Clinical Study Report Synopsis	
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BreCaReAl : Breast Cancers Registry in Algeria

Epidemiology of Breast Cancer in Women based on Diagnosis Data from Oncologists and Senologists in Algeria

Study dates: First subject enrolled: 29/05/2016
Last subject last visit: 31/03/2022

Phase of development: Non-interventional study

National Co-ordinating Investigator: [redacted]

Sponsor's Responsible Medical Officer: [redacted]

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

This submission /document contains trade secrets and confidential commercial information, disclosure of which is prohibited without providing advance notice to AstraZeneca and opportunity to object.

Study centre(s)

Twenty-three (23) sites participated to the study with 19 (82,6%) oncology departments and 4 (17,4%) senology departments of community and university hospitals, from the public sector in Algeria.

Publications

Smaili, F., et al, Cancer Treatment and Research Communications 25 (2020): 100220.

Objectives and criteria for evaluation

Table S1 Objectives and outcome variables

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Primary		To evaluate the survival status.	Survival status at 3, 6, 12, months then every 6 months until 05 years from inclusion (18, 24, 30, 36, 42, 48, 54 and 60 months of follow-up).
Secondary		To evaluate the incidence of women diagnosed with breast cancer, all stages combined, by oncologists and senologists in Algeria [8 months of recruitment duration],	Number of new diagnosed cases of breast cancer, all stages combined, by oncologists and senologists, in pre- and post-menopausal women, related to the general female population in Algeria [starting date – ending date of data collection].
Secondary		To evaluate the incidence of breast cancer by age during the 8 months of inclusion	Number of new cases diagnosed with breast cancer by age (18 - 20, 20-30, 30 - 40, 40 - 50, 50-60, 60 - 70 and > 70 years old).
Secondary		To evaluate the incidence of breast cancer by stage during the 8 months of inclusion	Number and frequency of new diagnosed patients by stage (TNM classification sub population).
Secondary		To evaluate the mortality of women diagnosed with breast cancer	Rate of recorded deaths, at 3, 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60 months of follow-up.
Secondary		To evaluate the mortality of women diagnosed with breast cancer by disease stages at the inclusion	Rate of recorded deaths, at 3, 6, 12, 18, 24, 30, 36, 42, 48, 54 and 60 months of follow-up by disease stages at the inclusion (TNM classification).

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Secondary		To describe the characteristics of patients with breast carcinomas pattern (anatomopathological types, cancer risk factors, clinical outcomes and histopathologic profile of young patients (<40 years)	Patient's profiles and characteristics (clinical information (menopausal status, performance status at diagnosis, cancer family history).
		To investigate the screening's conditions of breast cancer	Screening conditions: self-examination / medical consultation / mammography
Secondary		Identify and evaluate the molecular/cytopathologic testing considered by the investigators to take subsequent decisions regarding breast cancer management	Type and frequency of the molecular/cytopathologic markers considered by the investigators to take subsequent decisions regarding breast cancer management.
Secondary		Describe patients' treatment	Frequency of each first line treatment: chirurgical, chemotherapy, radiotherapy, targeted therapy, etc, for the whole study population and per disease stage (TNM classification).
Secondary		Evaluate the time from the diagnosis to the first line treatment	Mean time from the diagnosis to the first line treatment strategy implementation.
Secondary		To evaluate the quality of life of patients diagnosed with breast cancer	Quality of life questionnaires EORTC QLQ-C30

Study design

National, prospective, multicentric, non-interventional epidemiological study, conducted among oncologists and senologists in community and university hospitals, from the public sector in Algeria.

The study collected information on the characteristics, and breast carcinomas patterns of patients whose breast cancer diagnosis was confirmed by an anatomopathologist. The study was conducted over a representative, but not exhaustive sample of Algerian female patients.

Patients underwent clinical assessments and received the standard medical care as determined by the treating physician. Patients did not receive experimental intervention or experimental treatment as a consequence of their participation in this observational study. In addition, the study intended to collect data on patients diagnosed with breast cancer under conditions of routine clinical care.

The data for this observational study was collected with electronic case report forms (eCRF) (Appendix 2). It was anticipated that patient recruitment would last 8 months (expected from May 2016 to January 2017) and each patient would be followed for 60 months.

