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Study Design of Phase 3 Trials Evaluating Rocatinlimab Efficacy and Safety in Moderate-to-Severe Atopic Dermatitis: the ROCKET Program

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Introduction & Objectives:

Patients (pts) with moderate-to-severe atopic dermatitis (msAD) experience chronic symptoms resulting in significant clinical burden and impaired quality of life. Many pts fail to achieve or sustain an adequate response, cannot tolerate, and/or are not suitable for available treatment options. OX40, a key co-stimulatory molecule transiently expressed on activated effector and memory T cells, has been implicated in the pathogenesis and chronicity of AD. In a phase 2b study, rocatinlimab (AMG 451/KHK4083), an anti-OX40 monoclonal antibody that inhibits and reduces pathogenic OX40+ T cells, showed significant and progressive improvement in multiple measures of clinical severity compared with placebo, with a well-tolerated safety profile and no signs of immunosuppression (Guttman-Yassky E, et al. *Lancet*. 2023;401:204-14).

Materials & Methods:

The global ROCKET phase 3 program will evaluate rocatinlimab as monotherapy and combination therapy in 8 pivotal trials of adults and adolescents with msAD (Figure). Pts with or without prior exposure to biologics or systemic Janus kinase inhibitors (JAKi) are included. For adults with msAD, three 24-week, randomized, placebo-controlled studies will evaluate the efficacy and safety of rocatinlimab as monotherapy (IGNITE [NCT05398445], HORIZON [NCT05651711]) or in combination with topical corticosteroid and/or topical calcineurin inhibitor (SHUTTLE [NCT05724199]). ASTRO (NCT05704738) is a randomized study with an initial 24-week placebo-controlled period followed by 28-week rerandomized maintenance period evaluating the efficacy and safety of rocatinlimab as monotherapy or combination therapy in adolescents (aged ≥12 to <18 years) with msAD. The co-primary endpoints for IGNITE, HORIZON, SHUTTLE, and ASTRO are the achievement of a Validated Investigator's Global Assessment for Atopic Dermatitis (vIGA-ADTM) score of 0 (clear) or 1 (almost clear) with ≥ 2-point reduction from baseline and ≥ 75% reduction in Eczema Area and Severity Index (EASI) score from baseline at week 24. ORBIT (NCT05633355), a 52-week, open-label study, will assess the safety of rocatinlimab in adolescents with msAD. In addition, the effect of rocatinlimab on antibody responses to tetanus and meningococcal vaccinations will be evaluated in VOYAGER (NCT05899816). Adult or adolescent pts who complete a parent study (IGNITE, HORIZON, SHUTTLE, ASTRO, ORBIT, or VOYAGER) are eligible to enter ASCEND (NCT05882877), a long-term extension study evaluating the safety, tolerability, durability, and maintenance efficacy of rocatinlimab. Lastly, OUTPOST (NCT06224192) will evaluate the success of self-administered subcutaneous rocatinlimab in adults and adolescents with msAD.

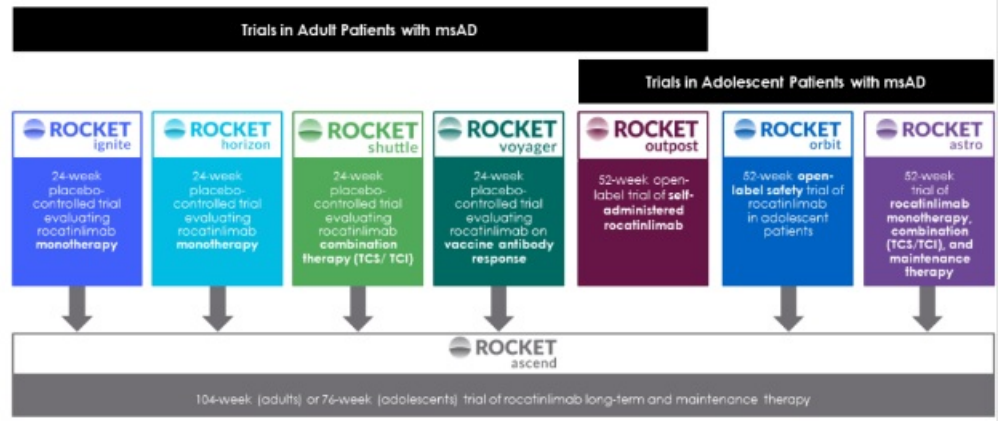
Results:

As of January 2024, ROCKET has enrolled 2235 pts from IGNITE, HORIZON, SHUTTLE (n=2065 adults), and ASTRO (n=170 adolescents). Mean (SD) age was 38.2 (14.7) and 14.7 (1.7) years for adults and adolescents, respectively, and 61.4% and 48.8% were White. Mean (SD) duration of AD was 23.3 (15.4) years in adults and 11.0 (4.8) years in adolescents. Baseline mean (SD) EASI score was 29.0 (11.1) in adults and 29.0 (10.8) in adolescents. Overall, 20.9% of adults and 14.7% of adolescents reported prior use of biologics or systemic JAKi for AD. The ROCKET program is ongoing.

Conclusion:

The comprehensive ROCKET phase 3 program will allow robust investigation of the efficacy and long-term safety of rocatinlimab in adults and adolescents with msAD.

Figure. ROCKET: Phase 3 Development Program Evaluating Rocatinlimab in Moderate-to-Severe AD



msAD, moderate-to-severe atopic dermatitis; SC, subcutaneous; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.