Name of Sponsor/Company: Astellas Pharma Ltd.		
Name of Finished Product: Eligard®		
Name of Active Ingredient: Leuprorelin acetate		

SYNOPSIS

Title of Study: An exploratory, open label, single-arm study to evaluate the effect of Eligard® 6-month on biomarkers of disease in patients with metastatic prostate cancer ISN: EGD-EC-005 (EFFECT)

Investigators /Coordinating Investigator: [redacted] MD, PhD [redacted] The Netherlands.

Study Center(s): This study was conducted at 5 sites in the Netherlands.

Publication (reference): Not applicable.

Study Period: August 2014 to August 2015

Study Initiation Date (Date of First Enrollment): 27 August 2014

Study Completion Date (Date of Last Evaluation): 05 August 2015

Phase of Development: Phase 4

Objectives: To explore the effect of Eligard® in subjects with metastatic prostate cancer responsive to androgen therapy on the following prostate cancer biomarkers: testosterone in serum, prostate specific antigen (PSA) in serum, prostate cancer antigen (PCA3) in urine, PSA mRNA in blood/peripheral blood mononuclear cells (PBMC), PCA3 mRNA in blood/PBMC, transmembrane protease, serine 2 (*TMPRSS2*)–v-ets erythroblastosis virus E26 oncogene homolog (*ERG*) fusion mRNA in blood/PBMC.

Methodology: This was a Phase IV prospective, exploratory, open-label, single-arm, multicenter study to evaluate the effect of Eligard® 6-month on biomarkers of disease in patients with confirmed metastatic prostate cancer for whom androgen deprivation therapy (ADT) was indicated. The duration of participation for a study subject was up to 26 weeks and consisted of a screening period (from 14 days prior to drug administration), a treatment visit where subjects received a single injection of Eligard® 45 mg (6-months formulation) and visits at week 6, 12 and 24 (end of study [EoS]).

Number of Patients/Subjects (planned, enrolled and analyzed): A total of 50 eligible patients were planned to be treated. 16 subjects signed informed consents, 14 were screen failures and 2 subjects were enrolled into the study, of which 1 received the study drug and the second enrolled subject did not receive study drug as the trial was terminated early.

Diagnosis and Main Criteria for Inclusion: A patient was eligible for the study if they fulfilled the following criteria:

1. Male aged 18 years or older.
2. Confirmed metastatic prostate cancer for whom androgen deprivation therapy (ADT) is indicated.
3. Non-castrate level of serum testosterone (≥ 8 nmol/L (i.e.230 ng/dL)) at screening.
4. Serum PSA ≥ 5 ng/mL at screening.

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5. Eastern Cooperative Oncology Group (ECOG) score of 0-2.
6. A life expectancy of at least 12 months.
7. Was able to tolerate injections of study drug and comply with the study requirements.
8. Positive blood PSA mRNA at screening. A positive PSA mRNA in PBMCs (defined as exceeding the Limit of Detection for the central lab assay, i.e. ≥ 10 copies per PCR).
9. Patient had given written informed consent.
10. History of bilateral orchidectomy.
11. History of any hormonal treatment/therapy with GnRH agonist, GnRH anti-agonist within 6 months of enrolment.
12. Treatment with anti-androgens (except where used to prevent testosterone flare up, starting up to 2 weeks prior to Eligard® injection, according to local treatment guidelines), 5-α reductase inhibitors, estrogens and/or other any investigational hormone-derivative within 3 months of enrolment or 5-times the half-life, whichever was longer.
13. Any previous treatment with chemotherapy treatment for prostate cancer prior to the screening visit or within 6 months prior to screening for any other cancer.
14. Patients previously treated for cancer with hormonal therapy in whom treatment was stopped due to lack of efficacy, progression of the disease or lack of tolerability.
15. Previous treatments for cancer (including prostate cancer) within 6 months prior to enrolment: immunotherapy, external beam radiotherapy, brachytherapy, thermotherapy, or biological response modifiers (e.g. cytokines).
16. Known or suspected spinal cord compression or evidence of spinal metastases with risk of spinal compression.
17. Uni- or bilateral uretric obstruction.
18. Required concomitant use of anti-androgens during the course of the study (except where used to prevent testosterone flare up, starting up to 2 weeks prior to Eligard® injection and continuing for up to 3 weeks, according to local treatment guidelines).

Test Product, Dose and Mode of Administration, Batch Numbers: Eligard® 45 mg (6-months formulation) is a single subcutaneous 6-month depot injection. The Eligard® 45 mg pack, contained two pre-filled cyclic olefin copolymer / polypropylene syringes, one containing the active compound 56.4 mg leuprorelin acetate powder (Syringe B), and one containing the solvent for suspension (Syringe A). These two syringes constituted a mixing system for subcutaneous injection after reconstitution with the sterile solvent to provide a 6-month depot injection.

Eligard® [redacted] (expiry date: Oct 2015)

Duration of Treatment (or Duration of Study, if applicable): The study treatment period was 6 months, with a screening visit 14 days previous to drug treatment.

Reference Product, Dose and Mode of Administration, Batch Numbers: Not applicable.

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Criteria for Evaluation: This study assessed changes in biomarker expression during Eligard® treatment. The biomarkers of interest of the study were serum testosterone, serum PSA, PCA3 score in urine, and blood/PBMC mRNA of PSA, PCA3 and TMPRSS2-ERG. There was no analysis of efficacy.

Statistical Methods: Standard descriptive statistics were planned to be reported at each time point for absolute values and for changes from baseline of the biomarker variables. The relationship between "classic" (testosterone and PSA) and "modern" biomarkers were to be explored by scatter plots with the calculated correlation coefficients and, if possible by regression analyses. Changes from the analyses planned in the protocol were made as a protocol amendment, including the change from inclusion criteria of PBMC PCA3 mRNA detection to PBMC PSA mRNA detection. This study was discontinued/terminated early due to Sponsor's decision. No statistical analyses were performed.

Summary of Results/Conclusions: This study was terminated early because of a lack of recruitment of eligible subjects. Out of the 16 subjects screened, 2 subjects met the inclusion/exclusion criteria and only 1 subject received study drug prior to the termination of the study. These low numbers were due in part to changes in the treatment landscape where other therapies were recommended first line treatment options whose use prior to entry to the study made subjects ineligible for study participation, as well as the lack of successful detection of PSA biomarker mRNA in PBMC at screening.

Population: The study population consisted of one subject: [redacted] with metastatic prostate cancer [redacted] and lower urinary tract symptoms (LUTS).

Efficacy Results: There was no analysis for efficacy.

Safety Results: The subject that received the study drug had 5 adverse events (AEs). [redacted] All AEs were considered non-drug related AEs.

CONCLUSIONS: This study was terminated early by Sponsor's decision, due to low overall recruitment and low number of subjects meeting the inclusion and exclusion criteria for entry into the study.

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