AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Zoladex 10,8 SafeSystem
ACTIVE INGREDIENT: Goserelin

Study No: NCT00540059
Zx-002: Evaluation of QoL, tolerabilty and use of Zoladex 10,8 SafeSystem for advanced PCa - German IPEP trial

Developmental phase: IV
Study Completion Date: 11-Dec-2007 (LSLV)
Date of Report: 5-Sep-2008

OBJECTIVES:
This PMS study had the main objective to verify if and how physicians (i.e. urologists) follow the therapy recommendation for men with advanced prostate cancer, which has been published (Altwein, J.E., Mohandessi, B: Prostata- und Samenblasentumoren; in Jocham, D., Miller, K. (Hrsg.): Praxis der Urologie (Band II). Kapitel 49, Thieme Verlag, Stuttgart, 2003) . The recommendation advises to switch to goserelin 10.8 mg

- if the prostate tumour is locally advanced,
- the PSA level has increased in the last months or
- the prostate tumour started to metastasize.

Therefore this PMS trial should help to assure that physicians follow the published therapy recommendation.

Another objective was to evaluate the tolerability of goserelin 10,8 mg under naturalistic conditions.

METHODS:

This project was a so-called ‘Anwendungsbeobachtung (AWB)’, i.e. a specific type of prospective Post Marketing Surveillance (PMS) project, performed in Germany by AstraZeneca GmbH. Under daily routine conditions and without any intervention by the sponsor regarding the selection of subjects, diagnostic procedures, therapeutic decisions (medicinal and non-medicinal therapy, dose, duration, etc.), routine assessments, the participating physicians (i.e. urologists)

were asked to document relevant data related to the goserelin 10.8 mg therapy as treatment in men with advanced prostate cancer.

The CRFs, obtained from the physicians, were sent from the responsible sponsor personnel to d.s.h. statistical service GmbH for further processing. All CRFs were entered into a MS Access data base using double data entry. The data from the MS Access data base system were then converted into SAS data sets for analysis. To improve the data quality, a thorough examination for plausibility and consistency of the data was performed using cleaning-checks based upon a Data Cleaning Plan. These checks were programmed in SAS V. 9.1. Invalid, inconsistent and/or implausible data were re-checked and corrected, if possible. However, no query process was used to try to get answers from the participating physicians.

Due to the non-interventional character of this PMS project, only an exploratory-descriptive statistical analysis has been performed.

RESULTS:

This PMS was performed in Germany between 15-JUN-2005 (first subject in) and 11-DEC-2007 (last subject last visit). This time-frame covers only those subjects with a prospective documentation, i.e. those with a baseline visit on 15-JUN-2005 or thereafter. However, there were also 169 subjects with a retrospective documentation, i.e. a baseline visit before 15-JUN-2005, or a missing date for the baseline assessment.

Overall, 2179 subjects were documented in this PMS by the participating physicians in 736 study centres. In the majority of the centres (96.9%) three subjects were documented. Out of these 2179 subjects, 2162 subjects were considered as treated with goserelin. In total, 498 of 2162 treated subjects [23.0%] had to be excluded from the statistical analysis because all these subjects fulfilled at least one of the criteria for non-evaluability (mainly retrospective documentation and no efficacy data after visit 1).

Overall, the mean age at Visit 1 was 73.4 years with a range from 41 to 97 years. The majority of subjects were between 71 and 80 years old.

With regard to the T-stage, the tumour of most men was classified as ‘3 *(tumour extends through the prostatic capsule)’* [44.1%] or as ‘2 *(tumour confined within the prostate)*’ [28.6%].

With regard to the N-stage, most of the tumours were categorised either as ‘X *(regional lymph node cannot be assessed)*’ [47.3%] or as ‘0 (*no regional lymph node metastasis*)’ [33.9%].

With regard to the M-stage, distant metastases could not be assessed for 21.8% of the tumours and were not evident for 55.4% of the tumours. Only 17.1% of the evaluable subjects had distant metastases.

According to the Gleason score 22.8% of tumours were moderately differentiated (5 – 6), 30.2% moderately to badly (7) and 30.2 % of the tumours were badly to not differentiated (8-10).

The main objective of this PMS was to verify if and how physicians (i.e. urologists) follow the therapy recommendation in men with advanced prostate cancer. The recommendation advises to switch to goserelin 10.8 mg if the prostate tumour is locally advanced, the PSA level has increased in the last months or the prostate tumour started to metastasize. According to this definition subjects were classified into one of the following classes:

- Metastasized PCA
- Locally advanced PCA
- PSA increase

If a subject fell into more than one category, he was counted in the highest category according to the above stated sequence.

A total of 1411 of 1681 evaluable subjects (83.9%) was included into the study according to the Zoladex SafeSystem therapy recommendation. A status of locally advanced PCA was documented for 767 (45.6%) subjects, metastasized PCA for 305 (18.1%) subjects and PSA increase for 339 (20.2%) subjects. For 199 (11.8%) subjects the assignment could not be performed due to missing information of TNM tumour status. Therapy recommendation was definitely not met for 71 (4.2%) subjects.

Of the 2162 treated subjects, 61 subjects (2.8%) experienced at least one AE with proper documentation on the (S)AE CRF. In total, 36 subjects (1.7%) reported AEs that were judged by the physicians to be related to goserelin. Thirteen subjects (0.6%) had a serious adverse event (SAE). Three subjects (0.1%) died. Taking also the additional events from the EOT CRF into account, 117 subjects (5.4%) experienced at least one AE. Thirty-eight subjects (1.8%) had an SAE. Twenty-eight subjects (1.3%) died during the study.

Based on the AEs from the (S)AE CRF, the primary system-organ classes with the highest numbers of subjects who experienced specific AEs were ‘vascular disorders’ (30 subjects [1.4%]; including “hot flushes”) and ‘Reproductive system and breast disorders’ (29 subjects [1.3%]; including “gynaecomastiae” and “erectile dysfunction”). Most of these events were considered to be drug related.