Changes in HER2 status between primary and metastatic disease in HR+ metastatic breast cancer highlights the clinical requirement for re-biopsy at relapse in the DigiONE OMOP federated oncology network

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Federated OMOP-based observational analysis of HR+/HER2- metastatic breast cancer across Europe: methodological development and clinical insights from the DigiONE network

Background

- Despite early detection and treatment, ~ 30% of early-stage **HR+ HER2- breast cancer (BC)** patients relapse. Re-biopsy at relapse is recommended and molecular profiling of metastatic sites to determine HER2 status is essential, to detect actionable mutations and to guide treatment selection and sequencing.
- This study aimed to assess natural history, treatments received and outcomes in patients with HR+/HER2- mBC, by metastasis presentation and HER2- status in the Digital Oncology Network in Europe (DigiONE) by leveraging **a network of federated OMOP databases.**

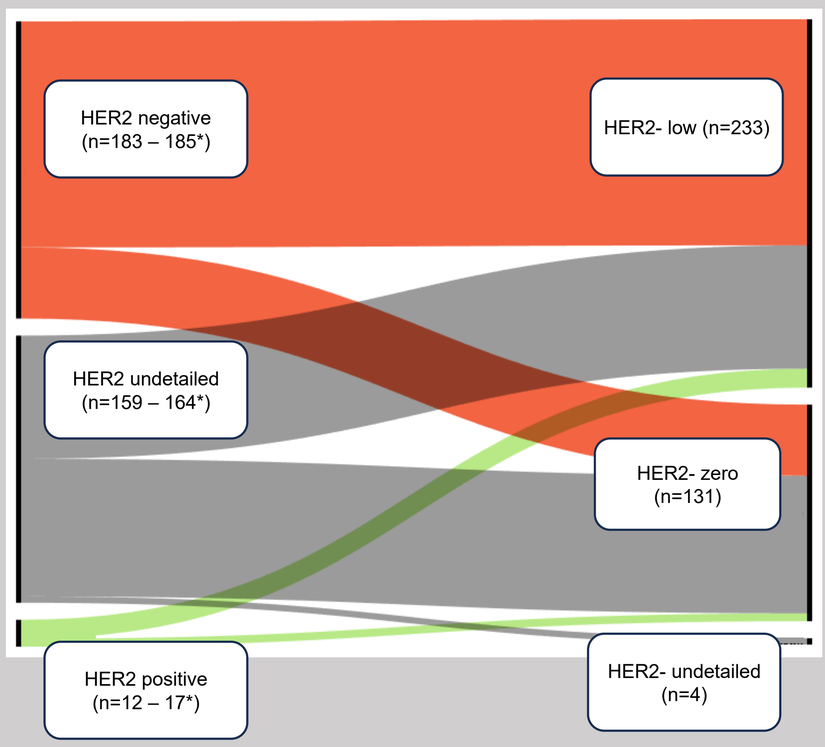
Results

A total of **1,387 HR+ HER2- mBC patients** were included in the cohort, with final analysis focusing on **551 patients** with deep phenotypic data available.

		De novo metastatic	Recurrent metastatic
Total patients (n)		183	368
Age at index (median* – min, max)		65 (25-93)	64 (27-99)
Disease stage at initial BC diagnosis (n, %)	I	N/A	64 (17.3%)
	II		175 (47.6%)
	III		74 (20.1%)
	IV		1** (0.3%)
	Unknown / Missing		54 (14.7%)
Genomic status at index (n, %)	Germline BRCA1/ BRCA2	15** (16.8%)	
	Somatic PIK3CA	37** (50%)	
	Somatic AKT1	3** (4%)	
	Somatic ERBB2	3** (4%)	

*federated median **federated range count

Of HER2 negative recurrent patients, **5.6% were HER2 positive** at early-stage BC

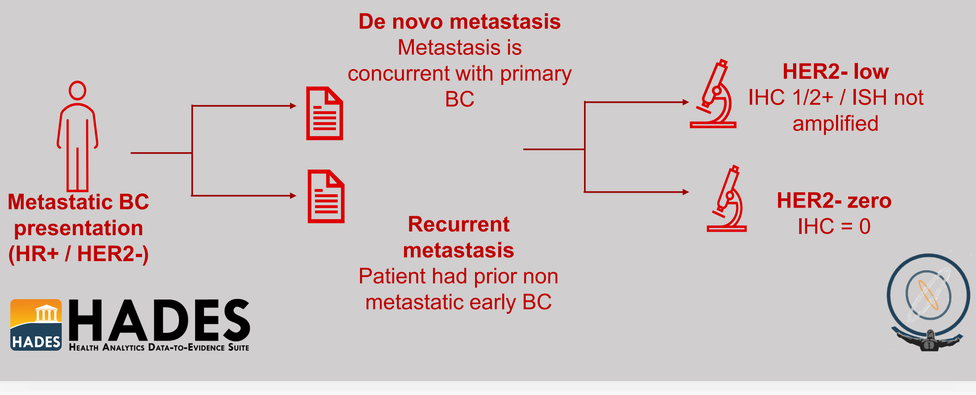


*federated range count

Methods

Cohort identification

- Metastatic HR+/ HER2- patients were identified between November 2018 and November 2023
- Cohorts were classified by metastasis presentation, and further stratified by HER2 status at index (metastatic) date



Data extraction

- Derived variables are extracted using study-specific packages written in R
- Data are stored locally in secure node

Federated analysis

- Local nodes are provided study specific configuration which dictates analytics for each derived variable
- Study schema is specified and local data are validated prior to federated analysis in Vantage6 using custom algorithms

Future directions

Changes in HER2 status between primary and metastatic disease highlight the **clinical requirement for re-biopsy at relapse.**

More than 50% of the HER2- mBC patients who underwent genomic testing **carried an actionable gene mutation**, indicating they could **benefit from targeted therapy**.

Future analyses will evaluate the **sequencing and clinical outcomes of therapies** in molecular phenotype and mutation subgroups and assess **clinical characteristics of patients who are re-biopsied.**

S Theophanous[1], L Revie[2], O Bouissou[3], F Duhoux[4], P Galgane Banduge[5], A Choudhury[5], A Collard[4], W Hai Deng[3], G Hall[1], RJ Geukes Foppen[6], V Gouthamchand[5], I Kaczmarczyk[2], E Krasniqi[6], L Licata[7],
A Lobo Gomes[8], L Sanchez Gomez[9], A van Maanen[4], G Podevijn[4], E Ross[3], J Thonnard[4], A Thomas[4], C Twelves[1], L Wagner[3], X Fernandez[10], C van Marcke[4]
[1]Leeds Teaching Hospitals NHS Trust, United Kingdom. [2]IQVIA Ltd, United Kingdom. [3]Oslo University Hospital, Norway. [4]Cliniques Universitaires Saint-Luc, Belgium. [5]Maastricht University, The Netherlands. [6] IFO, IRCCS Ospedale Regina Elena, Italy. [7]IRCCS Ospedale San Raffaele, Italy. [8]RWTH Aachen, Germany. [9]Medical Data Works, The Netherlands. [10]DigiCORE, Belgium.