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Non-Interventional Study (NIS) Primary Report Synopsis	
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LINE: Treatment patterns in postmenopausaL women wIth hormone receptor positive breast caNcEr

Study dates:	**First Subject In: 19/06/2012**
	Last Subject Last Visit: 15/01/2015

NIS REPORT SYNOPSIS (IF APPLICABLE)

LINE: Treatment patterns in postmenopausaL women wIth hormone receptor positive breast caNcEr

The current Non-Interventional Study was conducted to collect the data on clinical effectiveness of second-line hormone treatment and quality of life in patients with Breast Cancer (BC).

Study center(s): 25 Russian sites were selected in the study; 14 sites out of them were active and enrolled the subjects.

Publications: None.

Objectives:

Primary objective of the study was collection of data and analysis of routine (standard) regimens of endocrine therapy in postmenopausal women with hormone receptor-positive with recurrence after adjuvant hormone therapy or progression after initially inoperable locally advanced or metastatic breast cancer.

Secondary objective was to evaluate the impact of endocrine treatment on quality of life using a patient-rated, breast cancer specific, validated questionnaire (FACT-B) and to evaluate the anxiety inventory (Sbielberg-Khanin the State-Trait Anxiety Inventory); to collect real life data on the treatment habits in clinical practice across Russia; and to collect documented confirmation for clinical benefits of the treatment (within follow-up period) in this patient category.

Study Design:

This was a prospective, multicenter, observational, non-interventional study using a paper CRF.

Eligible women were defined as patients for whom the treating physician had decided to prescribe the first (with recurrence after adjuvant hormone therapy) or second (initially inoperable locally advanced or metastatic breast cancer) line therapy in his/her clinical judgement and who agreed to participate in the project. They were enrolled in the study at the first visit after reading and signing the Informed Consent Form. For each patient, the investigator recorded data of 4 visits which he/she conducted according to his/her current clinical practice.

Changes to the protocol:

Protocol Amendment # 1 issued 28 March 2012 was aimed to update section 7 "Study Conduct" with information regarding subject identification number assign procedure.

Protocol Amendment # 2 issued 11 May 2012 was aimed to clarify the procedures for the questionnaires usage during the visits and time limits of the treatment administration before the patients is enrolled into the study.

Protocol Amendment # 3 issued 28 November 2012 was aimed to clarify the criteria of patients discontinuation from the study.

Protocol Amendment # 4 issued 18 March 2013 was aimed to extend study timeframes because of slow enrolment rate.

Protocol Amendment # 5 issued 25 November 2012 was aimed to extend study timeframes because of slow enrolment rate.

Target subject population and sample size:

- Postmenopausal women with hormone receptor-positive breast cancer:
  - Recurrence after the adjuvant hormone therapy;
  - Or initially inoperable locally advanced or metastatic breast cancer progressed after the first line hormone therapy.

The sample size was estimated using the following rules and assumptions:

- Statistic power of tests should not be lower than 80% (probability of missing an existing effect is 0.8);
- Probability of type 1 error should not exceed 5% (probability of an erroneous decision on the presence of effect is less than 0.05);
- The used statistical criteria were two-sided due to the unavailability of reliable information about advantages of any treatment regimen over others;
- Since the primary study objective was collection of data and analysis of routine (standard) hormone therapy regimens in postmenopausal patients with hormone receptor-positive, locally advanced or metastatic breast cancer, who were receiving a second-line hormone treatment, the sample size was calculated based on the size of the parent population of postmenopausal patients with hormone receptor-positive BC in Russia, which is approximately 30,000-50,000 patients[1].
- The sampling error was assumed to be 7.5%.

Based on the above-listed assumptions, the minimum required total sample size was estimated to be 171 patients/

[1] Malignant Neoplasm in Russia in 2010 (Morbidity and Mortality). Ed. by V.I. Chissov, V.V. Starinsky, G.V. Petrova. Moscow, 2012.

However, adjusting for the predetermined 20% dropout rate, at least 205 patients should sign the informed consent.

Inclusion Criteria

All patients with BC on the first (after recurrence adjuvant hormone therapy) or the second (for initially inoperable locally advanced or metastatic breast cancer) line hormone therapy, who visit participating hospitals within not more than 1 month after the onset of the first or second-line treatment, will be considered eligible for the study.

Patients will be asked to sign the informed consent form stating that no changes in their treatment will be made in the study, and that the study will conduct only collection of information.

The patients who will be observed in this study must meet all of the following criteria:

- Postmenopausal women with hormone receptor-positive breast cancer:
  - Recurrence after the adjuvant hormone therapy;
  - Or initially inoperable locally advanced or metastatic breast cancer progressed after the first line hormone therapy;
- Ability to read and write and complete questionnaires.
- Provision of written informed consent.
- Patients who have already been prescribed endocrine therapy no more than 1 month ago with the above-mentioned lines and who can continue on the prescribed therapy in the investigator's opinion according to his/her regular clinical practice and current guidelines.

Drug prescription will be clearly demarcated from the decision on patient inclusion in this non-interventional study.

Exclusion Criteria

As per study design, to ensure high validity of data and to obtain accurate information on real-life practice, patients currently participating in other clinical studies will not be included in this study.

