 300mg/m^2; controls: 140mg/m^2. Multivariate analysis revealed anthracycline dose (per 100mg/m^2: OR=1.8, p<0.001), and chest radiation (OR=3.13, p=0.05) to be associated with cardiomyopathy. The role of polymorphisms in *CBR3/CBR1* was then examined, adjusting for chest radiation. There was a borderline association between *CBR3* V244M and cardiomyopathy (OR=1.5, p=0.08 for GG vs. GA/A); and no association for *CBR1* G1096A (OR=1.0, p=0.9). However, upon stratification by anthracycline does, the association with *CBR3* V244M became stronger among subjects exposed to ≤250mg/m^2 (OR=6.4, p=0.006), but disappeared for those exposed to >250mg/m^2 (OR=0.9, p=0.8). Similar but non-significant associations were observed for *CBR1* (OR=3.3, p=0.10; OR=0.8, p=0.7, respectively).
Conclusions: Using the largest cohort of documented cardiomyopathy, this report demonstrates a clear dose-response relation between anthracyclines and cardiomyopathy, and selectively greater impact of *CBR3* on risk of cardiomyopathy after low-dose anthracycline exposure. These data identify a definable subset of patients that may benefit from cardioprotection, surveillance or pharmacologic interventions.
Disclosures: Nothing to disclose.

Oral Abstract Session: Gynecologic Cancer
Sunday, June 6, 2010, 9:30-9:45 AM CDT

E Arie Crown Theater

Lead author: Karen Lu, MD
The University of Texas
M.D. Anderson Cancer Center
Houston, TX

Promising New Ovarian Cancer Screening Strategy Developed for Post-Menopausal Women at Average Risk

Researchers have tested a promising new screening approach for post-menopausal women at average risk of ovarian cancer. The strategy uses a mathematical model that combines trends in CA-125 blood test results and a patient's age, followed by transvaginal ultrasound and referral to a gynecologic oncologist, if necessary. The researchers found that this approach is feasible and produces very few false-positive results.

“More than 70 percent of ovarian cancers are diagnosed when they have already grown to an advanced stage, so identifying a reliable screening test for early-stage disease would be like finding the Holy Grail," said lead author Karen Lu, MD, professor of gynecologic oncology at The University of Texas MD Anderson Cancer Center. “This study is one step forward in that direction. If confirmed in larger studies, this approach could be a useful and relatively inexpensive tool for detecting ovarian cancer in its early, more curable stages, including the types of ovarian cancer that biologically are the most aggressive.”

While women at high risk of ovarian cancer may undergo more frequent screening or take other measures to reduce their risk, there are currently no screening tools for women at average risk of this disease. CA-125 is a protein that has been known for years to rise during ovarian cancer development, but because it can become elevated in response to other factors, it is not specific for ovarian cancer.

In this study, the researchers evaluated a “Risk of Ovarian Cancer Algorithm” (ROCA) -- which is based on a patient's age and trends in CA-125 blood test results over time -- followed by transvaginal sonography (TVS) in women with rising CA-125 levels, and, when needed, referral to a gynecologic oncologist to determine if surgery was necessary.

The study included 3,238 postmenopausal women aged 50 to 74 with no significant family history of breast or ovarian cancer who were followed for up to eight years. Ovarian cancer most commonly occurs in women over 50, and CA-125 is a more sensitive marker of ovarian cancer in postmenopausal than premenopausal women.

On an annual basis, less than 1 percent of the women required TVS. Eight women underwent surgery based on the ROCA results, three of whom had invasive but early-stage ovarian cancers (two had borderline ovarian tumors and three had benign ovarian tumors). The specificity of ROCA followed by TVS for referral to surgery was 99.7 percent, indicating that very few false-positives resulted from this approach.

A large-scale study of ROCA is under way in the United Kingdom in more than 200,000 women; the results are expected in 2015. If the algorithm is validated, CA-125 testing could be recommended as part of a woman's annual check-up with a physician.

