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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Melinda Gooderham[1], Charles Lynde[2,3], Maryam Shayesteh Alam[4], Neil Sadick[5,6], Craig A Rohan[7], William Philip Werschler[8], Adelaide A Hebert[9], Vivian T Laquer[10], Maxwell Sauder[2], James Q. Del Rosso[11], Timothy Rodgers[12], Ricardo Tan[13], Stephen Schleicher[14], Dedée F Murrell[15], Pablo Fernandez-Peñas[16,17], Adam Reich[18], Spyridon Gkalpakiotis[19], Juan Ruano Ruiz[20], Andreas Wollenberg[21], Jacek C Szepietowski[22], Michael Sticherling[23], Ansgar J. Weyergraf[24], Suzana Ljubojević Hadžavdić[25], Wojciech Baran[21], Trinidad Montero Vilchez[26], Telegdy Eniko[27], Michael Sebastian[28], Sohail Chaudhry[29], Zachary Lee[29], Danni Yu[29], Yi Liu[29], Wang Waltz[29], Jenny Gilbert[29], Lucinda M. Elko-Simms[29], Christie Fanton[29], Charleen Jue[29], Mary Tagliaferri[29], Jonathan Zalevsky[29], David Rosmarin[30]

[1]Department of Medicine, Queen's University, Kingston, ON, Canada; [2]Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada; [3]Lynde Institute for Dermatology, Markham, ON, Canada; [4]SimcoMed Health Ltd, Barrie, ON, Canada; [5]Department Of Dermatology, Weill Cornell Medicine, New York, NY, United States; [6]Sadick Research Group, New York, NY, United States; [7]Dermatology, Boonshoft School of Medicine at Wright State University, Dayton, OH, United States; [8]Department of Medicine/Dermatology, University of Washington, Seattle, WA, United States; [9]University of Texas Health Science Center Houston, Houston, TX, United States; [10]First OC Dermatology Research, Fountain Valley, CA, United States; [11]Lakes Dermatology and Del Rosso Dermatology Research Center, Las Vegas, NV, United States; [12]North Texas Center for Clinical Research, Frisco, TX, United States; [13]California Allergy & Asthma, Los Angeles, CA, United States; [14]DermDox Centers for Dermatology, Sugarloaf, PA, United States; [15]School of Medicine, University of Notre Dame, Sydney, NSW, Australia; [16]Department of Dermatology, Westmead Hospital, NSW, Australia; [17]Sydney Medical School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia; [18]Department of Dermatology, Institute of Medical Sciences, Medical College of Rzeszow University, Rzeszow, Poland; [19]Department of Dermatovenereology, Third Faculty of Medicine, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [20]Department of Dermatology, Reina Sofia University Hospital, Cordoba, Spain; [21]Department of Dermatology and Allergology, Ludwig-Maximilians-University, Munich, Germany; [22]Department of Dermatology, Venereology, and Allergology, Wroclaw Medical University, Wroclaw, Poland; [23]Department of Dermatology, University Hospital, Friedrich Alexander University Erlangen-Nuernberg, Erlangen, Germany; [24]Hautarztpraxis an der Hase, Bransche, Germany; [25]Department of Dermatology and Venereology University Hospital Center Zagreb, University of Zagreb School of Medicine, Zagreb, Croatia; [26]Department of Dermatology at Hospital Universitario Virgen de las Nieves, Granada, Spain; [27]Department of Dermatology, Markusovszky University Teaching Hospital, Szombathely, Hungary; [28]Dermatology Mahlow, Mahlow, Germany; [29]Nektar Therapeutics, San Francisco, CA, United States; [30]Indiana University School of Medicine, Indianapolis, IN, United States

BACKGROUND

- Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder.[1-3]
- Approximately 1 in 10 individuals have 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 in a 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 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

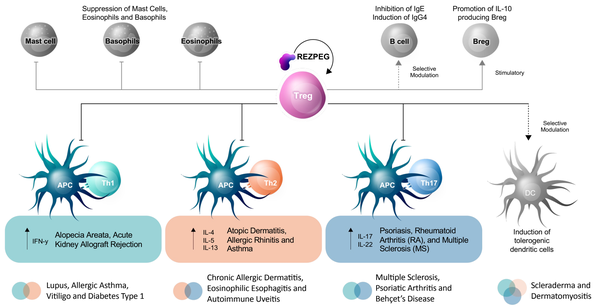
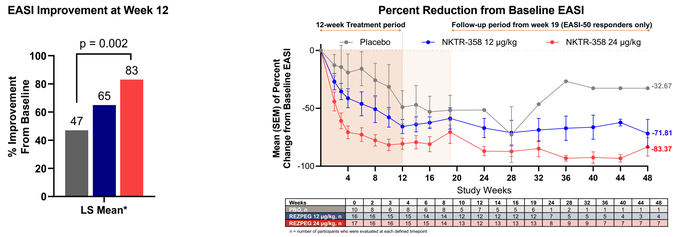


Figure 2: Phase 1b Study of REZPEG in Atopic Dermatitis-Percent Change From Baseline for EASI Score

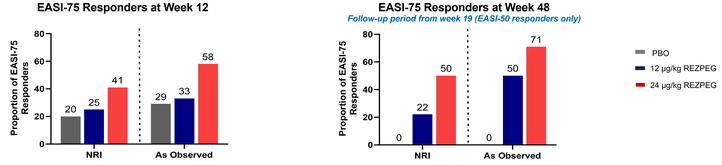


Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
Placebo	10	8	6	8	6	8	8	7	5	5	5	0	1	2	1	1	1	1
REZPEG 12 µg/kg q2w	16	16	15	15	14	14	12	12	12	12	12	12	7	5	5	5	4	3	4
REZPEG 24 µg/kg q2w	17	16	16	15	15	14	13	12	13	13	13	13	8	9	9	7	7	7	7

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)

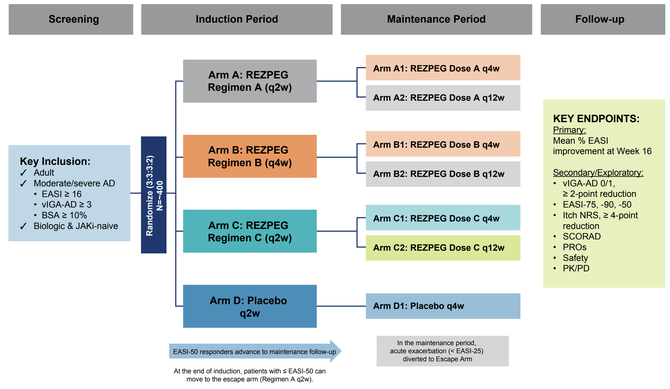
Figure 3: Phase 1b Study of REZPEG in Atopic Dermatitis-Proportion of EASI-75 Responders at Week 12 and at Week 48



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 and JAKi-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

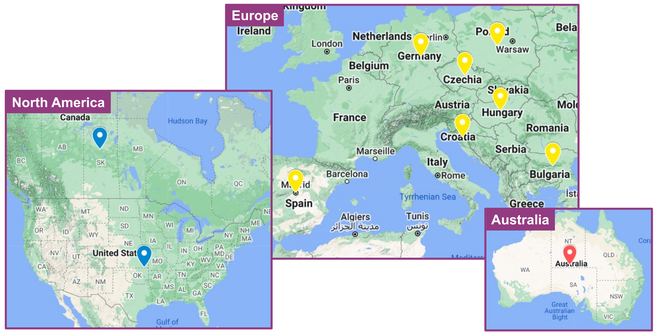
- The primary endpoint for this study is the least-square mean percent reduction in EASI from baseline at end of induction.

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 Therapeutics) with any questions (see NCT06136741)

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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Corresponding author Melinda Gooderham: mgooderham@centrefordermatology.com