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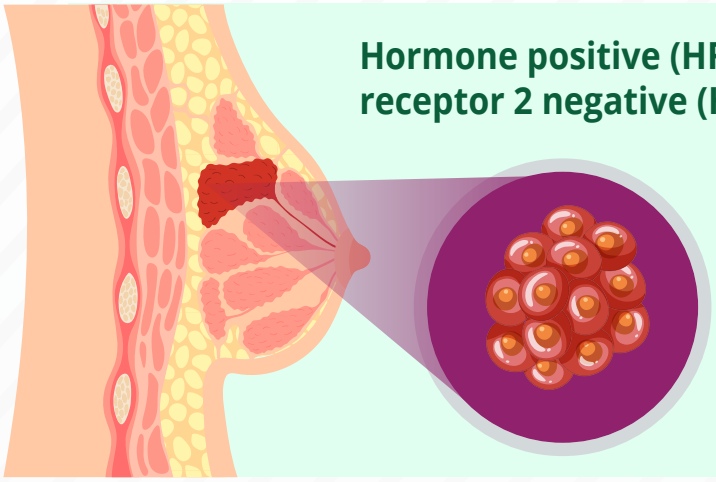
Hormone Positive (HR+)/Human Epidermal Growth Factor Receptor 2 Negative (HER2-) Early Breast Cancer

Risk factors and treatment



Hormone positive (HR+)/human epidermal growth factor receptor 2 negative (HER2-) early breast cancer (EBC)

EBC is a curable form of cancer that is contained in the breast or has only spread to the axillary lymph nodes[1]

Breast cancer cells express both oestrogen and progesterone receptors but lack HER2 receptors[1,2]

Tumours may exhibit endocrine therapy (ET) resistance and distant relapse[3]

Management must be multidisciplinary as treatments differ with molecular subtypes[1]

Why is risk assessment needed[1]?

Risk assessment must be done to determine

- Patients who need chemotherapy in addition to ET
- Optimal ET and its duration

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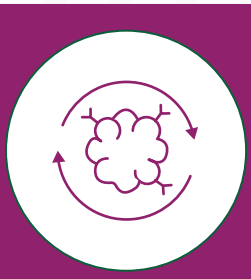
Various risk factors governing HR+/HER2- EBC prognosis and treatment

ER+

Only a few patients (approximately <5% of all HR+ patients) show a very low expression (1–9%) of ER; these tumours have poor sensitivity to ET and should be treated as HR-

Clinico-pathological factors[5]

- Tumour grade
- Nodal status



Relapse risk[5]

- Directly impacts treatment choice
- Strongly correlated with original tumour nodal status

Recurrence score (RS)[6,7]

The TAILORx and RxPONDER studies showed that RS strongly governs the long-term benefits of chemotherapy in patients

↑Score ∞ ↑Relapse ∞ ↑Chemotherapy benefits

Genomic risk (determined using the 70-gene signature test)[8]

- Specific to individual tumour
- Categorises tumours into low- and high-genomic-risk types
- Directly impacts chemotherapy decision

Dynamic Ki-67 protein[9,10,11]

- Important proliferation marker
- Ki-67/MIB-1 ↑ ∞ Relapse risk ↑
- Predicts patient outcomes for adjuvant therapy: POETIC trial
- No optimised, clinically relevant cut-off value available
- Promising outcomes when coupled with RS

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Various risk factors governing HR+/HER2- EBC prognosis and treatment

The clinical-pathologic stage + oestrogen receptor status, grade (CPS-EG) staging system for disease-specific survival[12,13]

- Categorises patients based on neoadjuvant therapy outcomes
- Can select candidates for post-neoadjuvant clinical trials
- Utilises the following criteria:
  - Clinico-pathologic stage
  - Oestrogen receptor status
  - Grade

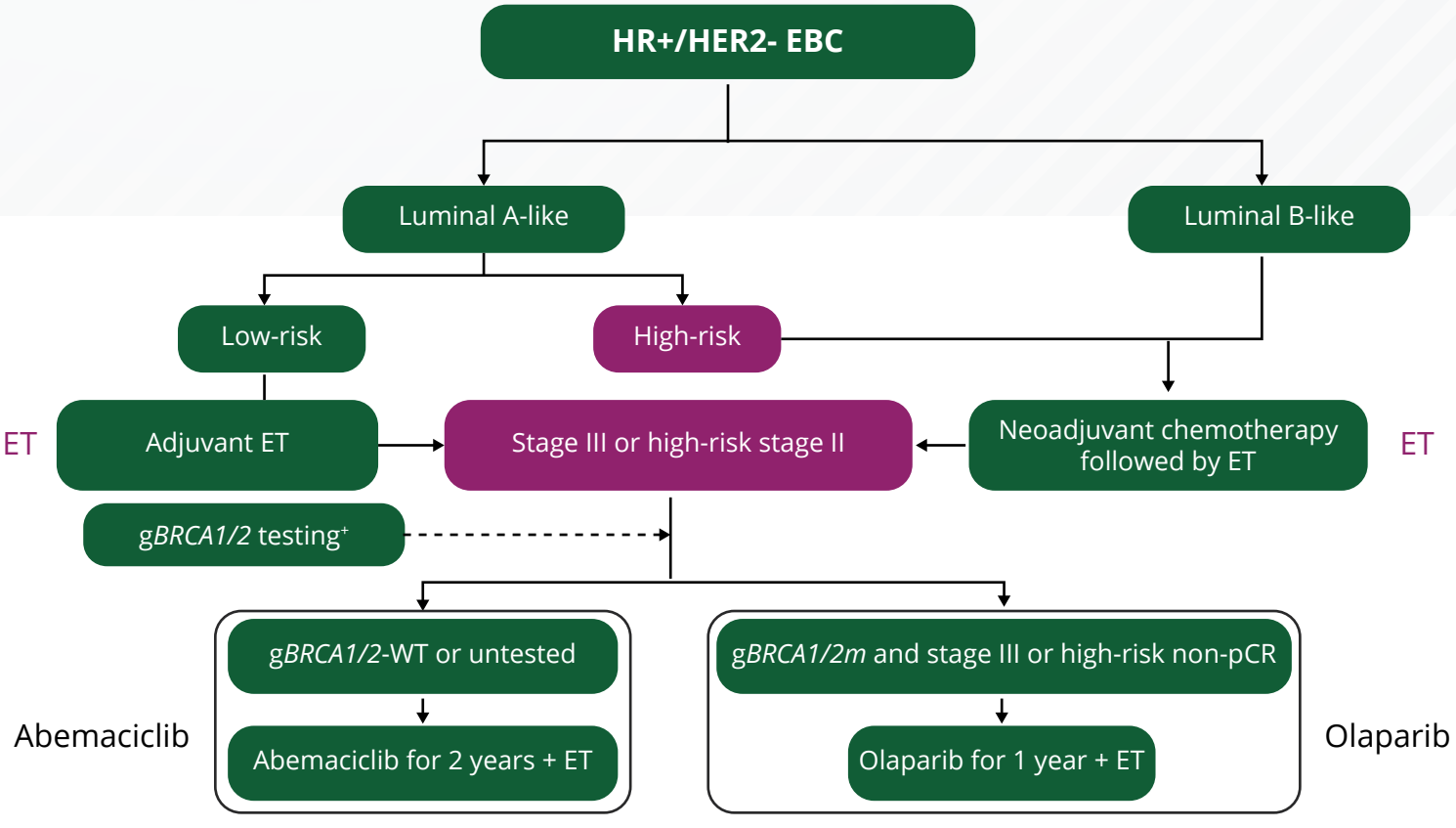
Treatment strategies

Two pillars of EBC management[1]

Locoregional treatment (surgery + radiation)

Systemic therapy

European Society for Medical Oncology clinical living guidelines for systemic therapy for HR+/HER2- EBC[14]



Cyclin-dependent kinase 4/6 inhibitors

Abemaciclib[15,16]

- Approved standard adjuvant treatment
- Blocks cancer cell progression
- MonarchE study (2 years): ET + abemaciclib > ↑Invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS)

Ribociclib[17]

- NATALEE study (3 years)
  - Ribociclib + ET vs. ET alone
  - 400 mg ribociclib/day
  - ↑IDFS and DRFS
  - Further investigations underway

Poly (ADP-ribose) polymerase inhibitors

Olaparib[18]

- Targets cancers with defects in homologous recombination repair by synthetic lethality
- Used to reduce recurrence in patients with breast cancer germline mutation(s)
- OlympiA study (3 years): Olaparib vs. placebo
  - ↑ Overall survival benefit
  - Manageable toxicity

Surgery of the axilla[19]

- Discussed at the 18th St. Gallen International Breast Cancer Conference held in March 2023, in Vienna, Austria
- Multiple studies underway for validation

Key message

A meticulous risk assessment and evaluation of clinico-pathological criteria must be conducted before deciding on the best systemic therapies for HR+/HER2- EBC

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