ROCKETing Forward: The Future of Atopic Dermatitis Treatment Targeting the OX40 Signalling Pathway

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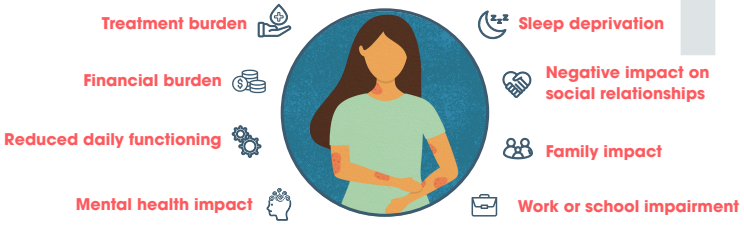
1 Burden and Unmet Need in Moderate-to-Severe AD

Complex Patient Burden[1-7]



Despite available therapies, treatment goals are not achieved or sustained for many patients with moderate-to-severe AD.[1-5]

Topical agents are widely used to treat AD; patients with moderate-to-severe AD often require systemic therapy as monotherapy or in combination.[2,4]

Systemic therapies, though effective for many patients, do not meet the needs of all patients and may be associated with treatment failure and adverse events that further impact patient QoL.[2,4]

There is still a need for novel, efficacious, well-tolerated therapeutic options that deliver durable benefits[2-4]

2 AD Pathophysiology and the OX40 Pathway

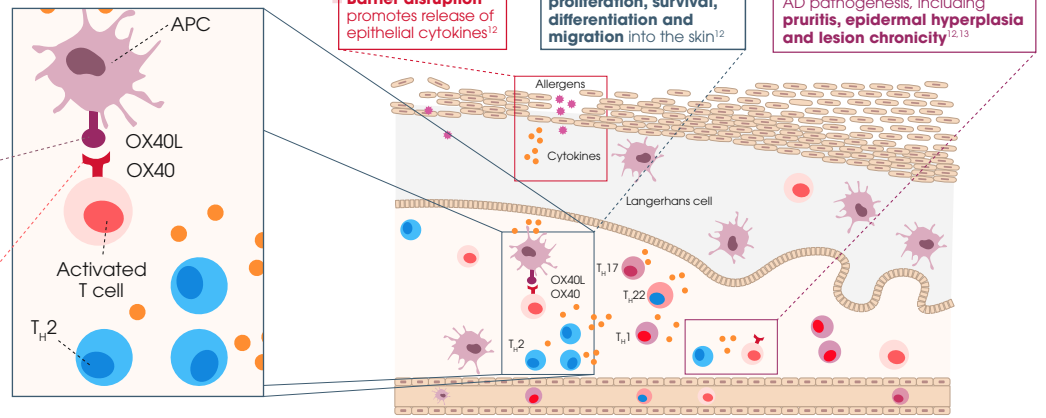
T cells are key drivers of AD pathophysiology. In AD, T cells become pathogenic when they receive signals to expand and mature into effector and memory T cells in the absence of an infectious threat.[8-11]

OX40 is expressed on the surface of activated T cells, which are more likely to contribute to AD pathogenesis.[12,13]

OX40 pathway activation drives the expansion, differentiation, and survival of pathogenic T cells, and promotes the development and reactivation of memory T cells[12,13]

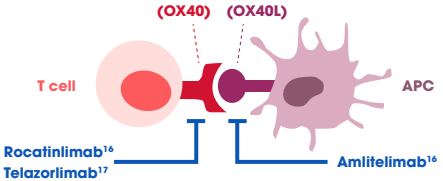
OX40L is expressed on activated APCs. No difference in OX40L expression on PBMs was observed in patients with AD versus healthy controls.[12,13]

OX40 is expressed on activated effector and memory T cells, but not in naïve T cells. Expression is increased in patients with AD.[12]



OX40 signalling represents a potential target for novel therapies[12,14,15]

3 OX40/OX40L Is a Novel Target Currently Under Investigation for the Treatment of Moderate-to-Severe AD

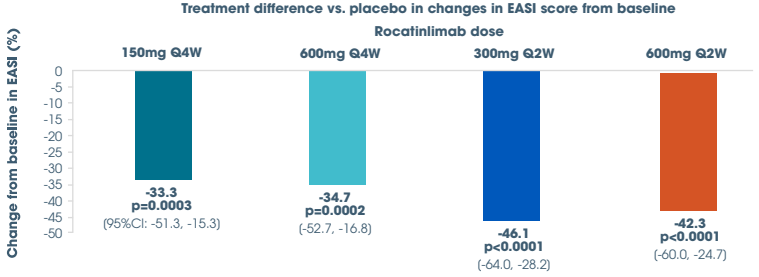


Rocatinlimab is a fully human mAb that blocks OX40 signalling, thereby preventing differentiation, expansion and survival of OX40+ pathogenic T cells. It also prevents the subsequent generation of memory T cells.[12,13,18]

Clinical Trials of Rocatinlimab in Moderate-to-Severe AD

A Phase II Study Demonstrated Efficacy and Favourable Safety Profile of Rocatinlimab in Adults with Moderate-to-Severe AD[18]

Significant reductions in EASI score versus placebo in moderate-to-severe AD (p<0.001).[18]



Overall, rocatinlimab was well tolerated, with most adverse events reported being mild-to-moderate.[18]

Improvements in disease severity were maintained throughout treatment and following discontinuation[18]

4 The Phase III ROCKET Programme is Designed to Evaluate the Efficacy, Safety, and Tolerability of Rocatinlimab in Patients with Moderate-to-Severe AD[19-25]

