Patient characteristics, diagnostic testing and treatment patterns in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+, HER2-), node-positive, high-risk early breast cancer (EBC) in Italy: a real-world study

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BACKGROUND

- Hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer accounts for ≈70% of all breast cancers[1]
- Treatment options for patients with early breast cancer (EBC) include:[2]
  - Primary treatment (surgery ± radiotherapy) with curative intent
  - Neoadjuvant systemic therapy if reduction in extent of surgery indicated: endocrine therapy (ET) in patients with oestrogen receptor positive (ER+) EBC; and/or chemotherapy (CT)
  - Adjuvant ET, recommended in patients with ER+ EBC
  - Adjuvant CT, recommended in patients at high risk of recurrence
- Following treatment, the risk of recurrence in the first 10 years is ~20% in patients diagnosed with ER+ EBC[3]
- Recognised predictive factors for high risk of recurrence include greater extent of nodal involvement, large primary tumour size, advanced tumour stage and grade, and expression of proliferative markers (e.g. Ki-67)[2]
  - Additional information from gene expression profiles (obtained using multi-gene assays, e.g. Oncotype DX) can be used to quantify the risk of recurrence and likely benefit from treatment with CT
- The open-label, phase III monarchE trial investigated oral abemaciclib (a cyclin-dependent kinase 4 and 6 inhibitor) + ET compared to ET alone in the treatment of patients with HR+, HER2-, node-positive EBC at high risk of recurrence[4]

BACKGROUND

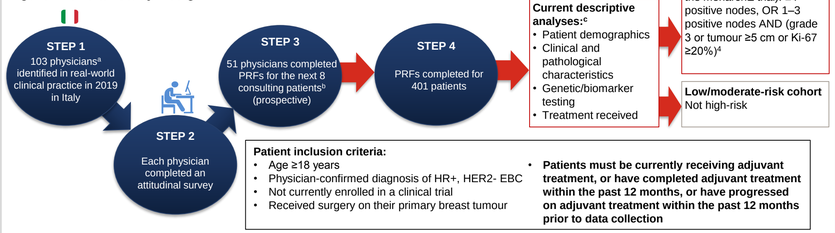
- monarchE included patients with HR+, HER2- EBC who had undergone definitive surgery for the primary tumour ± radiotherapy and/or (neo)adjuvant CT and who were considered at high-risk of recurrence according to the following criteria:
  - ≥4 positive nodes, OR
  - 1–3 positive nodes AND grade 3 or tumour ≥5 cm or Ki-67 ≥20%
- Eligible patients were randomised (1:1) to receive oral adjuvant abemaciclib (150 mg twice daily) plus standard-of-care ET or ET alone for 2 years (treatment period), with ET prescribed for ≥5 years

OBJECTIVE

- To describe patient characteristics, diagnostic testing and treatment patterns among patients with HR+, HER2- EBC in routine clinical practice in Italy, focusing on those at high risk of recurrence, defined according to monarchE inclusion criteria[4]

METHODS

Figure 1. Overall Study Design



Patient inclusion criteria:
- Age ≥18 years
- Physician-confirmed diagnosis of HR+, HER2- EBC
- Not currently enrolled in a clinical trial
- Received surgery on their primary breast tumour
- **Patients must be currently receiving adjuvant treatment, or have completed adjuvant treatment within the past 12 months, or have progressed on adjuvant treatment within the past 12 months prior to data collection**

[a]Oncologists, breast surgeons, and gynaecologists who treat patients with EBC, selected at random from public lists of healthcare professionals
[b]Physicians completed PRFs from June to August 2019 for up to the next 8 eligible patients with HR+, HER2- EBC
[c]Summarised using descriptive statistics
EBC, early breast cancer (stage I–IIIC); HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; PRF, patient record form

KEY RESULTS

Table 1. Numbers of patients meeting monarchE high-risk criteria (Italian cohort)

monarchE high-risk criterion	Number of patients
≥4 positive nodes[a]	24
1–3 positive nodes[a]	43
Grade 3 tumour[a]	39
Tumour >5 cm[b]	5
Ki-67 ≥20%[b]	38

[a]Assessed at data collection; [b]Assessed at diagnosis

- Among 401 patients in the Italian cohort, 67 (17%) met monarchE high-risk criteria
  - 52 (13%) patients met clinicopathologic high-risk criteria when Ki-67 expression levels were excluded

KEY RESULTS

Table 2. Patient demographics and characteristics at time of diagnosis[a]

Characteristic	Total cohort (N=401)	Low-/moderate-risk cohort (N=334)	High-risk cohort (N=67)
Median (IQR) age (years)[b]	57.5 (47.1–67.5)	57.9 (46.6–67.9)	54.8 (48.2–64.8)
Female, n (%)	388 (96.8)	324 (97.0)	64 (95.5)
Family history of breast cancer, yes, n (%)	72 (18.0)	61 (18.3)	11 (16.4)
Menopausal status[c,d], n (%)			
Pre/peri-menopausal	121 (31.2)	101 (31.2)	20 (31.3)
Post-menopausal	267 (68.8)	223 (68.8)	44 (68.8)
Stage I, n (%)	114 (28.4)	113 (33.8)	1 (1.5)
Stage II, n (%)	182 (45.4)	151 (45.2)	31 (46.3)
Stage III, n (%)	99 (24.7)	65 (19.5)	34 (50.7)
Histologic grade 1, n (%)[e]/n (%)[c]	49 (16.9)/58 (14.5)	46 (19.2)/57 (17.1)	3 (6.0)/1 (1.5)
Histologic grade 2, n (%)[e]/n (%)[c]	143 (49.3)/169 (42.1)	124 (51.7)/145 (43.4)	19 (38.0)/24 (35.8)
Histologic grade 3, n (%)[e]/n (%)[c]	82 (28.3)/93 (23.2)	55 (22.9)/54 (16.2)	27 (54.0)/39 (58.2)
Tumour size: <1 cm[f], n (%)	39 (11.1)	38 (13.3)	1 (1.6)
Tumour size: 1–3 cm[f], n (%)	253 (72.3)	211 (73.8)	42 (65.6)
Tumour size: 3.1–5 cm[f], n (%)	48 (13.7)	32 (11.2)	16 (25.0)
Tumour size: >5 cm, n (%)	10 (2.9)	5 (1.7)	5 (7.8)
Number of nodes affected[c]: 0, n (%)	271 (67.7)	271 (81.1)	0 (0.0)
Number of nodes affected[c]: 1–3, n (%)	69 (17.2)	26 (7.8)	43 (64.2)
Number of nodes affected[c]: ≥4, n (%)	24 (6.0)	0 (0.0)	24 (35.8)
ECOG PS: 0, n (%)	308 (76.8)	255 (76.3)	53 (79.1)
ECOG PS: 1, n (%)	78 (19.5)	67 (20.1)	11 (16.4)
ECOG PS: 2, n (%)	13 (3.2)	11 (3.3)	2 (3.0)

[a]Not all variables have data for all patients; some data were unknown
[b]Patients with a known date of diagnosis (total DSP cohort n=2224; Italian cohorts: total n=366; low/moderate-risk n=304; high-risk n=62)
[c]At time of data collection (not time of diagnosis)
[d]Percentage based on total number of female patients (overall DSP cohort n=2406; Italian cohorts: total n=388; low/moderate-risk n=324; high-risk n=64)
[e]For patients who received a biopsy at diagnosis (total DSP cohort n=1821; Italian cohorts: total n=290; low/moderate-risk n=240; high-risk n=50)
[f]Measured in patients with known tumour size at diagnosis (overall DSP cohort n=2235; Italian cohorts: total n=350; low/moderate-risk n=286; high-risk n=64)
DSP, Disease Specific Programme; EBC, early breast cancer; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; PS, performance status; SD, standard deviation

KEY TAKEAWAYS

- Among patients with HR+, HER2- EBC in this study conducted in Italy:
  - 17% had a high risk of recurrence as defined in monarchE
    - About one-third had ≥4 positive nodes
    - About two-thirds had 1–3 positive nodes
  - 13% met clinicopathologic high-risk criteria when Ki-67 expression levels were excluded
- Ki-67 testing was conducted more frequently in high-risk patients than in those with low/moderate-risk disease
- Around 94% of high-risk patients were receiving or had received adjuvant CT
- Evaluating the association between the clinical/pathological characteristics of high-risk patients and genomic profiling could provide an interesting avenue for future research

KEY RESULTS

Table 3. Biomarker and genetic tests performed at diagnosis (Italian cohort)[a]

Number (%) of patients with test[b]	Total cohort (N=401)	Low/moderate-risk cohort (N=334)	High-risk cohort (N=67)
BRCA1	73 (18.2)	65 (19.5)	8 (11.9)
Positive/mutated	31 (42.5)	31 (47.7)	0 (0.0)
Negative/wild type	31 (42.5)	29 (44.6)	2 (25.0)
BRCA2	70 (17.5)	62 (18.6)	8 (11.9)
Positive/mutated	29 (41.4)	29 (46.8)	0 (0.0)
Negative/wild type	30 (42.9)	28 (45.2)	2 (25.0)
PD-1/PD-L1	15 (3.7)	14 (4.2)	1 (1.5)
High	7 (46.7)	6 (42.9)	1 (100.0)
Low	8 (53.3)	8 (57.1)	0 (0.0)
Ki-67	303 (75.6)	242 (72.5)	61 (91.0)
≥20%[c]	106 (50.0)	68 (39.3)	38 (97.4)
Mean (SD)[d]	37.8 (16.5)	36.3 (17.4)	40.8 (14.2)

[a]Oestrogen (98.3% of patients), progesterone (97.0%) and androgen (6.7%) receptor, microsatellite instability (4.5%), and tumour mutation burden (7.0%) testing were also carried out
[b]Not all variables have data for all patients; test results do not show unknown/awaited/inconclusive results
[c]Proportion of patients with a Ki-67 test at diagnosis
[d]Analysed in patients with a Ki-67 expression test at or since diagnosis whose result was considered 'high' by the physician (total cohort n=174; low/moderate-risk cohort n=115; high-risk cohort n=59)
PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; SD, standard deviation

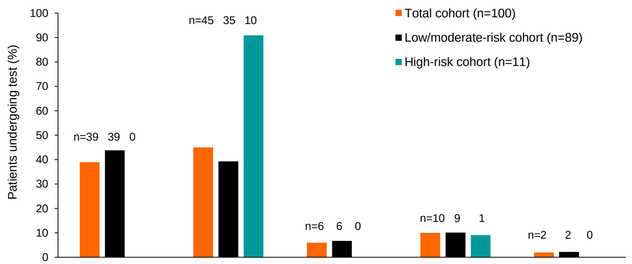
Methods

- A real-world, multinational, point-in-time observational study (Adelphi EBC I Disease Specific Programme™[.5]) was conducted in France, Germany, Italy, Spain, UK, USA and Japan in patients with HR+, HER2- EBC (stage I–IIIC)
  - The focus here is on the data collected in clinical practices in Italy

Other Results

- Only 24.9% (100/401) patients in the Italian cohort underwent tumour genomic testing
- Genomic testing was performed in 26.6% (89/334) low/moderate-risk patients and in 16.4% (11/67) high-risk patients

Figure 2. Genomic assays received at diagnosis for patients who underwent genomic testing at this time (Italian cohort)



[a]Since 2021, the Oncotype DX test has been reimbursed in Italy for HR+, HER2- patients in whom the benefits of chemotherapy need to be assessed[6]

- 100% of the 51 participating physicians in Italy were medical oncologists
- Nearly 60% of patients were seen by physicians in a public hospital/office setting
  - The remaining 40% were seen in Comprehensive Cancer Centres or privately

Table 4. Neoadjuvant treatment history (Italian cohort)[a]

Therapy, n (%) of patients who had received neoadjuvant therapy	Total cohort (N=401)	Low/moderate-risk cohort (N=334)	High-risk cohort (N=67)
Any neoadjuvant therapy[b], n (%)			
CT only	15 (3.7)	15 (4.5)	0 (0.0)
CT + ET	41 (10.2)	36 (10.8)	5 (7.5)
ET only	2 (0.5)	2 (0.6)	0 (0.0)
ET + Other	1 (0.2)	1 (0.3)	0 (0.0)

[a]Patients must have been currently receiving adjuvant treatment, or have completed adjuvant treatment within the past 12 months, or have progressed on adjuvant treatment within the past 12 months prior to data collection
[b]n (%) of each analysis population
CT: capecitabine, cyclophosphamide, docetaxel, doxorubicin, epirubicin, eribulin, gemcitabine, ixabepilone, methotrexate, mitomycin, mitoxantrone, nab paclitaxel, paclitaxel, vinorelbine, 5-fluorouracil; ET: anastrozole, exemestane, fulvestrant, goserelin, letrozole, raloxifene, tamoxifen, toremifene; Other: targeted therapy
CT, chemotherapy; ET, endocrine therapy

- A total of 59 patients in the total Italian cohort had received neoadjuvant therapy, 54 in the low/moderate risk cohort and 5 in the high-risk cohort
  - Of 5 patients in the high-risk cohort, 2 patients with ≥4 positive nodes and 3 patients with 1–3 positive nodes received neoadjuvant therapy

Acknowledgements

- Medical writing support was provided by Dr Gill Gummer and Dr Sue Chambers (Rx Communications, Mold, UK) and was funded by Eli Lilly and Company
- CB, AVT, MG and JB are employees of Eli Lilly and Company. AR and IS are employees of Adelphi Real World, who own the multi-sponsored Disease Specific Programme, and were paid by Eli Lilly and Company for the development of this analysis.

- Over 60% of patients in each of the three Italian cohorts were **currently** receiving adjuvant treatment

Table 5. First adjuvant treatment history (Italian cohort)[a]

	Total cohort (N=401)	Low/moderate-risk cohort (N=334)	High-risk cohort (N=67)
Mean (SD) duration of first adjuvant therapy[b], (days)	235.8 (409.1)	266.3 (444.6)	104.2 (127.1)
First adjuvant therapy, n (%)			
CT only	167 (41.6)	121 (36.2)	46 (68.7)
CT + ET	91 (22.7)	75 (22.5)	16 (23.9)
CT + ET + Other	4 (1.0)	3 (0.9)	1 (1.5)
ET only	133 (33.2)	129 (38.6)	4 (6.0)
Other only	1 (0.2)	1 (0.3)	0 (0.0)
ET + Other	5 (1.2)	5 (1.5)	0 (0.0)

[a]Includes 59 patients who also received neoadjuvant therapy (54 low/moderate-risk patients and 5 high-risk patients); patients must have been currently receiving adjuvant treatment, or have completed adjuvant treatment within the past 12 months, or have progressed on adjuvant treatment within the past 12 months prior to data collection
[b]For patients with a known start and end date (i.e. excluding patients with ongoing first adjuvant therapy): Italian cohorts: total n=335; low/moderate-risk n=272; high-risk n=63
CT: capecitabine, cyclophosphamide, docetaxel, doxorubicin, epirubicin, eribulin, gemcitabine, ixabepilone, methotrexate, mitomycin, mitoxantrone, nab paclitaxel, paclitaxel, vinorelbine, 5-fluorouracil; ET: anastrozole, exemestane, fulvestrant, goserelin, letrozole, raloxifene, tamoxifen, toremifene; Other: targeted therapy
CT, chemotherapy; ET, endocrine therapy; SD, standard deviation

Limitations

- The analysed data were reported by physicians; hence, no measures were clinically or independently validated
- The Adelphi EBC I Disease Specific Programme™ is more likely to collect data on patients who consult their physician frequently, which may contribute to potential selection bias
- As this was a point-in-time observational study, the numbers of patients receiving long-term ET might be an underestimate (i.e. some patients may have started ET after finishing CT)
- Analyses were descriptive in nature

Table 6. Tests conducted to support diagnosis (Italian cohort)

Number (%) of patients with test	Total cohort (N=401)	Low/moderate-risk cohort (N=334)	High-risk cohort (N=67)
Physical examination	354 (88.3)	290 (86.8)	64 (95.5)
Mammogram	344 (85.8)	284 (85.0)	60 (89.6)
Breast ultrasound	319 (79.6)	261 (78.1)	58 (86.6)
Biopsy[a]	289 (72.1)	239 (71.6)	50 (74.6)
CT scan	176 (43.9)	143 (42.8)	33 (49.3)
Lymph node ultrasound	154 (38.4)	136 (40.7)	18 (26.9)
Chest X-ray	126 (31.4)	101 (30.2)	25 (37.3)
MRI of the breast	125 (31.2)	96 (28.7)	29 (43.3)
PET scan	43 (10.7)	30 (9.0)	13 (19.4)
MRI scan	12 (3.0)	11 (3.3)	1 (1.5)
Other	19 (4.7)	17 (5.1)	2 (3.0)
None of the above	19 (4.7)	19 (5.7)	0 (0.0)

[a]Report of biopsy was not available for 111 patients
CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography

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