Clinical Update from a Phase 1, First-in-Human, Open-label Single Agent Study of SUPLEXA Therapeutic Cells in Patients with Metastatic Solid Tumors and Hematologic Malignancies

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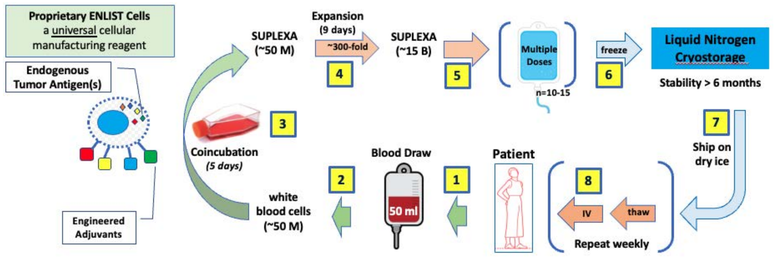
Background

SUPLEXA Therapeutic cells are a heterogeneous mixture of PBMC-derived activated white blood cells, comprised predominantly of natural killer (NK) cells, natural killer T (NKT) cells, γδ T cells, and αβ T cells of both the cytotoxic CD8-positive and CD4-positive T lymphocytes (CTL) variety. SUPLEXA cells are broadly cytolytic against of variety of tumor cell lines *in vitro* at exceedingly low effector to target cell ratios, while showing no adverse impact on normal resting peripheral blood mononuclear cells (PBMC) derived from either allogeneic or autologous sources. Additionally, SUPLEXA demonstrates no fratricide, indicating that normal activated immune cells are not targeted either.

Nonclinical studies in human tumor organoids, as well as in mouse patient-derived xenografts (PDX) and xenograft models support the anti-tumor activity of SUPLEXA.

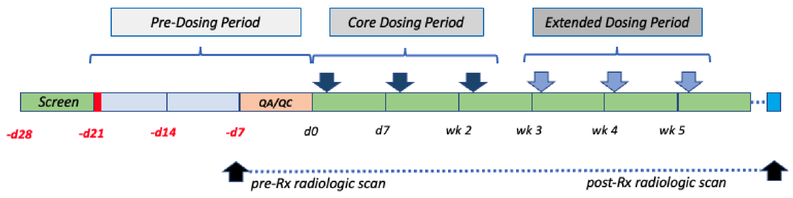
This first-in-human (FIH) Phase 1 open-label study is a non comparative, open label, single-agent, basket-design study designed to assess the safety, tolerability, and preliminary clinical efficacy of repeated intravenous (IV) infusions of SUPLEXA monotherapy in subjects with measurable metastatic solid tumours and haematologic malignancies. No chemo preconditioning or cytokine supportive are used in this study.

SUPLEXA manufacturing



Study Design

This poster reports on the first 11 patient of the **Solid tumor cohort**: This cohort includes subjects with histologically or cytologically confirmed measurable solid tumors. For example, various squamous cell carcinomas, such as skin, cervical, vaginal, esophageal, lung, as well as melanoma, prostate, and breast cancer, radiographically confirmed as Stage 2 to 4 cancer. All eligible subjects received a minimum of 3 weekly dose of SUPLEXA comprised of a median 2.5 billion cells per dose. At the discretion of the Investigator, and in agreement with the subject, treating physician and the Sponsor's Medical Monitor (or designee), dose extension for up to an additional 3 weekly SUPLEXA infusions was permitted.



Patient Specific Characteristics and Early Outcomes

Patient Number	Age/ Gender	Tumor Type	Stage at Screening	Metastasis Locations	Previous Lines of Treatment	SUPLEXA doses (start date)	RECIST (comment)
0101	M / 56	Rectal Squamous Cell Carcinoma	IIIA	Lung, Rectum, Lymph Node, Bone	• Surgery (3) • Radiation (2) • Anti-tumor (6)	5 (June 1)	SD (July 25) SD (Sept 19)
0102	F / 60	Ovarian	IV	Liver, Lymph Node	• Surgery (2) • Anti-tumor (9)	3 (June 21)	SD (Aug 1) PD (Sept 13)
0104	F / 34	Ovarian	IV	Lung, Ovary, Rectum, Lymph Node	• Surgery (3) • Anti-tumor (5)	3 (July 6)	PD (Aug 9) See SAE table.
0105	F / 67	Endometrioid carcinoma	IV	Lung	• Radiation (3) • Anti-tumor (9)	0	PD (Aug 3) (SUPLEXA manufacturing failure)
0106	F / 48	Cervical	IIC	Lung	• Surgery (1) • Radiation (1) • Anti-tumor (1)	6 (Sept 7)	SD (Oct 17)
0107	F/ 64	Pancreatic	IV	Lung, Spleen, Lymph Node, Ascites, Peritoneum	• Surgery (1) • Anti-tumor (5)	6 (Sept 7)	SD (Oct 17)
0201	F / 45	Ureteric Transitional cell carcinoma	IV	Pelvis	• Surgery (1) • Radiation (3) • Anti-tumor (5)	3 (Aug 3)	PD (Sept 12)
0202	F / 75	Uterus	IV	Lung, Liver, Lymph Node	• Surgery (3) • Radiation (4) • Anti-tumor (7)	3 (Aug 3)	PD (Sept 7) See SAE table.
0203	F / 70	Ovarian	IV	Omentum, Peritonium	• Surgery (5) • Anti-tumor (9)	6 (Aug 10)	SD (Sept 12) PD (Oct 10) (PD based on ascites worsening) See SAE table.
0204	F / 58	Ovarian	IV	Omentum	• Surgery (3) • Radiation (1) • Anti-tumor (7)	6 (Aug 31)	PD (Oct 4)
0205	F / 47	Bladder	IV	Lung, Peritoneal	• Anti-tumor (2)	5 (Aug 31)	SD (Sept 26)

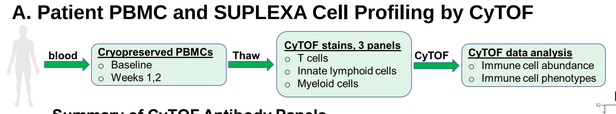
	SAE Verbatim	SAE duration	SAE reason	Relationship
0104	Bowel Obstruction	9 days	Hospitalisation	Not related (NR)
0202	Astrovirus infection Lower back pain Peri-rectal bleeding	9 days 7 days 7 days	Hospitalisation Hospitalisation Hospitalisation	NR NR NR
0203	Ascites worsening	6 days	Hospitalisation	NR

Conclusions

- Enrolled heavily pre-treated end-stage oncology population with a variety of tumor types.
- Excellent safety profile with no drug related adverse events observed to date. All SAEs were classified as not related to SUPLEXA.
- Encouraging signs of clinical activity in various tumor types, consistent with broad preclinical *in vitro* activity.
- Exploratory CyTOF characterization of first 3 patient samples demonstrate
  - Circulating cytokines levels were modulated by SUPLEXA therapeutic cells.
  - SUPLEXA cell manufacturing resulted in similar immune populations .
  - T cells, NK cells and NKT Cells in SUPLEXA showed cytotoxic phenotypes.
  - SUPLEXA cell therapy improved markers of immune health over initial time points.

Exploratory Scientific Results

A. Patient PBMC and SUPLEXA Cell Profiling by CyTOF



Summary of CyTOF Antibody Panels

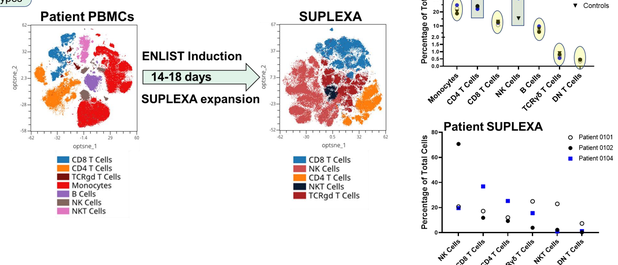
- Each panel contained 48 specific antibodies
- Panels designed to identify all major immune cell populations
- Antibodies for cell surface markers, intracellular markers, and transcription factors
- Panels included markers specific for SUPLEXA cells, *e.g.* CCR5, CCR6, CX3CR1,CXCR3, CD16, HLA-DR
- Staining was performed in batches using platinum-based barcoding reagents

Mass Cytometry (CyTOF) Workflow

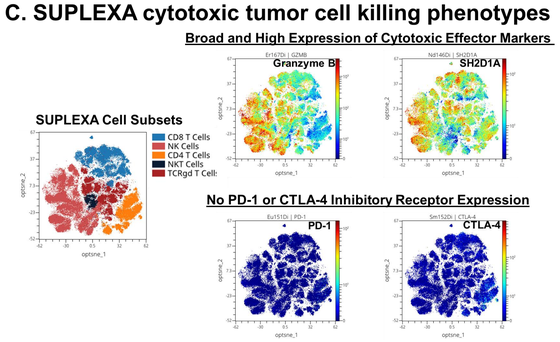
Thaw PBMCs/SUPLEXA, wash, count
↓
Plate at 1 x 10^6 cells, viability stain
↓
Stain with cell-surface CyTOF Abs
↓
Fix, permeabilize, palladium barcoding
↓
Stain with intracellular/nuclear Abs
↓
Fix, wash, DNA intercalator
↓
CyTOF-XT instrument data

1. CyTOF Data Analysis Workflow
2. Normalize, debarcode, OMIQ upload
3. Annotate with antibody information
4. Gaussian gating cleanup
5. Principal component analysis (PCA)
6. Dimensional reduction (optSNE)
7. Clustering by PARC
8. Identify immune cell types by heatmaps
9. Visualization by optSNE

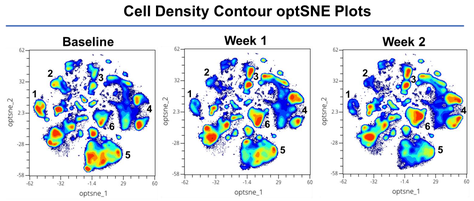
B. Patient PBMC and SUPLEXA Cellular Compositions



C. SUPLEXA cytotoxic tumor cell killing phenotypes

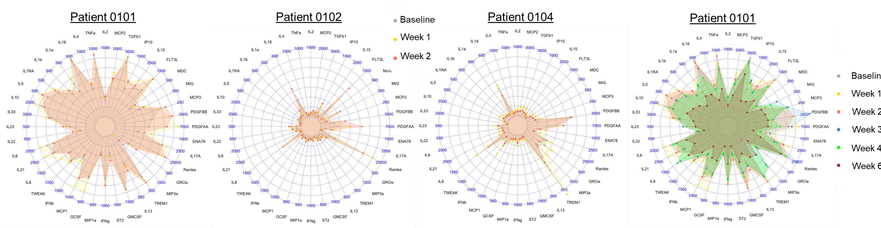


D. Longitudinal blood immune cell phenotyping in patients



1. ⬇ Exhausted CD4 T cells
2. ⬇ Exhausted CD8 T cells
3. ⬆ Cytotoxic NKT cells
4. ⬆ Activated proliferating monocytes
5. ⬇ CD16+/Arginase-1+ suppressive monocytes
6. ⬆ B cells

E. Patient Circulating Cytokines by Luminex Showing Different Immune Phenotypes



1. 3 patients displayed different systemic cytokine profiles
2. SUPLEXA treatments increased circulating levels of IL-8, Rantes, FLT3L, and PDGF-AA
3. Pro-inflammatory patient showed progressive reductions in inflammatory cytokine levels by 6-weeks after SUPLEXA treatments