Adult patients				**Adolescent** patients		**Both**
IGNITE	HORIZON	SHUTTLE	VOYAGER	ASTRO	ORBIT	ASCEND
24-week placebo-controlled trial evaluating rocatinlimab monotherapy in adult patients	24-week placebo-controlled trial evaluating rocatinlimab monotherapy in adult patients	24-week placebo-controlled trial evaluating rocatinlimab combination therapy in adult patients	24-week placebo-controlled trial evaluating rocatinlimab on vaccine antibody response in adult patients	52-week placebo-controlled trial evaluating rocatinlimab monotherapy, combination therapy, and maintenance therapy in adolescent patients	52-week open-label safety trial of rocatinlimab in adolescent patients	104-week trial evaluating rocatinlimab long-term and maintenance therapy in adult and adolescent patients

ROCKET is currently recruiting; find out more here

1. Eczema Society of Canada. Itch in atopic dermatitis. Available at: https://eczemahelp.ca/living-with-eczema/itch-in-atopic-dermatitis/. Last accessed: November 2023.
2. Wei W et al. A real-world study evaluating adeQUacy of Existing Systemic Treatments for patients with moderate-to-severe Atopic Dermatitis (QUEST-AD): Baseline treatment patterns and unmet needs assessment. Ann Allergy Asthma Immunol. 2019;123(4):381-8.
3. Augustin M et al. Unveiling the true costs and societal impacts of moderate-to-severe atopic dermatitis in Europe. J Eur Acad Dermatol Venereol. 2022;36(Suppl 7):3-16.
4. Kleyn CE et al. Burden of moderate to severe atopic dermatitis in adults from France, Italy, and the UK: patient-reported outcomes and treatment patterns. Dermatol Ther (Heidelb). 2022;12(8):1947-65.
5. Silverberg JI et al. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. Ann Allergy Asthma Immunol. 2018;121(3):340-7.
6. Kamata M, Tada Y. A literature review of real-world effectiveness and safety of dupilumab for atopic dermatitis. JID Innov. 2021;1(3):100042.
7. Capozza K et al. Divergent paths: the influence of pediatric atopic dermatitis on caregiver and family life decisions. Poster 583. 3rd RAD Annual Meeting. 11-13 December, 2021.
8. Czarnowicki T et al. Circulating CLA+ T cells in atopic dermatitis and their possible role as peripheral biomarkers. Allergy. 2017;72(3):366-72.
9. Kaufman BP et al. Atopic dermatitis in diverse racial and ethnic groups – variations in epidemiology, genetics, clinical presentation and treatment. Exp Dermatol. 2018;27(4):340-57.
10. Guttman-Yassky E et al. Atopic dermatitis: pathogenesis. Semin Cutan Med Surg. 2017;36(3):100-3.
11. De Bruyn Carlier T et al. Autoreactive T cells and their role in atopic dermatitis. J Autoimmun. 2021;120:102634.
12. Furue M, Furue M. OX40L-OX40 signaling in atopic dermatitis. J Clin Med. 2021;10(12):2578.
13. Croft M et al. The significance of OX40 and OX40L to T-cell biology and immune disease. Immunol Rev. 2009;229(1):173-91.
14. Lebwohl MG et al. Pathways to managing atopic dermatitis: consensus from the experts. J Clin Aesthet Dermatol. 2013;6 (7 Suppl):S2-18.
15. Boguniewicz M et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: a multidisciplinary consensus addressing current and emerging therapies. J Allergy Clin Immunol Pract. 2017;5(6):1519-31.
16. Lê AM, Torres T. OX40-OX40L inhibition for the treatment of atopic dermatitis – focus on rocatinlimab and amlitelimab. Pharmaceutics 2022;14(12):2753.
17. Tsuji G et al. Novel therapeutic targets for the treatment of atopic dermatitis. Biomedicines. 2023;11(5):1303.
18. Guttman-Yassky E et al. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023;401(10372):204-14.
19. Amgen. A study evaluating rocatinlimab in moderate-to-severe atopic dermatitis (ROCKET-IGNITE). NCT05398445. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05398445. Last accessed: November 2023.
20. Amgen. A study assessing rocatinlimab (AMG 451) monotherapy in moderate-to-severe atopic dermatitis (AD) (ROCKET HORIZON) NCT05651711. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05651711. Last accessed: November 2023.
21. Amgen. A study assessing rocatinlimab in combination with topical corticosteroid and/or topical calcineurin inhibitors in adult participants with moderate-to-severe atopic dermatitis (AD) (ROCKET-SHUTTLE). NCT05724199. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05724199. Last accessed: November 2023.
22. Amgen. A study assessing rocatinlimab on vaccine antibody response in moderate-to-severe atopic dermatitis (AD) (ROCKET-VOYAGER). NCT05899816. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05899816. Last accessed: November 2023.
23. Amgen. Study to evaluate rocatinlimab (AMG 451) in adolescent subjects with moderate-to-severe atopic dermatitis (AD) (ROCKET-ASTRO). NCT05704738. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05704738. Last accessed: November 2023.
24. Amgen. A study to assess the safety, tolerability, and efficacy of rocatinlimab in adolescent partic-ipants with moderate-to-severe atopic dermatitis (AD) (ROCKET). NCT05633355. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05633355. Last accessed: November 2023.
25. Amgen. A study to assess long-term safety, tolerability, and efficacy of rocatinlimab in adult and adolescent participants with moderate-to-severe atopic dermatitis (AD) (ROCKET-ASCEND). NCT05882877. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05882877. Last accessed: November 2023.

Abbreviations

AD: atopic dermatitis; APC: antigen presenting cell; CI: confidence interval; EASI: Eczema Area and Severity Index; mAb: monoclonal antibody; OX40L: OX40 ligand; PBM: peripheral blood monocyte; QoL: quality of life; Q2W: every 2 weeks; Q4W: every 4 weeks; T_H: T helper.