Abstract 5003
A prospective U.S. ovarian cancer screening study using the risk of ovarian cancer algorithm (ROCA).
K. H. Lu, S. Skates, T. B. Bevers, W. Newland, R. G. Moore, L. Leeds, S. Harris, O. W. Adeyinka, H. A. Fritsche, R. C. Bast

Background: There are currently no effective screening tools for the early detection of ovarian cancer in women at average population risk. We evaluated a screening strategy that incorporates change of CA-125 over time and age of the participant to estimate risk of ovarian cancer, referring a small fraction (~2%) of apparently healthy individuals annually to transvaginal sonography (TVS).
Methods: A single arm, prospective, multi-center screening study enrolled post-menopausal women age 50 to 74 with no significant family history of breast or ovarian cancer. Participants underwent a CA-125 blood test annually. Based on the Risk of Ovarian Cancer Algorithm (ROCA) result, women were triaged to the next annual CA-125 (low risk), repeat CA-125 in 3 months (intermediate risk), or TVS and referral to a gynecologic oncologist (high risk). Based on clinical findings and TVS, the gyn onc made the decision whether to proceed with surgery.
Results: 3238 women participated over an eight year period. The average annual rate of referral to 3 monthly CA125 was 6.8%, and the average annual rate of TVS and gyn onc referral was 0.9%. Cumulatively 85 women (2.6%) received TVS and referral to a gyn onc. Eight women subsequently underwent surgery based on the TVS and referral, with 3 invasive ovarian cancers, 2 borderline ovarian tumors and 3 benign ovarian tumors, providing a positive predictive value of 37.5% (95% CI 8.5%,75.5%).The combined specificity of ROCA followed by TVS for referral to surgery is 99.7% (95% CI 99.5%, 99.9%). The 3 invasive ovarian cancers were high grade epithelial tumors that were all early stage (two Stage 1C and Stage IIB). All 3 women with invasive ovarian cancer had at least 3 years with low risk, annual CA-125 values prior to a rising CA-125.
Conclusions: In this prospective, single arm study, the ROCA followed by TVS demonstrated excellent specificity and PPV in a population of U.S. women at average risk for ovarian cancer. As expected, less than 1% of participants annually required a TVS. In addition, the invasive high grade ovarian cancers that were detected were early stage. This study provides early evidence that ROCA followed by TVS is a feasible strategy for screening women over 50 years of age.
Disclosures: Herbert Fritsche, Research Funding, Roche Diagnostics; Robert Bast, Consultant or Advisory Role, Fujiresio Diagnostics Inc., Other Remuneration, Royalties for CA125.

Oral Abstract Session:
Patient and Survivor Care
Saturday, June 5, 2010, 4:45-5:00 PM CDT
Room E354b

Lead author: Karen Mustian, PhD, MPH

University of Rochester Medical Center, Rochester, NY

Yoga Improves Sleep and Quality of Life, Lessens Fatigue for Cancer Survivors

The largest randomized, controlled study to date examining the value of yoga designed specifically for cancer survivors found that a four-week yoga program helped them sleep better, experience less fatigue, and improved their quality of life.

"Very few, if any, treatments for the sleep problems and fatigue that cancer survivors experience work well for very long, if at all," said lead author Karen Mustian, PhD, MPH, assistant professor of radiation oncology and community and preventive medicine and at the University of Rochester Medical Center. "The study results point to a simple, non-pharmacological therapy that clinicians can recommend to help patients with several very common cancer-related problems."

Sleep problems and fatigue are among the most prevalent side effects experienced by cancer survivors, and they can impair quality of life. Approximately 80 percent of patients report sleep problems during treatment, and as many as 65 percent experience problems after therapy ends. Few effective treatments are available.

In this randomized, multicenter, Phase II/III trial -- conducted through the University of Rochester Cancer Center Community Clinical Oncology Program -- the benefits of yoga were assessed in 410 survivors of early-stage cancers (96 percent women, 75 percent breast cancer patients) who reported sleeping problems between two and 24 months after completing adjuvant therapy for their cancer. Participants received either usual care alone or usual care plus a four-week, twice-weekly YOCAS® (Yoga for Cancer Survivors) program, consisting of mindfulness exercises such as breathing, meditation, visualization, and poses in standing, seated and lying-down positions.

Patients who took yoga reported greater sleep quality, less use of drugs for sleep, less fatigue and better quality of life, while the control group reported increased use of sleeping medication. Specifically, patients in the yoga group reported greater improvement in sleep quality (22 percent vs. 12 percent), reduced incidence of clinically impaired sleep (31 percent vs. 16 percent), and less daytime sleepiness (29 percent vs. 5 percent), compared with patients in the control group. The yoga group showed these improvements in sleep while reducing sleep medication use by 21 percent. In contrast, the control group increased sleep medication use by 5 percent.

Additionally, researchers found that those in the yoga group reported a 42 percent reduction in fatigue, while the control group reported only 12 percent less fatigue after four weeks. Yoga participants reported an improved quality of life (6 percent) while the control group reported no change.

Abstract 9013
YOCAS® yoga significantly improves sleep, fatigue and quality of life: A URCC CCOP randomized, controlled clinical trial among 410 cancer survivors.
K. M. Mustian, O. Palesh, L. Sprod, L. J. Peppone, C. E. Heckler, J. S. Yates, P. S. Reddy, M. Melnik, J. K. Giguere, G. R. Morrow
Background: Impaired sleep quality (SQ) and fatigue are the most prevalent and troublesome side effects experienced by cancer survivors and both significantly impair quality of life (QOL). We conducted a nationwide, multi-site, phase II/III randomized, controlled, clinical trial examining the efficacy of yoga for improving SQ, fatigue and QOL among cancer survivors through the University of

Rochester (UR) Cancer Center Community Clinical Oncology Program (CCOP) Research Base.
Methods: Non-metastatic, cancer survivors suffering from moderate or greater sleep disruption between 2-24 months after completing adjuvant therapy with no participation in yoga during the previous 3 months were randomized into 2 arms: 1) standard care monitoring and 2) standard care plus the 4-week (wk) yoga intervention (2 x's/wk; 75 min./session). The yoga intervention utilized the UR Yoga for Cancer Survivors (YOCAS®) program consisting of pranayama (breathing exercises), 18 gentle Hatha and Restorative yoga asanas (postures) and meditation. SQ, fatigue and QOL were assessed pre- and post-intervention. **Results:** 410 survivors were accrued (96% female, mean age = 54, 75% breast cancer). ANCOVAs with baseline values as covariates revealed significant differences in SQ, fatigue and QOL (all $p<0.05$) between groups at post-intervention. Yoga participants demonstrated greater improvements in SQ (CS=change score; CS=1.96, standard error=SE; SE=0.25), fatigue (CS=7.82, SE=1.06) and QOL (CS=6.61, SE=1.11) from pre- to post-intervention compared to controls (SQ CS=1.07, SE=0.23, fatigue CS=2.34, SE=0.91 and QOL CS=1.58, SE=1.09). ANCOVAs also revealed the yoga group reduced sleep medication use (CS=-0.21, SE=0.09, $p<0.05$) while the control group increased medication use (CS=0.04, SE=0.07, p=0.09). **Conclusions:** The brief community-based YOCAS® yoga intervention significantly improves SQ, fatigue, and QOL while reducing sleep medication use among survivors. Clinicians should consider prescribing the YOCAS® program for survivors reporting impaired sleep and fatigue.
Disclosures: Nothing to disclose.
Funding: NCI U10CA37420 and K07CA120025.

Oral Abstract Session: Breast Cancer – Local, Regional and Adjuvant Therapy
Monday, June 7, 2010, 10:15-10:30 AM CDT
N Hall B1

Lead author: Kevin Hughes, MD

Massachusetts General Hospital
Boston, MA

Older Women with Early-Stage Breast Cancer Can Safely Forego Radiation Therapy

A follow-up study adds further evidence that women age 70 or older with early-stage breast cancer who undergo lumpectomy and receive tamoxifen may safely forego radiation therapy without significantly affecting their survival.

"The standard of care for women 70 and older with very small tumors that are estrogen-positive and node-negative – the largest group of breast cancer patients in this age group – had been lumpectomy and radiation," said lead author Kevin Hughes, MD, surgical director, breast screening, and co-director of the Avon Comprehensive Breast Evaluation Center at the Massachusetts General Hospital in Boston. "Earlier reports of this study with shorter median follow-up have shown the risk of recurrence without radiation to be only marginally worse than with radiation, but there was concern that longer follow-up would show a blossoming of recurrences. This study confirms that for older women with early-stage breast cancer, lumpectomy without radiation is a viable alternative, and tamoxifen may replace the need for radiation."

Radiation therapy after lumpectomy is the standard of care for younger women with early-stage breast cancer. Dr. Hughes and his colleagues looked at whether this therapy is also appropriate for older women, who often have less aggressive disease and are less likely to experience a recurrence.

The researchers randomly assigned 636 women aged 70 or older with stage I, estrogen receptor-positive, node-negative breast cancer who had a lumpectomy to receive tamoxifen (319 women) or tamoxifen and radiation (317 women). An earlier analysis by these investigators showed that after a median follow-up of 7.9 years, tamoxifen alone was an effective alternative to tamoxifen and radiation. This new analysis includes follow-up data after 10.5 years.

The risk of breast cancer recurrence in the same breast was lower among the women who received tamoxifen plus radiation therapy (2 percent) compared with those who received tamoxifen alone (8 percent). However, there were no significant differences between the two groups with respect to breast cancer-specific and overall survival: After 10 years, breast cancer-specific survival for women who received tamoxifen was 98 percent versus 96 percent for those who received tamoxifen and radiation. The tamoxifen-only group had a 10-year overall survival of 63 percent compared to 61 percent to the tamoxifen plus radiation group.

Abstract 507
Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer.
K. S. Hughes, L. A. Schnaper, C. Cirrincione, D. A. Berry, B. McCormick, H. B. Muss, B. Shank, C. Hudis, E. P. Winer, B. L. Smith, CALGB, ECOG, RTOG
Background: In women 70 years of age or older with early breast cancer undergoing lumpectomy, we had previously shown at a median follow-up (FU) of 7.9 years that tamoxifen alone (Tam) is an effective alternative to tamoxifen plus radiation (TamRT). To provide longer-term results we present outcomes at a median FU of 10.5 years.
Methods: Between July 1994 and February 1999, we randomly assigned 636 women 70 years of age or older with clinical stage I, estrogen receptor + (ER+) breast cancer treated by lumpectomy to receive Tam (N = 319) or TamRT (N = 317). Primary endpoints were time to locoregional recurrence, mastectomy for recurrence, distant metastases, and breast cancer-specific and all-cause mortality.

Results: The addition of RT to Tam prolonged the time to first recurrence ($p = 0.015$) due to improved local control by TamRT. Site of first recurrence was local for 9% vs. 2% (Tam vs. TamRT). Specifically, for Tam vs. TamRT, first recurrence occurred in the ipsilateral breast in 8% vs. 2% and solely in the axilla in 1% vs. 0%. The remaining endpoints did not differ by arm ($p > 0.05$). Comparing the Tam and TamRT arms, respectively, the probability at 10 years of being free from mastectomy was 96% vs. 98% and from distant mets was 95% vs. 93%. Similarly, the 10-year breast-cancer-specific survival was 98% vs. 96%, and overall survival was 63% vs. 61%.
Conclusions: At 10.5 years median FU, the data continue to demonstrate that TamRT results in an absolute reduction of 6% in ipsilateral breast tumor recurrence (IBTR) when compared to Tam alone in this population. Otherwise, the addition of radiation does not impact survival, distant disease free survival, breast cancer specific survival or breast conservation. At this time, 43% of women participating in this study have died (but only 7% of those deaths were due to breast cancer). This study demonstrates that with over a decade of follow-up, lumpectomy with antiestrogen therapy, but without the addition of radiation, is an appropriate treatment option for older women with node-negative hormone receptor positive disease. Further, the low rate of breast cancer deaths indicates that breast cancer mortality is not a major concern for this subset of older women.
Disclosures: Nothing to disclose.

Oral Abstract Session: Lymphoma
Saturday, June 5, 2010, 1:00-1:15 PM CDT
Room E354a

Lead author: Gilles Salles, MD
University of Lyon
Lyon, France

Maintenance Therapy with Rituximab Halves Risk of Lymphoma Recurrence

The Phase III international PRIMA trial has found that two years of rituximab (Rituxan) "maintenance" therapy reduced the risk of follicular lymphoma recurrence by 50 percent in patients who responded to initial chemotherapy. Maintenance therapy is longer-term treatment given after patients achieve remission with standard therapy, with the goal of prolonging remission.

"These findings provide hope for the way we manage this disease. Rituximab maintenance therapy is likely to become a new standard of care for these patients," said lead author Gilles Salles, MD, professor of medicine at the University of Lyon. He noted that most patients with this type of lymphoma are at risk for a relapse within three to six years of their initial therapy.

In this study, patients with primarily stage III or IV follicular lymphoma whose disease was reduced or eliminated by rituximab-based combination chemotherapy (induction therapy) were randomly assigned to receive two additional years of rituximab as maintenance therapy (505 patients) or no maintenance therapy (observation group, 513 patients).

After a median follow-up time of 25 months, disease progression occurred in 18 percent of the rituximab group compared with 34 percent of the observation group. The benefits of rituximab maintenance were observed regardless of patients' stage of remission, age, or prior treatment regimen. The researchers noted that longer follow-up of the patients is needed to confirm the benefits of maintenance rituximab therapy for reducing the risk of lymphoma relapse.

Rituximab maintenance therapy was well tolerated, with the most common side effects being infections (37 percent for the rituximab group compared with 22 percent of the observation group). Quality of life was similar between the two groups.

Based on these data, the manufacturer of rituximab has applied for approval in the United States and Europe for an expanded indication for rituximab as maintenance therapy in these patients.

Abstract 8004
Rituximab maintenance for 2 years in patients with untreated high tumor burden follicular lymphoma after response to immunochemotherapy.
G. A. Salles, J. F. Seymour, P. Feugier, F. Offner, A. Lopez-Guillermo, R. Bouabdallah, L. M. Pedersen, P. Brice, D. Belada, L. Xerri
Background: The GELA sponsored intergroup PRIMA Phase III study investigated 2 years of rituximab (R) maintenance in follicular lymphoma (FL) patients responding to first-line immunochemotherapy consisting of either 8 cycles of R-CVP, or 6 cycles of R-CHOP or R-FCM (plus 2 additional rituximab infusions).
Methods: 1,217 patients were enrolled from 223 centres (25 countries) between Dec 2004 and Apr 2007. Pre-induction characteristics: median age 56 years (range 22–87); 52% male; 90% Ann Arbor stage III-IV; 33% B symptoms; 56% bone marrow involvement; 4% ECOG performance status >1; 34% elevated LDH; 32% β2-microglobulin >3mg/L; 21% FLIPI 0-1: 36% FLIPI 2; 43% FLIPI 3-5. Most patients (75%) received R-CHOP induction (22% R-CVP, 3% R-FCM). 1,018 eligible patients responding to induction therapy were randomized (stratified by regimen and response to induction) to observation or R-maintenance, 375 mg/m^2 i.v. every 8 weeks for 2 years.

Results: The primary endpoint of PFS was met at the planned interim analysis (ITT: 513 observation, 505 rituximab maintenance). Median follow-up was 25 months from randomization (31 months from study entry). There was a significant (stratified log-rank, P<.0001) improvement in the primary endpoint PFS, for R-maintenance (hazard ratio [HR]=0.50; 95% CI [0.39-0.64]; 2-year PFS 82%; 95% CI [78-86%] vs 66% [61-70%] for observation). An independent response review committee confirmed the significant improvement in PFS in the R-maintenance arm (HR=0.53 [0.41-0.68]). Time to next anti-lymphoma treatment, as well as response rate at the end of maintenance or observation, were significantly improved in the R-maintenance arm. The most common AEs were infections (22% observation, 37% R-maintenance). Grade 3-4 AEs were reported in 16% (observation) and 22% (R-maintenance) of patients (neutropenia 1% vs 4%; infections 1% vs 4%, respectively**).**
Conclusions: The PRIMA study demonstrates that 2 years of R-maintenance therapy after induction immunochemotherapy in previously untreated FL significantly improves PFS with little additional toxicity. The PRIMA study provides evidence for a new standard of care for FL patients in need of treatment.
Disclosures: Gilles Salles, Consultant or Advisory Role, roche, Honoraria, roche, Research Funding, Genentech; John Seymour, Consultant or Advisory Role, roche, Honoraria, roche, Other Remuneration, roche, Research Funding, roche; Pierre Feugier, Consultant or Advisory Role, roche, Honoraria, roche; David Belada, Honoraria, roche, Other Remuneration, roche.
Research Funding Provided by: Roche Pharma

Oral Abstract Session: Myeloma
Sunday, June 6, 2010, 11:15-11:30 AM CDT
Room E354b

Lead author: Michel Attal, PhD
Purpan Hospital
Toulouse, France

Lenalidomide Maintenance Therapy Slows Myeloma Progression

Results from an interim analysis of a Phase III trial show that maintenance therapy with lenalidomide (Revlimid) slowed disease progression by 54 percent among patients with multiple myeloma who had prior high-dose chemotherapy and an autologous stem cell transplant. Maintenance therapy is longer-term treatment given after patients achieve remission with initial therapy, with the goal of prolonging remission.

