A prospective study to evaluate the safety and efficacy of AdvaCoat Mx sinus gel for treatment of chronic rhinosinusitis without nasal polyps.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON32392

Source
ToetsingOnline

Brief title
AdvaCoat Mx sinus gel study for chronic rhinosinusitis without nasal polyps

Condition

- Respiratory tract infections

Synonym
Chronic rhinosinusitis, chronic sinusitis

Research involving
Human

Sponsors and support

Primary sponsor: Carbylan BioSurgery, Inc.

Source(s) of monetary or material Support: het onderzoek wordt door de sponsor gefinancierd

Intervention

Keyword: Chronic Rhinosinusitis, Chronic sinusitis, Corticosteroid, Triamcinolone Acetonide

Outcome measures

Primary outcome

Safety;

- number, severity and product related 'adverse events'.

Secondary outcome

Efficacy;

- Percent change from baseline in total of subjective symptom evaluations

(using questionnaires)

- Change from baseline in CT-scan score

Study description

Background summary

Chronic rhinosinusitis (CRS) is a common disease, affecting 5 to 15% of urban populations in Europe and approximately 12% of Americans under the age of 45 years. CRS is differentiated, though not clearly, as with or without nasal polyps. Assessment of CRS for diagnostic evaluation and for the clinical studies should include both subjective and objective measures to determine the degree and duration of symptoms. Patients will score symptoms using a visual analogue scale to measure subjective symptoms scores associated with chronic sinusitis. Furthermore, CT scans and endoscopy have been widely used for diagnosis and management of CRS.

Treatment of CRS includes topical and oral corticosteroids, oral antibiotics, nasal decongestants, saline nasal and antral irrigations, antimycotics, antihistamines, cromones and endoscopic surgery. Studies provide evidence to suggest that CRS should be treated with a rigorous medical regimen before surgery is considered. Indeed, relapse of symptoms may be prevented or

inhibited with medical therapy for a sustained period of time to delay or prevent surgery. The goal of surgery is to facilitate sinus drainage, generally by widening the sinus ostia and removing anatomic obstructions. Surgery should be reserved for patients refractory to medical therapy. There is evidence that the endoscopic sinus surgery is effective in improving symptoms and quality of life in adult patients with CRS.

Various hyaluronan based biomaterials are now available and in common use to provide a post-surgical nasal dressing. In addressing the issue of failed medical therapy for CRS, a combination of a steroid with a hyaluronan applied to the sinonasal tissues is considered for treatment of chronic rhinosinusitis refractory to medical therapy.

The AdvaCoat Mx gel is intended to alleviate the symptoms of CRS after a single application. To support safety, biocompatibility testing of the materials was conducted in accordance with ISO 10993 Guidelines for the Biological Evaluation of Medical Devices, and included cytotoxicity, irritation, sensitization and acute toxicity. These tests demonstrated the device component of AdvaCoat Mx gel to be biocompatible.

Study objective

The purpose of the first part of the study is the evaluation of the first 9 subjects that will be conducted to confirm the 1.5 mL AdvaCoat Mx treatment volume per side as the desired volume for the expanded portion of the study.

The purpose of the second part of this study is to evaluate the safety and efficacy of AdvaCoat* Mx sinus gel. 80 subjects will be blinded in a three arm study that will compare the safety and efficacy of AdvaCoat Mx to placebo gel and saline placebo in a 2:1:1 randomization.

AdvaCoat Mx is a sustained release formulation of triamcinolone acetonide (TA) applied to the ostiomeatal complex (OMC) for the relief of symptoms associated with chronic rhinosinusitis. Upon application, the AdvaCoat Mx forms a gel conforming to mucosal surfaces. The anticipated symptom relief from a single dose is due to the sustained anti-inflammatory action of TA made possible by the physical form of the product which provides localization and retention at the OMC. The product has been developed to reduce the symptoms for CRS. The current treatment of CRS (nasal spray with corticosteroids) has been used for a long period of time, but is not well able to reach the ostiomeatal complex and to result in relief of teh symptoms. The sponsor and the investigators hope to prove that the product is safe and effective in reducing the symptoms for CRS.

Study design

The study will initiate as an open-label, AdvaCoat Mx volume escalation

evaluation of nine (9) subjects (9 subject cohort). The planned AdvaCoat Mx volumes are 0.5 mL per side (1.0 mL total volume delivered), 1.0 mL per side (2.0 mL total volume delivered) and 1.5 mL per side (3.0 mL total volume delivered), to be delivered to each side of the Ostiomeatal Complex (OMC). The evaluation of all subjects in the 9 subject cohort will be completed prior to initiation of the blinded portion of the study (80 subject cohort). The 9 subject cohort is intended to confirm 1.5 mL AdvaCoat Mx per side as the desired volume for the 80 subject cohort. In the absence of any treatment related and/or serious adverse events, patients in the second part of the trial will be treated with 1.5 ml AdvaCoat Mx per side.

Subjects in the first part of the trial will be treated with AdvaCoat Mx on each side of the OMC as follows (two treatments per subject):
- 3 subjects will be treated with 0.5 mL per side (1.0 mL total volume delivered) AdvaCoat Mx.
- After 1 week post-treatment of the third subject receiving 0.5 mL per side of AdvaCoat Mx, 3 additional subjects will be treated with 1.0 mL per side (2.0 mL total volume delivered) of AdvaCoat Mx.
- After 1 week post-treatment of the third subject receiving 1.0 mL per side AdvaCoat Mx, 3 additional subjects will be treated with 1.5 mL per side (3.0 mL total volume delivered) of AdvaCoat Mx.
- After 1 week post-treatment of the third subject receiving 1.5 mL per side of AdvaCoat Mx, the sponsor will review any reported adverse events to confirm acceptability of proceeding with treating 80 subjects in the blinded portion of the study with 1.5 mL per side (3.0 mL total volume delivered) of AdvaCoat Mx.

Subjects will return for post-treatment follow-up at 1, 2 and 4 weeks. Daily pain medication logs will be completed by the subject at home for the duration of the study. Adverse events will be solicited at all visits.

The second part of the study is a prospective, multicenter, randomized, controlled, single-blinded study to evaluate the safety and efficacy of AdvaCoat* Mx sinus gel for the treatment of chronic rhinosinusitis without nasal polyps.

The eligible patients will be treated as follows;
- If the patient fulfills all inclusion and exclusion criteria the sinus where the gel will be applied will be cleared using suction.
- the patient will be randomised to teh control or treatment group (AdvaCoat gel : placebo gel : placebo saline = 2:1:1).

Control group:
- Placebo (saline) will be applied to the ostiomeatal complex
- Placebo gel (only the gel componen of the AdvaCoat gel) will be applied to the ostiomeatal complex

Treatment group:

- The AdvaCoat gel will be applied to teh ostiomeatal complex

The patients will be followed for 12 weeks and need to visit the hospital at 2, 8 and 12 weeks after the treatment for follow-up visits.

Intervention

In total 89 patients will participate in this clinical trial. Half the 80 patient cohort will be treated with AdvaCoat, one quarter will be treated with the placebo gel and one quarter with the placebo saline.

Study burden and risks

Potential risks associated with the use of AdvaCoat Mx may include those events that have been reported in association with other absorbable hyaluronan nasal dressings. Potential risks to subjects in this study include, but are not limited to, the following: nasal obstruction, headache, epistaxis, infection and local irritation or sensitivity to the product.

Potential adverse reactions which may be associated with any corticosteroid therapy include conditions which affect the following systems: fluid and electrolyte balance, musculoskeletal, gastrointestinal, dermatologic, endocrine, ophthalmic, metabolic and other areas.

The patients need to visit the hospital 5 times. During the follow-up visits, they only need to answer a few questions. The 80 patient cohort needs to complete a questionnaire as well and during the visit at 8 weeks another CT scan will be performed. At the last visit, all patients need to have another endoscopy. However, this will not be much of a burden for the patients.

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. Diagnosis of CRS defined as:
- Symptoms present for >12 consecutive weeks
- At least two of the following:
* Anterior and/or posterior mucoid drainage
* Nasal congestion
* Facial pain / pressure / fullness
- Both of the following:
* Nasal endoscopic examination confirming inflammation and/or edema of the ostiomeatal complex without the presence of polyps and/or previous sinus surgical procedures
* Evidence of CRS on CT (minimum score of 4 with at least two points coming from the sinuses; reference Table 1 for grading scale);2. Average score of 40-80 mm on the Patient Subjective Symptom Score (PSSS) at the end of the run-in period
3. 18 - 85 years of age
4. Adequate access for application of 3.0 mL of material (1.5 mL per side) onto Ostiomeatal Complex (OMC)
5. Willing and able to return for all required follow-up study visits and complete study diary and questionnaires.
6. Signed an informed consent form
7. Females of childbearing potential are not pregnant or lactating and agree not to become pregnant for the duration of the study

Exclusion criteria

1. Unilateral sinus disease
2. Evidence of polyps within or beyond the middle meatus by nasal endoscopy
3. Samter*s Triad
4. Previous or planned nasal or sinus surgery, including sinuplasty

5. Steroid dependent asthma
6. A known sensitivity to hyaluronan products, corticosteroids or any excipients contained within the formulation of Kenacort A-10
7. Cystic fibrosis or any immune deficiency that may interfere with wound healing
8. Any disease or condition that interferes with safe completion of initial or follow-up assessments
9. Anatomical abnormalities within middle meatus by endoscopy
10. Current evidence of sinus mucocele
11. Nasal intubation within 4 weeks of study run-in period (Day -7)
12. Wegener*s granulomatosis or sarcoidosis
13. Suspicion of sinonasal neoplasm
14. Use of nasal irrigation during study duration
15. Use of systemic corticosteroids within 4 weeks of study run-in period (Day -7)
16. Pregnant or planning to get pregnant
17. Current use of orally inhaled corticosteroids
18. Active sinus infection as evidenced by frank purulence/pus
19. Current or planned use of systemic antibiotics
20. PRN use of nasal corticosteroids, oral and/or nasal decongestants/antihistamines, leukotriene inhibitors, and/or mast-cell stabilizers (i.e., all medications must be stable dosing for 14 days prior to study run-in period (Day -7)).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-10-2008
Enrollment:	49
Type:	Actual

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-09-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-10-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2008-004226-16-NL
CCMO	NL23740.040.08