



Clinical trial results:

A Multicenter, Open-label, Single-dose Study to Evaluate Pharmacokinetics, Safety and Tolerability of Solifenacin Succinate Suspension in Pediatric Subjects from 5 to less than 18 years of age with Neurogenic Detrusor Overactivity (NDO)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-000250-28 |
| Trial protocol | BE GB DK |
| Global end of trial date | 13 August 2012 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 22 February 2016 |
| First version publication date | 11 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 905-CL-079 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01539707 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | Astellas Pharma Europe B.V. |
| Sponsor organisation address | Sylviusweg 62, Leiden, Netherlands, 2333 BE |
| Public contact | Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.com |
| Scientific contact | Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., 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? | Yes |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 August 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 August 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 August 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics (PK) of solifenacin succinate suspension after single-dose administration in children and adolescents with NDO.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH 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 | 13 March 2012 |
| 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 | Poland: 11 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Worldwide total number of subjects | 15 |
| EEA total number of subjects | 15 |

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) | 7 |

| | |
|---------------------------|---|
| Adolescents (12-17 years) | 8 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Children and adolescents with NDO (confirmed by urodynamics), who consented to enter this study and fulfilled all the eligibility criteria, were enrolled in this study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | AD-PED 5.0 mg |

Arm description:

Male and female adolescents aged 12 to less than 18 years old who received pediatric equivalent dose (PED) of 5 mg of solifenacin succinate.

| | |
|----------------------------------------|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Solifenacin succinate suspension |
| Investigational medicinal product code | YM905 |
| Other name | |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Adolescents were given a single dose of solifenacin succinate liquid suspension orally via syringe in the morning of day 1 followed by a glass of water. Doses were calculated per weight of the participant, targeting to have equivalent dose of 5 mg dose of solifenacin once daily in adults (referred to as PED of 5 mg).

| | |
|------------------|---------------|
| Arm title | CH-PED 5.0 mg |
|------------------|---------------|

Arm description:

Male and female children aged 5 to less than 12 years old who received PED of 5 mg of solifenacin succinate.

| | |
|----------------------------------------|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Solifenacin succinate suspension |
| Investigational medicinal product code | YM905 |
| Other name | |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Children were given a single dose of solifenacin succinate liquid suspension orally via syringe in the morning of day 1 followed by a glass of water. Doses were calculated per weight of the participant, targeting to have equivalent dose of 5 mg dose of solifenacin once daily in adults (referred to as PED of 5 mg).

| Number of subjects in period 1 | AD-PED 5.0 mg | CH-PED 5.0 mg |
|---------------------------------------|---------------|---------------|
| Started | 8 | 7 |
| Treated | 7 | 7 |
| Completed | 7 | 7 |
| Not completed | 1 | 0 |
| Consent withdrawn by subject | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | AD-PED 5.0 mg |
|-----------------------|---------------|

Reporting group description:

Male and female adolescents aged 12 to less than 18 years old who received pediatric equivalent dose (PED) of 5 mg of solifenacin succinate.

| | |
|-----------------------|---------------|
| Reporting group title | CH-PED 5.0 mg |
|-----------------------|---------------|

Reporting group description:

Male and female children aged 5 to less than 12 years old who received PED of 5 mg of solifenacin succinate.

| Reporting group values | AD-PED 5.0 mg | CH-PED 5.0 mg | Total |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|---------------|-------|
| Number of subjects | 8 | 7 | 15 |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 0 | 7 | 7 |
| Adolescents (12-17 years) | 8 | 0 | 8 |
| Age continuous | | | |
| This baseline characteristic was based on the Safety Analysis Set (SAF), which consisted of all enrolled participants who received any dose of study drug. As a participant in the AD-PED 5.0 mg did not receive any study drug, his age was not included in this calculation. | | | |
| Units: years | | | |
| arithmetic mean | 14.4 | 8.6 | |
| standard deviation | ± 2.07 | ± 1.72 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 3 | 7 |
| Male | 4 | 4 | 8 |

End points

End points reporting groups

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title | AD-PED 5.0 mg |
| Reporting group description: Male and female adolescents aged 12 to less than 18 years old who received pediatric equivalent dose (PED) of 5 mg of solifenacin succinate. | |
| Reporting group title | CH-PED 5.0 mg |
| Reporting group description: Male and female children aged 5 to less than 12 years old who received PED of 5 mg of solifenacin succinate. | |

Primary: Maximum concentration (Cmax)

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|
| End point title | Maximum concentration (Cmax) ^[1] |
| End point description: The analysis population was the pharmacokinetic analysis set (PKAS), which consisted of all participants who received any dose of study drug and who had values of solifenacin concentration for a sufficient number of time points to reliably calculate at least 1 pharmacokinetic parameter. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples). | |
| End point type | Primary |
| End point timeframe: Day 1 predose up to Day 7 postdose | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 21.906 (± 7.931) | 17.666 (± 5.8884) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Time to attain Cmax (tmax)

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| End point title | Time to attain Cmax (tmax) ^[2] |
| End point description: The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples). | |
| End point type | Primary |
| End point timeframe: Day 1 predose up to Day 7 postdose | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6 | 7 | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 3.8 (\pm 1.208) | 4.16 (\pm 1.055) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Area under the curve extrapolated to infinity (AUCinf)

| | |
|-----------------|-----------------------------------------------------------------------|
| End point title | Area under the curve extrapolated to infinity (AUCinf) ^[3] |
|-----------------|-----------------------------------------------------------------------|

End point description:

The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 predose up to Day 7 postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: ng*h/mL | | | | |
| arithmetic mean (standard deviation) | 1614.771 (\pm 954.6774) | 831.873 (\pm 329.5083) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent terminal elimination half-life (t_{1/2})

| | |
|-----------------|----------------------------------------------------------------------------|
| End point title | Apparent terminal elimination half-life (t _{1/2}) ^[4] |
|-----------------|----------------------------------------------------------------------------|

End point description:

The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 predose up to Day 7 postdose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|-------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 52.877 (\pm 21.0715) | 30.653 (\pm 8.275) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent total body clearance (CL/F)

| | |
|-----------------|-----------------------------------------------------|
| End point title | Apparent total body clearance (CL/F) ^[5] |
|-----------------|-----------------------------------------------------|

End point description:

The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 predose up to Day 7 postdose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: L/h | | | | |
| arithmetic mean (standard deviation) | 7.707 (\pm 4.8032) | 7.216 (\pm 4.0233) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent volume of distribution during the terminal phase (V_z/F)

| | |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Apparent volume of distribution during the terminal phase (V _z /F) ^[6] |
|-----------------|----------------------------------------------------------------------------------------------|

End point description:

The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 predose up to Day 7 postdose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: liters | | | | |
| arithmetic mean (standard deviation) | 499.397 (\pm 195.1213) | 298.923 (\pm 108.4731) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve from the time of dosing until the last measurable concentration (AUClast)

| | |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area under the concentration-time curve from the time of dosing until the last measurable concentration (AUClast) ^[7] |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|

End point description:

The analysis population was the PKAS. The number of samples as well sampling times depended on the age of the participant (aged 5-less than 9 years old: 4 samples; aged 9-less than 12 years old: 6 samples; aged 12-less than 18 years old: 7 samples).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 predose up to Day 7 postdose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study was written with no planned statistical analyses (statistical hypothesis testing) to be performed for any end points due to the simple design and purpose of the study.

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: ng*h/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[8] - AUClast was not calculated since non-compartmental modeling was not used for PK analysis.

[9] - AUClast was not calculated since non-compartmental modeling was not used for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Safety as assessed by adverse events (AEs), vital signs, clinical laboratory evaluations, physical examination and electrocardiograms (ECGs)

| | |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Safety as assessed by adverse events (AEs), vital signs, clinical laboratory evaluations, physical examination and electrocardiograms (ECGs) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Safety was monitored by collecting AEs, which included abnormal laboratory tests, vital signs or ECG data that were defined as an AE if the abnormality induced clinical signs or symptoms, required active intervention, interruption or discontinuation of study medication or was clinically significant in the investigator's opinion. A treatment-emergent adverse event (TEAE) was defined as an AE that occurred or worsened after study drug administration. A serious AE was any untoward medical occurrence that at any dose: Resulted in death, was life-threatening, resulted in persistent or significant disability/incapacity, resulted in congenital anomaly, or birth defect, required inpatient hospitalization or led to prolongation of hospitalization. The analysis population was the SAF, which consisted of all enrolled participants who received the dose of study drug.

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

End point timeframe:

From the first dose of study drug up to 7 days postdose

| End point values | AD-PED 5.0 mg | CH-PED 5.0 mg | | |
|--------------------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: participants | | | | |
| Participants experienced AEs | 2 | 0 | | |
| Number of AEs | 5 | 0 | | |
| Participants experienced drug-related AEs | 0 | 0 | | |
| Deaths | 0 | 0 | | |
| Participants experienced SAEs | 0 | 0 | | |
| Participants with AEs leading to discontinuation | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to 7 days postdose

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | AD-PED 5.0 mg |
|-----------------------|---------------|

Reporting group description:

Male and female adolescents aged 12 to less than 18 years old who received PED of 5 mg of solifenacin succinate.

| | |
|-----------------------|---------------|
| Reporting group title | CH-PED 5.0 mg |
|-----------------------|---------------|

Reporting group description:

Male and female children aged 5 to less than 12 years old who received PED of 5 mg of solifenacin succinate.

| Serious adverse events | AD-PED 5.0 mg | CH-PED 5.0 mg | |
|---------------------------------------------------|---------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | AD-PED 5.0 mg | CH-PED 5.0 mg | |
|-------------------------------------------------------|----------------|---------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Renal and urinary disorders | | | |
| Micturition urgency | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 16 March 2012 | The reason for the substantial amendment was to clarify: the terminology of the exclusion criteria, the analysis of pharmacokinetics, the study design and the dose rationale, reporting of SAEs, the safety assessment, the test drug concentration and the events always considered to be serious. Two new exclusion criteria, clinical research contact information, and reference to a relevant newly completed study (Study 905-CL-075) were added. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported