Efficacy of systemic therapy in HER2-low breast cancer with CNS metastases: a "real-world" experience

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Introduction

Local therapy (radiation, surgery) is standard in the treatment of breast cancer with CNS metastases.[1]

Systemic therapy is showing promise in the treatment of CNS metastases, especially in HER2-positive breast cancer. Evidence is limited in HER2-low disease.[1]

We present our experience of systemic therapy in patients with HER2-low breast cancer and CNS metastases, in a "real world" setting at a single institution.

Methodology

Retrospective study of electronic medical records of patients with breast cancer and CNS metastases at Henry Ford Health from January 2014 to July 2024.

Eligible patients did not receive concurrent local therapy to the studied lesions.

HER2-low defined as: HER2 IHC 1+; or 2+ with negative FISH

End points (stratified according to regimens, receptor, race): CNS ORR (based on modified RANO-BM[2]; DCR; DOR; PFS

Results

Total number of patients: 16

African American (AA): 63% (10/16)

Caucasian: 25% (4/16)

Others: 13% (2/16)

Results

Patient Characteristics:

Patient Characteristics	All Patients (n=16)	AA patients (n=10)
Age	56 (38-93)	54 (48-66)
Receptor	HR+: 75% (12) TNBC: 25% (4)	90% (9) 10% (1)
HER2 IHC	1+: 81% (13) 2+ 19% (3)	80% (8) 20% (2)
Type of metastases	Parenchymal: 88% (14) Leptomeningeal: 6% (1) Both: 6% (1)	80% (8) 10% (1) 10% (1)
Prior CNS metastases	Yes: 50% (8) No: 50% (8)	50% (5) 50% (5)
Prior CNS RT	Yes: 38% (6) No: 62% (10)	30% (3) 70% (7)
Regimens	Chemotherapy: 7 (Taxanes: 4/7) T-DXd: 4 Abemaciclib: 2 Other CDK4/6i: 2 Sacituzumab: 1	Chemo: 4 (Taxanes: 3/4) T-DXd: 3 Abemaciclib: 2 Other CDK4/6i: 1

Measurable disease:

88% had non-measureable disease by RANO-BM criteria[2] (<10 mm)

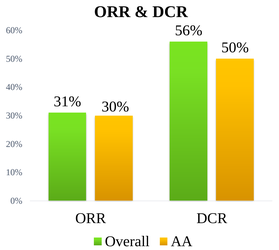
69% patients had lesions <5 mm

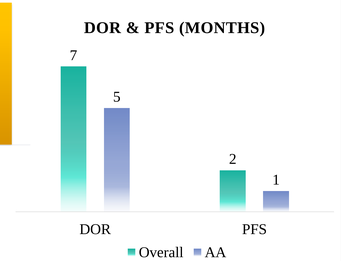
References:

1. Corti C, Antonarelli G, Criscitiello C, et al. Targeting brain metastases in breast cancer. *Cancer Treatment Reviews*. 2022;103:102324.
2. Lin NU, Lee EQ, Aoyama H, et al. Response Assessment in Neuro-Oncology (RANO) group. Response assessment criteria for brain metastases: proposal from the RANO group. Lancet Oncol. 2015 Jun;16(6):e270-8.

Results

Outcomes:





HER2 1+ vs 2+:

Outcomes	HER2-1+ (n=13)	HER-2+ (n=3)	P-value
ORR	23%	67%	p=0.24
DCR	46%	100%	p=0.23
mPFS	2.2 months	No progression	--

Common regimens: Response Rates

Response rates	T-DXd (n=4)	Chemotherapy (n=7)
ORR	50%	29%
DCR	75%	29%

Results

HER2-low vs HER2-positive:

Outcomes	HER2-low (n=16)	HER2-positive (n=17)	P-value
ORR	31%	53%	p=0.28
DCR	56%	94%	**p=0.017**
mDOR	7 months	5 months	--
mPFS	2 months	3 months	p=0.351

Conclusion

- ***Systemic therapy, especially T-DXd, shows encouraging CNS outcomes in HER2-low patients.***
- ***Response criteria for smaller brain metastases (<1 cm) need further exploration.***
- ***We highlight the need for larger prospective studies focused on HER-low CNS disease.***