ERLOTINIB IN >1,200 E/SE ASIAN PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER (NSCLC): FINAL RESULTS OF THE TRUST STUDY

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Introduction: Erlotinib, a potent orally active agent that inhibits the tyrosine-kinase domain of the human epidermal growth factor receptor (EGFR), has been shown to prolong survival versus best supportive care (BSC) in patients with pre-treated advanced NSCLC (Shepherd et al, 2005). The global, open-label, phase IV TRUST study was initiated to allow access to erlotinib for eligible patients in countries where it was not yet licensed. The main objectives of the study were to evaluate the safety and efficacy of erlotinib in a large, broad patient population, equivalent to that found in everyday clinical practice.

Methods: Patients who had failed to respond or who had relapsed following previous treatment with chemotherapy or radiotherapy, or those considered unsuitable to receive those treatments, were eligible to receive oral erlotinib (150mg/day) until disease progression, unacceptable toxicity or death. Dose interruption or reduction (in 50mg decrements) was permitted in the event of treatment-related adverse events (AEs). Data were gathered on AEs, serious AEs, dose reductions and withdrawals, incidence of rash, best response, progression-free survival (PFS), 1-year survival and overall survival (OS).

Results: Data are presented for the 1,242 E/SE Asian patients in the intent-to-treat (ITT) population of the TRUST study. These patients were enrolled from seven countries: mainland China (n=519); Taiwan (n=300); South Korea (n=201); Hong Kong (n=179); Thailand (n=30); Indonesia (n=8) and Malaysia (n=5). In this subpopulation, 111 patients (9%) received erlotinib as first line, 704 (57%) as second line, 420 (34%) as third line and seven patients (<1%) as fourth or later line of therapy. Seventy percent of this subpopulation had adenocarcinoma; 18% had squamous-cell carcinoma; 45% were current/former smokers; 54% were male. Seventeen percent of patients experienced one or more erlotinib-related AEs (other than the 15 most frequently occurring AEs pre-specified in the protocol); only 2% of patients experienced an erlotinib-related serious AE. Dose reductions were carried out in 171 patients (14%) and 32 patients (3%) withdrew due to treatment-related AEs. Eighty-two percent of E/SE Asian patients developed erlotinib-related rash, but the majority of cases (88%) were grade 1/2. ILD has previously been observed with EGFR inhibitor therapy in Asian patients, but this AE occurred in only 2 patients (<1%) in this study population. One ILD case (grade 2) resolved spontaneously while the other (grade 4) did not improve despite withdrawal of treatment; this patient subsequently had respiratory failure and died. Best response data were available

Efficacy outcome*	E/SE Asian population	Non-E/SE Asian population
Overall response rate (ORR)	27%	10%
Disease control rate (DCR = CR + PR + SD)	78%	66%
PFS	5.8 mos	2.9 mos
OS	14.7 mos	6.8 mos
1-year survival	58.3%	32.7%

*Note that patient numbers may vary for each analysis based on information available from CRFs

for 1,118 patients, with a reported overall response rate of 27% and a disease control rate of 78%. Median PFS was 5.8 months for the E/SE Asian population (n=1,242; 95% CI: 5.39-6.57), compared with 2.9 months (n=5,338; 95% CI: 2.79-3.02) for the non-Asian TRUST population. The 1-year survival rate was 58.3% for the E/SE Asian population, compared with 32.7% for the non-Asian population, and median OS was 14.7 months versus 6.8 months, respectively.

Conclusions: Erlotinib was well tolerated in E/SE Asian patients in the TRUST study, with no new safety signals reported. Impressive survival results were seen with erlotinib in this patient population, which may be explained by the higher incidence of EGFR mutations.