

**Clinical trial results:**

OPEN-LABEL, RANDOMIZED, THREE-ARM, PHASE IIIB CLINICAL STUDY TO INVESTIGATE THE SAFETY AND IMMUNOGENICITY OF A CONCOMITANT ADMINISTRATION OF GROUP C MENINGOCOCCAL POLYSACCHARIDE-TETANUS TOXOID CONJUGATE (MENC-TT) VACCINE AND 7-VALENT PNEUMOCOCCAL CRM197-CONJUGATE VACCINE (PCV7) IN TODDLERS PREVIOUSLY IMMUNIZED DURING INFANCY WITH PCV7

Summary

EudraCT number	2007-004276-39
Trial protocol	DE
Global end of trial date	30 July 2009

Results information

Result version number	v1 (current)
This version publication date	29 June 2016
First version publication date	05 August 2015

Trial information**Trial identification**

Sponsor protocol code	670701
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00617760
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: B9361010

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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	29 March 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the concomitant administration of a single dose of MenC-TT vaccine and a PCV7 booster dose does not influence the immune response to any of the seven pneumococcal strains contained in PCV7 as compared to administration of PCV7 alone.

To demonstrate that the concomitant administration of a single dose MenC-TT vaccine and a PCV7 booster dose does not influence the immune response to the MenC-TT vaccine as compared to administration of MenC-TT vaccine alone.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2008
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: 329
Worldwide total number of subjects	329
EEA total number of subjects	329

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)	329

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:

The study was conducted at 27 centers in Germany from 25 March 2008 to 30 July 2009. 333 subjects were enrolled in the study out of which 329 subjects were randomized. One subject randomized to the PCV7 group actually received both MenC-TT and PCV7. Subject disposition has been presented as per the actual treatment received.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenC-TT + PCV7

Arm description:

Subjects recieved MenC-TT as primary immunization dose in combination with PCV7 as booster dose on Day 0 (vaccination visit).

Arm type	Experimental
Investigational medicinal product name	MenC-TT
Investigational medicinal product code	
Other name	NeisVac-C
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received single 0.5 milliliter (mL) MenC-TT dose for primary immunization.

Investigational medicinal product name	PCV7
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received single 0.5 milliliter (mL) PCV7 dose for primary immunization.

Arm title	PCV7
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Arm description:

Subjects recieved intramuscularly 0.5 mL dose of Prevenar as a booster dose.

Arm type	Active comparator
Investigational medicinal product name	PCV7
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single 0.5 mL dose of Prevenar was administered as a booster dose on Day 0 (vaccination visit).

Arm title	MenC-TT
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Arm description:

Subjects recieved intramuscularly 0.5mL of MenC-TT dose for primary immunization.

Arm type	Active comparator
Investigational medicinal product name	MenC-TT
Investigational medicinal product code	
Other name	NeisVac-C
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single dose of 0.5mL of MenC-TT intramuscularly for primary immunization on Day 0 (vaccination visit).

Number of subjects in period 1	MenC-TT + PCV7	PCV7	MenC-TT
Started	166	81	82
Completed	165	78	82
Not completed	1	3	0
Consent withdrawn by subject	-	1	-
Protocol violation	1	2	-

Baseline characteristics

Reporting groups

Reporting group title	MenC-TT + PCV7
Reporting group description: Subjects recieved MenC-TT as primary immunization dose in combination with PCV7 as booster dose on Day 0 (vaccination visit).	
Reporting group title	PCV7
Reporting group description: Subjects recieved intramuscularly 0.5 mL dose of Prevenar as a booster dose.	
Reporting group title	MenC-TT
Reporting group description: Subjects recieved intramuscularly 0.5mL of MenC-TT dose for primary immunization.	

