GAG-therapy Efficacy Trial Solution for Bladder pain syndrome/ Interstitial cystitis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON54024

Source
ToetsingOnline

Brief title
GETSBI study

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
Bladder pain, urinary frequency

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Goodlife Pharma BV

Intervention

Keyword: bladder pain, BPS-IC, GAG therapy, interstitial cystitis

Outcome measures

Primary outcome

Primary outcome parameter: change from baseline in VAS pain score (3d average and maximal pain score).

Secondary outcome

Secondary outcome parameters:

- Change from baseline in VAS score (0-10) on self-reported secondary symptoms
- Change from baseline from self-reported Global Assessment of Improvement (Likert scale)
- Change from baseline from O*Leary-Sant IC Symptom Index & Problem Index questionnaire
- Change from baseline in urethrocystoscopical evaluation of bladder mucosa (inflammation, active Hunner lesions) (clinician assessed estimated % of inflammation & degree of inflammation)
- Change from baseline in Quality of Life using ED-5D 5L questionnaire (Dutch)
- Cost effectiveness analyses using iMCQ and iPCQ questionnaires
- Changes in Patient Reported Outcome questionnaire (incl. urinary frequency)
- Adverse events using Clavien-Dindo system

Study description

Background summary

Reimbursement of GAG-therapy for bladder pain syndrome / interstitial cystitis patients with Hunner lesion subtype (BPS-IC H+) is under debate, as evidence regarding its efficacy and cost-effectiveness is lacking.

Study objective

Main objective is to determine short and long term efficacy of GAG therapy (bladder instillations) for people with BPS-IC H+ as compared to placebo treatment on dominant symptoms such as pain. Secondary objectives are to determine the 1) cost-effectiveness of GAG therapy, 2) effectiveness of GAG therapy on quality of life and bladder inflammation evaluated by urethrocystoscopy

Study design

Multi-design study.

study is powered and set-up as double-blinded randomized intervention study and is extended with a double-blinded aggregated N-of-1 trial. As requested by the Zorginstituut Netherlands, the study will be further extended with a prospective, non-blinded intervention study to evaluate long term follow up with a low frequency therapy dose.

Intervention

GAG bladder instillations (hyaluronic acid + chondroitin sulfate; Ialuril) 50ml administered with a catheter. Placebo will be artificial Tears (three options: Hypromellose 0,3% (Artelac), Hypromellose 3mg/Dextran 70mg (Duratears) en Povidon 20mg (Protagens), with these products an 50mL placebo instillation will be made and administred per katheter. There are 3 periods of 6 wks with frequency of 1 instillation/wk (ratio intervention/placebo is 2:1). With wash-out periods 4 wks. After 3 periods of treatment / placebo (wk 30), blinding will cease and continue unblinded where all subjects will receive maintenance therapy Ialuril for 1x/4wk until 54 weeks (endpoint).
If needed (e.g. vacation patient), the wash-out period can be extended and the start of the treatment period postponed for a maximum of 5 weeks, minimal wash-out period of 4 weeks.

During the study we found out the production of articifial tears is very unstable and results in many delivery and storage problems. In the normal clinic the Pharmacist changes between artificial tears to prescribe (depending on availability). Because of this we have decided to have three placebo options, in case of storage Artelac is the first choice, followed by Duratears and final Protagens. In this way the study is less vunerable and continuity is maintained. On 29th of July 2022 we had to change the placebo acutely to another product because the production was stopped because of economical

issues.

Study burden and risks

All participants are capacitated adults and will receive a similar amount of intervention and placebo treatments. Treatment corresponds to the Dutch NVU guideline BPS. Therapy will be reimbursed for patients. During 54wks, patients will have a 6 week period where placebo is given. Due to the study design, patients can obtain a personal (individual) study efficacy result if therapy was successful in him/her.

Therapy and placebo: risks and burden

This study will be submitted as low-intervention trial. GAG therapy (instillations) has been used for >25 yrs in clinical practice to treat BPS-IC. GAG-therapies are registered as medical devices. The therapy is instilled into the bladder using a catheter (by nurse / patient). Catherization has a small increased risk for developing an urine tract infection (1.9%) [Herr 2015], urethral discomfort and in rare cases urethral trauma.

The placebo compound artificial tears are used as moisturizing drops to treat dry eyes. It is inert (non-irritating and hypo-allergenic). All artificial tears have no active compound, because the production of the tears is unstable we have included three possible options to use as placebo: In the first place: Hypromellose 0.3%, secondly Hypromellose/dextran and lastly Povidon 20mg. Rare side effects are reported in the Dutch *Farmacologisch Kompas*. They report local side effects of sensitivity (burning, itch, tears e.d.). Blurry vision. and very rare systemic effects as rash, itch.
Because of these reported side effects at inclusion the (over)sensitivity is checked by one drop in an eye, taking into account the possible blurry vision afterwards. In principle the Hypromellose 0.3% is checked for sensitivity, hence if in storage this is the first choice of placebo. If another drop is used as a placebo, together with the physician will be decided if that needs to be checked for sensitivity as well.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1) Adult patients (18 yrs or older) with symptomatic BPS with established Hunner lesions objectified with urethrocystoscopy in the 3 months prior to inclusion.
2) A VAS pain score (maximum pain during the last 3 days; scale 0-10) of at least 4.

Exclusion criteria

1) pain, discomfort in pelvic region of inflammatory bladder conditions due to any cause other than BPS with Hunner lesions, 2) a urine tract infection in the previous 6 weeks 3) received bladder instillations for BPS in the previous 3 months 4) received intradetrusor Botulinum toxin (BOTOX) injections within the previous 12 months 5) received transurethral coagulation/ablation therapy of Hunner lesions within the last 12 months 6) started a new treatment for (chronic) pain (pharmacotherapy) or urine tract infection in the last month. 7) Unable (also legal) to give informed consent. 8) Allergy/Sensibilisation for artificial tears (this will be tested by applying one drop in one eye).

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-10-2021
Enrollment:	80
Type:	Actual

Medical products/devices used

Generic name:	GAG therapy (bladder instillations); ialuril® Prefill
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	20-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-10-2021

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL76290.091.20