CT143

Whole Cell Antigen Presenting Immune Stimulating Cells (Bria-IMT) for the Treatment of Metastatic breast Cancer

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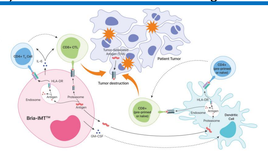
BACKGROUND

SV-BR-1-GM is an off-the-shelf whole tumor cell therapeutic vaccine that expresses class I & class II HLAs, secretes GM-CSF, and functions as antigen-presenting cells with subsequent enhancements improving in-vitro characteristics. By expressing cancer antigens such as HER2/Neu and PRAME, SV-BR-1-GM also serves as the reservoir of cancer 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 SV-BR-1-GM regimens.

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

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



SV-BR-1-GM expresses breast cancer antigens which are taken up by dendritic cells and presented to CD4+ and CD8+ T cells which thereafter may induce a tumor-directed immune response

Figure 1 Mechanism of Action: SV-BR-1-GM acts as an antigen-presenting cell for primed T cells.

METHOD

CO study: an ongoing prospective, phase 1/2 with a randomized phase 2 cohort (NCT03328026; 2018-present) using SV-BR-1-GM with a PD-1 inhibitor (pembrolizumab or retifanlimab) with cycles every 3 weeks (30 patients dosed to date).
SV study: SV-BR-1-GM "monotherapy" (NCT03066947; 2013-8), a completed prospective phase 1-2 study of the SV-BR-1-GM regimen every 2 weeks x 2 then monthly.

Both regimens (SV and CO) included cyclophosphamide 300 mg/m^2 i.v. 48-72 hours prior to SV-BR-1-GM (~20 x 10^6 cells) intradermally followed by interferon-alpha at the SV-BR-1-GM inoculation sites 2 days afterwards.

Candida skin test was performed at cycle 1 to determine if a patient can mount immune reactions (non-anergic). SV-BR-1-GM-specific delayed-type hypersensitivity (DTH) skin test is done by intradermal injection of a small dose of SV-BR-1-GM at every cycle prior to full dose SV-BR-1-GM inoculation.

SV and CO STUDIES

Table 1 Demographics of SV and CO studies

Study	SV (mono)	CO (combo)
N	26	30
Median Age (Rane)	59 (33 – 74)	62 (38 – 82)
HER2/neu [a] (%)	1 positive (4%) 4 low (15%)	0 positive 5 low (17%)
HR+ (%)	14 (54%)	21 (70%)
TNBC (%)	9 (35%)	9 (30%)
Prior Lines of Systemic Tx Median (Range)	5 (1-17)	5 (2-13)

Table 2 Disease Outcomes in SV and CO studies

Study	SV	CO
PFS[b] Median, day (Range)	77 (11-207) n = 23	80 (33-308) n = 24
Modified PFS[c] Median, day (Range)	83 (41-207) N = 16	91 (33-308) N = 20
Disease Control Rate[d] Best Overall (SD+PR+CR)	44% (n=16)	40% (n=20)
Objective Response Rate[e] Best Overall (PR+CR)	0[f]	10% (n=20)

Conclusion:
SV and CO patients are comparable in demographics, treatment history and biomarkers, but CO appears to have better ORR compared to SV.

[a] HER2 low is HER2-IHC 0 and HER2-FISH 1-2.
[b] PFS calculated only in patients who received at least 1 dose of SV-BR-1-GM. PFS defined from informed consent to study discontinuation, confirmed PD or death (whichever first).
[c] Modified PFS in patients who had assessable disease outcomes.
[d] Disease Control Rate is determined from the patient's best response among those who had available disease outcomes.
[e] Objective Response Rate is determined from the patient's best response among those who had available disease outcome.
[f] One patient had regression of 20 pulmonary nodules not measurable per RECIST criteria, but the liver metastasis showed SD.

SV-BR-1-GM regimen induces immune responses in anergic patients

Table 3 CO study patients classified by candida response

	N	Known CBR*	DTH Positive	Inoculation Site Positive
Non-anergic	12 (44%)	1xPR, 5xSD in 12 patients	10	12
		50%	83%	100%
Anergic	15 (56%)	1xPR, 1xSD in 8 patients	9	12
		25%	60%	80%
Total	27	2xPR, 6xSD in 20 patients	19	24
		40%	70%	89%

*CBR only in patients with known disease outcome at datacut.

- Candida antigen skin test positive (non-anergic) defined as either length or width of erythema/induration measures ≥5mm.
- DTH and inoculation site positive means either length or width of erythema/induration measures ≥5mm.

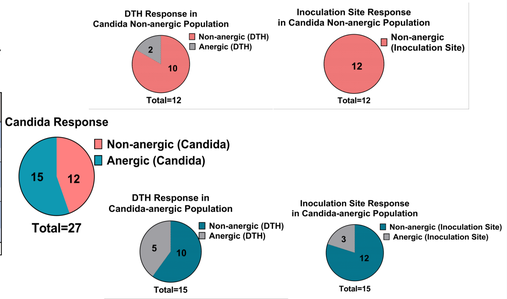


Figure 2 CO study patients classified by Candida response (Anergic vs Non-anergic) and the DTH- and inoculation site-responses of the two populations

Conclusion:
When starting treatment 56% of the patients were anergic. After receiving the SV-BR-1-GM combo-regimen, 70% and 89% of all patients had immune responses to the DTH test and SV-BR-1-GM inoculation, respectively. 80% of the originally anergic patients developed a positive inoculation site reaction.
Non-anergic patients has 50% (2-fold higher) CBR compared to 25% for anergic patients. Nevertheless, anergic patients still had disease benefit including one PR and SD.

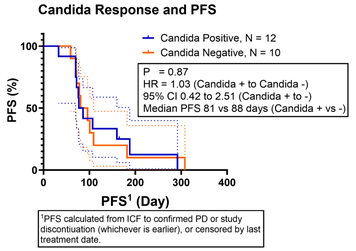


Figure 3 PFS Survival curve of anergic and non-anergic patients

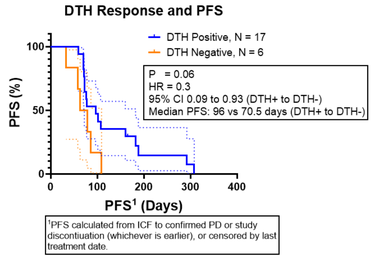


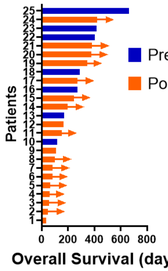
Figure 4 PFS Survival curve of DTH-positive and DTH-negative patients

Conclusion:
Candida response does not correlate with PFS, but positive DTH response correlates with better PFS.

Survival and PFS Difference

Survival of CO patients

PFS Difference = [on study PFS] - [last regimen treatment time]
On study PFS is based on time of disease progression not toxicity



- Five patients enrolled pre-2022 had not been followed-up for survival.
- Arrowheads indicate subjects currently being followed for survival.

Figure 5 Survival of CO patients

Conclusion:
- ***Of 18 patients recruited since the study reopened in 2021, 15 remain alive.***
- ***Of 17 patients enrolled ≥ 9-month to data-cut (before 6/17/22), 8 had OS>9mo (4 ongoing survival), 4 had OS<9mo and 5 were lost to follow-up.***

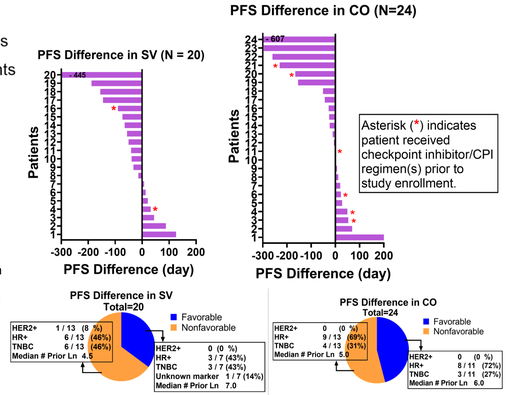


Figure 6 PFS difference in SV and CO patients

Conclusion:
In both studies, patients were heavily pre-treated with a median of 5 prior systemic therapies. When treated with the SV-BR-1-GM regimen, a good proportion of patients still had favorable on-study PFS compared to their prior regimen treatment time. The benefit is seen in 35% and 46% patients in SV and CO, respectively, suggesting an enhanced efficacy of the combination therapy. Prior CPI therapy(ies) does not attenuate clinical benefit.

DISCUSSION AND CONCLUSIONS

The SV-BR-1-GM cellular immunotherapy works by eliciting an immune response to the patient's tumor cells. In both mono- and combo-therapy studies, heavily pre-treated aMBC patients received benefit regardless of anergy at baseline. In combination with a PD-1 inhibitor, the SV-BR-1-GM regimen "turned on" the immune response in 80% of anergic patients. The DTH positive group has a favorable PFS.
The combination therapy showed better PFS compared with prior penultimate standard of care results. Promising CBR was observed with SV-BR-1-GM in combination with CPI (checkpoint inhibitor). Prior CPI use did not attenuate the clinical benefit.
The Randomized Phase 2 clinical trial to evaluate the efficacy of the SV-BR-1-GM regimen in combination with immune check point inhibition is currently ongoing. Future registration trials will incorporate these results.

References:
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2. Lopez-Lago M et al, AACR 2023, poster # 685
3. Adams DL et al, AACR 2023, poster # 2310
4. Kasabwala DM et al, AACR 2023, poster # 304