Bria-ABC vs physician choice in late stage MBC; early biomarker correlates of the randomized registration trial

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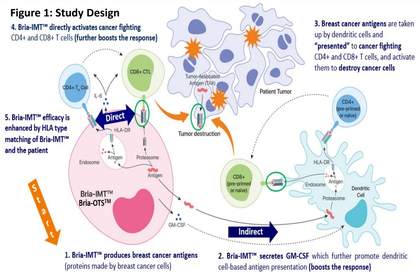
BACKGROUND

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 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.

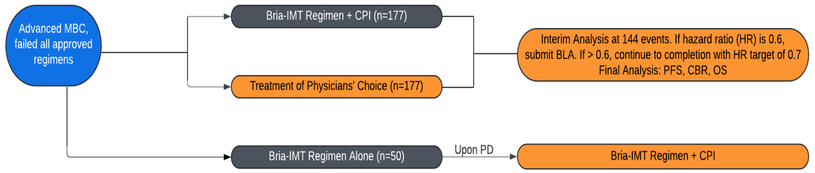
Figure 1: Study Design



METHODS

This is an ongoing, prospective, randomized phase 3 study (NCT06072612; initiated in 2024), evaluating the Bria-IMT regimen in combination with an anti–PD-1 checkpoint inhibitor (CPI). 3 arm randomized 1:1:1 (Bria-IMT, Bria-IMT+CPI, or PC) in late stage heavily pretreated pts with MBC. Pts can be ECOG ≤2, Pts w/ CNS mets and/or who have received prior CPI or ADCs are allowed. The Bria-IMT™ regimen includes preconditioning w/ cyclophosphamide (300 mg/m²) on day -2/-3, intradermal SV-BR-1-GM inoculations (x4) on day 0, and interferon at inoculation sites (Days 1-3). CPI (retifanlimab 375 mg) may be given between days -2 to 2. The regimen is administered every 3 weeks (Q3W). Pts randomized to the monotherapy arm (Bria-IMT™ alone) may cross over to the combo arm upon disease progression. Response assessments are planned Q6W for the first cycle, and then Q8W thereafter. Based on prior data, an interim HR of 0.6 at 144 events will constitute early success. Overall study design anticipates 404 total pts.

Figure 2: Study Design



Time to event analyses for the primary outcome will use the Kaplan-Meier method and stratified log-rank test with randomization stratification factors, for testing significance.

Patients with advanced metastatic breast cancer (MBC) who failed all approved regimens are randomized to receive either the Bria-IMT regimen plus checkpoint inhibitor (CPI), treatment of physician's choice, or Bria-IMT alone. An interim analysis is planned at 144 events, with a decision to submit a BLA if the hazard ratio (HR) is ≤ 0.6. Final analysis will assess progression-free survival (PFS), clinical benefit rate (CBR), and overall survival (OS). Patients progressing on Bria-IMT alone may cross over to Bria-IMT + CPI. Time-to-event outcomes will be analyzed using the Kaplan-Meier method with a stratified log-rank test.

RESULTS

Table 1: Patient Demographics

N = 70	N (%)
Age, Median (Range)	57 (32 – 83)
• White	59 (75)
• Black	8 (10)
• Hispanic	18 (23)
• Asian	3 (4)
• Other	7 (9)
• ECOG 0	42 (60)
• ECOG 1	23 (33)
• ECOG 2	5 (7)

Prior systemic therapy, Median (Range)	6 (2-13)
Previous therapies	N (%)
• ADC	53 (76)
• CPI	12 (17)
• CDK4/6 inhibitors	35 (50)
Number of HLA Match with SV-BR-1-GM	
• 0	11
• ≥ 1	40
• Unknown	19

CONCLUSIONS

Early Phase 3 data reinforce the relevance of biomarkers identified in Phase 2. While findings remain preliminary, consistent trends support their continued evaluation:

- DTH positivity is significantly associated with improved outcomes (4.5 vs 2.5 months, p = 0.001), consistent with Phase 2 observations.
- Presence of ≥1 CTC at first follow-up after treatment predicts worse PFS (2.4 vs 3.8 months, p = 0.04), supporting its role as a negative prognostic marker.
- Higher baseline CAML scores (≥ 5) trend toward improved prognosis (3.7 vs 2.2 months, p = 0.10), consistent with prior directional findings.
- An initial on-treatment NLR of > 2.3 or < 0.7, assessed after initiation of therapy, was significantly associated with shorter median progression-free survival (3.07 months vs undefined, p = 0.02).
- The Bria-IMT regimen remains well tolerated, with treatment-emergent adverse events (TEAEs) generally manageable.

RESULTS

Figure 3: Kaplan-Meier curve depicting median PFS across all arms of the trial.

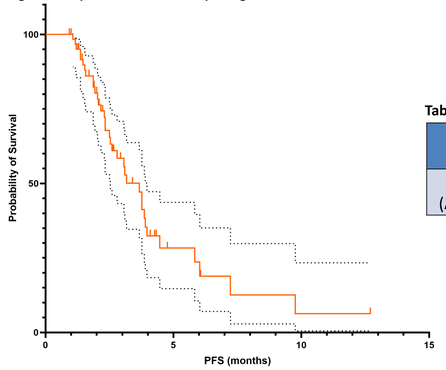


Table 2: Median PFS across all patient arms.

N = 62	Median PFS (Months)	95% CI
Overall (All Arms)	3.67	2.53 - 3.97

Table 3: Adverse events occurring in > 10% of patients

AE Term	Number of Patients (%)
Fatigue	17 (27.4)
Anemia	16 (25.8)
Nausea	15 (24.2)
AST/ALT increased	13 (20.9)
Constipation	11 (17.7)
Injection site reactions	11 (17.7)
Neutrophil count decreased	11 (17.7)
GGT increased	10 (16)
Vomiting	10 (16)
Headache	9 (14.5)
White blood cell count decreased	9 (14.5)
Back pain	8 (12.9)
Cough	8 (12.9)

RESULTS

Table 4: Median PFS in patients who matched or did not match the HLA alleles present in SV-BR-1-GM.

Treatment	Any HLA Match Median PFS (mo)	No HLA Match Median PFS (mo)	Hazard Ratio	95% CI	p Value
Bria-IMT With or Without CPI	3.10	4.00	0.77	0.29 to 1.99	0.59
TPC	3.16	2.80	2.226	0.5191 to 9.543	0.6803

Figure 5: Kaplan-Meier curve comparing median PFS in patients with a positive DTH response vs those without a DTH response.

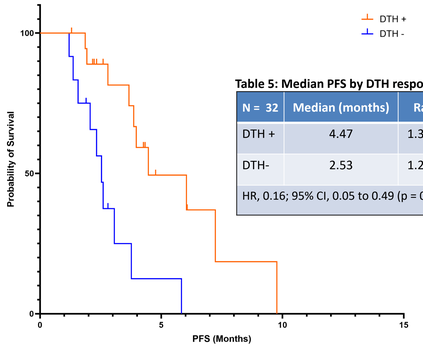


Table 5: Median PFS by DTH response

N = 32	Median (months)	Range
DTH +	4.47	1.3 – 9.8
DTH-	2.53	1.2 – 5.8
HR, 0.16; 95% CI, 0.05 to 0.49 (p = 0.001)		

Figure 6: Progression-free survival (PFS) by neutrophil-to-lymphocyte ratio (NLR) after 1st administration of therapy.

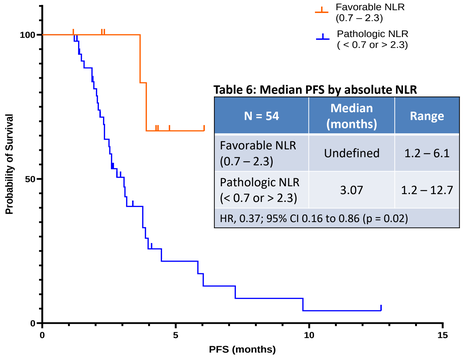


Table 6: Median PFS by absolute NLR

N = 54	Median (months)	Range
Favorable NLR (0.7 – 2.3)	Undefined	1.2 – 6.1
Pathologic NLR (< 0.7 or > 2.3)	3.07	1.2 – 12.7
HR, 0.37; 95% CI 0.16 to 0.86 (p = 0.02)		

Figure 7: Kaplan-Meier curve comparing patients with < 1 CTC vs 1+ CTC at 1st available follow up.

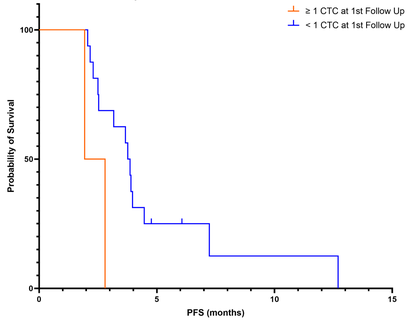


Table 7: Median PFS by absolute baseline CTC count

N = 18	Median (months)	Range
0 CTC at 1st Follow Up	3.8	2.1 – 12.7
≥ 1 CTC at 1st Follow Up	2.4	1.9 – 2.8
HR, 0.05 ; 95% CI 0.003 to 0.817 (p = 0.04)		

Figure 8: Kaplan-Meier curve of PFS in patients with ≥ 5 CAMLs vs < 5 CAMLs at baseline.

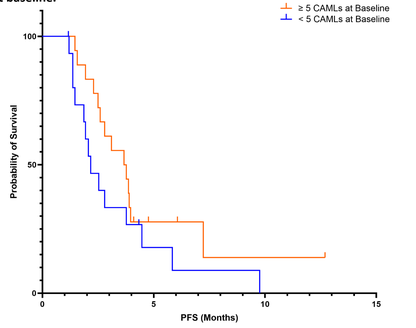


Table 8: Median PFS by absolute baseline CAML count

N = 34	Median (months)	Range
< 5 CAML at Baseline	2.2	1.2 – 9.8
≥ 5 CAML at Baseline	3.7	1.5 – 12.7
HR, 0.58 ; 95% CI 0.27 to 1.26 (p = 0.10)		