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Overall Survival Results of BRIA-IMT Allogenic Whole Cell-Based Cancer Vaccine

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Background

SV-BR-1-GM is an off-the-shelf whole-cell therapeutic vaccine that expresses class I & II HLAs, secretes GM-CSF, and functions as antigen-presenting cells, with subsequent enhancements improving in-vitro characteristics (Lopez-Lago SABC 2023). By expressing cancer antigens such as HER2 and PRAME, SV-BR-1-GM also serves as a reservoir of antigens to activate the patient's anti-tumor immune responses. We report prospective randomized and post hoc exploratory data for patients with advanced metastatic breast cancer (aMBC) treated with the Bria-IMT regimen (SV-BR-1-GM +CTX +IFNα) in combination with an anti-PD-1 immune checkpoint inhibitor.

Methods

Ongoing, prospective, phase 1-2 with randomized phase 2 cohort (NCT03328026; 2018-present) using the Bria-IMT regimen with an anti-PD-1 checkpoint inhibitor (CPI); cycles every 3 weeks; 54 patients dosed to date. The regimen includes CTX 300mg/m^2 I.V. 48 hours prior to irradiated SV-BR-1-GM intradermally (~20 million cells) followed by IFNα (0.1 mcg pegylated IFNα) at each inoculation site 2 days afterward. A Candida skin test was performed at cycle 1 to evaluate anergy. SV-BR-1-GM delayed-type hypersensitivity (DTH) skin test is done by intradermal injection of a test dose of SV-BR-1-GM at every cycle prior to full dose SV-BR-1-GM inoculation. Two formulations were evaluated, with and without IFNγ pre-treatment of SV-BR-1-GM cells. Two treatment sequences in randomized cohorts were evaluated: CPI during the first cycle (immediate) vs. initialing CPI at the second cycle (ie delayed).

Results

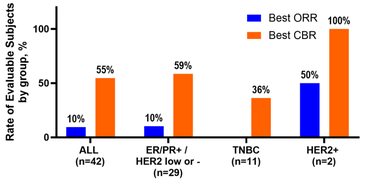
Table 1: Patient characteristics (N = 54)

Characteristics		N (%)
Age	Median (Range)	61 (38-81) years
BMI	Median (Range)	28.1 (18.1-42.7)
Race/Ethnicity	White	42 (78%)
	Black	6 (11%)
	Hispanic	10 (19%)
	Asian	3 (6%)
	Other	3 (6%)
ECOG	ECOG 0	29 (54%)
	ECOG 1	25 (46%)
Tumor Grade	Grade 1	6 (11%)
	Grade 2	15 (28%)
	Grade 3	30 (56%)
	Unknown	3 (5%)
Prior lines of Rx	Median (Range)	6 (2-13)
Previous Rx	Antibody-drug conjugate	23 (44%)
	Immune checkpoint	11 (20%)
	CDK4/6 inhibitor	34 (63%)
Metastatic sites	CNS	4 (7%)
	Visceral	35 (65%)
	Bone	12 (22%)
	Other	27 (50%)

Characteristics		N (%)
Number of HLA Match	0	13 (24%)
	1	17 (31%)
	≥ 2	22 (41%)
	Unknown	2 (4%)

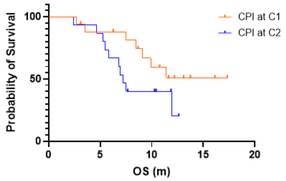
Table 2: Objective response rates (ORRs) by breast cancer subtypes (N = 54)

Subtypes	N (%)	Evaluable patients	ORR (CR, PR)	CBR (CR, PR, SD)
HER2+	3	2	50%	100%
HR + / HER2 -	33	29	10%	62%
TNBC	18	11	0%	36%
Totals	54	42	10%	50%



Results

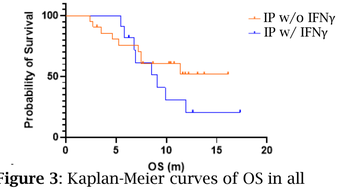
Figure 1: Kaplan-Meier curves comparing overall survival (OS) by treatment sequencing of a checkpoint inhibitor (CPI) with immediate cycle 1 vs. delayed cycle 2 in the randomized phase 2 cohort.



	Median (months)	Range
CPI at C1	Undefined	2.73 – 17.33
CPI at C2	7.23	2.43 – 12.63
HR, 0.53; 95% CI, 0.22 to 1.27 (p = 0.15)		

Conclusion: There was no significant difference in OS between the two arms: Immediate C1 (CPI starting at cycle 1, 2 days prior to SV-BR-1-GM; 8.9 months) and Delayed C2 (CPI starting at cycle 2, 2 days after SV-BR-1-GM; 7.4 months). As a result, the Immediate C1 approach was implemented in the Phase III trial.

Figure 2: Kaplan-Meier curves comparing OS by treatment formulation (without vs. with IFNγ incubation) in the randomized cohort (N = 32).



	Median, months	Range
Without IFNγ	Undefined	2.43 – 16.13
With IFNγ	9.1	5.47 – 17.33
HR, 0..58; 95% CI, 0.21 to 1.59 (p = 0.29)		

Conclusion: The formulation of SV-BR-1-GM without pulsed IFNγ in cell culture for 48 hours, then washed prior to harvesting significantly prolonged OS (13.4 vs 6.9 months Figure 3). The formulation without IFNγ treatment is being used in all future clinical trials.

Figure 3: Kaplan-Meier curves of OS in all patients by formulation (N = 54).

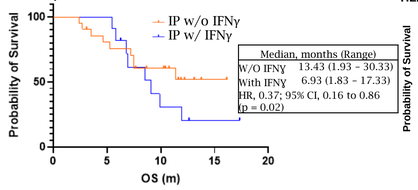


Figure 4: Kaplan-Meier curves by HLA matching.

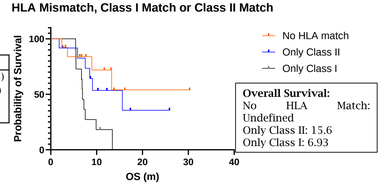


Table 3: Summary of adverse events (AEs).

	Maximum Grade (Number, %)				Total Number (%)
	Grade 1	Grade 2	Grade 3	Grade 4	
Fatigue	10 (18.5)	10 (18.5)	3 (5.6)	0	12 (22)
Injection Site Reaction	16 (29.6)	2 (3.7)	0	0	17 (31.5)
Nausea	12 (22)	5 (9.3)	0	0	8 (14.8)
Constipation	7 (13)	4 (7.4)	1 (1.9)	0	3 (5.6)
Diarrhea	7 (13)	3 (5.6)	0	0	1 (1.9)
Headache	8 (14.8)	2 (3.7)	0	0	2 (3.7)
Anemia	5 (9.3)	1 (1.9)	3 (5.6)	0	8 (14.8)
Rash/maculo-papular rash	6 (11.1)	1 (1.9)	1 (1.9)	0	2 (3.7)
Vomiting	4 (7.4)	3 (5.6)	1 (1.9)	0	4 (7.4)
TSH increase/Hypothyroidism	3 (5.6)/1 (1.9)	5 (9.3)/5 (9.3)	0, 0	0, 0	5 (9.3)/3 (5.6)
Back Pain	4 (7.4)	3 (5.6)	0	0	0

Results

Figure 5: Percent change of the sum of intracranial lesion diameters in patients across various studies.

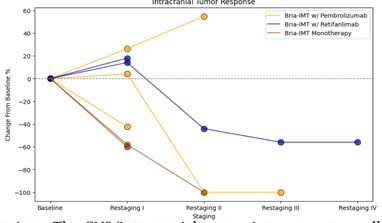


Table 4: Patient Demographics (N = 8)

Patients with Intracranial Metastasis				
Median Age	Median OS (months)	Median Prior Lines	Median Prior Lines of Radiation	Median Prior Surgeries
64	13.7	5	3	2

Table 5: Absolute Change in Tumor Size Before vs After Therapy.

Median Sum of Intracranial Lesion Diameters (mm)	
Before Bria-IMT™	After Bria-IMT™
26	13

Table 6: Summary of adverse events (AEs).

Median % Change in the Sum of Intracranial Lesion Diameters (mm)		
Bria-IMT™ w/ Pembrolizumab	**Bria-IMT™ w/ Retifanlimab**	**Bria-IMT™ Monotherapy**
-42%	-19%	-80%

Conclusion: The CNS/intracranial regression seen across all breast cancer subtypes among heavily pretreated patients highlights the potential of SV-BR-1-GM in managing CNS metastasis. Ongoing trials will further evaluate the efficacy of the Bria-IMT regimen in patients with CNS/intracranial metastasis.

Figure 6: Kaplan-Meier curves comparing OS by DTH responses in the randomized cohort (N = 32).

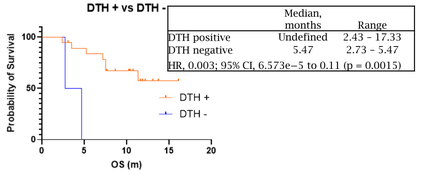


Figure 7: Kaplan-Meier curves comparing OS by CTC ≥ 5 or < 5 in the full cohort (N = 54)

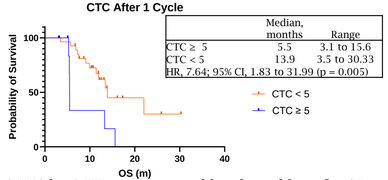
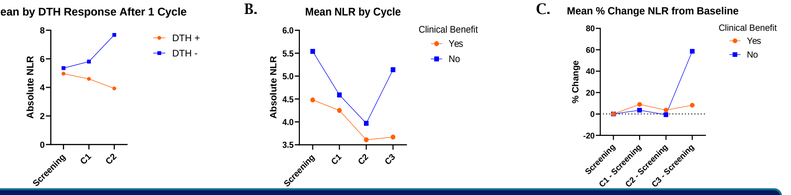


Figure 8: Mean changes of neutrophil to lymphocyte ratio (NLR) by DTH response and by clinical benefit. (N = 54)
A. Mean NLR by DTH response status. **B.** Median NLR by clinical benefit. **C.** Mean % Change NLR from Baseline measurement.



Conclusion

- The Bria-IMT regimen with an immune checkpoint inhibitor appears well tolerated and is capable of producing clinical benefit in heavily pretreated patients with metastatic breast cancer.
- The overall survival observed in patients treated with the phase 3 formulation exceeds that of contemporary studies with similar patient populations.
- Patients with a DTH reaction exhibited a mean reduction in NLR after one therapy cycle. Similarly, patients who achieved clinical benefit demonstrated sustained stability in NLR over multiple cycles compared to baseline, in contrast to those without clinical benefit, who showed marked variability and increases in NLR.
- These findings will inform the ongoing development for optimized outcomes in future studies.
- These preliminary results will be confirmed in the ongoing randomized phase 3 pivotal registrational trial (NCT06072612).

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