Survival Results of Randomized Phase II Bria-IMT Allogenic Whole Cell-Based Cancer Vaccine

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BACKGROUND

Bria-IMT™ is a combination immunotherapy comprising the allogeneic whole-cell vaccine SV-BR-1-GM, administered with low-dose cyclophosphamide (CTX), pegylated interferon alpha (IFNα), and an immune checkpoint inhibitor (CPI). SV-BR-1-GM breast cancer cells are engineered to express both class I and II HLA molecules, secrete GM-CSF to enhance dendritic cell activation, and present tumor-associated antigens such as HER2 and PRAME. Functioning as antigen-presenting cells, these cells serve as a reservoir of shared tumor antigens capable of activating anti-tumor immune responses. Subsequent enhancements to SV-BR-1-GM have improved in vitro immunologic characteristics (Lopez-Lago, SABC 2023). The addition of CPI is intended to potentiate SV-BR-1-GM–induced immune activation by overcoming tumor-induced immune suppression. We present updated findings from prospective randomized and post hoc exploratory analyses in patients with advanced metastatic breast cancer (aMBC) treated with the Bria-IMT regimen.

METHODS

This is an ongoing, prospective, phase 1–2 study with a randomized phase 2 cohort (NCT03328026; initiated in 2018), evaluating the Bria-IMT regimen in combination with an anti–PD-1 checkpoint inhibitor (CPI). Treatment cycles are administered every 3 weeks. To date, 54 patients have received at least one dose. The regimen includes intravenous cyclophosphamide (CTX; 300 mg/m²) administered 48 hours prior to intradermal inoculation of irradiated SV-BR-1-GM cells (~20 million cells), followed by pegylated interferon alpha (IFNα; 0.1 mcg) at each inoculation site 2 days later. A Candida skin test is performed at cycle 1 to assess anergy. At each cycle, a delayed-type hypersensitivity (DTH) skin test is conducted using an intradermal test dose of SV-BR-1-GM prior to full dosing. Two SV-BR-1-GM cell formulations, with and without IFNγ pre-treatment, have been evaluated. In the randomized cohorts, two CPI administration sequences are compared: initiation at cycle 1 (immediate) versus initiation at cycle 2 (delayed). For TWiST, restricted mean durations (area under the Kaplan-Meier curves) were calculated for TOX, PFS, and OS with 95% confidence intervals estimated via bootstrap resampling (1,000 iterations).

RESULTS

Table 1: Patient Demographics

Characteristic	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 systemic therapy, Median (Range)	6 (2-13)
Previous therapies	
• ADC	23 (44%)
• CPI	11 (20%)
• CDK4/6 inhibitors	34 (63%)
Number of HLA Match	
• 0	12 (22%)
• ≥ 1	40 (74 %)
• Unknown	2 (4%)

Table 2: Adverse Events

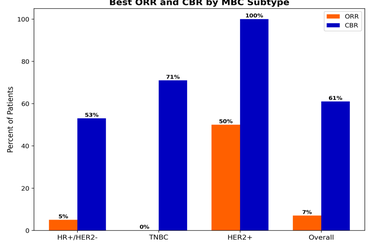
Adverse Event	Maximum Grade				Total Related
	Grade 1	Grade 2	Grade 3	Grade 4	
	N (percent)				
Injection Site Rxn	16 (50)	1 (3.1)	0	0	17 (53.1)
Nausea	9 (28.1)	3 (9.4)	1 (3.1)	0	14 (43.8)
Fatigue	5 (15.6)	6 (18.8)	2 (6.3)	0	13 (40.6)
Anemia	3 (9.4)	1 (3.1)	2 (6.3)	0	6 (18.8)
Diarrhea	6 (18.8)	0	0	0	6 (18.8)
Fever	5 (15.6)	1 (3.1)	0	0	6 (18.8)
TSH increased	5 (15.6)	1 (3.1)	0	0	6 (18.8)
Vomiting	3 (9.4)	2 (6.3)	1 (3.1)	0	6 (18.8)
AST/ALT increased	3 (9.4)	2 (6.3)	1 (3.1)	0	5 (15.6)
Alkaline phosphatase increased	1 (3.1)	2 (6.3)	2 (6.3)	0	5 (15.6)
Constipation	4 (12.5)	0	1 (3.1)	0	5 (15.6)
Cough	3 (9.4)	2 (6.3)	0	0	5 (15.6)
GGT increased	2 (6.3)	1 (3.1)	2 (6.3)	0	5 (15.6)
Headache	4 (12.5)	1 (3.1)	0	0	5 (15.6)
Anorexia/appetite decreased	2 (6.3)	2 (6.3)	0	0	4 (12.5)
Lymphocyte count decrease	1 (3.1)	2 (6.3)	1 (3.1)	0	4 (12.5)
Rash	4 (12.5)	0	0		4 (12.5)
UTI	0	2 (6.3)	2 (6.3)	0	4 (12.5)
Weight loss	4 (12.5)	0	0	0	4 (12.5)

Conclusion: Bria-IMT was well-tolerated with no discontinuations due to toxicity.

Table 3: Clinical Benefit in Evaluable Patients

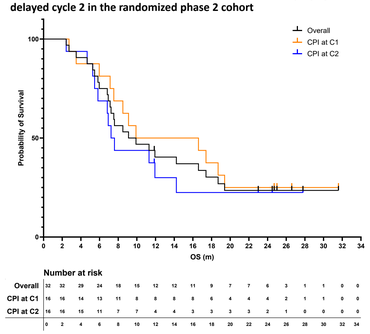
Biomarkers	N (%)	Patients with Evaluable Outcome	Best ORR [CR, PR] in Evaluable Patients	Best CBR [CR, PR, SD] in Evaluable Patients
HER2+	3	2	50%	100%
HR + / HER2 -	20	19	5%	53%
TNBC	9	7	0%	71%
Overall	32	28	7%	61%

Figure 1: Clinical Benefit in Evaluable Patients



RESULTS

Figure 2: 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

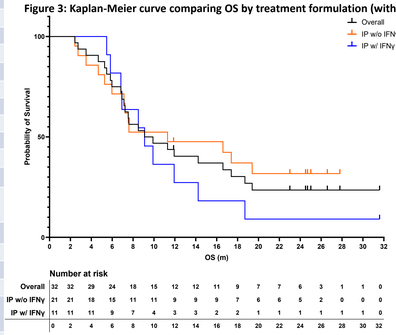


N = 32	Median (months)	Range
CPI at C1	13.3	2.73 – 31.6
CPI at C2	7.4	2.43 – 27.8
HR, 0.75; 95% CI, 0.34 to 1.7 (p = 0.49)		
Overall	9.5	2.43 – 31.6

There was a clinical but not statistically significant difference in OS between the two arms in the Phase II cohort: Immediate C1 (CPI starting at cycle 1, 2 days prior to SV-BR-1-GM; 13.3 months) and Delayed C2 (CPI starting at cycle 2, 2 days after SV-BR-1-GM; 7.4 months).

Conclusion: The immediate C1 approach was implemented in the Phase III trial.

Figure 3: Kaplan-Meier curve comparing OS by treatment formulation (with vs without IFNγ pretreatment) in the randomized cohort.

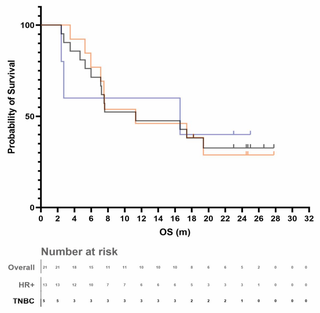


N = 32	Median (months)	Range
IP w/o IFNγ (Phase 3 formulation)	11.3	2.4 – 27.9
IP w/ IFNγ	9.1	5.5 – 31.6
HR, 0.62 ; 95% CI 0.26 to 1.49 (p = 0.29)		
Overall	9.5	2.43 – 31.6

There was a clinical but not statistically significant difference in OS between the formulation of SV-BR-1-GM with/without pulsed IFNγ in cell culture between the two arms in randomized phase II cohort (IP w/o IFNγ, 11.3 months vs IP w/ IFNγ, 9.1 months; p = 0.29).

Conclusion: The formulation without IFNγ pretreatment is being used in all future clinical trials.

Figure 4: Kaplan-Meier curve comparing OS by MBC Subtype in the randomized phase 2 cohort in Patients Receiving IP w/o IFNγ



N = 18	Median (months)	Range
ER/PR+/ HER2-	11.3	3.5 – 27.8
TNBC	16.6	2.4 – 25.0
HR, 1.04; 95% CI, 0.3 to 3.8 (p = 0.96)		
Overall (Ph3 formulation)	11.3	2.4 – 27.9

There was no statistically significant difference in OS between ER/PR+/HER2- and TNBC subtypes in patients receiving SV-BR-1-GM without IFNγ. Median OS was 11.3 months for ER/PR+/HER2- and 16.6 months for TNBC (HR 1.04; 95% CI, 0.3 to 3.8; p = 0.96).

Conclusion: As a result, both subtypes continue to be enrolled in the ongoing Phase III trial.

RESULTS

Figure 5: Status of Individual Intracranial Oligometastases by Patient

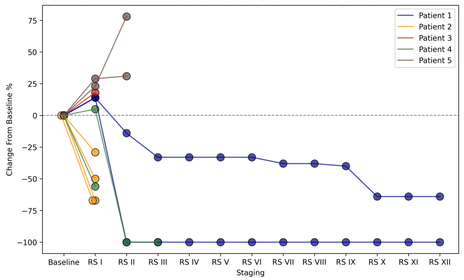


Table 4: Intracranial disease response rate in patients with intracranial metastases

MBC Subtype	N	Patients with Evaluable Outcome	Best ORR [CR, PR] in Evaluable Patients[a]	Best CBR [CR, PR, SD] in Evaluable Patients[a]
HER2+	1	1	100%	100%
HR + / HER2 -	1	1	100%	100%
TNBC	4	2	0%	50%
Overall	6	4	50%	75%

a. in patients with evaluable outcomes

Figure 6: Waterfall Plot Showing Best % Change in Sum of Target Lesion Diameters from Baseline

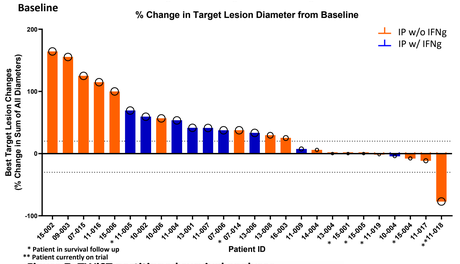


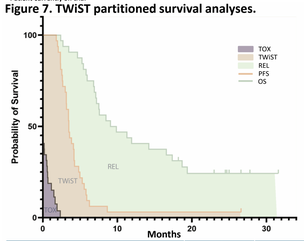
Table 5: Summary of patient tumor responses

N = 26	Measurement	%
Best Response	Greatest decrease in sum of lesion diameters from baseline	–77%
Tumor Burden Change	Percent of patients with no increase or a decrease in the sum of target lesion diameters from baseline (≤ 0% change)	25%
IP Formulation	Percent of patients exhibiting ≤ 0% change in target lesion sum who received the IP formulation without IFNγ	88%
Prior ADC Exposure	Percent of patients with decrease in sum of target lesions diameters vs baseline with prior ADC failure	60%

Among patients with at least one follow up tumor assessment (N = 26), 16% experienced a reduction in the sum of target lesion diameters from baseline, and 25% demonstrated either a decrease or no increase (≤ 0% change) at most recent tumor assessment vs baseline assessment. In those with ≤ 0% change in target lesion sum, 88% received the IP formulation without IFNγ. Of those with a decrease in lesion sum, 60% had experienced prior ADC failure.

Conclusion: The reduction in tumor burden reported in a sizeable number of patients suggests that treatment with the Bria-IMT regimen + CPI can overcome immune exhaustion in this heavily pretreated cohort.

Figure 7. TWIST partitioned survival analyses.

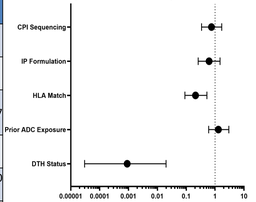


Metric	Duration (months)	95% CI	N
TOX (time with ≥ Grade 3 toxicity before progression)	0.38	0.15 to 0.54	13
TWiST (time without symptoms/toxicity before progression)	4.03	2.94 to 5.86	32
REL (time alive after disease progression)	9.86	6.59 to 13.03	32

Table 6: Overall Survival Metrics by Patient Subgroups

Analysis	N (%)	OS months (range)	HR; 95% CI	p-value
CPI at C1	16 (50	13.3 (2.7 – 31.6)	0.75; 0.34 to 1.7	0.49
CPI at C2	16 (50)	7.4 (2.4 – 27.8)		
IP w/o IFNγ	21 (66)	11.3 (2.4 – 27.9)	0.62 ; 0.26 to 1.49	0.29
IP w/ IFNγ	11 (34)	9.2 (5.5 – 31.6)		
HLA Match[a]	23 (72)	7.6 (2.7 – 24.5)	0.21; 0.09 to 0.52	0.0007
HLA No Match[a]	7 (22)	Undefined (2.4 – 31.6)		
Prior ADC	20 (63)	8.1 (2.4 – 31.6)	1.35; 0.6 to 3.0	0.47
No Prior ADC	12 (37)	15.4 (5.5 – 27.8)		
DTH -	3 (9)	4.7 (2.7 – 5.5)	0.0009; 0.000034 to 0.02	<0.000 1
DTH +	29 (91)	11.3 (2.4 – 31.6)		
Overall	32 (100)	9.5 (2.4 – 31.6)	95% CI 6.9 – 17.4	-

Figure 7 : Forest Plot of Hazard Ratios for Overall Survival from Secondary and Correlative Analyses



CONCLUSION

- This randomized phase 2 trial confirms previously reported tolerability and potential meaningful clinical benefit in late stage MBC.
- OS on Bria-IMT, even after 6 lines and most recent approved treatments, is highly meaningful and warrants additional trials.
- Bria-IMT shows potential across all breast cancer types including those without an existing IO indication..
- These updated findings support continued refinement of the Bria-IMT regimen to optimize clinical outcomes in future trials.