About the Calm-CAH Study

(CRN04894-12)

Study Purpose

The Calm-CAH Study (CRN04894-12) is a Phase 3, double-blind, placebo-controlled study evaluating the safety, efficacy, pharmacokinetics, and pharmacodynamics of an investigational drug, atumelnant, in adults living with classic congenital adrenal hyperplasia (CAH). The primary objective of this study is to reduce daily supraphysiological glucocorticoid (GC) dosage while maintaining adrenal androgen control. This global study is sponsored by Crinetics Pharmaceuticals, Inc.

About CAH

CAH is a set of autosomal recessive diseases of the adrenal glands due to genetic mutations leading to 21-hydroxylase deficiency (21-OHD). This can result in a lack of cortisol and aldosterone production, leading to lifelong adrenal insufficiency. Cortisol absence can elevate adrenocorticotropic hormone (ACTH) levels and drive excess adrenal androgen production. Prolonged exposure to elevated ACTH can cause adrenal hyperplasia and eventually hyperandrogenism, leading to premature puberty in childhood and infertility in adulthood, among other conditions.

Study Design

Participation in the study will last up to 42 weeks and enroll approximately 150 participants. The study includes up to 14 visits that will be conducted at the study site, at home if allowed and available, or over the phone. Participants will be randomized 2:1 to receive either atumelnant 80 mg or placebo, which will be taken orally once daily in the evening. An option for dose escalation to either atumelnant 120 mg or placebo 120 mg will occur later in the study. Participants who complete the 32-week treatment period of this study may be eligible to take part in a separate long-term open-label extension study.

The investigational drug, study lab tests, imaging, study procedures, and safety assessments are provided at no cost to participants. Additionally, costs for travel may be reimbursed.

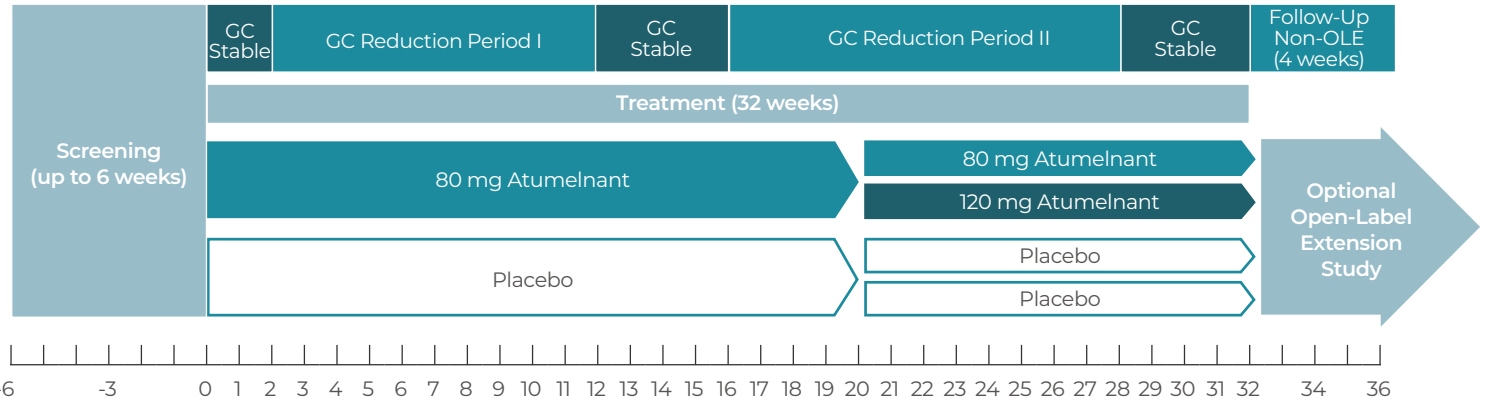
About Atumelnant

Atumelnant is a once-daily melanocortin-2 receptor (MC2R) antagonist. Atumelnant may offer a different mechanism and site (adrenal gland) of action that may allow for rapid and sustained normalization of adrenal androgens and clinically meaningful glucocorticoid reductions to physiologic levels for individuals living with CAH.

Crinetics® Pharmaceuticals

Calm-CAH

Study Schema



GC = glucocorticoid; OLE = open-label extension

About Atumelnant (cont'd)

In January 2025, Crinetics announced positive results from the TouCAHn Phase 2 sequential dose cohort study in adult individuals living with CAH. The study data showed a rapid, substantial, and sustained significant reduction in serum androstenedione (A4) levels, as well as a significant positive impact on CAH signs and symptoms. No participants in TouCAHn required dose reduction or discontinued from the study.[1]

Atumelnant is an investigational drug, and its safety and effectiveness have not been approved by any regulatory authority.

Key Eligibility Criteria

- Be between ≥ 18 and < 75 years of age
- Have classic CAH due to 21-OHD
- Be on a stable regimen of GC replacement (e.g., modified-release hydrocortisone, cortisone acetate, prednisolone, prednisone, methylprednisolone, dexamethasone)
- No history of bilateral adrenalectomy, hypopituitarism, or other condition requiring chronic GC therapy
- Other eligibility criteria will apply

Thank you for your interest in the Calm-CAH Study (CRN04894-12).

Endpoints

Primary Objective:

- To evaluate efficacy of atumelnant in reducing daily GC dosage while maintaining adrenal androgen control at the end of the 32-week treatment period

Secondary Objectives:

- To evaluate efficacy of atumelnant in reducing adrenal steroid levels and other CAH disease burden at Week 2
- To evaluate efficacy of atumelnant in reducing adrenal steroid levels and other CAH disease burden at the end of the 32-week treatment period
- To evaluate efficacy of atumelnant in reducing daily GC dosage while maintaining adrenal androgen control at the end of the 32-week treatment period

Learn More

To learn more or to refer a patient for the Calm-CAH Study, scan the QR code or visit **CrineticsCAH.com**. For questions on the mechanism of action or other studies within Crinetics' pipeline, please contact **ClinicalTrials@Crinetics.com**.

1. crinetics.com/crinetics-announces-positive-topline-results-from-phase-2-trial-of-atumelnant-in-congenital-adrenal-hyperplasia-cah

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