ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: February 7, 2020

ClinicalTrials.gov ID: NCT03974360

Study Identification

Unique Protocol ID:	2018-003943-46
Brief Title:	Efficacy and Tolerability of Erenumab in the Prophylactic Treatment of Persistent Post-Traumatic Headache
Official Title:	An Open Label Study to Evaluate the Efficacy and Tolerability of Erenumab in the Prophylactic Treatment of Persistent Headache Attributed to Mild Traumatic Injury to the Head
Secondary IDs:	

Study Status

Record Verification:	February 2020
Overall Status:	Completed
Study Start:	April 5, 2019 [Actual]
Primary Completion:	December 31, 2019 [Actual]
Study Completion:	December 31, 2019 [Actual]

Sponsor/Collaborators

Sponsor:	Danish Headache Center
Responsible Party:	Principal Investigator Investigator: Henrik Schytz [hschytz] Official Title: Associate Professor Affiliation: Danish Headache Center
Collaborators:	Novartis Amgen

Oversight

U.S. FDA-regulated Drug:	Yes
U.S. FDA-regulated Device:	No
Product Exported from U.S.:	Yes
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 2018-003943-46 Board Name: Ethics Committee of the Capital Region of Denmark Board Affiliation: Phone:

Email:
Address:

Data Monitoring: Yes

FDA Regulated Intervention: No

Study Description

Brief Summary: An exploratory open-label study of PPTH patients to study the efficacy and tolerability of erenumab in the prophylactic treatment of persistent headache attributed to mild traumatic injury to the head. Approximately 100 subjects will be included to erenumab 140 mg. Patients who have participated in study with prior provocation (Ethics Committee of the Capital Region of Denmark (H-1801147 and H-18050498) and who have consented to be contacted will primarily be included. The study will begin February 2019 and is expected to last one year. Patients responding to advertisement (see add) will be contacted by phone.

Detailed Description: The reasons and justification of choosing an open-label design are the following:

1. To date, there are no evidence for prophylactic drugs treating post-traumatic headache. Post-traumatic headache patients are notoriously known to be refractory to prophylactic treatment and have usually tried several prophylactic drugs such as amitriptylin, which is recommended as a prophylactic drug in migraine and chronic tension-type headache, and other drugs developed for the treatment of primary headache disorders. First step is therefore to show if there is an effect at all following erenumab treatment in these refractory PPTH patients.
2. The refractory nature of PPTH will lower the bias that could occur through placebo effects.
3. The treatment period is also quite long, and the endpoint is assessed in the last month of treatment, which will also minimize a placebo effect.
4. Furthermore, this relatively small exploratory open label study is needed to show if there is an effect of erenumab in post-traumatic headache at all and what this effect is, before initiating larger multicenter double-blind studies in this patient group.

Conditions

Conditions: Post-Traumatic Headache
Mild Traumatic Brain Injury
Post-Concussion Syndrome

Keywords:

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 2

Interventional Study Model: Single Group Assignment
Exploratory Open-Label Study

Number of Arms:	1
Masking:	None (Open Label)
Allocation:	N/A
Enrollment:	100 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Erenumab 100 subjects with persistent post-traumatic headache will be allocated to receive monthly subcutaneous injections of 140 mg erenumab at three time points (week 0, week 4, week 8)	Drug: AMG 334 100 subjects with persistent post-traumatic headache will be allocated to receive monthly subcutaneous injections of 140 mg erenumab at three time points (week 0, week 4, week 8) Other Names: • Erenumab

Outcome Measures

Primary Outcome Measure:

1. Effect of Erenumab on Headache Days with Moderate or Severe Intensity
   To evaluate the effect of erenumab on change in the monthly average number of headache days with moderate or severe intensity from baseline to week 9-12 in patients with persistent post-traumatic headache (PPTH). The assessment will be made using a headache diary.

   [Time Frame: 12 weeks]

Secondary Outcome Measure:

2. Erenumab on number of Headache Days
   To evaluate the effect of erenumab on change in the monthly average number of headache days from baseline to week 9-12 in PPTH patients. The assessment will be made using a headache diary.

   [Time Frame: 12 weeks]
3. Proportion of Patient reaching at least 75% reduction in monthly average number of headache days
   To evaluate the proportion of patients reaching at least 75% reduction in the monthly average number of headache days of any severity (Time frame: baseline – week 12). The assessment will be made using a headache diary.

   [Time Frame: 12 weeks]
4. Proportion of Patient reaching at least 50% reduction in monthly average number of headache days
   To evaluate the proportion of patients reaching at least 50% reduction in the monthly average number of headache days of any severity (Time frame: baseline – week 12). The assessment will be made using a headache diary.

   [Time Frame: 12 weeks]
5. Proportion of Patient reaching at least 25% reduction in monthly average number of headache days
   To evaluate the proportion of patients reaching at least 25% reduction in the monthly average number of headache days of any severity (Time frame: baseline – week 12). The assessment will be made using a headache diary.

   [Time Frame: 12 weeks]
6. Headache Impact Test (HIT-6)
   To evaluate the mean change in disability score, as measured by the 6-item Headache Impact Test (HIT-6) from baseline – week 12.

   HIT-6 consits of six items and is a global measure of adverse headache impact to assess headache severity in the previous month and change in a patient's clinical status over a short period of time. Each of the 6 questions is responded to using 1 of 5 response categories: "never," "rarely,""sometimes," "very often," or "always." For each HIT-6

item, 6, 8, 10, 11, or 13 points, respectively, are assigned to the response provided. Subjects will complete the HIT-6 monthly at each clinical visit.

[Time Frame: 12 weeks]

7. Tolerability of Erenumab will be assessed by recording number and type of adverse events
To evaluate the tolerability of erenumab. Tolerability will be assessed by recording number and type of adverse events at each follow-up visit.

[Time Frame: 12 weeks]

Other Pre-specified Outcome Measures:

8. CGRP induced change in AUC in responders versus non-responders*
* based on data from patients involved in the CGRP provocation (Ethics Committee of the Capital Region of Denmark (H-1801147 and H-18050498). Response is defined as patients reaching at least 50% reduction in the monthly average number of headache days of any severity from baseline to week 9-12

[Time Frame: 12 weeks]

9. CGRP induced incidence of exacerbations in responders versus non-responders*
* based on data from patients involved in the CGRP provocation (Ethics Committee of the Capital Region of Denmark (H-1801147 and H-18050498). Response is defined as patients reaching at least 50% reduction in the monthly average number of headache days of any severity from baseline to week 9-12

[Time Frame: 12 weeks]

10. CGRP induced change in AUC* correlated to change in number of headache days from baseline - week 9-12
* based on data from patients involved in the CGRP provocation (Ethics Committee of the Capital Region of Denmark (H-1801147 and H-18050498). Response is defined as patients reaching at least 50% reduction in the monthly average number of headache days of any severity from baseline to week 9-12

[Time Frame: 12 weeks]

11. Headache phenotype* in responders versus non-responders
*PPTH patients will be divided into patients with a migraine phenotype or a primarily tension-type headache phenotype. Headache phenotype will be assessed using a semi-structured interview.

[Time Frame: 12 weeks]

Eligibility

Minimum Age:	18 Years
Maximum Age:	65 Years
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Men and women between 18 – 65 years who suffer from PPTH following a concussion / mild traumatic brain injury more than 12 months ago.
- Fertile women must use safe contraceptives and present with a negative u-HCG on the experimental day. Safe contraceptives are defined as intra-uterine devices, contraceptive pills or implants and surgical sterilization.

Exclusion Criteria:

- Pre-trauma primary headache disorders, including tension-type headache > 1 days/months
- Medication-overuse headache
- Whiplash injury
- Cardiovascular disease of any kind, including cerebrovascular disease

- Hypertension on the experimental day (systolic blood pressure > 150 mmHg and/or diastolic blood pressure > 100 mmHg)
- Hypotension on the experimental day (systolic blood pressure < 90 mmHg and/or diastolic blood pressure < 50 mmHg)
- Pre-trauma psychiatric disorder of any kind – unless effectively treated
- Anamnestic or clinical symptoms of any kind that are deemed relevant for study participation by the physician who examines the patient
- Pregnant or breastfeeding, or is a female expecting to conceive during the study,
- including through 4 weeks after the last dose of erenumab
- Female subject of childbearing potential who is unwilling to use an acceptable
- Method of effective contraception during treatment through 4 weeks after the last dose of erenumab. Acceptable methods of effective birth control include not having intercourse (true abstinence, when this is in line with the preferred and usual lifestyle of the subject), hormonal birth control methods (pills, shots/injections, implants, or patches), intrauterine devices, surgical contraceptive methods (vasectomy with medical assessment of the surgical success of this procedure or bilateral tubal ligation), or two barrier methods (each partner must use one barrier method) with spermicide - males must use a condom with spermicide; females must choose either a diaphragm with spermicide, OR cervical cap with spermicide, OR contraceptive sponge with spermicide. Female subjects not of childbearing potential are defined as any female who: is post-menopausal by history, defined as:
    - Age ≥ 55 years with cessation of menses for 12 or more months, OR
    - Age < 55 years but no spontaneous menses for at least 2 years, OR
    - Age < 55 years and spontaneous menses within the past 1 year, but currently amenorrheic (eg, spontaneous or secondary to hysterectomy), AND with postmenopausal gonadotropin levels (luteinizing hormone and follicle-stimulating hormone levels > 40 IU/L) or postmenopausal estradiol levels (< 5 ng/dL) or according to the definition of "postmenopausal range" for the laboratory involved. OR
        - Underwent bilateral oophorectomy OR
        - Underwent hysterectomy OR
        - Underwent bilateral salpingectomy
- Known sensitivity to any component of erenumab
- Previously randomized into an erenumab study
- Member of investigational site staff or relative of the investigator
- Unlikely to be able to complete all protocol required study visits or procedures, and/or to comply with all required study procedures to the best of the subject’s and investigator’s knowledge

Contacts/Locations

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IPDSharing

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References

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