Reporting group values	MenC-TT + PCV7	PCV7	MenC-TT
Number of subjects	166	81	82
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	13.4 ± 1.48	13.3 ± 1.55	13.6 ± 1.59
Gender categorical Units: Subjects			
Female	88	33	34
Male	78	48	48

Reporting group values	Total		
Number of subjects	329		
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	155		
Male	174		

End points

End points reporting groups

Reporting group title	MenC-TT + PCV7
Reporting group description:	
Subjects recieved MenC-TT as primary immunization dose in combination with PCV7 as booster dose on Day 0 (vaccination visit).	
Reporting group title	PCV7
Reporting group description:	
Subjects recieved intramuscularly 0.5 mL dose of Prevenar as a booster dose.	
Reporting group title	MenC-TT
Reporting group description:	
Subjects recieved intramuscularly 0.5mL of MenC-TT dose for primary immunization.	

Primary: Percentage of Subjects With PCV7-Specific Antibody Concentrations of Greater than or Equal to (\geq) 0.2 Microgram/Milliliter (mcg/mL)

End point title	Percentage of Subjects With PCV7-Specific Antibody Concentrations of Greater than or Equal to (\geq) 0.2 Microgram/Milliliter (mcg/mL) ^[1]
End point description:	
Number of subjects achieving seroprotective PCV7-specific antibody concentrations for each of the 7 vaccine serotypes (14, 18C, 19F, 23F, 4, 6B, 9V) 1 month after the PCV booster vaccination were reported. Immunoglobulin G (IgG) antibody concentrations in response to the administration of PCV7 were determined by Enzyme linked immune sorbant assay (ELISA) with antibody concentrations \geq 0.2 mcg/mL considered the serological correlate of protection. The per protocol (PP) analysis data set included all randomized and vaccinated subjects who fulfilled all inclusion and exclusion criteria, had no major protocol deviation, and had data available for the respective analysis.	
End point type	Primary
End point timeframe:	
1 month after 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received booster vaccination with PCV7.

End point values	MenC-TT + PCV7	PCV7		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	77		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 14	100 (97.5 to 100)	100 (95.2 to 100)		
Serotype 18C	100 (97.6 to 100)	100 (95.2 to 100)		
Serotype 19F	100 (97.5 to 100)	98.7 (93 to 99.8)		
Serotype 23F	100 (97.5 to 100)	100 (95.2 to 100)		
Serotype 4	100 (97.6 to 100)	100 (95.2 to 100)		
Serotype 6B	100 (97.5 to 100)	98.7 (93 to 99.8)		

Serotype 9V	100 (97.6 to 100)	100 (95.2 to 100)		
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Statistical analyses

Statistical analysis title	Statistical Analysis of PVC7 \geq 0.2 mcg/mL: 14
Statistical analysis description:	
Non inferiority criteria margin is -10 percent (%). 95% Confidence Interval (CI) for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.	
Comparison groups	MenC-TT + PCV7 v PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.5

Statistical analysis title	Statistical Analysis of PVC7 \geq 0.2 mcg/mL: 18C
Statistical analysis description:	
Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.	
Comparison groups	PCV7 v MenC-TT + PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.4

Statistical analysis title	Statistical Analysis of PVC7 \geq 0.2 mcg/mL: 19F
Statistical analysis description:	
Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.	
Comparison groups	MenC-TT + PCV7 v PCV7

Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	1.4

Statistical analysis title	Statistical Analysis of PVC7 \geq 0.2 mcg/mL: 23F
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Statistical analysis description:

Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.

Comparison groups	MenC-TT + PCV7 v PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.5

Statistical analysis title	Statistical analysis PCV7 \geq 0.2 mcg/mL: 4
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Statistical analysis description:

Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.

Comparison groups	PCV7 v MenC-TT + PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.4

Statistical analysis title	Statistical analysis PCV7 \geq 0.2 mcg/mL: 6B
Statistical analysis description:	
Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.	
Comparison groups	MenC-TT + PCV7 v PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	1.4

Statistical analysis title	Statistical analysis PCV7 \geq 0.2 mcg/mL: 9V
Statistical analysis description:	
Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with PVC7-Specific Antibody Concentration of \geq 0.2 mcg/mL was calculated between MenC-TT + PCV7 vs PCV7.	
Comparison groups	MenC-TT + PCV7 v PCV7
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.4

Primary: Percentage of Subjects With Seroprotective Meningococcal Serogroup C (MenC)-Specific Serum Bactericidal Activity (SBA) Titers \geq 1:8

End point title	Percentage of Subjects With Seroprotective Meningococcal Serogroup C (MenC)-Specific Serum Bactericidal Activity (SBA) Titers \geq 1:8 ^[2]
End point description:	
Number of subjects achieving seroprotective MenC-specific SBA titers 1 month after administration of MenC-TT vaccine were reported. Protection against serogroup C meningococcal disease correlated with the presence of anticapsular antibodies with SBA. A SBA titer of \geq 1:8 was considered the serological correlate of protection for MenC vaccines. PP analysis data set contained all randomized and vaccinated subjects who fulfilled all inclusion and exclusion criteria, had no major protocol deviation, and had data available for the respective analysis.	
End point type	Primary
End point timeframe:	
1 month after vaccination	

Notes:

[2] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received vaccination with MenC-TT.

End point values	MenC-TT + PCV7	MenC-TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	80		
Units: Percentage of subjects				
number (confidence interval 95%)	100 (97.6 to 100)	100 (95.4 to 100)		

Statistical analyses

Statistical analysis title	Statistical analysis MenC-specific SBA titers $\geq 1:8$
Statistical analysis description:	
Non inferiority criteria margin is -10%. 95% CI for the difference on the proportion of subjects with MenC-specific SBA titers $\geq 1:8$ was calculated between MenC-TT + PCV7 vs MenC-TT.	
Comparison groups	MenC-TT + PCV7 v MenC-TT
Number of subjects included in analysis	239
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	2.4

Secondary: Number of Subjects With PCV7-Specific Antibody Concentrations ≥ 0.35 mcg/mL

End point title	Number of Subjects With PCV7-Specific Antibody Concentrations ≥ 0.35 mcg/mL ^[3]
End point description:	
Number of subjects achieving PCV7-specific antibody concentrations for each of the 7 vaccine serotypes (14, 18C, 19F, 23F, 4, 6B, 9V) 1 month after the PCV booster vaccination was determined by ELISA. The intent to treat (ITT) data set contained all randomized and vaccinated subjects with available data for the respective analysis.	
End point type	Secondary
End point timeframe:	
1 month after 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received booster vaccination with PVC7.

End point values	MenC-TT + PCV7	PCV7		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	80		
Units: Subjects				
number (not applicable)				
Serotype 14	156	80		
Serotype 18C	158	80		
Serotype 19F	155	79		
Serotype 23F	154	80		
Serotype 4	158	80		
Serotype 6B	155	79		
Serotype 9V	158	80		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With PCV7-Specific Antibody Concentrations ≥ 1 mcg/mL

End point title	Number of Subjects With PCV7-Specific Antibody Concentrations ≥ 1 mcg/mL ^[4]
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End point description:

Number of subjects achieving PCV7-specific antibody concentrations for each of the 7 vaccine serotypes (14, 18C, 19F, 23F, 4, 6B, 9V) 1 month after the PCV booster vaccination was determined by ELISA. ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
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End point timeframe:

1 month after vaccination

Notes:

[4] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received booster vaccination with PVC7.

End point values	MenC-TT + PCV7	PCV7		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	80		
Units: Subjects				
number (not applicable)				
Serotype 14	156	80		
Serotype 18C	145	73		
Serotype 19F	153	76		
Serotype 23F	150	77		
Serotype 4	153	80		
Serotype 6B	151	79		
Serotype 9V	152	80		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration (GMC) for PCV7-Specific Antibody 1 Month After Booster Vaccination With PVC7

End point title	Geometric Mean Concentration (GMC) for PCV7-Specific Antibody 1 Month After Booster Vaccination With PVC7 ^[5]
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End point description:

PCV7-specific antibody GMC's 1 month after the PCV7 booster were assumed to be log-normally distributed. Concentration values were log-transformed, and their means and 95% Confidence Intervals (CIs) were calculated based on the t-distribution. ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
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End point timeframe:

1 month after vaccination

Notes:

[5] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received booster vaccination with PVC7.

End point values	MenC-TT + PCV7	PCV7		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	80		
Units: microgram per millilitre				
geometric mean (confidence interval 95%)				
Serotype 14	10.94 (9.5 to 12.6)	11.47 (9.41 to 13.99)		
Serotype 18C	3.82 (3.3 to 4.41)	3.6 (2.91 to 4.45)		
Serotype 19F	7.14 (6.15 to 8.29)	5.98 (4.65 to 7.69)		
Serotype 23F	6.1 (5.15 to 7.23)	6.14 (4.89 to 7.7)		
Serotype 4	5.34 (4.56 to 6.24)	5.97 (4.85 to 7.36)		
Serotype 6B	11.05 (9.35 to 13.06)	11.69 (9.05 to 15.09)		
Serotype 9V	3.78 (3.34 to 4.28)	4.25 (3.6 to 5.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer (GMT) for MenC-Specific SBA 1 Month After Primary Vaccination with MenC-TT

End point title	Geometric Mean Titer (GMT) for MenC-Specific SBA 1 Month After Primary Vaccination with MenC-TT ^[6]
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End point description:

MenC-specific SBA GMTs 1 month after vaccination with MenC-TT were assumed to be log-normally distributed. The ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
End point timeframe:	
1 month after vaccination	
Notes:	
[6] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received vaccination with MenC-TT.	

End point values	MenC-TT + PCV7	MenC-TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	81		
Units: Titer				
geometric mean (confidence interval 95%)	1114.32 (946.63 to 1311.72)	1429.68 (1162.12 to 1758.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Seroconversion 1 Month After Vaccination With MenC-TT

End point title	Number of Subjects With Seroconversion 1 Month After Vaccination With MenC-TT ^[7]
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End point description:

Seroconversion is a 4-fold increase in MenC-specific SBA titers, one month after vaccination. ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
End point timeframe:	
1 month after vaccination	

Notes:

[7] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received vaccination with MenC-TT.

End point values	MenC-TT + PCV7	MenC-TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	81		
Units: Subjects				
number (not applicable)	164	81		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Increase in PCV7-Specific Antibody Concentrations From Before PCV7 Booster Vaccination to 1 Month After the PCV7 Booster

Vaccination

End point title	Geometric Mean Fold Increase in PCV7-Specific Antibody Concentrations From Before PCV7 Booster Vaccination to 1 Month After the PCV7 Booster Vaccination ^[8]
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End point description:

PCV7-specific antibody concentrations one month after booster vaccination with PCV7 were assumed to be log-normally distributed. Concentration values were log-transformed, and changes from baseline were calculated for each subject. Mean changes (95% CIs) from baseline were calculated based on the t-distribution. ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
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End point timeframe:

Before PCV7 vaccination, 1 month after PCV7 vaccination

Notes:

[8] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received booster vaccination with PVC7.

End point values	MenC-TT + PCV7	PCV7		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	80		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 14	4.62 (3.95 to 5.42)	4.69 (3.78 to 5.83)		
Serotype 18C	9.56 (8.36 to 10.93)	8.51 (7.12 to 10.17)		
Serotype 19F	10.08 (8.42 to 12.07)	9.02 (7.03 to 11.58)		
Serotype 23F	10.26 (8.81 to 11.96)	9.41 (7.63 to 11.61)		
Serotype 4	9.77 (8.36 to 11.41)	9.88 (7.88 to 12.39)		
Serotype 6B	9.16 (7.87 to 10.67)	8.4 (6.53 to 10.8)		
Serotype 9V	5.86 (5.21 to 6.6)	5.82 (4.89 to 6.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Increase in MenC-specific SBA Titers From Before MenC-TT Primary Immunization Vaccination to 1 Month After Primary Immunization With MenC-TT

End point title	Geometric Mean Fold Increase in MenC-specific SBA Titers From Before MenC-TT Primary Immunization Vaccination to 1 Month After Primary Immunization With MenC-TT ^[9]
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End point description:

MenC-specific SBA titers one month after vaccination with MenC-TT were assumed to be log-normally distributed. Titer values were log-transformed, and changes from baseline were calculated for each subject. Mean changes (95% CIs) from baseline were calculated based on the t-distribution. ITT data set contains all randomized and vaccinated subjects with available data for the respective analysis.

End point type	Secondary
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End point timeframe:

Before MenC-TT vaccination, 1 month after MenC-TT vaccination

Notes:

[9] - 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: The endpoint was planned to be assessed for only those reporting arms in which subjects received vaccination with MenC-TT.

End point values	MenC-TT + PCV7	MenC-TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	81		
Units: Titer				
geometric mean (confidence interval 95%)	547.82 (464.7 to 645.81)	690.79 (557.74 to 855.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Pre-Specified Injection Site Reactions

End point title	Number of Subjects Reporting Pre-Specified Injection Site Reactions
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End point description:

The severity of injection site reactions was rated for Redness, induration, or swelling (diameter) as Mild (1.0–2.5 cm), Moderate (2.5–5.0 cm) Severe (> 5.0 cm) and for Injection site pain or tenderness as Mild (No impairment of arm movement), Moderate (Impairment of arm movement) and Severe (Severe impairment, arm not moving). The safety analysis data set contains all vaccinated subjects. Unknown refers to injection site reactions whose severity score was missing because of a lesion size of less than 1 cm, i.e., less than mild.

End point type	Secondary
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End point timeframe:

Within 1 month after vaccination

End point values	MenC-TT + PCV7	PCV7	MenC-TT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	81	82	
Units: Subjects				
number (not applicable)				
Mild	30	12	10	
Moderate	18	12	3	
Severe	2	5	1	
Unknown	32	8	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Pre-Specified Systemic Reactions

End point title	Number of Subjects Reporting Pre-Specified Systemic Reactions
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End point description:

Systemic reactions are treatment-related systemic adverse events. Systemic reactions were reported in subject diary and includes vomiting, sweating, inconsolable or persisting crying, irritability, sleepiness, and food rejection. Unknown refers to injection site reactions whose severity score was missing because of a lesion size of less than 1 cm, i.e., less than mild. The safety analysis set contained all subjects vaccinated at least once with NeisVac-C.

End point type	Secondary
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End point timeframe:

Within 1 month after vaccination

End point values	MenC-TT + PCV7	PCV7	MenC-TT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	81	82	
Units: Subjects				
number (not applicable)				
Mild	51	28	17	
Moderate	14	8	8	
Severe	1	0	0	
Unknown	0	0	0	
Total with Reaction	66	36	25	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Local and Systemic Non-Serious Reactions Related to the Vaccination

End point title	Number of Subjects With Local and Systemic Non-Serious Reactions Related to the Vaccination
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End point description:

Local reactions include induration, injection site pain, swelling, redness, and tenderness. Systemic reactions includes vomiting, sweating, inconsolable and persisting crying, irritability, sleepiness, and food rejection. The safety analysis data set contains all vaccinated subjects.

End point type	Secondary
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End point timeframe:

Within 1 month after vaccination

End point values	MenC-TT + PCV7	PCV7	MenC-TT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	81	82	
Units: Subjects				
number (not applicable)				
Food rejection	4	2	5	
Inconsolable/persisting crying	1	7	11	
Induration	14	22	50	
Injection site pain	2	9	19	
Irritability	2	13	14	
Redness	11	27	67	
Sleepiness	7	13	16	
Sweating	1	2	4	
Swelling	3	16	27	
Tenderness	12	18	40	
Vomiting	1	1	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within 1 month after vaccination

Adverse event reporting additional description:

SAEs and AEs were grouped by system organ class and summarized. AEs included AEs collected in subject diary (local and pre specified systemic reactions) and AEs collected on case report form at each visit. MedDRA dictionary version was not captured, here 0.0 is included for the MedDRA version.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	0.0
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Reporting groups

Reporting group title	MenC-TT and PCV7
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Reporting group description:

Subjects recieved MenC-TT as primary immunization dose in combination with PCV7 as booster dose on Day 0 (vaccination visit).

Reporting group title	PCV7
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Reporting group description:

Subjects recieved intramuscularly 0.5 mL dose of Prevenar as a booster dose.

Reporting group title	MenC-TT
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Reporting group description:

Subjects recieved intramuscularly 0.5mL of MenC-TT dose for primary immunization.

Serious adverse events	MenC-TT and PCV7	PCV7	MenC-TT
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	1 / 82 (1.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 166 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple	Additional description: "Multiple" includes subjects with more than one event reported under a single Reported Term.		
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MenC-TT and PCV7	PCV7	MenC-TT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	105 / 166 (63.25%)	56 / 81 (69.14%)	34 / 82 (41.46%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Joint injury			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Mouth injury			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Poisoning			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Peripheral coldness			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Crying			
subjects affected / exposed	15 / 166 (9.04%)	8 / 81 (9.88%)	2 / 82 (2.44%)
occurrences (all)	15	8	2
Poor quality sleep			
subjects affected / exposed	5 / 166 (3.01%)	2 / 81 (2.47%)	1 / 82 (1.22%)
occurrences (all)	6	2	1
Somnolence			
subjects affected / exposed	19 / 166 (11.45%)	15 / 81 (18.52%)	7 / 82 (8.54%)
occurrences (all)	19	15	7
General disorders and administration site conditions			

Injection site pain			
subjects affected / exposed	0 / 166 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	18 / 166 (10.84%)	14 / 81 (17.28%)	2 / 82 (2.44%)
occurrences (all)	18	14	2
Pyrexia			
subjects affected / exposed	50 / 166 (30.12%)	32 / 81 (39.51%)	15 / 82 (18.29%)
occurrences (all)	56	37	19
Injection site erythema			
subjects affected / exposed	67 / 166 (40.36%)	27 / 81 (33.33%)	11 / 82 (13.41%)
occurrences (all)	86	27	11
Injection site haematoma			
subjects affected / exposed	3 / 166 (1.81%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	3	0	1
Injection site haemorrhage			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Injection site induration			
subjects affected / exposed	50 / 166 (30.12%)	22 / 81 (27.16%)	14 / 82 (17.07%)
occurrences (all)	69	22	14
Injection site pain (Local reaction)			
subjects affected / exposed	46 / 166 (27.71%)	19 / 81 (23.46%)	12 / 82 (14.63%)
occurrences (all)	86	27	14
Injection site swelling			
subjects affected / exposed	27 / 166 (16.27%)	16 / 81 (19.75%)	3 / 82 (3.66%)
occurrences (all)	32	16	3
Multiple	Additional description: "Multiple" includes subjects with more than one event reported under a single Reported Term".		
subjects affected / exposed	6 / 166 (3.61%)	6 / 81 (7.41%)	2 / 82 (2.44%)
occurrences (all)	8	7	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 166 (0.60%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	1	1	0
Eye disorders			

Conjunctivitis subjects affected / exposed occurrences (all)	5 / 166 (3.01%) 5	2 / 81 (2.47%) 2	1 / 82 (1.22%) 1
Gastrointestinal disorders			
Aphthous stomatitis subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	1 / 82 (1.22%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 166 (0.00%) 0	0 / 81 (0.00%) 0	1 / 82 (1.22%) 1
Diarrhoea subjects affected / exposed occurrences (all)	8 / 166 (4.82%) 8	6 / 81 (7.41%) 6	2 / 82 (2.44%) 2
Enteritis subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	0 / 82 (0.00%) 0
Faecal incontinence subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	1 / 81 (1.23%) 1	0 / 82 (0.00%) 0
Faeces hard subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	0 / 82 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	1 / 81 (1.23%) 2	0 / 82 (0.00%) 0
Teething subjects affected / exposed occurrences (all)	6 / 166 (3.61%) 9	1 / 81 (1.23%) 1	3 / 82 (3.66%) 3
Vomiting subjects affected / exposed occurrences (all)	5 / 166 (3.01%) 5	4 / 81 (4.94%) 5	4 / 82 (4.88%) 4
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	6 / 166 (3.61%) 6	2 / 81 (2.47%) 2	2 / 82 (2.44%) 2
Skin and subcutaneous tissue disorders			

Dermatitis			
subjects affected / exposed	0 / 166 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Dermatitis diaper			
subjects affected / exposed	5 / 166 (3.01%)	2 / 81 (2.47%)	1 / 82 (1.22%)
occurrences (all)	6	2	1
Eczema			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	1 / 82 (1.22%)
occurrences (all)	0	1	1
Hyperhidrosis			
subjects affected / exposed	4 / 166 (2.41%)	3 / 81 (3.70%)	1 / 82 (1.22%)
occurrences (all)	4	3	1
Neurodermatitis			
subjects affected / exposed	2 / 166 (1.20%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	2	0	0
Petechiae			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	3 / 166 (1.81%)	1 / 81 (1.23%)	2 / 82 (2.44%)
occurrences (all)	3	1	3
Rash maculo-papular			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 166 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Depressed mood			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	2	0
Food aversion			

subjects affected / exposed	10 / 166 (6.02%)	2 / 81 (2.47%)	4 / 82 (4.88%)
occurrences (all)	10	2	4
Insomnia			
subjects affected / exposed	2 / 166 (1.20%)	2 / 81 (2.47%)	2 / 82 (2.44%)
occurrences (all)	2	2	2
Nervousness			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	4 / 166 (2.41%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	4	1	0
Sleep disorder			
subjects affected / exposed	2 / 166 (1.20%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	2	0	1
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Acute tonsillitis			
subjects affected / exposed	1 / 166 (0.60%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	1	1	0
Bacterial infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 166 (0.60%)	2 / 81 (2.47%)	1 / 82 (1.22%)
occurrences (all)	1	2	1
Bronchopneumonia			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Candida nappy rash			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Eczema infected			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0

Erythema infectiosum			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Exanthema subitum			
subjects affected / exposed	1 / 166 (0.60%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	1	1	0
Febrile infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Fungal skin infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	4 / 166 (2.41%)	1 / 81 (1.23%)	3 / 82 (3.66%)
occurrences (all)	4	1	3
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Genital candidiasis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 166 (0.60%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	1	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 166 (4.22%)	3 / 81 (3.70%)	3 / 82 (3.66%)
occurrences (all)	7	3	3
Otitis media			
subjects affected / exposed	5 / 166 (3.01%)	2 / 81 (2.47%)	3 / 82 (3.66%)
occurrences (all)	5	2	3

Pharyngitis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	11 / 166 (6.63%)	5 / 81 (6.17%)	1 / 82 (1.22%)
occurrences (all)	11	5	1
Sinobronchitis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 166 (2.41%)	5 / 81 (6.17%)	2 / 82 (2.44%)
occurrences (all)	4	5	2
Urinary tract infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Varicella			
subjects affected / exposed	0 / 166 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	4 / 166 (2.41%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences (all)	4	1	0
Viral rash			
subjects affected / exposed	1 / 166 (0.60%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	0 / 82 (0.00%) 0
Metabolism and nutrition disorders			
Appetite disorder subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	0 / 82 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	0 / 166 (0.00%) 0	1 / 81 (1.23%) 1	0 / 82 (0.00%) 0
Fluid imbalance subjects affected / exposed occurrences (all)	1 / 166 (0.60%) 1	0 / 81 (0.00%) 0	0 / 82 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2008	The protocol was amended to restrict the withdrawal of blood following 3 unsuccessful attempts in order to limit the stress caused on the subject.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported