SUMMARY

ZENECA PHARMACEUTICALS
FINISHED PRODUCT: CASODEX™
ACTIVE INGREDIENT: Bicalutamide

Trial title (number): A Randomised, Double-blind Comparative Trial of Bicalutamide (CASODEX™) versus Placebo in Patients with Early Prostate Cancer (7054IL/0023).

Clinical phase: IIIb

First patient recruited: 1 August 1995
Last patient recruited: 29 August 1997
Data cut-off: 1 June 1999
Zeneca approval date: 10 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 2 years of adjuvant CASODEX (bicalutamide) 150 mg monotherapy with placebo in terms of time to clinical progression and overall survival.
Secondary objectives: To compare 2 years of adjuvant CASODEX 150 mg monotherapy with placebo in terms of time to treatment failure; to investigate the association of serial measurement of serum prostate specific antigen (PSA) and treatment outcome following 2 years of adjuvant CASODEX therapy versus placebo; to evaluate the tolerability of 2 years of CASODEX 150 mg therapy versus placebo.

METHODS

Design: This is a multicentre, randomised, double-blind trial comparing the effect of CASODEX 150 mg monotherapy with placebo as adjuvant therapy in patients with non-metastatic (NX, M0) prostate cancer. Baseline assessments were performed before randomisation and included a bone scan (not more than 30 weeks before randomisation), physical examination (4 weeks), lymph node assessment (if required, 30 weeks), and PSA (4 weeks). Eligible patients were randomised 1:1 to CASODEX 150 mg or placebo. Following randomisation, patients were assessed at 12-week intervals up to and including Month 24. For the next 2 years visits were to be made at 6-month intervals up to and including Month 48 after which visits were to be made annually until death. A minimum of 3000 patients were to be randomised at North American centres.

Population: At the data cut-off date (1 June 1999), a total of 3292 patients had been randomised into the trial; 81 patients had died and 274 patients were still receiving treatment.

Key inclusion criteria: Patients, aged 18 years or older, with histologically confirmed adenocarcinoma of the prostate gland; clinical or pathological confirmation of stage T1b, T1c, T2, T3, or T4 prostate cancer; radical prostatectomy or radiation to the prostatic bed within the 16 weeks before randomisation; absence of metastatic disease confirmed within the 30 weeks before randomisation by assessment of skeletal metastases on bone scan and pelvic lymph nodes via laparotomy or laparoscopy with histological confirmation.

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 prostate cancer or treated squamous/basal cell carcinoma of the skin, within the last 5 years; serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT) concentrations >2.5 times the upper limit of normal; any severe concomitant medical condition.

Dosage: Patients were randomised to receive 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 ADM49288/92, ADM59338/93, ADM27178/95, ADM35393F96, ADM36384K96, H96/2146, ADM35741K97, H97/2184). Placebo was supplied as a matched white tablet (formulation number F11192, batch numbers ADM59396/93, ADM28100/95, ADM35402G96, ADM34561/94, ADM35828E96, ADM35807E96, ADM37118H96, ADM37118H96, ADM37120F96, ADM38940F96).

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 (PSA, AST, ALT, and bilirubin), and physical examinations. Adverse events were summarised by Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) preferred term and primary body system.

RESULTS

Efficacy: On 1 June 1999, the data cut-off date 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: From the beginning of the trial (1 August 1995) to the data cut-off (1 June 1999) 81 patients had died: 8 from prostate cancer, 37 from an adverse event, and 36 from other causes. 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 3270 patients had received treatment and adverse events led to withdrawal of 637 (19.5%) of these patients. The most common adverse events were gynaecomastia (40.8%) and male breast pain (47.5%), leading to the withdrawal of 6.0% and 8.9% of patients, respectively. Increases in alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase [SGPT]) and aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]) were reported as adverse events in 2.9% and 2.0% of patients, respectively.