A Phase 1 Randomized, Double-Blind Study of Safety, Tolerability and Pharmacokinetics of Solrikitug in Healthy Participants

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Introduction

- Solrikitug (NSI-8226), a humanized immunoglobulin (Ig)G1 monoclonal antibody that selectively binds thymic stromal lymphopoietin (TSLP) and inhibits downstream receptor signaling. [1]
- TSLP is a master regulator of type 2 inflammation (IL-4, IL-5, and IL-13), also contributing to non-type 2 inflammation. [2-3]
- Inhibition of TSLP has a broad spectrum of anti-inflammatory effects in patients with Type 2 immunity, e.g., asthma, chronic obstructive pulmonary disease (COPD) and eosinophilic esophagitis (EoE). [4-5]
- These indications are currently under study with solrikitug: [NCT06496607, NCT06496620, NCT06598462].
- In previously completed Phase 1 studies [MK-8226-001], solrikitug was safe and well tolerated in healthy participants administered as single IV doses ranging from 0.1 mg/kg to 10 mg/kg and after multiple IV doses in patients with moderate to severe atopic dermatitis over 12-weeks, dosed from 0.3 mg/kg to 10 mg/kg Q2W [MK-8226-003]. [6]

Aims

This study assesses safety, tolerability, pharmacokinetics, immunogenicity and pharmacodynamics (PD) of subcutaneous (SC) and intravenous (IV) solrikitug in healthy participants.

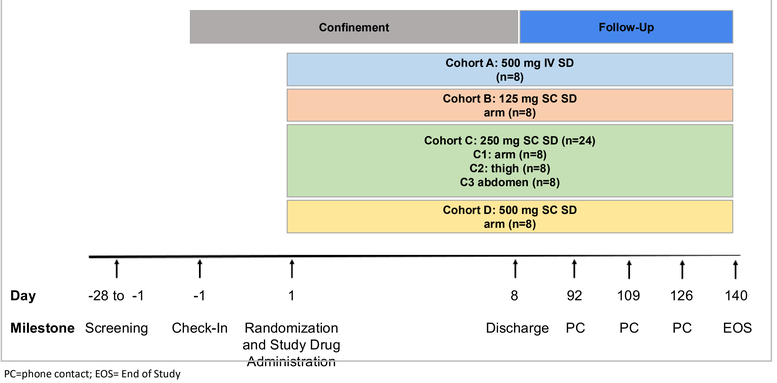
Methods

NCT06640920 enrolled 48 healthy participants; six participants in each cohort received either 125 (arm), 250 (arm, thigh, abdomen), 500 mg SC (arm) or 500 mg IV single-dose solrikitug; two participants per cohort received placebo (**Figure 1**).

Study included male or female healthy participants, 18 to 65 years of age, BMI 18-32 kg/m^2 with no medical history findings, assessed by the investigator.

Eosinophil cell counts were measured as an exploratory biomarker endpoint.

Figure 1. NSI-8226-101 Schema: Single Dose SC or IV Solrikitug



PC=phone contact; EOS= End of Study

Results: Safety

Solrikitug was generally well tolerated; all TEAEs were either mild or moderate in severity, and all study drug-related TEAEs were mild. There were no TEAEs of special interest. 15 (41.7%) participants receiving solrikitug experienced 36 TEAEs, and 5 (41.7%) receiving placebo experienced 6 TEAEs (**Table 1**).

Most of the study drug-related TEAEs were in the system organ class of general disorders and administration site conditions: injection site erythema, induration, pain, pruritus, and swelling.

There were no clinically meaningful trends between treatment groups, including between sites of SC drug administration, in the incidence rates of study drug-related TEAEs.

Table 1. Safety Results

	125 mg SC Solrikitug (N=6) n (%)	250 mg SC Solrikitug			500 mg SC Solrikitug (N=6) n (%)	500 mg IV Solrikitug (N=6) n (%)	Pooled Placebo (N=12) n (%)	Total Solrikitug (N=36) n (%)
		Arm (N=6) n (%)	Thigh (N=6) n (%)	Abdomen (N=6) n (%)				
Any TEAEs	1 (16.7)	2 (33.3)	6 (100)	3 (50.0)	3 (50.0)	0 (0.0)	5 (41.7)	15 (41.7)
Any TEAEs by maximum severity								
Mild	1 (16.7)	1 (16.7)	5 (83.3)	2 (33.3)	3 (50.0)	0 (0.0)	4 (33.3)	12 (33.3)
Moderate	0 (0.0)	1 (16.7)	1 (16.7)	1 (16.7)	0 (0.0)	0 (0.0)	1 (8.3)	3 (8.3)
Any study drug-related TEAEs	1 (16.7)	1 (16.7)	5 (83.3)	3 (50.0)	2 (33.3)	0 (0.0)	2 (16.7)	12 (33.3)
Any study drug-related TEAEs by maximum severity								
Mild	1 (16.7)	1 (16.7)	5 (83.3)	3 (50.0)	2 (33.3)	0 (0.0)	2 (16.7)	12 (33.3)
Any SAEs/TESAEs/Any AEs leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any TEAEs leading to discontinuation of study	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

% = 100 × n/N. AE reported terms were coded using the Medical Dictionary for Regulatory Activities (version 26.1). AE = adverse event; IV = intravenous(ly); N = number of participants in each treatment group; n = number of participants in each category; SAE = serious adverse event; SC = subcutaneous(ly); solrikitug = NSI-8226; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.

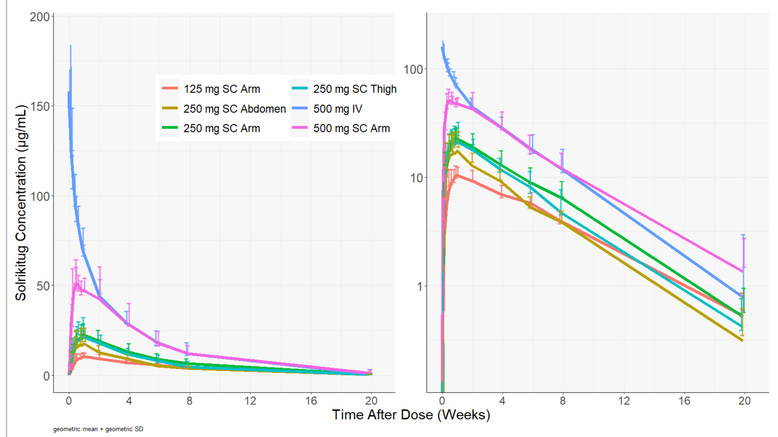
All injection site reactions were mild (Grade 1) in severity with no observed trends in incidence rates across treatment groups. No clinically meaningful trends were identified for any safety laboratory chemistry, hematology, or urinalysis parameters over time.

Results: PK and Immunogenicity

Solrikitug dose proportionality was established over the range of studied doses. Except for 2/602 measurements, all concentration-time data were above the lower limit of quantification over the 20 weeks post-dosing (**Figure 2**). Noncompartmental PK parameters for SD IV and SC are summarized in **Table 3**.

Given dose independence, bioavailability of SC solrikitug was 73.0%, based on dose-normalized geometric mean ratio of SC to IV $AUC_{0\text{-inf}}$. Numerically lower (18%) relative SC bioavailability of solrikitug is currently estimated for the abdomen, considering dose-normalized geometric mean ratio of $AUC_{0\text{-inf}}$ with 90% confidence interval (CI) expressed as percent, (71% [51% to 100%]) versus the thigh (89% [63% to 126%]) with administration in the arm as a reference. Given the CI overlap, these differences are likely of limited clinical importance.

Figure 2. Solrikitug Single Dose IV and SC Pharmacokinetics: Group Geometric Means + SD



7 confirmed positive anti-drug antibody (ADA) samples were detected in 4 out of 36 (11%) solrikitug-treated participants, with low titers.

Two out of 4 ADA positive or 2 out of 36 (5.6%) solrikitug-treated participants were detected as ADA incidence post-baseline; both cases were considered treatment-induced ADAs with confirmatory ADA positivity occurring transiently after solrikitug administration only on Day 8 and Day 15, respectively.

No neutralizing antibodies were detected in any of the samples that tested positive in the confirmatory ADA assay.

Table 2. Solrikitug PK Parameters

	125 mg SC Solrikitug Cohort B (N=6)	250 mg SC Solrikitug			500 mg SC Solrikitug Cohort D [2] (N=5)	500 mg IV Solrikitug Cohort A (N=6)
		Arm Cohort C1 [1] (N=6)	Thigh Cohort C2 (N=6)	Abdomen Cohort C3 (N=6)		
$AUC_{0\text{-inf}}$ (day*µg/mL)	552 (26.9)	897 (22.5)	848 (29.8)	679 (21.3)	2120 (21.4)	2510 (29.0)
$DNAUC_{0\text{-inf}}$ (day*µg/mL/mg)	4.41 (26.9)	3.59 (22.5)	3.39 (29.8)	2.71 (21.3)	4.23 (21.4)	5.01 (29.0)
C_{max} (µg/mL)	10.7 (21.8)	23.7 (29.3)	22.1 (33.1)	18.0 (46.4)	53.7 (23.0)	159 (23.5)
T_{max} (day)	6.5 (5.0, 14.0)	7.0 (6.0, 14.0)	7.0 (3.0, 7.0)	6.50 (3.0, 7.0)	4.00 (2.0, 7.0)	0.04 (0.04, 0.17)
$t_{½}$ (day)	29.1 (15.5)	25.0 (16.8)	23.2 (17.3)	23.9 (26.9)	26.9 (23.4)	22.2 (30.9)
CL or CL/F (L/day)	0.227 (26.9)	0.279 (22.5)	0.295 (29.8)	0.368 (21.3)	0.236 (21.4)	0.200 (29.0)
Vd or Vd/F (L)	9.51 (18.8)	10.0 (21.9)	9.89 (34.6)	12.7 (35.8)	9.18 (13.8)	6.40 (9.1)
V_{ss} (L)	–	–	–	–	–	5.74 (16.4)

