

VANDETANIB STUDY FACT SHEET: ZEAL

American Society of Clinical Oncology Meeting

Vandetanib plus pemetrexed vs pemetrexed as 2nd-line therapy in patients with advanced non-small-cell lung cancer (NSCLC): a randomized, double-blind phase III trial (ZEAL)

Presentation: Monday, June 1

ASCO Poster #8010

Display Time: 8 a.m. – 12 p.m.

Display Location: Level 3, W340A

Discussion Time: 11 a.m. – 12 p.m.

Display Location: Level 2, West Hall E2

Trial Design:	ZEAL (ZACTIMA [®] Efficacy with Alimta in Lung cancer) is a randomized, double-blind, placebo-controlled, phase III study evaluating the combination of vandetanib 100 mg with pemetrexed 500 mg/m ² given every 21 days (maximum 6 cycles) versus pemetrexed alone. ¹
Objectives:	<p><u>Primary objectives</u></p> <ul style="list-style-type: none">• Prolongation of progression-free survival <p><u>Secondary objectives</u></p> <ul style="list-style-type: none">• Overall survival• Objective response rate (RECIST-defined complete response, partial response or stable disease)• Time to deterioration of symptoms (FACT-L Lung Cancer Subscale)• Safety <p>Efficacy and safety were assessed in females as a co-primary analysis population</p>
Key Inclusion Criteria:	Patients with locally advanced (Stage IIIB/IV) non-small cell lung cancer (NSCLC) who received one prior chemotherapy and had a performance status between zero and two were eligible for the study.
Treatment Information:	Vandetanib (ZACTIMA [®]) is an investigational oral anti-cancer drug that that is directed at two clinically important mechanisms - blocking the development of tumor blood supply (anti-angiogenesis or anti-VEGFR) and blocking the growth and survival of the tumor (anti-EGFR).
Patient Characteristics:	<ul style="list-style-type: none">• The study involved 534 patients with a mean age of 59, who were randomized to receive vandetanib plus pemetrexed (n=256) or placebo plus pemetrexed (n=278); 38 percent of study participants were female• Twenty-one percent of patients had squamous cell carcinoma and 8 percent had brain metastases• Eighty-four percent of patients had Stage IV disease• Forty-one percent had a performance status of zero, 53 percent had a performance

	<p>status of 1 and 6 percent had a performance status of 2</p> <ul style="list-style-type: none"> • Median duration of follow-up was 9.0 months, with 83 percent patients progressed and 50 percent deceased
Results:	<ul style="list-style-type: none"> • While the study did not meet the primary endpoint of statistically significant progression-free prolongation versus pemetrexed alone , the combination of vandetanib plus pemetrexed demonstrated evidence of clinical benefit in patients with pretreated advanced NSCLC, <ul style="list-style-type: none"> ○ The combination of vandetanib plus pemetrexed showed positive trends for both progression-free survival (hazard ratio [HR] 0.86, 97.58% CI 0.69–1.06; P=0.108) and overall survival (HR 0.86, 97.54% CI 0.65–1.13; P=0.219); similar advantages were observed for the female co-primary analysis population ○ The vandetanib plus pemetrexed arm did achieve statistically significant advantages in objective response rate(19.1 percent vs. 7.9 percent, P<0.001) and time to deterioration of symptoms (HR 0.61, P=0.004) • The adverse event profile for vandetanib was consistent with previous vandetanib studies: <ul style="list-style-type: none"> • Common adverse events that occurred more frequently in the vandetanib arm included rash (38 percent vs. 26 percent), diarrhea (26 percent vs. 18 percent) and hypertension (12 percent vs. 3 percent) • Adverse events that occurred less frequently in the vandetanib arm included: anemia (8 percent vs. 22 percent), nausea (29 percent vs. 37 percent), vomiting (15 percent vs. 22 percent), fatigue (37 percent vs. 45 percent), and asthenia or weakness (11 percent vs. 17 percent) • The incidence of protocol defined QTc prolongation was less than one percent and there was no increase in bleeding or thrombotic events in the vandetanib arm
Investigators:	Richard H. de Boer, Óscar Arrieta, Maya Gottfried, Fiona H. Blackhall, Johann Raats, Chih-Hsin Yang, Peter Langmuir, Tsveta Milenkova, Jessica Read, and Johan Vansteenkiste

###

ⁱ De Boer, R. et al. Vandetanib plus pemetrexed vs pemetrexed as 2nd-line therapy in patients with advanced non-small-cell lung cancer (NSCLC): a randomized, double-blind phase III trial (ZEAL). ABS 31867, ASCO. 2009.