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Preliminary Analysis of a Phase 1 Study of NEXI-002 Autologous Multi-Antigen-Specific CD8+ T Cells for the Treatment of Relapsed or Refractory Multiple Myeloma (RRMM)

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NexImmune

Background

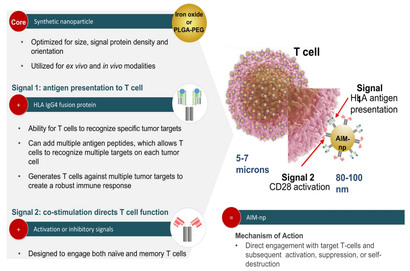
A novel approach to immunotherapy is being developed that employs the body's own T cells to generate a specific, potent, and durable immune response by utilizing a proprietary Artificial Immune Modulation (AIM™) nanoparticle technology platform. AIM constructed nanoparticles (AIM-np) function as synthetic dendritic cells capable of directing the immune function of antigen-specific T cells and employ natural biology to engage, activate and expand endogenous T cells.

Multiple myeloma remains an incurable malignancy of plasma cells in bone marrow and is the second most common hematologic cancer. Despite advances in therapy, including adoptively transferred T cells directed against the BCMA protein, virtually all patients relapse.

Within the emerging field of adoptive cell therapy for cancer, an ongoing challenge is the ex vivo expansion of high quantity and quality T cells capable of eliciting deep and durable anti-tumor activity.

Here we present the ability of the AIM technology platform to expand high quality T cell products from heavily pre-treated MM patients that are capable of in vivo persistence and expansion, tumor site infiltration and disease stabilizing activity.

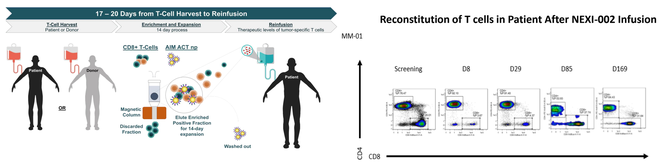
AIM Nano Technology



Target Antigens:
WT1, CS1, CD138, NY-ESO-1

AIM-np use fully human signaling proteins to engage with antigen-specific T cells, mimicking a natural cell-cell interaction

T cell Expansion Platform



NEXI-002 T cell Product: Healthy vs. Patient

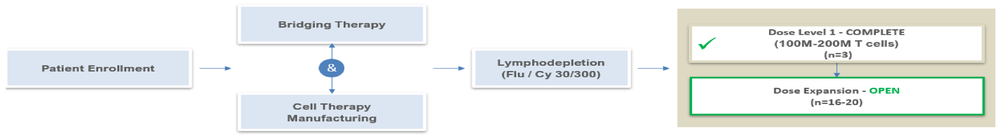
PBMC Source	Incoming cell count (PBMC)	Viability %	CD8+ Specificity %	Tscm + Tcm %	Tem %	Final T cell count
Healthy Donor	23.0e9	91.1	32	66.39	30.28	1.8e9
	32.8e9	84.3	35	51.3	44.7	1.57e9
MM r/r patient	6.9e9	92.7	29	40.1	49.5	1.32e8
	7.3e9	95.6	15	26.2	68.5	2.37e8

Products produced using HD PBMC and autologous PBMC have consistent product quality attributes as characterized by total antigen specificity, memory phenotype and viability. However, differences in the number of incoming apheresis-collected cells impacts final yield of clinical doses produced.

*NEXI-001 HD lots -20-007 and 21-006; NEXI-002 lots 20-003 and 21-002

NEXI-002: Multiple Myeloma Phase I/II Trial

- Design: Prospective, multi-center, open-label, single-arm Phase I/II study
- Eligibility: HLA-A*02.01 patients with relapsed/refractory MM who have failed ≥3 prior lines of therapy
- Objectives: Primary: Safety and tolerability
  Secondary: Immunologic and anti-tumor activity (ORR, PFS, OS)
- Biomarkers: Antigen-specific T cell persistence, immuno-phenotype, functionality, and TCR sequencing (blood and bone marrow)

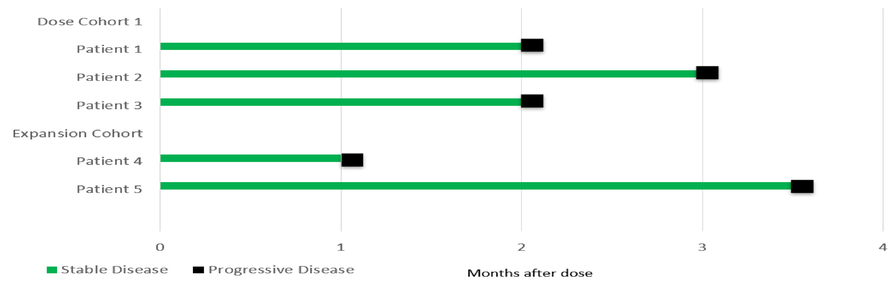


Patient Characteristics

	Age	Gender	# prior lines	M-protein	FISH	Remarks	Dose
Patient 1	59	Male	6	IgGλ	t(11;14)	20% plasma cells in BM	80M
Patient 2	55	Male	10	IgGκ	Gain of 9, 11, 15	95% plasma cells in BM; multiple LBLs	80M
Patient 3	39	Male	10	K light chain	No abnormalities	EM masses; multiple LBLs	100M
Patient 4	52	Female	9	K light chain	No abnormalities	Multiple LBLs	40M
Patient 5	56	Female	4 (includes 3 prior ASCTs)	IgGλ	t(8;22), t(11; 14) +5,+7,+9	50% plasma cells in BM; multiple LBLs	100M

Clinical Activity

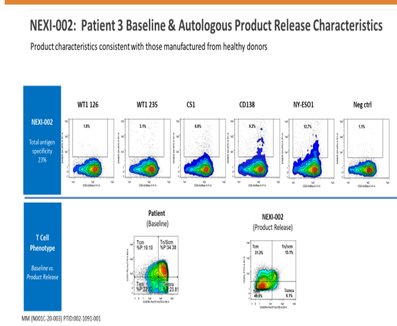
NEXI-002: Summary of Patient Experience

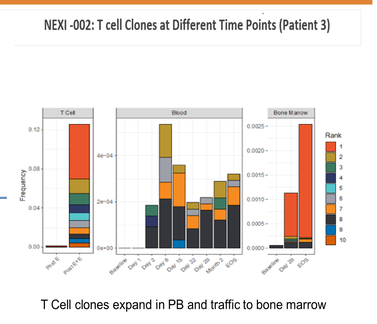


Conclusions

- NEXI-002 therapy was well tolerated without dose-limiting toxicities (No grade ≥3 CRS or any grade ICANS).
- TCR sequencing showed that NEXI-002 product contains T-cell clones that were undetectable in the PB of patients at baseline.
- The NEXI-002 product contains CD8+ antigen-specific T cells with memory phenotypes.
- A rapid lymphocyte recovery after NEXI-002 therapy, with reconstitution of both CD4 and CD8 + T cells.
- NEXI-002 T cells are detected in PB, proliferate and persist over time, and traffic to bone marrow.
- RRMM patients have achieved stable disease for 2-3 months duration at low doses of the NEXI-002 therapy.
- The quality and functionality of the NEXI-002 T Cells may be comparable to those expanded from healthy donors. Strategies that may yield higher product doses include evaluating patients with lower disease burden plasma cell dyscrasias.

Correlative Data

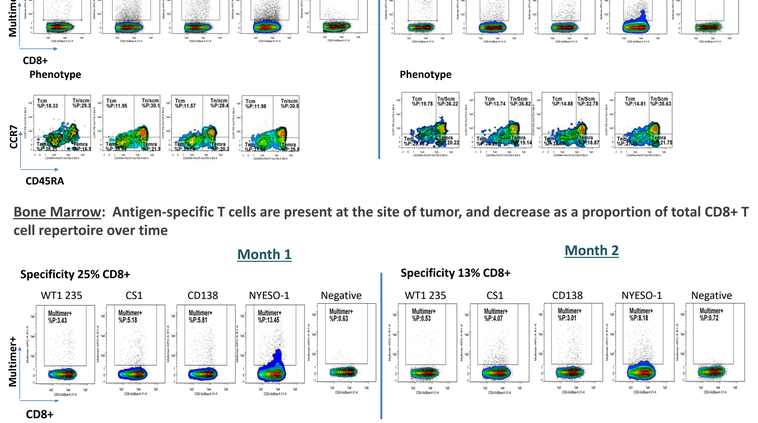




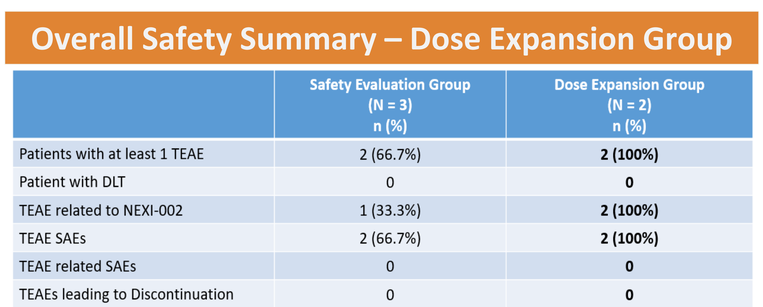
T Cell clones expand in PB and traffic to bone marrow

Biomarker Data

PBMC: Antigen-specific T cells continue to expand, and maintain a less differentiated phenotype over time



Bone Marrow: Antigen-specific T cells are present at the site of tumor, and decrease as a proportion of total CD8+ T cell repertoire over time



Overall Safety Summary – Dose Expansion Group

	Safety Evaluation Group (N = 3) n (%)	Dose Expansion Group (N = 2) n (%)
Patients with at least 1 TEAE	2 (66.7%)	**2 (100%)**
Patient with DLT	0	**0**
TEAE related to NEXI-002	1 (33.3%)	**2 (100%)**
TEAE SAEs	2 (66.7%)	**2 (100%)**
TEAE related SAEs	0	**0**
TEAEs leading to Discontinuation	0	**0**
TEAEs leading to Death	0	**0**
TEAE of Special Interest		
CRS	0	**1 (50%)**
IRR	1 (33.3%)	**0**
ICANS	0	**0**

CRS = cytokine release syndrome; DLT = dose limiting toxicity; ICANS = immune-effector cell-associated neurotoxicity syndrome; IRR = infusion-related reactions; TEAE = treatment-emergent adverse event

Data as of 13Sep2021