AstraZeneca

**STUDY REPORT SUMMARY**

**ASTRAZENECA PHARMACEUTICALS**

**FINISHED PRODUCT:** IRESSA
**ACTIVE INGREDIENT:** Gefitinib

| **Study No: 1839IL/0137** |
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| An open, randomised, non comparative phase II trial of docetaxel (Taxotere®) in combination with ZD1839 (IRESSA™) and docetaxel alone as second-line chemotherapy in patients with advanced or metastatic non-small cell lung cancer |

**Developmental phase:** II
**Study Completion Date: 08 April 2005**
**Date of Report:** 04 August 2008

## OBJECTIVES

The primary objective of the trial was to estimate the objective response rate (complete response [CR] and partial response [PR]) for docetaxel administered in combination with ZD1839 and docetaxel alone in patients with advanced or metastatic non-small cell lung cancer (NSCLC) using the Response Evaluation Criteria in Solid Tumors (RECIST).

The secondary objectives were:

Efficacy:

- To estimate disease control rate (CR, PR and stable disease [SD]) for each treatment arm
- To estimate progression-free survival (PFS) for each treatment arm
- To estimate overall survival for each treatment arm

Quality of life:

- To evaluate the patient's quality of life for each treatment arm using FACT-L questionnaire

Safety:

- To evaluate the safety and tolerability of the combination docetaxel and ZD1839 (treatment arm A) and docetaxel alone (treatment arm B)
- To further characterise the safety profile of ZD1839 at a 250 mg daily dose (treatment arm A only after docetaxel was discontinued)

## METHODS

A multicentre, open-label, randomised, two-arm, non-comparative phase II trial. Patients were randomised to receive docetaxel in combination with ZD1839 (treatment arm A) or docetaxel as a single agent (treatment arm B)

Duration of treatment:

Patients in both treatment arms received at least 6 cycles of docetaxel if obtaining clinical benefit. Docetaxel had to be stopped in case of disease progression, unacceptable toxicity or withdrawal of consent.

Patients in treatment arm A received ZD1839 daily in combination with docetaxel until disease progression, unacceptable toxicity or withdrawal of consent. ZD1839 may be continued as monotherapy after the end of the docetaxel treatment for patients who showed evidence of continuing response or clinical benefit, until disease progression, unacceptable toxicity or withdrawal of consent.

Stastistical methods:

All patients that were enrolled and received trial treatment were included into the intention-to-treat (ITT) population. The analysis population for all efficacy endpoints was the ITT population.

The standard summary statistics for continuous variables were mean, standard deviation, median, quartiles, maximum and minimum. The standard summary statistics for discrete variables were count and proportion. Response rates and controlled disease rates were summarised by proportions together with a 95% confidence interval (the objective response rate also had a 90% confidence interval calculated). Durations (of PFS and overall survival) were summarised by Kaplan-Meier methods.
Tolerability was summarised by the appropriate standard summary statistics. Quality of life was summarised by reporting subscale scores using the standard summary statistics for continuous variables.

There was no comparison between the two treatment arms.

## RESULTS

### Efficacy Results:

The analysis of the primary criteria gave consistent results with the literature. The overall best response to the study treatment was 6.8% and 9.1% of Partial Response in arms A and B respectively. However, these results did not show any positive effect of ZD1839 on the overall response rate when added to docetaxel.

The analysis of the secondary criteria showed that the proportion of patients with controlled disease at 6 months was slightly higher in arm A (ZD1839 + docetaxel) than in arm B (docetaxel alone), as well as the proportion of patients alive at 6 months. The proportion of patients alive at 6 months was estimated with the Kaplan-Meier method. In arm A, 61.4% (95% CI [47%; 75.8%]) of the patients were alive at 6 months, and they were 54.2% (95% CI [39.4%; 69%]) in arm B. The median overall survival was 232 days (95% CI [165; 357]) for arm-A patients and 188 days (95% CI [157; 220]) for arm-B patients.

The analysis of the Quality of Life showed that patients from arm A were often more numerous to express a worsening of the 3 scores compared to the patients from arm B. However, this tendency remained low during the study.

**Safety Results:**

During this study, there were more adverse events related to the study treatment and severe adverse events in arm A treated with Iressa™ + Taxotere® than in arm B treated with Taxotere®.

Indeed, more non-haematological AEs and more haematological grade 3-4 AEs were observed during the combination therapy. No difference was observed for biochemical toxicity between the 2 treatment arms.