SUMMARY

ZENECA PHARMACEUTICALS
FINISHED PRODUCT: CASODEX™
ACTIVE INGREDIENT: Bicalutamide

Trial title (number): A Randomised, Double-blind, Parallel-group Trial Comparing CASODEX™ 150 mg Once Daily with Placebo in Patients with Non-metastatic Prostate Cancer (7054IL/0024).

Clinical phase: IIIb

First patient recruited: 21 September 1995
Last patient recruited: 27 July 1998
Data cut-off date: 1 June 1999
Zeneca approval date: 13 December 1999

Principal investigator and location (centre number): Professor MP Wirth, Universitätsklinikum, Dresden, Germany (Centre 601).

OBJECTIVES

Primary objectives: To compare CASODEX (bicalutamide) 150 mg once daily with placebo in terms of time to clinical progression in patients with non-metastatic prostate cancer.
To evaluate the tolerability of CASODEX 150 mg compared with placebo.
Secondary objectives: To compare CASODEX 150 mg once daily with placebo in terms of overall survival and time to treatment failure; to investigate the role of serum prostate-specific antigen (PSA) as a predictor of outcome.

METHODS

Design: This is a multicentre, randomised, double-blind, parallel-group trial comparing the effect of CASODEX 150 mg once daily with placebo in patients with non-metastatic (NX, M0) prostate cancer. Patients are assessed at a pre-treatment visit, for which a bone scan should have been performed within the preceding 12 weeks (later amended to 24 weeks). Eligible patients were randomised 1:1 to CASODEX 150 mg or placebo. Following randomisation, patients were assessed at 12-week intervals until clinical progression and thereafter every 12 weeks if the patient continued on randomised therapy, or every 24 weeks if randomised therapy was discontinued. All patients were followed-up until death. A minimum of 3500 patients were to be enrolled from approximately 180 centres throughout Europe, Israel, Mexico, South Africa, and Australia.

Population: At the data cut-off date (1 June 1999), a total of 3603 patients were randomised into the trial; 136 patients had died, 157 patients had disease progression, and 2537 patients were continuing with trial therapy.

Key inclusion criteria: Aged 18 years and above; diagnosed with non-distant metastatic adenocarcinoma of the prostate gland (T1b/T1c/T2/T3/T4, NX, M0).

Key exclusion criteria: Any previous systemic therapy for prostate cancer (other than neoadjuvant therapy prior to primary therapy of curative intent, or therapy with 5-alpha-reductase inhibitors); previous history or presence of other malignancy, other than treated squamous/basal cell carcinoma of the skin within the last 5 years; serum bilirubin, aspartate aminotransferase (AST), or alanine aminotransferase (ALT) concentrations >2.5 times the upper limit of normal; treatment with any new chemical entity within the previous 3 months.

Dosage: Patients received either oral CASODEX 150 mg/day or matching placebo. CASODEX was supplied as a white, intagliated tablet containing 150 mg of micronised drug (formulation number F11156; batch numbers 27088/95, 27120/95, 35395K96, 35396H96, 3638C96, 35394C96, 38159D96, 39829G96, 37074K97, 38474F97, 38825C97, 00041J98, 00040B98, 01390D98, 01413K98, 02911G98, 03568A98). Placebo was supplied as a matched white tablet (formulation number F11192; batch numbers 34563/94, 34562/94, 59397/93, 35403D96, 35398B96, 37053A96, 35904I96, 35905F96, 37119E96, 37120F96, 38941C96, 36898B97, 37121C96, 36896H97, 36895K97, 36897E97, 38280B97, 38277G97, 38279A97, 38278D97).

Key assessments:

Efficacy: The protocolled efficacy assessments included analysis of survival and disease progression. However, as this trial is currently ongoing, efficacy results have yet to be analysed and are therefore not presented in this report.

Safety: Safety was assessed by the recording of adverse events, routine laboratory tests, and physical examinations. Adverse events were presented both individually for each patient and summarised by Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) preferred term and primary body system. As the trial is still ongoing, the randomisation code has not been broken and so the safety results are presented for the whole patient population irrespective of randomised treatment.

RESULTS

Efficacy: On 1 June 1999, the data cut-off for this report, the trial was ongoing and the results had not been analysed; therefore, no efficacy data are presented at this time. All efficacy data collected will be fully presented in a final clinical trial report.

Safety: The most common adverse events reported were gynaecomastia and male breast pain, in 34.1% and 33.6% of all patients, respectively. Although the data are still blinded, these events can be predicted from the pharmacological effects of antiandrogens. These were also the most frequent adverse events leading to withdrawal from treatment, with gynaecomastia leading to withdrawal of 4.2% of patients and male breast pain to 4.7% of patients. Other adverse events were much less common and were widely distributed across the body systems.
