



Clinical trial results:

A phase II, randomized, controlled, observer-blind study to assess the safety, reactogenicity and immunogenicity of GlaxoSmithKline (GSK) Biologicals' Streptococcus pneumoniae protein containing vaccine formulations when administered according to a 0-2-6 month schedule, in healthy children aged 12-23 months at the time of first vaccination.

Summary

EudraCT number	2009-012701-19
Trial protocol	CZ
Global end of trial date	02 March 2011

Results information

Result version number	v3 (current)
This version publication date	31 October 2020
First version publication date	01 August 2015
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	113171
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00985751
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 October 2010
Global end of trial reached?	Yes
Global end of trial date	02 March 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the two formulations of GSK Biologicals' S. pneumoniae protein containing vaccine combined with GSK Biologicals' 10-valent pneumococcal conjugate vaccine (pooled groups) versus GSK Biologicals' 10-valent pneumococcal conjugate vaccine with respect to the percentage of subjects reporting fever >40.0°C (rectal temperature) within 7 days after at least one dose of primary vaccination.

To compare the two formulations of GSK Biologicals' S. pneumoniae protein containing vaccine (pooled groups) versus GSK Biologicals' 10-valent pneumococcal conjugate vaccine with respect to the percentage of subjects reporting fever >40.0°C (rectal temperature) within 7 days after at least one dose of primary vaccination.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 2009
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	Czech Republic: 257
Worldwide total number of subjects	257
EEA total number of subjects	257

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	257

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Blinding implementation details:

Serological data was not available to any investigator or any person involved in the conduct of the study (including data cleaning).

Data were collected in an observer-blind manner: vaccine recipient and those responsible for evaluation of any endpoint (safety, reactogenicity, and immunogenicity) was unaware of which vaccine was administered. To do so, vaccine preparation and administration was done by authorised medical personnel who did not participate in any of the clinical evaluation assays

Arms

Are arms mutually exclusive?	Yes
Arm title	dPly-PhtD-LD Group

Arm description:

Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal protein vaccine (low dose formulation), adsorbed
Investigational medicinal product code	
Other name	GSK 2189242A , dPly/PhtD-LD
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

Arm title	dPly-PhtD-HD Group
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Arm description:

Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal protein vaccine (high dose formulation), adsorbed
Investigational medicinal product code	
Other name	GSK 2189242A , dPly/PhtD-LD
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was

not adequate).

Arm title	10Pn-dPly-PhtD-LD Group
Arm description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Arm type	Experimental
Investigational medicinal product name	10 valent pneumococcal conjugate vaccine combined with free pneumococcal proteins, adsorbed
Investigational medicinal product code	
Other name	10Pn/dPly/PhtD-LD
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

Arm title	10Pn-dPly-PhtD-HD Group
Arm description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Arm type	Experimental
Investigational medicinal product name	10 valent pneumococcal conjugate vaccine combined with free pneumococcal proteins, adsorbed
Investigational medicinal product code	
Other name	10Pn/dPly/PhtD-HD
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

Arm title	10Pn Group
Arm description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6.	
Arm type	Active comparator
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

Number of subjects in period 1	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group
Started	51	52	52
Completed	51	52	52
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	10Pn-dPly-PhtD-HD Group	10Pn Group
Started	51	51
Completed	51	50
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	dPly-PhtD-LD Group
Reporting group description:	
Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	dPly-PhtD-HD Group
Reporting group description:	
Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn-dPly-PhtD-LD Group
Reporting group description:	
Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn-dPly-PhtD-HD Group
Reporting group description:	
Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn Group
Reporting group description:	
Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6.	

Reporting group values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group
Number of subjects	51	52	52
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: months			
arithmetic mean	17	16.7	17.1
standard deviation	± 3.6	± 3.81	± 4.03
Gender categorical Units: Subjects			
Female	25	22	23
Male	26	30	29

Reporting group values	10Pn-dPly-PhtD-HD Group	10Pn Group	Total
Number of subjects	51	51	257
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: months			
arithmetic mean	16.8	16.3	
standard deviation	± 3.96	± 4.18	-
Gender categorical Units: Subjects			
Female	29	28	127
Male	22	23	130

End points

End points reporting groups

Reporting group title	dPly-PhtD-LD Group
Reporting group description: Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	dPly-PhtD-HD Group
Reporting group description: Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn-dPly-PhtD-LD Group
Reporting group description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn-dPly-PhtD-HD Group
Reporting group description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.	
Reporting group title	10Pn Group
Reporting group description: Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6.	
Subject analysis set title	dPly-PhtD Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pooled dPly-PhtD-LD and dPly-PhtD-HD groups	
Subject analysis set title	10Pn-dPly-PhtD Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pooled 10Pn-dPly-PhtD-LD and 10Pn-dPly-PhtD-HD groups	

Primary: Number of subjects with fever > 40.0°C (rectal temperature)

End point title	Number of subjects with fever > 40.0°C (rectal temperature) ^[1]
End point description:	
End point type	Primary
End point timeframe: Within 7 days (day 0-day 6) following at least one dose of the primary vaccination.	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is reporting the parameter for pooled groups containing the baseline groups.

End point values	10Pn Group	10Pn-dPly-PhtD Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	51	103		
Units: Subjects				
Fever >40°C	0	1		

Statistical analyses

Statistical analysis title	Fever >40°C -non-inferiority
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Statistical analysis description:

To compare the 2 formulations of GSK Biologicals' S. pneumoniae protein containing vaccine combined with 10Pn-PD-DiT vaccine (pooled groups) versus 10Pn-PD-DiT vaccine (10Pn-dPly-PhtD Group minus 10Pn Group) with respect to the percentage of subjects reporting fever > 40.0°C (rectal temperature) within 7 days after at least 1 dose of primary vaccination.

Comparison groups	10Pn Group v 10Pn-dPly-PhtD Group
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Parameter estimate	Difference in percentage
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	5.32

Notes:

[2] - The 95% CI for the difference between groups in the percentage of subjects with rectal temperature > 40.0°C within the 7-day follow-up period following primary vaccination was computed for the 10Pn-dPly-PhtD minus the 10Pn group. No statistically significant difference between groups in rectal temperature >40.0°C would be detected if the 95% CIs included 0 and non-inferiority would be expressed if the upper limit of the 2-sided 95% CI on the group difference < 10%.

Primary: Number of subjects with fever > 40.0°C (rectal temperature)

End point title	Number of subjects with fever > 40.0°C (rectal temperature) ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Within 7 days (day 0-day 6) following at least one dose of the primary vaccination.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is reporting the parameter for pooled groups containing the baseline groups.

