Anti-tumor function and long-term persistence of KSQ-001EX, a SOCS1-edited eTIL® therapy, independent of IL-2 co-administration

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Background

- Tumor Infiltrating Lymphocyte (TIL) therapy is an autologous adoptive cell therapy for cancer involving the isolation, ex vivo expansion, and infusion of polyclonal T cells from the patient's own tumor.
- KSQ-001EX is an engineered TIL (eTIL) therapy with CRISPR/Cas9-mediated inactivation of SOCS1, a negative regulator of cytokine signaling and T cell function.
- KSQ-001EX induces higher IFNγ cytokine secretion and higher effector function gene signature score in pre-clinical eTIL drug product (DP) compared to unedited TIL DP.
- KSQ-001EX is being investigated in a phase 1/2 clinical study (NCT06237881) in patients with advanced solid tumors. Metastatic melanoma patients received lymphodepleting chemotherapy followed by KSQ-001EX without IL-2 in Cohort 1 (n=4) or with high-dose IL-2 in Cohort 2 (n=8), at a dose range of 0.5-10 billion cells (median 5.25 billion cells).
- KSQ-001EX cells were directly monitored in blood and tissue samples via indel analysis at the SOCS1 gene locus.
- Correlative analyses were performed by integrating patient baseline characteristics, drug product (DP) manufacturing data, multi-modal and single-cell characterization of tumor starting material, KSQ-001EX DP, post-infusion PBMCs and on-treatment tumor tissue biopsies

KSQ-001EX clinical study

Phase 1: Dose Confirmation

Key eligibility criteria:
- Advanced cutaneous, acral or unknown primary melanoma that has progressed following ≥1 line of prior systemic therapy (including antiPD-1/antiPDL1 inhibitor alone or in combination)
- Resectable lesion for manufacturing
- At least one measurable lesion following resection

Primary Objective: To evaluate the safety and tolerability of KSQ-001EX

Primary and key Secondary Endpoints:
- Incidence of DLTs;
- Incidence/severity of TEAEs
- ORR, DOR, TTR per RECIST
- Manufacture success rate

Safety Lead-in Cohort 1 (n=6)
KSQ-001EX
(1 x 10^9 – 10 x 10^9 cells)
No IL-2
Advanced Melanoma

Safety Lead-in Cohort 2 (n=6)
KSQ-001EX
(1 x 10^9 – 10 x 10^9 cells)
High-dose IL-2 (up to 6 doses^)
Advanced Melanoma
^IL-2 dose: 600,000 IU/kg q 8-12 hrs

Study Treatment Schema

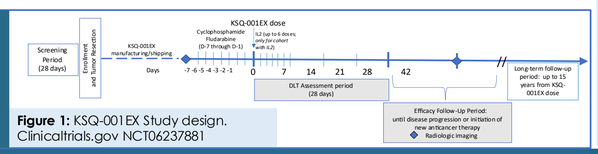


Figure 1: KSQ-001EX Study design. Clinicaltrials.gov NCT06237881

Clinical Results Summary*

- **No dose limiting toxicities with manageable safety profile**
- **100% patients (n=6) treated with above median cell dose (5.25 billon cells) had target lesion reduction**
- **33% ORR (2/6) in patients treated with above median cell dose**
- **1 patient ongoing with PR > 12 months**

**Data presented in Abstract #9820 at AACR 2026*

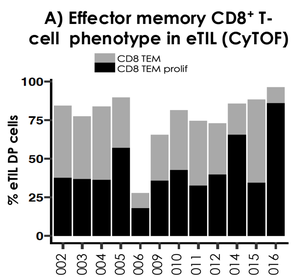
Translational and CMC Sample Analysis Plan

Sample type	Time Point	Objective	Assays
Tumor	Harvest, D28	Characterization	scRNAseq, bulkTCRseq, Targeted AmpSeq (indel)
Drug Product (eTIL DP)	Manufacturing	Characterization	scRNAseq, CyTOF, Flow, Targeted AmpSeq (indel)
		Functionality	IL2 and TCR stimulation, autologous co-culture
		Clonal tracking	Bulk TCRseq
		Quality	Cellularity, Viability, Yield
PBMC	Pre-infusion (Day –7) and post-infusion	Clonal tracking	Bulk TCRseq
		Characterization	CyTOF
		PK	Targeted NGS on edit
Serum	Characterization	PD, systemic immune activation	Cytokine panel

KSQ-001EX eTIL drug products exhibit a less differentiated, low exhaustion phenotype

Feature	KSQ-001EX median (min-max)	Attribute
% Live cells	93 (85 – 96)	High post-thaw viability
% SOCS1 edited	95 (92 – 97)	High editing efficiency during manufacturing
% CD8+	89 (65 – 98)	Majority of the cells are CD8+ cytotoxic T cells
% CD8+ CCR7-RA-RO+	95 (82 – 97)	Effector memory (T^{EM}) phenotype
% CD8+CD27+	37 (7 – 70)	Young, less differentiated TIL
% CD8+PD1+	10 (3 – 37)	Exhaustion/activation marker
% CD8+TIM3+	8 (5 – 28)	Exhaustion/activation marker
% CD8+CD39-CD69- (DN)	19 (1 – 63)	Stem-like TIL phenotype associated with clinical responses