The study consisted of:

- Four in-hospital visits (inclusion visit, visit at 3 months, visit at 6 months, visit at 12 months). All patients presenting to their oncologists/senologists during a routine visit were sequentially asked to participate to the study

- In addition to the 4 visits, a phone contact with the patients was done by the investigator or the CRO (independent person) or during a routine visit to the investigator, to check the patients' survival every 6 months for 5 years (8 phone contacts starting from year 1).

Target subject population and sample size

Algerian female patients with newly diagnosed breast cancer all stages and confirmed during the study period by an anatomopathologist.

Inclusion criteria:

1. Female patients

2. Aged 18 years and over

3. Newly diagnosed with breast cancer all stages confirmed during the study period by an anatomopathologist, defined as a first diagnosis of breast cancer based on anatopathological results from at least a microbiopsy

4. Provision of subject informed consent

Exclusion criteria:

1. Informed consent not obtained.

2. Patients with a mental or psychological disorder according to their treating clinicians.

3. Patients participating in an interventional study or already included in the study. A patient could be consulted and treated in two different centres; thus a codification system will be generated to avoid duplicate participation.

No formal sample size calculation was done given the epidemiological type of the study and because patient recruitment was open at the national level. Hence, all eligible patients were included in the study with an expected number of 1200–1500 patients.

Statistical methods

Data were summarized using descriptive analysis. Median and interquartile ranges are displayed for non-normal distribution. Survival data were analyzed using the Kaplan-Meier method and patients were censored in case of loss to follow up and at last time point with information. A Cox regression model (backward selection) was used to define the factors associated with relapse. Statistical significance was two-sided and set at an alpha level of 5%. Cumulative incidence was also estimated in each class of age categorized by the National Institute of statistics. For a given class of age, the number of breast cancers was divided by the corresponding population size. Statistical analysis was done using SAS software SAS 9.4 and SAS/ STAT software, version 14.3 for Windows (SAS Institute Inc Cary, NC, USA).

Subject population

1500 patients were included in the study. 55% patients were excluded because they had at least one major deviation, the final population of analysis was 1445 patients (96 %).

Twenty-three (23) sites participated to the study with 19 (82,6%) oncology departments and 4 (17,4%) senology departments of community and university hospitals, from the public sector in Algeria. The median of patient's inclusion per site was 58 (IQR [9; 195]).

Summary of efficacy results

Primary endpoint:

Survival rate was 97,2%, 93,2%, 90,6%, 88,7% and 86,9% at 1, 2, 3, 4 and 5 years respectively.

Secondary endpoint:

Incidence of breast cancer, estimated over the recruitment period, was 22.5 [95%CI: 21.6; 23.3] per 100,000 inhabitants. The incidence of breast cancer was highest in the age group [45-50 years [with 48,8 cases per 100,000 inhabitants [95%CI: 44.7; 52.9].

Overall, 150 (10,4%) patients died with a median delay from inclusion of 22 months. The main cause of death was related to breast cancer progression (121 (80,7%) patients). Chemotherapy toxicity involved 3 (2%) patients and an unknown cause of death was reported in 18 (12%) of cases.

Overall, 705 (48,8%) patients had adjuvant chemotherapy and 468 (32,4%) patients had neoadjuvant chemotherapy.

Targeted therapy was performed on a minority of patients.

In case a surgery was indicated, it was performed during the first year of follow up.

Radiotherapy was mostly prescribed at 12 months follow up visit.

Summary of safety results

Overall, 165 (11,4%) patients had at least one serious adverse event (SAE).

The only SAE present in more than 1% of cases was “begnin neoplasm, malignant and non-specified (incl kystes and polypes)” which was reported in 51 (3,5%) patients).

The action taken was a permanent cessation of breast cancer treatment in 150 (69,1%) of cases. A breast cancer treatment modification was undertaken in 20 (9,2%) of cases and temporary cessation of breast cancer treatment was decided in 10 (4,6%) of cases.

Conclusion(s)

The BreCaReAl study was conducted over 60 months with a survival assessment each 6 months until 60 months. The young age as well as the advanced stage at diagnosis make the burden of breast cancer greater and require effective breast cancer management.