Characteristics and treatment patterns in patients with locally advanced and metastatic hormone receptor positive (HR+), human epidermal growth factor 2 negative (HER2-) breast cancer in clinical practice: retrospective analysis from Leeds Cancer Centre

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- Breast cancer is the most common cancer in the UK and accounts for 15% of newly diagnosed cancers each year[1]
- An estimated 60-75% of patients with invasive breast cancer have hormone receptor (HR) +ve, human epidermal growth factor 2 (HER2) -ve disease[2-4]
- At the time of this cohort, the UK National Institute for Health and Care Excellence (NICE) recommended endocrine therapy as first-line treatment for most patients with HR+/HER2- breast cancer; treatment is tailored to menopausal status, response, tolerability, co-morbidities and patient preference[5]
- Chemotherapy is reserved for HR+/HER2- patients with rapidly progressive visceral disease and those whose disease is no longer sensitive to endocrine therapy
- There is little published information on real-world treatment patterns for UK patients with HR+/HER2- breast cancer
- This study aimed to characterise treatment patterns and resource use for patients with metastatic HR+/HER2- breast cancer treated in Leeds Cancer Centre (LCC) prior to the approval of CDK 4/6 therapies

Methods

Setting and participants

- LCC is a major regional NHS cancer centre serving a metropolitan catchment area of over 850,000 people for secondary care and 2.7 million for tertiary care
- Anonymised retrospective data was extracted for the study cohort (**Table 1**) directly from structured hospital electronic medical records (EMR) and by expert review of clinical notes

Table 1. Description of study cohort

Inclusion	Exclusion
Incident diagnosis of advanced or metastatic breast cancer (TNM stage IIIB-IV)[6]	Evidence of a second significant malignancy at diagnosis of advanced or metastatic disease
Advanced or metastatic diagnosis between January 2012 – March 2018	Patients for whom age, sex, TNM status, treatment or HR+/HER2- status could not be confirmed from records
Adults (≥ 18 years)	Patients receiving treatments not currently reimbursed in the UK
HR+/HER2- status	Patients participating in a clinical trial

Data variables

- Index date was the first date that advanced/metastatic HR+/HER2- breast cancer was confirmed
- Patients were followed until date of last record, death, or end of the study time period, whichever came first
- Receptor status was defined as follows from clinical review:
  - HR: positive if either oestrogen or progesterone receptor status score was at least 3 (out of 8) using immuno-histochemistry (IHC) or '+ve' on pathology report
  - HER2: negative if receptor status score was between 0-1+ by IHC, or 2+ by IHC but negative by fluorescence in-situ hybridisation (FISH) or '–ve' on pathology report
- Analyses were stratified by menopausal status at index date: patients aged ≥55 yrs were assumed to be post-menopausal; menopausal status (post- vs pre/peri-) was confirmed in clinical notes for patients <55 yrs
- Treatment was categorised as surgery, radiotherapy, endocrine therapy, targeted therapy (everolimus + endocrine) or chemotherapy; specific drug, regimen, line of therapy (LoT) and therapy sequence were derived
- Treatment use was stratified by treatment intent (curative, non-curative), distinguishing patients with locally advanced and metastatic disease at index date
- Healthcare resource use (HCRU) data included numbers of overnight inpatient stays, day case inpatient admissions (not including routine clinic appointments) and outpatient visits
- Crude HCRU rates were calculated for all hospitalisations (including overnight, day case and outpatient visits) and 95% CI derived from Poisson estimates
- Summary and descriptive statistics were calculated for categorical and continuous variables as appropriate

References

1. Cancer Registration Statistics UK, (2016) *Office for National Statistics UK* https://tinyurl.com/y89xdkbm
2. Lobbezoo D, et al (2016) *Ann Onc.* 27(2): 256-62
3. Howlader N, et al (2014) *JNCI* 106(5): dju055
4. Clarke C, et al.(2012) *J Natl Cancer Inst*. 104(14): 1094–1101
5. NICE (2017) https://tinyurl.com/ydfzjxzo
6. UICC (2018) UICC/AJCC TNM Classification of Malignant Tumours (7th ed.)

Results

Patient characteristics

- 243 patients were identified for inclusion in the study; 33 (14%) pre/peri-menopausal and 204 (84%) post-menopausal (menopausal status unknown in 6 patients (2%)). Median follow-up was 34 months (IQR: 17-58, range: <1-77).
- At index date, 124 (51%) patients had progressed to metastatic disease from a previous diagnosis, 72 (30%) were diagnosed with metastatic disease, and 47 (19%) with locally advanced disease
- Median age was 67yrs with ranges of 33-53yrs and 43-95yrs for pre/peri-menopausal and post-menopausal patients, respectively (**Table 2**)

Table 2. Patient characteristics at index date, by menopausal status

Characteristic n (% of sub-cohort)	Study cohort[a] (N = 243)	Pre/peri-menopausal (N = 33)	Post-menopausal (N = 204)
Age, median (range)	67 years (33-95)	45 years (33-53)	70 years (43-95)
Stage IIIB	19 (7.8%)	<5	15 (7.4%)
Stage IIIC	28 (11.5%)	<5	22 (10.8%)
Stage IV	196 (80.7%)	25 (75.8%)	167 (81.9%)
Morphology (1° tumour)			
Infiltrating duct carcinoma, NOS[b]	139 (57.2%)	24 (72.7%)	111 (54.4%)
Lobular carcinoma, NOS	38 (15.6%)	<5	35 (17.2%)
Carcinoma, NOS	33 (13.6%)	<5	28 (13.7%)
Infiltrating duct & lobular carcinoma	13 (5.3%)	<5	11 (5.4%)
Other	20 (8.2%)	<5	19 (9.3%)

[a] There were 6 patients for whom menopausal status was unknown
[b] NOS=not otherwise specified

- 196 (81%) patients had a record of distant metastasis and 62% of these had metastases in visceral sites, with no difference between pre and post-menopausal patients (**Table 3**). Bone, lymph, pulmonary and liver were the most common metastatic sites.

Table 3. All sites of metastasis recorded for patients with stage IV disease, by menopausal status

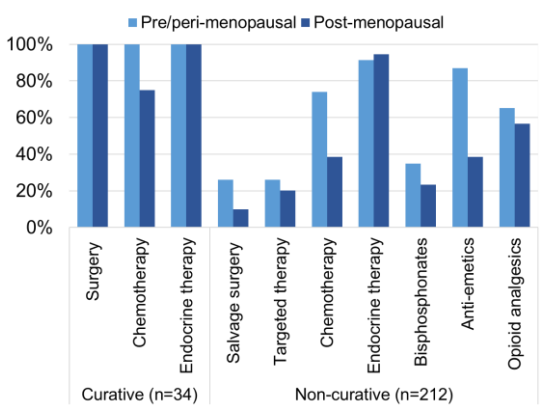
Site of metastasis[a] n (% of sub-cohort)	Study cohort[b] (N = 196)	Pre/peri-menopausal (N = 25)	Post-menopausal (N = 167)
Non-visceral	**163 (84.9%)**	**20 (83.3%)**	**139 (84.8%)**
Bone	133 (69.3%)	20 (83.3%)	110 (67.0%)
Lymph nodes	68 (35.4%)	6 (25.0%)	59 (36.0%)
Skin and soft tissue	29 (15.1%)	<5	27 (16.5%)
Visceral (incl. CNS)	**119 (62.0%)**	**15 (62.5%)**	**101 (61.6%)**
Pulmonary	64 (33.3%)	7 (29.2%)	55 (33.5%)
Liver	56 (29.2%)	9 (37.5%)	44 (26.8%)
Pleura	33 (17.2%)	<5	27 (16.5%)
Peritoneum	10 (5.2%)	<5	8 (4.9%)
CNS	8 (4.2%)	0	8 (4.9%)

[a] Patients may have multiple sites of mets; categories not mutually exclusive
[b] Menopausal status unknown for 4 metastatic patients; there were 4 metastatic patients with missing site data

Treatment categories

- 238 patients (98%) received treatment at some point during follow up, including 34 (13%) with locally advanced disease who were treated with curative intent
- 32 patients (13%) received radiotherapy and 5 patients received no treatment at all: the remaining treatment recorded is shown (**Figure 1**)
- Pre/peri menopausal patients received chemotherapy (either curative or non-curative) and salvage breast surgery more commonly than post-menopausal
- Supportive treatments included opioid analgesics, anti-emetics and bisphosphonates (to reduce skeletal morbidity)
- Median non-curative LoT was 2 per patient (range 1-9)

Figure 1. Patients receiving treatment during follow-up, by intent and menopausal status



Surgery: mastectomy, axillary node clearance, wide local incision and sentinel lymph node biopsy. Targeted therapy: everolimus + endocrine

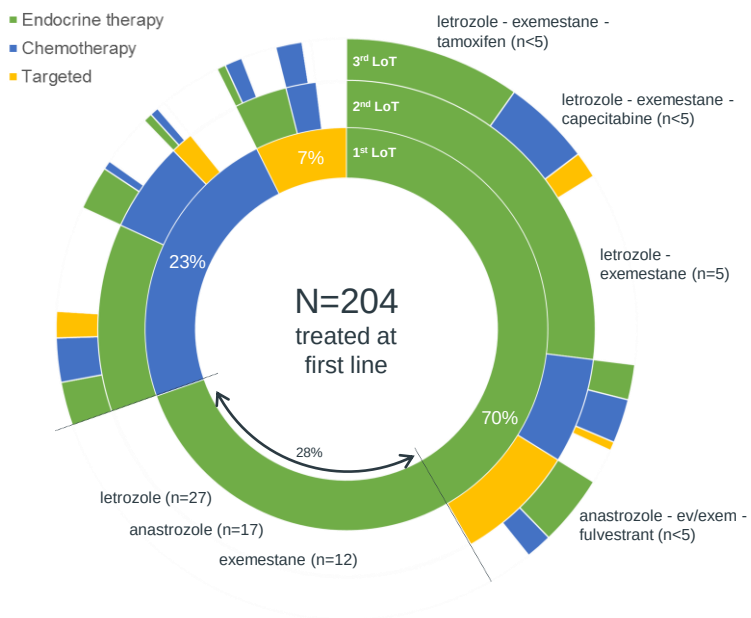
Healthcare Resource Use Rates for post-menopausal patients

- Total hospitalisation rate (per patient) for post-menopausal patients increased from 19.2 (95% CI: 18.6-19.8) visits per year during first line to 26.7 (95% CI: 25.1-28.4) visits per year at third line
- For patients using endocrine therapy, the overnight inpatient hospitalisation rate (per patient) increased from 1.5 (95% CI: 1.3-1.9) stays per year during first line to 2.1 (95% CI: 1.3-2.9) stays at third line
- Day case inpatient rate (per patient) also increased for patients using endocrine therapy from 6.5 (95% CI: 6.0-5.9) admissions per year during first line to 8.8 (95% CI: 7.5-10.1) admissions per year at third line

Treatment Sequence

- Among those receiving non-curative treatment, endocrine therapy was most commonly received at first LoT (70%) (**Figure 2**) as well as 2nd and 3rd lines
- Median treatment duration for first LoT was 128 days (range: 1-1708)
- A single line of endocrine therapy was the most common treatment sequence received (28% patients)
- Regimens used within treatment category sequences were diverse; the most common therapies were a single line of letrozole (13% of cohort) or anastrozole (8%) or exemestane (6%). All other specific regimen sequences were used in 2% of patients or less

Figure 2. Categories of sequential non-curative treatment received (up to 3 LoT shown). The 7 most common regimen sequences are named and corresponding numbers of patients shown



Targeted therapy: all targeted therapy recorded for this cohort was everolimus in combination with an endocrine, most usually everolimus/exemestane (ev/exem). Small number suppression in operation.

Conclusions

Real world treatment patterns for patients with HR+/HER2- metastatic breast cancer show:

- **Pre-/peri-menopausal patients receive chemotherapy more commonly than those who are post-menopausal**
- **The most commonly received treatment at first LoT is endocrine therapy and 28% receive no subsequent treatment following this**
- **For those receiving more than 1 LoT, successive lines are most commonly with endocrine therapy**
- **Individual patient treatment pathways are diverse, reflecting the range of treatment options and heterogeneity of this population**
- **HCRU tended to increase over sequential LoT**

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