



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, Multicenter, Phase 2a, Proof-of-Concept Study of ASP8302 in Subjects With Underactive Bladder

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-003693-13 |
| Trial protocol | SK PL NL DE GB |
| Global end of trial date | 28 April 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 22 April 2021 |
| First version publication date | 22 April 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | 8302-CL-0201 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03702777 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Astellas Pharma Europe B.V. (APEB) |
| Sponsor organisation address | Sylviusweg 62, 2333 BE Leiden, Netherlands, |
| Public contact | Clinical Trial Disclosure, Astellas Pharma Europe B.V. (APEB), astellas.resultsdisclosure@astellas.com |
| Scientific contact | Clinical Trial Disclosure, Astellas Pharma Europe B.V. (APEB), astellas.resultsdisclosure@astellas.com |

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 | 28 April 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 April 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The study objectives of this study are to evaluate the efficacy of ASP8302 compared with placebo in participants with underactive bladder (UAB), to investigate the safety and tolerability of ASP8302 compared with placebo in participants with UAB, to investigate the pharmacokinetics of ASP8302 in participants with UAB and to support the development of the UAB - Patient Reported Outcome (PRO).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 November 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Germany: 12 |
| Country: Number of subjects enrolled | Japan: 60 |
| Country: Number of subjects enrolled | Netherlands: 12 |
| Country: Number of subjects enrolled | Poland: 39 |
| Country: Number of subjects enrolled | Slovakia: 11 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Worldwide total number of subjects | 135 |
| EEA total number of subjects | 74 |

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) | 66 |
| From 65 to 84 years | 68 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Adult male and female participants diagnosed with underactive bladder (UAB), who were able to void spontaneously, with or without clean intermittent catheterization (CIC), without severe overactive bladder (OAB) and without significant bladder outlet obstruction (BOO) were enrolled in this study.

Pre-assignment

Screening details:

Prior to randomization, participants entered a single-blind placebo run-in period for 2 weeks and completed a 3-day micturition diary. After the placebo run-in period, participants' eligibility criteria were re-confirmed and participants were then randomized into the double-blind treatment period of the study.

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Overall Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject, Monitor, Carer |

Arms

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

Arm description:

Participants received ASP8302 matching placebo orally once daily for up to 4 weeks.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received ASP8302 matching placebo orally once daily for up to 4 weeks.

| | |
|------------------|----------------|
| Arm title | ASP8302 100 mg |
|------------------|----------------|

Arm description:

Participants received ASP8302 100 mg capsules orally once daily for up to 4 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | ASP8302 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received ASP8302 100 mg capsules orally once daily for up to 4 weeks.

| Number of subjects in period 1 | Placebo | ASP8302 100 mg |
|---------------------------------------|---------|----------------|
| Started | 70 | 65 |
| Completed | 65 | 62 |
| Not completed | 5 | 3 |
| Consent withdrawn by subject | 2 | 2 |
| Adverse event, non-fatal | 1 | - |
| Miscellaneous | 1 | - |
| Protocol deviation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|----------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received ASP8302 matching placebo orally once daily for up to 4 weeks. | |
| Reporting group title | ASP8302 100 mg |
| Reporting group description: | |
| Participants received ASP8302 100 mg capsules orally once daily for up to 4 weeks. | |

| Reporting group values | Placebo | ASP8302 100 mg | Total |
|--|---------|----------------|-------|
| Number of subjects | 70 | 65 | 135 |
| Age categorical | | | |
| Units: Participants | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 35 | 31 | 66 |
| From 65-84 years | 34 | 34 | 68 |
| 85 years and over | 1 | 0 | 1 |
| Age | | | |
| Units: years | | | |
| arithmetic mean | 61.4 | 62.7 | |
| standard deviation | ± 13.1 | ± 10.9 | - |
| Sex | | | |
| Units: Participants | | | |
| Female | 30 | 26 | 56 |
| Male | 40 | 39 | 79 |
| Race | | | |
| Units: Subjects | | | |
| ASIAN | 31 | 29 | 60 |
| WHITE | 39 | 36 | 75 |
| Post Void Residual Urine Volume (PVR) after standardized bladder filling measured by catheterization | | | |
| Volume of urine in the bladder after standardized bladder filling measured by catheterization (PVRc2). | | | |
| Units: milliliter (mL) | | | |
| arithmetic mean | 369.3 | 374.7 | |
| standard deviation | ± 234.6 | ± 248.6 | - |

End points

End points reporting groups

| | |
|---|----------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received ASP8302 matching placebo orally once daily for up to 4 weeks. | |
| Reporting group title | ASP8302 100 mg |
| Reporting group description: | |
| Participants received ASP8302 100 mg capsules orally once daily for up to 4 weeks. | |

Primary: Change From Baseline in PVR After Standardized Bladder Filling Measured by catheterization (PVRc2) at Week 4

| | |
|--|--|
| End point title | Change From Baseline in PVR After Standardized Bladder Filling Measured by catheterization (PVRc2) at Week 4 |
| End point description: | |
| Volume of urine in the bladder after standardized bladder filling measured by catheterization (PVRc2). | |
| The FAS-PVR Population (FAS-PVR) comprised of all randomized participants who took at least 1 dose of double-blind study medication and had a nonmissing PVRc2 value at baseline and end of trial (EoT). | |
| End point type | Primary |
| End point timeframe: | |
| Baseline and week 4 | |

| End point values | Placebo | ASP8302 100 mg | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 61 | | |
| Units: mL | | | | |
| median (inter-quartile range (Q1-Q3)) | -35 (-130 to 40) | -40 (-125 to 25) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Placebo versus ASP8302 100 mg |
| Comparison groups | Placebo v ASP8302 100 mg |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.96 ^[1] |
| Method | Stratified rank ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -42 |
| upper limit | 34 |

Notes:

[1] - The stratified rank analysis of covariance (ANCOVA) was used to compare the median change between placebo and ASP8302 treatment group.

Hodges-Lehmann method was used to obtain an estimate in the median (and 90% CI).

Secondary: Voided Volume After Standardized Bladder Filling (VV_St) at Week 4

| | |
|-----------------|--|
| End point title | Voided Volume After Standardized Bladder Filling (VV_St) at Week 4 |
|-----------------|--|

End point description:

VVst is thought to increase as the bladder emptying is improved. Standardizing the bladder filling is thought to increase accuracy in comparison with normal spontaneous bladder filling which will differ between time points.

No multiplicity correction was performed.

FAS-PVR Population

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 4

| End point values | Placebo | ASP8302 100 mg | | |
|---------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 61 | | |
| Units: mL | | | | |
| median (inter-quartile range (Q1-Q3)) | 306 (185 to 409) | 368 (265 to 456) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Placebo vs ASP8302 100 mg |
| Comparison groups | Placebo v ASP8302 100 mg |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.17 ^[2] |
| Method | Stratified rank ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | 62 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 8 |
| upper limit | 112 |

Notes:

[2] - The stratified rank ANCOVA was used to compare the median between placebo and ASP8302 treatment group.

Hodges-Lehmann method was used to obtain an estimate in the median (and 90% CI).

Secondary: Bladder Voiding Efficiency Calculated With PVRc2 and VV-St (BVEc2) at Week 4

| | |
|-----------------|--|
| End point title | Bladder Voiding Efficiency Calculated With PVRc2 and VV-St (BVEc2) at Week 4 |
|-----------------|--|

End point description:

Bladder voiding efficiency (BVE) is defined as the percentage of the total bladder capacity (BC) that is voided using the following formula: $BVE = [volume\ voided\ (VV) / (PVR + VV)] \times 100$.

BVEc2: BVE calculated for PVRc2 parameter i.e. $BVEc2 = [VV_St / (PVRc2 + VV_St)] \times 100$.

FAS-PVR Population

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 4

| End point values | Placebo | ASP8302 100 mg | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 61 | | |
| Units: percentage of BVE | | | | |
| median (inter-quartile range (Q1-Q3)) | 54.60 (28.40 to 76) | 53.10 (40.20 to 70) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Placebo vs ASP8302 100 mg |
| Comparison groups | Placebo v ASP8302 100 mg |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.489 ^[3] |
| Method | Stratified rank ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | 3.3 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -4.9 |
| upper limit | 10.6 |

Notes:

[3] - The stratified rank ANCOVA was used to compare the median between placebo and ASP8302 treatment group.

Hodges-Lehmann method was used to obtain an estimate in the median (and 90% CI).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to end of study (6 weeks)

Adverse event reporting additional description:

The SAF consisted of all participants who took at least 1 dose of double-blind study medication, and was used for safety analyses.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-------|
| Dictionary version | v21.0 |
|--------------------|-------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | ASP8302 100mg |
|-----------------------|---------------|

Reporting group description:

Participants received ASP8302 100 mg capsules orally once daily for up to 4 weeks.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received ASP8302 matching placebo orally once daily for up to 4 weeks.

| Serious adverse events | ASP8302 100mg | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 70 (2.86%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | ASP8302 100mg | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 6 / 70 (8.57%) | |
| Infections and infestations | | | |
| Cystitis | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 0 / 70 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 6 / 70 (8.57%) | |
| occurrences (all) | 0 | 8 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 14 June 2018 | The changes included: 1) Updated informed consent process to delete the possibility of the obtaining informed consent from a legally authorized representative. 2) Revised the inclusion criterion 5 to remove the specification that females are heterosexually active. Updated the concomitant medications to include information on how to treat urinary tract infections. 3) Updated the criteria for discontinuation of treatment based on liver function test abnormalities to specify that treatment was to be discontinued for certain liver function test abnormalities. 4) Updated the definition of adverse event (AE) so that it may or may not be considered related to the underlying disease. 5) Added the definition and reporting of suspected unexpected serious adverse reactions (SUSARs). 6) Added a section containing subject confidentiality and privacy to the protocol appendix. |
| 22 July 2019 | The changes included: 1) The number of participants enrolled in the placebo run-in period was increased to 163. This increased number provided 130 randomized participants (65 in each arm) in order to achieve 98 evaluable participants. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported