



## Clinical trial results:

### An Open-Label, Long-Term Extension, Multi-center, Sequential Dose Titration Study to Assess Safety and Efficacy of Solifenacin Succinate Suspension in Pediatric Subjects with Overactive Bladder (OAB)

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2011-002047-10          |
| Trial protocol           | GB BE NL DE DK SE NO FR |
| Global end of trial date | 08 October 2014         |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 24 February 2018 |
| First version publication date | 22 April 2015    |
| Version creation reason        |                  |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | 905-CL-077 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01655069 |
| 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 Europe B.V.,<br>Astellas.resultsdisclosure@astellas.com |
| Scientific contact           | Clinical Trial Disclosure, Astellas Pharma Europe B.V.,<br>Astellas.resultsdisclosure@astellas.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000573-PIP01-09 |
| 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                       | 08 October 2014 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 08 October 2014 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of solifenacin oral suspension once daily in children and adolescents with overactive bladder (OAB).

Protection of trial subjects:

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                          | 04 October 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 | Norway: 4             |
| Country: Number of subjects enrolled | Poland: 21            |
| Country: Number of subjects enrolled | Sweden: 8             |
| Country: Number of subjects enrolled | United Kingdom: 2     |
| Country: Number of subjects enrolled | Belgium: 34           |
| Country: Number of subjects enrolled | Denmark: 20           |
| Country: Number of subjects enrolled | Brazil: 9             |
| Country: Number of subjects enrolled | Canada: 5             |
| Country: Number of subjects enrolled | Mexico: 8             |
| Country: Number of subjects enrolled | Philippines: 2        |
| Country: Number of subjects enrolled | Serbia: 16            |
| Country: Number of subjects enrolled | South Africa: 5       |
| Country: Number of subjects enrolled | Turkey: 2             |
| Country: Number of subjects enrolled | Ukraine: 3            |
| Country: Number of subjects enrolled | United States: 2      |
| Country: Number of subjects enrolled | Korea, Republic of: 7 |
| Worldwide total number of subjects   | 148                   |
| EEA total number of subjects         | 89                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                     | 119 |
| Adolescents (12-17 years)                 | 29  |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Participants recruited for this study were children (5 to less than 12 years old) and adolescents (12 to less than 18 years old) with overactive bladder (OAB), who completed the 2-week placebo run-in period and 12-week treatment period of Study 905-CL-076.

### Pre-assignment

Screening details:

Children and adolescents with OAB, who completed study 905-CL-076, consented to enter this study and fulfilled all the eligibility criteria were enrolled at Week 12/13 (2-3 days after last dose was received during the 905-CL-076 study). The age of participant at informed consent signing in 905-CL-076 determined the age group 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                    |

Blinding implementation details:

All participants in this extension study received open-label solifenacin. However, the treatment which they received (solifenacin or placebo) in Study 905-CL-076 has been reflected to provide clarity on the baseline status of the participants.

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Children Treated With Placebo in 905-CL-076 |

Arm description:

Male and female children aged 5 to less than 12 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.

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

Dosage and administration details:

Children were given solifenacin liquid suspension once a day orally via syringe along with the completion of a 7-day diary prior to study visit (start of 905-CL-076 to end of 905-CL-077, 14 visits). The initial dose started with the equivalent of 5 mg in adults (referred to as PED5) except for participants who finished Study 905-CL-076 with PED2.5 (active or placebo), who could start at this dose for this study. Doses were calculated per weight determined at the first visit of this study, targeting to have equivalent doses of 2.5, 5, 7.5 and 10 mg doses of solifenacin once daily in adults (referred to as PED2.5, PED5, PED7.5 and PED10). There was a titration period of up to 12 weeks during which the participants would be up or down-titrated based on a combination of efficacy and safety parameters followed by a fixed dose period during which no dose adjustments were allowed.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Children Treated With Solifenacin in 905-CL-076 |
|------------------|---|

Arm description:

Male and female children aged 5 to less than 12 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

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

**Dosage and administration details:**

Children were given solifenacin liquid suspension once a day orally via syringe along with the completion of a 7-day diary prior to study visit (start of 905-CL-076 to end of 905-CL-077, 14 visits). The initial dose started with the equivalent of 5 mg in adults (referred to as PED5) except for participants who finished Study 905-CL-076 with PED2.5 (active or placebo), who could start at this dose for this study. Doses were calculated per weight determined at the first visit of this study, targeting to have equivalent doses of 2.5, 5, 7.5 and 10 mg doses of solifenacin once daily in adults (referred to as PED2.5, PED5, PED7.5 and PED10). There was a titration period of up to 12 weeks during which the participants would be up or down-titrated based on a combination of efficacy and safety parameters followed by a fixed dose period during which no dose adjustments were allowed.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Adolescents Treated With Placebo in 905-CL-076 |
|------------------|--|

**Arm description:**

Male and female adolescents aged 12 to less than 18 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents.

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

**Dosage and administration details:**

Adolescents were given solifenacin liquid suspension once a day orally via syringe along with the completion of a 7-day diary prior to study visit (start of 905-CL-076 to end of 905-CL-077, 14 visits). The initial dose started with the equivalent of 5 mg in adults (referred to as PED5) except for participants who finished Study 905-CL-076 with PED2.5 (active or placebo), who could start at this dose for this study. Doses were calculated per weight determined at the first visit of this study, targeting to have equivalent doses of 2.5, 5, 7.5 and 10 mg doses of solifenacin once daily in adults (referred to as PED2.5, PED5, PED7.5 and PED10). There was a titration period of up to 12 weeks during which the participants would be up or down-titrated based on a combination of efficacy and safety parameters followed by a fixed dose period during which no dose adjustments were allowed.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Adolescents Treated With Solifenacin in 905-CL-076 |
|------------------|--|

**Arm description:**

Male and female adolescents aged 12 to less than 18 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents.

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

**Dosage and administration details:**

Adolescents were given solifenacin liquid suspension once a day orally via syringe along with the completion of a 7-day diary prior to study visit (start of 905-CL-076 to end of 905-CL-077, 14 visits). The initial dose started with the equivalent of 5 mg in adults (referred to as PED5) except for participants who finished Study 905-CL-076 with PED2.5 (active or placebo), who could start at this dose for this study. Doses were calculated per weight determined at the first visit of this study, targeting to have equivalent doses of 2.5, 5, 7.5 and 10 mg doses of solifenacin once daily in adults (referred to as PED2.5, PED5, PED7.5 and PED10). There was a titration period of up to 12 weeks during which the participants would be up or down-titrated based on a combination of efficacy and safety parameters followed by a fixed dose period during which no dose adjustments were allowed.

| <b>Number of subjects in period 1</b> | Children Treated<br>With Placebo in 905-<br>CL-076 | Children Treated<br>With Solifenacin in<br>905-CL-076 | Adolescents Treated<br>With Placebo in 905-<br>CL-076 |
|---------------------------------------|--|---|---|
| Started                               | 61   | 58  | 14  |
| Safety Analysis Set (SAF)             | 61   | 57  | 14  |
| Full Analysis Set (FAS)               | 60   | 57  | 14  |
| Completed                             | 53   | 46  | 12  |
| Not completed                         | 8  | 12  | 2   |
| Lack of Efficacy                      | -  | 1   | -   |
| No Treatment Needed                   | -  | 1   | -   |
| Adverse Event                         | 6  | 7   | 2   |
| Physician Decision                    | -  | -   | -   |
| Withdrawal by Subject                 | 2  | 3   | -   |

| <b>Number of subjects in period 1</b> | Adolescents Treated<br>With Solifenacin in<br>905-CL-076 |
|---------------------------------------|--|
| Started                               | 15   |
| Safety Analysis Set (SAF)             | 15   |
| Full Analysis Set (FAS)               | 15   |
| Completed                             | 11   |
| Not completed                         | 4  |
| Lack of Efficacy                      | -  |
| No Treatment Needed                   | -  |
| Adverse Event                         | 3  |
| Physician Decision                    | 1  |
| Withdrawal by Subject                 | -  |

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Children Treated With Placebo in 905-CL-076        |
| Reporting group description:<br>Male and female children aged 5 to less than 12 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.            |  |
| Reporting group title   | Children Treated With Solifenacin in 905-CL-076    |
| Reporting group description:<br>Male and female children aged 5 to less than 12 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.        |  |
| Reporting group title   | Adolescents Treated With Placebo in 905-CL-076     |
| Reporting group description:<br>Male and female adolescents aged 12 to less than 18 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents.     |  |
| Reporting group title   | Adolescents Treated With Solifenacin in 905-CL-076 |
| Reporting group description:<br>Male and female adolescents aged 12 to less than 18 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents. |  |

| Reporting group values             | Children Treated With Placebo in 905-CL-076 | Children Treated With Solifenacin in 905-CL-076 | Adolescents Treated With Placebo in 905-CL-076 |
|------------------------------------|---|---|--|
| Number of subjects                 | 61  | 58  | 14   |
| Age categorical<br>Units: Subjects |   |   |  |

|   |       |       |       |
|---|-------|-------|-------|
| Age continuous  |       |       |       |
| The analysis population is Safety Analysis Set (SAF), which consisted of all participants who received at least 1 dose of open-label solifenacin and had any safety data reported after the first dose of open-label solifenacin. The baseline values measured for study 905-CL-076 were used as the baseline values for the present study. |       |       |       |
| Units: years  |       |       |       |
| arithmetic mean   | 7.2   | 7.5   | 13.9  |
| standard deviation  | ± 1.6 | ± 1.5 | ± 1.6 |
| Gender categorical<br>Units:  |       |       |       |
| Male  | 34    | 23    | 1     |
| Female  | 27    | 34    | 13    |
| Not recorded  | 0     | 1     | 0     |
| Ethnicity<br>Units: Subjects  |       |       |       |
| Hispanic or Latino  | 7     | 7     | 2     |
| Not Hispanic or Latino  | 54    | 50    | 12    |
| Unknown or Not Reported   | 0     | 1     | 0     |
| Race<br>Units: Subjects   |       |       |       |
| American Indian or Alaska Native  | 3     | 3     | 1     |
| Asian   | 4     | 5     | 1     |

|   |    |    |    |
|---|----|----|----|
| Native Hawaiian or Other Pacific Islander | 0  | 0  | 0  |
| Black or African American                 | 2  | 2  | 1  |
| White                                     | 49 | 47 | 11 |
| More than one race                        | 0  | 0  | 0  |
| Other                                     | 3  | 0  | 0  |
| Unknown or Not Reported                   | 0  | 1  | 0  |

| <b>Reporting group values</b> | Adolescents Treated With Solifenacin in 905-CL-076 | Total |  |
|-------------------------------|--|-------|--|
| Number of subjects            | 15   | 148   |  |
| Age categorical               |  |       |  |
| Units: Subjects               |  |       |  |

|   |       |     |  |
|---|-------|-----|--|
| Age continuous  |       |     |  |
| The analysis population is Safety Analysis Set (SAF), which consisted of all participants who received at least 1 dose of open-label solifenacin and had any safety data reported after the first dose of open-label solifenacin. The baseline values measured for study 905-CL-076 were used as the baseline values for the present study. |       |     |  |
| Units: years  |       |     |  |
| arithmetic mean   | 14.5  |     |  |
| standard deviation  | ± 1.8 | -   |  |
| Gender categorical  |       |     |  |
| Units:  |       |     |  |
| Male  | 4     | 62  |  |
| Female  | 11    | 85  |  |
| Not recorded  | 0     | 1   |  |
| Ethnicity   |       |     |  |
| Units: Subjects   |       |     |  |
| Hispanic or Latino  | 1     | 17  |  |
| Not Hispanic or Latino  | 14    | 130 |  |
| Unknown or Not Reported   | 0     | 1   |  |
| Race  |       |     |  |
| Units: Subjects   |       |     |  |
| American Indian or Alaska Native  | 0     | 7   |  |
| Asian   | 1     | 11  |  |
| Native Hawaiian or Other Pacific Islander   | 0     | 0   |  |
| Black or African American   | 2     | 7   |  |
| White   | 12    | 119 |  |
| More than one race  | 0     | 0   |  |
| Other   | 0     | 3   |  |
| Unknown or Not Reported   | 0     | 1   |  |



## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Children Treated With Placebo in 905-CL-076        |
| Reporting group description:<br>Male and female children aged 5 to less than 12 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.  |  |
| Reporting group title   | Children Treated With Solifenacin in 905-CL-076    |
| Reporting group description:<br>Male and female children aged 5 to less than 12 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 247.9 days in children.  |  |
| Reporting group title   | Adolescents Treated With Placebo in 905-CL-076     |
| Reporting group description:<br>Male and female adolescents aged 12 to less than 18 years old who received placebo in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents.   |  |
| Reporting group title   | Adolescents Treated With Solifenacin in 905-CL-076 |
| Reporting group description:<br>Male and female adolescents aged 12 to less than 18 years old who received solifenacin in Study 905-CL-076 and received open-label solifenacin once daily in this study. The mean time on study drug in this study was 240.1 days in adolescents.   |  |
| Subject analysis set title  | Children (aged 5 to less than 12 years) - FAS      |
| Subject analysis set type   | Full analysis                                      |
| Subject analysis set description:<br>Children aged 5 to less than 12 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults. The full analysis set (FAS) consisted of participants who received at least one dose of open-label solifenacin and for at least 1 efficacy variable had a valid baseline value (from 905-CL-076 study) and a valid postbaseline value from diary data completed after the first dose of open-label solifenacin (in 905-CL-077 study). |  |
| Subject analysis set title  | Adolescents (Aged 12 to Less Than 18 Years) - FAS  |
| Subject analysis set type   | Full analysis                                      |
| Subject analysis set description:<br>Adolescents aged 12 to less than 18 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults. This group is part of the FAS.  |  |
| Subject analysis set title  | Children (aged 5 to less than 12 years old) - SAF  |
| Subject analysis set type   | Safety analysis                                    |
| Subject analysis set description:<br>Children aged 5 to less than 12 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults. The safety analysis set (SAF) consisted of all participants who received at least 1 dose of open-label solifenacin and had any safety data reported after the first dose of open-label solifenacin.   |  |
| Subject analysis set title  | Adolescents (Aged 12 to Less Than 18 Years) - SAF  |
| Subject analysis set type   | Safety analysis                                    |
| Subject analysis set description:<br>Adolescents aged 12 to less than 18 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of   |  |

the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults. This group is part of the SAF.

## Primary: Number of Participants With and Severity of Treatment-Emergent Adverse Events (TEAEs)

|                 |  |
|-----------------|--|
| End point title | Number of Participants With and Severity of Treatment-Emergent Adverse Events (TEAEs) <sup>[1]</sup> |
|-----------------|--|

End point description:

The investigator assessed the severity of AEs, including abnormal clinical laboratory values, electrocardiogram (ECG), vital signs, as follows: (1) Mild: No disruption of normal daily activities; (2) Moderate: Affect normal daily activities; (3) Severe: Inability to perform daily activities. In participants treated with placebo in Study 905-CL-076, a TEAE was defined as an AE that started/worsened after the first dose of open-label solifenacin in Study 905-CL-077 up to 7 days after the last dose of solifenacin. In participants treated with solifenacin in Study 905-CL-076, a TEAE was defined as an AE that started/worsened after the first dose of double-blind solifenacin in Study 905-CL-076 up to 7 days after last dose of open-label solifenacin in Study 905-CL-077. The analysis population was the SAF. Participants who received placebo and participants who received solifenacin in Study 905-CL-076 are combined for analyses of efficacy and safety in this study.

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

End point timeframe:

From first dose of solifenacin (in Study 905-CL-076 or in current study) up to 7 days after last dose of open-label solifenacin (41 weeks for participants who received placebo in 076 and 53 weeks for those who received solifenacin in 076)

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: As this was simply an open-label, long-term safety study, there were no statistical analyses performed for the primary safety endpoint. However, statistical analyses were performed for the secondary efficacy endpoints, which used a repeated measures model to provide adjusted means per study period (window) and data is seen in the summary results. There were no comparisons and no p-values that resulted from these analyses.

| End point values  | Children (aged 5 to less than 12 years old) - SAF | Adolescents (Aged 12 to Less Than 18 Years) - SAF |  |  |
|---|---|---|--|--|
| Subject group type                                      | Subject analysis set                              | Subject analysis set                              |  |  |
| Number of subjects analysed                             | 118   | 29  |  |  |
| Units: participants                                     |   |   |  |  |
| number (not applicable)                                 |   |   |  |  |
| TEAE - Mild   | 72  | 10  |  |  |
| TEAE - Moderate   | 20  | 8   |  |  |
| TEAE - Severe   | 1   | 2   |  |  |
| Any TEAE  | 93  | 20  |  |  |
| Drug-related TEAEs                                      | 41  | 11  |  |  |
| Deaths  | 0   | 0   |  |  |
| Serious TEAEs   | 1   | 1   |  |  |
| Drug-related serious TEAEs                              | 0   | 0   |  |  |
| TEAEs leading to discontinuation                        | 12  | 5   |  |  |
| Drug related TEAEs leading to permanent discontinuation | 12  | 4   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Mean Number of Incontinence Episodes Per 24 Hours

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Mean Number of Incontinence Episodes Per 24 Hours |
|-----------------|---|

End point description:

The mean number of incontinence episodes was based on 7-day diary data completed by participants prior to each visit from the start of 905-CL-076 to the end of 905-CL-077. An Incontinence episode is defined as an episode with any involuntary loss of urine. Data are reported by duration of solifenacin treatment based on the number of days from the date of first dose of solifenacin in either study 905-CL-076 or 905-CL-077 up to and including the study visit. Using equivalent treatment duration periods, data were combined for participants who received placebo and solifenacin in study 905-CL-076 within each age group. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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

End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

| End point values                           | Children (aged 5 to less than 12 years) - FAS | Adolescents (Aged 12 to Less Than 18 Years) - FAS |  |  |
|--|---|---|--|--|
| Subject group type                         | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed                | 117   | 29  |  |  |
| Units: Incontinence episodes               |   |   |  |  |
| arithmetic mean (standard error)           |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28]  | -0.92 (± 0.18)                                | -1.05 (± 0.34)                                    |  |  |
| 6 weeks solifenacin treatment [N=116, 26]  | -1.11 (± 0.17)                                | -1.40 (± 0.33)                                    |  |  |
| 9 weeks solifenacin treatment [N=115, 29]  | -1.28 (± 0.19)                                | -1.48 (± 0.38)                                    |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | -1.39 (± 0.20)                                | -1.66 (± 0.39)                                    |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | -1.61 (± 0.19)                                | -1.73 (± 0.39)                                    |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | -1.66 (± 0.23)                                | -1.49 (± 0.36)                                    |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | -1.56 (± 0.22)                                | -1.34 (± 0.38)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Mean Number of Incontinence Episodes per 24 Hours – Repeated Measures ANCOVA

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Mean Number of Incontinence Episodes per 24 Hours – Repeated Measures ANCOVA |
|-----------------|--|

End point description:

Repeated measures ANCOVA (analysis of covariance) was used in this analysis, which included double-blind and/or open-label solifenacin treatment duration, gender, geographic region and randomized treatment group in Study 905-CL-076 as fixed effects, baseline as a covariate and "duration" repeated within participant. The analysis population was the FAS. N indicates the number of participants with

available data at each time point.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment |           |

| End point values                           | Children (aged 5 to less than 12 years) - FAS | Children (aged 5 to less than 12 years old) - SAF |  |  |
|--|---|---|--|--|
| Subject group type                         | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed                | 117   | 29  |  |  |
| Units: Incontinence episodes               |   |   |  |  |
| least squares mean (standard error)        |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28]  | -0.95 (± 0.12)                                | -0.93 (± 0.35)                                    |  |  |
| 6 weeks solifenacin treatment [N=116, 26]  | -1.11 (± 0.12)                                | -1.38 (± 0.36)                                    |  |  |
| 9 weeks solifenacin treatment [N=115, 29]  | -1.26 (± 0.13)                                | -1.40 (± 0.35)                                    |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | -1.39 (± 0.12)                                | -1.58 (± 0.35)                                    |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | -1.54 (± 0.11)                                | -1.80 (± 0.35)                                    |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | -1.56 (± 0.13)                                | -1.57 (± 0.36)                                    |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | -1.93 (± 0.13)                                | -2.00 (± 0.42)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Number of Dry (Incontinence-free) Days per 7 Days

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Number of Dry (Incontinence-free) Days per 7 Days |
|-----------------|---|

End point description:

The number of dry (incontinence-free) days was based on 7-day diary data completed by participants prior to each visit from start of 905-C L-076 to end of 905-C L-077. An incontinence-free day is a day without any incontinence episodes. Data are reported by duration of solifenacin treatment based on the number of days from the date of first dose of solifenacin in either study 905-CL-076 or 905-CL-077 up to and including the study visit. Using equivalent treatment duration periods, data were combined for participants who received placebo and solifenacin in study 905-CL-076 within each age group. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment |           |

| End point values                           | Children (aged 5 to less than 12 years) - FAS | Adolescents (Aged 12 to Less Than 18 Years) - FAS |  |  |
|--|---|---|--|--|
| Subject group type                         | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed                | 117   | 29  |  |  |
| Units: days                                |   |   |  |  |
| arithmetic mean (standard error)           |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28]  | 1.17 (± 0.16)                                 | 1.69 (± 0.53)                                     |  |  |
| 6 weeks solifenacin treatment [N=116, 26]  | 1.28 (± 0.19)                                 | 2.21 (± 0.56)                                     |  |  |
| 9 weeks solifenacin treatment [N=115, 29]  | 1.59 (± 0.21)                                 | 1.94 (± 0.50)                                     |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | 1.60 (± 0.21)                                 | 2.89 (± 0.51)                                     |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | 2.09 (± 0.22)                                 | 3.19 (± 0.51)                                     |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | 2.15 (± 0.25)                                 | 2.71 (± 0.59)                                     |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | 2.57 (± 0.40)                                 | 3.27 (± 0.73)                                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Number of Dry (Incontinence-free) Days per 7 Days – Repeated Measures ANCOVA

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Number of Dry (Incontinence-free) Days per 7 Days – Repeated Measures ANCOVA |
|-----------------|--|

End point description:

Repeated measures ANCOVA (analysis of covariance) was used in this analysis, which included double-blind and/or open-label solifenacin treatment duration, gender, geographic region and randomized treatment group in Study 905-CL-076 as fixed effects, baseline as a covariate and "duration" repeated within participant. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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

End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

| End point values                          | Children (aged 5 to less than 12 years) - FAS | Adolescents (Aged 12 to Less Than 18 Years) - FAS |  |  |
|---|---|---|--|--|
| Subject group type                        | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed               | 117   | 29  |  |  |
| Units: days                               |   |   |  |  |
| least squares mean (standard error)       |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28] | 1.35 (± 0.19)                                 | 1.53 (± 0.69)                                     |  |  |
| 6 weeks solifenacin treatment [N=116, 26] | 1.43 (± 0.20)                                 | 1.90 (± 0.70)                                     |  |  |

|  |                    |                    |  |  |
|--|--------------------|--------------------|--|--|
| 9 weeks solifenacin treatment [N=115, 29]  | 1.72 ( $\pm$ 0.22) | 1.75 ( $\pm$ 0.69) |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | 1.80 ( $\pm$ 0.22) | 2.69 ( $\pm$ 0.69) |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | 2.21 ( $\pm$ 0.23) | 3.07 ( $\pm$ 0.69) |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | 2.28 ( $\pm$ 0.25) | 2.45 ( $\pm$ 0.71) |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | 2.84 ( $\pm$ 0.33) | 3.93 ( $\pm$ 0.81) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Mean Number of Micturations per 24 Hours

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Mean Number of Micturations per 24 Hours |
|-----------------|--|

End point description:

The mean number of micturations (urinations) was based on 7-day diary data completed by participants prior to each visit from start of 905-CL-076 to end of 905-CL-077. Data are reported by duration of solifenacin treatment based on the number of days from the date of first dose of solifenacin in either study 905-CL-076 or 905-CL-077 up to and including the study visit. Using equivalent treatment duration periods, data were combined for participants who received placebo and solifenacin in study 905-CL-076 within each age group. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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

End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

| End point values                           | Children (aged 5 to less than 12 years) - FAS | Adolescents (Aged 12 to Less Than 18 Years) - FAS |  |  |
|--|---|---|--|--|
| Subject group type                         | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed                | 117   | 29  |  |  |
| Units: Micturations                        |   |   |  |  |
| arithmetic mean (standard error)           |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28]  | -0.78 ( $\pm$ 0.18)                           | -1.29 ( $\pm$ 0.39)                               |  |  |
| 6 weeks solifenacin treatment [N=116, 26]  | -0.96 ( $\pm$ 0.20)                           | -1.38 ( $\pm$ 0.63)                               |  |  |
| 9 weeks solifenacin treatment [N=115, 29]  | -1.15 ( $\pm$ 0.20)                           | -1.15 ( $\pm$ 0.61)                               |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | -1.09 ( $\pm$ 0.21)                           | -1.24 ( $\pm$ 0.49)                               |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | -1.42 ( $\pm$ 0.21)                           | -1.01 ( $\pm$ 0.49)                               |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | -1.43 ( $\pm$ 0.24)                           | -1.39 ( $\pm$ 0.75)                               |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | -1.80 ( $\pm$ 0.43)                           | -0.81 ( $\pm$ 0.34)                               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Mean Number of Micturitions per 24 Hours – Repeated Measures ANCOVA

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Mean Number of Micturitions per 24 Hours – Repeated Measures ANCOVA |
|-----------------|---|

End point description:

Repeated measures ANCOVA (analysis of covariance) was used in this analysis, which included double-blind and/or open-label solifenacin treatment duration, gender, geographic region and randomized treatment group in Study 905-CL-076 as fixed effects, baseline as a covariate and "duration" repeated within participant. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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

End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

| End point values                           | Children (aged 5 to less than 12 years) - FAS | Adolescents (Aged 12 to Less Than 18 Years) - FAS |  |  |
|--|---|---|--|--|
| Subject group type                         | Subject analysis set                          | Subject analysis set                              |  |  |
| Number of subjects analysed                | 117   | 29  |  |  |
| Units: Micturitions                        |   |   |  |  |
| least squares mean (standard error)        |   |   |  |  |
| 3 weeks solifenacin treatment [N=114, 28]  | -0.98 (± 0.15)                                | -0.93 (± 0.39)                                    |  |  |
| 6 weeks solifenacin treatment [N=116, 26]  | -1.15 (± 0.15)                                | -0.94 (± 0.26)                                    |  |  |
| 9 weeks solifenacin treatment [N=115, 29]  | -1.31 (± 0.15)                                | -0.81 (± 0.31)                                    |  |  |
| 12 weeks solifenacin treatment [N=111, 29] | -1.22 (± 0.15)                                | -0.91 (± 0.30)                                    |  |  |
| 24 weeks solifenacin treatment [N=108, 27] | -1.50 (± 0.15)                                | -0.71 (± 0.52)                                    |  |  |
| 40 weeks solifenacin treatment [N=97, 23]  | -1.52 (± 0.16)                                | -1.18 (± 0.36)                                    |  |  |
| 52 weeks solifenacin treatment [N=44, 11]  | -1.83 (± 0.20)                                | -1.79 (± 0.38)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Change from Baseline in Mean Number of Grade 3 or 4 Urgency Episodes per 24 Hours in Adolescents**

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Mean Number of Grade 3 or 4 Urgency Episodes per 24 Hours in Adolescents |
|-----------------|--|

## End point description:

Adolescent participants were also asked to record urgencies for at least 2 of the 7 diary days using the Perception of Intensity of Urgency Scale (PPIUS): (0 - no urgency, 1 - mild urgency, 2 - moderate urgency, 3 - severe urgency, 4 - urge incontinence). This data is based on 7-day diary data completed by participants prior to each visit from the start of 905-CL-076 to the end of 905-CL-077. Data are reported by duration of solifenacin treatment based on the number of days from the date of first dose of solifenacin in either study 905-CL-076 or 905-CL-077 up to and including the study visit. Using equivalent treatment duration periods, data were combined for participants who received placebo and solifenacin in study 905-CL-076 within each age group. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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

## End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | Adolescents<br>(Aged 12 to<br>Less Than 18<br>Years) - FAS |  |  |  |
| Subject group type                    | Subject analysis set                                       |  |  |  |
| Number of subjects analysed           | 29   |  |  |  |
| Units: Urgency episodes               |  |  |  |  |
| arithmetic mean (standard error)      |  |  |  |  |
| 3 weeks solifenacin treatment [N=27]  | -0.79 (± 0.26)   |  |  |  |
| 6 weeks solifenacin treatment [N=25]  | -1.36 (± 0.53)   |  |  |  |
| 9 weeks solifenacin treatment [N=27]  | -1.15 (± 0.54)   |  |  |  |
| 12 weeks solifenacin treatment [N=28] | -1.31 (± 0.38)   |  |  |  |
| 24 weeks solifenacin treatment [N=26] | -1.11 (± 0.47)   |  |  |  |
| 40 weeks solifenacin treatment [N=22] | -2.18 (± 0.81)   |  |  |  |
| 52 weeks solifenacin treatment [N=10] | -1.87 (± 0.44)   |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in Mean Number of Grade 3 or 4 Urgency Episodes per 24 Hours in Adolescents – Repeated Measures ANCOVA**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Mean Number of Grade 3 or 4 Urgency Episodes per 24 Hours in Adolescents – Repeated Measures ANCOVA |
|-----------------|---|

## End point description:

Repeated measures ANCOVA (analysis of covariance) was used in this analysis, which included double-blind and/or open-label solifenacin treatment duration, gender, geographic region and randomized treatment group in Study 905-CL-076 as fixed effects, baseline as a covariate and "duration" repeated within participant. The analysis population was the FAS. N indicates the number of participants with available data at each time point.

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



End point timeframe:

Baseline (of 905-CL-076 study) and after 3, 6, 9, 12, 24, 40, and 52 weeks of solifenacin treatment

| End point values                      | Adolescents<br>(Aged 12 to<br>Less Than 18<br>Years) - FAS |  |  |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Subject analysis set                                       |  |  |  |
| Number of subjects analysed           | 28   |  |  |  |
| Units: Urgency episodes               |  |  |  |  |
| least squares mean (standard error)   |  |  |  |  |
| 3 weeks solifenacin treatment [N=27]  | -0.74 ( $\pm$ 0.46)  |  |  |  |
| 6 weeks solifenacin treatment [N=25]  | -1.30 ( $\pm$ 0.47)  |  |  |  |
| 9 weeks solifenacin treatment [N=27]  | -1.14 ( $\pm$ 0.47)  |  |  |  |
| 12 weeks solifenacin treatment [N=28] | -1.28 ( $\pm$ 0.46)  |  |  |  |
| 24 weeks solifenacin treatment [N=26] | -1.04 ( $\pm$ 0.46)  |  |  |  |
| 40 weeks solifenacin treatment [N=22] | -1.96 ( $\pm$ 0.49)  |  |  |  |
| 52 weeks solifenacin treatment [N=10] | -2.20 ( $\pm$ 0.65)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Final Visit in Postvoid Residual (PVR) Volume

|  |   |
|--|---|
| End point title  | Change from Baseline to Final Visit in Postvoid Residual (PVR) Volume |
| End point description:<br>PVR volume was assessed by ultrasonography or bladder scan during 905-CL-076 and 905-CL-077. The value reported is the last PVR volume value after first dose of solifenacin up to 52 weeks.                           |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline (of 905-CL-076 study) to final visit (the most recent value after first dose of solifenacin up to 40 weeks for participants who received placebo in 076 and 52 weeks for those who received solifenacin in 076) |   |

| End point values                 | Children (aged<br>5 to less than<br>12 years old) -<br>SAF | Adolescents<br>(Aged 12 to<br>Less Than 18<br>Years) - SAF |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Subject analysis set                                       | Subject analysis set                                       |  |  |
| Number of subjects analysed      | 118  | 29   |  |  |
| Units: mL                        |  |  |  |  |
| arithmetic mean (standard error) | 1.3 ( $\pm$ 11.9)  | 0.7 ( $\pm$ 8.8)   |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of solifenacin (in Study 905-CL-076 or in current study) up to 7 days after last dose of open-label solifenacin (41 weeks for participants who received placebo in 076 and 53 weeks for those who received solifenacin in 076).

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 13.0   |

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Children (Aged 5 to Less Than 12 Years) |
|-----------------------|---|

Reporting group description:

Children aged 5 to less than 12 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults.

|                       |   |
|-----------------------|---|
| Reporting group title | Adolescents (Aged 12 to Less Than 18 Years) |
|-----------------------|---|

Reporting group description:

Adolescents aged 12 to less than 18 years old with OAB who received placebo or solifenacin in 905-CL-076, received a weight-based dose of open-label solifenacin oral suspension once daily for 40 weeks in this study. At the start of the 12-week titration period, the dose was adjusted according to the weight of the participant in order to deliver a plasma drug exposure equivalent to the 2.5 mg, 5 mg, 7.5 mg and 10 mg once daily oral tablet dose of solifenacin in adults.

| Serious adverse events                            | Children (Aged 5 to Less Than 12 Years) | Adolescents (Aged 12 to Less Than 18 Years) |  |
|---|---|---|--|
| Total subjects affected by serious adverse events |   |   |  |
| subjects affected / exposed                       | 1 / 118 (0.85%)                         | 1 / 29 (3.45%)                              |  |
| number of deaths (all causes)                     | 0                                       | 0   |  |
| number of deaths resulting from adverse events    |   |   |  |
| Infections and infestations                       |   |   |  |
| Gastroenteritis                                   |   |   |  |
| subjects affected / exposed                       | 1 / 118 (0.85%)                         | 0 / 29 (0.00%)                              |  |
| occurrences causally related to treatment / all   | 0 / 1                                   | 0 / 0                                       |  |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0                                       |  |
| Appendicitis                                      |   |   |  |
| subjects affected / exposed                       | 0 / 118 (0.00%)                         | 1 / 29 (3.45%)                              |  |
| 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 %

| <b>Non-serious adverse events</b>                     | Children (Aged 5 to Less Than 12 Years) | Adolescents (Aged 12 to Less Than 18 Years) |  |
|---|---|---|--|
| Total subjects affected by non-serious adverse events |   |   |  |
| subjects affected / exposed                           | 93 / 118 (78.81%)                       | 29 / 29 (100.00%)                           |  |
| Investigations  |   |   |  |
| Electrocardiogram QT prolonged                        |   |   |  |
| subjects affected / exposed                           | 10 / 118 (8.47%)                        | 4 / 29 (13.79%)                             |  |
| occurrences (all)                                     | 10                                      | 4   |  |
| Nervous system disorders                              |   |   |  |
| Headache  |   |   |  |
| subjects affected / exposed                           | 16 / 118 (13.56%)                       | 1 / 29 (3.45%)                              |  |
| occurrences (all)                                     | 21                                      | 1   |  |
| General disorders and administration site conditions  |   |   |  |
| Pyrexia   |   |   |  |
| subjects affected / exposed                           | 9 / 118 (7.63%)                         | 0 / 29 (0.00%)                              |  |
| occurrences (all)                                     | 11                                      | 0   |  |
| Immune system disorders                               |   |   |  |
| Seasonal allergy                                      |   |   |  |
| subjects affected / exposed                           | 1 / 118 (0.85%)                         | 2 / 29 (6.90%)                              |  |
| occurrences (all)                                     | 1                                       | 2   |  |
| Gastrointestinal disorders                            |   |   |  |
| Abdominal pain upper                                  |   |   |  |
| subjects affected / exposed                           | 7 / 118 (5.93%)                         | 1 / 29 (3.45%)                              |  |
| occurrences (all)                                     | 10                                      | 1   |  |
| Constipation  |   |   |  |
| subjects affected / exposed                           | 16 / 118 (13.56%)                       | 1 / 29 (3.45%)                              |  |
| occurrences (all)                                     | 19                                      | 1   |  |
| Diarrhoea   |   |   |  |
| subjects affected / exposed                           | 7 / 118 (5.93%)                         | 2 / 29 (6.90%)                              |  |
| occurrences (all)                                     | 7                                       | 3   |  |
| Abdominal pain  |   |   |  |
| subjects affected / exposed                           | 3 / 118 (2.54%)                         | 2 / 29 (6.90%)                              |  |
| occurrences (all)                                     | 3                                       | 2   |  |
| Nausea  |   |   |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 3 / 118 (2.54%)<br>4 | 3 / 29 (10.34%)<br>3 |  |
| Infections and infestations                      |                      |                      |  |
| Escherichia urinary tract infection              |                      |                      |  |
| subjects affected / exposed                      | 7 / 118 (5.93%)      | 2 / 29 (6.90%)       |  |
| occurrences (all)                                | 9                    | 4                    |  |
| Gastroenteritis                                  |                      |                      |  |
| subjects affected / exposed                      | 11 / 118 (9.32%)     | 2 / 29 (6.90%)       |  |
| occurrences (all)                                | 11                   | 2                    |  |
| Nasopharyngitis                                  |                      |                      |  |
| subjects affected / exposed                      | 16 / 118 (13.56%)    | 4 / 29 (13.79%)      |  |
| occurrences (all)                                | 21                   | 4                    |  |
| Urinary tract infection                          |                      |                      |  |
| subjects affected / exposed                      | 6 / 118 (5.08%)      | 2 / 29 (6.90%)       |  |
| occurrences (all)                                | 8                    | 2                    |  |
| Influenza  |                      |                      |  |
| subjects affected / exposed                      | 4 / 118 (3.39%)      | 3 / 29 (10.34%)      |  |
| occurrences (all)                                | 4                    | 4                    |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 20 April 2012     | Several changes to dose, risk-benefit assessment and other statistical analyses were made to align the current protocol with the updated opinion of the Paediatric Committee (PDCO) of the EMA (published as: opinion of the PDCO on the acceptance of a modification of an agreed PIP (EMA-000573-PIP01-09-M01). Other changes were: increase in number of sites, inclusion criterion 3 was updated to reflect differences in national legislation with regard to informed consent (IC) for adolescents in clinical studies, inclusion criterion 4 was updated to provide more clarity on who should be subject to birth control, the discontinuation criterion relating to the QT interval was updated to reflect the use of QT interval corrected for heart rate by Bazett formula (QTcB), acute urinary retention (AUR) was defined as "urinary retention for which an intervention is required or has taken place" to provide clarification to investigators, it was added that no important identified risks for solifenacin had been captured in a pediatric population to date, a requirement for leucocyturia, defined as white blood cell (WBC) count > 100/mcL as a prior step to urine culture was added, Tri- and tetracyclic antidepressants were added to the list of restricted medication, the recording of the urgency grade in adolescents according to the PPIUS was reduced from 7 days per diary period to 2 days, the requirement of a sitting position of the patient for these assessments and the use of the same arm for every blood pressure measurement was specified to further standardize the measurement, instructions were changed to repeat the PVR volume assessment only once when the initial PVR volume was > 20 mL, specifications (comparison to age-appropriate norms) were added to aid data interpretation and ensure consistency in the assessment and evaluation of vital signs, laboratory results and height and weight, the SAE reporting instruction was slightly rephrased to provide better guidance to investigators. |
| 19 July 2012      | After finalization and first regulatory submissions of Substantial Amendment 1 dated 20 Apr 2012 (Protocol version 2.0), inconsistencies were identified in the changes made to the respective paragraphs across the protocol (e.g., changes made only in the synopsis part of the protocol, but not in the body text of the protocol). These were corrected in Protocol version 2.1, including Substantial Amendment 1 dated 20 Apr 2012.   |
| 07 September 2012 | Germany country-specific amendment: A local substantial Amendment 1 dated 7 Sep 2012 was issued. This amendment corresponds to the global substantial Amendment 2 dated 30 Oct 2012. In addition, the pharmacokinetic samples scheduled to be taken in Study 905-CL-076 were instead to be taken in this unblinded extension Study 905-CL-077. No patients were enrolled at the study sites in Germany.  |
| 24 September 2012 | The Netherlands country-specific amendment: A local substantial Amendment 1 dated 24 Sep 2012 was issued. This amendment corresponds to the global substantial Amendment 2 dated 30 Oct 2012. No patients were enrolled at the study sites in the Netherlands before this amendment was implemented.   |
| 17 October 2012   | UK country-specific amendment: A local substantial Amendment 1 dated 17 Oct 2012 was issued. This amendment corresponds to the global substantial Amendment 2 dated 30 Oct 2012. No patients were enrolled at the study sites in the UK before this amendment was implemented.   |

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| 30 October 2012   | This global amendment was prepared and submitted after approval of the country specific amendments. The sections "Study Design", "Dose Rationale", "Discontinuation Criteria for Individual Subjects", "Dose/Dose Regimen and Administration Period", and "Increase or Reduction in Dose of the Study Drugs" were updated to reflect the inclusion of the possibility to down titrate to "no treatment" (i.e., interruption of treatment) for a period of 3 weeks and the subsequent possibility to discontinue the study in case no symptoms of OAB occur in this period. This amendment was developed to limit unnecessary exposure to solifenacin in patients who did no longer require treatment with OAB medication. The objective was to identify patients who did not require treatment with OAB medication.   |
| 23 September 2013 | Several changes were made to align current protocol with the updated opinion of the PDCO of the EMA regarding solifenacin (published as: opinion of the Paediatric Committee on the acceptance of a modification of an agreed PIP [EMA-000573-PIP01-09-M04]). Other changes were: the number of patients was changed from at least 120 patients (at least 60 children and 60 adolescents) to at least 120 patients (at least 100 children and at least 20 adolescents) evaluable for the primary endpoint, an additional inclusion criterion was added "Subject agrees not to participate in another interventional study while on treatment", as well as the main analyses of safety and efficacy, which were performed separately in both children and adolescent cohorts, further statistical methods were described that used the data from the patients in this study together with data from adults in the solifenacin phase 3 program, to interpolate between children and adults, and provide estimates of treatment effects in adolescents based on an extensive data set, in assessing the PVR volume, the instruction that the bladder was to be emptied when it was initially filled > 50% of the bladder capacity for age was changed such that the bladder should only be emptied when it was initially filled with preferably > 50% of the bladder capacity for age, the calculation of the baseline QTcB mean was revised to use the average of the QTcB means of the ECG triplicates from the 2 prerandomization visits (i.e., visits 2 and 3) of Study 905-CL-076 instead of using the QTcB mean from visit 3 ECG triplicates only, the definition of SAE was reworded for clarification and the events of interest that may require expedited reporting and/or safety evaluation were defined and categorized. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported