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 (SPCG-6) (7054IL/0025).

Clinical phase: IIIb

First patient recruited: 4 October 1995
Last patient recruited: 30 July 1998
Data cut-off date: 1 June 1999
Zeneca approval date: 13 December 1999

Publications: Wirth MP, See WA, McLeod DG, Iversen P, Klimberg I, Gleason D, et al. A clinical programme comparing bicalutamide (Casodex) 150 mg once daily with placebo in patients with non-metastatic prostate cancer: preliminary demographic data from 1 of the largest international early prostate cancer trials. European Urology 1998;33:136 (Abstract 541).

Wirth MP, See WA, McLeod DG, Iversen P, Klimberg I, Gleason D**,** et al. Bicalutamide (Casodex) Early Prostate Cancer (EPC) programme: final demographic data from over 8000 randomised patients. European Urology 1999;35:13 (Abstract 52).

OBJECTIVES

Primary objectives: To compare CASODEX (bicalutamide) 150 mg once daily with placebo in terms of overall survival and 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 time to treatment failure; to assess the time taken for prostate specific antigen (PSA) to double; to assess sexual function using the Golombok-Rusk Inventory of Sexual Satisfaction (GRISS) questionnaire.

CASODEX is a trademark, the property of Zeneca Limited.

METHODS

Design: This is a multicentre, randomised, double-blind, parallel-group trial comparing the effects 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 1000 patients were to be enrolled from centres throughout Scandinavia.

Population: At the data cut-off date (1 June 1999), a total of 1218 patients were randomised into the trial; 89 patients had died, 150 patients had disease progression, and 850 patients were continuing with trial therapy.

Key inclusion criteria: Aged 18 to 75 years; 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); patients for whom long-term therapy was considered inappropriate because of their expected survival time; previous history or presence of other malignancy, other than treated squamous/basal cell carcinoma of the skin within the last 10 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, 35394C96, 38159D96, 39829G96, 37074K97, 38494F97, 38825C97, 00041J98, 00040B98, 01413K98, 01390D98, 02911G98, 03568A98). Placebo was supplied as a matched white tablet (formulation number F11192; batch numbers 34562/94, 34563/94, 59397/93, 34558/94, 35403D96, 35398B96, 35904I96, 35905F96, 37119E96, 37053A96, 37120F96, 36898B97, 38941C96, 36896H97, 36895K97, 36897E97, 38277G97, 38280B97, 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 and routine laboratory tests. Adverse events were presented both individually for each patients 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 date for this report, the trial was ongoing and the efficacy data 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, reported by 25.0% and 31.1% of patients, respectively; both of these events led to the withdrawal of 1.3% of patients. Although the data are blinded, these effects can be predicted from the pharmacological effects of antiandrogens. The incidence of these events and the proportion of patients withdrawing from treatment as a result of these events appears comparable to that seen in other CASODEX 150 mg monotherapy trials. The incidence of other adverse events reported in this trial appears comparable with that reported previously, although definitive assessment of the adverse event profile of CASODEX 150 mg in this trial is not possible due its blinded nature.

The number of deaths due to adverse events was low with cardiovascular causes predominating as would be expected in this population of elderly males. A total of 115 (9.5%) patients withdrew because of adverse events. Approximately one-third of these withdrawals were due to just 4 events - gynaecomastia, male breast pain, nausea and liver function test abnormalities. The other events leading to withdrawal were widely distributed throughout the body systems.