SV-BR-1-GM after progression on ADC in patients with metastatic breast cancer

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BACKGROUND

Antibody-drug conjugates (ADCs) such as SG and T-DXd, though effective in metastatic breast cancer (MBC) treatment, are associated with significant challenges including severe adverse events like Interstitial Lung Disease (ILD) and potential for cross-resistance due to their shared mechanism of action. SV-BR-1-GM, an allogeneic whole cell therapeutic vaccine, utilizes a distinct therapeutic approach by expressing both class I and II HLAs, secreting GM-CSF, and functioning as an antigen-presenting cell. This vaccine has been enhanced for improved in-vitro characteristics and serves as a reservoir for cancer antigens such as HER2 and PRAME, activating a specific anti-tumor immune response, thereby offering a potentially safer and non-cross-resistant treatment option.

METHODS

This retrospective subset analysis include 23 ADC-resistant patients in the ongoing Ph2 trial (NCT03328026). The study assesses the efficacy of Bria-IMT (irradiated SV-BR-1-GM ~20 million cells, intradermally 48-72 hours after cyclophosphamide 300 mg/m^2, followed by low-dose interferon-alpha at the inoculation sites 2 days later), which was administered q3wks in combination with a check point inhibitor (CPI). DTH to Bria-IMT and anergy to Candin were evaluated. Bria-IMT PFS was defined as informed consent date to treatment termination. Penultimate PFS was defined as penultimate treatment start date to treatment termination.

RESULTS

Table 1: ADC-resistant Patient Demographics

N	23
Age, Median (Range)	62 (41 - 83)
Race / Ethnicity	White (65%) Black (22%) Asian (4%) Other (9%) Hispanic (30%)
ECOG	ECOG 0 (70%) ECOG 1 (30%)
Tumor Grade	Grade I (9%) Grade II (43%) Grade III (48%)

	N (%)
Metastatic or Recurrent Target Lesion sites	Brain: 2 (9%) Lung: 7 (30%) Liver: 11 (48%) Bone: 2 (9%) Other: 15 (65%)
Prior Systemic Tx, Median (Range)	6 (3 – 13)
Prior ADC Tx	1 prior ADC: 15 (65%) 2 prior ADC: 8 (35%)
Prior CPI Tx	7 (30%)

Conclusion: The ADC-resistant cohort was heavily pretreated

Table 2: Most Common Adverse Events in ADC-resistant patients

Adverse Event Term	Maximum Grade				Total Related
	Grade 1	Grade 2	Grade 3	Grade 4/5	N (%)
Injection Site Reaction	8 (35%)	2 (9%)	0	0	10 (44%)
Nausea / Vomiting	5 (22%)	4 (17%)	1 (4%)	0	5 (22%)
Fatigue	4 (17%)	3 (13%)	1 (4%)	0	8 (35%)
Anemia	3 (13%)	0	3 (13%)	0	5 (22%)
TSH increased / Hypothyroidism	5 (22%)	1 (4%)	0	0	4 (17%)
Constipation	2 (9%)	2 (9%)	1 (4%)	0	3 (13%)

Conclusion: Bria-IMT was well-tolerated with no discontinuations due to toxicity, the most commonly reported related AE was injection site reaction, and 1 patient (4%) reported an SAE (grade 3 intractable nausea and/or vomiting) related to the Bria-IMT regimen. Notably, no instances of Interstitial Lung Disease were reported.

RESULTS

Table 3: Treatment Efficacy by MBC Subtype in ADC-resistant patients

Histology	All (N)	Evaluable (N)	Best ORR[1]	Best CBR[2]
All ADC Resistant	23	17	12% (2 / 17)	53% (9 / 17)
ER/PR + / HER2 low or -	8	8	13% (1 / 8)	63% (5 / 8)
HER2 +	3	2	50% (1 / 2)	100% (2 / 2)
TNBC	12	7	0	29% (2 / 7)

1. Best ORR includes CR and PR by investigator or central read starting at first assessment at 3-month. *
2. Best CBR includes CR, PR and SD by investigator or central read starting at first assessment at 3-month.

Conclusion: The ADC-resistant cohort consisted of patients with advanced metastatic breast cancer (MBC) encompassing a spectrum of molecular subtypes. Best overall objective response rate (ORR) to the treatment was 12%, with HER2+ showing the highest ORR at 50%. Best clinical benefit rate (CBR) was favorable, with an overall rate of 53%. HER2+ subtype demonstrated a 100% CBR, suggesting a potential subtype-specific efficacy.

Figure 1: Absolute Bria-IMT PFS vs Absolute Penultimate PFS

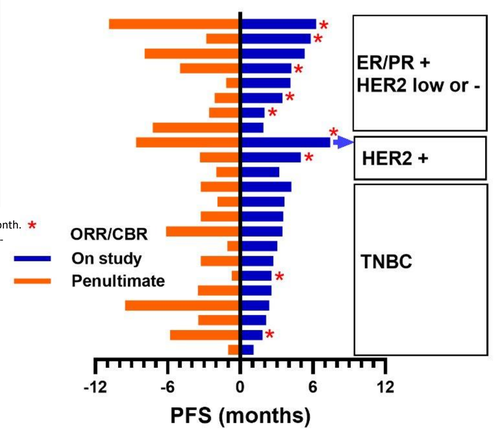
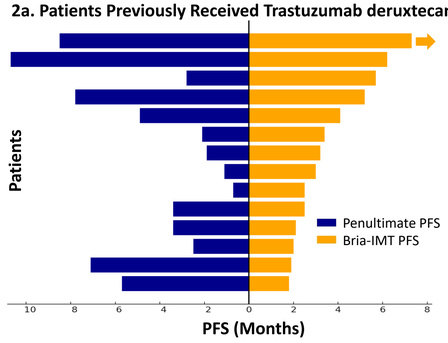
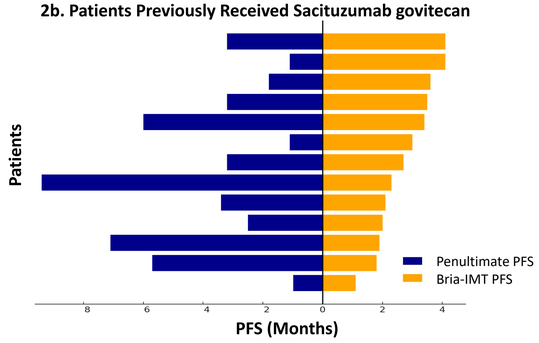


Figure 2: Penultimate Therapy PFS vs Bria-IMT PFS ratio by specific ADC.

2a. Patients Previously Received Trastuzumab deruxtecan



2b. Patients Previously Received Sacituzumab govitecan



2c. Patients Previously Received Trastuzumab emtansine

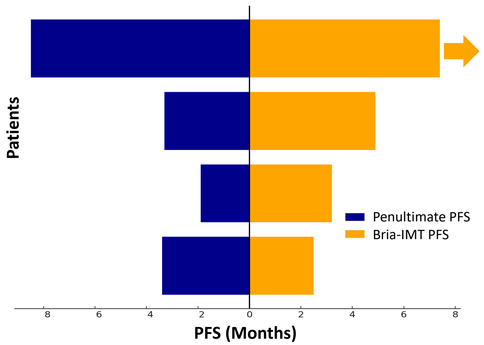


Table 4: Summary of PFS comparison in ADC-resistant patients

Prior ADC Treatment	Number of Patients (N)	% Patients with Improved PFS
Trastuzumab deruxtecan	14	36 %
Sacituzumab govitecan	13	46 %
Trastuzumab emtansine	4	50 %

Conclusion: Bria-IMT™ showed potential survival advantage over penultimate treatment, likely by reversing immune exhaustion in patients irrespective of specific prior ADC.

RESULTS

Figure 3: Cross-Trial Comparison: Kaplan-Meier curves presenting ADC-resistant patient data on PFS of the Bria-IMT + CPI Combination vs the TPC arms from two other trials.

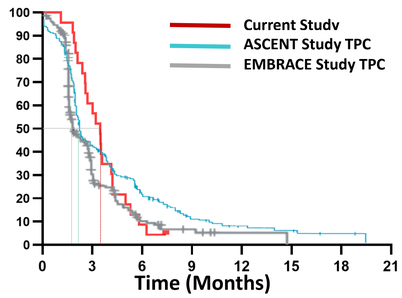


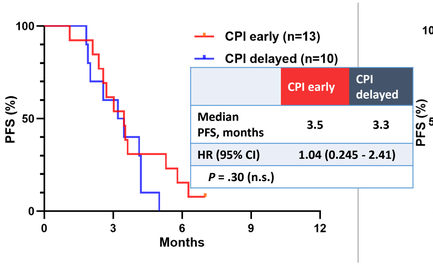
Table 5: Cross Trial Comparison of Median Progression-Free Survival (PFS) in Patients with Multiple Prior Lines of Therapy

Study	Treatment(s)	Prior Lines of Therapy, median (range)	Median PFS of TPC Arm in months	Median PFS of Experimental Arm in months
Bria-IMT (current trial, ADC-resistant subset)	Single Arm Bria-IMT regimen	6 (3-13) including 1-2 ADC	NA	3.5 (1.1 – 7.4+)
EMBRACE[3]	Eribulin vs TPC arm (2:1)	4 (2 – 7)	2.2 (2.0 – 2.6)	3.6 (3.3 – 3.7)
ASCENT[4]	Sacituzumab govitecan vs TPC arm (1:1)	4 (2-14) in TNBC	1.7 (1.5 – 2.5)	4.8 (4.1 – 5.8)

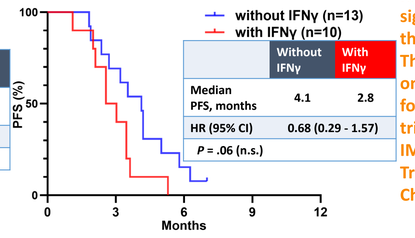
Conclusion: Compared to the Treatment of Physician's Choice (TPC) arms from two other Ph3 trials, Bria-IMT's ADC-resistant cohort had higher median PFS despite more prior lines of therapy, suggesting potential superior efficacy by overcoming immune exhaustion in heavily pretreated populations.

Figure 4: Kaplan-Meier curves presenting the effects on PFS by Treatment sequence (3a) and IP formulation (3b) in ADC-resistant cohort

4a. Treatment Sequence: CPI was administered either 1-2 days prior to the SV-BR-1-GM (CPI early) or skipped in cycle 1 and administered starting in Cycle 2 at 2-3 days after SV-BR-1-GM (CPI delayed)



4b. IP formulation: During manufacturing, SV-BR-1-GM was either pulsed with interferon-γ (IFN-γ) or omitted, before irradiation and formulation. The formulation omitting IFN-γ was chosen for the ongoing Bria-IMT phase 3 study (NCT06072612).



Conclusion: Sequencing of CPI and SV-BR-1-GM does not have an effect on PFS, while different IP formulations show near-significant effect on PFS in the ADC-resistant cohort. The IP formulation omitting IFN-γ is chosen for the ongoing Phase 3 trial comparing the Bria-IMT regimen + CPI vs Treatment of Physician's Choice.

CONCLUSION

This subset analysis of the Bria-IMT™ regimen in ADC resistant MBC patients suggests clinical benefit and a potential treatment option for this patient population. A CBR of 53% was observed among patients refractory to ADC therapy. No treatment discontinuations were attributed to SV-BR-1-GM and the lack of interstitial lung disease (ILD) underscores the Bria-IMT regimen's favorable safety profile. Future studies are warranted to confirm these results and explore the potential of Bria-IMT™ in broad clinical settings of heavily pretreated contemporary MBC patients.

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