"These results are very promising. If confirmed in the final analysis, they suggest that maintenance therapy with lenalidomide can improve quality of life in patients with myeloma by delaying the need for more intensive therapy to treat a relapse," said Michel Attal, PhD, professor of hematology at Purpan Hospital in Toulouse, France and the lead author of the study, which was conducted by the French-Speaking Intergroup for Myeloma (Intergroup Francophone du Myelome). Final data on progression-free survival and overall survival are expected to be reported in December 2010.

Multiple myeloma, a cancer of the bone marrow, is treated with high-dose chemotherapy and autologous stem cell transplantation (ASCT) -- a procedure in which some of a patient's stem cells are removed before therapy and returned after treatment to rebuild the patient's immune system. Despite this aggressive approach, however, more than 90 percent of patients eventually experience a cancer relapse. Prior research has shown that maintenance therapy with the chemically similar drug thalidomide can delay myeloma relapse, but this drug has significant toxic effects on the nervous system and was only effective in a limited group of patients.

Lenalidomide is an oral drug that is already used to treat myeloma that recurs or persists despite prior therapy. In this study, investigators compared the time it took for a patient's myeloma to progress (progression-free survival) between 307 patients who were randomly assigned to receive maintenance lenalidomide until relapse and 307 patients who received a placebo. All patients had previous treatment with high-dose therapy and ASCT within six months of randomization, followed by two months of lenalidomide "consolidation" therapy (lenalidomide treatment after initial therapy to achieve a complete remission; consolidation therapy uses a higher dose of lenalidomide than maintenance therapy).

Lenalidomide maintenance therapy improved three-year progression-free survival: 68 percent of patients in the lenalidomide group did not experience disease progression, compared with 35 percent of the placebo group. This benefit was observed whether or not patients had achieved a complete response after ASCT. Two-year overall survival was similar in both groups (95 percent). Maintenance lenalidomide was well tolerated.

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Lenalidomide maintenance after transplantation for myeloma.
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Background: High-dose therapy with autologous stem cell transplantation (ASCT) is a standard treatment for myeloma patients. However, a residual disease (RD) responsible for relapse is always present. Effective maintenance treatment would be required. However, such treatment is still to be defined. We previously reported that thalidomide reduced RD. However, neuropathy was a major limiting factor. Lenalidomide, a thalidomide analog devoid of neurological toxicity, was thus attractive to investigate.

Methods: Patients, under 65 years of age, with non-progressive disease after a first line ASCT (performed within the last 6 months) were randomized to receive a consolidation with lenalidomide (25 mg/d, 21 days/month, for 2 months) followed by a maintenance with either lenalidomide (10 to 15 mg/d) until relapse (Arm A) or placebo (Arm B). From July 2006 to August 2008, 614 patients were randomized. Patient's characteristics of each group were similar and no significant differences were found with regard to age (57 years), ISS stage, FISH analysis, induction regimen (VAD/bortezomib-dex/thalidomide-dex/others=49%/44%/3%/2%), diagnosis-randomization interval (10 months), and response at time of randomization.
Results: In December 2009, with a median follow up of 24 months from randomization, the first pre-planned interim analysis was performed. The independent data and safety monitoring committee recommended to unblind the trial due to the PFS superiority of arm B (primary end point). Consolidation improved the response in 20% of patients. Maintenance with LEN improved the 3-year PFS from randomization: 35% in arm A versus 68% in arm B (HR=0.46, $p<10^{-6}$). This benefit was observed both among patients achieving or not a complete response after ASCT. In multivariate analysis, PFS was related to response after consolidation, beta-2 microglobulin at diagnosis, and treatment arm. A strong interaction ($p<0.04$) was found between the efficacy of arm B and beta 2-microglobulin (HR=0.3, $p <10^{-4}$ for beta-2 m <=3 mg/l; HR=0.58, $p<0.003$ for beta-2 m > 3 mg/l). The 2-year survival was similar in both treatment arms (95%)
Conclusions: Lenalidomide is an effective maintenance treatment which prolongs PFS after ASCT.
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