End point values	10Pn Group	dPly-PhtD Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	51	103		
Units: Subjects				
Fever >40°C	0	1		

Statistical analyses

Statistical analysis title	Fever >40°C -non-inferiority
Statistical analysis description:	
To compare the 2 formulations of GSK Biologicals' S. pneumoniae protein containing vaccine (pooled groups) versus 10Pn-PD-DiT vaccine (dPly-PhtD Group minus 10Pn Group) with respect to the percentage of subjects reporting fever > 40.0°C (rectal temperature) within 7 days after at least 1 dose of primary vaccination.	
Comparison groups	10Pn Group v dPly-PhtD Group
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Parameter estimate	Difference in percentage
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	5.32

Notes:

[4] - The 95% CI for the difference between groups in the percentage of subjects with rectal temperature > 40.0°C within the 7-day follow-up period following primary vaccination was computed for the dPly-PhtD minus the 10Pn group. No statistically significant difference between groups in rectal temperature >40.0°C would be detected if the 95% CIs included 0 and non-inferiority would be expressed if the upper limit of the 2-sided 95% CI on the group difference < 10%.

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

End point title	Number of subjects reporting any and grade 3 solicited local symptoms
End point description:	
Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.	
End point type	Secondary
End point timeframe:	
During the 7-day (Days 0-6) post-vaccination period following each dose (Dose 1, Dose 2 and Booster dose)	

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	52	51
Units: Subjects				
Any Pain Dose 1 [N=51;52;52;51;51]	18	15	31	23
Grade 3 Pain Dose 1 [N=51;52;52;51;51]	0	0	1	2

Any Redness Dose 1 [N=51;52;52;51;51]	17	20	32	28
Grade 3 Redness Dose 1 [N=51;52;52;51;51]	1	0	5	4
Any Swelling Dose 1 [N=51;52;52;51;51]	8	5	19	17
Grade 3 Swelling Dose 1 [N=51;52;52;51;51]	0	0	2	2
Any Pain Dose 2 [N=51;52;52;51;50]	15	22	24	27
Grade 3 Pain Dose 2 [N=51;52;52;51;50]	0	0	2	2
Any Redness Dose 2 [N=51;52;52;51;50]	21	25	23	22
Grade 3 Redness Dose 2 [N=51;52;52;51;50]	1	1	4	1
Any Swelling Dose 2 [N=51;52;52;51;50]	11	9	18	11
Grade 3 Swelling Dose 2 [N=51;52;52;51;50]	0	0	5	1
Any Pain Booster [N=51;51;52;51;50]	18	22	32	26
Grade 3 Pain Booster [N=51;51;52;51;50]	0	0	3	2
Any Redness Booster [N=51;51;52;51;50]	19	20	28	22
Grade 3 Redness Booster [N=51;51;52;51;50]	2	2	5	4
Any Swelling Booster [N=51;51;52;51;50]	11	8	18	15
Grade 3 Swelling Booster [N=51;51;52;51;50]	0	3	3	1

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Subjects				
Any Pain Dose 1 [N=51;52;52;51;51]	26			
Grade 3 Pain Dose 1 [N=51;52;52;51;51]	4			
Any Redness Dose 1 [N=51;52;52;51;51]	25			
Grade 3 Redness Dose 1 [N=51;52;52;51;51]	2			
Any Swelling Dose 1 [N=51;52;52;51;51]	19			
Grade 3 Swelling Dose 1 [N=51;52;52;51;51]	1			
Any Pain Dose 2 [N=51;52;52;51;50]	27			
Grade 3 Pain Dose 2 [N=51;52;52;51;50]	3			
Any Redness Dose 2 [N=51;52;52;51;50]	24			
Grade 3 Redness Dose 2 [N=51;52;52;51;50]	3			
Any Swelling Dose 2 [N=51;52;52;51;50]	16			
Grade 3 Swelling Dose 2 [N=51;52;52;51;50]	2			

Any Pain Booster [N=51;51;52;51;50]	25			
Grade 3 Pain Booster [N=51;51;52;51;50]	1			
Any Redness Booster [N=51;51;52;51;50]	21			
Grade 3 Redness Booster [N=51;51;52;51;50]	3			
Any Swelling Booster [N=51;51;52;51;50]	13			
Grade 3 Swelling Booster [N=51;51;52;51;50]	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms
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End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectally temperature $\geq 38.0^{\circ}\text{C}$), irritability, and loss of appetite. Grade 3 drowsiness = drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectally temperature) above ($>$) 40.0°C . Grade 3 irritability = crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite = not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination.

End point type	Secondary
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End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose (Dose 1, Dose 2, Booster dose)

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	52	51
Units: Subjects				
Any Drowsiness Dose 1 [N=51;52;52;51;51]	16	13	24	20
Grade 3 Drowsiness Dose 1 [N=51;52;52;51;51]	0	0	0	0
Related Drowsiness Dose 1 [N=51;52;52;51;51]	6	6	13	10
Any Irritability Dose 1 [N=51;52;52;51;51]	21	16	31	27
Grade 3 Irritability Dose 1 [N=51;52;52;51;51]	0	0	0	0
Related Irritability Dose 1 [N=51;52;52;51;51]	6	9	17	16
Any Loss of appetite Dose 1 [N=51;52;52;51;51]	15	7	14	12
Grade 3 Loss of appetite Dose 1 [N=51;52;52;51;51]	2	0	1	0

Related Loss of appetite Dose 1 [N=51;52;52;51;51]	4	5	9	3
Any Fever Dose 1 [N=51;52;52;51;51]	7	8	14	12
Grade 3 Fever Dose 1 [N=51;52;52;51;51]	0	1	1	0
Related Fever Dose 1 [N=51;52;52;51;51]	3	2	7	8
Any Drowsiness Dose 2 [N=51;52;52;51;50]	12	16	17	15
Grade 3 Drowsiness Dose 2 [N=51;52;52;51;50]	0	0	0	0
Related Drowsiness Dose 2 [N=51;52;52;51;50]	6	11	11	10
Any Irritability Dose 2 [N=51;52;52;51;50]	12	18	22	24
Grade 3 Irritability Dose 2 [N=51;52;52;51;50]	0	0	0	0
Related Irritability Dose 2 [N=51;52;52;51;50]	3	11	17	18
Any Loss of appetite Dose 2 [N=51;52;52;51;50]	8	10	12	9
Grade 3 Loss of appetite Dose 2 [N=51;52;52;51;50]	1	0	0	0
Related Loss of appetite Dose 2 [N=51;52;52;51;50]	4	5	9	5
Any Fever Dose 2 [N=51;52;52;51;50]	9	12	8	9
Grade 3 Fever Dose 2 [N=51;52;52;51;50]	0	0	0	0
Related Fever Dose 2 [N=51;52;52;51;50]	2	6	5	7
Any Drowsiness Booster [N=51;51;52;51;50]	13	13	18	12
Grade 3 Drowsiness Booster [N=51;51;52;51;50]	0	0	0	0
Related Drowsiness Booster [N=51;51;52;51;50]	7	9	11	10
Any Irritability Booster [N=51;51;52;51;50]	15	17	26	17
Grade 3 Irritability Booster [N=51;51;52;51;50]	0	0	0	1
Related Irritability Booster [N=51;51;52;51;50]	9	11	15	13
Any Loss of appetite Booster [N=51;51;52;51;50]	6	10	13	15
Grade 3 Loss of appetite Booster [N=51;51;52;51;50]	2	0	1	1
Related Loss of appetite Booster [N=51;51;52;51;50]	4	4	7	7
Any Fever Booster [N=51;51;52;51;50]	8	10	10	5
Grade 3 Fever Booster [N=51;51;52;51;50]	0	0	0	0
Related Fever Dose 3 Booster [N=51;51;52;51;50]	5	3	7	2

