AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: CASODEX

ACTIVE INGREDIENT: Bicalutamide 150 mg

Study No:
ONCO/SORSE/NIS-OIT-CAS-2007/1

Developmental phase: IV (Observational Study)
Study Completion Date: 14th July 2008
Date of Report: 10 Giugno 2009

OBJECTIVES:

Study objective is to evaluate hormone response, in terms of duration and biochemical response, of the hormone treatment lines following a primary line with Bicalutamide 150 mg in subjects affected by prostate cancer.

Primary objectives

The primary objective is to identify the hormone response of the second-line hormone treatment after Bicalutamide 150 mg therapy, in terms of percentage of subjects (50% of analyzed subjects) that, after 6 months, in relation to the biochemical response, are still under hormone therapy.

Secondary objectives

- To evaluate the media of duration of the second line, time to PSA nadir achievement; percentage of patients with biochemical response.
- To evaluate medium duration of the third hormone line, time to PSA nadir achievement; percentage of patients with biochemical response.
- To evaluate starting time of chemotherapeutical treatment in relation to the sequence of the treatments already administered.

METHODS:

Retrospective observational study. A total number of 738 patients were screened, 156 of which were enrolled in the study. They were affected by prostate cancer without progression, with relapses during bicalutamide 150mg mono-therapy and undergoing the second-line hormone treatment for at least 6 months.

The percentage of subjects (with 95% CI) that completed *at least* 6 months of second-line hormone treatment without biochemical and/or clinical disease progression have been estimated.

Biochemical disease progression was defined as a PSA value increased by at least 10% with respect to the value observed at the beginning of the second-line hormone treatment, the biochemical disease progression has been actually defined as a PSA value increased by at least 10% with respect to the PSA nadir observed during the second-line hormone treatment.

Primary Endpoint

Will be evaluated the percentage of subjects that complete at least 6 months of therapy, starting from the date of the first administration of the second-line hormone treatment, without developing any biochemical disease progression intended as >10% PSA increase of the value collected at the beginning of the second-line therapy.

Secondary Endpoint

a) Will be evaluated medium duration of the second-line hormone therapy, intended as time between the first administration and the second disease relapse
b) Will be evaluated medium duration of the third-line hormone therapy, intended as time between the first administration and the third disease relapse
c) Will be evaluated the time between the first Bicalutamide 150 mg administration and the beginning of chemotherapy and this time it will be put into relation with the sequentiality of the second-line administered treatments (LHRH, MAB, antiandrogen monotherapy).
d) Will be evaluated the time to PSA nadir achievement; intended as time between PSA value at first disease recurrence and the lowest PSA value reached before the second relapse.
e) Will be evaluated the percentage of subjects that achieve a PSA reduction after the beginning of the second-line hormone therapy according to the following cases:

    a) **$\geq$20% $\leq$50%** PSA reduction, compared to PSA value at first disease recurrence

    b) **> 50%** PSA reduction, compared to PSA value at first disease recurrence

f) Will be evaluated the time to clinical relapse, intended as time between the first therapeutic intervention leading to a significant reduction of PSA value recorded at diagnosis, and clinical evidence of disease recurrence documented through instrumental methods.

RESULTS:

134 subjects (out of 156) fully met inclusion/exclusion criteria and represent the main analysis set. Except when a subject presented missing values, he has been included in each primary and secondary analysis.

Primary objective:

119 subjects (89%) completed at least 6 months of second-line hormone treatment without biochemical disease progression, while the null hypothesis was set at 40%.

Secondary variables

a. Duration of the second-line hormone therapy

All 134 subjects were treated with second-line hormone therapy and entered this analysis. Median duration of the second-line hormone therapy has been estimated through survival analysis methods and Kaplan-Meier curve has been obtained. The observed median duration of second-line hormone therapy was 24.87 months

b. Duration of the third-line hormone therapy

Only 36 subjects were treated with third-line hormone therapy and present analysis was limited to these ones. The median duration of the third-line hormone therapy has been estimated through survival analysis methods and Kaplan-Meier curve has been obtained. The observed median duration of third-line hormone therapy was 6.07 months.

c. Time between the first Bicalutamide 150mg administration and the beginning of chemotherapy

The time between the first Bicalutamide 150mg administration and the beginning of chemotherapy has been evaluated and its relation with the second- and third-line administered treatments has been investigated through survival analysis methods and Kaplan-Meier curves have been obtained.

Median time was assessed only for cases who received chemotherapy and came out to be 32.67 months. This value represents an obvious underestimation, as the major part of subjects could be still waiting to receive chemotherapy or will never be eligible to receive it.

d. Time to PSA nadir achievement

Time to PSA nadir achievement was intended as time between first disease recurrence and time when the lowest PSA value was reached before the second relapse. 125 subjects experienced a PSA nadir and median time to PSA nadir was 6.43 months.

e. Subjects that achieved a PSA reduction after the beginning of the second-line hormone therapy

PSA reduction after the beginning of the second-line hormone therapy has been compared to PSA value at first disease recurrence. 106 subjects (79%) had a PSA reduction higher than 50%.

f. Time to clinical disease progression

Clinical disease progression was defined as a disease progression revealed by clinical instrumental investigation. Only 28 subjects had a clinical disease progression and median time to clinical disease progression was 13.68 months.

Non-clinical disease progression indicates that disease progression was assessed only through PSA increase or no progression was revealed.