Study of the Bria-IMT Regimen and CPI vs Physicians' Choice in Advanced Metastatic Breast Cancer (BRIA-ABC)

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BACKGROUND

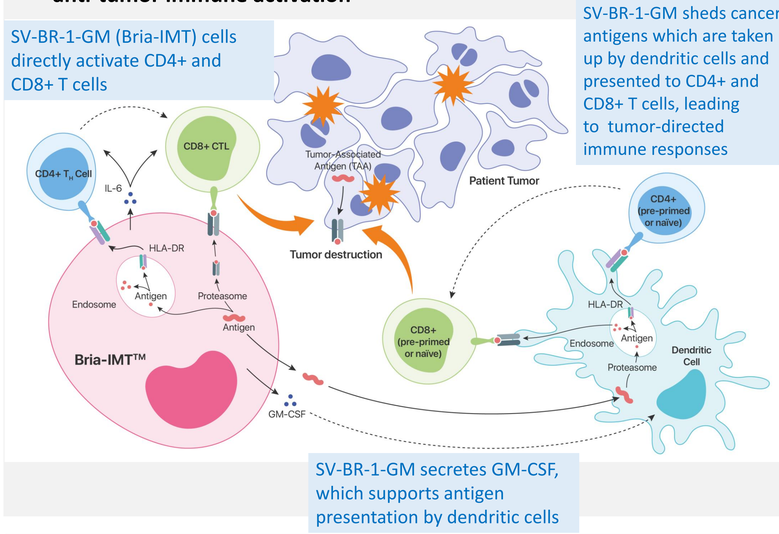
- SV-BR-1-GM (Bria-IMT™), BriaCell's engineered human immortalized cell line, is an off-the-shelf, allogeneic cellular immunotherapy
- Designed to work by triggering robust adaptive (T-cells) and innate (dendritic and NK cells) anti-tumor immune responses
- Bria-IMT enhances these responses through direct antigen presentation and activation of CD4+ and CD8+ T-cells, significantly increasing effectiveness when combined with immune checkpoint inhibitors (CPI).

FIGURE 1 DUAL MECHANISM of ACTION 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**

SV-BR-1-GM (Bria-IMT) cells directly activate CD4+ and CD8+ T cells

SV-BR-1-GM sheds cancer antigens which are taken up by dendritic cells and presented to CD4+ and CD8+ T cells, leading to tumor-directed immune responses



SV-BR-1-GM secretes GM-CSF, which supports antigen presentation by dendritic cells

PHASE 2 CLINICAL OUTCOMES

- In 54 heavily pretreated metastatic breast cancer patients, the Bria-IMT regimen demonstrated clinical benefits (Calfa C, 2024)
- 53% (9 out of 17 evaluable) of patients who had previously received antibody drug conjugates (ADCs) achieved disease control (Chumsri S 2024)
- Significant clinical benefits observed in 4 out of 5 patients with intracranial metastases (Figure 2, Figure 3 & Figure 4)
- CD8-ImmunoPET demonstrated increased post-treatment recruitment of CD8+ T-cells to metastatic sites (Figure 5)
- Optimized regimen for Phase 3 in treatment sequence (CPI early vs CPI delayed) and SV-BR-1-GM formulation (Treated with IFNγ vs untreated) (Chumsri S, 2024)

FIGURE 2 CLINICAL BENEFIT in INTRACRANIAL DISEASE

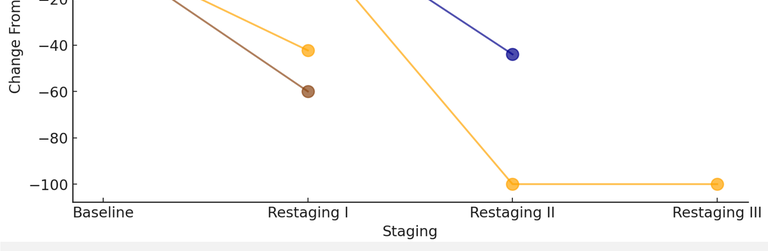


FIGURE 3 INTRACRANIAL DISEASE REGRESSION – SUBJECT 1

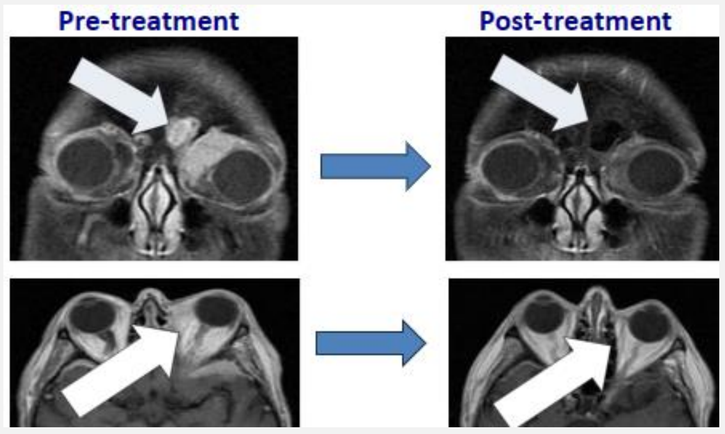


FIGURE 4 INTRACRANIAL DISEASE REGRESSION – SUBJECT 2

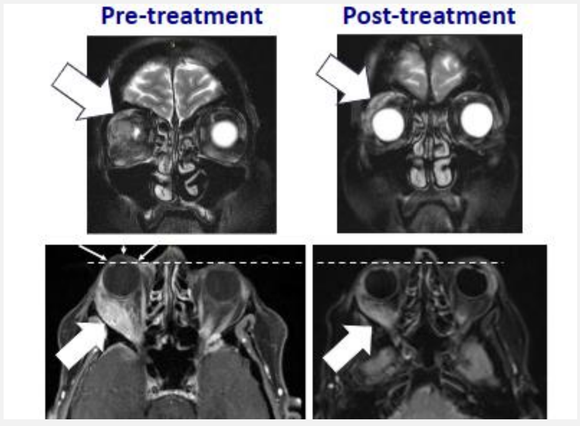
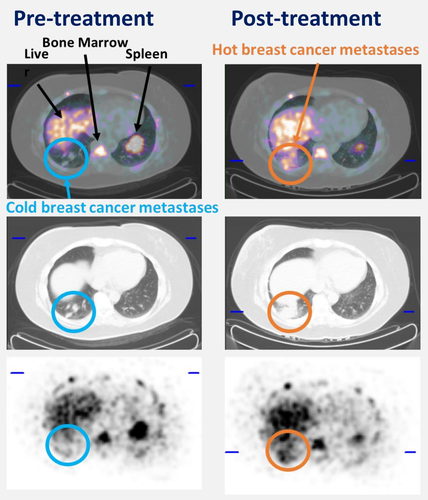


FIGURE 5 CD8-ImmunoPET IMAGING



Tumor Marker	Pre-treatment	Post-treatment
CEA	2.0	1.4
CA 15-3	17.0	9.7

REFERENCES

- Lopez-Lago M, et al. *Cancer Research* 83.7_Supplement (2023): 685-685.
- Calfa C, et al. J Clin Oncol 42, 2024 (suppl 16; abstr 1022)
- Chumsri S, et al. Clin Oncol 42, 2024 (suppl 16; abstr 1087)
- Kamarju S, et al. *Cancer Research* 84.7_Supplement (2024): CT204-CT204.
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ASCO 2024 PUBLICATIONS

Rapid Oral Session: Updated Phase 2 Results

Poster Session: Bria-IMT Post-ADC Progression

Online Publication: Bria-IMT Intracranial Disease Response

PHASE 3 STUDY DESIGN

- Multicenter, randomized, open-label trial
- Comparing the Bria-IMT regimen plus a checkpoint inhibitor (CPI) versus Treatment of Physicians' Choice (TPC) in metastatic breast cancer patients lacking alternative approved therapies

OBJECTIVES

- Primary: Overall survival with an interim analysis planned after 144 events, aiming for a hazard ratio of 0.6
- Secondary: Progression-free survival (PFS), objective response rate (ORR), clinical benefit rate (CBR), CNS event-free survival, and time without symptoms or toxicities (TWiST).

ELIGIBILITY

- Metastatic advanced breast cancer of all subtypes
- CNS metastases allowed
- ECOG 0, 1, or 2
- No limit on prior number of therapies
- 2 week wash out period from previous treatment

RANDOMIZATION and TREATMENT ARMS

- 1:1:1 ratio to 3 arms:
  Bria-IMT + CPI
  Treatment of Physicians' Choice
  Bria-IMT alone
- After 150 patients (50 in each arm), Bria-IMT alone will stop enrolling. The remaining subjects will be randomized 1:1 to the other 2 arms (total of 177 in each of the main comparison arms)

TREATMENT REGIMENS

- Bria-IMT: Cyclophosphamide 300 mg/m^2 administered two days prior to treatment, 20 million irradiated SV-BR-1-GM cells given intradermally in 4 sites, followed by peg-interferon α-2a (0.1 mcg) into each inoculation site
- CPI: retifanlimab infused once every cycle, 375mg, on any 1 of 3 visit days consistently
- Cycles every 3 weeks
- TPC Arm: Treatment of Physicians' Choice following standard of care (SOC)

BRIA-IMT™ REGIMEN – Every 3 Weeks

Day –2 or –3
Cyclophosphamide 300 mg/m^2 IV

Day 0
SV-BR-1-GM 1 million ID

If no immediate hypersensitivity
SV-BR-1-GM 20 million ID (thighs and upper back)

Day 2±1
Interferon alpha (IFNα) at inoculation sites:
Peg-IFNα-2a 0.4 mcg ID

CPI (retifanlimab 375 mg IV) can be any 1 of the 3 days consistently.

REGISTRATION & STATUS

- This study is registered at ClinicalTrials.gov: NCT06072612
- Approximately 100 sites planned in the US, Canada and EU
- Enrollment began in January 2024 and ongoing
- 16 locations open and enrolling