Clinical trial results:
A single center, open-label, dose escalation study of the safety and pharmacokinetics of rhLAMAN (recombinant human alpha-mannosidase or Lamazym) for the treatment of patients with alpha-mannosidosis.

Summary

EudraCT number	2010-022084-36
Trial protocol	DK
Global end of trial date	21 January 2011

Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	09 August 2015

Trial information

Trial identification

Sponsor protocol code	rhLAMAN-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01268358
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Chiesi Farmaceutici Spa
Sponsor organisation address	Via Palermo 26/A, Parma, Italy, 43122
Public contact	Clinical Trial Transparency Manager, Chiesi Farmaceutici Spa, clinicaltrials_info@chiesi.com
Scientific contact	Clinical Trial Transparency Manager, Chiesi Farmaceutici Spa, clinicaltrials_info@chiesi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001056-PIP02-12
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 January 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 January 2011
Global end of trial reached?	Yes
Global end of trial date	21 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are:
- To evaluate the safety profile of rhLAMAN (Lamazym)
- To determine the PK profile of rhLAMAN (Lamazym) in patients with alpha-mannosidosis as measured by rhLAMAN levels in plasma

Protection of trial subjects:

The study was conducted in accordance with the declaration of Helsinki, good clinical practice (GCP) guidelines and local law requirements. Other than routine care, no specific measures for protection of trial subjects were implemented.

Although an Independent Data Monitoring Committee was not formally established , a Safety Committee (SC) did exist for this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2010
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	Denmark: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	5
Adolescents (12-17 years)	5

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited at Copenhagen University Hospital, Denmark. Primary recruitment centers were:
St Mary's Hospital, Manchester, UK; Children's Hospital, Mainz, DE; Hospices Civils in Lyon, FR; The Children's Memorial Health Institute, Warsaw, PL; Universitair Ziekenhuis, Brussels, BE; Hospital Universitario Reina Sofia, ES.

Pre-assignment

Screening details:

Ten patients were screened, entered the study and subsequently stratified. No patients failed screening or withdrew from treatment or study.

Period 1

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

Blinding implementation details:

The present study was open-labeled, as the primary objective of this study was to evaluate safety.

Arms

Are arms mutually exclusive?	Yes
Arm title	Lamazym 6.25 U/kg - Group 1

Arm description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.
Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Arm type	Experimental
Investigational medicinal product name	Lamazym
Investigational medicinal product code	
Other name	recombinant human alpha-mannosidase
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were stratified into 5 groups (1-5) before entering the treatment phase, and each group was to receive one of the fixed doses (6.25, 12.5, 25, 50 or 100 U/kg).

Treatment phase (Visit 3-12)
Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.

Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only onefusion before entering phase IIa.

Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Arm title	Lamazym 12.5 U/kg - Group 2

Arm description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Arm type	Experimental
Investigational medicinal product name	Lamazym
Investigational medicinal product code	
Other name	recombinant human alpha-mannosidase
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were stratified into 5 groups (1-5) before entering the treatment phase, and each group was to receive one of the fixed doses (6.25, 12.5, 25, 50 or 100 U/kg).

Treatment phase (Visit 3-12)
Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.

Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only onefusion before entering phase IIa.

Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Arm title	Lamazym 25 U/kg - Group 3

Arm description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Arm type	Experimental
Investigational medicinal product name	Lamazym
Investigational medicinal product code	
Other name	recombinant human alpha-mannosidase
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were stratified into 5 groups (1-5) before entering the treatment phase, and each group was to receive one of the fixed doses (6.25, 12.5, 25, 50 or 100 U/kg).

Treatment phase (Visit 3-12)
Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.

Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only

onefusion before entering phase IIa.

Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Arm title	Lamazym 50 U/kg - Group 4

Arm description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Arm type	Experimental
Investigational medicinal product name	Lamazym
Investigational medicinal product code	
Other name	recombinant human alpha-mannosidase
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were stratified into 5 groups (1-5) before entering the treatment phase, and each group was to receive one of the fixed doses (6.25, 12.5, 25, 50 or 100 U/kg).

Treatment phase (Visit 3-12)
Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.

Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only onefusion before entering phase IIa.

Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Arm title	Lamazym 100 U/kg - Group 5

Arm description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Arm type	Experimental
Investigational medicinal product name	Lamazym
Investigational medicinal product code	
Other name	recombinant human alpha-mannosidase
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were stratified into 5 groups (1-5) before entering the treatment phase, and each group was to receive one of the fixed doses (6.25, 12.5, 25, 50 or 100 U/kg).

Treatment phase (Visit 3-12)
Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.

Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only onefusion before entering phase IIa.

Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Number of subjects in period 1	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3
Started	2	2	2
Completed	2	2	2

Number of subjects in period 1	Lamazym 50 U/kg - Group 4	Lamazym 100 U/kg - Group 5
Started	2	2
Completed	2	2

Baseline characteristics

Reporting groups

Reporting group title	Lamazym 6.25 U/kg - Group 1

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.
Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Reporting group title	Lamazym 12.5 U/kg - Group 2

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 25 U/kg - Group 3

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 50 U/kg - Group 4

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 100 U/kg - Group 5

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3
Number of subjects	2	2	2
Age categorical Units: Subjects			
Children (2-11 years)	0	1	2
Adolescents (12-17 years)	2	1	0
Age continuous Units: years			
arithmetic mean	15.1	13.2	8.1
standard deviation	± 0.1	± 3.9	± 0.5
Gender categorical Units: Subjects			
Female	0	1	2
Male	2	1	0

Reporting group values	Lamazym 50 U/kg - Group 4	Lamazym 100 U/kg - Group 5	Total
Number of subjects	2	2	10
Age categorical Units: Subjects			
Children (2-11 years)	1	0	4
Adolescents (12-17 years)	1	2	6
Age continuous Units: years			
arithmetic mean	9.8	16.7	
standard deviation	± 3.1	± 1.2	-
Gender categorical Units: Subjects			
Female	0	0	3
Male	2	2	7

End points

End points reporting groups

Reporting group title	Lamazym 6.25 U/kg - Group 1

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.
Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Reporting group title	Lamazym 12.5 U/kg - Group 2

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 25 U/kg - Group 3

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 50 U/kg - Group 4

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Reporting group title	Lamazym 100 U/kg - Group 5

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one infusion before entering phase IIa.

Primary: rhLaman level in plasma	
End point title	rhLaman level in plasma
End point description: The rhLaman level in plasma is measured as AUC.	
End point type	Primary
End point timeframe: At Visit 3 (first dose)	

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: µg*h/L				
arithmetic mean (standard deviation)	12221 (± 7388)	54684 (± 14056)	101930 (± 27336)	268538 (± 44872)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: µg*h/L				
arithmetic mean (standard deviation)	697375 (± 264080)			

Statistical analyses

Statistical analysis title	Evaluation of dose proportionality
Comparison groups	Lamazym 6.25 U/kg - Group 1 v Lamazym 12.5 U/kg - Group 2 v Lamazym 25 U/kg - Group 3 v Lamazym 50 U/kg - Group 4 v Lamazym 100 U/kg - Group 5
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	linear regression model
Point estimate	1.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.19
upper limit	1.64

Notes:

[1] - This is a dose finding (dose-escalation) study

Secondary: DBP

End point title	DBP

End point description:

Only descriptive statistical data of Diastolic Blood Pressure at Visit 3 - 24 Hours 30 Minutes Post Infusion Stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 3, 4, 5, 6 and 7 (pre-infusion, multiple post infusion start and multiple post infusion stop timepoints)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmHg				
arithmetic mean (standard deviation)	81 (± 2.8)	59.5 (± 2.1)	66.5 (± 0.7)	70 (± 12.5)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmHg				
arithmetic mean (standard deviation)	69 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: SBP

End point title	SBP

End point description:

Only descriptive statistical data on Visit 3 - 24h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 3, 4, 5, 6 and 7 (pre-infusion, multiple post infusion start and multiple post infusion stop timepoints).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmHg				
arithmetic mean (standard deviation)	142 (± 2.8)	112.5 (± 2.1)	95.5 (± 10.6)	113.5 (± 13.4)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmHg				
arithmetic mean (standard deviation)	135 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Heart rate

End point title	Heart rate

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 3, 4, 5, 6 and 7 (pre-infusion, multiple post infusion start and multiple post infusion stop timepoints)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: bpm				
arithmetic mean (standard deviation)	101 (± 1.4)	69 (± 22.6)	93 (± 1.4)	81 (± 18.4)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: bpm				
arithmetic mean (standard deviation)	64.5 (± 3.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Temperature

End point title	Temperature

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 3, 4, 5, 6 and 7 (pre-infusion, multiple post infusion start and multiple post infusion stop timepoints).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: Celsius degrees				
arithmetic mean (standard deviation)	36.8 (± 1)	36.9 (± 0.1)	37.6 (± 0.5)	36.8 (± 0.1)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Celsius degrees				
arithmetic mean (standard deviation)	37.7 (± 0.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Respiration rate

