Drug product:	Faslodex	**SYNOPSIS**	
Drug substance(s):	Fulvestrant		
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Faslodex Registry: a Belgian observational study to evaluate the use of fulvestrant in current clinical practice

Study centre(s)

A total of 16 centres in Belgium participated in this study.

Publications

None at the time of the report.

Study dates		**Phase of development**
First subject enrolled	22 September 2008	NIS
Last subject completed	14 December 2009	
Database lock	05 February 2010	

Objectives

The primary objective of this observational study was to collect real life data, according to Belgian physicians' clinical practice, on the use of fulvestrant to treat ABC patients fulfilling the criteria for its reimbursement.

The secondary objectives were to document treatment during observation period and number of fulvestrant injections and also to document reasons for fulvestrant treatment discontinuation when applicable.

Study design

This study was an open-label, multicentre, prospective, observational non-interventional study which took place in Belgium, upon recommendation of the Belgian Health Authorities (RIZIV/INAMI). It was composed of two visits aimed at collecting real life data on the use of fulvestrant in ABC patients fulfilling the criteria for reimbursement (Table S-1).

The final evaluation visit data were recorded at study closure, in the first half of December 2009, or earlier in case of discontinuation with fulvestrant treatment.

Eligible women were to be enrolled into the study after providing informed consent. Their assignment to a particular therapeutic strategy fell within current clinical practice. They returned to the centre independently of the course of this study, meaning that no additional visits or procedures were applied to the patient. Any intermediate visit of the patient to the centre prior to the final evaluation at study closure visit was not considered as part of the study.

Table S-1 Study plan

	Baseline	**Final evaluation**
Schedule	June 2008-June 2009	At fulvestrant treatment discontinuation or first half of December 2009
Visit	**1**	**2**
Informed consent	X	
Date of visit	X	X*
Patient's age	X	
Disease and treatment		
Date of diagnosis of initial breast cancer **	X	
Date of diagnosis of advanced breast cancer**	X	
Previous therapy (hormonal, chemotherapy)	X	
Date of first fulvestrant injection	X	
Number of fulvestrant injections during observation period		X
Total number of fulvestrant injections		X
Date of last fulvestrant injection		X
Discontinuation of treatment with fulvestrant (if applicable)		
Date of hormonal treatment discontinuation		X
Reason for treatment discontinuation		X
Type of alternative treatment		X

* If the patient was not present, the date of the last visit to the centre was collected.
** Date of initial and advanced breast cancer should be the same if the initial breast cancer diagnosis was metastatic.

Target subject population and sample size

Postmenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer, fulfilling the criteria for reimbursement of fulvestrant, who already received a prescription for fulvestrant and for which the investigator considered to continue prescribing fulvestrant in accordance with the current Summary of Product Characteristics (SmPC) and according to investigator's clinical practice.

The Belgian Health Authorities (RIZIV/INAMI) recommended the collection of real life data from approximately 200 patients on the use of fulvestrant in current clinical practice.

Investigational product: dosage and mode of administration

Faslodex®, a registered trademark of the AstraZeneca Group of Companies, is a solution for intramuscular injection. One pre-filled syringe contains 250mg of fulvestrant in 5 mL solution (excipients: ethanol 96%, benzyl alcohol, benzyl benzoate, castor oil). Doses and treatment regimens were to be prescribed according to the Belgian SmPC and according to current clinical practice.

In Belgium, fulvestrant is indicated for the treatment of postmenopausal women with hormone receptor positive, locally advanced or metastatic breast cancer with recurrence during or after adjuvant anti-oestrogen therapy or disease progression during therapy with an anti-oestrogen.

Due to the non interventional nature of this study, the assignment of a patient to a particular therapeutic strategy fell within the current clinical practice of the Investigator.

