AstraZeneca

SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: IRESSA

ACTIVE INGREDIENT: Gefitinib

Trial title: A randomised phase II study: Treatment with daily p.o. Iressa (ZD1839) or placebo in combination with weekly IV infusion of docetaxel in patients with metastatic breast cancer.

Developmental phase: II
First subject recruited: 01 August 2003
Last subject completed: 24 May 2006
Approval date: N/A

OBJECTIVES

Primary objective

The primary objective of the trial was to document the frequency of objective responses in measurable lesions by treatment with docetaxel (weekly intravenous infusions) and ZD1839 (250 mg daily per oral administration) in patients with metastatic breast cancer.

Secondary objective

- The characterization of the toxicity and the safety profile of the combined administration of both drugs.
- To estimate the time to progression.

Exploratory objectives

- To document the ER and PgR receptor status in addition to the erb-B1 and erb-B2 receptor status in patients included for treatment with the ZD1839/docetaxel combination, and to correlate these findings with the clinical responses in the patient.
- In patients where tumour material pre and post-treatment is available, investigate the apoptotic rate, the changes in vascularity and the expression of mediators of angiogenesis (VEGF and bFGF) present in the tumours before and after treatment.
- Investigate the response of the treatment on the presence of micrometastatic cells found in the bone marrow of the patient before and after treatment.

METHODS

Study design

Randomised double blind phase II placebo controlled protocol for first line treatment of patients with metastatic breast cancer. The patients will be randomised into treatment with ZD1839, 250 mg daily, and docetaxel 35 mg/m2 administered weekly for six of eight weeks, or placebo administered daily and docetaxel 35 mg/m2 administered weekly for six of eight weeks.

Target subject population

Patients with metastatic breast cancer, no previous taxane chemotherapy for metastatic breast cancer and more than one year since adjuvant or neoadjuvant administration of taxanes are eligible for the study. Patients must have measurable disease, according to RECIST to be included.

Investigational product, dosage and mode of administration

ZD1839 tablets 250mg. Daily per oral administration of ZD1839 250 mg or placebo during the whole treatment cycle.

Comparator, dosage and mode of administration

All patients will receive docetaxel 35 mg/m2 administered weekly for six weeks by IV infusion, followed by a two week treatment rest before the start of a new cycle.

Duration of treatment

Patients will continue the study medication until progression, DLT or until patient withdrawal of informed consent.

Outcome variables

The following endpoints have been evaluated in this study:

Efficacy

Primary outcome variable: Objective tumour response (CR + PR) per RECIST criteria

Secondary outcome variables:

- Time to progression
- Response duration

Exploratory:

- Objective tumour response in relation to ER, PgR, erb-B1 and erb-B2 receptor status and reduction in the number of malignant cells present in bone marrow
- Treatment mediated changes in the apoptosis, vascularity, and angiogenesis mediators and the nature, incidence and severity of adverse events

Safety

- Safety and tolerability of the combined administration of ZD1839 and docetaxel (Taxotere®).

RESULTS

The study was planned with the inclusion of 66 patients, 33 receiving gefitinib. Eleven of eighteen included patients progressed on the study medication, six receiving gefitinib and five control medication. The study was closed due to the relative large proportion of patients experiencing treatment related toxicity. Seven of the eighteen patients, three of which received gefitinib and four placebo medication, were taken out of the study due to toxicity. Six patients treated with gefitinib, but only two patients in the placebo control group were reported to have serious adverse events (SAE).

REFERENCE:

Citation: Abstract 1093 at SABCS 2006

As with any comprehensive clinical trial programme, individual studies may include both approved and non-approved treatment regimens, including doses higher than those approved for clinical use. Before prescribing Iressa™ (gefitinib), Healthcare Professionals should view their specific country information.