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Comparative study about the distribution of Ialuril® in the bladder wall using a normal catheter or a specific device named Ialuadapter®

Submission date
16/02/2021

Recruitment status
No longer recruiting

Registration date
03/03/2021

Overall study status
Completed

Last Edited
19/04/2022

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Ialuril® is a solution that contains components that are present in the healthy bladder walls. It has been observed that the loss of these components is associated to an increase of inflammation and infection (e.g. in cystitis due to different causes, bladder pain syndrome, recurrent urinary tract infection). This study is not aimed at assessing the effect of Ialuril®, but at assessing its distribution on the bladder wall using different instillation device, i.e. normal catheter vs Ialuadapter®.
The main aim of the study is to compare the distribution of Ialuril® solution in the bladder wall after instillation using the standard modality (catheter) or using a specific device named Ialuadapter.
A solution with Methylene Blue will also be instilled to stain Ialuril® adsorbed onto the bladder wall. The coloration of the bladder walls will permit to evaluate the performance of the device used for the instillation.

Who can participate?
Healthy women (all investigations) and female patients with damaged bladder (pilot 2 investigation only), aged 18-55 years inclusive.

What does the study involve?
The investigation plan foresees 3 parts, each with 2 periods separated by a wash-out interval of at least 7 days. The minimum investigation duration for each subject will be 16 days, screening period included. Written informed consent will be obtained before any investigation assessment or procedure.
The following phases, visits and procedures will be performed:
Screening phase: Screening – visit 1: between day -21 and day -7
Interventional phase:
Period 1 – visit 2: days 1
Wash-out interval of at least 7 days

Period 2 – visit 3: day 1
Final phase: Visit 4: final visit/early termination visit (ETV).

What are the possible benefits and risks of participating?
No specific benefits for the healthy or patients subjects participating in the current study are foreseen, except for the medical screening..
Ialuril® Pre-fill device will be administered using a catheter or Ialuadapter®, according to the clinical practice. No risks for the subjects are foreseen considering that all administrations will be performed by qualified personnel with a long experience in this field. Ialuril® Prefill is usually well tolerated and causes few, if any, adverse reactions. Occasionally subjects could experience local reactions (irritation, burning) as a result of the instillation procedure itself, rather than from the device. Cystoscopy could cause some discomfort to the subjects. However the personnel performing the procedure are well qualified and experienced and only minor discomfort is expected.

Where is the study run from?
The study is being run by and takes place at CROSS Research Phase I Unit, Switzerland and at Service for gynaecology and obstetrics, Regional Hospital, Mendrisio, Switzerland

When is the study starting and how long is it expected to run for?
June 2019 to August 2021

Who is funding the study?
IBSA Institut Biochimique SA (Switzerland)

Who is the main contact?
Milko Radicioni, MD
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
18CH-IAev11 (CRO-18-140)

Study information

Scientific Title
Adsorption of Ialuril® onto the bladder wall - A comparative investigation in healthy women between administration using a catheter and administration using Ialuadapter®

Study objectives
The present investigation has been designed to evaluate, through staining by methylene blue of Hyaluronic acid and Chondroitin sulphate components, the extent to which Ialuril® is actually adsorbed onto the bladder wall of healthy women administered the products by intravesical instillation.
The evidence gained from preliminary in vitro experiments and present in the literature support the selective methylene blue staining of the two glycosaminoglycans (GAGs), whereas the normal urothelium should not be bound .

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/06/2019, Ethics Committee of Canton Ticino (c/o Ufficio di sanità, Via Orico 5, 6501 Bellinzona, Switzerland; +41 91 814 30 57; dss-ce@ti.ch), ref: 3452, project ID: 2019-00363

Study design
Single dose three-part (2 pilot investigations and main investigation) 2-way cross-over main investigation randomized and exploratory investigation

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Evaluation of product adsorption onto the bladder walls of healthy women and patients with damaged bladder epithelium

Interventions
Pilot 1 investigation:
On day 1 of two periods, 3 subjects will receive by intravesical instillation a single dose of 20 mL Methylene blue 0.1% using Ialuadapter® in the first period (MT1) and through a catheter in the second period (MR1). . 30 min before Methylene blue administration, 50 mL saline solution will be intravescically instilled using Ialuadapter® in the first period and through a catheter in the second period. Three (3) other subjects (Group 2) will receive Ialuril® by intravesical instillation using Ialuadapter® (IMT1) in the first period and through a catheter (IMR1) in the second period. Ialuril® will be administered as a single dose of 50 mL in each period, on day 1. Thirty (30) min after the administration of Ialuril®, 20 mL of 0.1% Methylene Blue will be administered using Ialuadapter® in the first period and through a catheter in the second period.
A wash-out interval of at least 7 days will separate the two investigation periods' administrations.

Pilot 2 investigation:
On day 1 of the two periods, the enrolled subjects (3±1 healthy volunteers and 3±1 patients) will receive by intravesical instillation through a catheter 50 mL physiological (saline) solution in period 1 and 50 mL Ialuril® in period 2. Thirty (30) min after the administration of the saline solution (period 1) or Ialuril® (period 2), 20 mL of 0.1% Methylene Blue will be administered.
A wash-out interval of at least 7 days will separate the two investigation periods' administrations.

Main investigation:
Subjects will be assigned to two treatment sequences, i.e. T2R2 or R2T2 to receive Ialuril® by intravesical instillation using Ialuadapter® (T2) and through a catheter (R2) in the two main investigation periods according to the randomisation list and the crossover design. A wash-out interval of at least 7 days will separate the two periods' administrations.
In each period, on day 1, Ialuril® will be administered as a single dose of 50 mL. Thirty (30) min after the administration of Ialuril®, 20 mL of 0.1% Methylene Blue will be administered by intravesical instillation using the same method (Ialuadapter® or catheter) used for the intravesical instillation of Ialuril®.

All three investigation parts:
In pilot 1 and main investigation, cystoscopy will be performed approximately 30 min after Methylene blue administration (i.e. 60 min after Ialuril® or saline solution administration, as applicable). In pilot 2 investigation, cystoscopy will be performed approximately 60 min after Methylene blue administration. In all three investigation parts, from the end of administration of Ialuril® or saline solution, as applicable, to the cystoscopy, the subjects will be supine in bed and asked to rotate slightly to the left and to the right, alternatively.

Intervention Type
Device

Phase
Phase I

Drug/device/biological/vaccine name(s)

Ialuril® Prefill with Luer-Lock Adapter and Ialuadapter®

Primary outcome measure
Bladder walls stain distribution and intensity by cystoscopy imaging after Ialuril® administration followed (after 30 minutes) by Methylene blue administration using Ialuadapter® (Test treatment; T2) and through a catheter (Reference treatment; R2)

Secondary outcome measures
1. Treatment-Emergent Adverse Events (TEAEs) collected using specific data capture forms filled in by the Investigator during the study from screening up to Final Visit /ETV
2. Device Deficiencies (DDs) collected using specific data capture forms filled in by the Investigator during the study from screening up to Final Visit /ETV
3. Local tolerability at the administration site measured by collecting comments made by the subjects regarding discomfort or any other inconvenience during and after instillation
4. Physical abnormalities collected using specific data capture forms filled in by the Investigator during the study from screening up to Final Visit /ETV
5. Vital signs (blood pressure and heart rate) measured at screening, on day 1 and final visit/ETV
6. Body weight (kg) measured at screening and final visit/ETV
7. Safety laboratory analysis results measured at the screening visit and final visit/ETV

Overall study start date
12/06/2019

Completion date
30/12/2021

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the investigation
2. Sex and Age: women, 18-55 years old inclusive
3. Body Mass Index (BMI): 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 50-90 bpm, measured after 5 min at rest in the sitting position
5. Full comprehension: ability to comprehend the full nature and purpose of the investigation, including possible risks and side effects; ability to co-operate with the investigator and to comply with the requirements of the entire investigation
6. Contraception and fertility: women of child-bearing potential must be using at least one of the following reliable methods of contraception:
6.1. Hormonal oral, implantable, transdermal, or injectable contraceptives for at least 2 months before the screening visit
6.2. A non-hormonal intrauterine device [IUD] or female condom with spermicide or contraceptive sponge with spermicide or diaphragm with spermicide or cervical cap with spermicide for at least 2 months before the screening visit
6.3. A male sexual partner who agrees to use a male condom with spermicide
6.4. A sterile sexual partner
Women of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted. For all women, pregnancy test result must be negative at screening and day 1.

Additional inclusion criteria for Pilot 2 part only:
7. Patients with damaged bladder epithelium due to chronic cystitis, interstitial cystitis or painful bladder syndrome

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Female

Target number of participants
24

Total final enrolment
12

Key exclusion criteria
1. Electrocardiogram (ECG 12-leads, supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with the objectives of the investigation
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Urinary diseases: presence of any specific urinary symptoms detected through questioning at Screening during the physical examination visit, except for the patients enrolled in pilot 2 part (see inclusion criterion N. 7)
5. Bladder status: Bladder urine volume after spontaneous urination before treatment ≥ 100 mL as detected by suprapubical ultrasound examination (day 1)
6. Infection history: history of bacterial urinary tract or bacterial or fungal vaginal infections for 3 weeks before the screening visit, except for the patients enrolled in pilot 2 part (see inclusion criterion N. 7)
7. Systemic infections: bacterial or fungal infections that may interfere with the aim of the investigation or affect the subject’s safety (positive urino-culture for E.coli, other gram negative bacteria, Staphylococcus spp, Streptococcus spp, Enterococcus spp, Corynebacterium spp or Yeasts), except for the patients enrolled in pilot 2 part (see inclusion criterion N. 7)
8. Urethral opening conditions: altered urethral opening conditions affecting the site of insertion (e.g. irritation or other).
9. Allergy: ascertained or presumptive hypersensitivity to the active principle and/or formulations' ingredients of the investigational product, to Methylene Blue (AxP) or to any other thiazine dies; history of anaphylaxis to drugs or allergic reactions in general, which the investigator considers may affect the outcome of the investigation
10. Diseases: moderate or severe renal disease or significant history of urinary tract, hepatic,

gastrointestinal, cardiovascular, respiratory, skin, hematological, endocrine, psychiatric or neurological diseases that may interfere with the aim of the investigation and in particular asthma, anemia (Hb values < 11 g/dL), deficiency of glucose-6-phosphate dehydrogenase, deficiency in nicotinamide adenine dinucleotide phosphate, or abnormal urinary function. . For pilot 2 part only: damaged bladder epithelium due to chronic cystitis, interstitial cystitis or painful bladder syndrome is allowed (see inclusion criterion N. 7)
11. Medications: medications, including over-the-counter medications and herbal remedies for 2 weeks before the start of the investigation. Concurrent or previous treatment, within 2 weeks before screening, with any of the prohibited psychiatric medications that may interact with methylene blue as listed in the drug safety alert published by the US FDA, which include selective serotonin reuptake inhibitors (SSRI), serotonin-norepinephrine reuptake inhibitors (SNRI), tricyclic anti-depressants or monoamine oxidase A inhibitors, other psychiatric drugs, bupropion, buspirone, clomipramine, mirtazapine and venlafaxine. Previous or concomitant treatment with fluoxetine within 5 weeks prior to screening, and/or previous or concomitant treatment with anticoagulants or antiaggregant agents inducing an international normalized ratio (INR) > 1.5. Hormonal contraceptives will be allowed. Treatments taken by the patients enrolled in Pilot 2 part for chronic cystitis, interstitial cystitis or painful bladder syndrome will be allowed according to the investigators opinion
12. Investigative drug or medical devices studies: participation in the evaluation of any investigational product or medical device for 3 months before this investigation. The 3-month interval is calculated as the time between the first calendar day of the month that follows the last visit of the previous investigation and the first day of the present investigation
13. Drug, alcohol: history of drug or alcohol abuse
14. Drug test: positive result at the drug test at screening
15. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this investigation
16. Pregnancy: positive or missing pregnancy test at screening or day 1, pregnant or lactating women

Date of first enrolment
01/01/2020

Date of final enrolment
30/08/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research Phase I Unit, Switzerland
Via F. A. Giorgioli 14
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Study participating centre
Service for gynaecology and obstetrics, Regional Hospital, Mendrisio
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Funder(s)

Funder type
Industry

Funder Name
IBSA Institut Biochimique (Switzerland)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
30/12/2022

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date