Criteria for evaluation

Primary variables

- Previous hormonal or chemotherapies for breast cancer and for advanced breast cancer (ABC).
- Duration of previous hormonal or chemotherapies for breast cancer and for ABC
- Number of previous hormonal or chemotherapies for breast cancer and for ABC

Other variables

- Patient's age
- Time interval between initial and advanced breast cancer diagnoses
- Time interval between ABC diagnosis and first injection of fulvestrant
- Number of fulvestrant injections during observation period (between Visit 1 and Visit 2)
- Total number of fulvestrant injections
- Duration of fulvestrant treatment

- Reason for discontinuation of treatment with fulvestrant
- Alternative treatment after the end of the study.

Safety

Due to the non-interventional character of this study, no-pro-active safety data collection was performed.

Statistical methods

All analyses were based on the full analysis set.

Due to the non-interventional design of this observational study, most statistical analyses were descriptive. Categorical analysis variables were summarised by frequency and percentage of each category. Continuous analysis variables were described by number of non-missing observation, mean, standard deviation, median and range.

Student's t-test was used to detect differences between means. In case of unequal variances between groups, the Alpin Welch test was used.

Subject population

A total of 161 patients were included into the study under the supervision of 16 investigators. The mean follow-up time (time between visits) during the study for all patients was 5.2 ± 3.6 months.

The mean age for the 161 patients was 67.2 years (range: 41 to 92 years).

The median time interval between initial breast cancer and ABC was 59 months (range: 0 to 267 months). The median time interval between ABC diagnosis and the first injection of fulvestrant was 38 months (range: 0 to 222 months).

Previous therapies

Treatment lines

Adjuvant therapies

Most patients had adjuvant chemotherapy and adjuvant hormonal treatments (33.5%) or hormonal therapies only (32.9%). Patients treated only with chemotherapy represented 6.2% of all patients. A total of 44 patients (27.3%) had no previous adjuvant treatment.

Most patients (53.4 %) had one previous adjuvant hormonal treatment. Patients never treated with adjuvant hormonal therapy represented 33.5% of all patients. Most patients treated with hormonal therapies had tamoxifen (91.6%), with 72.0% of patients only treated with this medication and 19.6% also treated with AI.

Regarding patients previously treated with adjuvant chemotherapy, 76.1 % of adjuvant hormonal treatments were given as first-line treatment and 19.7% were given as second-line

treatment. First-line treatments were the longest treatments with a median duration of 31.9 months. For the patients not previously treated with chemotherapy, 88.3% of all adjuvant hormonal treatments were given as first-line treatments and none of the patients had third or fourth-line treatments. The median duration of first-line treatments was 36 months.

Amongst patients whom started fulvestrant treatment within the month before enrolment or during study period, most had no previous adjuvant chemotherapy (61.6 %). Approximately one third (32.9%) had one line of adjuvant chemotherapy.

Therapies for ABC

A total of 84 patients (52.2%) had previous hormonal therapy without chemotherapy for ABC whereas 74 (46%) had both treatments.

Regarding patients treated with hormonal therapies for ABC, 155 patients out of 158 (98.1 %) were treated with aromatase inhibitors (AIs) and 61 patients were treated with tamoxifen (38.6%). Almost all patients treated with tamoxifen for ABC were also treated with AIs (58 patients out of 61). Overall, the number of previous hormonal therapies for ABC per patient ranged from 1 to 7 and 74.5% of the patients had two or more treatments.

The number of hormonal treatment lines was similar between patients previously treated with chemotherapy (up to 7 hormonal treatment lines) and patients not previously treated with chemotherapy (up to 6 hormonal treatment lines). In both groups, most treatments were given as first-line treatments (38.6% and 51.2% of all hormonal treatments, respectively) and the longest treatment was the first one (median duration: 16.1 and 19.1 months, respectively).

Type of therapy

Hormonal therapies

A total of 28 patients out of 38 were treated with tamoxifen for at least 5 years; none of the 38 patients was treated with AIs for at least 5 years. A switch between tamoxifen and AI treatments was observed for 10 patients.

Before inclusion into the study, 131 hormonal **adjuvant breast cancer therapies** were administered to 107 patients (66, 5% of all patients); the mean number of therapies in previously treated patients was 1.2 ± 0.5 (range: 1 to 4). The most frequent therapy administered was tamoxifen (74.8%). Tamoxifen was the longest administered treatment (median= 36 months) whereas exemestane was the shortest (median= 12.3 months).

A total of 158 patients (98.1% of all patients) had previous hormonal **ABC therapies**, with a mean number of 2.3 ± 1.1 therapies per treated patient (range: 1 to 7). The most frequent treatments were exemestane (32.3%) and letrozole (27.0%). Anastrozole was the longest administered treatment (median= 28.4 months).

Chemotherapies

Amongst the 161 study patients, 64 (39.8%) had an **adjuvant chemotherapy** prior to enrolment. The mean number of adjuvant chemotherapies per treated patient was 1.2 ± 0.5. The median duration was 4.9 months and ranged from 2.1 to 14.0 months

The proportion of patients whom received previous **chemotherapy for ABC** was 46.0% and the mean number of chemotherapies per treated patient was 2.6 ± 1.9 (range: 1 to 10). The median duration was 4.1 months and ranged from 0.0 to 36.7 months.

Treatment with fulvestrant

Start and duration of fulvestrant treatments

Faslodex® has been granted reimbursement by the Belgian Health Authorities on 1st of March, 2008. Five study patients (3.1%) started a treatment with fulvestrant before that date. Most of the patients (70.8%) started their treatment between the 1st of March 2008 and the day of their enrolment into the study. Approximately 26% of patients received their first injection of fulvestrant the day of their enrolment or during the study.

The median duration of treatment with fulvestrant for all patients was 5 months (range: 0 to 64 months).

There was no significant difference in the duration of treatments with fulvestrant between patients treated or not with chemotherapy for ABC (mean duration ± SD: 7.39 ± 9.68 vs. 7.15 ± 6.20; p-value > 0.05).

Number of fulvestrant injections

The median total number of fulvestrant injections for all study patients was 6 (range: 1 to 65) and the most frequent numbers of injections was 3 and 4 (13.7% of all patients, each). During the study, the median number of injection was 4 (range: 0 to 16).

The median number of fulvestrant injections per patient was lower for patients treated with hormonal therapy and chemotherapy for ABC than for patients only treated with hormonal therapy (5 vs 6.5 injections). In addition, patients who had tamoxifen and AIs for ABC had fewer fulvestrant injections than patients treated only with AIs (median =5 vs. 7 injections).

There was no significant difference in the number of fulvestrant injections between patients previously treated or not with chemotherapy for ABC (mean duration± SD: 8.36 ± 9.84 vs. 8.26 ± 6.73; p-value >> 0.05)

Discontinuation from treatment with fulvestrant

At the final evaluation (Visit 2), 75.2% of the patients discontinued from treatment with fulvestrant. The main reason was the progression of the disease (92.6%).

The mean total duration of treatment for the 112 patients who discontinued due to progression of cancer was 6.5 ± 5.9 months (median: 5 months, range: 1 to 56 months) and the median total number of fulvestrant injection was 3.89.

Ongoing treatments with fulvestrant

The mean total duration of treatment with fulvestrant for the 40 patients (24.8%) who continued with this therapy at study closure was 13.3 ± 10.4 months (median: 11 months, range: 6 to 64 months) and the median total number of fulvestrant injections was 12.

Treatments after the end of the study

At study closure, 8.8% of patients had no treatment, 85.5% had one, and 5.7% had more than one. The most frequent prescribed therapies were chemotherapy (46%) and fulvestrant (24.8%). The percentage of patients with treatment with tamoxifen or AIs ranged from 0.6% to 1.9%. Other therapies were prescribed for 7.5% of the patients.

Safety results

None of the reasons for treatment discontinuation with fulvestrant was related to intolerance.

Date of the report

13 April 2010