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	51			

Units: Subjects				
Any Drowsiness Dose 1 [N=51;52;52;51;51]	26			
Grade 3 Drowsiness Dose 1 [N=51;52;52;51;51]	0			
Related Drowsiness Dose 1 [N=51;52;52;51;51]	16			
Any Irritability Dose 1 [N=51;52;52;51;51]	23			
Grade 3 Irritability Dose 1 [N=51;52;52;51;51]	0			
Related Irritability Dose 1 [N=51;52;52;51;51]	14			
Any Loss of appetite Dose 1 [N=51;52;52;51;51]	14			
Grade 3 Loss of appetite Dose 1 [N=51;52;52;51;51]	0			
Related Loss of appetite Dose 1 [N=51;52;52;51;51]	7			
Any Fever Dose 1 [N=51;52;52;51;51]	12			
Grade 3 Fever Dose 1 [N=51;52;52;51;51]	0			
Related Fever Dose 1 [N=51;52;52;51;51]	9			
Any Drowsiness Dose 2 [N=51;52;52;51;50]	23			
Grade 3 Drowsiness Dose 2 [N=51;52;52;51;50]	0			
Related Drowsiness Dose 2 [N=51;52;52;51;50]	18			
Any Irritability Dose 2 [N=51;52;52;51;50]	27			
Grade 3 Irritability Dose 2 [N=51;52;52;51;50]	1			
Related Irritability Dose 2 [N=51;52;52;51;50]	21			
Any Loss of appetite Dose 2 [N=51;52;52;51;50]	13			
Grade 3 Loss of appetite Dose 2 [N=51;52;52;51;50]	0			
Related Loss of appetite Dose 2 [N=51;52;52;51;50]	7			
Any Fever Dose 2 [N=51;52;52;51;50]	7			
Grade 3 Fever Dose 2 [N=51;52;52;51;50]	0			
Related Fever Dose 2 [N=51;52;52;51;50]	7			
Any Drowsiness Booster [N=51;51;52;51;50]	17			
Grade 3 Drowsiness Booster [N=51;51;52;51;50]	0			
Related Drowsiness Booster [N=51;51;52;51;50]	11			
Any Irritability Booster [N=51;51;52;51;50]	19			
Grade 3 Irritability Booster [N=51;51;52;51;50]	1			
Related Irritability Booster [N=51;51;52;51;50]	13			
Any Loss of appetite Booster [N=51;51;52;51;50]	8			

Grade 3 Loss of appetite Booster [N=51;51;52;51;50]	1			
Related Loss of appetite Booster [N=51;51;52;51;50]	6			
Any Fever Booster [N=51;51;52;51;50]	7			
Grade 3 Fever Booster [N=51;51;52;51;50]	0			
Related Fever Dose 3 Booster [N=51;51;52;51;50]	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)
End point description:	
An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined as an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.	
End point type	Secondary
End point timeframe:	
During the 31-day (Days 0-30) follow-up period after each primary dose	

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	52	51
Units: Subjects				
Any AE(s)	25	24	31	24

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Subjects				
Any AE(s)	22			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)
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End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined as an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type Secondary

End point timeframe:

During the 31-day (Days 0-30) follow-up period after the booster dose

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	52	51
Units: Subjects				
Any AE(s)	14	12	13	4

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Subjects				
Any AE(s)	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title Number of subjects with serious adverse events (SAEs)

End point description:

End point type Secondary

End point timeframe:

During the entire study period starting at the administration of the first vaccine dose up to study end

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	52	51
Units: Subjects				
Any SAE(s)	5	3	5	0

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Subjects				
Any SAE(s)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti- pneumococcal dPly and PhtD proteins antibody concentrations

End point title	Anti- pneumococcal dPly and PhtD proteins antibody concentrations
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End point description:

Seropositivity status, defined as anti-pneumococcal dPly antibody concentrations ≥ 599 Luminex Units per millilitre (LU/mL) and anti-pneumococcal PhtD antibody concentrations ≥ 391 LU/mL .

End point type	Secondary
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End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster:

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	47	41
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-dPly, Post-dose 2 [N=45;43;45;39;41]	135703.5 (95376.62 to 193081.3)	148447.5 (101599.9 to 216896.7)	32436.07 (25523.77 to 41220.35)	57149.83 (44908.69 to 72727.64)
Anti-dPly, Pre-booster [N=44;45;46;40;40]	100811.4 (74005.55 to 137326.8)	96552.52 (73753.5 to 126399.3)	19573.55 (14948.37 to 25629.82)	29592.91 (22065.25 to 39688.66)
Anti-dPly, Post-booster [N=44;43;47;41;41]	224726.2 (178187.6 to 283419.8)	305912.3 (248087.9 to 377214.4)	44123.43 (34299.98 to 56760.29)	85805.02 (67740.53 to 108686.8)
Anti-PhtD, Post-dose 2 [N=45;43;45;39;41]	30402.84 (20723.61 to 44602.88)	35043.91 (24164.16 to 50822.19)	23438.06 (16617.86 to 33057.36)	22141.18 (15065.44 to 32540.15)
Anti- PhtD, Pre-booster [N=44;45;46;40;40]	24350.58 (17056.09 to 34764.74)	23918.77 (17724.59 to 32277.63)	14375.59 (9338.31 to 22130.1)	12721.01 (8498 to 19042.62)
Anti- PhtD, Post-booster [N=44;43;47;41;41]	65584.24 (50985.27 to 84363.43)	77312.07 (58589.49 to 102017.6)	32609.19 (23615.58 to 45027.88)	36098.18 (26620.97 to 48949.34)

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-dPly, Post-dose 2 [N=45;43;45;39;41]	3759.82 (2376.77 to 5947.68)			
Anti-dPly, Pre-booster [N=44;45;46;40;40]	4654.16 (2879.42 to 7522.78)			
Anti-dPly, Post-booster [N=44;43;47;41;41]	4553.43 (2878.04 to 7204.12)			
Anti-PhtD, Post-dose 2 [N=45;43;45;39;41]	3795.68 (2268.23 to 6351.73)			
Anti- PhtD, Pre-booster [N=44;45;46;40;40]	4814.97 (2881.25 to 8046.46)			
Anti- PhtD, Post-booster [N=44;43;47;41;41]	5072.43 (3023.97 to 8508.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pneumococcal serotypes and cross-reactive serotypes antibody concentrations

End point title	Anti-pneumococcal serotypes and cross-reactive serotypes antibody concentrations
End point description: Seropositivity status, defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and cross-reactive serotype 6A and 19 antibody concentrations ≥ 0.05 microgram per millilitre ($\mu\text{g/mL}$).	
End point type	Secondary
End point timeframe: One month post-dose 2, prior to the booster dose and one month post-booster	

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	44	47	41
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				

Anti-1, Post-Dose 2 [N=40;36;46;40;41]	0.04 (0.03 to 0.05)	0.05 (0.04 to 0.06)	2.5 (2.01 to 3.11)	2.08 (1.56 to 2.77)
Anti-1, Pre-booster [N=43;42;45;40;40]	0.05 (0.03 to 0.06)	0.05 (0.04 to 0.07)	0.87 (0.68 to 1.12)	0.75 (0.57 to 0.99)
Anti-1, Post-booster [N=40;41;47;41;41]	0.04 (0.03 to 0.06)	0.05 (0.04 to 0.08)	2.69 (2.13 to 3.39)	2.47 (2.03 to 3)
Anti-4, Post-Dose 2 [N=37;37;46;40;41]	0.05 (0.03 to 0.08)	0.03 (0.02 to 0.03)	6.42 (5.23 to 7.87)	6.6 (5.12 to 8.52)
Anti-4, Pre-booster [N=41;41;46;41;40]	0.05 (0.03 to 0.07)	0.03 (0.03 to 0.03)	2.3 (1.82 to 2.91)	2.36 (1.79 to 3.11)
Anti-4, Post-booster [N=40;41;47;41;41]	0.05 (0.03 to 0.07)	0.04 (0.03 to 0.05)	5.26 (4.14 to 6.69)	5.61 (4.46 to 7.07)
Anti-5, Post-Dose 2 [N=31;34;44;39;41]	0.06 (0.04 to 0.08)	0.06 (0.05 to 0.08)	2.42 (1.85 to 3.17)	2.41 (1.85 to 3.13)
Anti-5, Pre-booster [N=42;43;45;41;40]	0.07 (0.05 to 0.1)	0.06 (0.05 to 0.08)	1.08 (0.83 to 1.41)	1.05 (0.81 to 1.36)
Anti-5, Post-booster [N=41;43;47;41;41]	0.07 (0.05 to 0.09)	0.07 (0.05 to 0.09)	3.57 (2.79 to 4.57)	3.45 (2.7 to 4.41)
Anti-6B, Post-Dose 2 [N=43;39;46;40;41]	0.04 (0.03 to 0.05)	0.03 (0.02 to 0.03)	0.55 (0.37 to 0.81)	0.48 (0.32 to 0.72)
Anti-6B, Pre-booster [N=42;41;44;40;40]	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)	0.39 (0.28 to 0.54)	0.42 (0.3 to 0.59)
Anti-6B, Post-booster [N=41;42;47;41;40]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.06)	1.08 (0.74 to 1.57)	1.14 (0.83 to 1.57)
Anti-7F, Post-Dose 2 [N=37;38;46;40;41]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.04)	5.03 (4.16 to 6.09)	4.73 (3.89 to 5.74)
Anti-7F, Pre-booster [N=42;44;46;41;40]	0.04 (0.03 to 0.06)	0.03 (0.03 to 0.04)	2.6 (2.14 to 3.15)	2.36 (1.94 to 2.86)
Anti-7F, Post-booster [N=41;43;47;41;41]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.05)	5.9 (4.83 to 7.2)	5.25 (4.36 to 6.32)
Anti-9V, Post-Dose 2 [N=42;40;46;40;41]	0.04 (0.03 to 0.06)	0.03 (0.02 to 0.03)	2.81 (2.24 to 3.51)	2.49 (1.95 to 3.19)
Anti-9V, Pre-booster [N=41;42;45;41;40]	0.04 (0.03 to 0.05)	0.03 (0.03 to 0.04)	1.44 (1.15 to 1.81)	1.26 (0.94 to 1.67)
Anti-9V, Post-booster [N=39;40;47;41;40]	0.04 (0.03 to 0.06)	0.03 (0.02 to 0.04)	3.13 (2.48 to 3.93)	3.21 (2.45 to 4.19)
Anti-14, Post-Dose 2 [N=43;36;46;40;41]	0.1 (0.07 to 0.14)	0.09 (0.06 to 0.14)	5.18 (3.91 to 6.86)	3.78 (2.92 to 4.91)
Anti-14, Pre-booster [N=40;40;46;40;40]	0.11 (0.08 to 0.17)	0.11 (0.07 to 0.18)	2.86 (2.25 to 3.65)	2.3 (1.81 to 2.91)
Anti-14, Post-booster [N=42;43;47;41;41]	0.13 (0.09 to 0.18)	0.16 (0.1 to 0.26)	7.74 (6.03 to 9.94)	6.62 (5.22 to 8.4)
Anti-18C, Post-Dose 2 [N=39;39;45;40;41]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.05)	13.92 (10.75 to 18.03)	16.92 (13.61 to 21.03)
Anti-18C, Pre-booster [N=41;42;45;41;40]	0.05 (0.03 to 0.07)	0.04 (0.03 to 0.05)	4.94 (3.83 to 6.38)	5.51 (4.3 to 7.05)
Anti-18C, Post-booster [N=42;44;47;41;40]	0.05 (0.03 to 0.07)	0.05 (0.03 to 0.07)	16.12 (12.2 to 21.32)	21.98 (16.67 to 28.99)
Anti-19F, Post-Dose 2 [N=33;35;45;39;41]	0.05 (0.03 to 0.08)	0.06 (0.03 to 0.12)	8.6 (6.37 to 11.63)	10.08 (7.21 to 14.09)
Anti-19F, Pre-booster [N=38;40;46;41;40]	0.06 (0.04 to 0.1)	0.05 (0.03 to 0.09)	4.15 (2.94 to 5.85)	4.72 (3.54 to 6.3)
Anti-19F, Post-booster [N=41;40;47;41;41]	0.06 (0.04 to 0.09)	0.07 (0.04 to 0.13)	10.46 (7.35 to 14.88)	14.38 (10.53 to 19.63)
Anti-23F, Post-Dose 2 [N=38;38;45;39;41]	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.05)	1.19 (0.82 to 1.74)	0.91 (0.62 to 1.33)
Anti-23F, Pre-booster [N=42;41;45;41;40]	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.06)	0.71 (0.5 to 0.99)	0.62 (0.45 to 0.85)
Anti-23F, Post-booster [N=41;43;47;41;40]	0.03 (0.03 to 0.04)	0.05 (0.03 to 0.06)	1.92 (1.42 to 2.6)	2.04 (1.56 to 2.65)
Anti-6A, Post-Dose 2 [N=33;37;43;40;41]	0.04 (0.03 to 0.07)	0.03 (0.03 to 0.04)	0.32 (0.2 to 0.51)	0.27 (0.16 to 0.45)

Anti-6A, Pre-booster [N=42;42;44;41;40]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.04)	0.24 (0.17 to 0.34)	0.24 (0.15 to 0.38)
Anti-6A, Post-booster [N=42;40;47;41;40]	0.04 (0.03 to 0.06)	0.04 (0.03 to 0.06)	0.53 (0.35 to 0.79)	0.56 (0.36 to 0.87)
Anti-19A, Post-Dose 2 [N=33;35;43;39;41]	0.07 (0.04 to 0.12)	0.05 (0.03 to 0.06)	1.08 (0.71 to 1.62)	0.97 (0.63 to 1.48)
Anti-19A, Pre-booster [N=43;42;44;41;40]	0.07 (0.04 to 0.1)	0.05 (0.04 to 0.06)	0.85 (0.61 to 1.17)	0.68 (0.47 to 0.98)
Anti-19A, Post-booster [N=41;39;47;41;41]	0.07 (0.05 to 0.11)	0.05 (0.04 to 0.07)	2.76 (1.92 to 3.96)	2.98 (2.08 to 4.26)

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1, Post-Dose 2 [N=40;36;46;40;41]	2.13 (1.62 to 2.79)			
Anti-1, Pre-booster [N=43;42;45;40;40]	0.73 (0.55 to 0.97)			
Anti-1, Post-booster [N=40;41;47;41;41]	2.4 (1.85 to 3.12)			
Anti-4, Post-Dose 2 [N=37;37;46;40;41]	5.67 (4.56 to 7.06)			
Anti-4, Pre-booster [N=41;41;46;41;40]	2.11 (1.68 to 2.64)			
Anti-4, Post-booster [N=40;41;47;41;41]	5.18 (4.05 to 6.63)			
Anti-5, Post-Dose 2 [N=31;34;44;39;41]	2.36 (1.88 to 2.97)			
Anti-5, Pre-booster [N=42;43;45;41;40]	1.18 (0.94 to 1.48)			
Anti-5, Post-booster [N=41;43;47;41;41]	3.84 (2.98 to 4.95)			
Anti-6B, Post-Dose 2 [N=43;39;46;40;41]	0.55 (0.39 to 0.78)			
Anti-6B, Pre-booster [N=42;41;44;40;40]	0.46 (0.34 to 0.62)			
Anti-6B, Post-booster [N=41;42;47;41;40]	1.08 (0.78 to 1.52)			
Anti-7F, Post-Dose 2 [N=37;38;46;40;41]	3.72 (3.17 to 4.36)			
Anti-7F, Pre-booster [N=42;44;46;41;40]	2.14 (1.82 to 2.51)			
Anti-7F, Post-booster [N=41;43;47;41;41]	4.65 (3.77 to 5.72)			
Anti-9V, Post-Dose 2 [N=42;40;46;40;41]	1.55 (1.21 to 2)			
Anti-9V, Pre-booster [N=41;42;45;41;40]	0.95 (0.73 to 1.24)			
Anti-9V, Post-booster [N=39;40;47;41;40]	2.18 (1.71 to 2.79)			
Anti-14, Post-Dose 2 [N=43;36;46;40;41]	4.63 (3.71 to 5.77)			
Anti-14, Pre-booster [N=40;40;46;40;40]	2.71 (2.17 to 3.38)			

Anti-14, Post-booster [N=42;43;47;41;41]	5.98 (4.68 to 7.63)			
Anti-18C, Post-Dose 2 [N=39;39;45;40;41]	12.56 (9.8 to 16.1)			
Anti-18C, Pre-booster [N=41;42;45;41;40]	4.79 (3.69 to 6.21)			
Anti-18C, Post-booster [N=42;44;47;41;40]	14.62 (10.9 to 19.6)			
Anti-19F, Post-Dose 2 [N=33;35;45;39;41]	8.87 (6.2 to 12.7)			
Anti-19F, Pre-booster [N=38;40;46;41;40]	4.33 (3.06 to 6.12)			
Anti-19F, Post-booster [N=41;40;47;41;41]	11.32 (7.94 to 16.13)			
Anti-23F, Post-Dose 2 [N=38;38;45;39;41]	0.73 (0.54 to 0.98)			
Anti-23F, Pre-booster [N=42;41;45;41;40]	0.51 (0.39 to 0.67)			
Anti-23F, Post-booster [N=41;43;47;41;40]	1.47 (1.04 to 2.06)			
Anti-6A, Post-Dose 2 [N=33;37;43;40;41]	0.31 (0.2 to 0.48)			
Anti-6A, Pre-booster [N=42;42;44;41;40]	0.27 (0.18 to 0.4)			
Anti-6A, Post-booster [N=42;40;47;41;40]	0.58 (0.37 to 0.9)			
Anti-19A, Post-Dose 2 [N=33;35;43;39;41]	0.93 (0.61 to 1.43)			
Anti-19A, Pre-booster [N=43;42;44;41;40]	0.62 (0.42 to 0.93)			
Anti-19A, Post-booster [N=41;39;47;41;41]	2.06 (1.3 to 3.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes and cross-reactive serotypes

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes and cross-reactive serotypes
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End point description:

Seropositivity status, defined as Opsonophagocytic activity against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and cross-reactive serotypes 6A and 19A ≥ 8

