Impact of Prior Therapy, Genotype Matching, and Biomarkers in the Bria-ABC Phase 3 Trial

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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 secrete GM-CSF to enhance dendritic cell activation, express both class I and II HLA molecules and present tumor associated antigens such as HER2 and PRAME. Exhibiting antigen presenting cell activity, these cells serve as a reservoir of shared tumor antigens capable of enhancing anti-tumor immune responses. Subsequent enhancements to SV-BR-1-GM have improved in vitro immunologic characteristics (Lopez-Lago, SABC 2023)[1]. 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

Patients are randomized 1:1:1 to receive Bria-IMT +CPI, Bria-IMT monotherapy, or TPC. The Bria-IMT regimen includes Day -2 CTX (300 mg/m²), Day 0 intradermal SV-BR-1-GM (20x10⁶M irradiated cells), and Day 2-3 pegylated IFNα (0.1 mcg/site). CPI is administered q3w per protocol. Imaging assessments are performed every 6 weeks (×2) then every 8 weeks. ECOG2, CNS metastases, prior checkpoint inhibitor (CPI), antibody drug conjugate (ADC), or CDK4/6 inhibitor (CDK4/6i) exposure, are eligible, with no limit on prior lines. This interim report was conducted to evaluate trial feasibility, biomarker validation, and arm blind PFS stratified by prior treatment failures, immunologic matching, and cellular biomarkers. Median PFS was calculated using Kaplan Meier curves and further assessed by log rank tests. For TWiST, restricted mean durations (area under the Kaplan-Meier curves) were calculated for TOX, and PFS with 95% confidence intervals estimated via bootstrap resampling (1,000 iterations).

RESULTS

Table 1: Patient Demographics

Characteristic	N (%) N = 118
Age, Median (Range)	60 (32-91)
BMI, Median (Range)	25.1 (8.7 – 45.7)
• White	89 (75)
• Other	29 (25)
• ECOG 0	57 (45)
• ECOG 1	53 (43)
• ECOG 2	7 (6)
Tumor Grade 1	3 (3)
Grade 2	16 (14)
Grade 3	26 (22)
• Undetermined or Not Reported	76 (64)
Prior systemic therapy, Median (Range)	6 (2-15)
Prior ADC Exposure	96 (81)
Prior CPI Exposure	33 (28)
Prior CDK4/6 inhibitor Exposure	70 (59)
Intracranial Metastases	11 (9)

Table 2: Adverse Events

Adverse Event	Maximum Grade			
	Grade 1	Grade 2	Grade 3	Grade 4
	Number of subjects (percent)			
Fatigue	20 (16.9)	18 (15.3)	4 (3.4)	0
Nausea	23 (19.5)	11 (9.3)	2 (1.7)	0
Anemia	12 (10.2)	8 (6.8)	8 (6.8)	1 (0.85)
Vomiting	16 (13.6)	10 (8.5)	2 (1.7)	0
Constipation	15 (12.7)	8 (6.8)	1 (0.85)	0
Lymphocyte count decrease	6 (5.1)	9 (7.6)	4 (3.4)	0
Anorexia	11 (9.3)	8 (6.8)	0	0
Injection site reaction	16 (13.6)	1 (0.85)	0	4 (3.4)
Neutrophil count decrease	6 (5.1)	4 (3.4)	3 (2.5)	0
Alkaline phosphatase increase	9 (7.6)	6 (5.1)	1 (0.85)	0
Back Pain	7 (5.9)	6 (5.1)	3 (2.5)	0
Cough	6 (5.1)	10 (8.5)	0	0

CONCLUSIONS

- Results show feasibility for recruitment and treatment of MBC patients with ECOG 0 to 2
- The population is very heavily pretreated with median 6 prior lines of therapy
- 9% of patients reported intracranial metastases
- PFS was higher in patients with no CTCs at baseline, favorable NLR, HLA class I A2 expression
- The biomarkers that correlated with PFS and OS in the phase 2 study continue to show correlation with PFS in the phase 3 study.
- Bria-IMT + CPI regimen may be a treatment option for patients who have exhausted other therapeutic options including ADC, CPI, and CDK4/6 inhibitors.
- Adverse events are consistent with those expected in late stage MBC patient population.

