SYNOPSIS OF RESEARCH REPORT [redacted] (PROTOCOL BO18279)

COMPANY: NAME OF FINISHED PRODUCT: NAME OF ACTIVE SUBSTANCE(S):	(FOR NATIONAL AUTHORITY USE ONLY)

TITLE OF THE STUDY / REPORT No. / DATE OF REPORT	Final CSR: MERIT – A Phase II Marker Identification Trial for Tarceva in Second Line NSCLC Patients / Report no. [redacted] / December 2012 This CSR focuses on data from cut-off for the primary analysis (Dec 1, 2006) through to last patient last visit.		
INVESTIGATORS / CENTERS AND COUNTRIES	This study was conducted in 26 sites in 12 countries: Germany, Hong Kong, Poland, Spain, Taiwan, Bulgaria, Italy, United Kingdom, France, Russia, Singapore and Estonia.		
PUBLICATION (REFERENCE)	Tan et al. Ann Oncol. 2010;21:217-22.		
PERIOD OF TRIAL	July 29, 2005 – June 9, 2009 (last patient, last visit)	CLINICAL PHASE	II
OBJECTIVES	The primary objective was the identification of differentially expressed genes that are predictive for benefit of erlotinib treatment. The secondary objective was to assess alterations in the epidermal growth factor receptor (EGFR) signaling pathways with respect to benefit from treatment. This final CSR focuses on efficacy data and safety data from cut-off for the primary analysis through to end of study.		
STUDY DESIGN	An open label, non-randomized phase II study		
NUMBER OF SUBJECTS	264		
DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION	Patients with histologically documented advanced non-small cell lung cancer (NSCLC), with performance status 0-2, who had failed at least one course of standard chemotherapy or were unsuitable for chemotherapy, and whose tumor was accessible to biopsy by bronchoscopy.		
TRIAL DRUG / STROKE (BATCH) No.	Erlotinib 150 mg: [redacted] Erlotinib 100 mg: [redacted] Erlotinib 25 mg: [redacted]		
DOSE / ROUTE / REGIMEN / DURATION	Erlotinib 150 mg, once daily, by mouth		

CRITERIA FOR EVALUATION	
POTENTIALLY PREDICTIVE MARKERS	• Assessment of gene expression profiles in tumor tissue and normal cells • Gene mutation analysis for EGFR and other molecules involved in EGFR signal transduction • Other marker assessments that may correspond with erlotinib efficacy (Results presented in the primary CSR)
EFFICACY:	• Overall response and clinical benefit rates assessed by using RECIST criteria • Time to progression (TTP), progression-free survival (PFS) and overall survival
SAFETY:	• Adverse events and serious adverse events • Laboratory tests
STATISTICAL METHODS	Descriptive statistics were used to analyze the safety and efficacy data presented in this final CSR.

METHODOLOGY

This was an open-label, single-arm predictive marker identification Phase II study conducted in 26 sites in 12 countries. Erlotinib was administered orally at a dose of 150 mg/day (with dose reductions allowed based on tolerability to drug therapy). Clinical and laboratory parameters were assessed to evaluate disease control and toxicity. Treatment continued until disease progression, unacceptable toxicity or death.

EFFICACY RESULTS

Although there were small changes in the number of responders with follow-up through to the end of study (see table below), the number of patients with clinical benefit—the primary outcome measure—remained the same.

Response and Clinical Benefit at Cut-off for the Primary Analysis and at Study End

	Primary Cut-off (N=264) n (%, 95% CI)	End of Study (N=264) n (%, 95% CI)
Responders	36 (13.6%; 9.7%-18.4%)	40 (15.2%; 11.1%-20.1%)
Complete response	0 (0%; 0.0%-1.4%)	0 (0%; 0.0%-1.4%)
Partial response	36 (13.6%; (9.7%-18.4%)	40 (15.2%; 11.1%-20.1%)
Stable disease	80 (30.3%; 24.8%-36.2%)	76 (28.8%; 23.4%-34.7%)
Progressive disease	116 (43.9%; 37.9%-50.2%)	118 (44.7%; 38.6%-50.9%)
Clinical benefit[a]	83 (31.4%; 25.9%-37.4%)	83 (31.4%; 25.9%-37.4%)

[a] Complete response, partial response or stable disease for at least 12 weeks after study entry

At cut-off for the primary analysis, 213 patients (80.7%) had progressed or died and 140 patients (53.0%) had died. By the end of study, 252 (95.5%) had progressed or died and 224 (84.8%) had died. The median PFS of 11.4 months was almost the same as the PFS reported in the primary CSR (11.3 months). Likewise, the median OS of 7.8 months was almost the same as the OS reported in the primary CSR (7.6 months).

Thirty-six patients were included in the duration of response analysis at cut-off for the primary analysis compared to 40 patients at the end of study. In the end-of-study analysis, the median duration of response extended to 41.9 weeks at the end of study compared to 32.1 weeks at cut-off for the primary analysis. Four patients still had response at the end of study.

SAFETY RESULTS

An additional 98 AEs were reported after cut-off for the primary analysis. There were 87 deaths after cut-off for the primary analysis; all but one of these deaths was considered due to disease progression. An additional 5 serious AEs occurred after cut-off for the primary analysis. Only one of these events, gait disturbance, was considered treatment-related. This event was also the only event after cut-off for the primary analysis that led to treatment discontinuation.

CONCLUSIONS

The original conclusions of the primary analysis were unaffected by the extended follow-up through to the end of study, either in terms of efficacy or safety.