AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Nolvadex
ACTIVE INGREDIENT: Tamoxifen

Study No: NIS-OIT-DUM-2006/1
Retrospective observational trial on reasons for withdraw of Adjuvant Tamoxifen in Breast Cancer patients (SOSTA)

Developmental phase: Observational Study
Study Completion Date: Last patient completed: 30 May 2008
Date of Report: 09 April 2009

OBJECTIVES:

Primary Objective:

To detect the incidence of Tamoxifen adjuvant therapy interruption due to intolerance in menopausal subjects affected by breast cancer

Secondary objectives:

1. To evaluate the nature of adverse events which caused the interruption of Tamoxifen adjuvant therapy due to intolerance.
2. To evaluate the percentage of subjects interrupting the Tamoxifen therapy due to gynecological side effects
3. To evaluate the percentage of subjects interrupting the Tamoxifen therapy due to thromboembolic side effects.
4. To evaluate which treatments subjects interrupting the Tamoxifen therapy due to intolerance undergo.
5. To evaluate the onset of side effects in terms of time and resolution.

METHODS:

Case histories of post-menopausal subjects under Tamoxifen treatment in a period of time between January 2003 and December 2004 have been retrospectively reviewed. Subjects have been screened to identify those interrupting the treatment with Tamoxifen due to intolerance, in order to firstly estimate the interruption incidence rate The study involved 13 centers

Subjects interrupting the treatment with Tamoxifen due to intolerance have then been evaluated and included in the study respecting inclusion and exclusion criteria. Data concerning diagnosis, staging, disease biological features, side effects causing the interruption of Tamoxifen therapy, and therapy undergone after the interruption have been collected.

RESULTS:

Primary objective

The incidence of Tamoxifen adjuvant therapy interruption due to intolerance observed in this study was 19.5 (95% CI = 0 – 52.67). However, due to the extremely wide variation of enrollment rate, ranging between 3.85% and 100% of the screened subjects, this value could be somewhat biased. Excluding center with 100% of screened subjects enrolled in the observational study, the incidence of Tamoxifen intolerance-related interruptions decreased to 11.16 (0 – 36.24) that should be closer to reality

Secondary objectives

The nature of adverse events, which caused the interruption of Tamoxifen adjuvant therapy due to intolerance, is described in table 4, according to CTC classification. Each subject could have had more than one adverse event.

Table 4 - Adverse events related to the interruption of Tamoxifen adjuvant therap

CTC adverse event	Number of AE	%
Renal/Genitourinary	104	50.73
Vascular	32	15.61
Neurology	19	9.27
Endocrine	13	6.34
Gastrointestinal	8	3.90
Allergy/Immunology	7	3.41

Dermatology/skin	5	2 44
Ocular/visual	5	2 44
Coagulation	4	1 95
Hepatobiliary/Pancreas	4	1.95
Cardiac general	3	1.46
Syndromes	1	0.49
Total	**205**	**100**

The percentage of subjects interrupting the Tamoxifen therapy due to renal/genitourinary adverse events (endometrial alterations, mainly) side effects was of 50.73%

The percentage of subjects interrupting the Tamoxifen therapy due to vascular adverse events (thromboembolic events, mainly) was of 15 61%.

Treatments subjects interrupting the Tamoxifen therapy due to intolerance undergo are described in Table 5.

Table 5 - Treatment taken by subjects interrupting the Tamoxifen therapy

Post Tamoxifen Therapy	Subjects N.	%
None	**20**	**10.58**
Anastrozole	**94**	**49.74**
Letrozole	**52**	**27.51**
Exemestane	**22**	**11.64**
Other*	**1**	**0.53**

Tamoxifen therapy was interrupted due to side effects after a median time of 11 83 months (95% CI: 8.93-15.90) and adverse events were resolved in a median time of 2.53 (95% CI: 1.80 – 4.40).