



## Clinical trial results:

### An Open-Label, Inpatient Dose Escalation Study to Evaluate the Safety, Tolerability, Immunogenicity, and Biological Activity of ATYR1940 in Patients with Limb Girdle and Facioscapulohumeral Muscular Dystrophies

#### Summary

EudraCT number	2015-001910-88
Trial protocol	DK
Global end of trial date	05 October 2016

#### Results information

Result version number	v1 (current)
This version publication date	13 April 2018
First version publication date	13 April 2018

#### Trial information

##### Trial identification

Sponsor protocol code	ATYR1940-C-004
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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, IND number: 132865

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	30 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2016
Global end of trial reached?	Yes
Global end of trial date	05 October 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and immunogenicity of the weekly and twice weekly intravenous (IV) administration of ATYR1940, at doses of 0.3, 1.0, and 3.0 mg/kg, to patients with Limb Girdle Muscular Dystrophy 2B (LGMD2B, dysferlinopathy) and Facioscapulohumeral Muscular Dystrophy (FSHD).

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	02 October 2015
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	France: 8
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	18
EEA total number of subjects	13

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)	0
Adults (18-64 years)	18

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	26 <sup>[1]</sup>
Number of subjects completed	18

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failures: 8
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number corresponds to the number of patients randomized (18) and not to the number of patients screened (26).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A – FSHD

Arm description:

Starting at a dose of 0.3 mg/kg, with the potential for inpatient dose escalation to 1.0 mg/kg over the dosing period

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 were to receive a single, 90-minute IV placebo infusion followed by administration of ATYR1940 as a 90-minute IV infusion once a week for 8 weeks, then twice weekly for 4 weeks, for a total of 12 weeks

<b>Arm title</b>	Group B – LGMD2B and FSHD
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Arm description:

Starting at a dose of 0.3 mg/kg/week, with the potential for inpatient dose escalation to a dose of 3.0 mg/kg and up to 3.0 mg/kg twice a week over the dosing period

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 were to receive a single, 90-minute IV placebo infusion followed by administration of ATYR1940

as a 90-minute IV infusion once a week for 8 weeks, then twice weekly for 4 weeks, for a total of 12 weeks

<b>Number of subjects in period 1</b>	Group A – FSHD	Group B – LGMD2B and FSHD
Started	4	14
Completed	4	10
Not completed	0	4
Consent withdrawn by subject	-	1
Other	-	2
Infusion-related reaction	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Group A – FSHD
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Reporting group description:

Starting at a dose of 0.3 mg/kg, with the potential for inpatient dose escalation to 1.0 mg/kg over the dosing period

Reporting group title	Group B – LGMD2B and FSHD
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Reporting group description:

Starting at a dose of 0.3 mg/kg/week, with the potential for inpatient dose escalation to a dose of 3.0 mg/kg and up to 3.0 mg/kg twice a week over the dosing period

Reporting group values	Group A – FSHD	Group B – LGMD2B and FSHD	Total
Number of subjects	4	14	18
Age categorical			
Units: Subjects			
Adults (18-64 years)	4	14	18
Age continuous			
Units: years			
arithmetic mean	45.0	36.3	
full range (min-max)	39 to 51	22 to 62	-
Gender categorical			
Units: Subjects			
Female	1	7	8
Male	3	7	10

## End points

### End points reporting groups

Reporting group title	Group A – FSHD
Reporting group description: Starting at a dose of 0.3 mg/kg, with the potential for inpatient dose escalation to 1.0 mg/kg over the dosing period	
Reporting group title	Group B – LGMD2B and FSHD
Reporting group description: Starting at a dose of 0.3 mg/kg/week, with the potential for inpatient dose escalation to a dose of 3.0 mg/kg and up to 3.0 mg/kg twice a week over the dosing period	

### Primary: Hematocrit

End point title	Hematocrit <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe: Change from baseline to 1-week post-treatment follow-up	

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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	1.25 (0.0 to 3.6)	0.09 (-3.9 to 5.1)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Hemoglobin

End point title	Hemoglobin <sup>[2]</sup>
End point description:	

End point type	Primary
End point timeframe: Change from baseline to 1-week 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.

