STUDY REPORT SYNOPSIS

ARTEMIS: ARimidex Therapy compliance Electronic MonitorIng System

A study to evaluate the impact of educational material on the adherence to adjuvant anastrozole for postmenopausal women with hormone sensitive early breast cancer

First patient recruited: 10 July 2009
Last patient recruited: 30 December 2009
Last patient completed: 14 March 2011
Database locked: 5 May 2011

OBJECTIVES:

The primary objective of this study is to assess how educational material affects overall adherence to anastrozole in a non-controlled real-life setting. In this study patients' adherence to the prescribed treatment was expected to be improved by modifying patients' motivation and changing their behaviour through the mailed educational material that covered several topics such as characteristics of early breast cancer, the risk of recurrence, the benefits, and side-effects of the treatment, and importance of adherence to a long-term hormonal medication.

If on a given day, the medication was not taken there can be two reasons: (1) the patient had previously discontinued treatment (non-persistence) or (2) the patient was still engaged with the dosing regimen but neglected to take a dose on that particular day (non-execution). Adherence analysis does not distinguish non-persistence and non-execution. The secondary objectives of this study are to analyze the impact of educational materials by mail on persistence with anastrozole (how long the patient stayed with the regimen) and how well the execution of once daily anastrozole dosing regimen while the patient is still engaged to the treatment. Patients' reported reasons why they discontinued the anastrozole treatment were evaluated in this study.

METHODS:

This is a randomised, open label, parallel-group, multi centre study. Postmenopausal women with hormone sensitive early breast cancer that have been prescribed anastrozole according to the SmPC and current clinical practice were recruited from 5 centres in Belgium. Patients were randomised 1:1 in the two study arms:

- Standard: 12-month follow-up of anastrozole treatment according to SmPC and current clinical practice.

- Educational: 12-month follow-up of anastrozole treatment according to SmPC and current clinical practice plus reception of educational material by mail.

During this study, the subjects received anastrozole according to the SmPC and current clinical practice. Electronic monitoring using Medication Event Monitoring System (MEMS™) was used to compile patients' dosing histories.

RESULTS:

A total of 107 patients (54 Standard, 53 Educational) with an average age of 61 (+/- 10) and an average post-menopausal age of 49 (+/- 6) were recruited from 5 centres in Belgium. 53% of the patients had chemotherapy; 75% of the patients had diseases other than breast cancer, and 15% of the patients used herceptine as other treatment for breast cancer. Baseline characteristics were similar for the two groups.

Primary outcome: adherence to anastrozole

Adherence to anastrozole for both groups was analyzed by looking at the percent of patient with correct dosing (at least one dose) in each group over time (Figure A). The daily average of percent of patients with correct dosing for 365 days is 80.15% (SD = 4.16%) for the Standard group and 86.72% (SD = 4.94%) for the Educational group, however the difference between the two groups are not significant (GEE model, p=0.2358). The daily average of percent of patients with correct dosing of both groups combined is 83.40% (SD=4.22%). The adherence to anastrozole of both groups decreased over time, due to patients who discontinued the treatment during the study period. The diminishing rate is not significantly different between the two groups (p=0.5630).

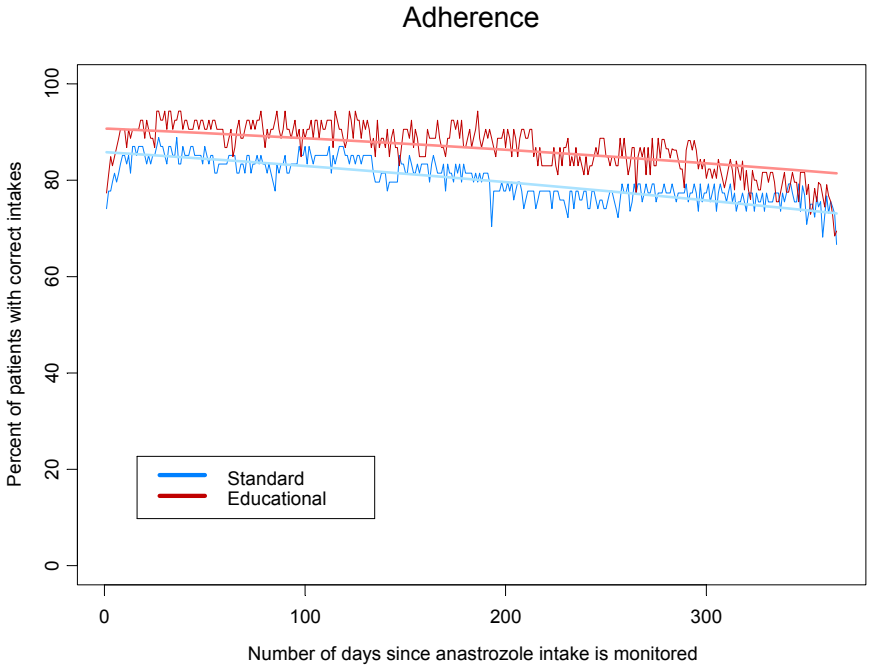

Figure A: Adherence to anastrozole: daily percentage of patients with correct intakes in both groups

Secondary outcome: persistence with anastrozole

Persistence is the length of time during which the medication is taken, i.e. the time from the first-taken dose to the last taken dose. The Kaplan-Meier curve was used to estimate the percentage of patients who stayed with the regimen based on MEMS data (Figure B). At one year, 77.8% [SE=5.66%] of patients in the Standard group and 84.7% [SE=4.97%] of patients in the Educational group stayed with the regimen. A log-rank test showed that there is no significant difference of the persistence curves between the two groups (p = 0.0782).

The reported reasons of early discontinuation are shown by Table A. During the study period 16 patients dropped out from the study: 9 patients from the Standard group and 7 patients from the Educational group. Based on the MEMS data, 4 patients (3 Standard, 1 Educational) were detected of having stopped taking the medication earlier than the end of the study but never claimed it in the CRF. Two patients in the Standard group had a recurrence; one of them reported a metastasis.

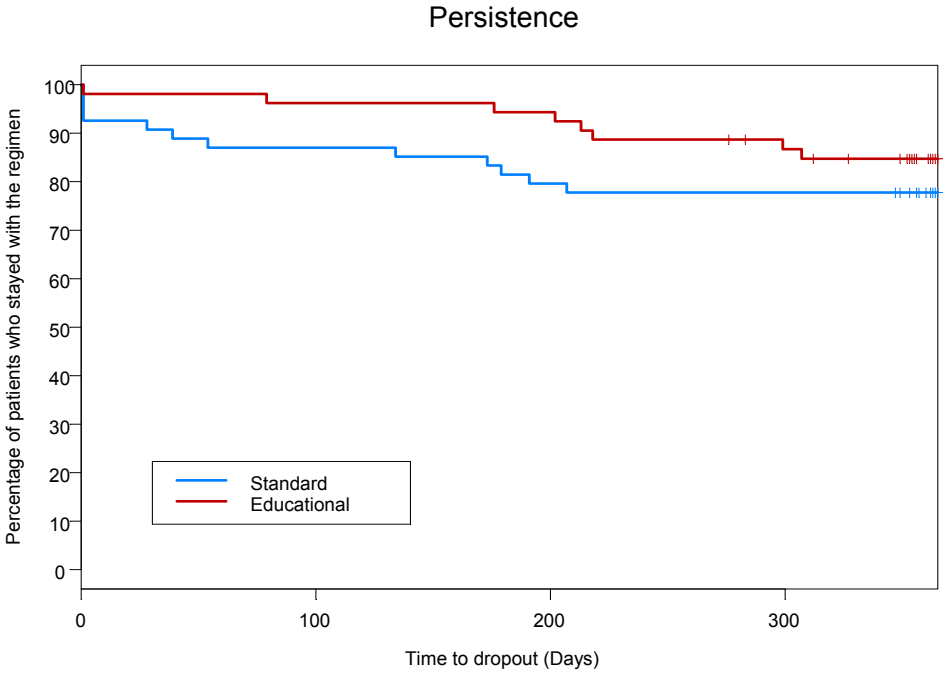

Figure B: Persistence with anastrozole based on MEMS data compared between both groups

