



Clinical trial results:

Prospective, open-label, multicentre clinical trial, phase I/IIa, to investigate the safety and tolerability of allogeneic B-cell concentrates CD3+-depleted, CD19+-enriched, cryopreserved (single administration after day 120 following allogeneic stem cell transplantation, donor-identical) in 4 groups with escalating doses for immune response enhancement, measured as response to a preponed single vaccination

Summary

EudraCT number	2012-003033-42
Trial protocol	DE
Global end of trial date	21 March 2018

Results information

Result version number	v1 (current)
This version publication date	10 June 2022
First version publication date	10 June 2022

Trial information

Trial identification

Sponsor protocol code	UKER-BLZ-PH1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
Sponsor organisation address	Ulmenweg 18, Erlangen, Germany, 91054
Public contact	Medizinische Klinik 5, Universitätsklinikum Erlangen, +49 91318543112, julia.winkler@uk-erlangen.de
Scientific contact	Medizinische Klinik 5, Universitätsklinikum Erlangen, +49 91318543112, julia.winkler@uk-erlangen.de

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	21 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2018
Global end of trial reached?	Yes
Global end of trial date	21 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and tolerability of escalating doses of the study medication in patients after allogeneic stem cell transplantation (donor-identical)

Protection of trial subjects:

Treatment with antihistamines 30min Prior to IMP Administration to avoid allergic reactions; cardiopulmonal Monitoring during the first 4 Hours following IMP Administration; inpatient Setting for at least 18 Hours following IMP Administration; sterility testing Prior to IMP Administration to avoid Transmission of infectious agents; only patients at low Risk for EBV reactivation and GvHD could be enrolled

Background therapy:

Additional pilot vaccination with Pentavac (Diphtherie, Tetanus, pertussis, Polio, HiB) and Prevenar 13 (Pneumokokken) at day 8 +/- 3 days after IMP Administration to determine the functionality of transferred B lymphocytes.

Basic immunization following stem cell transplantation according EBMT scheme

Evidence for comparator: -

Actual start date of recruitment	01 July 2013
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	Germany: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	22
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

male or female subjects, 18 - 75 years, with Status post allogeneic SCT 120 - 160 days before IMP Administration; EBV-serostatus as follows: R-/D- or R+/D- or R+/D+; no EBV reactivation > 10.000 copies/ml, no acute GvHD grade III or IV, no chronic GvHD (middle/high Risk accord. to NIH staging), initial donor willing to participate in leukapheresis

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Dose group I
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Arm description:

0,5 x 1.000.000 B-lymphocytes per kg BW

Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

0,5 x 1.000.000 B-lymphocytes per kg BW once

Arm title	Dose group II
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Arm description:

1 x 1.000.000 B-lymphocytes per kg BW

Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

1 x 1.000.000 B-lymphocytes per kg BW once

Arm title	Dose group III
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Arm description:

2 x 1.000.000 B-lymphocytes per kg BW

Arm type	Experimental
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Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 2 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group IV
Arm description: 4 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 4 x 1.000.000 B-lymphocytes per kg BW once	

Number of subjects in period 1	Dose group I	Dose group II	Dose group III
Started	6	5	10
Pre-treatment examination	6	5	10
Completed	3	3	6
Not completed	3	2	4
Physician decision	3	-	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
IMP unavailable	-	-	2
donor unavailable	-	2	-

Number of subjects in period 1	Dose group IV
Started	7
Pre-treatment examination	7
Completed	3
Not completed	4
Physician decision	1
Consent withdrawn by subject	1
Adverse event, non-fatal	1
IMP unavailable	-
donor unavailable	1

Period 2	
Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Dose group I
Arm description: 0,5 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 0,5 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group II
Arm description: 1 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 1 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group III
Arm description: 2 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 2 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group IV
Arm description: 4 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental

Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

4 x 1.000.000 B-lymphocytes per kg BW once

Number of subjects in period 2	Dose group I	Dose group II	Dose group III
Started	3	3	6
Completed	3	3	6

Number of subjects in period 2	Dose group IV
Started	3
Completed	3

Period 3

Period 3 title	Post-treatment
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose group I

Arm description:

0,5 x 1.000.000 B-lymphocytes per kg BW

Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

0,5 x 1.000.000 B-lymphocytes per kg BW once

Arm title	Dose group II
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Arm description:

1 x 1.000.000 B-lymphocytes per kg BW

Arm type	Experimental
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Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 1 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group III
Arm description: 2 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 2 x 1.000.000 B-lymphocytes per kg BW once	
Arm title	Dose group IV
Arm description: 4 x 1.000.000 B-lymphocytes per kg BW	
Arm type	Experimental
Investigational medicinal product name	Allogeneic B-cell concentrate CD3+-depleted, CD19+-enriched, cryopreserved
Investigational medicinal product code	EV substance code SUB112494
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use
Dosage and administration details: 4 x 1.000.000 B-lymphocytes per kg BW once	

Number of subjects in period 3	Dose group I	Dose group II	Dose group III
Started	3	3	6
Completed	3	3	6
Not completed	0	0	0
Adverse event, serious fatal	-	-	-

Number of subjects in period 3	Dose group IV
Started	3
Completed	2
Not completed	1
Adverse event, serious fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Screening
Reporting group description: -	

Reporting group values	Screening	Total	
Number of subjects	28	28	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	54		
full range (min-max)	18 to 79	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	20	20	

Subject analysis sets

Subject analysis set title	SES
Subject analysis set type	Safety analysis
Subject analysis set description: all subjects treated with the IMP at any dose level	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: all treated subjects with Primary and secondary Parameters available	
Subject analysis set title	SES Dose level I / II
Subject analysis set type	Safety analysis
Subject analysis set description: all subjects treated with IMP at a dose level of 0,5x10.000.000 cells/kg bw or 1x10.000.000 cells/kg bw	
Subject analysis set title	SES Dose level III / IV
Subject analysis set type	Safety analysis
Subject analysis set description: all subjects treated with IMP at a dose level of 2x10.000.000 cells/kg bw or 3-4x10.000.000 cells/kg bw	

Reporting group values	SES	FAS	SES Dose level I / II
Number of subjects	15	14	6
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	52	51	
full range (min-max)	21 to 70	21 to 70	
Gender categorical Units: Subjects			
Female	6	6	
Male	9	8	

Reporting group values	SES Dose level III / IV		
Number of subjects	9		
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	Dose group I
Reporting group description: 0,5 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group II
Reporting group description: 1 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group III
Reporting group description: 2 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group IV
Reporting group description: 4 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group I
Reporting group description: 0,5 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group II
Reporting group description: 1 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group III
Reporting group description: 2 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group IV
Reporting group description: 4 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group I
Reporting group description: 0,5 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group II
Reporting group description: 1 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group III
Reporting group description: 2 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group IV
Reporting group description: 4 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group I
Reporting group description: 0,5 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group II
Reporting group description: 1 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group III
Reporting group description: 2 x 1.000.000 B-lymphocytes per kg BW	
Reporting group title	Dose group IV
Reporting group description: 4 x 1.000.000 B-lymphocytes per kg BW	
Subject analysis set title	SES
Subject analysis set type	Safety analysis
Subject analysis set description: all subjects treated with the IMP at any dose level	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: all treated subjects with Primary and secondary Parameters available	
Subject analysis set title	SES Dose level I / II
Subject analysis set type	Safety analysis

Subject analysis set description:

all subjects treated with IMP at a dose level of 0,5x10.000.000 cells/kg bw or 1x10.000.000 cells/kg bw

Subject analysis set title	SES Dose level III / IV
Subject analysis set type	Safety analysis

Subject analysis set description:

all subjects treated with IMP at a dose level of 2x10.000.000 cells/kg bw or 3-4x10.000.000 cells/kg bw

Primary: Number and severity of TEAEs

End point title	Number and severity of TEAEs ^[1]
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End point description:

Severity: 3 TEAEs severity grade 3 (hypertriglyceridaemia, CRP increase, CMV colitis), others grade 1/2

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

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: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	39	29	35	38

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	141			

Statistical analyses

No statistical analyses for this end point

Primary: Number and severity of ARs

End point title	Number and severity of ARs ^[2]
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End point description:

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	0	0	0	0

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number and severity of TESAEs

End point title	Number and severity of TESAEs ^[3]
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End point description:

Severity: 1 TESAe severity grade 5 (fatal, septic shock), 2 TESAEs severity grade 2 (moderate; fever, diarrhea)

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	1	0	0	2

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number and severity of SARs

End point title	Number and severity of SARs ^[4]
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End point description:

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	0	0	0	0

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number and severity of AESIs

End point title	Number and severity of AESIs ^[5]
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End point description:

The following Events were defined as AESI:

De-novo acute GvHD or Deterioration of a pre-existing acute GvHD

De-novo chronic GvHD or Deterioration of a pre-existing chronic GvHD

Severe allergic reaction CTCAE grade 3 or higher

EBV reactivation within <14d after IMP Administration requiring immediate treatment

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	1	1	1	1

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	4			

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of PTLD

End point title	Occurrence of PTLD ^[6]
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End point description:

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	0	0	0	0

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	0			

Statistical analyses

No statistical analyses for this end point

Primary: Frequency of >50.000 EBV DNA copies/ml plasma

End point title	Frequency of >50.000 EBV DNA copies/ml plasma ^[7]
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End point description:

End point type	Primary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Notes:

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

Justification: Safety Parameters were analysed for treated subjects (SES) in a descriptive manner only. No formal statistical hypothesis was tested.

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	3
Units: number of events	0	0	0	0

End point values	SES			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: number of events	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in percentage of antibody-producing cells

End point title	Change in percentage of antibody-producing cells
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End point description:

percentage v10 - percentage v1

End point type	Secondary
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End point timeframe:

visit 1 (screening) to v10 EoS visit (day 120 - 127 after IMP Administration)

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	2 ^[8]
Units: percent				
arithmetic mean (standard deviation)	-2.2 (± 0.5)	-0.7 (± 0.6)	-4.9 (± 0.4)	1.2 (± 1.9)

Notes:

[8] - 1 subject died due to septic shock on day 63 after IMP administration

Statistical analyses

No statistical analyses for this end point

Secondary: Change in number of B-lymphocytes

End point title	Change in number of B-lymphocytes
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End point description:

value v10 - value v1

End point type	Secondary
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End point timeframe:

visit 1 (screening) to v10 EoS visit (day 120 - 127 after IMP Administration)

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	2 ^[9]
Units: cells/microlitre				
arithmetic mean (standard deviation)	324.3 (± 86.4)	421.3 (± 245)	383.3 (± 297.4)	188 (± 171.8)

Notes:

[9] - 1 subject died due to septic shock on day 63 after IMP administration

Statistical analyses

No statistical analyses for this end point

Secondary: Change in percentage of naive B-lymphocytes

End point title	Change in percentage of naive B-lymphocytes
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End point description:

percentage v10 - percentage v1

End point type	Secondary
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End point timeframe:

visit 1 (screening) to v10 EoS visit (day 120 - 127 after IMP Administration)

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	2 ^[10]
Units: percent				
arithmetic mean (standard deviation)	-13 (± 4.3)	3.9 (± 22.7)	-1 (± 6.3)	-3.6 (± 9.9)

Notes:

[10] - 1 subject died due to septic shock on day 63 after IMP administration

Statistical analyses

No statistical analyses for this end point

Secondary: Change in percentage of memory B-lymphocytes

End point title	Change in percentage of memory B-lymphocytes
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End point description:

percentage v10 - percentage v1

End point type	Secondary
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End point timeframe:

visit 1 (screening) to v10 EoS visit (day 120 - 127 after IMP Administration)

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	2
Units: percent				
arithmetic mean (standard deviation)	0 (\pm 1.5)	1.5 (\pm 2.5)	-1.5 (\pm 2.3)	0.6 (\pm 4.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in antigen-specific antibody-concentration: Tetanus titer

End point title	Change in antigen-specific antibody-concentration: Tetanus titer
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End point description:

value v7 - value v5

End point type	Secondary
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End point timeframe:

Visit 5 (day 8 +/- 3 days after IMP administration) to visit 7 (day 39 +/- 3 days after IMP administration)

End point values	SES Dose level I / II	SES Dose level III / IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: IU/ml				
arithmetic mean (standard deviation)	0.3137 (\pm 1.038)	1.9056 (\pm 2.394)		

Statistical analyses

No statistical analyses for this end point

Secondary: CMV-reactivation requiring specific treatment

End point title	CMV-reactivation requiring specific treatment
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End point description:

End point type	Secondary
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End point timeframe:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

End point values	Dose group I	Dose group II	Dose group III	Dose group IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	2
Units: number of subjects	0	0	0	0

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: number of subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in antigen-specific antibody-concentration: Diphteria titer

End point title	Change in antigen-specific antibody-concentration: Diphteria titer
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End point description:

v7 - v5

End point type	Secondary
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End point timeframe:

Visit 5 (day 8 +/- 3 days after IMP administration) to visit 7 (day 39 +/- 3 days after IMP administration)

End point values	SES Dose level I / II	SES Dose level III / IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: IU/ml				
arithmetic mean (standard deviation)	1.82867 (\pm 3.042)	1.6919 (\pm 2.254)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in antigen-specific antibody-concentration: Pertussis titer

End point title	Change in antigen-specific antibody-concentration: Pertussis titer
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End point description:

value v7 - value v5

End point type	Secondary
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End point timeframe:

Visit 5 (day 8 +/- 3 days after IMP administration) to visit 7 (day 39 +/- 3 days after IMP administration)

End point values	SES Dose level I / II	SES Dose level III / IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: IU/ml				
arithmetic mean (standard deviation)	29.75 (± 92.98)	26.91 (± 38.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in antigen-specific antibody-concentration: HiB titer

End point title	Change in antigen-specific antibody-concentration: HiB titer
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End point description:

value v7 - value v5

End point type	Secondary
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End point timeframe:

Visit 5 (day 8 +/- 3 days after IMP administration) to visit 7 (day 39 +/- 3 days after IMP administration)

End point values	SES Dose level I / II	SES Dose level III / IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: IU/ml				
arithmetic mean (standard deviation)	9.9867 (± 14.58)	3.0752 (± 3.352)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in antigen-specific antibody-concentration: Polio titer

End point title	Change in antigen-specific antibody-concentration: Polio titer
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End point description:

value v7 - value v5

End point type	Secondary
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End point timeframe:

Visit 5 (day 8 +/- 3 days after IMP administration) to visit 7 (day 39 +/- 3 days after IMP administration)

End point values	SES Dose level I / II	SES Dose level III / IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: IU/ml				
arithmetic mean (standard deviation)	2.64 (± 50.97)	-0.15 (± 8.276)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

day 1 (IMP Administration) to EoS visit (day 120 - 127 after IMP Administration)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Dose group I
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Reporting group description:

0,5 x 1.000.000 B-lymphocytes per kg BW

Reporting group title	Dose group II
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Reporting group description:

1 x 1.000.000 B-lymphocytes per kg BW

Reporting group title	Dose group III
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Reporting group description:

2 x 1.000.000 B-lymphocytes per kg BW

Reporting group title	Dose group IV
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Reporting group description:

4 x 1.000.000 B-lymphocytes per kg BW

Serious adverse events	Dose group I	Dose group II	Dose group III
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Pyrexia	Additional description: Fever and CRP increase following 3rd vaccination with Prevenar/Pentavac; Outcome: resolved		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dose group IV		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
General disorders and administration site conditions			
Pyrexia	Additional description: Fever and CRP increase following 3rd vaccination with Prevenar/Pentavac; Outcome: resolved		
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Dose group I	Dose group II	Dose group III
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Hypotonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertensive crisis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Body temperature increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Vaccination site pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Adverse drug reaction	Additional description: coagulation disorder		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Acute graft versus host disease			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Acute graft versus host disease in skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chronic graft versus host disease			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	0 / 6 (0.00%)
occurrences (all)	0	7	0
Chronic graft versus host disease in skin			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Graft versus host disease in liver			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Immunisation reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Cortisol decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Liver function test abnormal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Blood creatine increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Scrotal haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mouth injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Spinal fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			

Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Hypergammaglobulinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Leukopenia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral lichen planus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Trichoglossia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Proctitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Alcoholic liver disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Erythema			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	1	4
Night sweats			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pigmentation disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Autoimmune thyroiditis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gouty arthritis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Osteoarthropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Febrile infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Folliculitis			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Paronychia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	1	0

Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cervicitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	2	2	1
Cytomegalovirus colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Folate deficiency			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Vitamin B12 deficiency			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Non-serious adverse events	Dose group IV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Hypotonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypertensive crisis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypertonia			

subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vaccination site pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Adverse drug reaction	Additional description: coagulation disorder		
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Acute graft versus host disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Acute graft versus host disease in skin			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Chronic graft versus host disease			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Chronic graft versus host disease in skin			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Graft versus host disease in liver			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Immunisation reaction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Investigations			
Cortisol decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Liver function test abnormal			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Blood creatine increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Injury, poisoning and procedural complications Vaccination complication subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Skin abrasion subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Scrotal haematoma subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Mouth injury subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Ligament sprain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Spinal fracture subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Cardiac disorders Extrasystoles subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Nervous system disorders Tremor subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Sciatica			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypergammaglobulinaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Oral lichen planus			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Trichoglossia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Proctitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Abdominal distension			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Alcoholic liver disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatic steatosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Night sweats			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pigmentation disorder			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Adrenal insufficiency			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Autoimmune thyroiditis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gouty arthritis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Osteoarthropathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Campylobacter gastroenteritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Clostridium difficile colitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Febrile infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Folliculitis subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2		
Paronychia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Bronchitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2		

Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cervicitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Septic shock			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oesophageal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Cytomegalovirus colitis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Cytomegalovirus infection			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Folate deficiency			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Vitamin B12 deficiency			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Vitamin D deficiency			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2013	Changes due to deficiency letter
28 July 2014	NIMP: altern. vaccination allowed
20 June 2016	Dose Level IV changed from 4x10.000.000 cells/kg bw to 3-4x10.000.000 cells/kg bw (manufacturing issue)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported