NCT07075185 — KLN-1010 (Kelonia Therapeutics)

Safety: Relevant Links and Summary

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The product being studied in trial NCT07075185 is KLN-1010, a novel in vivo gene therapy developed by Kelonia Therapeutics for relapsed/refractory multiple myeloma. It uses an engineered lentiviral vector (the iGPS® platform) to directly generate anti-BCMA CAR-T cells inside the patient's body following a single IV infusion — without the need for apheresis, ex vivo cell manufacturing, or lymphodepleting chemotherapy.

Relevant Links

- AACR Abstract (preclinical safety/efficacy)
- Kelonia press release — 2023 NHP/mouse preclinical data
- Kelonia press release — April 2024 preclinical data
- Kelonia press release — ASH 2025 first-in-human data
- CancerNetwork — FDA IND clearance, Phase 1 safety data
- OncLive — ASH 2025 Phase 1 data summary
- PMC review — in vivo CAR-T landscape including KLN-1010
- Nature Medicine — long-term safety of lentiviral T-cell therapies (783 patients)
- Leukemia (Nature) — vector safety and genotoxicity review
- Human Gene Therapy — Skysona case and LV genotoxicity risk

Summary of Content

The Drug and the Trial

The inMMyCAR study is a Phase 1, open-label, dose-escalation trial designed to assess the safety, tolerability, pharmacology, and preliminary efficacy of a single dose of KLN-1010 in up to 40 patients. The primary endpoints are the incidence and severity of treatment-emergent adverse events (TEAEs), including dose-limiting toxicities (DLTs), and establishing the recommended Phase 2 dose. KLN-1010 employs an engineered lentiviral vector with a VSV-G mutant and a T-cell-specific CD3 scFv fused into the viral membrane.

(1) Safety Studies in Mice and Non-Human Primates (NHPs)

The preclinical safety data for KLN-1010 comes from both mouse and NHP models, and the results were favorable:

In mouse models, KLN-1010 treatment resulted in T cell–specific CAR expression with no evidence of off-target modification, including in the lung and liver, except for

phagocytes. Clinical application of the iGPS technology was modeled in non-human primates using an NHP T cell–targeting particle expressing an anti-CD20 CAR. CAR-T cell activity — assessed by B cell depletion — and tolerability were evaluated without prior lymphodepleting chemotherapy across a 10x dose range. Even at a low dose of 1.3×10^8 IU/kg, potent and durable CAR-T cell activity was observed, with complete B cell depletion lasting over two months. The treatment at all dose levels was highly tolerable with no observed toxicities, cytokine release syndrome, or neurotoxicity.

In mouse xenograft models of myeloma, KLN-1010 delivered in vivo led to more profound tumor killing compared with ex vivo manufactured ciltacabtagene autoleucel (cilta-cel; Carvykti)–like CAR-T cells. KLN-1010–generated CAR-T cells showed diverse T-cell developmental phenotypes with a higher proportion of central memory and STEM-like CAR-T cells. In multiple animal models, the vast majority of CAR-positive cells were confirmed to be T cells.

Early Human Safety Data (Phase 1, as of ASH 2025)

Highlights from the first four patients presented at ASH 2025 included a 100% MRD-negative response rate, a favorable toxicity profile with no CRS grade 3 or above and no ICANS, and potent CAR-T expansion from a single, off-the-shelf infusion without chemotherapy. Safety data from the dose-escalation portion revealed no immune effector cell–associated neurotoxicity syndrome (ICANS) events, and all instances of cytokine release syndrome (CRS) were low-grade events. [Note, total is now 10 patients, all doing well.]

(2) Potential Long-Term Adverse Effects in Humans

This is where the picture is more nuanced. KLN-1010 uses an integrating lentiviral vector, which means it permanently inserts genetic material into the DNA of patients' T cells. The field of lentiviral gene therapy has grappled seriously with the long-term risk of insertional mutagenesis — the possibility that vector integration near proto-oncogenes could, over time, drive abnormal cell growth or malignancy.

Broader lentiviral T-cell therapy data:
A large study evaluating safety outcomes in 783 patients across 38 T-cell therapy trials using integrating gammaretroviral or lentiviral vectors found that 2.3% of patients developed secondary malignancies after treatment, with a median onset of about 1.94 years (range: 51 days to 14 years). Where tumor samples were analyzed for vector copy number, no evidence of high-level marking or insertional mutagenesis was found. Analysis of vector integration sites in 176 patients revealed no pathological insertions linked to secondary malignancies, though integration in or near certain genes — including tumor suppressor genes — was associated with modest clonal expansion in some cases.

The Skysona precedent (a cautionary case involving a different LV product):
Seven cases of hematological malignancy in recipients of Skysona™ reignited concerns about insertional mutagenesis in lentiviral gene therapy. However, analysis showed these cancers were mechanistically linked to the use of a potent viral MNDU3 promoter, probably combined with intensive conditioning and growth-factor support, whereas lentiviral products employing weak or physiological promoters continue to display an

excellent safety profile. With event rates below 0.6 per 100 patient-years, the therapeutic index of approved LV-based therapies remains favorable.

Residual theoretical risk:
Vector integration can drive clonal expansions, and these may carry long-term safety risks. Documented cases of hematological malignancy after self-inactivating lentiviral gene therapy have recently emerged, particularly where heterologous retroviral promoters were employed, with concerns also around certain insulator elements and other possible contributors. Among lentiviral vector safety concerns, insertional mutagenesis — the upregulation or disruption of cellular genes by the retroviral integration event — remains the biggest concern and has been identified as a crucial initiation event for malignant transformation in some contexts.

Key Takeaways

- In mouse and NHP models, KLN-1010 demonstrated a clean safety profile: T-cell–specific gene delivery, no off-target transduction of non-T cells (except phagocytes), no CRS, and no neurotoxicity across a 10x dose range.
- In the first [10] human patients, early results are encouraging: all low-grade or absent CRS, no ICANS, robust CAR-T expansion without chemotherapy conditioning.
- Long-term risk: Because KLN-1010 is an integrating lentiviral vector, the theoretical risk of insertional mutagenesis — and downstream secondary malignancy — cannot be fully ruled out at this early stage. The broader lentiviral T-cell therapy literature suggests this risk is real but low (roughly 2.3% secondary malignancy rate across thousands of patient-years), and appears to be substantially lower when vectors use weaker, physiological promoters rather than strong viral ones. Whether the specific promoter design in KLN-1010 carries elevated or mitigated risk is not yet publicly detailed. Long-term follow-up of trial participants will be essential.
