Allogeneic, Antigen-Presenting, GM-CSF-secreting, SV-BR-1-GM Whole Cell Therapeutic Vaccine in Advanced Metastatic Breast Cancer

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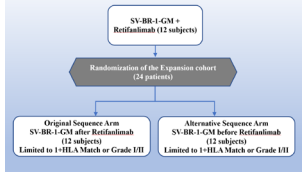
BACKGROUND

SV-BR-1-GM is an irradiated allogeneic cell line derived from a hormone receptor-negative (HR-) HER2 positive (HER2+) breast cancer, expressing HLA class I and II molecules, engineered to secrete GM-CSF and function as an antigen-presenting cell. SV-BR-1-GM cancer cell antigens are taken up by dendritic cells and presented to $CD4^+$ and $CD8^+$ T cells, which induce a tumor-directed immune response. SV-BR-1-GM cells can also directly activate T cells to stimulate cancer fighting T cells, as an additional boost to the immune response (SABC 2022 posters #P3-06-08, #P1-05-28 and AACR 2022). Here we report post-hoc exploratory data for metastatic breast cancer patients (MBC) treated with the SV-BR-1-GM regimen (SV) alone (NCT03066947) and in combination (CO) with immune checkpoint inhibitors (ICIs) (NCT03328026). CO recently completed its phase 1 and is now enrolling into an HLA-matched randomized phase 2 (Figure 1).

METHODS



Open label Phase I/II. Both regimens (SV and CO) included cyclophosphamide 300 mg/m² i.v. 48-72 hours prior to SV-BR-1-GM (~20 x 10^6 irradiated cells) intradermally followed by interferon-alpha-2b at the SV-BR-1-GM inoculation sites (1-4 hours and again 2 days afterwards), q3 weeks. HLA typing using PacBio Sequencing was used to determine patient matching status to SV-BR-1-GM at any of the HLA-A, -B, -C, -DRB1, and -DRB3/4/5 loci.

***Figure 1 Study Design of the current SV-BR-1-GM regimen in combination with PD1 inhibitor (Retifanlimab)**. To date, 12 patients have been treated in the phase 1; Subjects are now being randomized 1:1 into 2 different treatment sequences (n=24)*

RESULTS

Demographics were typical of a heavily pretreated MBC patient population (see table 1).

Table 1 Demographics of the intent to treat population in SV and CO studies with SV-BR-1-GM

Study	N	Age Median (Range)	BMI Median (Range)	Prior Systemic Tx Median (Range)	Time Since Initial Dx Median (Range)
SV	26	59 (33 – 74)	31.5 (17.2 – 41.6)	2 (0-9)	3.1 yrs (0.4-8.1)
CO	22	62 (38 – 82)	27.7 (17.5 – 41.4)	6.5 (2 - 13)	3.0 yrs (0.2 – 15.0)

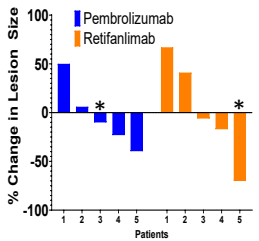
***Table 2 Clinical Benefit with SV-BR-1-GM**. Patients with refractory advanced MBC were treated either with the SV-BR-1-GM regimen (SV) or in combination (CO) with a PD-1 inhibitor (either pembrolizumab or retifanlimab) every 2-4 weeks. *Disease control includes 1 partial response (PR) and 7 stable disease (SD) in the monotherapy studies and 2 PR and 5 SD in combination therapy. The combination therapy study is ongoing as a randomized phase 2 (see figure 1).*

Patients	HLA Match	Disease Control*	Disease Control in Immune Responders**
Monotherapy Studies (SV)			
N=6	≥ 2	50%	75%
N=20	≥ 1	25%	33%
N=7	0	29%	29%
PD-1 Inhibitor Combination Study (CO)			
N=7	≥2	43%	40%
N=9	≥1	56%	57%
N=5	0	40%	40%

***Measured by delayed-type hypersensitivity.*

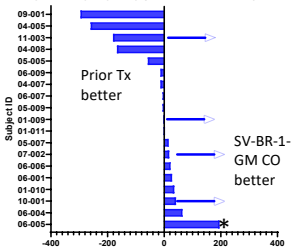
***Conclusion:** Clinical benefit with the SV-BR-1-GM regimen is achievable especially with HLA matching between patients and the cell line*

***Figure 2 Tumor Size with the SV-BR-1-GM Regimen and PD-1 Inhibitors** in combination (CO) with either pembrolizumab (blue) or retifanlimab (orange). The sum of diameters of measurable lesions are shown. Note that patient 3* with pembrolizumab transitioned to the retifanlimab combination patient 5*.*



***Conclusion:** Patients with refractory MBC can respond to the SV-BR-1-GM regimen with PD-1 inhibition with marked tumor reductions.*

***Figure 3 Progression Free Survival (PFS) Compared with Prior Therapy**. Time on study for patients treated in the combination study CO (SV-BR-1-GM + PD-1 inhibitor) was compared with the time on study for their last regimen prior to the CO study. The results shown are days on study minus days on their prior (last) regimen. (ongoing patient = arrows).*



***Conclusion:** Patients treated with the SV-BR-1-GM regimen in combination with PD-1 inhibition have PFS in many cases better than their last therapy.*

RESULTS IMAGING

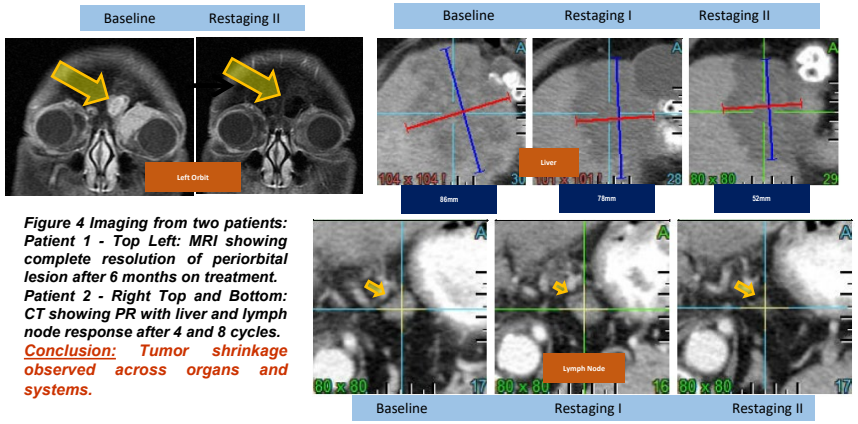


Figure 4 Imaging from two patients: Patient 1 - Top Left: MRI showing complete resolution of periorbital lesion after 6 months on treatment. Patient 2 - Right Top and Bottom: CT showing PR with liver and lymph node response after 4 and 8 cycles.

***Conclusion:** Tumor shrinkage observed across organs and systems.*

SAFETY PROFILE

Table 3 Adverse Events in ≥2 patients received SV-BR-1-GM regimen with Pembrolizumab (N=11)

Adverse Event Term	Number of Subjects Affected	Highest Toxicity Grade
Injection site reaction (All)	6 (55%)	1
Injection Site Reaction, Erythema	4 (36%)	
Injection Site Reaction, Induration	6 (55%)	
Injection site reaction (unspecified)	2 (18%)	
Injection Site Reaction, Pruritus	1 (9%)	
Fatigue	5 (45%)	2
Constipation	3 (27%)	2
Headache	3 (27%)	1
Diarrhea	2 (18%)	2
Dizziness	2 (18%)	2
Edema Limbs	2 (18%)	1
Hypothyroidism	2 (18%)	2

Table 4 Adverse Events in ≥2 patients received SV-BR-1-GM regimen with Retifanlimab (N=12)

Adverse Event Term	Number of Subjects Affected	Highest Toxicity Grade
Constipation	4 (33%)	2
Fatigue	4 (33%)	2
Urinary Tract Infection	3 (25%)	2
Injection Site Reaction: Erythema	2 (17%)	1
Injection Site Reaction: Induration	2 (17%)	1
Diarrhea	2 (17%)	2

***Conclusion:** SV-BR-1-GM regimen in combination with PD1 inhibitors appear to be safe and well-tolerated.*

QUALITY OF LIFE

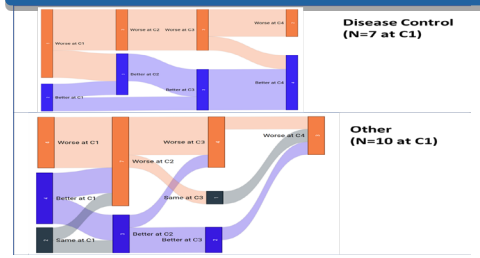


***Figure 5 Change of Quality of Life in Patients Receiving SV-BR-1-GM CO Regimen, stratified by Disease Outcome (Top, Disease Control; Bottom, Other)** SF-36 score sum was used to calculate quality of life changes [=0, Same (gray); >0, Better (blue), <0, Worse (orange)] at Cycle 1 through Cycle 4.*

***Conclusion:** Patients who had disease control have an increasing proportion in "Better" with treatment.*

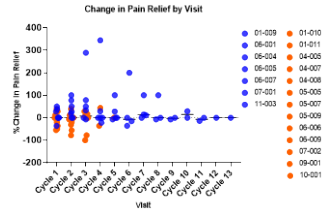


***Figure 6 Change in Pain Relief in Patients Receiving SV-BR-1-GM CO Regimen, stratified by Disease Outcome (Blue, Disease Control; Orange, Other)** Score sum from two SF-36 questions on pain was used to calculate pain relief changes.*

***Conclusion:** Many patients receiving the SV-BR-1-GM CO regimen have an improvement in the level of pain from baseline, especially patients who have clinical benefit from the regimen*

RESULTS

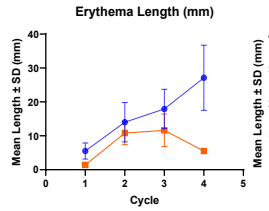


***Figure 7 Delayed Type Hypersensitivity (DTH) Reactions and Disease Outcome**. Erythema and Induration Length (longest diameter) in patients treated with CO regimen stratified by Best Outcome (local or central read). 4 subjects rolled over from SV to CO; their SV portion results of DTH are used.*

***Conclusion:** DTH responses are more pronounced in patients who received clinical benefit from the SV-BR-1-GM regimen in combination with PD-1 inhibitors.*

***Figure 8 Cancer Antigen and Disease Outcome in SV-BR-1-GM combination study** assessed during study treatment. Patient IDs are shown, and color coded by disease control (blue) and other (orange). Y axis log scale*

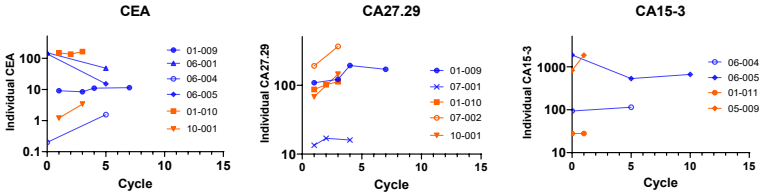


***Table 5 Summary of Clinical Experience with SV-BR-1-GM by MBC biomarkers**. Patients with available disease outcome were classified by the original biomarkers and HLA matching status with SV-BR-1-GM. HR+ = ER or PR positive; HER2+ = HER2/neu positive; TNBC = triple negative MBC; unknown = biomarker unknown.*

SV (N=20)	HR+				HR-/HER2+		TNBC			unknown
	All	HLA-matched	Grade I/II	Grade III	All	HLA-matched	All	Grade I/II	Grade III	All
# of Subjects	11	8	4	4	1	0	5	1	4	3
Best ORR (%, #)	9% (1/11)	13% (1/8)	0%	0%	0	0	0	0	0	0
Best CBR (%, #)	45% (5/11)	38% (3/8)	75% (3/4)	25% (1/4)	0	0	40% (2/5)	100% (1/1)	25% (1/4)	33% (1/3)
PFS (m)	2.8±1.9	2.6±2.1	4.5±1.5	2.5±0.5	4.3	NA	2.1±1.4	1.4	2.5±1.4	5.4±0.9

CO (N=18)	HR+				HR-/HER2+		TNBC			unknown
	All	HLA-matched	Grade I/II	Grade III	All	HLA-matched	All	Grade I/II	Grade III	All
# of Subjects	14	9	8	5	0	0	4	0	3	0
Best ORR (%, #)	14% (2/14)	11% (1/8)	25% (2/8)	0%	0	0	0	0	0	0
Best CBR (%, #)	43% (6/14)	44% (4/9)	63% (5/8)	20% (1/5)	0	0	25% (1/4)	0%	33% (1/3)	0%
PFS (m)	3.2±2.7	2.5±3.2	5.8±2.9	2.4±0.6	NA	NA	2.9±0.6	NA	2.4±0.6	NA

DISCUSSION AND CONCLUSIONS

SV-BR-1-GM demonstrated promising activity in patients with MBC. Treatment was well tolerated with no concerning AEs. The PFS ratio compares favorably with prior penultimate standards of care results, more notably in patients with matched HLA. Clinical benefits were observed across multiple subtypes of MBC, particularly in patients with HR+ disease receiving combination therapy. The Randomized Phase II clinical trial to evaluate the efficacy of SV-BR-1-GM in combination with immune check point inhibitor is currently ongoing. Future registration trials will incorporate these results.

References

1. Lopez-Lago et al AACR 2022 https://aacrjournals.org/cancerres/article/82/12_Supplement/3557/699627/Abstract-3557-Toward-a-personalized-off-the-shelf
2. Lopez-Lago et al SITC 2022 https://jitc.bmj.com/content/10/Suppl_2/A272
3. Lopez-Lago et al SABC 2022 #P3-06-08 Wednesday Dec 7
4. Adams et al SABC 2022 #P1-05-28 Tuesday Dec 6