

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: No applicable

ACTIVE INGREDIENT: No applicable

Study No: NIS-OFR-DUM-2007/1

French national prospective survey on women with a invasive breast cancer

Developmental phase: No applicable

Study Completion Date: LSLV = 15 July 2008

Date of Report: 18 June 2009

OBJECTIVES:

The objective of the CSI observatory, held in France in 2007-2008, was to describe the radiological, clinical and pathological characteristics of a population of women with invasive breast cancer in comparison to a previous non interventional study, set up in 2001-2002 (RH2001).

METHODS and RESULTS:

A total of 162 physicians accepted to partake in the survey. Among them, 130 included at least one patient (80.2%). The 130 active physicians included a total of 1761 patients (14 patients per physician on average). Mean age of active physicians was 48 years, 71% were male, about one-third (33.8%) were gynaecological surgeons, 30.8% were radiotherapists, 23.8% were medical oncologists, about one half (48.5%) worked in a private hospital, and 23.1% in a cancer centre. The activity of the physicians was only private in 45.2% of cases, and exclusively hospital in 42.1% of cases. In about 75% of cases, more than 100 new patients with breast cancer were seen per year in their unit.

Among the 1761 patients included in this observatory, 1647 met the eligibility criteria. Mean age at the time of diagnosis was 58.5 years \pm 13.0 years, 72.4% were over 50 years. More than two-thirds of patients (69%) had no known risk factor for breast cancer.

Family history of breast cancer was found in 29.8% of the patients. More than two-thirds of patients (67.3%) were post-menopausal at the time of diagnosis, with a mean period between first menses and menopausal status of 37 years \pm 5 years. Diagnosis of breast cancer was made by screening in more than half of patients (52.6%) and in 60.8% of those over 50 years.

At the time of diagnosis, 61.3% of patients were symptomatic. The main sign was the presence of a nodule or a tumour, observed in 54% of symptomatic patients. Cancer was unilateral in the vast majority of cases (98.3%) and mainly located in the superior-extern quadrant of the breast (42.6%). At the time of diagnosis, a mammography was performed for 98.2% of patients, and an anomaly suggesting cancer (ACR5) was found in 59.0% of patients. In 42.3% of cases, the tumour measured less than 2 cm (T1); the majority of patients had no active flare-up (93.8%), no regional lymph invasion (81.2%) and no distant metastases (96.4%). Mammary ultrasound was also performed for 85.4% of patients, and a percutaneous sample biopsy performed for 80.4% of patients. Main histological type was infiltrating ductal carcinoma, in 80.4% of patients, and for 56% of patients an in situ component was associated. A SBR2 histoprognostic score was found in 48.1% of all patients, and in 70.7% of patients with ILC. On pathological examination, maximum tumour size was 20.1 mm \pm 16.3 mm on average. Tumour size was greater for infiltrating lobular carcinomas than for infiltrating ductal carcinomas. The mean number of lymph nodes sampled was 8 lymph nodes \pm 6 lymph nodes, in all. Sentinel lymph node was sampled in 37.5% of patients, and axillary curage was performed in 44.3% of patients. No regional lymph node invasion was found in two-thirds of the patients (66%). Hormone receptors were assayed for 99.4% of patients mainly by immunohistochemical methods. Hormone receptors were positive in 83% of tumours. The tumours of 81.4% of patients expressed oestrogen receptors, and those of 69.6% of patients expressed progesterone receptors. The proportion of patients in whom oestrogen receptors were positive increased significantly with age ($p < 0.001$).

In a very large majority of patients (91%), the HER2 protein had been assayed, and the latter was overexpressed in 14.2% of patients. The proportion of tumours overexpressing the protein increased in a statistically significant manner with lower age ($p < 0.001$).

Equivalent results were found when patients with metastatic cancer and patients having received neoadjuvant treatment were excluded from the analysis. A vast majority of patients (99.6%) were operated on. Surgical procedure was mainly a conservative surgery (70.4%). Moreover, 42.6% of patients had axillary curage and 41.0% had removal of the sentinel lymph node. Approximately 94% of patients had received or were to receive radiotherapy, and 50.7% of patients had received or were to receive chemotherapy. Main chemotherapy regimen consisted of 3 FEC 100 followed by 3 Docetaxel (58.6% of adjuvant chemotherapy regimens). Administration schedule of Trastuzumab to patients overexpressing the HER2 protein was once every three weeks in 91.7% of cases, and for a mean duration of 11.5 months \pm 2 months.

Hormone therapy was planned, performed or under way in 83% of patients of the eligible population, including 14 patients whose tumours expressed no hormone receptor.

Hormone therapy was mainly based on a non-steroidal aromatase inhibitor (63.3% of cases).

Nearly half of physicians who participated in the RH 2001 observatory were medical oncologists (49.2%), in contrast with less than one-quarter (23.8%) in the CSI observatory. In the RH 2001 observatory, the majority of participating physicians were practising in teaching hospitals, regional hospitals or general hospitals, while this was only the case for 28.5% of them in the CSI observatory. In the 2008 survey, nearly half of physicians (48.5%) were practising in a private hospital, and 23.1% in a cancer centre versus 13.7% in RH 2001.

Mean ages of patients on the day of their inclusion were similar in the 2 observatories (58.5 years). More than two-thirds of patients included in the 2 observatories had brought 2 pregnancies to term. More than one-fifth of patients in the CSI observatory had brought 3 pregnancies to term (21.3%), while an equivalent proportion of patients in the RH 2001 (21.9%) had only brought one to term. Mean ages of 1st pregnancy were similar in the 2 surveys (24.5 years), as were mean ages of menopause (50 years). A slightly lower proportion of patients included in 2008 had received hormone replacement therapy (34.5%) as compared to patients from the previous survey (38.3%). One-quarter of patients in the RH 2001 observatory and 29.9% of those in the CSI observatory had a previous family history of breast cancer. At the time of diagnosis, the tumours measured

by mammography were smaller in the 2008 survey, which may be explained by earlier diagnosis today, and therefore detection of tumours at an earlier stage due to the generalisation of breast cancer screening in France since 2004. A greater proportion of patients included in the CSI observatory had no regional adenopathy (81.2% vs. 73.3% for RH 2001). The proportions of patients with distant metastases at the time of diagnosis were similar (3.5%). However, the locations of these metastases were different between the 2 populations: more bone, pulmonary and pleural metastases in 2001 than in 2008 and, conversely, more hepatic and skin metastases in 2008. The distributions of histological types of invasive breast cancers were similar in the 2 populations. Hormone receptors, both ER and PR, were positive in equivalent proportions of patients in the 2 populations. The HER2 protein, which had been assayed only in 30.6% of patients in 2001, was assayed in 91.1% of the population in 2008. The protein was overexpressed in 20.6% of patients included in 2001, versus 14.2% of patients included in 2008.

The median of maximal tumour size determined by pathological examination was 19 mm in 2001, and 15 mm in 2008. This may also be explained by an earlier screening of breast tumour nowadays. Tumour margins superior to 1 mm were more frequent in the CSI observatory than in the previous survey (84.7% Vs 75.5% of patients).

Management of patients has changed between 2001 and 2008. In 2001, 58.7% of patients received adjuvant chemotherapy, and 75.4% received adjuvant hormonotherapy, while in 2008, 51% of patients received adjuvant chemotherapy and 83% adjuvant hormonotherapy. Chemotherapy regimens have changed over this period of time, since in 2001 the main regimen administered was a FEC 100 regimen (46.2%), while this regimen was only prescribed in 22.2% of cases in 2008, replaced by 3 FEC 100 followed by 3 Docetaxel (58.4% of patients). Other regimens prescribed in 2001 were only rarely prescribed 7 years later (FEC 75, FEC 50, FAC and AC regimens). Hormonotherapy has also greatly changed, since 2001 the main treatment prescribed (90.0% of patients) was Tamoxifen, while in 2008, only 32.1% of patients included in the CSI observatory had received that treatment. In 2008, the main hormonotherapy prescribed was a non-steroidal aromatase inhibitor (62.2%).

Surgical managements of tumours of patients without metastatic cancer and not having received any neoadjuvant treatment were equivalent in the 2 populations : 99.6% to 100% of patients were operated in the CSI and in RH 2001 observatories, respectively. Node

dissection also evolved. In 2001, 79.0% of patients received a lymph node curage, and only 2.8% had a sentinel lymph node procedure. In 2008, only 42.6% of the patients had a lymph node curage, and 41.0% had a sentinel lymph node procedure. Thus, the surgical management of the lymph nodes seems to evolve toward less extended procedures.

Management by radiotherapy of non-metastatic patients not having received neoadjuvant treatment and having received partial surgery changed little over the period of time, since 94.6% of patients included in 2001 and 93.7% of patients included in 2008 were irradiated.