End point title	Respiration rate

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 3, 4, 5, 6 and 7 (pre-infusion, multiple post infusion start and multiple post infusion stop timepoints).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: beats/min				
arithmetic mean (standard deviation)	27 (± 4.2)	21 (± 4.2)	21 (± 1.4)	21 (± 1.4)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: beats/min				
arithmetic mean (standard deviation)	20 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Basophilocytes

End point title	Hematology - Basophilocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	0.05 (± 0.07)	0.1 (± 0)	0 (± 0)	0.05 (± 0.07)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E9/L				
arithmetic mean (standard deviation)	0.05 (± 0.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Eosinophilocytes

End point title	Hematology - Eosinophilocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	0.1 (± 0)	0.05 (± 0.07)	0.15 (± 0.21)	0.05 (± 0.07)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E9/L				
arithmetic mean (standard deviation)	0.8 (± 0.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Haemoglobin (Fe)

End point title	Hematology - Haemoglobin (Fe)

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	9.5 (± 0.14)	7.7 (± 0.28)	7.45 (± 0.35)	7.05 (± 0.78)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	9 (± 0.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Mean cell haemoglobin concentration

End point title	Hematology - Mean cell haemoglobin concentration

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	21.5 (± 0.7)	21 (± 0)	21 (± 0)	21 (± 0)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	21 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Mean cell haemoglobin

End point title	Hematology - Mean cell haemoglobin

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: fmol				
arithmetic mean (standard deviation)	1.85 (± 0.07)	1.85 (± 0.21)	1.75 (± 0.07)	1.65 (± 0.07)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: fmol				
arithmetic mean (standard deviation)	1.8 (± 0.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Lymphocytes

End point title	Hematology - Lymphocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	1.65 (± 0.49)	1.45 (± 0.21)	1.6 (± 0.57)	2.3 (± 0.42)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E9/L				
arithmetic mean (standard deviation)	3.05 (± 1.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Monocytes

End point title	Hematology - Monocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	0.35 (± 0.07)	0.4 (± 0.14)	0.1 (± 0)	0.3 (± 0)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E9/L				
arithmetic mean (standard deviation)	0.35 (± 0.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Neutrophilocytes

End point title	Hematology - Neutrophilocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	2.85 (± 1.63)	2.85 (± 0.64)	2.5 (± 0.92)	2.1 (± 0.28)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			

Units: 10E9/L				
arithmetic mean (standard deviation)	3.15 (± 1.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Platelets

End point title	Hematology - Platelets

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	206.5 (± 30.4)	177 (± 7.1)	223.5 (± 60.1)	167.5 (± 14.8)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E9/L				
arithmetic mean (standard deviation)	194.5 (± 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Erythrocytes

End point title	Hematology - Erythrocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E12/L				
arithmetic mean (standard deviation)	5.1 (± 0.14)	4.2 (± 0.42)	4.2 (± 0)	4.25 (± 0.35)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: 10E12/L				
arithmetic mean (standard deviation)	5.05 (± 0.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology - Leucocytes

End point title	Hematology - Leucocytes

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: 10E9/L				
arithmetic mean (standard deviation)	4.95 (± 1.06)	4.75 (± 0.21)	3.95 (± 0.07)	4.8 (± 0.14)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			

Units: 10E9/L				
arithmetic mean (standard deviation)	7.35 (± 3.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Chemistry - S-Alat

End point title	Blood Chemistry - S-Alat

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: U/L				
arithmetic mean (standard deviation)	14.5 (± 3.5)	18.5 (± 7.8)	15 (± 4.2)	25 (± 11.3)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: U/L				
arithmetic mean (standard deviation)	14 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Alkaline phosphatase

End point title	Blood chemistry - S-Alkaline phosphatase

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: U/L				
arithmetic mean (standard deviation)	121.5 (± 19.1)	183 (± 124.5)	246 (± 79.2)	248.5 (± 106.8)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: U/L				
arithmetic mean (standard deviation)	120.5 (± 13.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Amilase

End point title	Blood chemistry - S-Amilase

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: U/L				
arithmetic mean (standard deviation)	57 (± 8.5)	52 (± 4.2)	43 (± 24)	35.5 (± 3.5)

End point values	Lamazym 100 U/kg - Group 5			

Subject group type	Reporting group			
Number of subjects analysed	2			
Units: U/L				
arithmetic mean (standard deviation)	63 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Bilirubin

End point title	Blood chemistry - S-Bilirubin

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: µmol/L				
arithmetic mean (standard deviation)	23 (± 4.2)	23.5 (± 23.3)	8.5 (± 0.7)	6 (± 2.8)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: µmol/L				
arithmetic mean (standard deviation)	17 (± 8.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Calcium

End point title	Blood chemistry - S-Calcium

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	2.36 (± 0.01)	2.38 (± 0.14)	2.36 (± 0.04)	2.37 (± 0.04)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	2.4 (± 0.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Creatin kinase

End point title	Blood chemistry - S-Creatin kinase

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: U/L				
arithmetic mean (standard deviation)	74.5 (± 20.5)	61 (± 22.6)	63 (± 5.7)	102.5 (± 50.2)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: U/L				
arithmetic mean (standard deviation)	72.5 (± 23.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Creatininium substr.c.