Parameters as group geometric mean (geometric CV), Tmax as median (minimum, maximum). [1]N=5 for Cohort C1 parameters ($t_{½}$, CL/F, Vd/F, AUC0-inf) as extrapolated AUC was 28.5% in one pt. [2]One participant in Cohort D was excluded from the summary due to an outlier profile. Geometric CV = SQRT(100*(exp(SD^2)-1), where SD is the standard deviation of the log-transformed data. $AUC_{0\text{-inf}}$ = area under the observed serum conc. vs time curve, time 0 to infinity; CL = clearance after IV; CL/F = apparent serum clearance (after extravascular [SC] administration); Cmax = maximum observed serum conc.; CV = coefficient of variation; $DNAUC_{0\text{-inf}}$ = dose-normalized $AUC_{0\text{-inf}}$; N = number of participants in each treatment group; PK = pharmacokinetic(s); SC = subcutaneous(ly); SD = standard deviation; SQRT=square root; $t_{½}$ = apparent first-order terminal elimination half-life; Tmax = time to Cmax; Vd = volume of distribution during terminal elimination phase after IV administration; Vd/F = apparent volume of distribution during terminal elimination phase (after extravascular [subcutaneous] administration); Vss = volume of distribution at steady state after IV administration.

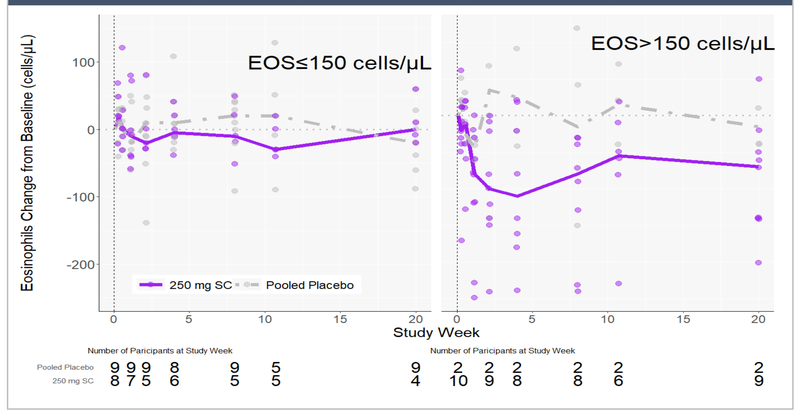
Results: PD (Eosinophils)

Sustained blood eosinophil count reduction was evident in solrikitug treated participants with higher blood eosinophils at baseline (>150 cells/µL), in contrast to pooled placebo and lower (<150 cells/µL) eosinophil participants at baseline (**Figure 3**).

More participants with ≥150 cells/µl eosinophils at baseline achieved a >75 cells/µl decrease: 11/19 (58%) for solrikitug treated participants vs 2/19 (11%) for placebo.

There were 4/27 (5%) solrikitug treated and 1/27 (4%) placebo participants that achieved the same (>75 cells/µl) eosinophil cell count decrease from baseline in the ≤150 cells/µl at baseline group.

Figure 3 Eosinophil Counts after a Single Dose of Solrikitug



Conclusions

- Solrikitug was well tolerated. TEAEs were either mild or moderate in severity, and all study drug-related TEAEs were mild in severity. There were no SAEs or TEAEs leading to discontinuation of the study.
- Solrikitug SC bioavailability, linear PK and low immunogenicity reflect its unmodified Fc region and mAb class.
- This contrasts with Fc-modified, and/or mAbs binding receptor targets which generally exhibit nonlinear PK and higher rates of immunogenicity, possibly leading to increased pharmacodynamic variability [7].
- Marked and sustained eosinophil reduction reflects solrikitug pharmacodynamics, consistent with high in vitro potency and functional assay activity [1].
- The results of this study support the SC route of administration for solrikitug and evaluation of PK/PD of biomarkers and clinical endpoints in Phase 2 clinical studies.

Reference:
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5. Lancet Respir Med. 2025 Jan;13(1):47-58
6. MK-8226-001 data on file; MK-8226-003 results on clinicaltrials.gov

Poster presented at ERS, Amsterdam, NL 2025

Conflict of Interest Disclosures:
BL, AW, HKK, AL, LW are employees and shareholders of Uniquity Bio
HO and TH were employees and shareholders of Uniquity Bio at the time the study was conducted