



Clinical trial results:

Prospective, double-blind, randomized, multicenter phase III study evaluating efficacy and safety of three different dosages of NewGam in patients with chronic inflammatory demyelinating poly(radiculo) neuropathy.

Summary

EudraCT number	2015-005443-14
Trial protocol	DE DK SE HU CZ PL BG
Global end of trial date	05 September 2019

Results information

Result version number	v1 (current)
This version publication date	29 August 2020
First version publication date	29 August 2020

Trial information

Trial identification

Sponsor protocol code	NGAM-08
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02638207
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 14096

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H.
Sponsor organisation address	Oberlaaer Strasse 235, Vienna, Austria, 1100
Public contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., 43 610321716, clinical.department@octapharma.com
Scientific contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., 43 610321716, clinical.department@octapharma.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	31 January 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary:

To provide confirmatory data on the effect of 1.0 g/kg NewGam every three weeks in patients with active CIDP based on the percentage of responders at Week 24, which should corroborate the existing evidence on efficacy of IGIV in CIDP as known from published literature.

Protection of trial subjects:

The study described herein is conducted in accordance with the ethical principles of the Declaration of Helsinki, and ICH-GCP (Note for Guidance CPMP/ICH/135/95), and national regulatory requirements. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product.

Throughout the study safety was assessed, such as of monitoring of AEs, SAEs, vital signs and concomitant medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 August 2017
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	Poland: 14
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Ukraine: 41
Country: Number of subjects enrolled	Romania: 39
Worldwide total number of subjects	142
EEA total number of subjects	78

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)	97
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with documented diagnosis of chronic inflammatory demyelinating poly(radiculo)neuropathy (ProCID Study) were screened according to predefined in- and exclusion criteria.

Period 1

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

Blinding implementation details:

In the event of medical emergency, the investigator was able to unblind a patient immediately by accessing the IWRS system.

Arms

Are arms mutually exclusive?	Yes
Arm title	0.5 g/kg NewGam

Arm description:

All patients received a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (0.5g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).

Arm type	Experimental
Investigational medicinal product name	NewGam
Investigational medicinal product code	
Other name	Panzyga
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients received a loading dose of 2.0 g/kg NewGam (administered over 2 consecutive days), followed by 7 infusions of the maintenance dose the patient has been randomized to (i.e., 0.5, 1.0 or 2.0 g/kg NewGam), also administered over 2 consecutive days every 3 weeks (± 4 days). The same volumes and infusion rates were used regardless of the randomized group, with supplementation with an authorized 0.9% w/v isotonic sodium chloride solution as appropriate to maintain the blinding. There was the option of rescue treatment with two consecutive blinded infusions of 2.0 g/kg NewGam at 3-week intervals (± 4 days) for all patients in the 0.5 and 1.0 g/kg NewGam arms who were either stable at Week 6 or deteriorated after Week 3 and before Week 18.

Arm title	1.0 g/kg NewGam
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Arm description:

All patients will receive a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (1.0g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).

Arm type	Experimental
Investigational medicinal product name	NewGam
Investigational medicinal product code	
Other name	Panzyga
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients received a loading dose of 2.0 g/kg NewGam (administered over 2 consecutive days), followed by 7 infusions of the maintenance dose the patient has been randomized to (i.e., 0.5, 1.0 or

2.0 g/kg NewGam), also administered over 2 consecutive days every 3 weeks (± 4 days). The same volumes and infusion rates were used regardless of the randomized group, with supplementation with an authorized 0.9% w/v isotonic sodium chloride solution as appropriate to maintain the blinding. There was the option of rescue treatment with two consecutive blinded infusions of 2.0 g/kg NewGam at 3-week intervals (± 4 days) for all patients in the 0.5 and 1.0 g/kg NewGam arms who were either stable at Week 6 or deteriorated after Week 3 and before Week 18.

Arm title	2.0 g/kg NewGam
Arm description:	
All patients will receive a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (2.0g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).	
Arm type	Experimental
Investigational medicinal product name	NewGam
Investigational medicinal product code	
Other name	Panzyga
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients received a loading dose of 2.0 g/kg NewGam (administered over 2 consecutive days), followed by 7 infusions of the maintenance dose the patient has been randomized to (i.e., 0.5, 1.0 or 2.0 g/kg NewGam), also administered over 2 consecutive days every 3 weeks (± 4 days). The same volumes and infusion rates were used regardless of the randomized group, with supplementation with an authorized 0.9% w/v isotonic sodium chloride solution as appropriate to maintain the blinding. There was the option of rescue treatment with two consecutive blinded infusions of 2.0 g/kg NewGam at 3-week intervals (± 4 days) for all patients in the 0.5 and 1.0 g/kg NewGam arms who were either stable at Week 6 or deteriorated after Week 3 and before Week 18.

Number of subjects in period 1	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam
Started	35	69	38
Completed	28	61	34
Not completed	7	8	4
Adverse event, non-fatal	3	2	1
Patient Decision	3	3	1
Administrative reasons	-	-	1
Safety Reasons	-	1	1
other	1	2	-

Baseline characteristics

Reporting groups

Reporting group title

Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	142	142	
Age categorical			
Units: Subjects			
18-64 years	97	97	
65-83 Years	45	45	
Age continuous			
Units: years			
arithmetic mean	55.84		
full range (min-max)	18 to 83	-	
Gender categorical			
Units: Subjects			
Female	58	58	
Male	84	84	

End points

End points reporting groups

Reporting group title	0.5 g/kg NewGam
Reporting group description: All patients received a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (0.5g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).	
Reporting group title	1.0 g/kg NewGam
Reporting group description: All patients will receive a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (1.0g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).	
Reporting group title	2.0 g/kg NewGam
Reporting group description: All patients will receive a loading dose of 2.0 g/kg Newgam (administered over two consecutive days), followed by seven infusions of the maintenance dose the patient has been randomized to (2.0g/kg NewGam), also administered over two consecutive days every 3 weeks (± 4 days).	

Primary: Decrease in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score in the 1.0 g/kg Group

End point title	Decrease in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score in the 1.0 g/kg Group ^[1]
End point description: Efficacy - Proportion of responders in the 1.0 g/kg NewGam arm at Week 24 (Termination Visit) relative to baseline (Week 0). A responder being defined as a patient with a decrease of at least 1 point on the adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score (a scale from 0 to 10, from healthy to unable to make any purposeful movements with arms and/or legs)	
End point type	Primary
End point timeframe: at week 24	

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: Primary endpoint was evaluated by comparing the lower limit of the 95% Wilson-Score CI for the percentage of responders on the adjusted INCAT disability scale in the 1.0 g/kg dose group with a predefined threshold of 42%. The response rates in the alternative dose groups were compared descriptively to the 1.0 g/kg treatment group, and the CIs for the differences were presented. Descriptive summaries are presented for each of the primary, secondary and exploratory variables.

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Responders	22	55	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score in the 0.5 g/kg and 2.0 g/kg Group

End point title	Decrease in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score in the 0.5 g/kg and 2.0 g/kg Group
End point description: Proportion of responders in the 0.5 g/kg and 2.0 g/kg NewGam arms at Week 24 relative to baseline compared to the 1.0 g/kg arm, based on the adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score.	
End point type	Secondary
End point timeframe: at week 24	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Responders	22	55	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Grip Strength Score

End point title	Grip Strength Score
End point description: Proportion of responders in the 0.5 g/kg and 2.0 g/kg NewGam arms at Week 24 relative to Baseline at Week 0 compared to the 1.0 g/kg arm, based on the grip strength (Martin Vigorimeter) using the previously published minimum clinically important difference (MCID) cut-off of 8 kPa .	
End point type	Secondary
End point timeframe: at Week 24	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Responders	19	45	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Rasch-built Overall Disability Scale (I-RODS Score)

End point title	Inflammatory Rasch-built Overall Disability Scale (I-RODS Score)
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End point description:

Proportion of responders in the 0.5 g/kg and 2.0 g/kg NewGam arms at Week 24 relative to Baseline at Week 0 compared to the 1.0 g/kg arm, based on the I-RODS scores using the MCID concept related to the varying standard errors (MCID-SE).

End point type	Secondary
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End point timeframe:

at Week 24

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Responders	13	38	26	

Statistical analyses

No statistical analyses for this end point

Secondary: Worsening in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score

End point title	Worsening in the Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score
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End point description:

Time to first confirmed worsening on the adjusted INCAT disability scale by at least 1 point from the value at Baseline (Week 0)

End point type	Secondary
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End point timeframe:

24 weeks

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: days				

Notes:

[2] - No patients with worsening in this group, analysis not possible.

[3] - Only 1 patient with worsening thus an analysis of the time to first worsening was not possible.

[4] - No patients with worsening in this group, analysis not possible

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Grip Strength

End point title	Mean Change in Grip Strength
End point description: Mean change from baseline (Week 0) to Termination Visit in grip strength of both hands (assessed by Martin vigorimeter).	
End point type	Secondary
End point timeframe: Termination Visit	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: kPa				
arithmetic mean (standard deviation)				
Dominant Hand	23.91 (± 25.290)	19.38 (± 20.377)	26.06 (± 25.030)	
Non-dominant Hand	23.94 (± 24.600)	17.43 (± 19.916)	24.53 (± 22.247)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Rasch-built Overall Disability Scale (I-RODS)

End point title	Inflammatory Rasch-built Overall Disability Scale (I-RODS)
End point description: Mean change from baseline (Week 0) to Termination Visit in Inflammatory Rasch-built overall disability sum score (I-RODS using the concept of MCID-SE as recently reported) and number of improvers.	
End point type	Secondary
End point timeframe: Termination Visit	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Score				
arithmetic mean (standard deviation)	11.38 (± 12.485)	10.32 (± 10.836)	13.86 (± 11.981)	

Statistical analyses

No statistical analyses for this end point

Secondary: Motor Nerves

End point title	Motor Nerves
End point description: Mean change from baseline (Week 0) to Termination Visit in sum of the distal evoked amplitude of 4 right sided and 4 left sided motor nerves (peroneal, tibial, ulnar and median).	
End point type	Secondary
End point timeframe: Termination Visit	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	68	36	
Units: mV				
arithmetic mean (standard deviation)	2.16 (\pm 6.332)	2.69 (\pm 6.688)	3.93 (\pm 9.298)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Pain Intensity Numerical Rating Scale (PI-NRS Scale)

End point title	Mean Change in Pain Intensity Numerical Rating Scale (PI-NRS Scale)
End point description: Mean change from baseline (Week 0) to Termination Visit in Pain Intensity Numeric Rating Scale (PI-NRS)	
End point type	Secondary
End point timeframe: Termination Visit	

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: Score				
arithmetic mean (standard deviation)	-2.29 (\pm 3.040)	-2.19 (\pm 2.907)	-2.17 (\pm 3.256)	

Statistical analyses

No statistical analyses for this end point

Secondary: Worsening on the Inflammatory Rasch-built Overall Disability Scale (I-RODS Scale)

End point title	Worsening on the Inflammatory Rasch-built Overall Disability Scale (I-RODS Scale)
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End point description:

Time to first confirmed worsening on the I-RODS scale.

End point type	Secondary
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End point timeframe:

24 weeks

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[5]	0 ^[6]	0 ^[7]	
Units: days				

Notes:

[5] - Only 1 patient with worsening , thus an analysis of the time to first worsening was not possible.

[6] - Only 2 patients with worsening , thus an analysis of the time to first worsening was not possible.

[7] - No patients with worsening in this group, analysis not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: 1 Point Decrease in the INCAT Disability Score

End point title	1 Point Decrease in the INCAT Disability Score
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End point description:

Time to 1 point decrease (improvement of disability) in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score.

End point type	Secondary
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End point timeframe:

24 weeks

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	69	36	
Units: days				
median (confidence interval 95%)	22.0 (22.0 to 24.0)	26.0 (22.0 to 43.0)	23.0 (22.0 to 43.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in Inflammatory Rasch-built Overall Disability Scale (I-RODS Scale)

End point title	Decrease in Inflammatory Rasch-built Overall Disability Scale (I-RODS Scale)
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End point description:

Time to decrease in Inflammatory Rasch-built overall disability scale (I-RODS) scores.

End point type	Secondary
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End point timeframe:

24 weeks

End point values	0.5 g/kg NewGam	1.0 g/kg NewGam	2.0 g/kg NewGam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[8]	0 ^[9]	0 ^[10]	
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[8] - No patients with worsening thus an analysis of the time to first worsening was not possible.

[9] - Only 1 patient with worsening thus an analysis of the time to first worsening was not possible.

[10] - No patients with worsening thus an analysis of the time to first worsening was not possible

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the whole study from week 0 up to week 24 (end of study visit)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Safety Population
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Reporting group description: -

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 142 (4.23%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness unilateral			

subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory arrest			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Encephalitis			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Osteomyelitis			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 142 (61.97%)		
Investigations			
Blood pressure increased			
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	14		
Body temperature increased			
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	12		
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 142 (3.52%)		
occurrences (all)	5		
Heart rate decreased			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		
Transaminases increased			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	3		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		

Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 142 (2.82%)		
occurrences (all)	6		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 142 (13.38%)		
occurrences (all)	26		
Somnolence			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	4		
Tension headache			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	7		
Dizziness			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 142 (7.75%)		
occurrences (all)	13		
Chills			
subjects affected / exposed	7 / 142 (4.93%)		
occurrences (all)	8		
Influenza like illness			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Leukopenia			

subjects affected / exposed occurrences (all)	6 / 142 (4.23%) 7		
Anaemia subjects affected / exposed occurrences (all)	3 / 142 (2.11%) 4		
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 142 (1.41%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	5 / 142 (3.52%) 8		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 142 (2.82%) 4		
Vomiting subjects affected / exposed occurrences (all)	2 / 142 (1.41%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 142 (1.41%) 2		
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all)	13 / 142 (9.15%) 19		
Skin exfoliation subjects affected / exposed occurrences (all)	4 / 142 (2.82%) 5		
Urticaria subjects affected / exposed occurrences (all)	3 / 142 (2.11%) 4		
Rash subjects affected / exposed occurrences (all)	2 / 142 (1.41%) 6		
Pruritus			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Seborrhoeic dermatitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 142 (1.41%)</p> <p>3</p> <p>2 / 142 (1.41%)</p> <p>2</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 142 (4.23%)</p> <p>6</p> <p>3 / 142 (2.11%)</p> <p>3</p>		
<p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Respiratory tract infection viral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 142 (3.52%)</p> <p>5</p> <p>4 / 142 (2.82%)</p> <p>4</p> <p>4 / 142 (2.82%)</p> <p>4</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2018	Amendment 2: -addition of an upper limit for age of patients of <80 years to inclusion criteria; -addition of 'severe' to exclusion criterion regarding hypersensitivity to blood products -material of infusion bags (ethylene vinyl acetate) deleted and period of storage of infusion bags reduced from 72 to 24 hours -PGIC assessment at Screening deleted -viral testing added at Visit 2 (in addition to the screening sample)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported