KOREA study

Open Label, Multicenter, Real World Treatment Study of Single Agent Tagrisso for Patients with Locally Advanced/Metastatic Epidermal Growth Factor Receptor (EGFR) T790M Mutation-Positive Non-Small Cell Lung Cancer (NSCLC), Who Have Been Previously Treated with EGFR tyrosine kinase receptor (TKI) therapy;

Milestones:	Date of Fist Subject In: 29 Sep 2016 Date of Last Subject Last Visit: 19 Mar 2020
Phase of development:	Not Applicable – Observational study
Sponsor:	AstraZeneca Korea Ltd.

Background/rationale:

This study was conducted to investigate the occurrence and frequency of AEs·adverse drug reactions (ADRs), unexpected AEs·ADRs and serious AEs·ADRs (SAEs·SADRs) in a real world setting and look into factors that might affect safety and effectiveness, in the patients who are eligible for, or on active study drug treatment according to the approved prescribing information; patients with locally advanced or metastatic, epidermal growth factor receptor (EGFR) T790M mutation-positive NSCLC, who have been previously treated with EGFR tyrosine kinase receptor (TKI) therapy in Korea**.**

Objectives:

The objectives of this study are to assess the safety and efficacy of single agent Tagrisso (Osimertinib, hereinafter “the study drug”) in a real world setting in patients with locally advanced or metastatic, epidermal growth factor receptor (EGFR) T790M mutation-positive Non-Small Cell Lung Cancer (NSCLC), who have been previously treated with EGFR tyrosine kinase receptor (TKI) therapy.

Study design:

This will be an open-label, single-arm, multicenter, real world treatment study.

Data source:

The sources of information for all study variables collected for this study will be patient medical records or charts and patients surveys. All data collected will be entered by the investigator into a CRF.

Study population:

The sample size is at least 300. In principle, all patients treated with study drug in accordance with local prescribing information are eligible for enrolment in this study and can be recruited for at least 2 years from marketing approval. Subjects will be followed until disease progression, withdrawal of consent, loss to follow-up, or death, whichever comes first, for up to one year since the first dose of the study drug. The study period may extend to enrol at least 300 patients to detect AEs which occur with an incidence of at least 1% based on binomial probabilities.

Inclusion criteria:

1. Eligible for, or on active study drug treatment according to the approved label; patients with locally advanced or metastatic, EGFR T790M mutation-positive NSCLC, who have been previously treated with EGFR tyrosine kinase inhibitor (TKI) therapy

2. Provision of signed and dated written informed consent by the patient or legally acceptable representative

Exclusion criteria:

1. History of hypersensitivity to excipients of the study drug or to drugs with a similar chemical structure or class to the study drug

2. Pregnancy and/or breast feeding

3. Current participation in any interventional trial

Statistical methods:

All data will be presented for the overall full analysis set, and also by pre-defined subgroups. Descriptive statistics will be used for all variables, as appropriate. Continuous variables will be summarised by the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarised by frequency counts and percentages for each category. The objective response rate (ORR) will be calculated with the exact 95% confidence interval (CI). Progression-free survival (PFS) will be summarized using Kaplan-Meier estimates of the median time to progression or death or censoring and quartiles together with their 95% CIs.

Results:

Safety Result

In this study, the incidence proportion of AEs were investigated by demographic informa tion (sex and age), confirmation of T790M mutation (Mutation status of EGFR), characte ristics of NSCLC (disease duration and tumor histology), cancer treatment history (anti-c ancer agent, radiation therapy, and surgery), medical history, concomitant medication, , a nd study drug administration status (starting dosage and total administration period), and by special subjdects including pediatrics, geriatrics, subjects with renal or hepatic impair ment, and long-term users.

The investigation revealed that the difference in the incidence proportion of AEs accordi ng to 1 factor of administration/non-administration of concomitant medication (p=0.002) was statistically significant. Subjects with concomitant medications had a tendancy to ha ve higher incidence proportions of AEs than those without concomitant medications.

Logistic regression was not performed, because only 1 factor was statistically significant.

Effectiveness Result

In this study, the ORR was investigated by demographic information (sex and age), conf irmation of T790M mutation (Mutation status of EGFR), characteristic of NSCLC (diseas e duration and tumor histology), cancer treatment history (anti-cancer agent, radiation the rapy, and surgery), medical history, concomitant medication, study drug administration st atus (starting dosage and total administration period), and by special subjdects including pediatrics, geriatrics, subjects with renal or hepatic impairment, and long-term users.

The investigation revealed that the difference in the ORR according to 2 factors of total administration period of the study drug and long-term user were statistically significant ($p<0.0001$, respectively). The longer the administration period, the higher the ORR tende d to be, and the ORR was higher in long-term users.

Logistic regression was not performed, long-term users had a total administration period of 6 months or more, it could be judged that the results were the same.

Conclusion:

In conclusion, no specific issues that may affect the safety and the effectiveness of the s tudy drug were found in the Real world Evidence study. Administration/non-administrati on of concomitant medication in the safety analysis and total administration period of th e study drug in the response analysis were statistically significant, but not factors to affe ct the safety or the effectiveness. And it was confirmed that there's no major differences in safety and effectiveness from the latest information of approved label/package insert i n Korea. The incidence of AEs and their causal relationship will be continuously monito red in spontaneous reports and literature to identify the unexpected ADRs and serious A DRs.