



Clinical trial results:

12-week, Multicenter, Open-label, Non-comparative Study to Investigate Pharmacodynamic and Safety of Alfuzosin 0.2 mg/kg/Day in the Treatment of Children and Adolescents 2 - 16 Years of Age With Hydronephrosis Associated With Elevated Detrusor Leak Point Pressure of Neuropathic Etiology Followed by a 40-week Open-label Extension Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2007-000983-26 |
| Trial protocol | PL EE BG SK ES |
| Global end of trial date | 09 October 2009 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 01 April 2016 |
| First version publication date | 06 December 2014 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | EFC6269 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00576823 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi aventis recherche & développement |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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 | 10 November 2009 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 October 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary objective was to determine efficacy of Alfuzosin in the treatment of children and adolescents 2-16 years of age with newly diagnosed or progressive hydronephrosis due to elevated detrusor Leak Point Pressure (LPP) of neuropathic etiology.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Subjects continued their standard treatment including clean intermittent catheterization and anticholinergic/antimuscarinic agents. Antibiotics, over the counter analgesics, vitamins, dietary measures and/or laxatives were permitted if indicated.

Evidence for comparator:

NA

| | |
|---|---------------|
| Actual start date of recruitment | 06 March 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Slovakia: 2 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Taiwan: 2 |
| Country: Number of subjects enrolled | Malaysia: 1 |
| Country: Number of subjects enrolled | Singapore: 1 |
| Country: Number of subjects enrolled | Turkey: 1 |
| Country: Number of subjects enrolled | Russian Federation: 7 |
| Country: Number of subjects enrolled | India: 3 |
| Worldwide total number of subjects | 25 |
| EEA total number of subjects | 10 |

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) | 21 |
| Adolescents (12-17 years) | 4 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 19 sites in 12 countries. A total of 43 subjects were screened between December 2007 and September 2008.

Pre-assignment

Screening details:

18/43 screened subjects were not included: Inclusion/Exclusion criteria not respected (16), Subject's request (1), Other (2).

Subjects could have several reasons for not being included. Eligible subjects received alfuzosin 0.2 mg/kg/day. Formulation/frequency assigned by Interactive Voice Response System as per age group, ability to swallow tablet.

Period 1

| | |
|------------------------------|------------------------|
| Period 1 title | 12-week Efficacy Phase |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Alfuzosin Solution 12 weeks - 2-7 Years |

Arm description:

Alfuzosin solution for 12 weeks to children 2-7 years of age.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin solution 0.066 milligram per kilogram (mg/kg) three times daily (0.2 mg/kg/Day) administered orally for 12 weeks.

| | |
|------------------|--|
| Arm title | Alfuzosin Solution 12 weeks - 8-16 Years |
|------------------|--|

Arm description:

Alfuzosin solution 12 weeks to children and adolescents 8-16 years of age who were not able to swallow the tablets or preferred to take the solution or had a body weight less than (<) 30 kilogram (kg).

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin solution 0.066 mg/kg three times daily (0.2 mg/kg/Day) administered orally for 12 weeks.

| | |
|------------------|--|
| Arm title | Alfuzosin Tablet 12 weeks - 8-16 Years |
|------------------|--|

Arm description:

Alfuzosin tablet for 12 weeks to children and adolescents 8-16 years of age who were able to swallow the tablets and had a body weight greater than or equal to (>=) 30 kg.

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

| | |
|--|-----------|
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin tablet 0.1 mg/kg two times daily (0.2 mg/kg/Day) administered for 12 weeks.

| Number of subjects in period 1 | Alfuzosin Solution 12 weeks - 2-7 Years | Alfuzosin Solution 12 weeks - 8-16 Years | Alfuzosin Tablet 12 weeks - 8-16 Years |
|---------------------------------------|---|---|---|
| Started | 12 | 6 | 7 |
| Completed | 11 | 6 | 7 |
| Not completed | 1 | 0 | 0 |
| Parent's schedule issue | 1 | - | - |

Period 2

| | |
|------------------------------|--------------------------------|
| Period 2 title | 40-week Safety Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Alfuzosin Solution 40 weeks - 2-7 Years |

Arm description:

Alfuzosin solution for additional 40 weeks to children 2-7 years of age.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin solution 0.066 mg/kg three times daily (0.2 mg/kg/Day) administered orally for 40 weeks.

| | |
|------------------|--|
| Arm title | Alfuzosin Solution 40 weeks - 8-16 Years |
|------------------|--|

Arm description:

Alfuzosin solution for additional 40 weeks to children and adolescents 8-16 years of age who were not able to swallow the tablets or preferred to take the solution or had a body weight <30 kg.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin solution 0.066 mg/kg three times daily (0.2 mg/kg/Day) administered orally for 40 weeks.

| | |
|---|--|
| Arm title | Alfuzosin Tablet - 8-16 Years - 40 weeks |
| Arm description: Alfuzosin tablet for additional 40 weeks to children and adolescents 8-16 years of age who were able to swallow the tablets and had a body weight ≥ 30 kg. | |
| Arm type | Experimental |
| Investigational medicinal product name | Alfuzosin |
| Investigational medicinal product code | SL770499 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Alfuzosin tablet 0.1 mg/kg two times daily (0.2 mg/kg/Day) administered for 40 weeks.

| Number of subjects in period 2^[1] | Alfuzosin Solution 40 weeks - 2-7 Years | Alfuzosin Solution 40 weeks - 8-16 Years | Alfuzosin Tablet - 8-16 Years - 40 weeks |
|---|---|--|--|
| Started | 11 | 6 | 6 |
| Completed | 10 | 6 | 6 |
| Not completed | 1 | 0 | 0 |
| Lack of efficacy | 1 | - | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject in the Alfuzosin Tablet 12 weeks - 8-16 Years arm refused to continue in the extension phase.

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Alfuzosin Solution 12 weeks - 2-7 Years |
| Reporting group description: Alfuzosin solution for 12 weeks to children 2-7 years of age. | |
| Reporting group title | Alfuzosin Solution 12 weeks - 8-16 Years |
| Reporting group description: Alfuzosin solution 12 weeks to children and adolescents 8-16 years of age who were not able to swallow the tablets or preferred to take the solution or had a body weight less than (<) 30 kilogram (kg). | |
| Reporting group title | Alfuzosin Tablet 12 weeks - 8-16 Years |
| Reporting group description: Alfuzosin tablet for 12 weeks to children and adolescents 8-16 years of age who were able to swallow the tablets and had a body weight greater than or equal to (>=) 30 kg. | |

| Reporting group values | Alfuzosin Solution 12 weeks - 2-7 Years | Alfuzosin Solution 12 weeks - 8-16 Years | Alfuzosin Tablet 12 weeks - 8-16 Years |
|---|---|---|---|
| Number of subjects | 12 | 6 | 7 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean standard deviation | 4.3 ± 1.5 | 10 ± 1.7 | 11.2 ± 2.3 |
| Gender categorical Units: Subjects | | | |
| Female Male | 7 5 | 4 2 | 5 2 |
| Type of hydronephrosis Units: Subjects | | | |
| Bilateral hydronephrosis (both kidneys affected) Unilateral hydronephrosis (one kidney affected) | 11 1 | 4 2 | 5 2 |
| Urinary Tract Infection (UTI) history within the last 3 months Units: Subjects | | | |
| No UTI episode One UTI episode Two UTI episodes | 9 2 1 | 4 2 0 | 6 1 0 |

| | | | |
|--|--------|--------|--------|
| Grade of hydronephrosis - Left kidney | | | |
| Hydronephrosis was investigated by ultrasound of the kidneys, and graded using the Society of Fetal Urology (SFU) classification (5-point ordinal scale grading hydronephrosis from 0 [No hydronephrosis] to 4 [worst condition]). | | | |
| Units: grade | | | |
| median | 2 | 1.5 | 2 |
| full range (min-max) | 1 to 3 | 1 to 3 | 1 to 3 |
| Grade of hydronephrosis - Right kidney | | | |
| Units: grade | | | |
| median | 1 | 2 | 1 |
| full range (min-max) | 0 to 3 | 0 to 3 | 0 to 3 |
| Duration of diagnosis for hydronephrosis | | | |
| Units: years | | | |
| arithmetic mean | 1.83 | 5.45 | 3.35 |
| standard deviation | ± 2.3 | ± 4.2 | ± 3.05 |

| | | | |
|--|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 25 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | | |
| Male | 9 | | |
| Type of hydronephrosis | | | |
| Units: Subjects | | | |
| Bilateral hydronephrosis (both kidneys affected) | 20 | | |
| Unilateral hydronephrosis (one kidney affected) | 5 | | |
| Urinary Tract Infection (UTI) history within the last 3 months | | | |
| Units: Subjects | | | |
| No UTI episode | 19 | | |
| One UTI episode | 5 | | |
| Two UTI episodes | 1 | | |

| | | | |
|--|---|--|--|
| Grade of hydronephrosis - Left kidney | | | |
| Hydronephrosis was investigated by ultrasound of the kidneys, and graded using the Society of Fetal Urology (SFU) classification (5-point ordinal scale grading hydronephrosis from 0 [No hydronephrosis] to 4 [worst condition]). | | | |
| Units: grade median full range (min-max) | - | | |
| Grade of hydronephrosis - Right kidney Units: grade median full range (min-max) | - | | |
| Duration of diagnosis for hydronephrosis Units: years arithmetic mean standard deviation | - | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Alfuzosin Solution 12 weeks - 2-7 Years |
| Reporting group description: Alfuzosin solution for 12 weeks to children 2-7 years of age. | |
| Reporting group title | Alfuzosin Solution 12 weeks - 8-16 Years |
| Reporting group description: Alfuzosin solution 12 weeks to children and adolescents 8-16 years of age who were not able to swallow the tablets or preferred to take the solution or had a body weight less than (<) 30 kilogram (kg). | |
| Reporting group title | Alfuzosin Tablet 12 weeks - 8-16 Years |
| Reporting group description: Alfuzosin tablet for 12 weeks to children and adolescents 8-16 years of age who were able to swallow the tablets and had a body weight greater than or equal to (>=) 30 kg. | |
| Reporting group title | Alfuzosin Solution 40 weeks - 2-7 Years |
| Reporting group description: Alfuzosin solution for additional 40 weeks to children 2-7 years of age. | |
| Reporting group title | Alfuzosin Solution 40 weeks - 8-16 Years |
| Reporting group description: Alfuzosin solution for additional 40 weeks to children and adolescents 8-16 years of age who were not able to swallow the tablets or preferred to take the solution or had a body weight <30 kg. | |
| Reporting group title | Alfuzosin Tablet - 8-16 Years - 40 weeks |
| Reporting group description: Alfuzosin tablet for additional 40 weeks to children and adolescents 8-16 years of age who were able to swallow the tablets and had a body weight >=30 kg. | |
| Subject analysis set title | 2-7 Years Subjects Exposed to Alfuzosin Solution |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All subjects, 2-7 years of age, who received at least one dose of Alfuzosin 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received. | |
| Subject analysis set title | 8-16 Years Subjects Exposed to Alfuzosin Solution |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All subjects, 8-16 years of age, who received at least one dose of Alfuzosin solution 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received. | |
| Subject analysis set title | 8-16 Years Subjects Exposed to Alfuzosin Tablet |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All subjects, 8-16 years of age, who received at least one dose of Alfuzosin tablet 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received. | |

Primary: Number of Subjects With a Decrease From Baseline ≥ 1 in the Society of Fetal Urology (SFU) Grade of Hydronephrosis

| | |
|---|--|
| End point title | Number of Subjects With a Decrease From Baseline ≥ 1 in the Society of Fetal Urology (SFU) Grade of Hydronephrosis ^[1] |
| End point description: Hydronephrosis was investigated by ultrasound and graded using SFU classification at each time point. 'Complete response' was assessed when bilateral hydronephrosis at baseline and grade decrease from baseline ≥ 1 for both kidneys, or, unilateral hydronephrosis at baseline and grade decrease from baseline ≥ 1 for the affected kidney without worsening of the other kidney. 'Partial response' was assessed when bilateral hydronephrosis at baseline and grade decrease from | |

baseline ≥ 1 for one kidney without worsening of the other kidney.

The analysis was performed on the intent-to-treat (ITT) population (that is, all included subjects who received at least one dose of Alfuzosin) excluding the subjects who didn't have baseline SFU grade. Subjects without post-baseline SFU grade before Week 12 were included as non-responders.

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

End point timeframe:

baseline and 12 weeks (efficacy study phase)

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 was an exploratory, open label, non-comparative trial. Analysis were purely descriptive.

| End point values | Alfuzosin Solution 12 weeks - 2-7 Years | Alfuzosin Solution 12 weeks - 8-16 Years | Alfuzosin Tablet 12 weeks - 8-16 Years | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 6 | 7 | |
| Units: subjects | | | | |
| Complete response | 2 | 5 | 3 | |
| - Bilateral hydronephrosis | 1 | 3 | 1 | |
| - Unilateral hydronephrosis | 1 | 2 | 2 | |
| Partial response | 3 | 0 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Symptomatic Urinary Tract Infection (UTI) Episodes

| | |
|-----------------|--|
| End point title | Number of Subjects With Symptomatic Urinary Tract Infection (UTI) Episodes |
|-----------------|--|

End point description:

When a subject presented with symptoms such as pain, fever or hematuria (discretion of the Investigator), an urinalysis was performed including a dipstick and a quantitative urine culture.

A symptomatic UTI was defined as the presence of symptoms and a positive culture with $> 100\,000$ Colony Forming Units (CFUs) with a single organism.

The analysis was performed on the ITT population (that is, all included subjects who received at least one dose of Alfuzosin).

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

End point timeframe:

12 weeks (efficacy study phase)

| End point values | Alfuzosin Solution 12 weeks - 2-7 Years | Alfuzosin Solution 12 weeks - 8-16 Years | Alfuzosin Tablet 12 weeks - 8-16 Years | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 6 | 7 | |
| Units: subject | | | | |
| No symptomatic UTI | 11 | 5 | 7 | |
| One symptomatic UTI | 0 | 1 | 0 | |
| Two symptomatic UTI | 1 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Symptomatic Urinary Tract Infection (UTI) Episodes

| | |
|------------------------|--|
| End point title | Number of Subjects With Symptomatic Urinary Tract Infection (UTI) Episodes |
| End point description: | The analysis was performed on the exposed population (that is, all subjects who received at least one dose of Alfuzosin regardless of the amount of treatment received). |
| End point type | Secondary |
| End point timeframe: | 52 weeks (efficacy and extension study phases) |

| End point values | 2-7 Years Subjects Exposed to Alfuzosin Solution | 8-16 Years Subjects Exposed to Alfuzosin Solution | 8-16 Years Subjects Exposed to Alfuzosin Tablet | |
|-----------------------------|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 12 | 6 | 7 | |
| Units: subjects | | | | |
| No symptomatic UTI | 8 | 5 | 5 | |
| One symptomatic UTI | 2 | 0 | 2 | |
| Two symptomatic UTI | 2 | 0 | 0 | |
| Three symptomatic UTI | 0 | 1 | 0 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (52 weeks) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Treatment-emergent AEs are reported that is AEs that developed/worsened during on treatment period (time from 1st dose of drug up to 48 h [5 half lives] after last dose of drug of 12-week efficacy phase and up to time before 1st administration of extension phase for subjects continuing in the extension or after last dose of drug [for whole study]).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 12.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Afluzosin Solution - 2-7 years |
|-----------------------|--------------------------------|

Reporting group description:

All subjects, 2-7 years of age, who received at least one dose of Alfuzosin 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Afluzosin Tablets - 8-16 years |
|-----------------------|--------------------------------|

Reporting group description:

All subjects, 8-16 years of age, who received at least one dose of Alfuzosin tablet 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Afluzosin Solution - 8-16 years |
|-----------------------|---------------------------------|

Reporting group description:

All subjects, 8-16 years of age, who received at least one dose of Alfuzosin solution 0.2 mg/kg/Day during the overall study period (efficacy phase and/or safety extension phase) regardless of the amount of treatment received.

| Serious adverse events | Afluzosin Solution - 2-7 years | Afluzosin Tablets - 8-16 years | Afluzosin Solution - 8-16 years |
|---|-----------------------------------|-----------------------------------|------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 7 (0.00%) | 2 / 6 (33.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Femur Fracture | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteric Injury | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Calculus Urinary | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal Impairment | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyelonephritis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Afluzosin Solution - 2-7 years | Afluzosin Tablets - 8-16 years | Afluzosin Solution - 8-16 years |
|---|-----------------------------------|-----------------------------------|------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 12 (75.00%) | 5 / 7 (71.43%) | 5 / 6 (83.33%) |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Forearm Fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Iatrogenic Injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 7 (14.29%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb Injury | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urethral Injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 7 (14.29%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 7 (14.29%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|--|
| Dizziness subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders Eosinophilia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| General disorders and administration site conditions Oedema Peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 2 / 12 (16.67%) 2 | 0 / 7 (0.00%) 0 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 2 / 6 (33.33%) 2 |
| Gastrointestinal disorders Abdominal Pain Upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry Mouth subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 | 1 / 7 (14.29%) 1 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders Vaginal Discharge subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| Cough subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 |
| Respiratory Disorder subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dermatitis Allergic subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Conjunctivitis Infective subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 |
| Cystitis subjects affected / exposed occurrences (all) | 3 / 12 (25.00%) 3 | 1 / 7 (14.29%) 1 | 0 / 6 (0.00%) 0 |
| Ear Infection subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Gastrointestinal Infection subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 7 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Gastrointestinal Viral Infection | | | |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 1 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 7 (14.29%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 7 (14.29%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 7 (14.29%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Viral Infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral Pharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral Rhinitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 7 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral Upper Respiratory Tract | | | |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| Infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 7 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 05 May 2008 | Several aspects of original protocol were modified in order to change the grading of hydronephrosis in the inclusion criteria (Grade 3 hydronephrosis was added), to clarify the grading of the Vesicoureteral Reflux (VUR) and grading of ureteral dilatation, to better characterize the assessment of vital signs, and to modify the schedule of the collection of pharmacokinetic samples and the schedule of the ultrasound assessments. |
| 17 July 2008 | Additional ultrasound assessments were scheduled and provided further clarification on the grading of the VUR and grading of ureteral dilatation. A detailed Investigator instruction letter for VUR grading was also provided to the sites. |
| 06 October 2008 | The temporary treatment discontinuation procedure was revised and characterized the collection of laboratory results in more detail. In addition, a few minor editorial changes were made to the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported