Abstract #97: Breast cancer grade and clinical benefit in patients with advanced breast cancer treated with an engineered whole tumor cell-targeted immunotherapy alone or in combination with checkpoint inhibition.

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Background/Methods:

- Breast cancer is the most common cause of cancer death in women.
- Immunotherapy for breast cancer has had only limited success.
- Here we describe a cellular immunotherapy for breast cancer based on a breast cancer cell line with features of an antigen presenting cell[1].
- **SV-BR-1 is a breast cancer cell line derived from a grade II (moderately differentiated) tumor**. SV-BR-1 was transfected with the CSF2 gene (encoding GM-CSF) to form SV-BR-1-GM.
- SV-BR-1-GM expresses HLA class I & II antigens and has functional **antigen-presenting cell activity**, directly stimulating CD4+ T cells in an HLA-DR restricted fashion.
- **The SV-BR-1-GM regimen** consists of low-dose cyclophosphamide (300 mg/m^2) to reduce immune suppression, intradermal inoculation with irradiated SV-BR-1-GM (20x10^6 cells divided into 4 sites) and interferon-α2b (10,000 IU into each inoculation site ~2 & 4 days later) as a booster.
- Here, we evaluate the impact of tumor grade on clinical benefit following treatment with the SV-BR-1-GM regimen.

Methods:

- Patients with advanced breast cancer were treated with either the SV-BR-1-GM regimen alone or with the SV-BR-1-GM regimen with anti-PD-1 (αPD-1).
  - For the SV-BR-1-GM regimen alone, cycles were every 2 weeks x 3 and then monthly, while combination with αPD-1 was administered every 3 weeks.
  - The combination began with pembrolizumab then transitioned to INCMGA00012, a similar PD-1 inhibitor.
- Tumor restaging was every 6-12 weeks.
- 33 patients were treated, 27 with the SV-BR-1-GM regimen alone, of whom 4 rolled over into the combination with pembrolizumab, and 7 more with the αPD-1 combination.

[1]Lacher et al. SV-BR-1-GM, a Clinically Effective GM-CSF- Secreting Breast Cancer Cell Line, Expresses an Immune Signature and Directly Activates CD4+ T Lymphocytes. Frontiers in Immunology 2018; 9:Article 776

The SV-BR-1-GM regimen with or without αPD-1 appears safe and able to induce ***clinical responses in heavily pre-treated patients with well/intermediate grade advanced breast cancer***. Further study of the combination of the SV-BR-1-GM regimen with checkpoint inhibitors appears warranted, especially in patients with grade I or grade II tumors.

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Results:

- The treatment was generally safe with inoculation site pruritis, erythema and induration the most common adverse events.
- 23 patients had grade III tumors, 9 had grade II and one had a grade I tumor.
- None of the patients with grade III tumors exhibited clinical benefit.
- 7 patients with grade I/II tumors received the SV-BR-1-GM regimen alone, 2 received the SV-BR-1-GM/αPD-1 combo and 1 received both regimens.
- All 10 patients had metastatic breast cancer.
- Only 1 patient in the grade I/II group had triple negative breast cancer with most ER/PR+
- 7 patients experienced disease control (Table) including all 3 patients treated in combination with pembrolizumab. This included 6 patients with stable disease and one with a partial response.

Patients with Grade I or Grade II Tumors Treated with SV-BR-1-GM

Patient Characteristics	Monotherapy Study (n=8)	αPD-1 Combo Study (n=3)	All Patients (n=10)
Grade I	1	0	1
Grade II	7	3	9
Immune Responders (IR+)	7	3	9
Age	64 ± 2	67 ± 9	64 ± 7
Median (Range) Prior Systemic Regimens	5 (0-13)	10 (9-12)	8 (0-13)
% Triple Negative	14%	0%	11%
% ER/PR +	86%	100%	89%
% Her2/neu +	11%	0%	33%
Disease Control	**63%**	**100%**	**70%**
Disease Control IR+	**71%**	**100%**	**78%**
Days on Study (Median, Range)	**114 (32 – 181)**	**255 (133 – 259)**	**118 (32-259)**