RESULTS

Figure 1. Progression-Free Survival by Metastatic Breast Cancer Subtype

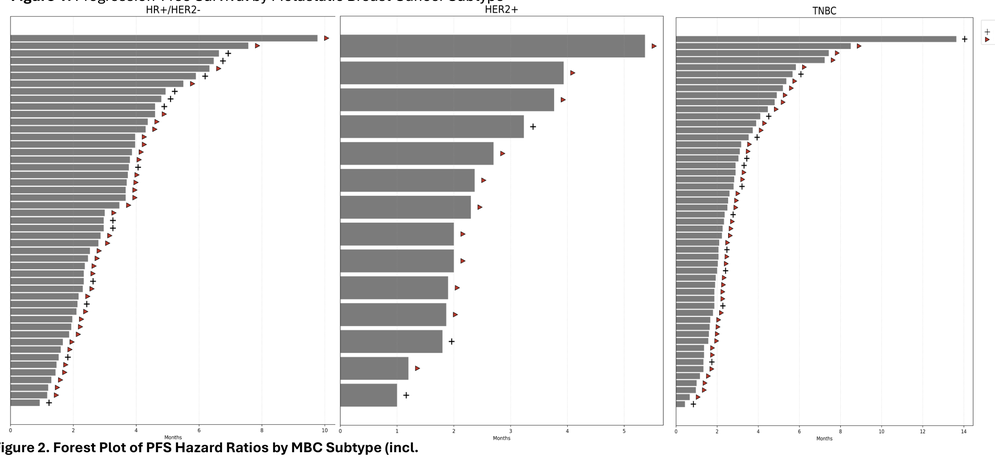


Figure 2. Forest Plot of PFS Hazard Ratios by MBC Subtype (incl. HER2low as a HER2 expression subsets)

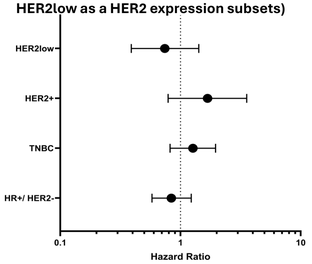


Figure 2. Hazard ratios for progression free survival (PFS) across metastatic breast cancer subtypes. Points represent estimated HRs and horizontal bars indicate 95 percent confidence intervals. The dotted vertical line marks HR = 1.

Table 3: Median PFS by MBC Subtype

Biomarker	n	PFS Events n (%)	Median PFS (months)
HR+/HER2-	49	36 (41)	3.7
TNBC	43	32 (37)	2.3
HER2+	14	11 (13)	2.4
HER2-Low	10	8 (9)	3.9
Overall	116[a]	87 (100)	3.0

[a] **MBC Subtype of 2 patients in cohort not yet reported**

RESULTS

Figure 3. Forest Plot of PFS Hazard Ratios by Prior CDK4/6i, CPI, and ADC Exposure

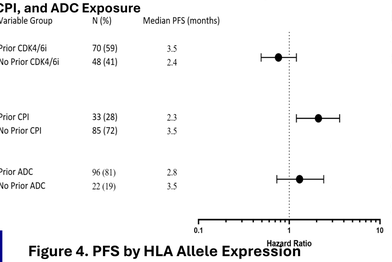


Figure 3. Hazard ratios for progression-free survival (PFS) by prior therapy exposure. Points represent estimated HRs and horizontal bars indicate 95 percent confidence intervals. Median PFS and sample sizes for each subgroup are shown on the left for reference.

Figure 4. PFS by HLA Allele Expression

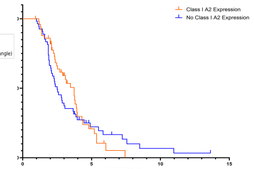


Table 4. PFS by HLA

HLA Status	Median	Range
Class I A2 Expression	3.7	0.9 – 7.4
No Class I A2 Expression	2.5	1.0 - 13.6
HR: 0.9 ; 95% CI 0.6 to 0.1.4, p = 0.72		

Figure 5. PFS by Neutrophil to Lymphocyte Ratio After 1 Treatment

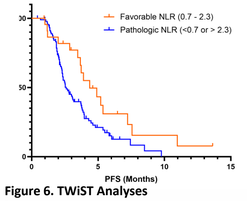
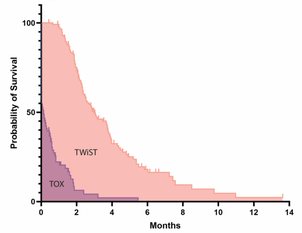


Table 5. Kaplan Meier curves showing PFS in patients with (after 1 treatment administration) an NLR of 0.7 – 2.3 (4.4 mo) vs those with NLR < 0.7 or > 2.3 (2.6 mo).

NLR Status	Median	Range
Favorable NLR	4.4	0.9 - 13.6
Pathologic NLR	2.6	0.4 – 9.8
HR: 0.6 ; 95% CI 0.3 to 0.9, p = 0.02		

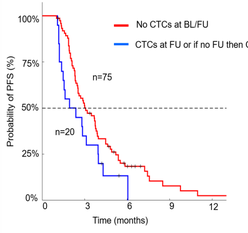
Figure 6. TWiST Analyses



Metric	Duration (months)	95% CI	N
TOX[a]	0.6	0.3 – 0.7	57
TWiST	3.3	2.8 – 3.8	118

[a] **time with ≥ Grade 3 toxicity before progression**

Figure 7. PFS by CTC



Metric	Median PFS (months)
No CTC at BL or FU	5.3
CTCs at FU	2.2
HR: 1.93; 95% CI 1.0 – 3.6, p = 0.06	

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