Th1-biased cytokine signatures as biomarkers of clinical benefit following SV-BR-1-GM cancer vaccination in breast cancer

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Abstract - 1614

BACKGROUND

Although cancer immunotherapy has shown great promises, many cancers remain resistant to treatment due to tumor heterogeneity, immune tolerance, and insufficient immune activation . Bria-IMT is a therapeutic cancer vaccine composed of SV-BR-1-GM , a breast cancer cell line engineered to release GM-CSF. This therapy has completed a phase I/II clinical trial (NCT03066947) and is under evaluation in a phase III study (NCT06072612) for advance metastatic breast cancer. Mechanistically, SV-BR-1-GM cells function as antigen-presenting cells, directly activating CD4+ T cells in an antigen-specific, HLA-restricted manner (as shown in vitro). They also deliver a broad repertoire of cancer antigens to stimulate endogenous immune responses. Building on evidence that changes in circulating cytokines and chemokines can reflect treatment-induced immune activation, this study aims to characterize serum cytokine and chemokine profiles as potential biomarkers of immunological response and clinical outcome following cancer immunotherapy.

OBJECTIVES

- To characterize serum cytokine and chemokine profiles in patients treated with Bria-IMT
- To identify immune-related changes in circulating cytokines and chemokines following therapy, particularly in patients with stable disease (SD), partial response (PR), or progressive disease (PD).
- To explore associations between cytokine dynamics and clinical outcomes, including progression free survival (PFS), and overall survival (OS).

METHODS

This retrospective analysis evaluated 35 different cytokines/chemokines in serum samples collected from 30 patients enrolled in the Phase I/II trial (NCT03066947) of Bria-IMT alone or in combination with an anti-PD-1 checkpoint inhibitor (CPI). Serum was isolated from blood pre- and post-therapy. We used multiplex ELISA using meso-scale-discovery (MSD) technology to measure 35 different cytokines/chemokines (*Cytokines:* GM-CSF, IFN-γ, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10,IL-12p70, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-21, IL-22, IL-23, IL-27, IL-31, TNF-α, TNF-β, VEGF; *Chemokines:* Eotaxin, Eotaxin-3, IP-10, IL-8, MCP-1, MCP-4, MDC, MIP-1α, MIP-1β, MIP-3α, TARC), known to be associated with immune regulation. Data was analyzed using MSD discovery workbench, and plotted using Origin 2025.

DEMOGRAPHICS

Patient/samples studied ↓ (RECIST1.1→)	SD	PR	PD	NE	Total
Patient studied	13	5	10	2	30
Samples before therapy (Baseline)	13	5	10	2	30
Post-treatment samples	17	18	11	4	50
Post cycle 2 samples	4	1	2	1	8
Post cycle 3, 4 and 5 samples	12	6	8	2	28
Post cycle 6-10	1	5	1	1	8
Monotherapy	9	3	4	0	16
Combination	21	20	17	6	64
Multiple time-points post therapy	4	4	1	2	11

RESULTS

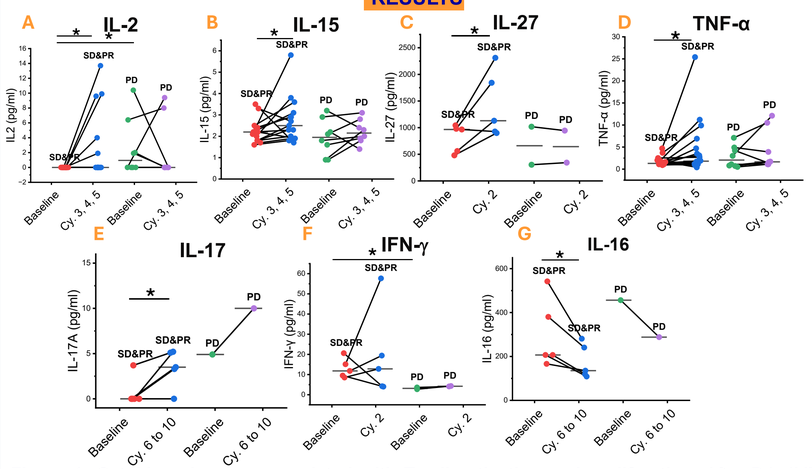

Figure 1: Cytokine changes associated with T-cell activation and proliferation. After Bria-IMT treatment, pro-inflammatory cytokines associated with Th1 response increased in stable disease (SD) and partial response (PR) groups (**A–D**), but not in progressive disease (PD). Similarly SD&PR group demonstrated an increase in IL-17A (Th17/Tc17 cytokine) post Bria-IMT (**E**). Baseline IFN-γ (**F**) was higher in SD & PR than in baseline PD. IL-16 (**G**) decreased after Bria-IMT treatment. * $p < 0.05$

RESULTS

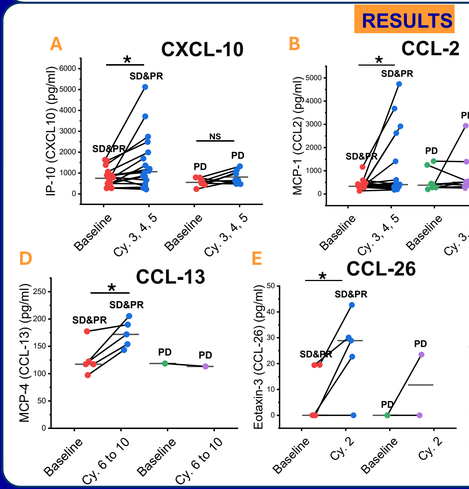

Figure 2: Increase in chemokines for immune cell recruitment. Increase in post-Bria-IMT treatment in SD&PR associated with Th1/Antitumor chemokine (**A**), monocyte/macrophage recruitment (**B** to **D**), and eosinophil-associated chemokines (**E**). Significant increase was not observed in PD groups post-Bria-IMT * $p < 0.05$

RESULTS

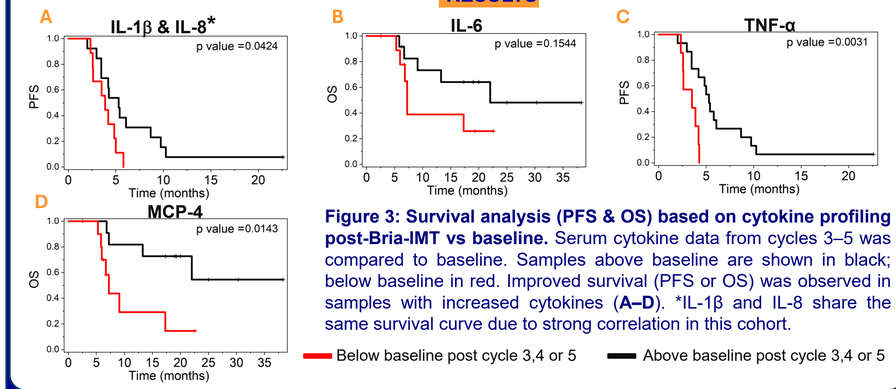

Figure 3: Survival analysis (PFS & OS) based on cytokine profiling post-Bria-IMT vs baseline. Serum cytokine data from cycles 3–5 was compared to baseline. Samples above baseline are shown in black; below baseline in red. Improved survival (PFS or OS) was observed in samples with increased cytokines (**A–D**). *IL-1β and IL-8 share the same survival curve due to strong correlation in this cohort.

RESULTS

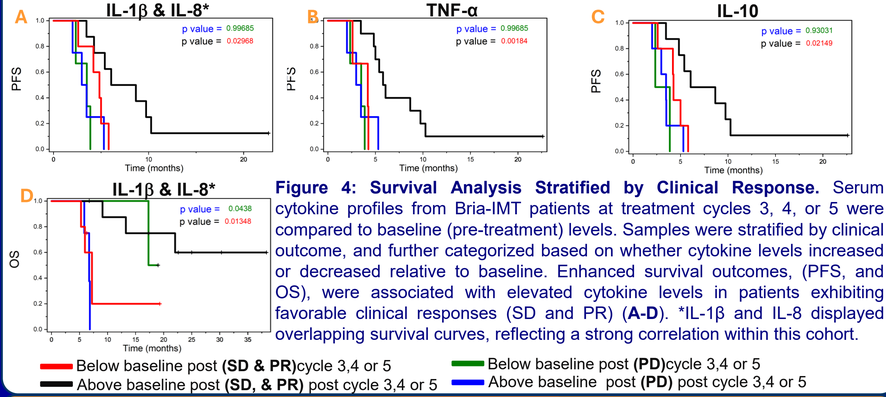

Figure 4: Survival Analysis Stratified by Clinical Response. Serum cytokine profiles from Bria-IMT patients at treatment cycles 3, 4, or 5 were compared to baseline (pre-treatment) levels. Samples were stratified by clinical outcome, and further categorized based on whether cytokine levels increased or decreased relative to baseline. Enhanced survival outcomes, (PFS, and OS), were associated with elevated cytokine levels in patients exhibiting favorable clinical responses (SD and PR) (**A-D**). *IL-1β and IL-8 displayed overlapping survival curves, reflecting a strong correlation within this cohort.

CONCLUSIONS

- *Bria-IMT–based immunotherapy induced measurable, predominantly Th1 biased cytokine and chemokine changes consistent with immune activation.*
- *Patients with SD or PR showed increased levels of IL-2, IL-15, IL-27, TNF-α, CXCL10, CCL2, CCL13, CCL26, and IL-17A post-treatment, suggesting enhanced T-cell activation and pro-inflammatory signaling.*
- .In contrast, there was no induction of Th2- or regulatory-associated cytokines, suggesting that the vaccine does not promote an immunosuppressive or tolerogenic environment.
- *Elevated post-treatment levels of IL-1β, IL-6, IL-8, TNF-α, and MCP-4 were associated with improved OS.*
- *These findings support cytokine and chemokine signatures as potential predictive biomarkers of immune activation and clinical benefit following SV-BR-1-GM vaccination.*