A randomised, double-blind, parallel group Phase III study to assess the efficacy and safety of 100 mg SC depemokimab in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) - ANCHOR-1 (depemokimAb iN CHrOnic Rhinosinusitis)

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Primary objective:To evaluate the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP.Secondary Objectives:To evaluate the efficacy of depemokimab 100 mg SC + SoC compared to placebo…

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON56281

Source
ToetsingOnline

Brief title
217095 - ANCHOR-1

Condition

- Miscellaneous and site unspecified neoplasms benign
- Upper respiratory tract disorders (excl infections)

Synonym
Soft growths inside the nose; chronic inflammation of the mucous membranes in the nose or sinuses

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline B.V.

Intervention

Keyword: chronic rhinosinusitis with nasal polyps, Depemokimab, Interleukin-5, Standard of care

Outcome measures

Primary outcome

c) Change from baseline in total endoscopic NP score at Week 52 (centrally read)

a) Change from baseline in mean nasal obstruction score (verbal response scale

[VRS]) from Week 49 through to Week 52

Secondary outcome

• Change from baseline in mean symptom score for rhinorrhoea (runny nose) (VRS)

from Week 49 through to Week 52

• Change from baseline in mean symptom score for loss of smell (VRS) from Week

49 through to Week 52

• Change from baseline in Lund Mackay CT score at Week 52

• Change from baseline in SNOT-22 total score at Week 52

• Change from baseline in mean nasal obstruction score (VRS) from Week 21

through to Week 24

• Change from baseline in total endoscopic NP score at Week 26

Study description

Background summary

Nasal polyposis (NP) is a chronic inflammatory disease of the nasal passage linings and/or sinuses leading to soft tissue growth in the upper nasal cavity. The resultant swellings which can grow in both nostrils (bilateral), greatly impact a patient*s health-related quality of life through increases in nasal obstruction, loss of smell, facial pain, facial pressure and nasal discharge.
The persistence of these symptoms due to NP leads to CRS. The condition is therefore also described as CRS with NP (CRSwNP). The European Position Paper on Rhinosinusitis and NP defines the severity of disease using a total severity visual analogue scale (VAS) in which a patient is asked to indicate on a 10 cm VAS how troublesome they consider their symptoms. An overall VAS symptom score of 0-3 is defined as mild disease, >3-7 as moderate and >7-10 as severe. Symptoms are invariably accompanied with findings of inflammation of the nasal mucosa and the presence of a polyp seen through nasal endoscopy or positive imaging findings, for example using computerized tomography (CT). The aetiology of CRSwNP is currently unknown.
The current SoC for CRSwNP is treatment with saline washes, INCS and, for severe symptoms, when short term relief is required, intermittent courses of systemic corticosteroids. Antibiotic courses may also be required for intercurrent sinus infection, which often complicates severe NP. Although many patients with CRSwNP can be adequately controlled with simple medical care (INCS and oral corticosteroid [OCS], occasional nasal douching and antibiotic courses), progression to surgery as a result of severe symptoms and disruption to quality of life is common. Surgery, when ultimately indicated, involves the removal of the polyp tissue and diseased mucosa, restoring aeration of the nasal passage and sinuses. Over 250,000 NP surgeries are performed in the US annually. However, polyps have a strong tendency to recur, often requiring repeat surgery with a timescale that can vary from a few months to years. Data suggests patients with NP associated with tissue eosinophilia constitute the majority of those who have a recurrence after surgery. Repeat (revision) surgery is associated with diminishing success and a higher potential for adverse effects, hence alternative treatment options are needed for this patient group.
While the recurrence of bilateral NP despite surgery is common and known to be associated with the IL-5/eosinophilic pathway in adults, this is less so for children. The number of eosinophils and cells expressing messenger RNA for IL-4, IL-5 and IL-10 is higher in patients with CRS excluding cystic fibrosis (CF) versus those with CF and controls. Antrochoanal polyps are also another form of NP more common in children that are usually unilateral and associated with low eosinophil tissue levels.

Study objective

Primary objective:
To evaluate the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP.
Secondary Objectives:
To evaluate the efficacy of depemokimab 100 mg SC + SoC compared to placebo + SoC at Week 52 in terms of symptom scores for rhinorrhoea (runny nose) and loss of smell.
To evaluate the efficacy of depemokimab 100 mg SC + SoC compared to placebo + SoC at Week 52 in terms of the Lund Mackay CT score.
To evaluate the efficacy of depemokimab 100 mg SC + SoC compared to placebo + SoC prior to Week 26 in participants with a diagnosis of CRSwNP.

Study design

This is a randomized, double-blind, placebo-controlled, parallel group, Phase III study of depemokimab + SoC in adults with CRSwNP. The objective of the study is to evaluate the efficacy and safety of depemokimab 100 mg, administered SC by the site staff, via a pre-filled safety syringe device (SSD) every 6 months + SoC for 52 weeks. Efficacy of depemokimab will be assessed using co primary endpoints of change from baseline in total endoscopic NP score at Week 52 and change from baseline in mean nasal obstruction VRS (verbal response scale) score from Week 49 through to Week 52. Nasal surgery will be assessed from a pre-specified pooled analysis of study 217095 (this study) and study 218079.

Intervention

The study will include an approximate 4 week run-in period followed by randomization to a 52 week treatment period. Randomization will be stratified based on occurrence of previous surgery for nasal polyps and country. Participants will be randomised in a 1:1 ratio into one of the two treatment groups, receiving 100 mg of depemokimab SC + SoC or placebo + SoC for a total of 2 doses (26 weeks apart).

Study burden and risks

• Risks associated with study procedures are listed below.
- When giving blood, participants may feel faint or experience mild pain, bruising, irritation, or redness from the needle.
- It is possible that the symptoms of participants* condition will not improve during the study or may even worsen.
- The study drug is given by subcutaneous injection. This means participants will receive injections in the upper arm or thigh, directly under the skin. There is a chance participants may feel faint, or experience mild pain, bruising, irritation, or redness where the needle is placed for each injection.
- During an ECG, small sticky pads are applied to certain parts of participants

body. Some areas on which the patches are placed may need to be shaved. participants may also feel a small amount of irritation, itching, or redness on the skin after these pads are removed. This should disappear in a few days.
- During a computerized tomography (CT) scan of participant*s nose and surrounding area, participants will be exposed to X-ray radiation. It is thought that exposure to radiation during CT scans could slightly increase your chances of developing cancer. The additional risk of developing cancer as a result of this radiation exposure is around 1 in 5000.
- During nasal endoscopy participants might feel discomfort due to the pressure of the endoscope. Nasal endoscopy is a routine procedure; however, it may have rare complications like nosebleed, fainting, harmful reaction to the anaesthetic spray (if physician decides to numb participant*s nose before the procedure).
Burden:
Participants will be expected to complete 17 visits altogether. The time between each visit is approximately 4 weeks. The time between Visit 8, Visit 9 and Visit 10 is shorter, there will be approximately 2 weeks between each of these visits.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Participant is >=18 years old
2. Participant has a endoscopic bilateral NP score of at least 5 out of a maximum score of 8 (with a minimum score of 2 in each nasal cavity) assessed by the investigator
3. Participants who have had at least one of the following at Visit 1:
• previous nasal surgery for the removal of NP;
• have used at least three consecutive days of systemic corticosteroids in the previous 2 years for the treatment of NP;
• medically unsuitable or intolerant to systemic corticosteroid.
4. Participants must be on daily treatment with INCS (including intranasal liquid steroid wash/douching) for at least 8 weeks prior to screening.
5. Participants presenting with severe NP symptoms defined as symptoms of nasal congestion/blockade/obstruction with moderate or severe severity and loss of smell or rhinorrhoea (runny nose) based on clinical assessment by the investigator.
6. Presence of symptoms of chronic rhinosinusitis as described by at least 2 different symptoms for at least 12 weeks prior to Visit 1, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip), plus
• facial pain/pressure
and/or
• reduction or loss of smell
7. Male or eligible female participants:
8. Capable of giving signed informed consent

Exclusion criteria

1. As a result of medical interview, physical examination, or screening investigation the physician responsible considers the participant unfit for the study
2. Participants who have cystic fibrosis
3. Participants who have antrochoanal polyps
4. Nasal cavity tumor (malignant or benign)
5. Fungal rhinosinusitis
6. Participant has severe nasal septal deviation occluding one nostril preventing full assessment of nasal polyps in both nostrils

7. Participants who had a sino-nasal or sinus surgery changing the lateral wall structure of the nose making impossible the evaluation of nasal polyp score
8. Participants who have acute sinusitis or upper respiratory tract infection at screening or in 2 weeks prior to screening
9. Participants who have ongoing rhinitis medicamentosa (rebound or chemical induced rhinitis)
10. Participants who have had an asthma exacerbation requiring admission to hospital within 4 weeks of Screening
11. Participants who have undergone any intranasal and/or sinus surgery within 6 months prior to Visit 1; nasal biopsy prior to Visit 1 for diagnostic purposes only is excepted.
12. Participants where NP surgery is contraindicated in the opinion of the Investigator
13. Participants with other conditions that could lead to elevated eosinophils such as hyper-eosinophilic syndromes including (but not limited to) EGPA (formerly known as Churg-Strauss Syndrome) or Eosinophilic Esophagitis
14. Participants with a known, pre-existing parasitic infestation within 6 months prior to Visit 1
15. Participants with a known immunodeficiency (e.g. human immunodeficiency virus - HIV), other than that explained by the use of corticosteroids (CSs) taken as therapy for asthma
16. Participants with a current malignancy or previous history of cancer in remission for less than 12 months prior to screening (NOTE: Participants that had localised carcinoma of the skin which was resected for cure will not be excluded).
17. Participant is ineligible if any of the following hepatic characteristics are present:
• Alanine aminotransferase (ALT) >2x ULN
• Total bilirubin >1.5x ULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%)
• Cirrhosis or current unstable liver or biliary disease per investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminaemia, oesophageal or gastric varices, persistent jaundice.

18. Other Concurrent Medical Conditions: Participants who have known, pre-existing, clinically significant cardiac, endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, haematological or any other system abnormalities that are uncontrolled with standard treatment.
19. Vasculitis: Participants with current diagnosis of vasculitis. Participants with high clinical suspicion of vasculitis at screening will be evaluated and current vasculitis must be excluded prior to enrolment.
20. Participants with allergy/intolerance to the excipients of depemokimab in Section 6.1, a monoclonal antibody, or biologic.
21. Participants that, according to the investigator's medical judgment, are likely to have active COVID-19 infection must be excluded. Participants with known COVID-19 positive contacts within the past 14 days must be excluded for at least 14 days following the exposure during which the participant should

remain symptom-free. Reported smell/ taste complications from COVID-19 must be used as exclusion.
22. Participants that have been exposed to ionising radiation in excess of 10mSv above background over the previous 3-year period as a result of occupational exposure or previous participation in research studies

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-12-2022
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Depemokimab
Generic name:	depemokimab

Ethics review

Approved WMO

Date:	15-03-2022
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	15-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-05-2024
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	-
EudraCT	EUCTR2021-005037-16-NL
CCMO	NL79949.018.22