Study variable(s):

- Primary variable is treatment patterns
- Other variables
  - Quality of life (QoL): the extent of reduction in QoL deficit from 1 visit.
  - The extent of reduction anxiety inventory
  - Effectiveness: Tumor regression; number (%) of patients with complete response (CR), partial response (PR) or stable disease

- Historical data analysis: treatment patterns effectiveness, duration of the adjuvant or first-line hormone treatment
- Response duration
- Performance status (ECOG)
- Epidemiological data (age, etc.)
- Co-morbidities
- Pharmacoeconomical analysis

Results

Disposition of subjects and baseline characteristics of study population:

- 139 subjects were enrolled in LINE study that is 67,8 % of estimated enrollment rate. The study was prolonged twice in order to reach the recruitment cap. 9 subjects (6,5 %) out of them were enrolled incorrectly – did not meet the protocol inclusion/exclusion criteria.
- 76 subjects (55 %) finished the study according to the protocol (e.g. were at all 4 study visits and performed all procedures). 22 subjects (15,8 %) had early termination due to disease progression. 23 subjects (16,5 %) were lost for follow-up.
- All subjects were female, the mean age of study population was 61,4 years. Minimal age was 37 years, maximum age was 83 years.
- All subjects were postmenopausal women and had diagnosis "hormone receptor positive breast cancer".
- TNM classification: the most common indications were T2 (48 %), N1 (36 %), M0 (83 %).
- Localization of metastasis: the most common localization was in bone – in 66 subjects (47 %), in soft tissues – in 30 subjects (22 %) and in lung – in 28 subjects (20 %) .
- Histological type of the primary tumor: the most common histological type was invasive ductal carcinoma – in 87 subjects (63 %) and invasive lobular carcinoma – in 30 subjects (22 %).
- Limitation of diagnosis:
    - the mean age of breast cancer diagnosis was 3,7 years,
    - the mean age of advanced breast cancer diagnosis was 0,6 years.
- Concomitant diseases and conditions: the most common concomitant deseases were cardiovascular – essential hypertension in 52 subjects (37 %), ischemic heart disease in 47 subjects (34 %) and atherosclerotic cardiosclerosis in 19 subjects (14 %). 31 subjects had not any concomitant diseases and/or conditions.

Therapy:

- Prior therapy:
    - 137 subjects had prior endocrine therapy;
    - 109 subjects had surgery;
    - 93 subjects had prior chemotherapy;
    - 90 subjects had prior radiotherapy.

  More than half of subjects had all 4 types of therapy in the past.
- 100 subjects had prior adjuvant hormone therapy; 37 subjects had prior first line hormone therapy; 2 subjects had not prior hormone therapy and were incorrectly enrolled into the study.
- The whole mean duration of prior endocrine therapy was 24,7 months: the mean duration of adjuvant hormone therapy was 25,6 months; the mean duration of the first line hormone therapy was 23,4 months.
- The most common trade marks of hormone medication used in the study were:
    - Tamoxifen – 121 subjects;
    - Anastrozole – 7 subjects;
    - Letrozole – 5 subjects.

Outcome and quality of life status:

- Effectiveness status by Visit 4:
    - Complete response – 4 subjects;
    - Partial response – 9 subjects;
    - Stable disease – 56 subjects;
    - Previous metastases progression – 4 subjects;
    - New metastases – 4 Subjects.
- Effectiveness: Total tumor regression – number (%) of patients with complete response (CR) + partial response (PR) + stable disease:
    - By Visit 2: 100 subjects (93,46 %) from 107 people;
    - By Visit 3: 86 subjects (86,00 %) from 100 people;
    - By Visit 4: 69 subjects (89,61 %) from 77 people.

- ECOG Status: at 4th visit 6 subjects had decline according to ECOG scale (the grades grew up) and 5 subjects had improvement (the grades dropped off).

- Subjects weight dynamics: mean subjects weight at Visit 1 was 75,5 kg and increased till 76,5 kg by Visit 4.

- Subjects quality of life status:

    - FACT-B Trial Outcome Index (TOI): mean indication of all subjects was 52,1 at Visit 1 and increased till 53,2 by Visit 4; mean indication of subjects who performed all 4 visits was 50,6 at Visit 1 and increased till 53,5 by Visit 4.

    - FACT-G Total Score: mean indication of all subjects was 64,2 at Visit 1 and decreased till 62,5 by Visit 4; mean indication of subjects who performed all 4 visits was 63,6 at Visit 1 and decreased till 62,7 by Visit 4.

    - FACT-B Total Score: mean indication of all subjects was 84,0 at Visit 1 and decreased till 83,3 by Visit 4; mean indication of subjects who performed all 4 visits was 82,3 at Visit 1 and increased till 83,7 by Visit 4.

    - STAI – State Anxiety Scale: mean indication of all subjects was 51,7 at Visit 1 and decreased till 48,5 by Visit 4; mean indication of subjects who performed all 4 visits was 52,3 at Visit 1 and decreased till 48,3 by Visit 4.

    - STAI – Triat Anxiety Scale: mean indication of all subjects was 50,4 at Visit 1 and decreased till 50,3 by Visit 4; mean indication of subjects who performed all 4 visits was 51,1 at Visit 1 and decreased till 50,2 by Visit 4.

Overall results:

- There were difficulties in subjects enrollment as hormone therapy is rarely prescribed in Russia. Hormone therapy is needed in popularization among the Russian doctors-oncologists.

- The most reason of the second line hormone therapy prescription was recurrence after the adjuvant hormone therapy: 100 subjects (71,94 %) from 139 people.

- The most popular trade mark of hormone medication was Tamoxifen: 121 subjects (87,05 %) from 139 people.

- Comparative evaluation showed that increased quality of life (QoL) levels occured during hormonal therapy in patients with breast cancer. The QoL level increased from 82,3 points to 83,7 points (plus 1,4 points) according to scale of FACT-B Total Score in subjects group who performed all 4 visits.

– The STAI results show that there is a slight decrease (that is a positive result) in State Anxiety Scale from 52,3 to 48,3 points (minus 4 points) in subjects group who performed all 4 visits, and no significant changes were observed in Triat Anxiety Scale.