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-- PRESS BRIEFING SATURDAY, MAY 30, 11:00 AM EDT --

STUDIES ADVANCE TREATMENT AND UNDERSTANDING OF LUNG CANCER

Orlando, Fla.— The findings from several large studies on lung cancer were released today at a press briefing at the 45th Annual Meeting of the American Society of Clinical Oncology (ASCO).

“Lung cancer is one of the most challenging cancers to treat, but the studies presented today highlight promising new targeted therapies and milder treatment regimens that improve survival,” said Bruce E. Johnson, MD, Director of the Dana-Farber Harvard Medical Center Lung Cancer Program and moderator of the press briefing.

“Researchers also report that hormone therapy among menopausal women with lung cancer is associated with a higher risk of death. These findings add to growing concerns about the safety of hormone therapy.”

Studies highlighted in the press briefing include:

- *Pemetrexed extends survival as maintenance therapy:* A phase III study reports that maintenance therapy with pemetrexed (Alimta) improves overall survival in nonsquamous forms of advanced non-small cell lung cancer (NSCLC).
- *Maintenance therapy with two targeted therapies is superior to one alone:* A phase III trial finds that adding erlotinib (Tarceva) to bevacizumab-based (Avastin) maintenance therapy in patients with advanced NSCLC delays cancer progression more than maintenance treatment with bevacizumab alone.
- *Menopausal hormone therapy with estrogen and progestin linked to increased risk of death in women with lung cancer:* A secondary analysis from the Women’s Health Initiative reports that use of hormone therapy with estrogen plus progestin increases the risk of dying from NSCLC for women with the disease.
- *Novel therapy that targets two receptors benefits patients with advanced lung cancer:* A phase III trial demonstrates that vandetanib (Zactima), a novel drug that targets two key receptors associated with lung cancer growth, improves progression-free survival in patients with advanced NSCLC.

For consumer-oriented information on these studies and more than 120 cancer types, please refer your readers to ASCO’s patient website, www.Cancer.Net.

**ORAL PRESENTATION
SUNDAY, MAY 31, 9:00 AM EDT
LEVEL 2, WEST HALL E1
LUNG CANCER - METASTATIC**

**Lead Author: Chandra P. Belani, MD
Penn State Cancer Institute
Hershey, Pa.**

**Maintenance Therapy with Pemetrexed Improves Overall Survival
in Advanced Non-Small Cell Lung Cancer**

An international, multi-institutional study finds that use of pemetrexed (Alimta) as maintenance therapy following standard treatment improves overall survival for patients with advanced non-small cell lung cancer (NSCLC); the study also further confirms that this benefit is primarily limited to those with the nonsquamous subtype.

The efficacy, tolerability and ease of administration provided a strong rationale for evaluating pemetrexed as maintenance therapy in patients with advanced non-small cell lung cancer whose cancer had not progressed following four cycles of platinum-based chemotherapy. The drug was given on an ongoing basis until patients' disease progressed.

"This study will change the overall standard of care," said Chandra P. Belani, MD, Deputy Director of the Penn State Cancer Institute and the study's lead author. "Maintenance therapy with pemetrexed offers a new paradigm for patients who have advanced lung cancer, because it has a low toxicity and can be given on an ongoing basis over a prolonged period of time to extend patients' lives."

Pemetrexed is currently approved as a first-line treatment for advanced nonsquamous non-small cell lung cancer in combination with the chemotherapy agent cisplatin and as a single agent in patients with recurrent disease. Preliminary results of the current study presented at the 2008 ASCO Annual Meeting had demonstrated that maintenance therapy with pemetrexed delayed disease progression, but this is the first time a significant improvement in overall survival has been shown in this setting.

In this randomized, double-blind, phase III study, patients were given either pemetrexed (441 patients) or placebo (222 patients), along with the best supportive care. All patients had advanced or metastatic (stage 3B or 4) NSCLC (both squamous and nonsquamous subtypes) that had not progressed after four cycles of platinum-based chemotherapy.

Patients who received pemetrexed had an overall survival of 13.4 months, versus 10.6 months for patients in the placebo group. For the nonsquamous subgroup (482 patients), overall survival was 15.5 months for patients on pemetrexed, versus 10.3 months for patients on placebo. Patients with the squamous subtype do not seem to benefit with pemetrexed, confirming what has been shown in other studies. Researchers suspect the possible mechanism for this difference in effectiveness may be related to the expression of biomarkers such as thymidylate synthetase, which has been shown to correlate with sensitivity to pemetrexed.

Severe (grade 3 or 4) side effects were low but more common in the pemetrexed group, specifically fatigue (five percent in the pemetrexed group, versus 0.5 percent in the placebo group) and low white blood cell counts (2.9 percent versus 0 percent). Side effects did not increase for patients who received pemetrexed for a longer period of time, and there were no drug-related deaths.

CRA8000

Maintenance pemetrexed (Pem) plus best supportive care (BSC) versus placebo (Plac) plus BSC: A randomized phase III study in advanced non-small cell lung cancer (NSCLC)

C. P. Belani, T. Brodowicz, T. Ciuleanu, J. H. Kim, M. Krzakowski, E. Laack, Y. L. Wu, P. Peterson, K. Krejcy, C. Zielinski

Background: Pemetrexed's efficacy, favorable tolerability profile and ease of administration provided a strong rationale for evaluation as maintenance therapy in patients (pts) with advanced NSCLC. We present the final analyses for all outcomes, including overall survival (OS), from a phase III study of Pem vs. Plac (Ciuleanu, *J Clin Oncol* 26, 2008, A 8011) in pts with stage IIIB/IV NSCLC who had not progressed on four cycles of platinum-based chemotherapy.

Methods: In this double-blind trial, pts were randomized 2:1 to receive Pem (500 mg/m², day 1) plus BSC or Plac plus BSC in 21-day cycles until disease progression. All pts received vitamin B₁₂, folic acid, and dexamethasone. The final OS analysis was performed using an unadjusted Cox model. Overall $\alpha=0.05$ for PFS and OS. **Results:** In the 663 randomized pts (Pem 441: Plac 222), Pem resulted in significantly better OS (13.4 vs. 10.6 mos [HR 0.79, 95% CI: 0.65-0.95, $P=0.012$]). As reported earlier, Pem also had better PFS ($P<0.00001$) and response ($P<0.001$) (Table). The improvements in PFS and OS were observed primarily in patients with non-squamous histology (PFS HR = 0.47 and OS HR = 0.70). Treatment by histology interaction for OS was significant ($P=0.038$). Drug-related grade 3/4 toxicities were higher for Pem (16% vs 4%; $P<0.001$); specifically, fatigue (5% vs 0.5%) and neutropenia (2.9% vs. 0%). Grade 3/4 toxicities did not increase significantly in pts who received ≥ 6 and ≥ 10 cycles of Pem. There were no Pem-related deaths. Fewer pts in the Pem arm (51.5% vs 67.1%; $P<0.001$) received systemic post-discontinuation therapy. **Conclusions:** Pem maintenance therapy is well tolerated and offers superior OS and PFS compared with Plac, making it a new treatment paradigm for patients with advanced NSCLC who respond to initial therapy. This trial further validates that Pem has greater efficacy in patients with non-squamous histology.

| | Median OS months | | p value (HR) | Median PFS*, months | | p value (HR) | CR+PR+SD*, % | | p value |
|---------------------|------------------|---------|--------------|---------------------|---------|-----------------|--------------|---------|---------|
| | Pem | Placebo | | Pem | Placebo | | Pem | Placebo | |
| Overall population | 13.4 | 10.6 | 0.012 (0.79) | 4.3 | 2.6 | <0.0001 (0.50) | 51.7 | 33.3 | <0.001 |
| Nonsquamous (n=482) | 15.5 | 10.3 | 0.002 (0.70) | 4.37 | 1.84 | <0.00001 (0.47) | 54.3 | 26.6 | <0.001 |
| Adeno (n=329) | 16.8 | 11.5 | 0.026 (0.73) | 4.60 | 2.66 | <0.00001 (0.51) | 58.2 | 29.6 | <0.001 |
| Large Cell (n=20) | 8.4 | 7.9 | 0.964 (0.98) | 4.53 | 1.45 | 0.104 (0.40) | 30.0 | 25.0 | 0.999 |
| Other (n=133) | 11.3 | 7.7 | 0.025 (0.61) | 4.11 | 1.58 | 0.0001 (0.44) | 47.5 | 18.9 | 0.004 |
| Squamous (n=181) | 9.9 | 10.8 | 0.678 (1.07) | 2.43 | 2.50 | 0.896 (1.03) | 33.3 | 34.5 | 1.000 |