End point type	Secondary
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End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	36	37	36
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1, Post-Dose 2 [N=27;33;35;30;30]	4 (4 to 4)	5.4 (3.8 to 7.8)	71.8 (40.9 to 126.1)	48.2 (26.5 to 87.6)
OPSONO-1, Pre-booster [N=35;35;33;35;34]	4 (4 to 4)	4.3 (3.7 to 5)	23 (13.1 to 40.3)	12.4 (7.6 to 20.3)
OPSONO-1, Post-booster [N=31;35;37;36;37]	5.2 (4 to 6.9)	8.1 (4.8 to 13.7)	169.5 (96.1 to 298.8)	200 (138.2 to 289.4)
OPSONO-4, Post-Dose 2 [N=20;29;32;29;29]	7 (3.1 to 15.6)	8.9 (4.5 to 17.6)	1260.2 (856.1 to 1855.2)	1197.9 (784.1 to 1830.2)
OPSONO-4, Pre-booster [N=28;29;29;33;30]	12.6 (5.6 to 28.4)	16.2 (7 to 37.2)	247.9 (117.4 to 523.2)	259.9 (120.6 to 560)
OPSONO-4, Post-booster [N=24;31;35;32;34]	15.5 (6.1 to 39.5)	17.8 (7.3 to 43.4)	1206.2 (888.9 to 1636.8)	1385 (974.5 to 1968.4)
OPSONO-5, Post-Dose 2 [N=27;33;33;30;31]	4 (4 to 4)	4.7 (3.4 to 6.5)	43.8 (27.1 to 70.8)	37.3 (21.7 to 64)
OPSONO-5, Pre-booster [N=34;35;34;33;34]	4.5 (3.5 to 5.8)	4 (4 to 4)	12.8 (8.2 to 19.9)	14.8 (9.6 to 23)
OPSONO-5, Post-booster [N=30;36;37;34;36]	4 (4 to 4)	5.1 (3.8 to 6.7)	99.3 (62.1 to 158.8)	110.4 (73.1 to 166.8)
OPSONO-6B, Post-Dose 2 [N=16;21;27;25;28]	15 (4.2 to 53.1)	23.4 (6.1 to 90.3)	361.9 (120 to 1091.7)	527.5 (202.6 to 1372.9)
OPSONO-6B, Pre-booster [N=23;27;30;30;30]	56.7 (16.2 to 198.4)	61.6 (19.2 to 197.3)	213.8 (79 to 578.1)	513.1 (243.9 to 1079.6)
OPSONO-6B, Post-booster [N=24;33;33;34;35]	26.1 (7.7 to 88.7)	30.8 (11.2 to 84.7)	804.6 (343.5 to 1884.9)	982.7 (527.6 to 1830.4)
OPSONO-7F, Post-Dose 2 [N=27;33;33;29;30]	734.6 (369.7 to 1459.6)	807.4 (445 to 1465.2)	5703.7 (4143.6 to 7851.2)	4936.6 (3320.7 to 7338.7)
OPSONO-7F, Pre-booster [N=33;30;32;34;33]	670.4 (317.5 to 1415.6)	462.3 (187.5 to 1139.8)	2450.1 (1637.4 to 3666.2)	2713.5 (1836.1 to 4010.1)
OPSONO-7F, Post-booster [N=30;35;35;33;36]	936.8 (510 to 1720.7)	785.5 (428 to 1441.6)	4109.3 (3086.9 to 5470.3)	5730.4 (4262 to 7704.7)
OPSONO-9V, Post-Dose 2 [N=22;29;34;29;30]	26.5 (8.2 to 85.9)	50.1 (17.5 to 143.7)	4455 (2803.3 to 7079.9)	3542.8 (2271.5 to 5525.5)
OPSONO--9V, Pre-booster [N=30;28;32;33;32]	172.4 (68.9 to 431.4)	172 (57.6 to 513.2)	2126.1 (1140.2 to 3964.4)	2622.4 (1786.7 to 3849)
OPSONO-9V, Post-booster [N=26;32;37;34;36]	173.5 (59.1 to 509.8)	137.6 (51.7 to 366)	4643.1 (3418.3 to 6306.9)	5802.4 (4453 to 7560.8)
OPSONO-14, Post-Dose 2 [N=18;23;33;29;31]	21.1 (6.7 to 66.8)	11.9 (4.7 to 30.4)	3324.8 (2324.8 to 4754.8)	2580.7 (1788.4 to 3724)
OPSONO-14, Pre-booster [N=30;30;32;34;33]	21 (8.5 to 51.6)	27.9 (10.4 to 75.1)	1390.5 (615.7 to 3140.4)	1725.8 (972.1 to 3064)
OPSONO-14, Post-booster [N=27;33;34;36;37]	32.3 (11.5 to 90.9)	46.7 (17 to 127.8)	2911.6 (1841.3 to 4604)	3729.8 (2693.2 to 5165.4)
OPSONO-18C, Post-Dose 2 [N=24;29;33;28;27]	4 (4 to 4)	7.4 (3.7 to 15.1)	1398.3 (810.6 to 2412)	2538.4 (1787.3 to 3605)
OPSONO-18C, Pre-booster [N=33;33;31;34;34]	5.4 (3.4 to 8.3)	5 (3.7 to 6.8)	420.1 (192.8 to 915.3)	1041 (699.6 to 1548.9)

OPSONO-18C, Post-booster [N=26;32;34;32;33]	6 (3.3 to 10.7)	8 (4.4 to 14.6)	1764.6 (1243.6 to 2503.8)	2640.6 (2083.3 to 3346.8)
OPSONO-19F, Pre-booster [N=31;34;30;34;34]	5 (3.1 to 8.2)	8 (4.3 to 14.7)	794.3 (476.6 to 1324)	420.7 (197.4 to 896.4)
OPSONO-19F, Post-booster [N=30;36;36;34;34]	4.9 (3.5 to 6.8)	4.4 (3.7 to 5.2)	173.3 (86.1 to 349)	210.1 (118.4 to 373)
OPSONO-19F, Post-Dose 2 [N=17;28;32;28;27]	5.6 (3.4 to 9.1)	7.3 (4.3 to 12.6)	1248.5 (740.4 to 2105.3)	1823.7 (1252.9 to 2654.5)
OPSONO-23F, Post-Dose 2 [N=20;28;34;28;29]	17.9 (5.1 to 62.9)	107.8 (28.1 to 412.8)	1735.5 (833.6 to 3613.3)	3621.8 (2431.4 to 5395.2)
OPSONO-23F, Pre-booster [N=30;33;32;33;33]	23.2 (7.6 to 70.3)	136.3 (36.1 to 514.6)	989.7 (419.2 to 2336.8)	1635.9 (691.7 to 3868.8)
OPSONO-23F, Post-booster [N=25;33;35;35;36]	68.6 (17.3 to 271.2)	106.7 (28.5 to 399.4)	3598.5 (2422.2 to 5345.9)	6108 (4335.9 to 8604.5)
OPSONO-6A, Post-Dose 2 [N=19;26;31;21;27]	9.3 (3.5 to 24.7)	5.7 (3.4 to 9.5)	225.3 (83.3 to 608.8)	186.2 (55.3 to 627.2)
OPSONO-6A, Pre-booster [N=27;30;31;33;32]	18.4 (7.6 to 44.5)	9.4 (4.5 to 19.5)	58.9 (21.6 to 160.3)	99.4 (39.9 to 247.8)
OPSONO-6A, Post-booster [N=22;32;34;31;32]	11.8 (4.7 to 29.5)	17.3 (7.9 to 37.9)	308 (141 to 672.9)	348.2 (154.9 to 782.5)
OPSONO-19A, Post-Dose 2 [N=25;31;34;28;29]	5.8 (3.4 to 9.9)	4.6 (3.7 to 5.6)	246 (109.7 to 551.7)	363.2 (202.1 to 652.8)
OPSONO-19A, Pre-booster [N=35;35;33;35;32]	6 (4 to 9.1)	4.5 (3.8 to 5.3)	56.7 (25.2 to 127.9)	76.4 (36.3 to 160.7)
OPSONO-19A, Post-booster [N=30;36;34;34;34]	6.7 (4.3 to 10.3)	6.3 (4.4 to 9.1)	746.3 (407.8 to 1365.6)	989.3 (652.5 to 1500)

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1, Post-Dose 2 [N=27;33;35;30;30]	90 (52.9 to 153)			
OPSONO-1, Pre-booster [N=35;35;33;35;34]	19.3 (11.1 to 33.6)			
OPSONO-1, Post-booster [N=31;35;37;36;37]	206.9 (123.1 to 347.5)			
OPSONO-4, Post-Dose 2 [N=20;29;32;29;29]	1220.4 (913.8 to 1629.9)			
OPSONO-4, Pre-booster [N=28;29;29;33;30]	478.9 (309.3 to 741.3)			
OPSONO-4, Post-booster [N=24;31;35;32;34]	1476 (1076 to 2024.6)			
OPSONO-5, Post-Dose 2 [N=27;33;33;30;31]	42 (26.6 to 66.4)			
OPSONO-5, Pre-booster [N=34;35;34;33;34]	17 (10.9 to 26.4)			
OPSONO-5, Post-booster [N=30;36;37;34;36]	160.7 (113 to 228.7)			
OPSONO-6B, Post-Dose 2 [N=16;21;27;25;28]	915.3 (543.4 to 1541.8)			

OPSONO-6B, Pre-booster [N=23;27;30;30;30]	371.9 (172.5 to 801.8)			
OPSONO-6B, Post-booster [N=24;33;33;34;35]	1523.1 (875.8 to 2649)			
OPSONO-7F, Post-Dose 2 [N=27;33;33;29;30]	6154.4 (4244.4 to 8923.7)			
OPSONO-7F, Pre-booster [N=33;30;32;34;33]	3844.5 (2725.7 to 5422.4)			
OPSONO-7F, Post-booster [N=30;35;35;33;36]	7404.7 (5271.1 to 10401.8)			
OPSONO-9V, Post-Dose 2 [N=22;29;34;29;30]	3947.2 (2612.7 to 5963.5)			
OPSONO--9V, Pre-booster [N=30;28;32;33;32]	3450 (2357.5 to 5048.7)			
OPSONO-9V, Post-booster [N=26;32;37;34;36]	6016.6 (4617.2 to 7840)			
OPSONO-14, Post-Dose 2 [N=18;23;33;29;31]	2487.6 (1703.4 to 3632.7)			
OPSONO-14, Pre-booster [N=30;30;32;34;33]	1776.6 (1009.5 to 3126.5)			
OPSONO-14, Post-booster [N=27;33;34;36;37]	3094 (2353.3 to 4068)			
OPSONO-18C, Post-Dose 2 [N=24;29;33;28;27]	1905.4 (1271.4 to 2855.6)			
OPSONO-18C, Pre-booster [N=33;33;31;34;34]	766.4 (468.4 to 1253.8)			
OPSONO-18C, Post-booster [N=26;32;34;32;33]	2123.4 (1493 to 3020.1)			
OPSONO-19F, Pre-booster [N=31;34;30;34;34]	625.4 (266.5 to 1467.7)			
OPSONO-19F, Post-booster [N=30;36;36;34;34]	260.7 (138 to 492.5)			
OPSONO-19F, Post-Dose 2 [N=17;28;32;28;27]	1625.3 (931.7 to 2835.3)			
OPSONO-23F, Post-Dose 2 [N=20;28;34;28;29]	2502.5 (1610.5 to 3888.6)			
OPSONO-23F, Pre-booster [N=30;33;32;33;33]	897.4 (381.6 to 2110.4)			
OPSONO-23F, Post-booster [N=25;33;35;35;36]	5296.1 (3857.9 to 7270.4)			
OPSONO-6A, Post-Dose 2 [N=19;26;31;21;27]	364.5 (158.7 to 837.1)			
OPSONO-6A, Pre-booster [N=27;30;31;33;32]	221.7 (93.8 to 524)			
OPSONO-6A, Post-booster [N=22;32;34;31;32]	554.3 (248.3 to 1237.6)			
OPSONO-19A, Post-Dose 2 [N=25;31;34;28;29]	349.9 (177.1 to 691.6)			
OPSONO-19A, Pre-booster [N=35;35;33;35;32]	87.8 (40.6 to 189.7)			
OPSONO-19A, Post-booster [N=30;36;34;34;34]	725.9 (367.8 to 1432.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD)

End point title	Antibody concentrations to protein D (Anti-PD)
End point description:	
Seropositivity status, defined as anti-PD antibody concentrations ≥ 100 ELISA units per millilitre (EL.U/mL)	
End point type	Secondary
End point timeframe:	
One month post-dose 2, prior to the booster dose and one month post-booster	

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	45	47	41
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD Post-Dose 2 [N=45;43;45;39;41]	90.9 (71.1 to 116.3)	100.4 (76.3 to 132.1)	1105.4 (833.7 to 1465.7)	600.2 (426.5 to 844.7)
Anti-PD Pre-booster [N=44;45;46;40;40]	89.1 (71.8 to 110.7)	118.2 (89.6 to 155.9)	734.6 (523.9 to 1030.1)	463 (330.2 to 649.3)
Anti-PD Post-booster [N=44;43;47;41;41]	97.9 (78 to 122.9)	130.6 (93.1 to 183.3)	1882.6 (1407.4 to 2518.1)	1474.6 (1103.7 to 1970.3)

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD Post-Dose 2 [N=45;43;45;39;41]	860 (659.2 to 1121.9)			
Anti-PD Pre-booster [N=44;45;46;40;40]	691.8 (527.6 to 907.1)			
Anti-PD Post-booster [N=44;43;47;41;41]	1963.8 (1560.1 to 2472)			

Statistical analyses

No statistical analyses for this end point

Secondary: Level of anti-dPly antibodies inhibiting Ply haemolysis activity

End point title	Level of anti-dPly antibodies inhibiting Ply haemolysis activity
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End point description:

Inhibition of haemolysis activity of pneumolysin (Ply) by anti-dPly antibodies was measured in vitro by mean of a haemolytic assay. The haemolysis activity could be followed by measuring the level of haemoglobin released. Anti-dPly titres (for inhibition of haemolytic activity) ≥ 140

End point type	Secondary
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End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster

End point values	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group	10Pn-dPly-PhtD-HD Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	38	43	39
Units: % of inhibition				
geometric mean (confidence interval 95%)				
Anti-Hem-dPly Post-Dose 2 [N=43;38;43;39;40]	3080 (2555.3 to 3712.5)	2988.7 (2410.1 to 3706.2)	1278.9 (1048.2 to 1560.3)	1814 (1495.3 to 2200.8)
Anti- Hem-dPly Pre-booster [N=37;37;37;34;35]	2441.1 (1867.1 to 3191.7)	2193.7 (1737.3 to 2770)	1141.5 (950.6 to 1370.6)	1344.2 (1087.6 to 1661.3)
Anti- Hem-dPly Post-booster [N=31;32;36;32;30]	4332.4 (3327.6 to 5640.4)	5931.9 (4744.5 to 7416.4)	1346.2 (1068.2 to 1696.5)	2388.3 (1830.6 to 3115.9)

End point values	10Pn Group			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: % of inhibition				
geometric mean (confidence interval 95%)				
Anti-Hem-dPly Post-Dose 2 [N=43;38;43;39;40]	913.2 (699.1 to 1192.8)			
Anti- Hem-dPly Pre-booster [N=37;37;37;34;35]	995.9 (788.3 to 1258.2)			
Anti- Hem-dPly Post-booster [N=31;32;36;32;30]	818.6 (662.5 to 1011.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms during the 4-day post-primary and post booster vaccination period; Unsolicited AEs during the 31-day post-primary and post-booster vaccination period; SAEs: during the whole study period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	dPly-PhtD-LD Group
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Reporting group description: -

Reporting group title	dPly-PhtD-HD Group
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Reporting group description: -

Reporting group title	10Pn-dPly-PhtD-LD Group
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Reporting group description: -

Reporting group title	10Pn-dPly-PhtD-HD Group
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Reporting group description: -

Reporting group title	10Pn Group
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Reporting group description: -

Serious adverse events	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 51 (9.80%)	3 / 52 (5.77%)	5 / 52 (9.62%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			

subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Open wound			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			

subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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			
Gastroenteritis salmonella			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Bronchitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Bronchopneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
Laryngitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Oral herpes			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngo-tonsillitis			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	10Pn-dPly-PhtD-HD Group	10Pn Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	4 / 51 (7.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open wound			

subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Affective disorder			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis salmonella			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngo-tonsillitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	dPly-PhtD-LD Group	dPly-PhtD-HD Group	10Pn-dPly-PhtD-LD Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 51 (92.16%)	49 / 52 (94.23%)	49 / 52 (94.23%)
General disorders and administration site conditions			
Pain Primary			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 51 (52.94%)	28 / 52 (53.85%)	34 / 52 (65.38%)
occurrences (all)	27	28	34
Redness Primary			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 51 (47.06%)	30 / 52 (57.69%)	36 / 52 (69.23%)
occurrences (all)	24	30	36
Swelling Primary			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 51 (33.33%)	11 / 52 (21.15%)	25 / 52 (48.08%)
occurrences (all)	17	11	25
Pain Booster			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 51 (35.29%)	22 / 52 (42.31%)	32 / 52 (61.54%)
occurrences (all)	18	22	32
Redness Booster			
alternative assessment type: Systematic			

subjects affected / exposed	19 / 51 (37.25%)	20 / 52 (38.46%)	28 / 52 (53.85%)
occurrences (all)	19	20	28
Swelling Booster			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 51 (21.57%)	8 / 52 (15.38%)	18 / 52 (34.62%)
occurrences (all)	11	8	18
Drowsiness Primary			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 51 (49.02%)	21 / 52 (40.38%)	34 / 52 (65.38%)
occurrences (all)	25	21	34
Irritability Primary			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 51 (50.98%)	23 / 52 (44.23%)	35 / 52 (67.31%)
occurrences (all)	26	23	35
Loss of appetite Primary			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 51 (37.25%)	15 / 52 (28.85%)	20 / 52 (38.46%)
occurrences (all)	19	15	20
Temperature/Rectally Primary			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 51 (25.49%)	16 / 52 (30.77%)	18 / 52 (34.62%)
occurrences (all)	13	16	18
Drowsiness Booster			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 51 (25.49%)	13 / 52 (25.00%)	18 / 52 (34.62%)
occurrences (all)	13	13	18
Irritability Booster			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 51 (29.41%)	17 / 52 (32.69%)	26 / 52 (50.00%)
occurrences (all)	15	17	26
Loss of appetite Booster			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 51 (11.76%)	10 / 52 (19.23%)	13 / 52 (25.00%)
occurrences (all)	6	10	13

Temperature/Rectally Booster alternative assessment type: Systematic subjects affected / exposed occurrences (all)	8 / 51 (15.69%) 8	10 / 52 (19.23%) 10	10 / 52 (19.23%) 10
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 52 (0.00%) 0	3 / 52 (5.77%) 3
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	6 / 51 (11.76%) 6	3 / 52 (5.77%) 3	2 / 52 (3.85%) 2
Infections and infestations Nasopharyngitis Primary subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	8 / 52 (15.38%) 8	9 / 52 (17.31%) 9
Nasopharyngitis Booster subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	3 / 52 (5.77%) 3	2 / 52 (3.85%) 2
Rhinitis Primary subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	1 / 52 (1.92%) 1	4 / 52 (7.69%) 4
Rhinitis Booster subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	1 / 52 (1.92%) 1	1 / 52 (1.92%) 1
Bronchitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	3 / 52 (5.77%) 3	4 / 52 (7.69%) 4
Gastroenteritis subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	2 / 52 (3.85%) 2	3 / 52 (5.77%) 3
Viral infection subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 52 (1.92%) 1	4 / 52 (7.69%) 4
Laryngitis			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Varicella			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	1 / 52 (1.92%)
occurrences (all)	0	1	1

Non-serious adverse events	10Pn-dPly-PhtD-HD Group	10Pn Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 51 (96.08%)	49 / 51 (96.08%)	
General disorders and administration site conditions			
Pain Primary			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 51 (64.71%)	34 / 51 (66.67%)	
occurrences (all)	33	34	
Redness Primary			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 51 (64.71%)	30 / 51 (58.82%)	
occurrences (all)	33	30	
Swelling Primary			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 51 (41.18%)	26 / 51 (50.98%)	
occurrences (all)	21	26	
Pain Booster			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 51 (50.98%)	25 / 51 (49.02%)	
occurrences (all)	26	25	
Redness Booster			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 51 (43.14%)	21 / 51 (41.18%)	
occurrences (all)	22	21	
Swelling Booster			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 51 (29.41%)	13 / 51 (25.49%)	
occurrences (all)	15	13	
Drowsiness Primary			

alternative assessment type: Systematic			
subjects affected / exposed	28 / 51 (54.90%)	35 / 51 (68.63%)	
occurrences (all)	28	35	
Irritability Primary			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 51 (70.59%)	35 / 51 (68.63%)	
occurrences (all)	36	35	
Loss of appetite Primary			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 51 (37.25%)	23 / 51 (45.10%)	
occurrences (all)	19	23	
Temperature/Rectally Primary			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 51 (35.29%)	17 / 51 (33.33%)	
occurrences (all)	18	17	
Drowsiness Booster			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 51 (23.53%)	17 / 51 (33.33%)	
occurrences (all)	12	17	
Irritability Booster			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 51 (33.33%)	19 / 51 (37.25%)	
occurrences (all)	17	19	
Loss of appetite Booster			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 51 (29.41%)	8 / 51 (15.69%)	
occurrences (all)	15	8	
Temperature/Rectally Booster			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 51 (9.80%)	7 / 51 (13.73%)	
occurrences (all)	5	7	
Eye disorders			
Conjunctivitis			

subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 51 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	4 / 51 (7.84%) 4	
Infections and infestations Nasopharyngitis Primary subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	7 / 51 (13.73%) 7	
Nasopharyngitis Booster subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 51 (3.92%) 2	
Rhinitis Primary subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 51 (1.96%) 1	
Rhinitis Booster subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 51 (0.00%) 0	
Bronchitis subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	3 / 51 (5.88%) 3	
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 51 (1.96%) 1	
Viral infection subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	1 / 51 (1.96%) 1	
Laryngitis subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	2 / 51 (3.92%) 2	
Varicella subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	2 / 51 (3.92%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported