Efficacy of Bria-IMT Regimen in Inducing CNS Metastasis Regression

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BACKGROUND

Breast cancer metastasis to the central nervous system (CNS) often leads to severe morbidity and mortality, and while systemic treatments manage primary tumors, their impact on CNS metastases is limited. 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, Bria-IMT also serves as the reservoir of antigens to activate the patient's anti-tumor immune responses.

METHODS

This retrospective analysis evaluates the efficacy of Bria-IMT (SV-BR-1-GM ~$20x10^6$ cells, intradermally 48-72 hours after cyclophosphamide 300 mg/m^2, followed by low-dose interferon-alpha at the inoculation sites 2 days later) as a monotherapy or in combination with an immune checkpoint inhibitor (CPI) on CNS tumor regression. MRI imaging was reviewed to assess progression / regression of intracranial lesions.

RESULTS

Table 1: Patient Demographics

Subject	Age	Prior lines of therapy	Treatment	Overall Survival (months)	HLA Matching with SV-BR-1-GM	DTH Positive (≥5mm) or Negative (< 5mm)	Intracranial Response	MBC Subtype
1	61	3	Bria-IMT	>6	1 locus	Negative	Yes	TNBC
2	70	13	Bria-IMT + Pembrolizumab	22	2 loci	Positive	Yes	HR+/HER2-
3	69	3	Bria-IMT + Pembrolizumab	14	2 loci	Positive	Yes	HR+/HER2-
4	64	3	Bria-IMT + Pembrolizumab	4	2 loci	Positive	No	HR-/HER2low
5	66	8	Bria-IMT + Retifanlimab	6+	No match	Positive	Yes	HR+/HER2+
6	45	6	Bria-IMT + Pembrolizumab	9	No match	Positive	No	TNBC
7	58	Unknown	Bria-IMT	>33	2 loci	Positive	Yes	HR+/HER2-

Table 2a: Safety

Most common AE (more than one subject reported):		
AE Term	# Subjects	Highest Toxicity Grade
Fatigue	6	3**
Injection Site Induration	4	1*
Injections Site Erythema	4	1
Cough	2	1*
Diarrhea	2	2
Headache	2	1
Hemorrhoids	2	2**
Hypothyroidism	2	2

* 1 patient in subset reported severity as mild without Toxicity Grade

** 1 patient in subset reported severity as moderate without Toxicity Grade

Table 2b: Safety

AE Toxicity Grades 3 and 4 (any occurrence)			
AE Term	Highest Toxicity Grade	# Subjects	Relatedness
Altered mental status	4*	1	Unrelated
Allergic reaction	3	1	Unrelated
E. Coli septicemia	3	1	Unrelated
Fall	3	1	Unrelated
Fatigue	3**	2	Possibly related to cyclophosphamide
Weakness	3	1	Possibly related to cyclophosphamide
Hemorrhoids	moderate	1	Unrelated

* The highest AE toxicity grade of 4 reported with altered mental status was found to be unrelated to study drug

** 1 patient in subset reported severity as moderate without toxicity grade and unrelated to study drug

IMAGING

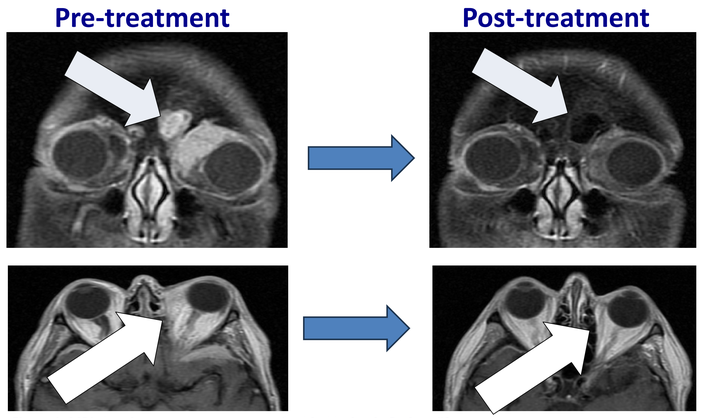


Figure 1: MRI showing complete response of orbital lesion in Patient #2

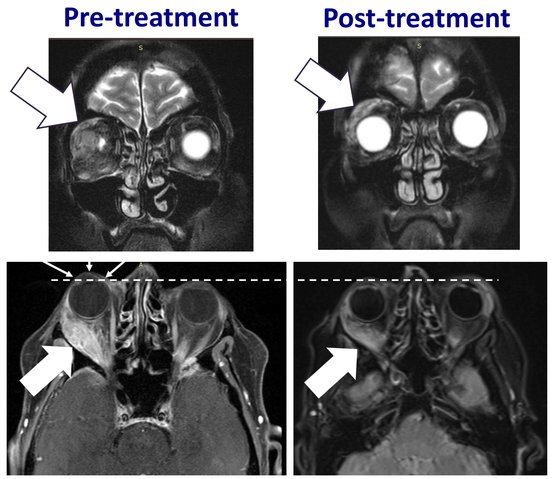
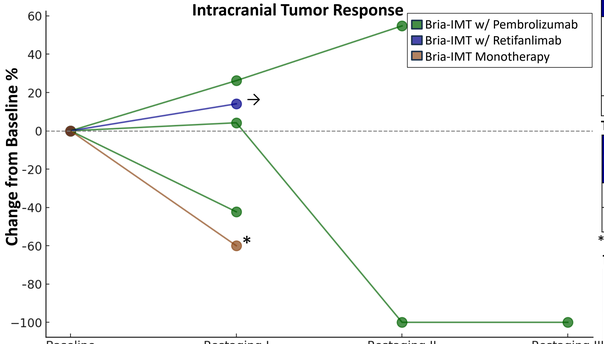


Figure 2: MRI showing regression of orbital lesion in Patient #5.

Patient #5 mentioned in this figure was a patient at Sylvester Comprehensive Cancer Center Site, University of Miami, Miami, FL, under the study led by Dr. Carmen Calfa (PI). Imaging analyzed by Dr. Russ Kuker.

RESULTS

Figure 3: Percent Change of the Sum of Intracranial Lesion Diameters



→ indicates patient currently enrolled

* Restaging was performed 5 weeks post Tx discontinuation

Table 3: Patient Demographics

Patients with Intracranial Metastasis				
Median Age	Median OS (months)	Median Prior lines of therapy	Median Prior Lines of Radiation	Median Prior Surgeries
64	9	5	3	2

Table 4: Change in Sum of Intracranial Lesions

Median Sum of Intracranial Lesion Diameters (mm)**	
Before Bria-IMT™	After Bria-IMT™
24	15

**in 5 evaluable patients with measurable outcomes

Table 5: Change in Sum of Intracranial Lesions by Regimen

Median % Change in the Sum of Intracranial Lesion Diameters (mm)**		
Bria-IMT™ w/ Pembrolizumab	Bria-IMT™ w/ Retifanlimab	Bria-IMT™ Monotherapy
-42.3%	14.1%	-60%

**in 5 evaluable patients with measurable outcomes

Table 6: Intracranial Tumor Response

Observed Intracranial Tumor Reduction				
Patient ID	Total Number of Bria-IMT Cycles	Measurable Change in Sum of Diameters	Number of Lesions Pre-Treatment	Number of Lesions Post-Treatment
1	5	-60% [a]	2	1
2	9	CR [b]	2	1
3	3	-42%	4	4
4	5	55%	2	2
5	8	14%	2	2
6	3	NA	0	≥ 2
7	12	CR of CNS lesions	≥3	CR of ≥3 lesions

[a] An additional small left parietal lobe lesion experienced CR in this patient. [b] An additional 9mm -> 4mm reduction in a left anterior temporal lobe lesion was observed in this patient after 3 cycles of Bria-IMT.

Table 7: Cancer Antigens

Cancer Antigens						
Patient ID	CEA at Screening (or First Available Value)	CEA Final or Most Recent Value	CA 15-3 at Screening (or First Available Value)	CA 15-3 Final or Most Recent Value	CA 27.29 at Screening (or First Available Value)	CA 27.29 Final or Most Recent Value
1	13.3	22.7	3	5	NA	NA
2	139.2	28.55	1886	666.2	NA	NA
3	1.8	5.35	62.4	60.3	NA	NA
4	12.9	1.3	15.7	16.2	NA	NA
5*	5.1	1.5	199.4	32.9	209.2	29.1
6	1.95	1.41	97.9	153	NA	NA
7	0.5	1.5	NA	NA	23.6	25.0

* Patient currently enrolled in study. Most recent CA levels evaluated after 9 cycles.

CONCLUSION

This review consolidates evidence for the efficacy of the Bria-IMT regimen in CNS metastasis regression, both alone and with CPIs. The consistent regression seen across all breast cancer subtypes among heavily pretreated patients highlights the potential of Bria-IMT in managing CNS metastasis. Ongoing trials will determine the full extent.