HR+/HER2- metastatic breast cancer in a large Italian database: incidence, prescription patterns, disease progression and direct costs

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OBJECTIVE

Breast cancer is the second incident neoplasm and the second leading cause of cancer death worldwide, accounting for the highest healthcare costs in European countries. **The epidemiology knowledge of different breast cancer types is crucial for planning and funding effective health services**. This holds particularly for **metastatic breast cancer (MBC) where information on its epidemiology are scarce.** The aim of this study was **to estimate the burden of HR+/HER2- metastatic breast cancer (MBC) in Italy**, in terms of incidence, prescription patterns, healthcare resource utilisation and costs for the National Health System (NHS).

METHODS

A cohort study based on healthcare administrative data (**Fondazione ReS database), covering >10 millions of Italians (Fig. 1)**, was performed. Incident cases of HR+/HER2- MBC were identified among adult women, at 2013. A woman was defined affected by MBC if she was hospitalized with concomitant diagnosis of "Malignant neoplasm of female breast" and "Secondary and malignant neoplasms". Incident cases were identified by excluding women responding to these criteria in the previous year. **The expression of receptors was derived using drugs as proxies: HR+ if a patient received a prescription of tamoxifen, aromatase inhibitors or fulvestrant; HER2– if she did not receive any prescription of trastuzumab or lapatinib.** The cohort was followed-up for 24 months **(Fig. 2)** to describe healthcare utilisation and integrated costs (pharmaceuticals, hospitalisations and outpatients visits and services) paid by NHS. **Prescription patterns were described in terms of first-line choice (active substance, monotherapy or combination therapy) and therapeutic changes (switches, drug addition or removal). Specific changes in drug therapy were used as proxies of disease progression. A survival analysis was performed to estimate the time from diagnosis to first disease progression**.

Fig.1 – ReS Database structure

ReS DB is a patient-centred data warehouse where all data sources are linked trough a unique anonymous patient code.

ReS DB, for the period 2012-2015, collected information of more than 10 million of Italian inhabitants of different Regions and Local Health Units.
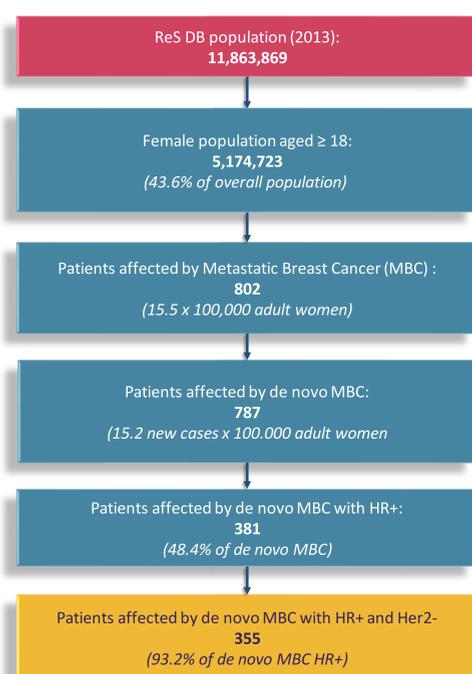
Fig.2 – Study design
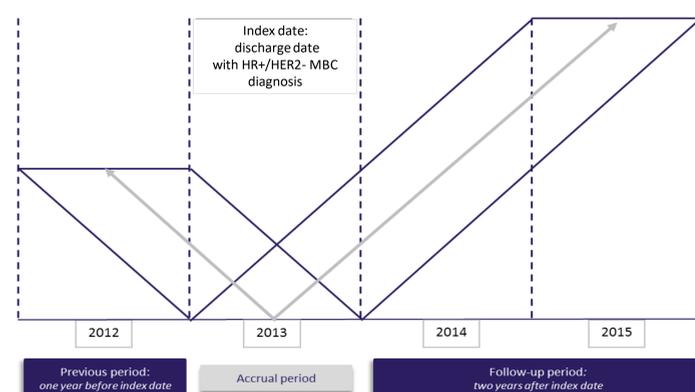
RESULTS

Out of a population of 5,174,723 adult women, **355 new cases of HR+/HER2- MBC were selected, with an incidence of 6.9 per 100,000 (Fig. 3 and Tab. 1)**. These women generated **an average cost of €3,888 for the hospitalization required to entry in the cohort (Tab. 2)**. During the **first follow-up year**, they generated an average cost of **€7,543**, whereas **€4,834 in the second year**. The 85.9% of the cohort received a monotherapy, whereas the remaining 14.1% a combination therapy. The most commonly used monotherapy was nonsteroidal aromatase inhibitors (45.9%), while the most prescribed combination therapy was tamoxifen + luteinizing hormone releasing hormone analogues (6.2%). Therapeutic changes occurred in 45.4% of the cohort, especially from chemotherapy to nonsteroidal aromatase inhibitors, after on average 276.8 days from the first treatment. **Disease progression was identified in 22.5% of patients and it occurred after a mean of 13±6 months from diagnosis (Fig. 4).**

Fig. 3 – Selection of the study cohort: incident cases of de novo MBC with HR+ and Her2- in 2013

Tab. 2 – Integrated healthcare costs for NHS generated by de novo HR +/HER2 metastatic breast cancer at the index date and during the first and second year of follow-u

Healthcare resource	Index date Average cost per patient (€)	1st year of follow-up Average cost per patient (€)	1st year of follow-up NHS expenditure (%)	2nd year of follow-up Average cost per patient (€)	2nd year of follow-up NHS expenditure (%)
Outpatient drug prescriptions		854	11.3	852	17.6
Specific drugs		*421*		*548*	
Concomitant drugs		*433*		*304*	
Chemotherapy*		1,601	21.2	737	15.2
Hospital admissions	3,888	1,708	22.6	1,861	38.5
Outpatient services and visits		3,380	44.8	1,384	28.6
Total	**3,888**	**7,543**	**100.0**	**4,834**	**100.0**

* Administered in day-hospital or ambulatory service

Fig. 4 – Survival analysis (Kaplan–Meier curve) for disease progression during 2-year follow-up
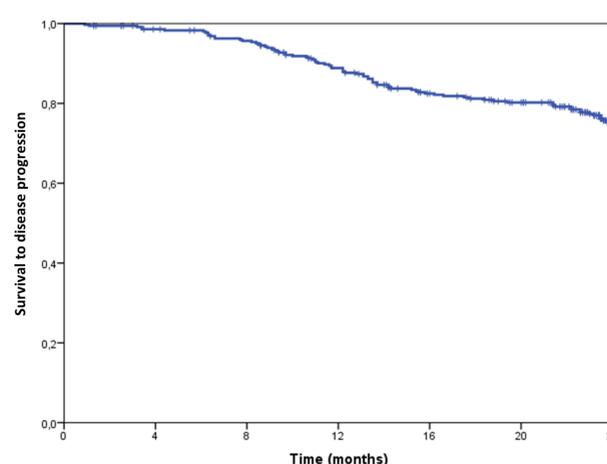
Survival analysis, performed on 355 women, corresponding to 7,061 person-months (an average of 19.9 months for patient), found that the first disease progression occurred, in average, 13±6 months after diagnosis.

Tab. 2 – Incidence of de novo HR+/HER2- MBC: distribution by age classes

Age class (years)	Population of adult women	De novo cases of HR+/HER2- metastatic breast cancer N	De novo cases of HR+/HER2- metastatic breast cancer %	Incidence (x 100,000)
18-49	2,408,995	72	20.3	3.0
50-59	837,437	74	20.8	8.8
60-69	723,361	73	20.6	10.1
70-79	641,531	89	25.1	13.9
≥80	563,399	47	13.2	8.3
Total	**5,174,723**	**355**	**100.0**	**6.9**

CONCLUSIONS

The study provided a **detailed picture of HR+/HER2- MBC**. Real-world data were used to describe the current management of this type of breast cancer and related direct costs paid by NHS. **These findings could be helpful in health technology assessment and expenditure forecasts of future therapeutic strategies for HR+/HER2- MBC**, particularly in the field of "precision medicine" or "personalized medicine".

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