Impact of Metaplastic Histology in Triple-Negative Breast Cancer Patients Receiving Neoadjuvant Systemic Therapy

**Background**

- Metaplastic breast cancers (MpBC) are rare and aggressive breast cancers characterized by glandular epithelial components admixed with non-glandular cell types.
- MpBCs are often triple-negative breast cancers (TNBC) and are considered to be resistant to chemotherapy.
- Here, we compare the clinicopathological characteristics and outcomes between patients with MpBC and non-metaplastic TNBC using data from the prospective ARTEMIS trial (NCT02276443).

**Methods**

- **Study Design**
  - Prospective neoadjuvant ARTEMIS trial (NCT02276443)
- **Major inclusion criteria:**
  - Stage I-III triple-negative breast cancer
  - Primary tumor ≥ 1.5 cm
- **Major exclusion criteria:**
  - Contraindication to anthracyclines and/or taxanes
  - Patients were initiated on 4 cycles of anthracycline-based chemotherapy (AC).
  - Volumetric change by ultrasound (vUS) was performed after 2 cycles (optional) and 4 cycles of AC.
- **Patients**
  - Patients with evidence of chemotherapy-resistant disease while receiving or after completion of 4 cycles of AC were offered enrollment in targeted therapy trials (TT).
  - Interim volumetric ultrasound in MpBC patients with ≥ 60% reduction in tumor volume on ultrasound after 2 cycles of AC were more likely to have a pathologic complete response (pCR)/minimal residual disease (RCB-I) following neoadjuvant systemic therapy (80% vs 0%, p=0.005).

**Results**

- **Table 1: Baseline Clinicopathological Characteristics**
  - MpBC (n=21) Non-MpBC (n=149) p value
  - Median age at diagnosis – years (range)
    - MpBC: 56 (34-74)
    - Non-MpBC: 54 (27-78)
    - 0.64
  - Mean clinical tumor size – cm
    - MpBC: 4.2 (3.4)
    - Non-MpBC: 3.4 (1.9)
    - 0.08
  - Clinical Nodal Status
    - Negative – n (%)
      - MpBC: 18 (86)
      - Non-MpBC: 74 (50)
      - 0.002
    - Positive – n (%)
      - MpBC: 3 (14)
      - Non-MpBC: 75 (50)
    - Histologic Grade
      - 1 – n (%)
        - MpBC: 1 (5)
        - Non-MpBC: 0
      - 2 – n (%)
        - MpBC: 5 (24)
        - Non-MpBC: 14 (9)
      - 3 – n (%)
        - MpBC: 15 (71)
        - Non-MpBC: 135 (91)

- **Outcomes**
  - MpBC patients had higher rates of disease progression on AC (24% vs 8%, p=0.041, Table 2)
  - MpBC patients were more likely to have significant residual disease (RCB II/III) after neoadjuvant systemic therapy (67% vs 42%, p=0.036, Table 2)
  - Among the 7 MpBC patients who had a pathologic complete response (pCR)/minimal residual disease (RCB-I) after neoadjuvant systemic therapy, 6 received anthracycline-taxane based chemotherapy and 1 received a targeted agent on a clinical trial following completion of AC.

**Conclusions**

- A clinically acceptable pCR/RCB-I rate of 33% and the opportunity to participate in neoadjuvant and adjuvant trials supports the use of neoadjuvant systemic therapy in MpBC.
- MpBC patients should be monitored closely for disease progression while receiving neoadjuvant therapy.

**References**