End point title	Blood chemistry - S-Creatininium substr.c.

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: µmol/L				
arithmetic mean (standard deviation)	88.5 (± 7.8)	67.5 (± 0.7)	61 (± 2.8)	63.5 (± 9.2)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: µmol/L				
arithmetic mean (standard deviation)	83 (± 4.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood chemistry - S-Potassium ion subst.c.

End point title	Blood chemistry - S-Potassium ion subst.c.

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	3.65 (± 0.21)	3.85 (± 0.07)	4 (± 0)	4.05 (± 0.07)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	3.65 (± 0.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Chemistry - S-LDH

End point title	Blood Chemistry - S-LDH

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion).

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: U/L				
arithmetic mean (standard deviation)	183.5 (± 3.5)	187.5 (± 94)	214.5 (± 10.6)	232.5 (± 21.9)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: U/L				
arithmetic mean (standard deviation)	187.5 (± 4.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Chemistry - S-Phosphate inorg.

End point title	Blood Chemistry - S-Phosphate inorg.

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	1.03 (± 0.04)	1.04 (± 0.03)	1.32 (± 0.11)	1.3 (± 0.18)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	1.09 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Chemistry - S-Sodium ion

End point title	Blood Chemistry - S-Sodium ion

End point description:

Only descriptive statistical data at Visit 3 - 24 h post infusion stop are reported here.

End point type	Secondary

End point timeframe:

At Visit 2 (baseline), 3 (pre infusion, 24 h post infusion stop), and 7 (pre-infusion)

End point values	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3	Lamazym 50 U/kg - Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	2	2
Units: mmol/L				
arithmetic mean (standard deviation)	140.5 (± 0.7)	140.5 (± 0.7)	139 (± 0)	138.5 (± 0.7)

End point values	Lamazym 100 U/kg - Group 5			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mmol/L				
arithmetic mean (standard deviation)	139 (± 2.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Visit 2 (baseline) to Visit 12

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Lamazym 6.25 U/kg - Group 1

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one fusion before entering phase IIa.
Group 1 was expected to receive a total of 5 doses, group 2, 4 doses and so on until group 5, which was expected to receive only 1 dose.

Reporting group title	Lamazym 12.5 U/kg - Group 2

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one fusion before entering phase IIa.

Reporting group title	Lamazym 25 U/kg - Group 3

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one fusion before entering phase IIa.

Reporting group title	Lamazym 50 U/kg - Group 4

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one fusion before entering phase IIa.

Reporting group title	Lamazym 100 U/kg - Group 5

Reporting group description:

A fixed dose regimen was chosen (6.25, 12.5, 25, 50 or 100 U/kg).
The dose was determined after an evaluation at baseline and on the basis of which group the patient

was stratified to (from 1-5). Each patient was to receive an infusion once a week. The number of infusions was dependant on the group number the patient was stratified to hence the onset of the first infusion for each patient.
Infusions were administered weekly commencing with group 1, where patients received their first dose at Day 0 (Visit 3). One week later (7 days ± 2 days) group 2 received their first infusion (Visit 3) whereas group 1 received their second dose (Visit 4) and so on until group 5 who would have only one fusion before entering phase IIa.

Serious adverse events	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Lamazym 50 U/kg - Group 4	Lamazym 100 U/kg - Group 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Lamazym 6.25 U/kg - Group 1	Lamazym 12.5 U/kg - Group 2	Lamazym 25 U/kg - Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	1 / 2 (50.00%)
Investigations			
Urine analysis abnormal			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Reflux gastritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Skin infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Lamazym 50 U/kg - Group 4	Lamazym 100 U/kg - Group 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	
Investigations			
Urine analysis abnormal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Reflux gastritis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Skin infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2010	• Addition of a pregnancy test in the post-menarchal adolescents women at inclusion and throughout the study as requested by the IEC. • Reduction of the infusion rate from 1.5 mg/min to 0.5 mg/min as requested by the SC. • Addition of an ECG taken immediately after the infusion stop, as requested by the SC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NO limitations or caveats are applicable to this summary.

Notes: