Central nervous system disease in patients with metaplastic breast cancer receiving antibody-drug conjugates: a multi-institutional study

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BACKGROUND

Metaplastic breast cancer (MpBC) represents a rare subtype, constituting <1% of all breast cancer cases[1]. It is pathologically characterized by epithelial and mesenchymal cellular components exhibiting a basal molecular pattern, hormone receptor and HER2-negativity, and high grade. Clinically, MpBC exhibits an aggressive course with early disease progression and poor survival[2]. Antibody-drug conjugates (ADCs) have been shown to penetrate the central nervous system (CNS)[3]; however, little is known about the response of ADCs in MpBC, particularly in patients with CNS disease.

OBJECTIVES

- To describe features of CNS disease in a subset of patients (pts) who received an ADC or multiple ADCs for MpBC.
- To further characterize CNS specific treatments and outcomes within this subset.

METHODS

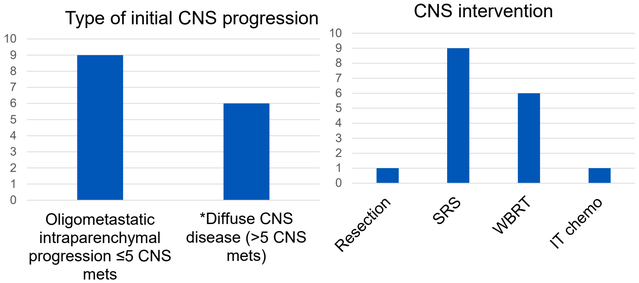
We conducted a multi-institutional retrospective observational study of pts with advanced MpBC treated with ADCs at 4 NCI-designated cancer centers (abstract #A-345). This analysis includes a subset of this cohort with CNS metastases, with the aim of examining the incidence, characteristics, and treatment patterns. Clinical outcomes were evaluated for pts with information available, including CNS median progression-free survival (mPFS; defined from initiation of systemic therapy to time of further documented CNS progression or death) and median real world PFS (rwPFS; defined from time of treatment initiation to documented disease progression or death).

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RESULTS

Table 1. Patient Characteristics and CNS Outcomes

Characteristics		
Tumor Subtype	**Patients (n)**	**%**
ER+	0	0%
HER2+	4	27%
TNBC	11	73%
Demographics		
Median Age	50 yrs (range 32-75 yrs)	
White	11/15	73%
Black	2/15	13%
Hispanic/Latino	2/15	13%
CNS disease characteristics		
Time from MpBC dx to CNS mets	13 mos (range 0-54 mos)	
Time from metastatic dx to development of CNS mets	3 mos (range 0-22 mos)	
CNS de-novo metastatic disease	2/15	27%
Screening CNS imaging prior to dx of CNS disease	4/15	27%



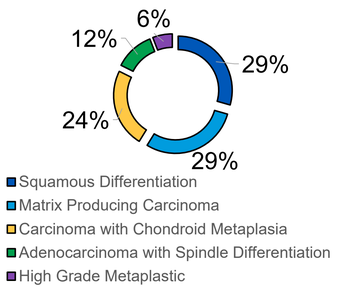
*A patient who initially developed diffuse CNS disease subsequently developed leptomeningeal disease

CNS, central nervous system; Dx, diagnosis; IT chemo, intrathecal chemotherapy; Mos, months; MpBC metaplastic breast cancer; Med, median; Mets, metastasis; SG, Sacituzumab Govitecan; SRS, stereotactic radiosurgery; T-DXd Trastuzumab Deruxtecan; T-DM1, Trastuzumab Emtansine; TNBC, triple negative breast cancer; WBRT, whole brain radiotherapy; Yrs, years

KEY FACTS:

- 15/48 (31%) developed CNS disease in the full cohort
- 3 patients were on an ADC at time of CNS disease development (1= T-DM1, 2 = SG)
- Majority of patients with CNS disease were symptomatic (14/15) 93%
- Most patients underwent a change in systemic therapy at time of CNS disease (13/15) 87%
  - 60% were switched to an ADC based treatment at the time of CNS progression
- Median time from first CNS event to further CNS progression was 6.5 months
- CNS PFS was 3.5 months (1-74 months)
  - Median rwPFS was 4.4 months
  - Among pts who utilized ADCs after dx of CNS met disease median rwPFS was 4 months
- At the time of this analysis, 11/15 (73%) of patients in this cohort passed away

Figure 1. Metaplastic Breast Cancer Histology



ADC received	Patients (n=15)	%
SG	12	80%
T-DXd	6	40%
T-DM1	1	7%

4 patients received both SG and T-DXd over their treatment course

DISCUSSION

Given the high rate of CNS metastasis within a short timeframe from diagnosis with a poor survival outcome, CNS screening should be considered. The extremely short CNS PFS and low median rwPFS of this cohort highlight the guarded prognosis associated with MpBC. Given the small sample size of this cohort, larger studies are warranted to validate these findings.

CONCLUSIONS

- Within this CNS sub-cohort study, we found that 31% of pts with MpBC developed CNS metastasis.
- The majority of pts had neurological symptoms at diagnosis.
- Most patients did not undergo routine screening for CNS disease.

REFERENCES

1. Reddy, T. P., Rosato, R. R., Li, X., Moulder, S., Piwnica-Worms, H., & Chang, J. C. (2020). A comprehensive overview of metaplastic breast cancer: clinical features and molecular aberrations. *Breast Cancer Research, 22(1), 121.* https://doi.org/10.1186/s13058-020-01353-z
2. Thapa, B., Arobelidze, S., Clark, B. A., Xuefei, J., Daw, H., Cheng, Y. C., Patel, M., Spiro, T. P., & Haddad, A. (2022). Metaplastic Breast Cancer: Characteristics and Survival Outcomes. *Cureus*, *14*(8), e28551. https://doi.org/10.7759/cureus.28551
3. Thomas A, Douglas E, Reis-Filho JS, Gurcan MN, Wen HY. Metaplastic Breast Cancer: Current Understanding and Future Directions. *Clin Breast Cancer.* 2023;23(8):775-783. doi:10.1016/j.clbc.2023.04.004

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