AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT:
FASLODEX
ACTIVE INGREDIENT:
FULVESTRANT

Study No: NIS-ORU-FAS-2007/1
Quality of life and symptoms in postmenopausal women with hormone receptor positive disseminated breast cancer while receiving faslodex

Developmental phase: Non Interventional Study
Study start: 1st June 2007
Study Completion Date: 28th March 2009
Date of Report: 28th March 2009
Centers-participants – 42

OBJECTIVES:

To study QoL related response, symptom spectrum and severity in disseminated breast cancer patients receiving Faslodex hormonal therapy.

To Achieve These Objectives

To stratify population of disseminated breast cancer patients receiving Faslodex according to grading of QoL related response.

To determine spectrum and severity of primary symptoms and to evaluate their dynamics in disseminated breast cancer patients receiving Faslodex hormonal therapy

DESIGN:

Prospective, multicenter, open-label, non-randomized study.

Time-points of assessment:

T0 - (Faslodex treatment);

T1 – 8 weeks after entry;

T2 – 16weeks after entry;

T3 – 24 weeks after entry;

T4 – 52 weeks after entry.

The following forms for each patient will be completed:

Generic QoL questionnaire SF-36 - filled out by every patient at each time point.

Symptom assessment questionnaire MDASI - filled out by every patient at each time point.

Checklist T0 (contains disease, treatment and demographic information) - filled out by a physician at T0 for each patient.

Checklists T1-4 (contain disease and treatment information) - filled out by a physician at T1-4 for each patient.

Comorbidity checklist - filled out by a physician at T0 for each patient.

NUMBER OF SUBJECTS:

Minimal sample size for the pilot study - 68 patients

Sample size for the main study will be determined on the basis of the results of the pilot study.

TARGET POPULATION: Postmenopausal women with hormone receptor positive metastatic breast cancer with disease progression.

LENGTH OF STUDY:

2 years

ASSESSMENTS OF:

- EFFECTIVENESS - Tumor response – number (%) of subjects with CR, PR or stabilization

- QUALITY OF LIFE - Quality of life response – the level of reduction of QoL deficit as compared to the population norm.

PROCEDURES (summary):

Measurements

SF-36-R, MDASI-R. SF-36 is a set of generic, coherent, and easily administered quality-of-life measures (available at www.rand.org). The M. D. Anderson Symptom Inventory (MDASI, Cleeland et al., 2000) is a multisymptom assessment tool which includes 13 symptoms that are reported with high frequency or unusual severity in cancer population. The Russian versions of SF-36 and the MDASI – SF-36-R and MDASI-R were validated by the Multinational Center of Quality of Life Research (2001).

Comorbidity Checklist. Modified Kaplan-Feinstein Index is a method of coding comorbidity. In this index, specific diseases and conditions are classified into four groups: none, mild, moderate, or severe according to the extent of organ decompensation and its prognostic impact (http://oto.wustl/clinepi/calc.html).

Measure of Performance Status. The ECOG Performance Status Scale will be used to assess the health care provider's estimate of the patient's functional status (Oken et al., 1982).

Patient Samples

Subjects will be postmenopausal women with hormone receptor positive metastatic breast cancer with disease progression who are prescribed Faslodex treatment. The recruitment includes a minimum of 68 patients for pilot study. Patients eligible for the study include those who are eligible to participate in the program "The study of the effectiveness and tolerance of Faslodex as I-II line hormonal therapy in postmenopausal women with advanced breast cancer", those who are able to fill in the questionnaires and those who have no comorbidities dominating at the moment of the study.

Recruitment of Participants:

The project staff in each study site will review the patients' medical records to determine their eligibility and will enter eligible patients into a patient-recruitment log. They will approach the patients, explain the study, ask them to participate, and acquire their signed informed consent(s).

Data Collection Procedure:

Data will be collected at five time points: at baseline and at 8, 16, 24 and 36 weeks after commencement of the protocol. Patients will complete SF-36-R and MDASI-R at each time-point. All of these measures can be presented in either a paper-and-pencil or interview format. At baseline physicians will complete a checklist that includes demographics, disease and treatment characteristics, and the comorbidity checklist. At the following time-points T1-T4 physicians will complete Checklists T1-4, respectively.

Research investigators from each site will receive training in interviewing, questionnaire administration, and data recording. Designated study staff will explain the purpose of the study and the instructions for completing the survey to all eligible patients.

The site investigator will review all collected data (patient and physician questionnaire responses, site evaluations, demographics) for content and completion. In the event of incomplete data, study staff will attempt to acquire the data either by medical record review or contacting the patient.

STATISTICAL ANALYSES:

The calculation of the sample size for the pilot study is made on the assumption of clinically significant differences of 0.1 or more between groups in the means of the values of Integral QOL Index. The p-level has been set at 0.05. The statistical test power has been set at 0.85. Sample size for the main study will be determined on the basis of the results of the pilot study.

We will use descriptive statistics to define: 1) central tendency (arithmetical mean, median), 2) variability (standard deviation) and 3) number of patients in the groups and the proportions of patients with different QoL response grades and symptom severity within the groups.

Statistically significant differences between frequencies of patients with different QoL response grades and symptom severity will be studied using Friedman's ANOVA or Chi-square test. Pairwise comparison is planned to be conducted with post hoc statistical criteria.

Comparison of parameters between patient groups at different time-points will be made using ANOVA with Repeated Measures.

p less than 0.05 is considered to be statistically significant. The statistical power of criteria will be at 0.85.

In case missing data is detected in more than 10 % of patients, the Missing Value Analysis EM (procedure of statistical software package SPSS 13.0) will be applied to input the missing data.

The statistical analysis will be made in: SPSS 13.0, Sigma Stat 3.0.

RESULTS:

Number of patients enrolled – 115 postmenopausal women with hormone receptor positive metastatic breast cancer

Information about the number of patients and the number of Faslodex injections across the study time-points is presented in Table 1.

Table 1

The number of patients and the number of Faslodex injections across the study time-points

Time-point	Number of injections	Number of patients
P1	1	115
P2	2	112
P3	4	91
P4	6	82
P5	≥ 11	57

Fifty eight patients discontinued treatment (Table 2). The majority of them (69%) had disease progression.

Table 2

Reasons of withdrawn from study treatment (*n*=58)

Reason	Patients, n (%)
Disease progression*	40 (69.0)
Treatment rejection	8 (13.7)
Death **	2 (3.4)
Others (not present at the scheduled appointment, not willing to continue participation in the study, Faslodex not available)	8 (13.8)

- one woman died after disease progression
- **both women died due to acute heart failure

Information about symptom management during the Faslodex treatment is presented in Table 3.

Table 3

Symptom management during Faslodex treatment

Symptom	Symptom management	No. of Patients (%)				
		P1 – at 4 weeks (*n*=115)	P2 – at 8 weeks (*n*=112)	P3 – at 16 weeks (*n*=91)	P4 – at 24 weeks (*n*=82)	P5 – at 48 weeks (*n*=57)
Pain	NAIDs	28 (24)	26 (23)	20 (22)	12 (15)	9 (16)
	Weak opioids	11 (10)	6 (5)	5 (5)	8 (10)	4 (7)
Fatigue	Blood transfusion	1(0,8)	-	-	1 (1)	-
	Iron supplement	10 (9)	11 (10)	6 (7)	6 (7)	6 (11)
	Erythropoetines	6 (5)	3 (3)	1 (1)	1(1)	3 (5)
	Vitamins	27 (23)	30 (27)	19 (21)	15 (18)	7 (12)
Other symptoms	Antidepressants	16 (14)	5 (4)	4 (4)	5 (6)	4 (7)
	Sedative/hypnotic drugs	13 (11)	12 (10)	9 (10)	7 (9)	5 (9)
	Anxiolytics	5 (4)	4 (4)	7 (8)	3 (4)	1(2)
	Antibiotics	4 (3)	2 (2)	1 (1)	1 (1)	-
	Antifungal drugs	3 (2)	2 (2)	-	1(1)	-
	Antiemetics	7 (6)	2 (2)	3 (3)	-	-
	Corticosteroids	8 (7)	4 (2)	1 (1)	3(4)	-
	Others	8 (7)	8 (7)	3 (3)	5 (6)	-

ADVERSE EVENTS:

The reported adverse events in the patients receiving Faslodex included drowsiness, hot flushes, injection site rash, sleep disturbance, hyperglycemia, nausea, lack of appetite, headache, gastrointestinal syndrome, bone pain, and pain in kidney zone after injection. The adverse events at different time-points are listed in Table 4.

Table 4

Adverse events registered during Faslodex treatment

Adverse events	No. of Patients (%)				
	P1 – at 4 weeks (n=115)	P2 – at 8 weeks (n=113)	P3 – at 16 weeks (n=92)	P4 – at 24 weeks (n=82)	P5 – at 48 weeks (n=57)
Drowsiness	1 (0.98)	1 (0.95)	-	-	-
Hot flushes	2 (1.8)	2 (1.9)	2 (2.56)	1 (1.63)	1 (4.54)
Injection site rash	1 (0.98)	-	-	-	-
Sleep disturbance	-	1 (0.95)	1 (1.28)	-	-
Hyperglycemia	-	1 (0.95)	-	-	-
Nausea	-	-	1 (1.28)	-	-
Lack of appetite	-	-	1 (1.28)	-	-

Headache	-	-	1 (1.28)	-	-
Gastrointestinal syndrome	-	-	1 (1.28)	-	-
Bone pain	-	-	1 (1.28)	2 (3.27)	-
Pain in kidney zone after injection	-	-	-	1 (1.63)	-

EFFICACY:

For postmenopausal women with hormone – sensitive ABC receiving Faslodex clinical benefit rate (complete response + partial response + stable disease ≥24 weeks) was 54.5% (at a median follow-up of 11 months)

QUALITY OF LIFE:

Faslodex treatment in postmenopausal women with hormone-positive ABC significantly improves physical, psychological and social functioning with a maximum at 48 weeks after the onset of treatment.

During Faslodex treatment the number of patients with no QoL impairment increases whereas the number of patients with critical QoL impairment decreases.

Quality of life treatment response (QoL improvement or QoL stabilization) was achieved in the majority of patients with hormone-positive ABC receiving Faslodex.

Faslodex treatment in patients with hormone-positive ABC yields reduction of the number of patients with moderate-to-severe symptoms. Prolongation of treatment is associated with decline of symptom severity.

Faslodex treatment of patients with hormone-positive ABC within a year results in improvement of the majority of quality of life domains. Quality of life profile is characterized by less compression and deformation at 24 and at 48 weeks after the onset of treatment. The longer the treatment, the larger the number of patients with no QoL impairment and the less the number of patients with critical QoL impairment decreases.

Decrease of the number of moderate-to-severe (score ≥ 5) symptoms in patients with hormone-positive ABC during Faslodex treatment was noted.

Symptom treatment response in terms of improvement or stabilization was achieved in the majority of patients with hormone-positive ABC receiving Faslodex within a year.