PD-L1 Upregulation in Circulating Tumor Associated Cells Predicts for Clinical Outcomes in a Phase 1/2 Clinical Trial Using SV-BR-1-GM Vaccine with the Check Point Inhibitor Retifanlimab in Metastatic Breast Cancer Patients, an Interim Analysis

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BriaCell

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BACKGROUND

Circulating Tumor Cells (CTCs) are clinical indicators of poorer clinical outcomes in metastatic Breast Cancer (mBC) and may be monitored post therapy induction to identify patients not responding to treatment. However, CTCs are rare in mBC (i.e. <20% of patients), and many patients without CTCs also often progress. Recently an inflammatory pro-tumorigenic PD-L1 expressing macrophage (Cancer associated macrophage-like cell [CAML]) was identified in the blood along with CTCs which are common in mBC (i.e. >90% of patients) and also indicate tumor response to new therapies. SV-BR-1-GM, which is a mBC cell line derived vaccine with antigen presenting characteristics, developed for treatment of mBC as a monotherapy, or in combination with checkpoint inhibitors (**Fig 1**). Here we report the results of CTC & CAML changes and their PD-L1 expression profiles pre and post inoculation with SV-BR-1-GM. We present Progression Free Survival (PFS) and Overall Survival (OS) at 24 months as part of the exploratory portion of an open label roll over phase 1/2 trial (NCT03328026).

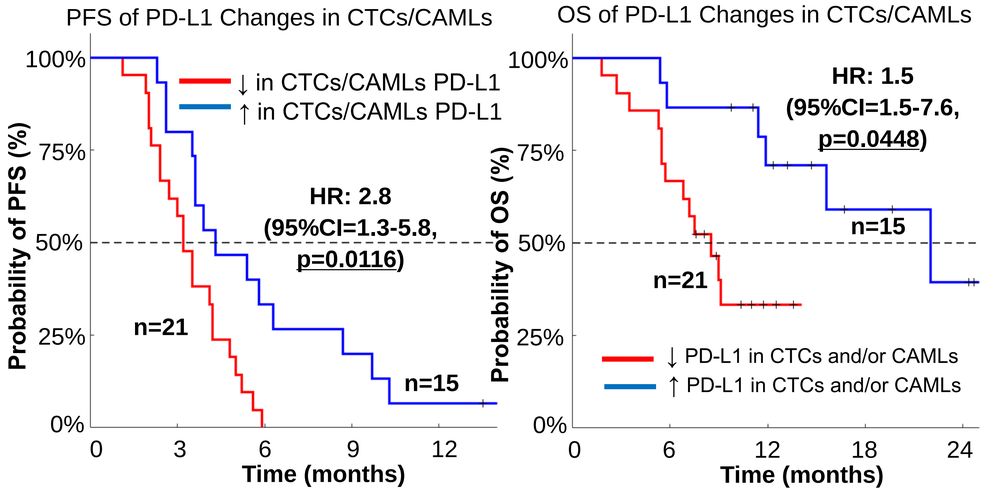
MATERIALS AND METHODS

SV-BR-1-GM treatment includes low pre-dose cyclophosphamide, intradermal inoculation of ~20 million irradiated SV-BR-1-GM cells, post-dose local interferon-α and an anti-PD-1 inhibitor (retifanlimib), with cycles every 3 weeks. Baseline (BL) anonymized blood samples were taken prior to starting SV-BR-1-GMT, after initiation of therapy (T1) at ~23 days, and if possible at the standard tumor assessment (T2) ~75 days to evaluate the predictive value of CTCs/CAMLs and their PD-L1 expressions. Cells were isolated and quantified using the LifeTracDx® liquid biopsy test. The quantities of CTCs & CAMLs and their respective PD-L1 were analyzed based on PFS using RECIST v1.1 and OS hazard ratios (HRs) by censored univariate analysis at 24 months.

RESULTS

- Blood samples were available from 93% (n=41/44) of all patients
- At BL, CTCs were found in 44% (n=18/41) and CAMLs in 90% (n=37/41)
- BL CTCs predicted significantly worse OS, but not PFS (**Table 1**).
- T1 samples were available from 88% (n=36/41) of pts.
- Decreases in CTCs or CAMLs after SV-BR-1-GM therapy was seen in 40% of pts, correlating with better PFS. (**Table 1**)
- PD-L1 in CTCs or CAMLs at BL was not associated with improved clinical responses (**Table 1**).
- An increase in PD-L1 in CTCs or CAMLs after SV-BR-1-GM therapy was seen in 42% (n=15/36) of pts, correlating with better PFS and OS. (**Fig 2**)

Figure 2. PFS and OS Based on PD-L1 Changes in CTCs/CAMLs



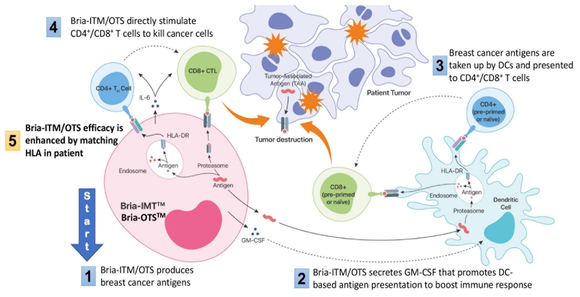


Figure 1. Dual mechanism of action. *SV-BR-1-GM cells secret GM-CSF that supports presentation of breast cancer antigens by Dendritic Cells (DCs). SV-BR-1-GM also directly presents antigens to CD4+ and CD8+ T cells.*

Table 1. Hazard ratio comparisons of CTCs/CAMLs after SV-BR-1-GM Therapy

HR (95%CI) p value	CTCs at BL 0 vs ≥1	CTCs at T1 0 vs ≥1	↑ vs ↓ CTCs/CAMLs BL vsT1	Low vs High CTC/CAML PD-L1 (BL)	↑ vs ↓ CTC/CAML PD-L1 (BL vsT1/T2)
n value	23 vs 18	24 vs 12	21 vs 14	18 vs 23	15 vs 21
PFS	2.1 (1.0-4.3) p=0.0596	1.7 (0.8-3.8) p=0.2374	**2.7 (1.3-5.7) p=0.0157**	1.7 (0.9-3.4) p=0.1621	**2.8 (1.3-5.8) p=0.0116**
OS	**4.1 (1.7-10.0) p=0.0044**	1.3 (0.5-3.4) p=0.8203	2.7 (1.0-7.5) p=0.0887	1.2 (0.5-2.8) p=0.8649	**3.0 (1.5-7.6) p=0.0448**

CONCLUSIONS

- In an interim analysis of heavily treated mBC patient population, we observed that treatment with the SV-BR-1-GM regimen was associated with decreases in CTCs and CAMLs in 40% of patients
- A drop in CTCs/CAMLs significantly correlated with better PFS and trended for better OS.
- SV-BR-1-GM therapy appeared to upregulate PD-L1 in n=15 patients which correlated with better responses to combination treatment with the anti-PD-1 check point inhibitor retifanlimab.

References

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