



Clinical trial results:

Phase III, randomized, open-label, multicenter evaluation of efficacy and tolerability of Ialuril (sodium hyaluronate-chondroitin sulfate) vs. dimethyl sulfoxide (DMSO) in women with interstitial cystitis / painful bladder syndrome (IC / BPS)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2010-021556-25 |
| Trial protocol | IT |
| Global end of trial date | 30 September 2013 |

Results information

| | |
|-----------------------------------|-----------------------------------|
| Result version number | v1 (current) |
| This version publication date | 21 March 2019 |
| First version publication date | 21 March 2019 |
| Summary attachment (see zip file) | cervigni-2016 (cervigni-2016.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | IBSA 01-2010 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | IBSA Institut Biochimique SA |
| Sponsor organisation address | Via del Piano 29, Pambio-Noranco, Switzerland, 6915 |
| Public contact | Valeria Frangione, IBSA Institut Biochimique SA, +41 583601000, valeria.frangione@ibsa.ch |
| Scientific contact | Valeria Frangione, IBSA Institut Biochimique SA, valeria.frangione@ibsa.ch |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 08 January 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 September 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 September 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was the assessment of the efficacy of Ialuril as compared to DMSO (RIMSO-50) in patients suffering from BPS/IC

Protection of trial subjects:

No other intravesical drug was allowed throughout the study, either during the treatment or during the follow-up period.

No other restrictions in prior or concomitant therapy were considered in the protocol.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 30 June 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 3 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Italy: 110 |
| Worldwide total number of subjects | 110 |
| EEA total number of subjects | 110 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 91 |
| From 65 to 84 years | 18 |

| | |
|-------------------|---|
| 85 years and over | 1 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Italy

FPFV: 30-Jun-2011

LPLV: 30-Sep-2013

Pre-assignment

Screening details:

110 female patients older than 18 with diagnosis of BPS/IC were screened

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | Study Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ialuril |

Arm description:

intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ialuril |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Intravesical solution |
| Routes of administration | Intravesical use |

Dosage and administration details:

intravesical instillation every 7 days for a total of 13 instillations over 3 months

| | |
|------------------|------|
| Arm title | DMSO |
|------------------|------|

Arm description:

intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment

| | |
|--|-----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | RIMSO-50 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Intravesical solution |
| Routes of administration | Intravesical use |

Dosage and administration details:

one instillation every 7 days for a total of 13 instillations, over 3 months

| Number of subjects in period 1 | Ialuril | DMSO |
|---------------------------------------|---------|------|
| Started | 74 | 36 |
| Completed | 59 | 29 |
| Not completed | 15 | 7 |
| Consent withdrawn by subject | 5 | 3 |
| Adverse event, non-fatal | 1 | 2 |
| Lost to follow-up | 6 | - |
| Lack of efficacy | 2 | 2 |
| Protocol deviation | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | Ialuril |
| Reporting group description: intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment | |
| Reporting group title | DMSO |
| Reporting group description: intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment | |

| Reporting group values | Ialuril | DMSO | Total |
|---|---------|---------|-------|
| Number of subjects | 74 | 36 | 110 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 50.95 | 48.78 | |
| standard deviation | ± 14.97 | ± 17.70 | - |
| Gender categorical Units: Subjects | | | |
| Female | 74 | 36 | 110 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | Ialuril |
| Reporting group description: intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment | |
| Reporting group title | DMSO |
| Reporting group description: intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment | |

Primary: VAS pain reduction

| | |
|--|--------------------|
| End point title | VAS pain reduction |
| End point description: | |
| End point type | Primary |
| End point timeframe: at 6 months (end of follow-up) versus baseline | |

| End point values | Ialuril | DMSO | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 36 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | 39.15 (± 29.14) | 30.36 (± 30.53) | | |

Statistical analyses

| | |
|--|------------------------|
| Statistical analysis title | Primary Endpoint |
| Statistical analysis description: Difference Ialuril vs. RIMSO-50 in VAS pain reduction | |
| Comparison groups | DMSO v Ialuril |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.111 ^[1] |
| Method | ANCOVA |
| Notes: [1] - between treatment groups | |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The study was divided into 3 periods: screening (Visit 1), treatment (13 weekly visits), follow-up (Visit 15 after 3 months without any treatment). Adverse Events were evaluated at each visit.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 16.1 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Ialuril |
|-----------------------|---------|

Reporting group description:

intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment

| | |
|-----------------------|------|
| Reporting group title | DMSO |
|-----------------------|------|

Reporting group description:

intravesical instillation every 7 days for a total of 13 instillations over 3 months + 3 months of follow-up without treatment

| Serious adverse events | Ialuril | DMSO | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | 0 / 36 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Ialuril | DMSO | |
|---|----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | 8 / 36 (22.22%) | |
| Renal and urinary disorders | | | |
| Bladder pain | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | 1 / 36 (2.78%) | |
| occurrences (all) | 1 | 1 | |
| Bladder irritation | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | 1 / 36 (2.78%) | |
| occurrences (all) | 0 | 1 | |
| Cystitis | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 0 / 74 (0.00%) | 2 / 36 (5.56%) | |
| occurrences (all) | 0 | 4 | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | 4 / 36 (11.11%) | |
| occurrences (all) | 0 | 4 | |
| Strangury | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | 1 / 36 (2.78%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 16 January 2012 | Urodynamic test, Cystourethroscopy and Vulvoscopy were considered as "Optional" at screening and during the study. Some inclusion criteria were better specified and, in particular: - criterion n. 2 was changed to reflect the ESSIC guideline nomenclature, as for what regards the disease under study (from "IC/PBS" to "BPS/IC") - criterion n. 4 was changed to allow the recruitment of patients who are not sexually active. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27654012>