



## Clinical trial results:

### A Placebo-Controlled, Randomized, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Biological Activity of ATYR1940 in Adult Patients with Molecularly Defined Genetic Muscular Dystrophies

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-001753-17  |
| Trial protocol           | NL IT           |
| Global end of trial date | 04 January 2017 |

#### Results information

|                                   |                                                                             |
|-----------------------------------|-----------------------------------------------------------------------------|
| Result version number             | v1 (current)                                                                |
| This version publication date     | 30 November 2018                                                            |
| First version publication date    | 30 November 2018                                                            |
| Summary attachment (see zip file) | ATYR1940-C-002 CSR synopsis (ATYR1940-C-002 FINAL CSR Synopsis 12JUN17.pdf) |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | ATYR1940-C-002 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |                    |
|------------------------------------|--------------------|
| ISRCTN number                      | -                  |
| ClinicalTrials.gov id (NCT number) | -                  |
| WHO universal trial number (UTN)   | -                  |
| Other trial identifiers            | IND number: 122045 |

Notes:

#### Sponsors

|                              |                                                                                             |
|------------------------------|---------------------------------------------------------------------------------------------|
| Sponsor organisation name    | aTyr Pharma, Inc.                                                                           |
| Sponsor organisation address | 3545 John Hopkins Court, Suite #250, San Diego, CA, United States, 92121                    |
| Public contact               | Clinical Trial Operations, Voisin Consulting, clinicaltrialinformation@voisinconsulting.com |
| Scientific contact           | Clinical Trial Operations, Voisin Consulting, clinicaltrialinformation@voisinconsulting.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 12 June 2017     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 21 December 2015 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 04 January 2017  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Evaluate the safety, tolerability, pharmacokinetics (PK), and immunogenicity of multiple doses of intravenous (IV) ATYR1940 in adults 18 to 65 years of age, inclusive, with FSHD.

All clinically significant laboratory abnormalities were reported as adverse events and therefore appear in the Adverse events section of this dataset. As a consequence, the endpoints reported in this dataset are limited to the most relevant safety endpoints, as well as the pharmacodynamic endpoints.

Cohort 4 was optional in the study and the Sponsor elected to not move forward with Cohort 4.

Protection of trial subjects:

The study process, benefits and risks of participating in the study were explained to each subject. In addition, if the study drug needed to be stopped for safety, the doctor, his/her staff along with the medical monitor, were to continue to monitor participant's health and determine what treatment should be given (if any) until the symptoms or findings had resolved or until a satisfactory conclusion was reached.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 04 September 2014 |
| 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 | Netherlands: 7   |
| Country: Number of subjects enrolled | France: 6        |
| Country: Number of subjects enrolled | Italy: 5         |
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects   | 20               |
| EEA total number of subjects         | 18               |

Notes:

### Subjects enrolled per age group

|                                        |   |
|----------------------------------------|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|                                          |    |
|------------------------------------------|----|
| wk                                       |    |
| 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)                     | 18 |
| From 65 to 84 years                      | 2  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Cohorts 1 to 3 were completed and the data are described herein. The sponsor elected not to move forward with cohort 4.

### Pre-assignment

Screening details:

A total of 44 patients were screened. Out of that number, 20 patients were randomized.

### Period 1

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

### Arms

|                              |                      |
|------------------------------|----------------------|
| Are arms mutually exclusive? | No                   |
| <b>Arm title</b>             | Cohort 1 - 0.3 mg/kg |

Arm description:

Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | ATYR1940                              |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Patients received an initial Study Drug infusion of placebo, followed by once weekly IV Study Drug administration (ATYR1940) for 4 weeks. All Study Drug was administered via IV infusion over 30 minutes.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Cohort 2 - 1 mg/kg |
|------------------|--------------------|

Arm description:

Cohort 2 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | ATYR1940                              |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Patients received an initial Study Drug infusion of placebo, followed by once weekly IV Study Drug administration (ATYR1940) for 4 weeks. All Study Drug was administered via IV infusion over 30 minutes.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Cohort 3 - 3 mg/kg |
|------------------|--------------------|

Arm description:

Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.

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

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | ATYR1940                              |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Patients received an initial Study Drug infusion of placebo, followed by once weekly IV Study Drug administration (ATYR1940) for 12 weeks. All Study Drug was administered via IV infusion over 30 minutes.

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Cohorts 1, 2 and 3 - Placebo |
|------------------|------------------------------|

**Arm description:**

Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). Cohorts 2 and 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the placebo patient from Cohort 1, the 2 placebo patients from Cohort 2 and the 2 placebo patients from Cohort 3.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Placebo                               |
| Investigational medicinal product name | Placebo                               |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Patients received an initial Study Drug infusion of placebo, followed by once weekly IV Study Drug administration (placebo) for 4 weeks. All Study Drug was administered via IV infusion over 30 minutes.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Cohort 3 - Placebo |
|------------------|--------------------|

**Arm description:**

Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the 2 placebo patients from Cohort 3.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Placebo                               |
| Investigational medicinal product name | Placebo                               |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Patients received an initial Study Drug infusion of placebo, followed by once weekly IV Study Drug administration (placebo) for 12 weeks. All Study Drug was administered via IV infusion over 30 minutes.

| <b>Number of subjects in period 1</b> | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg |
|---------------------------------------|----------------------|--------------------|--------------------|
| Started                               | 3                    | 6                  | 6                  |
| Completed                             | 3                    | 6                  | 6                  |

| <b>Number of subjects in period 1</b> | Cohorts 1, 2 and 3 - Placebo | Cohort 3 - Placebo |
|---------------------------------------|------------------------------|--------------------|
| Started                               | 5                            | 2                  |
| Completed                             | 5                            | 2                  |



## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                    |                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                              | Cohort 1 - 0.3 mg/kg         |
| Reporting group description:                                                                                                                                                                                                                                                       |                              |
| Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                              | Cohort 2 - 1 mg/kg           |
| Reporting group description:                                                                                                                                                                                                                                                       |                              |
| Cohort 2 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                              | Cohort 3 - 3 mg/kg           |
| Reporting group description:                                                                                                                                                                                                                                                       |                              |
| Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                              | Cohorts 1, 2 and 3 - Placebo |
| Reporting group description:                                                                                                                                                                                                                                                       |                              |
| Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). Cohorts 2 and 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the placebo patient from Cohort 1, the 2 placebo patients from Cohort 2 and the 2 placebo patients from Cohort 3. |                              |
| Reporting group title                                                                                                                                                                                                                                                              | Cohort 3 - Placebo           |
| Reporting group description:                                                                                                                                                                                                                                                       |                              |
| Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the 2 placebo patients from Cohort 3.                                                                                                                                                        |                              |

| Reporting group values | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg |
|------------------------|----------------------|--------------------|--------------------|
| Number of subjects     | 3                    | 6                  | 6                  |
| Age categorical        |                      |                    |                    |
| Units: Subjects        |                      |                    |                    |
| Adults (18-64 years)   | 3                    | 6                  | 5                  |
| From 65-84 years       | 0                    | 0                  | 1                  |
| Age continuous         |                      |                    |                    |
| Units: years           |                      |                    |                    |
| arithmetic mean        | 44.3                 | 44.5               | 45.3               |
| full range (min-max)   | 25 to 55             | 33 to 52           | 25 to 72           |
| Gender categorical     |                      |                    |                    |
| Units: Subjects        |                      |                    |                    |
| Female                 | 1                    | 4                  | 2                  |
| Male                   | 2                    | 2                  | 4                  |

| Reporting group values | Cohorts 1, 2 and 3 - Placebo | Cohort 3 - Placebo | Total |
|------------------------|------------------------------|--------------------|-------|
| Number of subjects     | 5                            | 2                  | 20    |
| Age categorical        |                              |                    |       |
| Units: Subjects        |                              |                    |       |
| Adults (18-64 years)   | 4                            | 2                  | 18    |
| From 65-84 years       | 1                            | 0                  | 2     |
| Age continuous         |                              |                    |       |
| Units: years           |                              |                    |       |
| arithmetic mean        | 54                           | 56.5               |       |
| full range (min-max)   | 39 to 66                     | 49 to 64           | -     |

|                    |   |   |    |
|--------------------|---|---|----|
| Gender categorical |   |   |    |
| Units: Subjects    |   |   |    |
| Female             | 1 | 0 | 8  |
| Male               | 4 | 2 | 12 |



## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                    |                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                              | Cohort 1 - 0.3 mg/kg         |
| Reporting group description:<br>Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                                                              | Cohort 2 - 1 mg/kg           |
| Reporting group description:<br>Cohort 2 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                                                              | Cohort 3 - 3 mg/kg           |
| Reporting group description:<br>Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). For the purpose of reporting the results, separate arms were created for the placebo patients.                                                                                                                 |                              |
| Reporting group title                                                                                                                                                                                                                                                                                              | Cohorts 1, 2 and 3 - Placebo |
| Reporting group description:<br>Cohort 1 included 4 patients randomized 3 (ATYR1940) : 1 (placebo). Cohorts 2 and 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the placebo patient from Cohort 1, the 2 placebo patients from Cohort 2 and the 2 placebo patients from Cohort 3. |                              |
| Reporting group title                                                                                                                                                                                                                                                                                              | Cohort 3 - Placebo           |
| Reporting group description:<br>Cohort 3 included 8 patients randomized 3 (ATYR1940) : 1 (placebo). This arm includes the 2 placebo patients from Cohort 3.                                                                                                                                                        |                              |

### Primary: Anti-drug antibodies (ADA)

|                                                                                                                                                                                                                                                                                |                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| End point title                                                                                                                                                                                                                                                                | Anti-drug antibodies (ADA) <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                         |                                           |
| End point type                                                                                                                                                                                                                                                                 | Primary                                   |
| End point timeframe:<br>Screening and weeks 3 to 9 for Cohorts 1 and 2, screening and weeks 3 to 6, 10, 14, 17, 25 for Cohort 3                                                                                                                                                |                                           |
| Notes:<br>[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.<br>Justification: No statistical analysis was performed for any of the primary/safety endpoints. |                                           |

| End point values                                | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg | Cohorts 1, 2 and 3 - Placebo |
|-------------------------------------------------|----------------------|--------------------|--------------------|------------------------------|
| Subject group type                              | Reporting group      | Reporting group    | Reporting group    | Reporting group              |
| Number of subjects analysed                     | 3                    | 6                  | 6                  | 5                            |
| Units: number (frequency) of confirmed positive | 2                    | 1                  | 3                  | 0                            |

| End point values            | Cohort 3 - Placebo |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 2                  |  |  |  |

|                                                 |   |  |  |  |
|-------------------------------------------------|---|--|--|--|
| Units: number (frequency) of confirmed positive | 0 |  |  |  |
|-------------------------------------------------|---|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Primary: Jo-1 antibodies

|                 |                                |
|-----------------|--------------------------------|
| End point title | Jo-1 antibodies <sup>[2]</sup> |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

Screening and weeks 3 to 9 for Cohorts 1 and 2, screening and weeks 3 to 14, 17, 25 for Cohort 3

Notes:

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

Justification: No statistical analysis was performed for any of the primary/safety endpoints.

| End point values                                | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg | Cohorts 1, 2 and 3 - Placebo |
|-------------------------------------------------|----------------------|--------------------|--------------------|------------------------------|
| Subject group type                              | Reporting group      | Reporting group    | Reporting group    | Reporting group              |
| Number of subjects analysed                     | 3                    | 6                  | 6                  | 5                            |
| Units: number of patients positive or equivocal | 0                    | 0                  | 0                  | 0                            |

| End point values                                | Cohort 3 - Placebo |  |  |  |
|-------------------------------------------------|--------------------|--|--|--|
| Subject group type                              | Reporting group    |  |  |  |
| Number of subjects analysed                     | 2                  |  |  |  |
| Units: number of patients positive or equivocal | 0                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Treatment Emergent Adverse Events (TEAEs)

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Treatment Emergent Adverse Events (TEAEs) <sup>[3]</sup> |
|-----------------|----------------------------------------------------------|

End point description:

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

End point timeframe:

All study visits until the end of the study

Notes:

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

Justification: No statistical analysis was performed for any of the primary/safety endpoints.

| End point values                               | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg | Cohorts 1, 2 and 3 - Placebo |
|------------------------------------------------|----------------------|--------------------|--------------------|------------------------------|
| Subject group type                             | Reporting group      | Reporting group    | Reporting group    | Reporting group              |
| Number of subjects analysed                    | 3                    | 6                  | 6                  | 5                            |
| Units: number of subjects with at least 1 TEAE | 3                    | 6                  | 6                  | 5                            |

| End point values                               | Cohort 3 - Placebo |  |  |  |
|------------------------------------------------|--------------------|--|--|--|
| Subject group type                             | Reporting group    |  |  |  |
| Number of subjects analysed                    | 2                  |  |  |  |
| Units: number of subjects with at least 1 TEAE | 2                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Manual Muscle Testing (MMT)

|                 |                             |
|-----------------|-----------------------------|
| End point title | Manual Muscle Testing (MMT) |
|-----------------|-----------------------------|

End point description:

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

End point timeframe:

Cohorts 1 and 2: shift from baseline to Week 6

Cohort 3: shift from baseline to Week 14

| End point values                       | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg | Cohort 3 - 3 mg/kg | Cohorts 1, 2 and 3 - Placebo |
|----------------------------------------|----------------------|--------------------|--------------------|------------------------------|
| Subject group type                     | Reporting group      | Reporting group    | Reporting group    | Reporting group              |
| Number of subjects analysed            | 3                    | 6                  | 6                  | 5                            |
| Units: percentage                      |                      |                    |                    |                              |
| arithmetic mean (full range (min-max)) | 2.83 (1.0 to 4.4)    | 3.07 (0.7 to 5.6)  | 0.70 (-5.9 to 9.2) | 1.34 (-3.3 to 7.8)           |

| End point values            | Cohort 3 - Placebo |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 2                  |  |  |  |

|                                        |                      |  |  |  |
|----------------------------------------|----------------------|--|--|--|
| Units: percentage                      |                      |  |  |  |
| arithmetic mean (full range (min-max)) | -1.40 (-1.5 to -1.3) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Individualized Neuromuscular Quality of Life (INQoL) - Overall QoL

|                                                |                                                                    |
|------------------------------------------------|--------------------------------------------------------------------|
| End point title                                | Individualized Neuromuscular Quality of Life (INQoL) - Overall QoL |
| End point description:                         |                                                                    |
| End point type                                 | Secondary                                                          |
| End point timeframe:                           |                                                                    |
| Cohorts 1 and 2: shift from baseline to Week 6 |                                                                    |
| Cohort 3: shift from baseline to Week 14       |                                                                    |

| End point values                       | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg   | Cohort 3 - 3 mg/kg   | Cohorts 1, 2 and 3 - Placebo |
|----------------------------------------|----------------------|----------------------|----------------------|------------------------------|
| Subject group type                     | Reporting group      | Reporting group      | Reporting group      | Reporting group              |
| Number of subjects analysed            | 3                    | 5                    | 6                    | 5                            |
| Units: PP                              |                      |                      |                      |                              |
| arithmetic mean (full range (min-max)) | 2.77 (-5.0 to 6.7)   | -2.98 (-16.1 to 8.4) | -9.90 (-19.4 to 5.0) | 4.12 (-8.3 to 22.2)          |

| End point values                       | Cohort 3 - Placebo  |  |  |  |
|----------------------------------------|---------------------|--|--|--|
| Subject group type                     | Reporting group     |  |  |  |
| Number of subjects analysed            | 2                   |  |  |  |
| Units: PP                              |                     |  |  |  |
| arithmetic mean (full range (min-max)) | 15.55 (3.9 to 27.2) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug to the last follow-up assessment (EOS Visit) or after the end of the study if the TEAE was thought to be related to study drug

Adverse event reporting additional description:

TEAEs reported for  $\geq 2$  patients treated with ATYR1940 are listed in the section below.

The number of occurrences per TEAE is not available in the source data, the field "Occurrences all number" therefore corresponds to the number of subjects affected per TEAE.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 18.0   |

### Reporting groups

|                                |                              |
|--------------------------------|------------------------------|
| Reporting group title          | Cohorts 1, 2 and 3 - Placebo |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 1 - 0.3 mg/kg         |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 2 - 1 mg/kg           |
| Reporting group description: - |                              |
| Reporting group title          | Cohort 3 - 3 mg/kg           |
| Reporting group description: - |                              |

| Serious adverse events                               | Cohorts 1, 2 and 3 - Placebo                                                                                                           | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg |
|------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------|
| Total subjects affected by serious adverse events    |                                                                                                                                        |                      |                    |
| subjects affected / exposed                          | 0 / 5 (0.00%)                                                                                                                          | 0 / 3 (0.00%)        | 0 / 6 (0.00%)      |
| number of deaths (all causes)                        | 0                                                                                                                                      | 0                    | 0                  |
| number of deaths resulting from adverse events       |                                                                                                                                        |                      |                    |
| General disorders and administration site conditions |                                                                                                                                        |                      |                    |
| Infusion related reaction                            | Additional description: Not assessed by the Investigator as serious; upgraded by Sponsor as medically-important, and therefore, an SAE |                      |                    |
| subjects affected / exposed                          | 0 / 5 (0.00%)                                                                                                                          | 0 / 3 (0.00%)        | 0 / 6 (0.00%)      |
| occurrences causally related to treatment / all      | 0 / 0                                                                                                                                  | 0 / 0                | 0 / 0              |
| deaths causally related to treatment / all           | 0 / 0                                                                                                                                  | 0 / 0                | 0 / 0              |

| Serious adverse events                            | Cohort 3 - 3 mg/kg |  |  |
|---------------------------------------------------|--------------------|--|--|
| Total subjects affected by serious adverse events |                    |  |  |
| subjects affected / exposed                       | 1 / 6 (16.67%)     |  |  |
| number of deaths (all causes)                     | 0                  |  |  |
| number of deaths resulting from adverse events    |                    |  |  |

|                                                      |                                                                                                                                        |  |  |
|------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|--|--|
| General disorders and administration site conditions |                                                                                                                                        |  |  |
| Infusion related reaction                            | Additional description: Not assessed by the Investigator as serious; upgraded by Sponsor as medically-important, and therefore, an SAE |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%)                                                                                                                         |  |  |
| occurrences causally related to treatment / all      | 1 / 1                                                                                                                                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                                                                                                                                  |  |  |

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

| <b>Non-serious adverse events</b>                     | Cohorts 1, 2 and 3 - Placebo | Cohort 1 - 0.3 mg/kg | Cohort 2 - 1 mg/kg |
|-------------------------------------------------------|------------------------------|----------------------|--------------------|
| Total subjects affected by non-serious adverse events |                              |                      |                    |
| subjects affected / exposed                           | 5 / 5 (100.00%)              | 3 / 3 (100.00%)      | 6 / 6 (100.00%)    |
| Vascular disorders                                    |                              |                      |                    |
| Flushing                                              |                              |                      |                    |
| subjects affected / exposed                           | 0 / 5 (0.00%)                | 0 / 3 (0.00%)        | 1 / 6 (16.67%)     |
| occurrences (all)                                     | 0                            | 0                    | 1                  |
| Nervous system disorders                              |                              |                      |                    |
| Headache                                              |                              |                      |                    |
| subjects affected / exposed                           | 2 / 5 (40.00%)               | 0 / 3 (0.00%)        | 1 / 6 (16.67%)     |
| occurrences (all)                                     | 2                            | 0                    | 1                  |
| Presyncope                                            |                              |                      |                    |
| subjects affected / exposed                           | 0 / 5 (0.00%)                | 0 / 3 (0.00%)        | 0 / 6 (0.00%)      |
| occurrences (all)                                     | 0                            | 0                    | 0                  |
| Gastrointestinal disorders                            |                              |                      |                    |
| Nausea                                                |                              |                      |                    |
| subjects affected / exposed                           | 0 / 5 (0.00%)                | 0 / 3 (0.00%)        | 2 / 6 (33.33%)     |
| occurrences (all)                                     | 0                            | 0                    | 2                  |
| Respiratory, thoracic and mediastinal disorders       |                              |                      |                    |
| Cough                                                 |                              |                      |                    |
| subjects affected / exposed                           | 0 / 5 (0.00%)                | 1 / 3 (33.33%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                     | 0                            | 1                    | 0                  |
| Musculoskeletal and connective tissue disorders       |                              |                      |                    |
| Arthralgia                                            |                              |                      |                    |
| subjects affected / exposed                           | 0 / 5 (0.00%)                | 2 / 3 (66.67%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                     | 0                            | 2                    | 0                  |
| Back pain                                             |                              |                      |                    |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 3 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all)           | 1              | 1              | 3              |
| Myalgia                     |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 1              | 1              |

| <b>Non-serious adverse events</b>                     | Cohort 3 - 3 mg/kg |  |  |
|-------------------------------------------------------|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 6 / 6 (100.00%)    |  |  |
| Vascular disorders                                    |                    |  |  |
| Flushing                                              |                    |  |  |
| subjects affected / exposed                           | 1 / 6 (16.67%)     |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Nervous system disorders                              |                    |  |  |
| Headache                                              |                    |  |  |
| subjects affected / exposed                           | 2 / 6 (33.33%)     |  |  |
| occurrences (all)                                     | 2                  |  |  |
| Presyncope                                            |                    |  |  |
| subjects affected / exposed                           | 2 / 6 (33.33%)     |  |  |
| occurrences (all)                                     | 2                  |  |  |
| Gastrointestinal disorders                            |                    |  |  |
| Nausea                                                |                    |  |  |
| subjects affected / exposed                           | 0 / 6 (0.00%)      |  |  |
| occurrences (all)                                     | 0                  |  |  |
| Respiratory, thoracic and mediastinal disorders       |                    |  |  |
| Cough                                                 |                    |  |  |
| subjects affected / exposed                           | 2 / 6 (33.33%)     |  |  |
| occurrences (all)                                     | 2                  |  |  |
| Musculoskeletal and connective tissue disorders       |                    |  |  |
| Arthralgia                                            |                    |  |  |
| subjects affected / exposed                           | 1 / 6 (16.67%)     |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Back pain                                             |                    |  |  |
| subjects affected / exposed                           | 0 / 6 (0.00%)      |  |  |
| occurrences (all)                                     | 0                  |  |  |
| Myalgia                                               |                    |  |  |

|                             |               |  |  |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 6 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                            |
|-------------------|--------------------------------------|
| 02 September 2014 | 2.0 (Amendment 1; 02 September 2014) |
| 10 January 2015   | 3.0 (Amendment 2; 10 January 2015)   |
| 05 February 2015  | 4.0 (Amendment 3; 05 February 2015)  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported