ASTRO-VAC CNS : Bria-IMT in the Management of Tumor Agnostic Metastatic CNS Lesions

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Background

- ❑ SV-BR-1-GM(Bria-IMT), BriaCell's engineered human immortalized cell line, is an off-the-shelf, allogeneic cellular immunotherapy.
- ❑ Designed to work by triggering robust adaptive (T-cells) and innate (dendritic and NK cells) anti-tumor immune responses.
- ❑ Bria-IMT enhances these responses through direct antigen presentation and activation of CD4+ and CD8+ T-cells, significantly increasing effectiveness when combined with immune checkpoint inhibitors (CPI).
- ❑ Prior presentations report that Bria-IMT is able to induce regression of intracranial metastases.
- ❑ In the ongoing randomized phase 2 and (NCT03328026) and previously completed trials, a reduction in the size and/or number of intracranial lesions was observed in 5 out of 7 evaluable patients with a median maximal decrease of 42% (range -19% to -100% decrease) in the sum of the diameters in multiple BC subtypes.
- ❑ Disease control after prior antibody-drug conjugates (ADCs) has been observed in 40% of patients.
- ❑ Bria-IMT is well tolerated with no concerning adverse events (AEs).

Dual Mechanistic Pathways of Bria-IMT

1. Direct – Bria-IMT directly stimulates CD4+ and CD8+ T cells.
2. Indirect – Bria-IMT secretes GM-CSF and provides tumor antigens for anti-tumor immune activation.

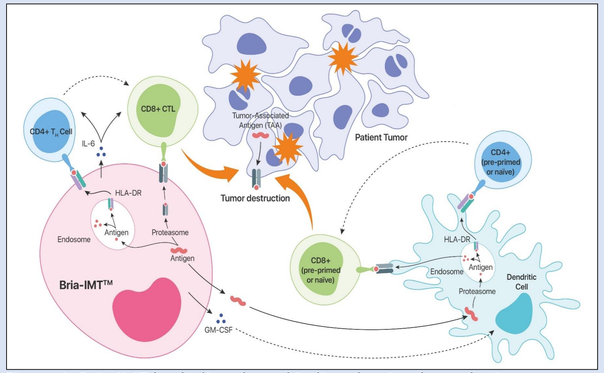


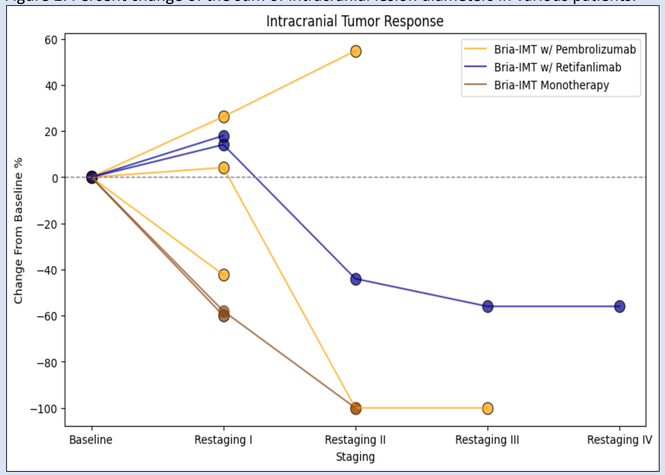
Figure 1. Bria-IMT both directly and indirectly stimulates the immune cells.

Phase 2 and Other Clinical Outcomes

- ❑ In 54 heavily pretreated metastatic breast cancer patients, the Bria-IMT regimen demonstrated clinical benefits. (Calfa C, 2024)
- ❑ In the randomized patient cohort (N = 32), evaluable patients demonstrated a clinical benefit rate (CBR) of 54%.
- ❑ 53% (9 out of 17 evaluable) of patients who had previously received antibody drug conjugates (ADCs) achieved disease control. (Calfa C, 2024)
- ❑ Intracranial tumor response observed in 5 out of 8 patients with intracranial metastases across various studies. (Chumsri S, 2024)
- ❑ CD8-ImmunoPET demonstrated increased post-treatment recruitment of CD8+ T-cells to metastatic sites. (Parent E, 2024)

Clinical Benefit in Intracranial Disease

Figure 2. Percent change of the sum of intracranial lesion diameters in various patients.



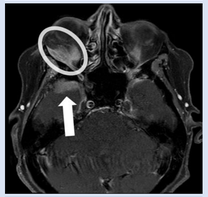
Patients with Intracranial Metastasis		
Median Age	**Median OS (months)**	**Median Prior Lines**
64	13.7	5

Table 1. Patient Demographics

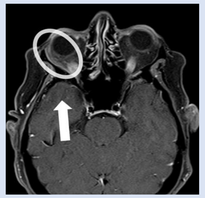
Median % Change in the Sum of Intracranial Lesion Diameters (mm)**		
Bria-IMT™ w/ Pembrolizumab	**Bria-IMT™ w/ Retifanlimab**	**Bria-IMT™ Monotherapy**
-42%	-19%	-80%

Table 2. Change in the Sum of Intracranial Lesions in 7 evaluable patients

Pre-treatment



6 Months



11 Months

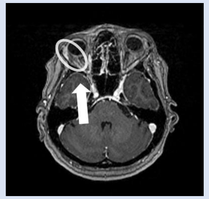


Figure 3. MRI imaging showing regression of right orbital and temporal lobe lesion in patient who received Bria-IMT w/ retifanlimab. (Parent E, 2024)

Tumor Marker	Before Bria-IMT (U/mL)	After 9 Cycles of Bria-IMT (U/mL)
CEA	**5.1**	**1.5**
CA 27.29	**209.2**	**29.1**
CA 15-3	**199.4**	**32.9**

Table 3. Comparison of tumor marker levels before and after Bria-IMT Regimen in the patient seen above.

Study Design

- ❑ ASTRO-VAC CNS: Allogeneic SV-BR-1-GM Therapeutic Response Optimizer VACcine for Central Nervous System Metastases.
- ❑ Single-center, prospective, phase 1 basket trial.
- ❑ Evaluating the safety and feasibility of administering SV-BR-1-GM in combination with pembrolizumab to solid tumor oncology patients.

Objectives

- ❑ Primary: Determine the safety, feasibility of delivery, and patient adherence to the investigational agent in patients with solid tumor CNS metastasis.
- ❑ Secondary: Intracranial and extracranial PFS, intracranial and extracranial objective response rate, and overall survival.

Eligibility

- ❑ History of CNS metastases (brain and/or LMD) with progression on ≥ one line of SOC therapy.
- ❑ ECOG ≤ 2
- ❑ No limit on prior number of therapies.
- ❑ Extracranial disease without visceral crisis.
- ❑ Asymptomatic and untreated brain metastasis are allowed at the discretion of the treating providers.
- ❑ 3 week wash out period from previous treatment.

Treatment Regimen

- ❑ SV-BR-1-GM, the investigational product, will be administered with:
  - ❑ Low-dose cyclophosphamide (300 mg/m²), given 2-3 days before SV-BR-1-GM
  - ❑ Peg-interferon alfa 2a (0.18 mcg, subcutaneous [SC]), administered on the day of SV-BR-1-GM inoculation to boost the immune response.
- ❑ Each SV-BR-1-GM administration consists of 4 intradermal injections.
- ❑ Pembrolizumab (200 mg) will be administered 2-3 days before SV-BR-1-GM inoculation during every cycle.
- ❑ Cycles q3w

Treatment Schema

Day 1
- Cyclophosphamide: 300 mg/m², IV
- Pembrolizumab: 200 mg/m², IV

Day 3-4
- Hypersensitivity Skin Test:
  - Inject SV-BR-1-GM (1 x 10^6 cells) into forearm skin
  - If no acute hypersensitivity, proceed to full dose of SV-BR-1-GM
- SV-BR-1-GM: 20 x 10^6 total cells, 4 intradermal injections
  - 2x upper back
  - 2x thighs
- Interferon:
  - 0.18 mcg, subcutaneous to the upper arm

Day 5-6
- Delayed-Type Hypersensitivity Test:
  - Patient self evaluation and reporting

Figure 4. Treatment schema for the Phase 1 ASTRO-VAC CNS clinical trial.

References:
1. Calfa, C. J., et al. (2024). Outcomes of advanced/metastatic breast cancer (aMBC) treated with BRIA-IMT, an allogeneic whole cell immunotherapy. Journal of Clinical Oncology, 42(16_suppl), 1022-1022. https://doi.org/10.1200/JCO.2024.42.16_suppl.1022
2. Chumsri, et al. Overall Survival Results of BRIA-IMT Allogenic Whole Cell-Based Cancer Vaccine. ***SABCS 2024 Poster.***
3. Parent, et al. Bria-IMT CD8+ Tumor Infiltrating Lymphocytes Turn "Cold" Tumor "Hot" in Metastatic Breast Cancer. ***SABCS 2024 Poster.***