Clinical Study Report Synopsis	
Drug Substance	Fulvestrant
Study Code	D6997L00018
Edition Number	1
Date	06 October 2014

Faslodex (fulvestrant) Post-marketing surveillance

Study dates: First subject enrolled: 06 February 2009
Last subject last visit: 24 October 2013

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Objectives and criteria for evaluation

This Post Marketing Surveillance aims to assess the efficacy, the safety and tolerability profile of Faslodex(fulvestrant) in everyday practice. Secondary objective of this PMS is to identify the frequency of serious adverse events or any unknown adverse events of Faslodex.

Study design

Time Perspective: Prospective

Inclusion will start from October 2008 and last until October 2013. Patients will be selected with a minimum of 120.

Target subject population and sample size

Postmenopausal women with locally advanced or metastatic breast cancer who have failed 2 or more prior hormone therapies, or were intolerant to prior hormone therapy and have no endocrine therapeutic options. (The prior hormone therapies should contain both anti-estrogen and non-steroidal aromatase inhibitor, irrespective of order.)

This PMS will be conducted by physicians who are taking care of breast cancer patients in about 30 centers in Korea.

Investigational product and comparator(s): dosage, mode of administration and batch numbers

Fulvestrant 500mg i.m. once monthly, with an additional 500 mg dose given 2 weeks after the initial dose

Statistical methods

Efficacy will be analysed through *t*-test or *chi* square-test. Safety will also be analyzed by *chi* square-test or other adequate methods.

Subject population

Case report forms (CRFs) were collected from a total of 42 subjects during this re-examination period. As 2 subjects assessed before contract date were excluded from the safety analysis, a total of 40 subjects were included in the safety analysis and only 27 subjects except 13 subjects who received study drug less than twice were included in the efficacy analysis.

Subjects included in the safety evaluation are all women due to the features of the indications of study drug. Mean age of subjects included in the safety evaluation was 54.35±9.59 years with 50.00% (20/40 subjects) in ‘50~59 years’ group, 30.00% (12/40 subjects) in ‘40~49 years’ group and 10.00% (4/40 subjects) in ‘60~69 years’ group. When subjects aged ‘under 18 years’ were classified into children group based on 18 years old, there were no children in subjects. Meanwhile when subjects aged ‘over 65 years’ were classified into elderly group based on 65 years old, 12.50% (5/40 subjects) were classified into the elderly group. Mean height of subjects was 157.91±4.11cm and mean weight was 57.54±8.25kg.

Summary of safety results

8 adverse events occurred in 4 out of 40 subjects included in the safety evaluation during this re-examination period, and consequently the AE incidence rate was 10.00%. One case of 'MUSCLE WEAKNESS' out of "MUSCULO-SKELETAL SYSTEM DISORDERS" was reported as a SAE during this re-examination period and it was not an adverse drug reaction whose causal relationship with study drug could not be excluded. 8 unexpected AEs were reported in 4 subjects (10.00%) during this re-examination period. The analysis of unexpected AEs by body system showed 'RESPIRATORY SYSTEM DISORDERS' were reported in 5.00% of subjects (2/40 subjects), 'MUSCULO-SKELETAL SYSTEM DISORDERS,' 'BODY AS WHOLE – GENERAL DISORDERS', 'CENTRAL & PERIPHERAL NERVOUS SYSTEM DISORDERS', 'SKIN AND APPENDAGES DISORDERS' and 'PLATELET, BLEEDING & CLOTTING DISORDERS' in 2.50% (1/40 subjects), respectively. In the analysis of unexpected AEs by detailed symptom, 'COUGHING' was reported in 5.00% of subjects (2/40 subjects), 'SPUTUM INCREASED', 'MUSCLE WEAKNESS', 'OEDEMA', 'NEUROPATHY', 'URTICARIA' and 'THROMBOCYTOPENIA' in 2.50% (1/40 subjects), respectively. Adverse drug reactions (ADRs) whose causal relationship with study drug could not be excluded included 'OEDEMA' and 'URTICARIA' (one case each). 8 adverse events occurred in 4 subjects (10.00%) during this re-examination period. In the analysis of AEs by body system, 'RESPIRATORY SYSTEM DISORDERS' was observed in 5.00% of subjects (2/40 subjects) and 'MUSCULO-SKELETAL SYSTEM DISORDERS,' 'BODY AS WHOLE – GENERAL DISORDERS', 'CENTRAL & PERIPHERAL NERVOUS SYSTEM DISORDERS', 'SKIN AND APPENDAGES DISORDERS' and 'PLATELET, BLEEDING & CLOTTING DISORDERS' in 2.50% (1/40 subjects), respectively. Adverse drug reactions (ADRs) whose causal relationship with study drug could not be excluded included 'OEDEMA' and 'URTICARIA' (one case each).

In the analysis of the severity of adverse events by classifying it into 'mild', 'moderate' and 'severe,' 'mild' AEs accounted for 62.50% (5/8 cases), 'moderate' for 25.00% (2/8 cases) and 'severe' for 12.50% (1/8 cases).

In the analysis of actions against study drug after the occurrence of adverse events by classifying them into 'None', 'Dose changed', 'Temporary stopped' and 'Permanently stopped,' 'None' accounted for 87.50% (7/8 cases) and 'Permanently stopped' for 12.50% (1/8 cases).

In the analysis of the results of adverse events observed in this study by classifying them into 5 categories like 'Recovered', 'Not changed', 'Deteriorated', 'Death' and 'Lost to follow-up,' Not changed' accounted for 62.50% (5/8 cases) and 'Recovered' for 37.50% (3/8 cases).

In the evaluation of the causal relationship between AEs and study drug, 'Probably not related/Unlikely'relationship was shown in 75.00% (6/8 cases), 'Probably related/Probably/likely' and 'Possibly related/Possible' in 12.50% (1/8 cases), respectively.

In the analysis of re-administration status of study drug, 'No (not re-administered)' accounted for 25.00% (2/8 cases) and 'Yes (re-administered)' for 75.0% (6/8 cases). And in the analysis of AE occurrence status after the re-administration, 'No relapse' was shown in 33.33% (2/6 cases) and 'Relapse' in 66.67% (4/6 cases).

Summary of efficacy results

Efficacy evaluation was made by classifying the status into 5 steps like 'Complete Response (CR)', 'Partial Response (PR)', 'Stable Disease (SD)', 'Progressive Disease (PD)' and 'Not evaluable' according to overall improvement assessed by an investigator at the end of the study. As a result, 'PD' was shown in 48.15% (13/27 subjects), 'SD' in 44.44% (12/27 subjects) and 'Not evaluable' in 7.41% (2/27 subjects). Among the efficacy evaluation criteria, 'Complete Response (CR)', 'Partial Response (PR)', 'Stable Disease (SD)' were re-classified into "Effectiveness" and 'Progressive Disease (PD)' and 'Not evaluable' into "Ineffectiveness" and efficacy evaluation was re-made. As a result, 'Effectiveness' was shown in 44.44% (12/27 subjects), 'Ineffectiveness' in 55.56% (15/27 subjects).