Decreases in Circulating Tumor Associated Cells Predict PFS and OS in a Pooled Analysis of Phase I Clinical Trials Using SV-BR-1-GM Therapy with or without Immune Check-Point Inhibitors in Metastatic Breast Cancer Patients

Daniel L. Adams1, Mingjin Chang2, Miguel Lopez-Lago2, Cha-Mei Tang1, William V. Williams2, Giuseppe Del Priore2

1Creativ MicroTech, Inc. Monmouth Junction, NJ 2Briacell Therapeutics Corporation, Philadelphia, PA

BACKGROUND

In metastatic Breast Cancer (mBC), Circulating Tumor Cells (CTCs) are critical indicators of worsening prognosis and patients (pts) not responding to current therapy. However, CTCs are rare, found in <20% of mBC pts, and many without CTCs may also progress. Recently an antigen presenting pro-tumorigenic macrophage (Cancer Associated Macrophage-like cell [CAML]) was identified in the blood, found in >90% of mBC pts, and appears to indicate tumor response to new therapies.

The SV-BR-1-GM is a mBC cell line (Figure 1) with antigen presenting characteristics that was developed for treating mBC1-2. SV-BR-1-GM is given in combination with low dose cyclophosphamide to reduce immune suppression, and local interferon alpha to boost the response. This regimen is given as a monotherapy (monoTx), or in combination with PD-1 checkpoint inhibitors (comboTx).

We report post-hoc results of a pooled analysis of n=18 monoTx mBC pts and interim results of n=21 comboTx (with an additional 4 pts that rolled from monoTx to comboTx) to analyze the predictive value of CTCs and/or CAML PD-L1 expression, isolated from peripheral blood pre & post treatment to predict Progression-Free Survival (PFS) and Overall Survival (OS) at 24 months.

MATERIALS AND METHODS

The SV-BR-1-GM regimen includes low pre-dose cyclophosphamide, intradermal inoculation of ~20 million irradiated SV-BR-1-GM cells and post-dose local interferonα with cycles every 2 weeks x 3, then monthly. ComboTx adds an anti-PD-1 antibody with cycles every 3 weeks. Blinded blood samples were taken at baseline (BL) prior to starting SV-BR-1-GM therapy (n=39), and a 2nd sample (TI) taken after therapy initiation (~32 days) obtained as part of the exploratory portion of 2 prospective phase III clinical studies, NCT03066947 & NCT03328026, to evaluate the predictive value of CTCs/CAMLs and CAML PD-L1 measured either high or low as previously described by LifetracDX™ liquid biopsy3. The quantities of CTCs & CAMLs were analyzed based on PFS using RECIST v1.1 and OS hazard ratios (HRs) by censored univariate analysis at 24 months.

RESULTS

- CTCs were found in 38% (n=15/39) and CAMLs in 95% (n=37/39) of pts (Table 1)
- N=39 mBC pts had BL samples from monoxo or comboTx.
- BL CTCs predicted worse OS (HR=5.2, p=0.0396), but not PFS.
- TI CTCs were available from 54% (n=21/39) pts.
- Drop in CTCs/CAMLs after SV-BR-1-GM therapy was seen in 67% of pts, correlating with better PFS HR=11.9, p=0.0012. (Figure 2)
- Drop in CTCs/CAMLs after SV-BR-1-GM Tx had a ~450% increase in mPFS (18.9 mo vs 3.3 mo) and ~170% increase in OS (7.1 mo vs 12.0 mo).
- Drop in CTCs/CAMLs correlated better to PFS (HR 20.6, p=0.0096) in the monoTx group and in the comboTx group (HR 12.1, p=0.0031).
- CAML PD-L1 at BL was correlated with significantly better OS HR=13.8, p=0.0037, consistent with long term benefit of SV-BR-1-GM therapy.

CONCLUSIONS

- CTCs and/or CAMLs were observed in 100% of the pt population.
- Treatment with SV-BR-1-GM regimen was associated with decreases in the presence of CTCs or CAMLs in 67% of pts, correlating with ~460% better mPFS and ~170% better OS in 2 years.
- SV-BR-1-GM therapy alone, or in combination with anti-PD-1, appears to improve long term clinical outcomes in heavily pre-treated mBC patients.

References


Figure 2. PFS Based on 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.