

VANDETANIB STUDY FACT SHEET: ZEST

American Society of Clinical Oncology Meeting

Vandetanib versus erlotinib in patients with advanced non-small-cell lung cancer (NSCLC) after failure of at least 1 prior cytotoxic chemotherapy: a randomized, double-blind phase III trial (ZEST)

Presentation: Monday, June 1

ASCO Poster #8009

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:	ZEST (ZACTIMA [®] Efficacy when Studied versus Tarceva) is a phase III randomized, double-blind, multicenter, placebo-controlled study to assess the efficacy of vandetanib 300 mg/day versus erlotinib 150 mg/day in patients with non-metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior anti-cancer therapy. ⁱ
Objectives:	<u>Primary objectives</u> <ul style="list-style-type: none">• Prolongation of progression-free survival <u>Secondary objectives</u> <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 (EORTC QoL Questionnaire)• Safety
Key Inclusion Criteria:	Patients with locally advanced or metastatic (Stage IIIB/IV) NSCLC who received one to two prior chemotherapy treatments and had a performance status between zero and two were eligible for the study.
Treatment Information:	Vandetanib (ZACTIMA [®]) is an oral anti-cancer drug 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 included 1,240 patients with a mean age of 61, who were randomized to receive vandetanib (n=623) or erlotinib (n=617) therapy; 38 percent of study participants were female and 22 percent had squamous cell carcinoma• Median duration of follow-up was 14 months, with 88 percent of patients progressed and 67 percent deceased
Results:	<ul style="list-style-type: none">• The study did not meet its primary objective of demonstrating progression-free survival prolongation with vandetanib versus erlotinib in patients with previously treated

	<p>advanced NSCLC; however, in a preplanned non-inferiority analysis vandetanib and erlotinib showed similar efficacy for progression-free survival and overall survival.</p> <ul style="list-style-type: none"> ○ There was no difference in progression-free survival for patients treated with vandetanib versus erlotinib (hazard ratio [HR] 0.98, 95.22% CI 0.87–1.10; P=0.721), and no difference in the secondary endpoints of overall survival (HR 1.01, 95.08% CI 0.89–1.16; P=0.830), overall response rate (both 12 percent) and time to deterioration of symptoms (pain: HR 0.92, P=0.289; dyspnea: HR 1.07, P=0.407; cough: HR 0.94, P=0.455) ● The adverse event profile for vandetanib was generally consistent with previous vandetanib 300 mg studies: <ul style="list-style-type: none"> ● Common adverse events (any grade) that occurred more frequently on the vandetanib arm included: diarrhea (50 percent vs. 38 percent) and hypertension (16 percent vs. 2 percent). Rash was more frequent on the erlotinib arm (50 percent vs. 40 percent) ● The vandetanib arm had a higher overall incidence of Common Terminology Criteria for Adverse Events (CTCAE) grade 3 and higher events than the erlotinib arm (50 percent vs. 40 percent) ● The incidence of protocol-defined QTc prolongation in the vandetanib arm was 5 percent
Investigators:	Ronald B. Natale, Sumitra Thongprasert, F. Anthony Greco, Michael Thomas, Cheun-Ming Tsai, Patrapim Sunpaweravong, David Ferry, Peter Langmuir, Jacqui A. Rowbottom, and Glenwood D. Goss

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ⁱ Natale, R. et al. Vandetanib versus erlotinib in patients with advanced non-small-cell lung cancer (NSCLC) after failure of at least 1 prior cytotoxic chemotherapy: a randomized, double-blind phase III trial (ZEST). ABS 31610. ASCO. 2009.