A Phase 2b, Randomized, Double-Blinded, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Rezpegaldesleukin in Adults with Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

- Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder.[1-3]
- Approximately 1 in 10 individuals has a lifetime risk of developing AD.[1-5]
- Dysfunction of regulatory T cells (Treg) may play a role in AD immunopathogenesis.[6]
- Targeting the Treg pathway is a novel therapeutic approach for restoring immune homeostasis in patients with moderate-to-severe AD.[7]
- Rezpegaldesleukin (REZPEG: NKTR-358) is a polyethylene glycol (PEG)-conjugated recombinant human interleukin 2 (rhIL-2) with the ability to selectively promote the activation and expansion of Tregs, while having relatively minimal effect on conventional T cells (Tcons).[7]
- In healthy volunteers and patients with SLE, REZPEG treatment resulted a in dose-dependent, selective, and up-to 17-fold increase in $CD25^{bright}$ Tregs over baseline that was sustained for 20–30 days.[7]
- A Phase 1b study of REZPEG for patients with moderate-to-severe AD demonstrated a rapid time to response (2-4 weeks) during induction therapy and a prolonged durability of response (i.e., majority of responders retained that response throughout the 36-week follow-up without additional systemic therapy).[8]
- These results support further development of REZPEG for patients with AD.

Figure 1: Role of Regulatory T Cells in Autoimmune Disease

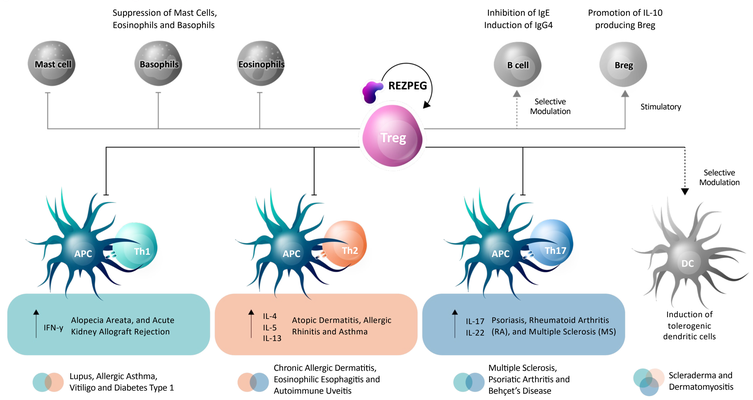
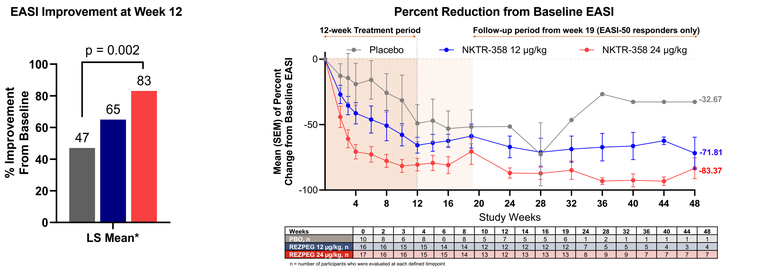


Figure 2: Phase 1b Study of REZPEG in Atopic Dermatitis

Percent Change From Baseline for EASI Score



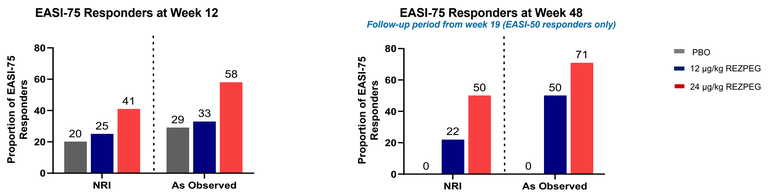
Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
PBO, n	10	8	6	8	6	8	5	7	5	5	6	1	2	1	1	1	1	1
REZPEG 12 µg/kg, n	16	16	15	15	14	14	12	12	12	12	7	5	5	5	4	3	4	
REZPEG 24 µg/kg, n	17	16	16	15	15	14	13	12	13	13	8	9	9	7	7	7	7	

n = number of participants who were evaluated at each defined timepoint

SEM: Standard error of the mean; continuous endpoint using observed data; *EASI Improvement results are least squares (LS) mean percent change from baseline obtained from Mixed Model for Repeated Measures (MMRM) as specified in the statistical analysis plan (SAP) defined in the protocol (generated by independent statistical audit firm)

Figure 3: Phase 1b Study of REZPEG in Atopic Dermatitis

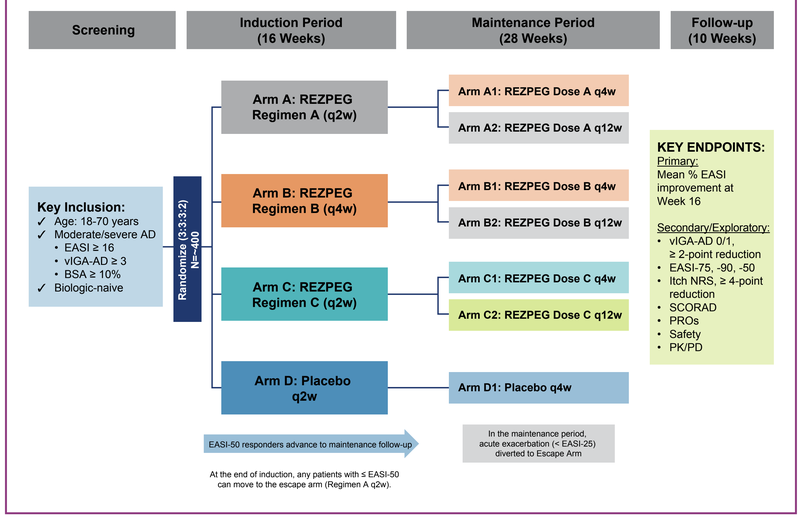
Proportion of EASI-75 Responders at Week 12 and at Week 48



Patients were followed until Week 19, and those with ≥EASI-50 response at Week 19 were followed until Week 48 or until EASI-25 response criteria were no longer met. NRI: non-responder imputation

STUDY DESIGN

Figure 4: Phase 2b Study Design



Phase 2b Study for Patients with Atopic Dermatitis

- This trial is a Phase 2b, randomized, double-blinded, placebo-controlled, international, multicenter study of REZPEG vs placebo for biologic-naïve patients with moderate-to-severe AD.
- Patients will be randomly assigned in a 3:3:3:2 ratio to 3 different REZPEG dosing regimens vs. placebo, administered subcutaneously, during the induction period.
- Patients on the REZPEG arms with an at-least EASI-50 response following the 16 week induction period will be re-randomized to a maintenance REZPEG administration every 4 or 12 weeks.
- Re-randomized patients with an acute exacerbation defined as <EASI-25 and patients that do not achieve an EASI-50 at end of induction will be placed in an open-label escape arm and administered REZPEG.

Key inclusion criteria

- ✓ Adult patients aged 18-70 years
- ✓ Chronic AD for at least 1 year and for whom topical treatment was inadequate or inadvisable
- ✓ Moderate-to-severe atopic dermatitis:
  - Eczema Area and Severity Index (EASI) score ≥ 16
  - Investigator's Global Assessment (IGA) AD score ≥ 3
  - Total Body Surface Area (BSA) affected ≥ 10%
- ✓ Systemic biologic and JAK-inhibitor naive

Primary Endpoints

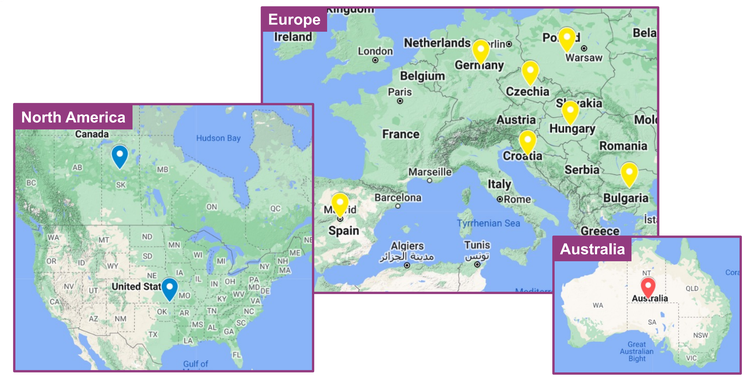
- The primary endpoint for this study is the least-square mean percent reduction in EASI from baseline at end of induction.

Secondary Endpoints

- To evaluate proportion of patients at the end of induction with:
  - IGA 0/1 with at-least 2 point reduction
  - EASI-75, -90, -50
  - SCORAD-75, -50
  - Itch Numerical Rating Scale [NRS] improvement of ≥ 4 points
  - Improvement in % BSA involvement
- Additional endpoints at the end of induction:
  - Safety/tolerability
  - Various patient reported outcomes (PROs)
  - Pharmacokinetics and Pharmacodynamics
- To evaluate the assessed efficacy and safety endpoint at all other timepoints
  - During Induction
  - During Maintenance
  - During Follow-up

STUDY STATUS

Figure 5: Countries Included in the Study



- This study is initiating in North America and other parts of the world (**Figure 5**):
  - North America (Canada, United States)
  - Europe (Bulgaria, Croatia, Czech Republic, Germany, Hungary, Poland, Spain)
  - APAC (Australia)
- Please contact the Sponsor (Nektar) with any questions

ACKNOWLEDGMENTS

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The study will be approved by the institutional review board of each participating site.

ABBREVIATIONS

AD, Atopic dermatitis; Treg, regulatory T cells; PEG, polyethylene glycol; rhIL-2, recombinant human interleukin 2; Tcons, conventional T cells; Th1, Type 1 T helper cells; Th2, Type 2 T helper cells; Th17, Type 17 T helper cells; RA, rheumatoid arthritis; MS, multiple sclerosis; APC, antigen-presenting cells; EASI, Eczema Area and Severity Index; vIGA-AD, Validated Investigator Global Assessment scale for Atopic Dermatitis; BSA, Body Surface Area; q2w, once every 2 weeks; q4w, once every 4 weeks; q12w, once every 12 weeks; Itch NRS, Itch Numerical Rating Scale; SCORAD, Scoring of Atopic Dermatitis Index; PROs, patient reported outcomes; PK, Pharmacokinetics; PD, Pharmacodynamics; APAC, Asia-Pacific

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