AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: NA
ACTIVE INGREDIENT: NA

Study No: NIS-OIT-ARI-2008/1
TIME 2 CHANGE

Developmental Phase: NA
Study Completion Date: February 28th 2010
Date of Report: December 17th 2010

OBJECTIVES:

The TIME-2-CHANGE was a retrospective, multicentre, observational (non-interventional) study, carried out in 3 Oncology Centres in Veneto (Aviano, Trento and Verona) based on the use of adjuvant hormonal therapies in the treatment of hormone-responsive breast cancer in two successive time periods, in relation to the recent changes in national and international recommendations (ASCO and AIOM guidelines).

The primary aims of the study were:

1. relative frequencies of the first adjuvant hormonal treatment (tamoxifen vs aromatase inhibitor) started during two time periods of 12 months each (2006 and 2008).

The secondary aim was:

1. relative frequencies of the type of initial treatment: *upfront* (a single drug - tamoxifen or aromatase inhibitor) or *early switch* (planned sequence of tamoxifen and inhibitor);
2. type of treatment and relative percentages of treatment undertaken subsequently by the patients after interruption of the first hormonal therapy;
3. types of adverse events and their relative frequencies.

METHODS:

Each of the investigators recruited patients according the following steps:

Inclusion criteria

- Post-menopausal patients with surgically treated breast cancer who started adjuvant hormonal therapy between January 2006 and December 2006 or between January 2008 and December 2008.
- Documented evidence of the way adjuvant hormonal treatment was initiated.

Exclusion criteria

- Pre- or peri-menopausal patients with surgically treated breast cancer who started adjuvant hormonal therapy.
- Patients already enrolled in clinical studies aimed at investigating hormone therapies.

Data were collected retrospectively. The information that were recorded includes: diagnosis, stage and biological characterization of the disease, way of first use of adjuvant hormonal therapy, updating of the stage of the disease and type of hormone treatment being used 24 months after the initiation of adjuvant hormonal therapy.

Adverse events that caused any interruption of therapy and the treatment prescribed after such an interruption were also recorded.

Data from the eligible patients were recorded in specific CRF, which included: documentation of the pathology: (histological type, pathological stage, receptor status, HER2), documentation of loco-regional treatment received (surgery / radiotherapy), documentation of the adjuvant hormone therapy initially prescribed and of any substitution (other than that prescribed), documentation of any interruptions of adjuvant hormone therapy administered (because of toxicity, disease recurrence, other), documentation of symptoms that could be related to the adjuvant hormone therapy and treatment-related events, as well as documentation of any recurrence of the breast cancer.

RESULTS:

At the end of the study 500 individuals were recruited.

243 pts starting in 2006; 257 pts starting in 2008

Primary Endpoint:

In patients starting in 2006 adjuvant hormonal therapy 54% of them were treated with aromatase inhibitor (AI), tamoxifen in 44% and a combination therapy of tamoxifen and AI in the remaining 2%.

Among women that start hormone therapy in 2008, the percentages were 75% for AI, 23% for tamoxifen and 2% for the combination of the two drugs.

The 21% increase in prescriptions of aromatase inhibitors as up-front treatment, confirming an alignment with new guidelines.

Separate analysis of the two major sites showed an increased use of tamoxifen for Aviano (AI at 40% and 54% in 2006 and 2008), in Verona (AI of 68% and 90% in 2006 and 2008).

The differences between the two groups were significant time in both sites ($p = 0.0438$ for Aviano and $p < 0.0001$ for Verona).

Between 2006 and 2008, there was a decreased use of anastrozole in the overall sample (from 51% to 31%) for the of increased use of letrozole (5% to 44%).

Secondary Endpoint:

1- Type of adjuvant hormone therapy prescribed (up fornt vs. switch).

The most prescribed treatment regimen was upfront, defined as taking a single type of treatment (tamoxifen or AI-aromatase inhibitor) for all the first 5 years of therapy: both in 2006 as in 2008.

2- Variations of adjuvant hormonal therapy prescribed. The proportion of patients characterized by a change in the initial hormonal adjuvant therapy appeared generally low and decreasing over time: 33 patients in 2006 (14%) and 22 patients (8%) in 2008. The reasons for change consisted mainly of the onset of adverse events, and to a lesser extent by the onset of a new tumor, recurrence or progression of the disease, in reaching guidelines, or by request of the patient, globally but also in the two sites when considered individually

3- Variations of adjuvant hormonal therapy prescribed due to adverse events. In 5% of patients that start hormonal therapy in 2006 (11 women out of 243) and 4% of those that start in 2008 (9 women out of 257) there was a change in the adjuvant treatment due to the onset of at least one adverse event.

Safety:

The proportion of patients affected by the occurrence of at least one adverse event decreased significantly during the transition from one time frame to the next: 30% observed in 2006 was reduced to 14% in 2008.

The majority of women (both within the two time windows), complained one adverse event.

At 24 months after adjuvant hormonal therapy, 93% of the patients enrolled in 2006 said they were disease free, while the remaining patients reported having suffered a locoregional recurrence (3%) or visceral disease (3%), without differences between centers.

Overall, patients that start adjuvant hormonal therapy in 2008 at the last clinical observation made were healthy. The 98% of patients on this study were recurrence free, in Aviano 99% and Verona 97%.