Reasons	Standard (N=54)	Educational (N=53)	Total (N=107)
Side effects N(%)	1(1.9%)	4(7.4%)	5(4.7%)
Subject's wish N(%)	2(3.7%)	2(3.8%)	4(3.7%)
Recurrence N(%)	2(3.7%)	0	2(1.9%)
Physician recommendation: Resumption of ovarian function N(%)	2(3.7%)	1(1.9%)	3(2.8%)
Others: Arthralgia N(%)	1(1.9%)	0	1(0.9%)
Physician recommendation: Augmentation of confusion N(%)	1(1.9%)	0	1(0.9%)
TOTAL RECORDED IN THE CRF N(%)	9(16.7%)	7(13.2%)	16(15.0%)
Discontinuation not recorded in the CRF – based on MEMS N(%)*	3(5.6%)	1(1.9%)	4(3.7%)
TOTAL N(%)	12(22.2%)	8(15.1%)	20(18.7%)

Table A: Reasons of early discontinuations

Secondary outcome: execution of the once daily anastrozole regimen

Execution of the anastrozole regimen was analyzed by looking at the day to day percent of patients with correct dosing among patients who were still engaged to the anastrozole regimen (Figure C). The daily average probability of correct dosing is 96.46% (SD=3.05%) for the Standard group and 93.99% (SD=3.11%) for the Educational group. The average probability of correct dosing of both groups combined is 95.17% (SD=2.52%). There is no significant difference between Educational and Standard group in the quality of the regimen execution (GEE model, p=0.1674). The probability of correct dosing increased over time (p=0.0126), due to the fact that patients who had poor quality of execution tend to quit early, leaving patients with good quality of execution in the observed population. The increasing rate is not significantly different between the two groups (p=0.5573).

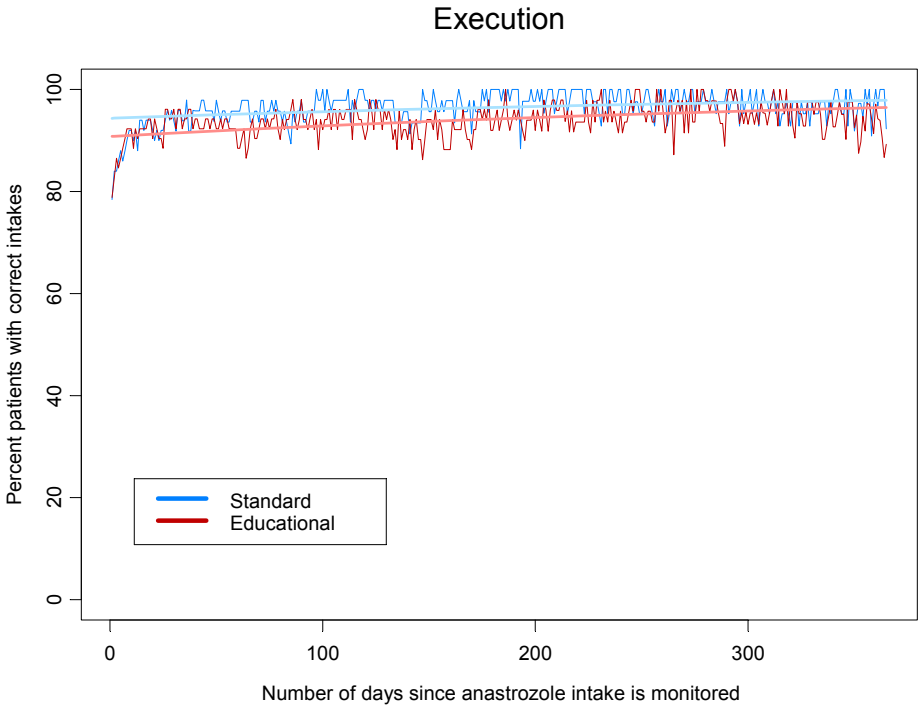

Figure C: Execution of anastrozole: daily percentage of patients with correct intakes in both groups among patients who are still engaged to the treatment

The association between execution and persistence with anastrozole is confirmed by the Cox model with percent of correct dosing during the execution period as explanatory variable. The model shows a relative risk of early discontinuation of 0.956 (p<0.0001): any additional percent of correct dosing during the execution period on average reduces the risk of early discontinuation by 4.4%.