SUPLEXA, A MULTIMODAL AUTOLOGOUS CELLULAR THERAPY, SHOWS IMMUNOMODULATORY BEHAVIOR IN CANCER PATIENTS CONSISTENT WITH IMPROVED ANTI-TUMOR IMMUNE FUNCTION

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Background SUPLEXA cells are populations of NK cells, CD8/CD4 T cells, γδ T cells, and NKT cells generated from cancer patients’ PBMCs using novel immune training immunomodulatory cells. Results of a first-in-human SUPLEXA clinical trial show safe and beneficial responses in patients. Here, we report on blood immune profiling providing first insights into the immunomodulatory behavior of SUPLEXA.

Methods This clinical study is ongoing in Australia in patients with progressive solid tumor and metastatic disease. Blood was prepared at baseline and at weekly intervals after SUPLEXA treatments. SUPLEXA cells and peripheral blood mononuclear cells (PBMCs) were stained with three 48-marker mass cytometry (CyTOF) panels designed to deeply profile SUPLEXA cell phenotypes and circulating immune cell types. Plasma was analyzed using 41-cytokine Luminex or Olink Discovery plasma proteomic assays. Computational clustering and dimensional reduction were used for CyTOF data analysis. Olink data was analyzed by R packages for statistics and enriched functional networks/pathways.

Results SUPLEXA cells from all patients showed mixtures of NK cells, CD8/CD4 T cells, γδ T cells, and NKT cells with granzymes A/B, perforin, granulysin, and SH2D1A expression consistent with cytolytic activity. They uniquely express HLA-DR and capacity to act as antigen presenting cells. No Tregs, myeloid cells, or B cells were detected. Longitudinal profiling of PBMCs from patients and controls indicated individualized immune cell signatures that were modulated by SUPLEXA treatments. Patients with high percentages of PMN-type myeloid suppressor cells (PMN-MDSCs), CD15+/CD16+/CD170+Arginase1−, at baseline showed progressive reduction in PMN-MDSCs after treatments (figure 1). Concomitant increases in classical monocytes (CD14+/CD64+/CD16−) occurred reaching percentages close to controls. Patients with high exhausted CD8 or CD4 T cells (CD57+/KLRG1+/TIGIT+) showed reductions. Some patients demonstrated increases in NKG2D+ CD8+ cytotoxic T cells or B cells. Plasma proteomics identified patients with high inflammatory cytokines, which were reduced by treatments. Patients with suppressed cytokine levels showed specific increases in IL-6, IL-8, IFN-γ, FLT3L, and G-CSF. Olink technology identified factors in SUPLEXA treated patients (baseline to week 2), 36 factors by adjusted p<0.01. Gene set enrichment analysis (GSEA) identified IL-6, IL-8, and TNF family cytokine production, extracellular matrix proteins, and positive regulation of immune defense response and signaling as enriched functional pathways.

Conclusions SUPLEXA therapeutic cells from patients’ PBMCs develop potent tumor cytolytic phenotypes. Longitudinal changes in circulating immune cell types and cytokine levels in SUPLEXA treated cancer patients indicate improved anti-tumor immune function and homeostasis.

Ethics Approval Approval was obtained from BellBerry 2021–10-1150. All participants signed PICF before starting the trial.