RANDOMIZED PHASE 2 OF BRIA-IMT, AN ALLOGENIC HUMAN CELL LINE WITH ANTIGEN PRESENTING ACTIVITY IN HEAVILY PRETREATED METASTATIC BREAST CANCER

Carmen Calfa, MD[1], Chaitali Nangia, MD[2], Minal Barve, MD[3], John Knecht, MD[4], Jarrod Holmes, MD[5], Kendrith Roland, MD[6], Ralph Boccia, MD[7], Frances Valdes-Albini, MD[8], Zach Gostout, BS[9], Mingjin Chang, PhD[9], William Williams, MD[9], Charles Wiseman, MD[9], Bonnie Guerin, MD[10], Shakar Dakhil, MD[11], Giuseppe Del Priore, MD MPH[9], Saranya Chumsri, MD[12].

University of Miami Sylvester Comprehensive Cancer Center Miami FL[1], Hoag Memorial Hospital Newport Beach[2], Mary Crowley Cancer Research Dallas TX[3], Tranquil Clinical Research Friendswood TX[4], St Joseph's Heritage Health Santa Rosa CA[5], Carle Cancer Center Urbana IL[6], The Center for Cancer and Blood Disorders[7], University of Miami[8], Atlantic Health Summit NJ[10], Cancer Center of Kansas KC KS[11], Mayo Clinic FL[12], BriaCell Therapeutics Corp., Philadelphia, PA[9]

SABC 2023
Poster ID P03-05-12

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 the reservoir of antigens to activate the patient's anti-tumor immune responses. We report post-hoc exploratory data for patients with advanced metastatic breast cancer (aMBC) treated with the Bria-IMT regimen (SV-BR-1-GM +CTX +IFNα).

METHODS

On going, prospective, phase 1-2 with randomized phase 2 cohort (NCT03328026; 2018-present) using the Bria-IMT regimen with a PD-1 checkpoint inhibitor (CPI); cycles every 3 weeks; 54 patients dosed to date. The regimen includes cyclophosphamide 300mg/m^2 I.V., 48 hours prior to irradiated SV-BR-1-GM intradermally (~20 x 10^6 cells), followed by IFNα at each inoculation site 2 days afterwards. 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 first vs SV-BR-1-GM first.

RESULTS

Table 1: Patient Demographics

N	Age, Median (Range)	BMI, Median (Range)	Prior Systemic Tx Median (Range)
48	62 (38 – 81)	28.1 (18.1 – 42.7)	6 (2 – 13)

Conclusion: Patients were heavily pre-treated

Table 2: Summary of Clinical Experience with SV-BR-1-GM by MBC Biomarkers at Metastatic Site

Biomarkers	N (%)	Patients with Evaluable Outcome	ORR [CR, PR] in Evaluable Patients	CBR [CR, PR, SD] in Evaluable Patients
HR+/HER2-	20 (42 %)	9	2	6
TNBC	11 (23 %)	4	0	1
HER2+	1 (2 %)	1	0	0
unknown	16 (33 %)	3	0	1
Total	48	17	2 (12 %)	8 (47%)

Conclusion: Clinical benefit was seen in 47% of evaluable patients, including those with HR+ and TNBC disease

Table 3: Summary of Adverse Events (AEs)

AE Term	# of Subjects	Highest Toxicity Grade
Constipation	11	3
Fatigue	11	3
Nausea	9	2
Injection Site Reaction	8	2
Headache	7	2
Hypothyroidism	6	2
Diarrhea	5	2
Injection Site Erythema	5	1
Injection Site Induration	5	1
Dizziness	4	2

Conclusion: Treatment with the Bria-IMT regimen with an immune CPI was generally well tolerated.

Table 4: Progression Free Survival (PFS) analysis using Cox Proportional Hazards Regression Model

PFS analysis Cox PH Regression Model		
Parameter	**Parameter Estimate**	**P-value**
Sequence	-0.11702	0.7865
Age	-0.10216	0.0003
NLR Baseline	0.11531	0.0442
Induration Max Change	-0.0871	0.0046

Conclusion: The Cox Proportional Hazards Regression Model for Progression Free Survival (PFS) adjusted for sequence, age, baseline NLR, maximum change in induration. *Age (>60), NLR (lower), and induration (>5 mm), were significant* in predicting improved PFS (available data in evaluable patients).

Table 5: Overall Survival (OS) analysis using Cox Proportional Hazards Regression Model

OS analysis Cox PH Regression Model		
Parameter	**Parameter Estimate**	**P-value**
Sequence	0.10053	0.8701
Age	-0.02849	0.3635
NLR Baseline	0.01221	0.8616
Induration Max Change	-0.04218	0.2001

Conclusion: The Cox Proportional Hazards Regression Model for OS analysis, did not reveal any statistically significant predictors among the tested parameters at this time based on available data in evaluable patients.

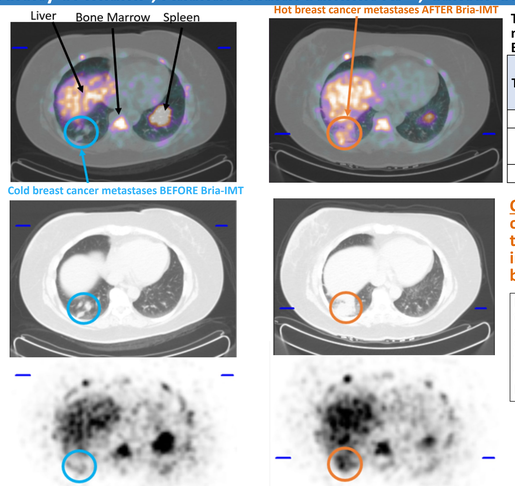

Figure 1: Multi Organ Anti CD8+ Immuno PET scan demonstrating Bria-IMT induced CD8+ TILS into breast cancer metastases

Table 6: Comparison of tumor marker levels before and after Bria-IMT regimen.

Tumor Marker	Before Bria-IMT (U/mL)	After Bria-IMT (U/mL)
CEA	2.0	1.4
CA 27.29	34.0	Not Available
CA 15-3	17.0	9.7

Conclusion: Bria-IMT combination therapy is able to induce CD8+ T cell infiltration into metastatic breast cancer tumors.

For complementary studies on this topic, please refer to our additional poster: **Kuker et al SABC 2023 PO1-20-12: "CD8+ Tumor Infiltrating Lymphocytes Turn a Cold Tumor Hot in Metastatic Breast Cancer"**

Table 7: Distribution of Disease Control Rate Based on Maximum Induration Diameter

Disease Control Rate by Maximum Induration			
Induration	No	Yes	Total
< 5mm	16 84.21%	3 15.79%	19
≥ 5mm	13 68.42%	**6** **31.58%**	19
Total	29	9	38

Table 8: Distribution of Disease Control Rate Based on Maximum Erythema Diameter

Disease Control Rate by Maximum Erythema			
Erythema	No	Yes	Total
< 5mm	14 82.35%	3 17.65%	17
≥ 5mm	15 71.43%	**6** **28.57%**	21
Total	29	9	38

Conclusion: The trend observed in available data from evaluable patients indicates that induration and/or erythema ≥ 5mm are predictive of an enhanced Disease Control Rate compared to those with induration or erythema < 5mm. These findings imply a correlation with local immune response and improved outcomes. Further investigation into the underlying mechanisms could provide valuable insights into patient stratification for treatment, potentially leading to more personalized and effective clinical approaches.

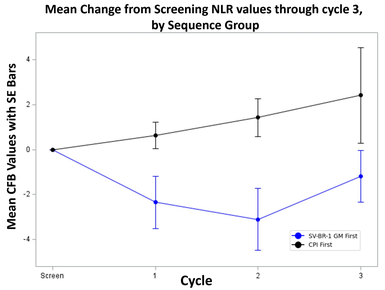

Figure 2: Mean Change from Screening Neutrophil to Lymphocyte Ratio (NLR) Through Cycle 3 by Treatment Sequence Group

Conclusion: NLR nadir on treatment was associated with OS (p = 0.004) and may act as an early indicator of therapeutic benefit. Sequencing SV-BR-1-GM before a CPI had a prolonged reduction in NLR. This sequence is being used in the ongoing pivotal phase 3 RCT (NCT06072612)

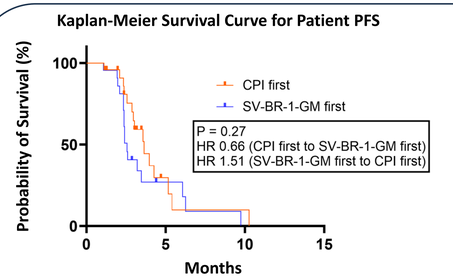

Figure 2: Kaplan-Meier curves presenting available data on progression free survival (PFS) for patients enrolled in BRI-ROL-001 trial.

Conclusion: No statistically significant difference in PFS treating with CPI or SV-BR-1-GM first in this interim analysis.

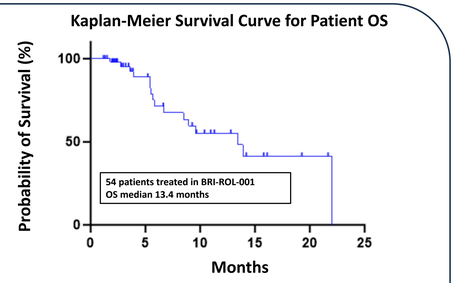

Figure 3: Kaplan-Meier curves presenting available data on overall survival (OS) for patients enrolled in BRI-ROL-001 trial.

Conclusion: OS for all patients is 13.4 months in this interim analysis.

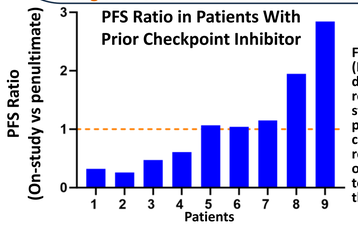

Figure 4: Bar chart of PFS ratio (PFS on the current study divided by PFS on their most recent therapy prior to this study) for nine patients previously treated with checkpoint inhibitors. Patient responses vary, with similar or increased PFS for patients 5 to 9. A dashed line indicates the PFS ratio of 1.

Conclusion: Bria-IMT has potential efficacy in reversing immune exhaustion among heavily pre-treated patients, as evidenced by the improved PFS ratios in patients 5-9. This suggests that these patients have benefitted from the therapy, achieving better outcomes despite failing prior CPI therapy.

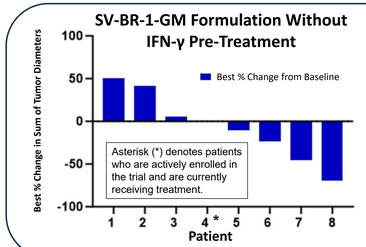

Figure 5: Bar graph displaying the best change from baseline in tumor diameter for subjects treated with SV-BR-1-GM formulation without IFNγ. 6 of 8 subjects with available data had no progression or death compared to 2 of 7 using a IFNγ exposed cell formulation (Fisher's Exact p = 0.057)

Conclusion: A simplified SV-BR-1-GM formulation without IFNγ treatment appears more effective in reducing tumor size than the formulation with IFNγ treatment (not shown). The formulation without IFNγ treatment is being used in all future subjects and trials.

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.
- Most patients who had failed prior CPI therapy showed improved PFS compared to patient's last regimen.
- Sequencing of CPI with SV-BR-1-GM is associated with differential clinical outcome trends but is not statistically significant in this interim analysis.
- CD8+ Immuno PET shows an increase in CD8+ peripheral infiltrating lymphocytes suggesting systemic activation and infiltration into cancer metastatic sites.
- Older patients were able to derive clinical benefit
- NLR decrease was associated with therapeutic benefits.
- These findings will inform the ongoing development for optimized outcomes in future studies.
- These preliminary results will be confirmed in an ongoing randomized phase 3 pivotal registrational trial (NCT06072612).