AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable.
ACTIVE INGREDIENT: Not applicable.

Study No: NIS-ORO-XXX-2012/1
Epidemiology and Therapeutic Management of Metastatic Breast Cancer in Romania: A retrospective cohort study **EMER study**

Developmental Phase: No
Study Completion Date: 30 June 2013
Date of Report: 23 June 2014

OBJECTIVES:

Primary Objectives

To calculate the incidence rate of progression of disease in a cohort of subjects newly diagnosed with Metastatic Breast Cancer (MBC), either de novo or having progressed from a non-metastatic stage. In participating centre, all subjects meetig inclusion criteria were enrolled.

Secondary Objectives

The secondary objectives of this study were the following:
- To estimate the progression free survival (PFS) rates at 12 and 18 months after diagnosis;
- To estimate the progression free survival (PFS) time;
- To estimate time to progression (TTP);
- To describe the clinical and pathological characteristics of newly diagnosed MBC subjects, including type and location of metastasis, tumor size, co-morbidities and performance status;
- To describe the socio-demographic and anthropometric characteristics of newly diagnosed MBC subjects;
- To describe the diagnostic and clinical management patterns of MBC subjects since confirmed diagnosis;

To describe health care utilization associated with the disease in Romania.

Inclusion Criteria

- Female aged 18 years and over
- Diagnosis of breast cancer according to ICD-10 diagnostic criteria with confirmed metastasis
- Confirmed diagnosis between 1st July 2010 and 30th June 2011
- Female subject managed for her disease at the same setting where final diagnosis of MBC was performed

Exclusion criteria

History of concurrent or other primary malignancies (except curatively resected non-melanoma skin cancer or in situ cervical cancer).

METHODS:

This was a multicenter, national, observational, 18-month retrospective cohort study. The Study was conducted through medical chart review of MBC female subjects diagnosed between 1st October 2010 and 31st March 2011. A representative sample of sites according to the MBC management reality in Romania was selected. Representativeness was inferred from available publications and/or a panel of experts from the country.

Centers were selected based on their experience in treating subjects with advanced breast cancer and their ability to comply with study guidelines. It was planned to enroll approximately 200 subjects but finally 125 subjects were enrolled.
All subjects (n=125) were included in All Patient Population and Full Analysis Set. Due to missing progression data after MBC diagnosis 123 subjects (97.4%) were included in the Per Protocol Population.

Statistical methods

Primary variable
Number of progression events on a per patient-year-basis was determined with descriptive statistical tools. The 95% confidence interval of the incidence rate was calculated with the Byar's confidence limits method.

Secondary variables
The first three endpoints were modelled and estimated with the help of Kaplan-Meier method. The remaining endpoints were characterized by descriptive statistical tools.

RESULTS:

Primary endpoint:
The incidence rate of progression of disease progression per patient-year was 0.545, the associated confidence interval is [0.439; 0.669].

Secondary endpoints:

Eighty-six events were observed (69.9%). The estimated probability (with the corresponding 95% CI) of PFS is 0.6013 (0.5079, 0.6826) at 360 days (~12 months) from diagnosis of MBC, and 0.4367 (0.3459, 0.5237) at 540 days (~18 months) from diagnosis of MBC.

Eighty events were observed (65.0%). The median of Time to Event is 469 days, (95% confidence interval is [399, 632]).The estimated probability (with the corresponding 95% CI) of TTP is 0.6436 (0.5495; 0.7230) at 360 days (~12 months) from diagnosis of MBC, and 0.4674 (0.3729, 0.5563) at 540 days (~18 months) from diagnosis of MBC.

Eighty-six events were observed (69.9%). The median of Time to Event is 456 days, (95% confidence interval is [368, 565]);
There were 123 subjects with non-missing death status in the study. 34 subjects (27.64%) died due to any cause which implies a death rate of 0.159 per patient-year. 28 subjects (22.76%) died due to MBC which implies a death rate of 0.131 per patient-year.

Ninety-nine subjects (79.2%) lived in the city and 26 subjects (20.8%) lived in the county. The average height of the subjects was 161.8 cm (SD: 5.7 cm) and the average weight of the subjects was 69.3 kg (13.8 kg). The average age was 58.7 year (SD: 11.3 year).

The Menopausal status at metastatic disease diagnostic was menopausa for 111 subjects (88.8%), while 10 subjects were in premenopausal and 4 subjects in perimenopausal status. The average age for menarche was 13.7 year (SD: 1.5 year), while average age at menopause was 46.9 years (SD: 5.3 year). Average age at first delivery was 22.1 year (SD: 4.4 year, n = 97). One hundred subjects are known to have given birth at least once. The average number of live births is 1.77 (SD: 0.81). Sixty-five subjects (65%) are known to have breast feeding history. The average duration of breast feeding was 9.4 month (SD: 7.9 month). Only 4 subjects were known to have taken oral contraceptives (for 8 years on average). Only 2 subjects were known to have received hormone replacement therapy.

The average age at metastatic disease diagnosis was 57.3 years. The most frequent metastasic tumor types were Invasive ductal carcinoma with 22 subjects (17.6%), Ductal carcinoma with 17 subjects (13.6%) and Infiltrating ductal carcinoma with 6 subjects (4.8%). The most frequent locations of metastasis were Bone with 75 subjects (60%), Liver with 36 subjects (28.8%) and Lung with 35 subjects (28%). The most frequent comorbidities were Cardiovascular disease (HTA) with 25 subjects (20%), Cardiac disease (IHD) with 15 subjects (12%) and Osteoporosis with 10 subjects (8%).

The most frequent methods of assessment for metastatic stage were Computer tomography (CT) scans with 90 subjects (72%), Clinical breast examination with 71 subjects (56.8%) and Tumor markers with 54 subjects (43.2%). Twenty-nine subjects (23.2%) had palliative surgery and 38 subjects (30.4%) had radiotherapy. The mean duration of Chemotherapy in MBC line 1 was 8.57 months with regiments of: Taxane base: 42 subjects (33.6%), Antracicline base: 15 subjects (12%) and Other: 18 subjects (14.4%). The mean duration of Hormonal therapy in MBC line 1 was 12.89 months with

regiments of: a LHRH: 4 subjects (3.2%), a LHRH + tamoxifen: 0 subjects (0%), tamoxifen: 10 subjects (8%), aromatase inhibitor: 36 subjects (28.8%), SERD: 12 subjects (9.6%) and other: 2 subjects (1.6%).

Thirty-four subjects (27.2%) had emergency department visits with an average number of visits of 2.59. Seventy-seven subjects (61.6%) had outpatient visits with an average number of outpatient visits to oncology service of 18.84. Ninety-six (76.8%) of the subjects needed hospital admission with an average number of admissions of 6.93 and an average number of total days of hospitalisation of 36.03. Ninety-four (75.2%) of the subjects needed one day hospitalisation with an average number of one day hospitalisations of 22.84. Seven subjects used home healthcare services. Six subjects used hospice services. Thirty-one subjects (24.8%) were treated with other concomitant therapy for breast cancer and 49 subjects (39.2%) were treated with other concomitant therapy for pre-existent comorbidities.