

VANDETANIB STUDY FACT SHEET: ZODIAC

American Society of Clinical Oncology Meeting

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

ORAL Presentation: Sunday, May 31 at 10 a.m.

Presentation #: CRA8003

Location: Level 2, West Hall E1

Discussant: Roy Herbst

Trial Design:	ZODIAC (ZACTIMA [®] in combination with Docetaxel in non-small cell lung Cancer) is a randomized, open-label, multicenter, phase III study evaluating the combination of vandetanib 100 mg with docetaxel at 75 mg/m ² every 21 days (for a maximum of 6 cycles) versus docetaxel 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 in females was assessed as a co-primary analysis population</p>
Treatment Information:	Vandetanib (ZACTIMA [®]) is an investigational 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).
Key Inclusion Criteria:	Patients with Stage IIIB/IV non-small cell lung cancer (NSCLC) who previously received 1 st -line chemotherapy treatment and had a performance status of zero or one.
Patient Characteristics:	<ul style="list-style-type: none">• The study involved 1,391 patients with a mean age of 58 (who were randomized to vandetanib plus docetaxel (n=694) or placebo plus docetaxel (n=697); 30 percent of study participants were female• Twenty-five percent of study patients had squamous-cell carcinoma and 10 percent of patients had brain metastases• Median duration of follow-up was 12.8 months with 87 percent of patients progressed and 59 percent deceased
Results:	<ul style="list-style-type: none">• The study met its primary objective of progression-free survival prolongation with vandetanib plus docetaxel versus docetaxel alone (hazard ratio [HR] 0.79, 97.58% CI

	<p>0.70–0.90; P<0.001), with a similar advantage in the female co-primary analysis population (HR 0.79; P=0.024).</p> <ul style="list-style-type: none"> • The vandetanib plus docetaxel arm had a median progression-free survival of 17.3 weeks vs. 14.0 weeks in the comparator arm. • The vandetanib plus docetaxel arm also had a significantly higher overall response rate than the comparator arm (17 percent vs. 10 percent, P<0.001) and demonstrated statistically significant advantages in terms of time to deterioration of symptoms (HR 0.78, P=0.002; FACT-L Lung Cancer Subscale). • Vandetanib plus docetaxel showed a positive trend for increased overall survival though the benefit was not statistically significant (HR 0.91, 97.52% CI 0.78–1.07; P=0.196). • The adverse event profile was consistent with that previously observed for vandetanib in NSCLC: <ul style="list-style-type: none"> ○ Common adverse events occurring more frequently in the vandetanib plus docetaxel arm included: diarrhea (42 percent vs. 33 percent), rash (42 percent vs. 24 percent) and neutropenia (32 percent vs. 27 percent). ○ Adverse events occurring less frequently in the vandetanib arm included: Nausea (23 percent vs. 32 percent), vomiting (16 percent vs. 21 percent) and anemia (10 percent vs. 15 percent). ○ The incidence of protocol-defined QTc prolongation was less than 2 percent in patients receiving vandetanib.
Investigators:	Roy S. Herbst, Yan Sun, Sönke Korfee, Paul Germonpré, Nagahiro Saijo, Caichun Zhou, Jie Wang, Peter Langmuir, Sarah J. Kennedy, and Bruce E. Johnson

###

ⁱ Herbst, R. et al. Vandetanib plus docetaxel vs docetaxel as 2nd-line treatment for patients with advanced non small-cell lung cancer (NSCLC): a randomized, double-blind phase III trial (ZODIAC). ABS 31495. ASCO. 2009.