AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: N/A
ACTIVE INGREDIENT: N/A

Study No: NIS-OTH-IRE-2009/1
Management of Advanced non-Small Cell Lung Cancer and Clinical Outcomes in Patients who Received Gefitinib (Iressa) in Tertiary Care Setting in Thailand

Developmental Phase: NIS
Study Completion Date: 3 August 2010
Date of Report: 23 November 2010

OBJECTIVES:

To determine the progression free survival of advanced NSCLC patients who received gefitinib as part of their clinical management. Other objectives were to describe clinical practice outcomes from advanced NSCLC treatment, pattern of care, and analysis for the clinical prognostic factors.

METHODS:

This is a retrospective cohort study. Patients from two tertiary hospitals were included if they had been treated with gefitinib for at least 3 months and was not as a part of any clinical study. Kaplan-Meier method was used to estimate median time to progression-free duration and overall survival. Cox regression was used to determine prognostic factors of the disease progression.

RESULTS:

A total of 205 patients with lung cancer were screened, 101 were excluded per inclusion and exclusion criteria. A total of 104 patients were enrolled and analyzed. On average, patients were 61±8 years old when they were diagnosed having NSCLC. Almost three quarters, 72.3%, were females and 84.5% had never smoked. Tumor histology of the patients was predominantly adenocarcinoma, 84.5%. More than half of them, 55.7%, had TNM stage 4. Based on 99 patients whose follow-up period can be determined, the total duration of the period was 12,713.6 months. Mean period of follow-up was 42.8±23.2 months. There were 3 major sites of metastasis – 38.5% was bone, 31.7% was lung, and 30.8% was pleura. Upon diagnosis, about two thirds, 67.9%, of them had WHO performance status of 1 – the patients cannot carry out heavy physical work, but can do anything else.

There are a total of 304 therapeutic lines undergone to the 104 patients. About 9 out of 104 patients received up to the 5th line chemotherapy. On average, duration under each therapeutic line was 6.7±10.1 months. The mean duration of treatment with gefitinib was 12.5±12.8 months. Although all patients received gefitinib at least one therapeutic lines,

they also received other regimens in other therapeutic lines which includes mainly platinum/gemcitabine (25.3%), followed by pemetrexed (11.8%), docetaxel (9.9%), and platinum/paclitaxel (8.9%).

Of 304 treatment lines provided to the 104 patients, there was 2,398.6 months duration of the treatment. Of the 304 lines of chemotherapy, 34.2% received gefitinib. Gefitinib was mainly used as the 2nd and the 3rd line therapy for 46.4% and 57.5%, respectively. Based on an assessment for the maximum responses, there was only one, 0.4%, complete response. Clinical benefit defined by complete responses, partial responses, or stable disease, achieved in 64.5% of all therapeutic lines where gefitinib yielded a highest (82.7%) benefit. More than half, 58.4%, had stable disease.

Among a total of 283 therapeutic lines with availability of information on progression free duration, the total treatment duration was 2,398.6 months. There were 198 disease progression occurred. Overall progression-free median survival was 12.10 (95% CI: 11.18 to 13.44) months after starting the treatments. Therapeutic lines that involved gefitinib had a significantly longer time to progression than those that used other regimens (Log-rank test p-value < 0.001), with median survival time of 16.6 (95%CI: 13.4 to 22.0) and 9.9 (95%CI: 8.5 to 11.9), respectively. Figure 4 displays progression free survival according to lines of gefitinib used, omitting the 4th line therapy due to small sample. The early therapeutic lines had a slightly better progression-free survival than the late one but there was no statistically significance (Log-rank test p-value = 0.384).

This section investigated effects of selected factors on disease progression among a total of 104 patients under 304 therapeutic lines using any treatment regimens where there were 198 (65.1%) therapeutic lines yielded disease progression. Univariate cox regression model indicated that significant predictors of progression include longer duration of smoking (p-value = 0.006), longer duration under treatments (p-value < 0.001), and not used gefitinib (p-value < 0.001). That is, for example, the disease progression increased by 88% in therapeutic lines that used other regimens rather than gefitinib (HR = 1.88; 95%CI: 1.40 to 2.52).

Multivariable cox regression model indicated that, there were 3 significant predictors of the disease progression – used other regimens rather than gefitinib, longer duration of smoking, and metastasis to the liver. The disease progression increased by 83% in therapeutic lines that used other regimens rather than gefitinib (HR = 1.83; 95%CI: 1.28 to 2.61). Other predictors of the disease progression included increasing duration of smoking for every 5 years (HR = 1.15; 95%CI: 1.04 to 1.28; p=0.008), and metastasis to the liver (HR = 2.10; 95%CI: 1.13 to 3.88; p=0.019). It is interesting to note that treatment with gefitinib as 2nd or 3rd line therapy yielded similar benefit in the study populations.

At the last follow-up, 44 (42.3%) patients were reported dead. Cause of death was mainly due to lung cancer (72.7%). Therefore the lung cancer death rate was 1.17 (95% CI: 0.80 to 1.65) per 100 person-years since birth. Five-year survivals and their 95%CIs were 59.9% (44.1 to 72.5) since diagnosis.