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Subcutaneous CINRYZE With Recombinant Human Hyaluronidase for Prevention of Angioedema Attacks

This study has been completed.

Sponsor:
Shire

Collaborator:
Halozyme Therapeutics

Information provided by (Responsible Party):
Shire

ClinicalTrials.gov Identifier:
NCT01756157

First received: June 29, 2012
Last updated: May 29, 2015
Last verified: June 2014
History of Changes

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Purpose

The primary objectives of the study are to evaluate the safety, tolerability, and efficacy of two doses of CINRYZE with recombinant human hyaluronidase (rHuPH20) administered by subcutaneous (SC) injection to prevent angioedema attacks.

Condition	Intervention	Phase
Hereditary Angioedema	Biological: CINRYZE with rHuPH20	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Intervention Model: Crossover Assignment
Masking: Double Blind (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose: Prevention

Official Title: A Phase 2, Randomized, Double-Blind, Multicenter, Dose-Ranging, Crossover Study to Evaluate the Safety and Efficacy of Subcutaneous Administration of CINRYZE® (C1 Esterase Inhibitor [Human]) With Recombinant Human Hyaluronidase (rHuPH20) for the Prevention of Angioedema Attacks in Adolescents and Adults With Hereditary Angioedema

Resource links provided by NLM:

Genetics Home Reference related topics: hereditary angioedema

Drug Information available for: Hyaluronidase SERPING1 protein, human

Genetic and Rare Diseases Information Center resources: Hereditary Angioedema

U.S. FDA Resources

Further study details as provided by Shire:

Primary Outcome Measures:

- Normalized Number of Angioedema Attacks During the Treatment Period [Time Frame: From Visit 1 (Week 1) up to Visit 16 (Week 8) during each treatment period]

  Angioedema attack was defined as the participant-reported indication of symptoms or signs such as swelling or pain at any location following a report of no swelling or pain on the previous day. Manifestations of an attack that progress from one site to another, prior to complete resolution, was considered a single attack. Attacks that began to regress and then worsened before complete resolution was also considered one attack. Participants who were dosed but did not have any attacks in the period were assigned a value of zero. The number of attacks was normalized for the number of days participants participated in a given period and expressed as the monthly frequency.

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Secondary Outcome Measures:

- Cumulative Attack-severity During the Treatment Period [Time Frame: From Visit 1 (Week 1) up to Visit 16 (Week 8) during each treatment period]

  Cumulative Attack-severity score was the sum of maximum symptom severity recorded for each angioedema attack, determined on the last day of symptoms and recorded as None=0, Mild=1, Moderate=2, and Severe=3 and summing over the unique attacks, yields a Cumulative Attack-severity score. None: no angioedema attack symptom; Mild: the angioedema attack symptom was noticeable to the participant but was easily tolerated and did not interfere with routine activities; Moderate: the angioedema attack symptom interfered with work/school or the ability to participate in family life and social activities; Severe: the angioedema attack symptom significantly limited the participant's ability to attend work/school or participate in family life and social activities. Cumulative attack-severity was normalized for the number of days participants participated in a given period and expressed as the monthly frequency. The scores ranged from 0 to 168 and higher scores represent worse symptoms.

- Cumulative Daily-severity During the Treatment Period [Time Frame: From Visit 1 (Week 1) up to Visit 16 (Week 8) during each treatment period]

  Cumulative Daily-severity score was the sum of the severity scores recorded for every day of reported symptoms during the treatment period. Severity scores were recorded as None=0, Mild=1, Moderate=2, and Severe=3. None: no angioedema attack symptom; Mild: the angioedema attack symptom was noticeable to the participant but was easily tolerated and did not interfere with routine activities; Moderate: the angioedema attack symptom interfered with work/school or the ability to participate in family life and social activities; Severe: the angioedema attack symptom significantly limited the participant's ability to attend work/school or participate in family life and social activities. Cumulative daily severity was normalized for the number of days participants participated in a given period and expressed as the monthly frequency. The scores ranged from 0 to 168 and higher scores represent worse symptoms.

- Cumulative Symptomatic Days During the Treatment Period [Time Frame: From Visit 1 (Week 1) up to Visit 16 (Week 8) during each treatment period]

  Cumulative symptomatic days was defined as the sum of the symptomatic days of each angioedema attack reported during the treatment period. Participants who were dosed but did not have any attacks in the period were assigned a value of zero. Cumulative symptomatic days was normalized for the number of days participants participated in a given period and expressed as the monthly frequency.

- Number of Angioedema Attacks Requiring Acute Treatment During the Treatment Period [Time Frame: From Visit 1 (Week 1) up to Visit 16 (Week 8) during each treatment period]

  Angioedema attack was defined as the participant-reported indication of symptoms or signs such as swelling or pain at any location following a report of no swelling or pain on the previous day. Manifestations of an attack that progress from one site to another, prior to complete resolution, was considered a single attack. Attacks that began to regress and then worsened before complete resolution was also considered one attack. Participants who were dosed but did not have any attacks in the period were assigned a value of zero. The number of attacks was normalized for the number of days participants participated in a given period and expressed as the monthly frequency.

Enrollment: 47
Study Start Date: December 2012
Study Completion Date: September 2013
Primary Completion Date: August 2013 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: SC CINRYZE with rHuPH20 Dose Level 1 followed by Dose Level 2 SC CINRYZE with rHuPH20 Dose Level 1 twice weekly (every 3 or 4 days) for 8 weeks followed by SC CINRYZE with rHuPH20 Dose Level 2 twice weekly (every 3 or 4 days) for 8 weeks.	Biological: CINRYZE with rHuPH20 Other Names: • C1 esterase inhibitor (human) • Recombinant human hyaluronidase
Experimental: SC CINRYZE with rHuPH20 Dose Level 2 followed by Dose Level 1 SC CINRYZE with rHuPH20 Dose Level 2 twice weekly (every 3 or 4 days) for 8 weeks followed by SC CINRYZE with rHuPH20 Dose Level 1 twice weekly (every 3 or 4 days) for 8 weeks.	Biological: CINRYZE with rHuPH20 Other Names: • C1 esterase inhibitor (human) • Recombinant human hyaluronidase

Eligibility

Ages Eligible for Study: 12 Years and older (Child, Adult, Senior)
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Be ≥12 years of age.
- Have a confirmed diagnosis of Hereditary Angioedema.

Exclusion Criteria:

- Receipt of any C1 inhibitor (C1 INH) therapy or any blood products for treatment or prevention of an angioedema attack within 7 days before the first dose of study drug.
- Be receiving prophylactic intravenous CINRYZE that exceeds 1000 units every 3 or 4 days (maximum weekly dose 2000 units).
- Have received any androgen therapy (e.g., danazol, oxandrolone, stanozolol, testosterone) within 7 days prior to the first dose of study drug.
- If female, have started taking or changed the dose of any hormonal contraceptive regimen or hormone replacement therapy (i.e., estrogen/progestin containing products) within 3 months prior to the first dose of study drug.
- History of allergic reaction to C1 INH products, including CINRYZE or other blood products.
- History of abnormal blood clotting.
- Have a known allergy to hyaluronidase or any other ingredient in the study formulation.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01756157

Show 23 Study Locations

Sponsors and Collaborators

Shire

Halozyme Therapeutics

Investigators

Study Director: Jennifer Schranz, MD ViroPharma

More Information

Responsible Party: Shire
ClinicalTrials.gov Identifier: NCT01756157 History of Changes
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Study First Received: June 29, 2012
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Keywords provided by Shire:
Crossover
Prevention
Hereditary Angioedema
C1 esterase inhibitor
C1 inhibitor
Subcutaneous
Recombinant human hyaluronidase

Additional relevant MeSH terms:

Angioedemas, Hereditary
Angioedema
Vascular Diseases
Cardiovascular Diseases
Genetic Diseases, Inborn
Urticaria
Skin Diseases, Vascular
Skin Diseases
Hypersensitivity, Immediate
Hypersensitivity
Immune System Diseases
Complement C1 Inhibitor Protein
Complement C1 Inactivator Proteins
Complement C1s
Complement Inactivating Agents
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs

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