



## Clinical trial results: The effect of tetanus revaccination in patients with myasthenia gravis Summary

EudraCT number	2014-004344-35
Trial protocol	NL
Global end of trial date	16 February 2015

### Results information

Result version number	v1 (current)
This version publication date	15 January 2022
First version publication date	15 January 2022
Summary attachment (see zip file)	Tetanus (Strijbos vaccine 2017 tetanus.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	50993
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#### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	LUMC
Sponsor organisation address	Albinusdreef 2, Leiden, Netherlands, 2333ZA
Public contact	Tetanus study contact, Leiden University Medical Center, 0031 715262118, myasthenie@lumc.nl
Scientific contact	Tetanus study contact, Leiden University Medical Center, 0031 715262118, myasthenie@lumc.nl

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	16 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2015
Global end of trial reached?	Yes
Global end of trial date	16 February 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the effectiveness of the humeral and cellular immune response after tetanus revaccination in patients with AChR MG, MuSK MG, or LEMS.

Protection of trial subjects:

Vital signs were measured directly after the revaccination and before leaving the hospital.

Background therapy:

Mestinon  
Prednisolone  
Azathioprine  
Mycofenolate mofetil  
Ciclosporine

Evidence for comparator: -

Actual start date of recruitment	20 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 65
Worldwide total number of subjects	65
EEA total number of subjects	65

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)	61
From 65 to 84 years	4



## Subject disposition

### Recruitment

Recruitment details:

Patients were asked to consider participation in the longitudinal experimental study by their treating physician at the LUMC and/or through the patient organisation "Spierziekten Nederland".

### Pre-assignment

Screening details:

1. Males and females aged between 18 years and 65 years at the time of the injection.
2. Patient with ocular or generalized AChR MG, MuSK MG or LEMS; and
3. A positive serologic test for AChR antibodies > 0.5 nmol/l or MuSK antibodies >0.1 nmol/l or VGCC antibodies >20 fmol/l.
4. Patient with prednisone dose lower than 30mg and stable (dose +/-)

### Period 1

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

### Arms

<b>Arm title</b>	Tetanus vaccin in patients
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Arm description:

All patients in the study received tetanus

Arm type	Active comparator
Investigational medicinal product name	Tetanus vaccine
Investigational medicinal product code	17639
Other name	
Pharmaceutical forms	Concentrate for dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5ml contains 40 IU tetanus toxoid (TT), 1.5 mg aluminium phosphate and 0.05 mg thimerosal

<b>Number of subjects in period 1</b>	Tetanus vaccin in patients
Started	65
Completed	65

## Baseline characteristics

### Reporting groups

Reporting group title	Tetanus vaccin in patients
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Reporting group description:

All patients in the study received tetanus

Reporting group values	Tetanus vaccin in patients	Total	
Number of subjects	65	65	
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)	0	0	
Adults (18-64 years)	61	61	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	55		
full range (min-max)	21 to 65	-	
Gender categorical			
Units: Subjects			
Female	46	46	
Male	19	19	

### Subject analysis sets

Subject analysis set title	AChR
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

AChR MG patients

Subject analysis set title	MuSK MG
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients with MuSK MG

Subject analysis set title	LEMS
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients with LEMS

Subject analysis set title	HC
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Subject analysis set type	Full analysis
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Subject analysis set description:

Healthy controls

Subject analysis set title	AChR Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AChR MG patienten met placebo (saline)

<b>Reporting group values</b>	AChR	MuSK MG	LEMS
Number of subjects	50	6	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	46	6	9
From 65-84 years	4	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56	44.5	49.3
full range (min-max)	21 to 65	21 to 65	21 to 65
Gender categorical Units: Subjects			
Female	37	3	6
Male	13	3	3

<b>Reporting group values</b>	HC	AChR Placebo	
Number of subjects	20	23	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean			
full range (min-max)			
Gender categorical Units: Subjects			
Female			
Male			



## End points

### End points reporting groups

Reporting group title	Tetanus vaccin in patients
Reporting group description: All patients in the study received tetanus	
Subject analysis set title	AChR
Subject analysis set type	Sub-group analysis
Subject analysis set description: AChR MG patients	
Subject analysis set title	MuSK MG
Subject analysis set type	Full analysis
Subject analysis set description: Patients with MuSK MG	
Subject analysis set title	LEMS
Subject analysis set type	Full analysis
Subject analysis set description: Patients with LEMS	
Subject analysis set title	HC
Subject analysis set type	Full analysis
Subject analysis set description: Healthy controls	
Subject analysis set title	AChR Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: AChR MG patienten met placebo (saline)	

### Primary: MG Composite

End point title	MG Composite
End point description:	
End point type	Primary
End point timeframe: Before vaccination and 4 weeks after vaccination	

End point values	AChR	AChR Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	23		
Units: 50	5	6		

<b>Attachments (see zip file)</b>	Clinical scores/Color figure 4.tif
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### Statistical analyses

<b>Statistical analysis title</b>	MG composite pre and post
Comparison groups	AChR Placebo v AChR
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	paired t-test

### Primary: Tetanus IgG titer

End point title	Tetanus IgG titer
End point description:	
End point type	Primary
End point timeframe:	
Before and 4 weeks after vaccination	

<b>End point values</b>	AChR	HC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	20		
Units: microgram(s)/litre				
geometric mean (confidence interval 95%)	34.04 (22.2 to 52.1)	77.2 (54.2 to 110.2)		

<b>Attachments (see zip file)</b>	IgG pre and post/Color figure 1a_b.tif
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### Statistical analyses

<b>Statistical analysis title</b>	IgG post
Statistical analysis description:	
Comparison of IgG total post vaccination between HC and ACHR MG	
Comparison groups	AChR v HC
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	unpaired t-test

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Untill 3 months after revaccination

Adverse event reporting additional description:

Swelling and redness at injection site

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	none
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Dictionary version	x
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### Reporting groups

Reporting group title	Overall study
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Reporting group description: -

<b>Serious adverse events</b>	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 65 (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>	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 65 (72.31%)		
Skin and subcutaneous tissue disorders			
Pain of skin	Additional description: Swelling and redness at injection site		
subjects affected / exposed	47 / 65 (72.31%)		
occurrences (all)	47		

## **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

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### **Online references**

<http://www.ncbi.nlm.nih.gov/pubmed/28992975>