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

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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 ARTEMS 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 (optional) and 4 cycles of AC.
  - 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).
  - Patients with chemotherapy-sensitive disease received taxane-based chemotherapy (T).
  - Residual Cancer Burden (RCB) Index was assessed during pathology evaluation after surgery.
- **Statistical Methods**
  - Categorical/Ordinal variables: Fisher's exact/Wilcoxon Rank Sum test
  - Continuous variables: Student's t-test

Results

- **Patients**
  - 170 patients (21 MpBC, 149 non-metaplastic TNBC) were included
  - Baseline characteristics are summarized in Table 1.
  - Patients with MpBC were less likely to have node-positive disease (p=0.002) and were more likely to have lower grade disease (p=0.009).

Table 1: Baseline Clinicopathological Characteristics

	MpBC (n=21)	Non-MpBC (n=149)	p value
Median age at diagnosis – years (range)	56 (34-74)	54 (27-78)	0.64
Mean clinical tumor size – cm (standard deviation)	4.2 (3.4)	3.4 (1.9)	0.08
Clinical Nodal Status			
Negative – n (%)	18 (86)	74 (50)	**0.002**
Positive – n (%)	3 (14)	75 (50)	
Histologic Grade			
1 – n (%)	1 (5)	0	**0.009**
2 – n (%)	5 (24)	14 (9)	
3 – n (%)	15 (71)	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.

Results

Table 2: Treatment and Outcomes

	MpBC (n=21)	Non-MpBC (n=149)	p value
Targeted therapy trial			
No – n (%)	13 (62)	115 (77)	0.17
Yes – n (%)	8 (38)	34 (23)	
Progression on AC			
No – n (%)	16 (76)	137 (92)	**0.041**
Yes – n (%)	5 (24)	12 (8)	
RCB Index			
pCR/RCB-I – n (%)	7 (33)	87 (58)	**0.036**
RCB-II/III – n (%)	14 (67)	62 (42)	

- **Interim volumetric ultrasound in MpBC**
  - 14 MpBC patients underwent volumetric ultrasound after 2 cycles of AC.
  - Among these 14 MpBC patients, 21% (3/14) had evidence of disease progression on the interim volumetric ultrasound.
  - 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).

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

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