* Independent review data.

Disclosures: Chandra Belani,.,Consultant or Advisory Role,Eli LillyChandra Belani,.,Honoraria,Eli LillyY Wu,.,Honoraria,RocheY Wu,.,Honoraria,PfizerY Wu,.,Honoraria,Eli Lilly and CompanyY Wu,.,Honoraria,AstraZenecaP Peterson,.,Employment or Leadership Position,Eli Lilly and CompanyP Peterson,.,Stock Ownership,Eli Lilly and CompanyK Krejcy,.,Employment or Leadership Position,Eli Lilly and CompanyK Krejcy,.,Stock Ownership,Eli Lilly and CompanyC Zielinski,.,Honoraria,Eli Lilly and CompanyC Zielinski,.,Other Remuneration,Eli Lilly and CompanyC Zielinski,.,Consultant or Advisory Role,Eli Lilly and Company

**ORAL PRESENTATION
SUNDAY, MAY 31, 9:30 AM EDT
LEVEL 2, WEST HALL E1
LUNG CANCER, METASTATIC**

**Lead Author: Vincent A. Miller, MD
Memorial Sloan-Kettering Cancer Center
New York, N.Y.**

**Adding Erlotinib to Bevacizumab Maintenance Therapy in Patients
with Advanced Non-Small Cell Lung Cancer Improves Outcomes**

An international team of researchers has shown that adding erlotinib (Tarceva) to bevacizumab (Avastin) maintenance therapy after initial treatment with chemotherapy and bevacizumab in patients with advanced non-small cell lung cancer delays disease progression better than bevacizumab alone.

“There is ongoing interest among medical oncologists about the potential role of maintenance therapy for patients with advanced non-small cell lung cancer,” said Vincent A. Miller, MD, Associate Attending Physician on the Thoracic Oncology Service at Memorial Sloan-Kettering Cancer Center and lead author of the study, known as ATLAS. “Bevacizumab is a core component of the treatment of advanced non-small cell lung cancer (NSCLC), and we’ve shown here we can delay progression with the addition of a targeted agent, erlotinib. Critical future work will try to determine which patients will get the greatest benefit from this combination, based in large part on the identification of genetic biomarkers.”

Maintenance therapy, a relatively new concept in NSCLC, refers to the continuation of one or more agents of a chemotherapy regimen but not the whole regimen to delay progression of disease and potentially improve survival after patients have received several months of stronger standard chemotherapy, which can carry significant side effects. This is the first study to show that adding erlotinib to maintenance therapy with bevacizumab delays disease progression in patients who have already received bevacizumab as part of their initial chemotherapy. Both bevacizumab and erlotinib have fewer side effects than traditional cytotoxic chemotherapy.

Previous research has shown that bevacizumab along with chemotherapy improved progression-free and overall survival among patients with advanced, metastatic, or recurrent non-squamous NSCLC when compared to chemotherapy alone. In that study, bevacizumab was continued after chemotherapy until disease progression. The purpose of the current study was to determine if progression could be further delayed by the addition of erlotinib.

In this randomized, double-blind, phase III trial, 768 patients were randomized to receive bevacizumab plus erlotinib or bevacizumab plus placebo. All patients had already received four cycles of chemotherapy and bevacizumab as first-line therapy. Patients who had not progressed then continued bevacizumab and were blinded and randomized to receive placebo or erlotinib.

This study reports the results of the trial’s second planned interim analysis of the data, which identified a statistically significant improvement in efficacy, favoring the erlotinib group; the trial was stopped early based on these findings. Patients in the erlotinib group experienced a 29 percent reduced risk of disease progression. Median progression-free survival (the time it took for the cancer to get worse) was 4.8 months for patients in the erlotinib plus bevacizumab group, compared with 3.7 months for patients in the bevacizumab-placebo group. There were no unexpected side effects in either arm.

LBA8002

A randomized, double blind, placebo controlled, Phase IIIb trial (ATLAS) comparing bevacizumab (B) therapy with or without erlotinib (E) after completion of chemotherapy with B for 1st - line treatment of locally advanced, recurrent, or metastatic non - small cell lung cancer (NSCLC)

V. A. Miller, P. O'Connor, C. Soh, F. Kabbinavar, for the ATLAS investigators

Background: B when added to chemotherapy, and E alone, each lead to improved survival in the treatment of patients (pts) with NSCLC (Sandler et al, NEJM 2006, 355:2542 - 2550; Shepherd et al, NEJM 2005, 353:123 - 132). Pre - clinical and clinical data (Herbst, J Clin Oncol 2007, 25: 4743 - 4750) suggest that the combination of B and E may improve the efficacy of NSCLC treatment. This potential was demonstrated in the BETA (B in combination with E compared with E alone for treatment of advanced NSCLC after failure of standard first - line chemotherapy) trial, a phase III trial in which progression free survival (PFS) was improved for patients treated with B + E (Hainsworth, Thoracic Oncol 2008, 3(11) Supp. 4:S302). **Methods:** The ATLAS study was designed to evaluate B + E (150 mg daily) versus B alone, following B + platin - containing doublet chemotherapy, in pts with stage IIIb/IV NSCLC. Enrolled pts were B - eligible, including pts with treated brain metastases, and pts anticoagulated with low molecular weight heparin(s). Pts with peripheral and/or

extra - thoracic squamous tumors were also eligible. Pts received 4 cycles of B (15 mg/kg every 3 weeks) with chemotherapy. Pts who had not experienced disease progression (DP) or significant toxicity were then randomized to receive B + E or B + placebo (P). The primary objective of ATLAS was to compare PFS in pts receiving B + E versus B + placebo. Secondary objectives included the assessment of safety, and overall survival. A data safety monitoring committee (DSMC) monitored safety and efficacy. **Results:** 1160 patients were enrolled and 768 randomized from May, 2005 to May, 2008. The DSMC recommended stopping the trial at the 2nd planned interim efficacy analysis, because it met the primary endpoint. The median PFS after randomization was 4.8 mos for (B + E) vs. 3.7 mos for (B + P), HR= 0.722 (95% CI: 0.592 - 0.881), p = 0.0012. The safety profile for B + E was consistent with known profiles for B and E. **Conclusions:** E added to B treatment after chemotherapy with B significantly improves the PFS of patients treated in the 1st - line setting for locally - advanced, recurrent, or metastatic NSCLC.

Disclosures: Vincent Miller,,Honoraria,Genentech, Inc.Paula O'Connor,,Employment or Leadership Position,Genentech, Inc.Paula O'Connor,,Stock Ownership,Genentech, Inc.Chang-Heok Soh,,Stock Ownership,Genentech, Inc.Chang-Heok Soh,,Employment or Leadership Position,Genentech, Inc.Fairooz Kabbinar, for the ATLAS Investigators,,Honoraria,Genentech, Inc.

**ORAL PRESENTATION
SATURDAY, MAY 30, 3:00 PM EDT
LEVEL 2, W203C
CANCER PREVENTION**

**Lead Author: Rowan T. Chlebowski, MD, PhD
Harbor-UCLA Medical Center
Los Angeles, Calif.**

Menopausal Hormone Therapy with Estrogen and Progestin Linked to Increased Risk of Death from Non-Small Cell Lung Cancer

Researchers have shown that use of hormone therapy with estrogen plus progestin increases the risk of dying from non-small cell lung cancer (NSCLC) in women with the disease. Lung cancer is the leading cause of cancer death in U.S. women.

These findings are based on secondary analyses from the Women's Health Initiative, a randomized, placebo-controlled clinical trial evaluating the health effects of conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA) in 16,608 mostly healthy postmenopausal women.

Previous research suggested that hormones play a role in non-small cell lung cancer because women tend to have higher survival rates than men and respond better to certain therapies. However, this is the first study to examine a specific correlation in a randomized clinical trial setting.

"Many women entering menopause have symptoms that make them consider hormone therapy," said Rowan Chlebowski, MD, PhD, a medical oncologist at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center and the study's lead author. "We already know that combined hormone therapy has more risks than benefits, including a higher risk of stroke and breast cancer, the most common cancer in U.S. women. The link we describe between hormone therapy with CEE plus MPA and death from non-small cell lung cancer should influence discussions between physicians and women considering hormone therapy use, especially for those with a smoking history."

This study looked at non-small cell lung cancer incidence and mortality during 5.6 years of intervention with hormone therapy or placebo and 2.4 years of additional follow-up. While there was no significant difference in NSCLC incidence between the two randomized groups, mortality after a NSCLC diagnosis was significantly higher in the combined hormone therapy group: women in the hormone therapy group were 61 percent more likely to die from non-small cell lung cancer than women in the placebo group (67 versus 39 deaths, respectively).

The researchers noted that the magnitude of the mortality risk of CEE plus MPA use in current smokers raises particular concerns. The researchers report that one in 100 current smokers in the trial using combined hormone therapy experienced an avoidable death from non-cell lung cancer during the eight years of this study. The mortality rate was 3.4 percent among smokers in the hormone therapy group, versus 2.3 percent among smokers in the placebo group over the 7.9 year study period.

Researchers noted that study strengths include the randomized, double-blind study design and the large, ethnically diverse population; limitations include the secondary nature of the analyses as these findings were not a primary objective of the trial. The researchers suspect their finding will prompt reconsideration of the risk-to-benefit balance of combined hormone therapy use for menopause symptoms and prompt further studies, both preclinical and clinical, on hormonal effects in NSCLC.

CRA1500

Non-small cell lung cancer and estrogen plus progestin use in postmenopausal women in the Women's Health Initiative randomized clinical trial

R. T. Chlebowski, A. Schwartz, H. Wakelee, G. L. Anderson, M. L. Stefanick, J. E. Manson, J. W. Chien, C. Chen, J. Wactawski-Wende, M. Gass, For the Women's Health Initiative Investigators

Background: Sex differences in lung cancer outcome suggest a potential hormonal influence; however, observational studies provide mixed findings regarding menopausal hormone therapy (HT) and lung cancer. **Methods:** Secondary analyses of the WHI randomized, placebo-controlled trial of daily conjugated equine estrogen (CEE, 0.625 mg) plus medroxyprogesterone acetate (MPA, 2.5 mg) in 16,608 multi-ethnic postmenopausal women, aged 50-79 were conducted on lung cancer incidence and mortality. Lung cancers were confirmed by medical record review. **Results:** Groups were balanced for age,

race/ethnicity, and prior HT. Smoking status was also comparable (never 50%, past 40%, current 10% in both groups). Cumulative risk for lung cancer was highest in current (0.51%), compared to past (0.14%) and never (0.04%) smokers. After 5.6 years on trial intervention and 2.4 years additional follow-up (median), small cell lung cancer incidence was comparable between randomization groups (total n=26), as was subsequent small cell lung cancer mortality. Although a trend for more non-small cell lung cancer (NSCLC) diagnoses in the active hormone group was not significant (p=0.12), an apparent divergence emerged after five years, with more diagnoses in the CEE+MPA group. In addition, mortality after NSCLC diagnosis was significantly higher for the CEE+MPA group (46.3% vs 27.0%, respectively, hazard ratio (HR) 1.59, 95% CI 1.03-2.46, p=0.04). As a result, CEE+MPA group women were more likely to die from NSCLC than those on placebo (p=0.02). **Conclusion:** Use of CEE + MPA for over 5 years increases a woman's risk for NSCLC mortality, the leading cause of cancer death in women. These data, together with recent results indicating higher breast cancer risk (*Cancer Res* 2009;69(2):78s), suggest cancer impact should influence risk-to-benefit consideration for combined HT use.

NSCLC outcomes (annualized %) by randomization group

| | CEE+MPA | | Placebo | | HR | 95% CI | P-Value |
|------------------|---------|-------|---------|-------|------|------------|---------|
| | N | % | N | % | | | |
| NSCLC Incidence | 96 | 0.14% | 72 | 0.11% | 1.28 | 0.94, 1.73 | 0.12 |
| NSCLC Mortality* | 67 | 0.10% | 39 | 0.06% | 1.61 | 1.09-2.39 | 0.02 |

* Analyses begins at entry randomization

Disclosures: Rowan Chlebowski,,Consultant or Advisory Role,AmgenRowan Chlebowski,,Honoraria,Eli LillyRowan Chlebowski,,Consultant or Advisory Role,WyethRowan Chlebowski,,Consultant or Advisory Role,Eli LillyRowan Chlebowski,,Honoraria,AmgenRowan Chlebowski,,Honoraria,AstraZenecaRowan Chlebowski,,Honoraria,WyethRowan Chlebowski,,Honoraria,NovartisRowan Chlebowski,,Consultant or Advisory Role,NovartisRowan Chlebowski,,Research Funding,AmgenRowan Chlebowski,,Consultant or Advisory Role,AstraZenecaChu Chen,,Honoraria,WyethChu Chen,,Honoraria,Wyeth

**ORAL PRESENTATION
SUNDAY, MAY 31, 10:00 AM EDT
LEVEL 2, WEST HALL E1
LUNG CANCER - METASTATIC**

**Lead Author: Roy S. Herbst, MD, PhD
M.D. Anderson Cancer Center
Houston, Texas**

Experimental Targeted Therapy Vandetanib Improves Progression-Free Survival in Patients with Advanced Non-Small Cell Lung Cancer

The results of an international trial have shown that adding the experimental targeted therapy vandetanib (Zactima) to docetaxel improves progression-free survival in patients with advanced non-small cell lung cancer (NSCLC) whose disease has progressed after first-line treatment. This is the first phase III study to show that adding a targeted therapy to second-line chemotherapy with docetaxel results in a clinical benefit for patients with advanced NSCLC. It is also the first phase III trial of vandetanib for NSCLC, which is being evaluated for certain types of thyroid cancer as well.

Vandetanib is a pill that targets two receptors already known to play a role in NSCLC – epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF). These receptors are targeted separately by other drugs, but vandetanib is the first drug to target both.

In this study, 1,391 patients who had previously been treated with chemotherapy were randomized to receive the docetaxel and vandetanib, or docetaxel and placebo. After a median follow-up of 12.8 months, patients in the vandetanib group had a 21 percent reduction in the risk of disease progression compared with patients in the placebo group. The median progression-free survival time was 17.3 weeks in the vandetanib arm versus 14 weeks in the control arm.

While there was no statistical difference in overall survival, a significant improvement in objective response rate was observed. Vandetanib treatment was also associated with an improvement in symptoms related to the underlying cancer and a 22 percent reduction in the risk that symptoms would worsen. For example, it took longer for patients in the vandetanib group to report that their disease symptoms, such as cough, weight loss, and difficulty breathing, had worsened.

Some side effects were more common in the vandetanib arm, including diarrhea (42 percent versus 33 percent in the placebo group), rash (42 percent versus 24 percent), and low white blood cell counts (32 percent versus 27 percent). Other side effects (nausea, vomiting, and anemia) were more common in the control group. About 22 percent of patients in the study discontinued vandetanib due to side effects, which is relatively low for a second-line therapy in advanced lung cancer.

“Clearly in a disease as heterogeneous as lung cancer the need to target multiple pathways has become clear – hence, this agent targeting two key pathways critical for NSCLC growth and metastasis is novel and could play a key role,” said Roy S. Herbst, MD, PhD, chief of thoracic medical oncology at the University of Texas M. D. Anderson Cancer Center and the study’s lead author. “The fact that more patients had an improvement in the symptoms from their lung cancer suggests that the drug could be important for the future management of this disease.”

CRA8003

Vandetanib plus docetaxel versus docetaxel as 2nd-line treatment for patients with advanced non-small-cell lung cancer (NSCLC): A randomized, double-blind phase III trial (ZODIAC)

R. S. Herbst, Y. Sun, S. Korfee, P. Germonpré, N. Saijo, C. Zhou, J. Wang, P. Langmuir, S. J. Kennedy, B. E. Johnson

Background: Vandetanib is a once-daily oral inhibitor of VEGFR, EGFR and RET signaling. Addition of vandetanib to docetaxel (doc) prolonged progression-free survival (PFS) in a randomized phase II study in patients (pts) with previously treated NSCLC (Heymach *et al*, JCO, 2007). **Methods:** The primary objective was to determine whether vandetanib 100 mg/day + doc 75 mg/m² every 21 days (max 6 cycles) prolonged PFS vs placebo + doc. Secondary endpoints included overall survival, objective response rate (ORR), time to deterioration of symptoms (TDS) and safety. Efficacy and safety in females were assessed as a co-primary analysis population. Eligibility criteria included stage IIIB/IV NSCLC, PS 0-1, and previous 1st-line chemotherapy. **Results:** Between May 06-Apr 08, 1391 pts (mean age, 58 years; 30% female; 25% squamous; 10% brain mets) were randomized to vandetanib + doc

(n=694) or placebo + doc (n=697). Baseline characteristics were similar in both arms. Median duration of follow-up was 12.8 months, with 87% patients progressed and 59% dead. Addition of vandetanib to doc showed a statistically significant improvement in PFS vs doc (hazard ratio [HR] 0.79, 97.58% CI 0.70-0.90; $P<0.001$), and a similar advantage in females (HR 0.79; $P=0.024$). Significant advantages for vandetanib + doc were also seen for ORR (17% vs 10%, $P<0.001$) and TDS (HR 0.78, $P=0.002$; FACT-L Lung Cancer Subscale). Overall survival showed a positive trend for vandetanib + doc that was not statistically significant (HR 0.91, 97.52% CI 0.78-1.07; $P=0.196$). The adverse event (AE) profile was consistent with that previously observed for vandetanib in NSCLC. Common AEs occurring more frequently in the vandetanib arm included diarrhea (42% vs 33%), rash (42% vs 24%) and neutropenia (32% vs 27%). Nausea (23% vs 32%), vomiting (16% vs 21%) and anemia (10% vs 15%) were less frequent in the vandetanib arm. The incidence of protocol-defined QTc prolongation was $<2\%$ in pts receiving vandetanib. **Conclusions:** The study met its primary objective of PFS prolongation with vandetanib + doc vs doc. Vandetanib is the first oral targeted therapy in phase III trials to show significant evidence of clinical benefit when added to standard chemotherapy in NSCLC.

Disclosures: Roy Herbst, Consultant or Advisory Role, AstraZeneca Oncology; Roy Herbst, Research Funding, AstraZeneca Oncology; Yan Sun, Research Funding, Wyeth; Paul Germonpré, Honoraria, AstraZeneca Oncology; Nagahiro Saijo, Stock Ownership, Takeda; Nagahiro Saijo, Research Funding, AstraZeneca Oncology; Nagahiro Saijo, Research Funding, Takeda; Nagahiro Saijo, Research Funding, Taiho; Nagahiro Saijo, Research Funding, Chugai; Peter Langmuir, Employment or Leadership Position, AstraZeneca Oncology; Sarah Kennedy, Employment or Leadership Position, AstraZeneca Oncology; Bruce Johnson, Consultant or Advisory Role, Genzyme; Bruce Johnson, Other Remuneration, Genzyme

Moderator Dr. Johnson made the following disclosures: Consultant or Advisory Role with Genzyme; Stock Ownership in Boston Scientific, Celgene and Johnson and Johnson; And royalty payments on a license to genzyme for doing EGFR mutation testing.

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

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