KSQ-001EX drug products have predominantly proliferative effector memory (T^{EM}) phenotype



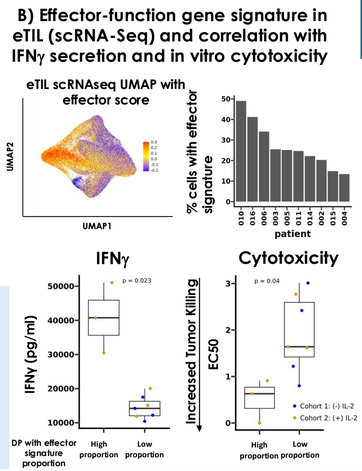


Figure 2: A) Proportion of CD8 T^{EM} phenotype with a proliferative (Ki67+) subset in eTIL DP; **B)** UMAP of eTIL DP scRNAseq data with effector gene signature (top left); Proportion of eTIL DP with a effector-function score (top right);Effector-function score is higher in KSQ-001EX compared to unedited TIL from same donors. Association of eTIL DP with High (>30% cells) and Low (<30 % cells) functional scores with with IFNγ secretion levels and EC50 in a A375-mOKT3 spheroid coculture assay (bottom)

Dose dependent eTIL cell expansion post-infusion, independent of IL-2 treatment

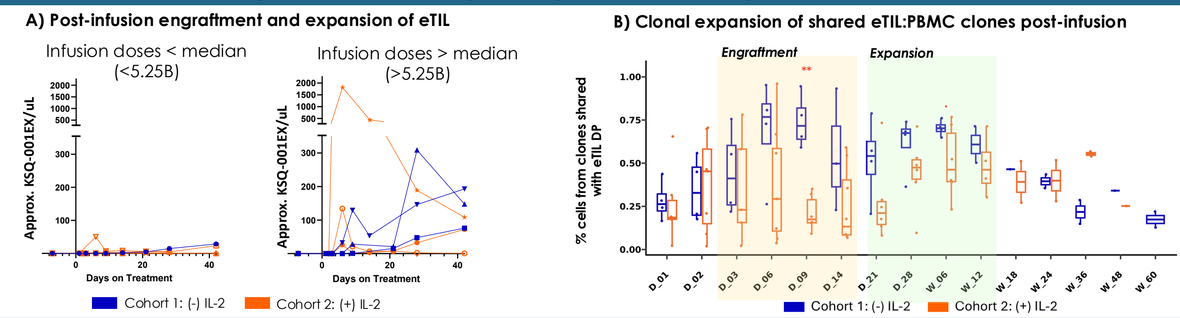


Figure 4: A) eTIL frequency was tracked in post-infusion PBMC by targeted amplicon sequencing. eTIL counts show dose dependent expansion, independent of IL-2 treatment; **B)** TCR repertoire of post-infusion T-cells shared with eTIL DP ("depth") expands in a biphasic manner: initial engraftment from Days 1 – 14 ("D_"), followed by a second expansion from day 21 to week 12 ("W_")

Increase in serum IFNγ independent of IL-2 treatment reflects SOCS1 biology

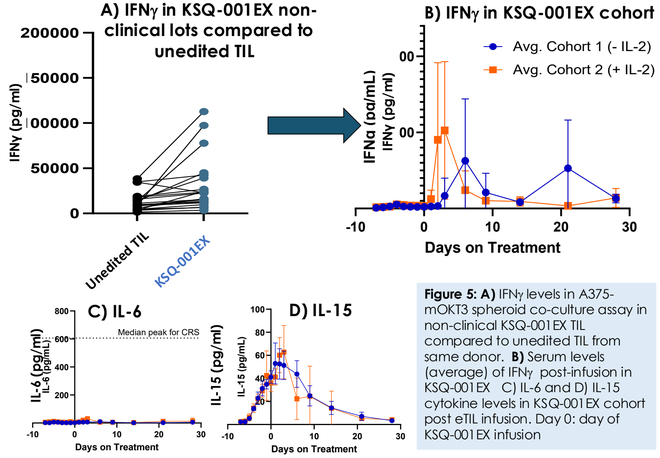


Figure 5: A) IFNγ levels in A375-mOKT3 spheroid co-culture assay in non-clinical KSQ-001EX TIL compared to unedited TIL from same donor. **B)** Serum levels (average) of IFNγ post-infusion in KSQ-001EX C) IL-6 and D) IL-15 cytokine levels in KSQ-001EX cohort post eTIL infusion. Day 0: day of KSQ-001EX infusion

Total $CD8^+$ $CD27^+$ DP cells correlates with engraftment, expansion and tumor infiltration

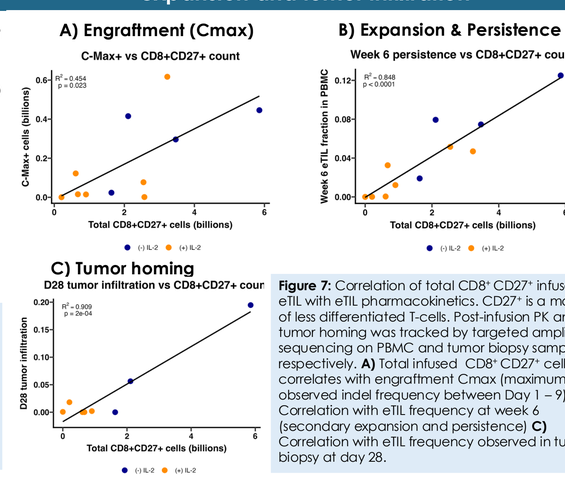


Figure 7: Correlation of total $CD8^+$ $CD27^+$ infused eTIL with eTIL pharmacokinetics. $CD27^+$ is a marker of less differentiated T-cells. Post-infusion PK and tumor homing was tracked by targeted amplicon sequencing on PBMC and tumor biopsy samples respectively. **A)** Total infused $CD8^+$ $CD27^+$ cells correlates with engraftment Cmax (maximum observed indel frequency between Day 1 – 9) **B)** Correlation with eTIL frequency at week 6 (secondary expansion and persistence) **C)** Correlation with eTIL frequency observed in tumor biopsy at day 28.

KSQ-001EX drug products have high cytotoxicity and tumor reactivity

Anti-Tumor Function = Functionality x Tumor Reactivity

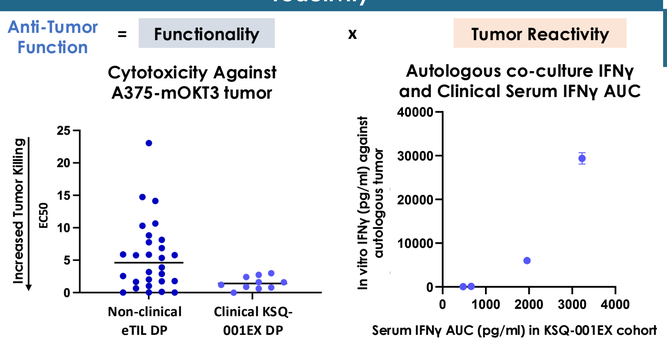


Figure 3: A) KSQ-001EX DP showed comparable or superior cytotoxicity to A375-mOKT3 tumor spheroids than non-clinical lots **B)** KSQ-001EX DP from 4 patients for which autologous tumors were available were co-cultured in vitro with digested autologous tumor for 24hr with tumor reactivity measured by IFNγ production; IFNγ production in vitro is plotted against serum IFNγ AUC calculated between day 1-day 28 post infusion.

Expansion of activated CD8 T^{EM} phenotype post-infusion independent of IL-2 treatment

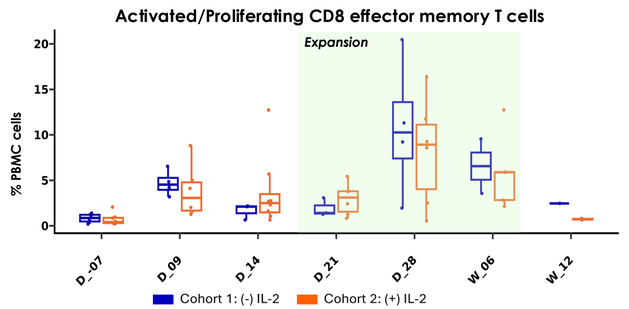


Figure 6: CyTOF analysis of and pre- post-infusion PBMC reveals a secondary expansion of activated/proliferating $CD8^+$ T effector memory (T^{EM}) cells in both no-IL2 and IL-2 cohorts.

Conclusion

- KSQ-001EX eTIL DP have a highly edited, CD8 enriched, less differentiated "young TIL" phenotype
- eTIL DP have a proliferative effector memory phenotype, correlated with in vitro cytotoxic activity and IFNγ levels in patients, indicating SOCS1 biology.
- Post-infusion, eTILs engraft and expand in a dose dependent manner, independent of IL-2 treatment. eTILs show a secondary expansion with persistence currently observed up to 60 weeks.
- Clinical efficacy observed in patients treated with higher doses (> median dose), independent of IL-2 treatment.
- Total $CD8^+CD27^+$ eTIL cells infused correlates with eTIL engraftment (Cmax), tumor homing at day 28, and persistence at week 6.
- Phase I/II study with SOCS1 and Regnase-1 dual edited eTIL, KSQ-004EX currently enrolling (Clinicaltrials.gov: NCT06598371).