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: g/L				
arithmetic mean (full range (min-max))	5.5 (0 to 10)	-1.2 (-13 to 13)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Erythrocytes

End point title	Erythrocytes <sup>[3]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment 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.

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: 10/L				
arithmetic mean (full range (min-max))	0.165 (0.07 to 0.32)	0.024 (-0.48 to 0.51)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Leukocytes

End point title	Leukocytes <sup>[4]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

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

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

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: 10/L				
arithmetic mean (full range (min-max))	0.63 (-0.6 to 1.4)	0.23 (-3.1 to 2.1)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Platelets

End point title	Platelets <sup>[5]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

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

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

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: 10/L				
arithmetic mean (full range (min-max))	4.0 (-35 to 46)	4.1 (-33 to 45)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Neutrophils

End point title	Neutrophils <sup>[6]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

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

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

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	-2.63 (-11.6 to 4.5)	0.21 (-13.9 to 14.6)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Lymphocytes

End point title	Lymphocytes <sup>[7]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

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

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

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	1.78 (-1.2 to 4.9)	0.91 (-14 to 16.5)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Monocytes

End point title	Monocytes <sup>[8]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[8] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	0.65 (-1.5 to 4.6)	-0.24 (-2.9 to 1.6)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Eosinophils

End point title	Eosinophils <sup>[9]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[9] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	0.73 (0.0 to 1.8)	-0.81 (-5.2 to 0.5)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Basophils

End point title	Basophils <sup>[10]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[10] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: percent				
arithmetic mean (full range (min-max))	-0.53 (-2.3 to 0.3)	-0.06 (-0.7 to 0.7)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Aspartate Aminotransferase

End point title Aspartate Aminotransferase<sup>[11]</sup>

End point description:

End point type Primary

End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[11] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: U/L				
arithmetic mean (full range (min-max))	0.5 (-11 to 13)	0.6 (-29 to 41)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Alanine Aminotransferase

End point title Alanine Aminotransferase<sup>[12]</sup>

End point description:

End point type Primary

End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[12] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: U/L				
arithmetic mean (full range (min-max))	-1.5 (-16 to 11)	-2.8 (-49 to 42)		

### Statistical analyses

No statistical analyses for this end point

#### Primary: Bilirubin

End point title	Bilirubin <sup>[13]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[13] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	12		
Units: mcmol/L				
arithmetic mean (full range (min-max))	1.97 (-2.6 to 4.3)	0.39 (-2.6 to 4.4)		

### Statistical analyses

No statistical analyses for this end point

#### Primary: Blood Urea Nitrogen

End point title	Blood Urea Nitrogen <sup>[14]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[14] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.268 (-1.43 to 1.07)	-0.001 (-1.79 to 1.42)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Creatinine

End point title	Creatinine <sup>[15]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[15] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	8		
Units: mcmol/L				
arithmetic mean (full range (min-max))	-2 (-8 to 0)	2.1 (-9 to 9)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Creatine Kinase

End point title	Creatine Kinase <sup>[16]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[16] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: U/L				
arithmetic mean (full range (min-max))	-25.3 (-100 to 56)	-38.2 (-1561 to 1204)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Cholesterol

End point title	Cholesterol <sup>[17]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[17] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	0.223 (-0.05 to 0.36)	0.014 (-0.90 to 0.83)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Sodium

End point title	Sodium <sup>[18]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[18] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	-1.5 (-7 to 1)	-0.2 (-3 to 5)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Potassium

End point title	Potassium <sup>[19]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[19] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	0.05 (-0.3 to 0.4)	-0.16 (-0.8 to 0.5)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Bicarbonate

End point title	Bicarbonate <sup>[20]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[20] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	-1.3 (-2 to 1)	-0.9 (-9 to 6)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Calcium

End point title	Calcium <sup>[21]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 1-week post-treatment follow-up

Notes:

[21] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: mmol/L				
arithmetic mean (full range (min-max))	0.080 (0.00 to 0.20)	-0.020 (-0.13 to 0.08)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Electrocardiogram - Heart rate

End point title	Electrocardiogram - Heart rate <sup>[22]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline (Week 2 preinfusion) to 1-week post-treatment follow-up

Notes:

[22] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: beats/min				
arithmetic mean (full range (min-max))	-5.0 (-11 to 3)	-0.2 (-18 to 16)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Electrocardiogram - PR duration

End point title	Electrocardiogram - PR duration <sup>[23]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline (Week 2 preinfusion) to 1-week post-treatment follow-up

Notes:

[23] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: msec				
arithmetic mean (full range (min-max))	-8.5 (-18 to -2)	-2.4 (-12 to 8)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Electrocardiogram - QRS duration

End point title	Electrocardiogram - QRS duration <sup>[24]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline (Week 2 preinfusion) to 1-week post-treatment follow-up

Notes:

[24] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: msec				
arithmetic mean (full range (min-max))	-3.3 (-17 to 8)	0.4 (-10 to 14)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Electrocardiogram - QTcF Interval

End point title	Electrocardiogram - QTcF Interval <sup>[25]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline (Week 2 preinfusion) to 1-week post-treatment follow-up

Notes:

[25] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	14		
Units: msec				
arithmetic mean (full range (min-max))	-15.5 (-23 to -8)	-1.1 (-17 to 25)		

## Statistical analyses

No statistical analyses for this end point

### Primary: PFT - FEV1/FVC Ratio

End point title	PFT - FEV1/FVC Ratio <sup>[26]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Change from baseline to 4-week post-treatment follow-up

Notes:

[26] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	12		
Units: percent				
arithmetic mean (full range (min-max))	0.448 (-3.00 to 6.66)	-0.876 (-6.59 to 5.00)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Anti-drug antibodies

End point title	Anti-drug antibodies <sup>[27]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Level of ADA titers: Screening, weeks 4, 6, 8 and 10 to 25 (follow-up period)

Notes:

[27] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: number (frequency) of confirmed positive	2	9		

### Statistical analyses

No statistical analyses for this end point

### Primary: Anti-Jo1 antibodies

End point title	Anti-Jo1 antibodies <sup>[28]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Screening, weeks 3 to 13, 14, 17 and 25 (follow-up period)

Notes:

[28] - 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	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: number of patients positive	0	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Manual Muscle Testing - Overall Total Score

End point title	Manual Muscle Testing - Overall Total Score
End point description:	
End point type	Secondary
End point timeframe:	
Percent change from baseline to 1-week post-treatment follow-up	

End point values	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: N/A				
arithmetic mean (full range (min-max))	-7.1 (-26 to 4)	4.3 (-2 to 21)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: INQoL - QoL

End point title	INQoL - QoL
End point description:	
End point type	Secondary
End point timeframe:	
Change from baseline to 1-week post-treatment follow-up	

<b>End point values</b>	Group A – FSHD	Group B – LGMD2B and FSHD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	14		
Units: N/A				
arithmetic mean (full range (min-max))	3.20 (-5.0 to 25.6)	1.04 (-10.5 to 17.2)		

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All AEs were to be collected and recorded from the time written informed consent is obtained through the EOS visit, or after the end of the study, if 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
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

### Reporting groups

Reporting group title	Group A – FSHD
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Reporting group description:

Starting at a dose of 0.3 mg/kg, with the potential for inpatient dose escalation to 1.0 mg/kg over the dosing period

Reporting group title	Group B – LGMD2B and FSHD
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Reporting group description:

Starting at a dose of 0.3 mg/kg/week, with the potential for inpatient dose escalation to a dose of 3.0 mg/kg and up to 3.0 mg/kg twice a week over the dosing period

Serious adverse events	Group A – FSHD	Group B – LGMD2B and FSHD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Group A – FSHD	Group B – LGMD2B and FSHD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	14 / 14 (100.00%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	4 / 14 (28.57%)	
occurrences (all)	0	4	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	7 / 14 (50.00%) 7	
Presyncope subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	2 / 14 (14.29%) 2	
Fatigue subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	1 / 14 (7.14%) 1	
Pyrexia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	2 / 14 (14.29%) 2	
Nausea subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 14 (14.29%) 2	
Pain in extremity			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 14 (7.14%) 1	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 14 (21.43%) 3	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2016	Protocol ATYR1940-C-004, Version 2.0, 08 January 2016

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported