



## Clinical trial results:

### An Open-Label Extension Study to Evaluate the Long-Term Safety, Tolerability, and Biological Activity of ATYR1940 in Patients with Limb Girdle and Fascioscapulohumeral Muscular Dystrophy

#### Summary

EudraCT number	2016-000624-25
Trial protocol	DK IT
Global end of trial date	18 April 2017

#### Results information

Result version number	v1 (current)
This version publication date	23 December 2018
First version publication date	23 December 2018
Summary attachment (see zip file)	ATYR1940-C-006 CSR Synopsis (synopsis.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	ATYR1940-C-006
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##### 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	05 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 April 2017
Global end of trial reached?	Yes
Global end of trial date	18 April 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and immunogenicity of long-term treatment with intravenous (IV) ATYR1940 in patients with limb girdle muscular dystrophy 2B (LGMD2B) or fascioscapulohumeral muscular dystrophy (FSHD) previously enrolled in clinical study ATYR1940-C-003 or ATYR1940-C-004.

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.

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	01 June 2016
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	Italy: 2
Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Denmark: 2
Worldwide total number of subjects	8
EEA total number of subjects	4

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	1
Adults (18-64 years)	7
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients who participated in and completed the treatment period in the parent studies.

### Pre-assignment

Screening details:

Patients who completed treatment in either parent study ATYR1940-C-003 or ATYR1940-C-004; demonstrated acceptable tolerability of study drug; were considered by the Investigator to be compliant with study drug and the study procedures; and did not meet any criterion for discontinuation.

### Period 1

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

### Arms

<b>Arm title</b>	Treatment period
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	ATYR1940
Investigational medicinal product code	ATYR1940
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For the first 12 weeks in this extension study, patients received ATYR1940 at the highest tolerated dose received in the parent study; no dose adjustments were allowed during this 12-week period. After 12 weeks, if the patient demonstrated good tolerability, the ATYR1940 dose may have been increased on a patient-specific basis to a maximum weekly dose of 3 mg/kg.

All patients received ATYR1940 on a weekly basis in this study, regardless of the frequency of dosing in the parent study.

ATYR1940 was administered via IV infusion over 90 minutes.

<b>Number of subjects in period 1</b>	Treatment period
Started	8
Completed	8

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment period (overall period)
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Reporting group description: -

Reporting group values	Treatment period (overall period)	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	7	7	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	30.0		
full range (min-max)	16 to 62	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	7	7	

## End points

### End points reporting groups

Reporting group title	Treatment period
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Reporting group description: -

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

End point title	Incidence of Treatment Emergent Adverse Events (TEAEs) <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

All study visits until the end of the study.

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

End point values	Treatment period			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: number of subjects with at least 1 TEAE	7			

### Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-drug antibodies (ADA) <sup>[2]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Week 1 then every 6 weeks (on-treatment), then 1-4- and 12-weeks post-treatment follow-up.

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.

<b>End point values</b>	Treatment period			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: number of confirmed positive	3			

### Statistical analyses

No statistical analyses for this end point

### Primary: Jo-1 antibodies

End point title	Jo-1 antibodies <sup>[3]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Weekly from Week 1, 1-week follow-up, 4-week follow-up, 12-week follow-up

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.

<b>End point values</b>	Treatment period			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: number of subjects Jo-1 positive	0			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent form to EOS visit

Adverse event reporting additional description:

Due to the small study size (N=8), 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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### Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

<b>Serious adverse events</b>	Treatment period		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

<b>Non-serious adverse events</b>	Treatment period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)  Myalgia subjects affected / exposed occurrences (all)  Pain in extremity subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3  3 / 8 (37.50%) 3  3 / 8 (37.50%) 3		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported