Clinical trial results:
A Phase 4, Open-label Trial to Assess the Safety, Tolerability, and Immunogenicity of Prevenar in Older Infants and Young Children in China Who Are Naive to Previous Pneumococcal Vaccination

Summary

EudraCT number	2014-004178-40
Trial protocol	Outside EU/EEA
Global end of trial date	25 September 2012

Results information

Result version number	v1 (current)
This version publication date	29 June 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	B1841008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01193582
WHO universal trial number (UTN)	-
Other trial identifiers	Protocol: 6114A1-4000

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Clinical Trials.gov Call Center, Pfizer Inc., 001 8007181021, linicalTrials.govInquiries@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc., 001 8007181021, linicalTrials.govInquiries@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	11 June 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the serotype-specific pneumococcal immune responses induced by Prevenar when measured 1 month after the last dose of Prevenar in each age group.
To assess the pre-vaccination antibody levels to the 7 pneumococcal serotypes in Prevenar in each age group.

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 505
Worldwide total number of subjects	505
EEA total number of subjects	0

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)	325
Children (2-11 years)	180
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:

This report presents results following completion of all vaccinations, including data from the 12-month follow-up. This study was conducted at one site in China.

Pre-assignment

Screening details:

Subjects were enrolled into 1 of 4 groups based on inclusion/exclusion criteria without a screening period. A total of 506 subjects were enrolled in this study, 505 received at least 1 dose of vaccine Subject disposition and baseline characteristics are represented for the treated subjects.

Period 1

Period 1 title	Vaccination Series
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Subjects 121 to less than (<) 212 days of age and received 4 doses of Prevenar.

Arm type	Experimental
Investigational medicinal product name	7-valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 4 doses of Prevenar administered as a single 0.5 milliliter (mL) dose intramuscularly.

Arm title	Group 2

Arm description:

Subjects 212 days to <12 months of age (before the first birthday) and received 3 doses of Prevenar.

Arm type	Experimental
Investigational medicinal product name	7-valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Prevenar administered as a single 0.5 mL dose intramuscularly.

Arm title	Group 3

Arm description:

Subjects 12 to <24 months of age (before the second birthday) and received 2 doses of Prevenar.

Arm type	Experimental

Investigational medicinal product name	7-valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of Prevenar administered as a single 0.5 mL dose intramuscularly.

Arm title	Group 4

Arm description:

Subjects 24 to <72 months of age (before the sixth birthday) and received 1 dose of Prevenar.

Arm type	Experimental
Investigational medicinal product name	7-valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received single 0.5 mL intramuscular doses of Prevenar.

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	100	100	125
Vaccinated Dose 1	100	100	125
Vaccinated Dose 2	92	91	118
Vaccinated Dose 3	90	89	0 [1]
Vaccinated Dose 4	90	0 [2]	0 [3]
Completed	89	88	117
Not completed	11	12	8
Consent withdrawn by subject	11	12	8

Number of subjects in period 1	Group 4
Started	180
Vaccinated Dose 1	180
Vaccinated Dose 2	0 [4]
Vaccinated Dose 3	0 [5]
Vaccinated Dose 4	0 [6]
Completed	177
Not completed	3
Consent withdrawn by subject	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 2 doses of vaccination (Dose1 and Dose 2).

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 3 doses of vaccination (Dose1, Dose 2 and Dose 3).

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 2 doses of vaccination (Dose1 and Dose 2).

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 1 dose of vaccination (Dose1).

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 1 dose of vaccination (Dose1).

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Subjects were planned to recieve only 1 dose of vaccination (Dose1).

Period 2

Period 2 title	12 Month Follow-up
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 Follow up period

Arm description:

Included subjects 121 to less than (<) 212 days of age who received 4 doses of Prevenar during vaccination series (period 1).

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 2 Follow up period

Arm description:

Included subjects 212 days to <12 months of age (before the first birthday) who received 3 doses of Prevenar during vaccination series (period 1).

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 3 Follow up period

Arm description:

Included subjects 12 to <24 months of age (before the second birthday) who received 2 doses of Prevenar during vaccination series (period 1).

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 4 Follow up period

Arm description:

Included subjects 24 to <72 months of age (before the sixth birthday) who received 1 dose of Prevenar during vaccination series (period 1).

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Group 1 Follow up period	Group 2 Follow up period	Group 3 Follow up period
Started	89	88	117
Completed	83	88	113
Not completed	6	0	4
Consent withdrawn by subject	6	-	3
Death	-	-	1

Number of subjects in period 2	Group 4 Follow up period
Started	177
Completed	166
Not completed	11
Consent withdrawn by subject	11
Death	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects 121 to less than (<) 212 days of age and received 4 doses of Prevenar.	
Reporting group title	Group 2
Reporting group description:	
Subjects 212 days to <12 months of age (before the first birthday) and received 3 doses of Prevenar.	
Reporting group title	Group 3
Reporting group description:	
Subjects 12 to <24 months of age (before the second birthday) and received 2 doses of Prevenar.	
Reporting group title	Group 4
Reporting group description:	
Subjects 24 to <72 months of age (before the sixth birthday) and received 1 dose of Prevenar.	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	100	100	125
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	5.3	9.7	17.5
standard deviation	± 0.88	± 1.45	± 4.15
Gender categorical Units: Subjects			
Female	55	53	62
Male	45	47	63
Unknown	0	0	0

Reporting group values	Group 4	Total	
Number of subjects	180	505	
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	44.42		
standard deviation	± 12.9	-	
Gender categorical Units: Subjects			
Female	95	265	
Male	85	240	
Unknown	0	0	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
Subjects 121 to less than (<) 212 days of age and received 4 doses of Prevenar.	
Reporting group title	Group 2
Reporting group description:	
Subjects 212 days to <12 months of age (before the first birthday) and received 3 doses of Prevenar.	
Reporting group title	Group 3
Reporting group description:	
Subjects 12 to <24 months of age (before the second birthday) and received 2 doses of Prevenar.	
Reporting group title	Group 4
Reporting group description:	
Subjects 24 to <72 months of age (before the sixth birthday) and received 1 dose of Prevenar.	
Reporting group title	Group 1 Follow up period
Reporting group description:	
Included subjects 121 to less than (<) 212 days of age who received 4 doses of Prevenar during vaccination series (period 1).	

Reporting group title	Group 2 Follow up period
Reporting group description:	
Included subjects 212 days to <12 months of age (before the first birthday) who received 3 doses of Prevenar during vaccination series (period 1).	

Reporting group title	Group 3 Follow up period
Reporting group description:	
Included subjects 12 to <24 months of age (before the second birthday) who received 2 doses of Prevenar during vaccination series (period 1).	
Reporting group title	Group 4 Follow up period
Reporting group description:	
Included subjects 24 to <72 months of age (before the sixth birthday) who received 1 dose of Prevenar during vaccination series (period 1).	

Primary: Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prenevar

End point title	Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prenevar[1]
End point description:	
Serotype-specific Pneumococcal Immunoglobulin G (IgG) antibody geometric mean concentration (GMC) after 1 month of last dose for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95 percent (%) confidence intervals (CI) were evaluated. Geometric means (GMs) were calculated using all subjects with available data for the specified blood draw. Evaluable immunogenicity population consisted of eligible participants in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.	
End point type	Primary
End point timeframe:	
1 month after last dose in each group	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	87	115	177
Units: microgram per millilitre (mcg/mL)				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 88, 87, 115, 177)	6.9 (5.61 to 8.48)	7.16 (6.09 to 8.42)	7.53 (6.7 to 8.46)	9.45 (8.38 to 10.65)
Serotype 6B (n= 88, 87, 114, 177)	8.01 (6.24 to 10.3)	5.79 (4.64 to 7.23)	4.81 (3.89 to 5.96)	6.36 (5.32 to 7.59)
Serotype 9V (n= 88, 87, 115, 177)	4.11 (3.4 to 4.96)	4.64 (3.93 to 5.47)	4.67 (4.18 to 5.21)	6.14 (5.42 to 6.95)
Serotype 14 (n= 88, 87, 115, 177)	12.75 (10.32 to 15.76)	13.02 (10.89 to 15.57)	11.98 (10.51 to 13.65)	9.86 (8.03 to 12.1)
Serotype 18C (n= 88, 87, 115, 177)	4.65 (3.81 to 5.69)	4.65 (3.86 to 5.61)	5.4 (4.78 to 6.1)	7.39 (6.41 to 8.51)
Serotype 19F (n= 87, 87, 115, 177)	4.05 (3.07 to 5.36)	4.02 (3.05 to 5.31)	4.03 (3.26 to 4.98)	4.53 (3.73 to 5.49)
Serotype 23F (n= 88, 87, 115, 177)	4.75 (3.77 to 5.99)	3.95 (3.19 to 4.89)	4.18 (3.51 to 4.96)	5.64 (4.84 to 6.57)

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at Baseline in Each Group

End point title	Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at Baseline in Each Group[2]

End point description:

End point description: Serotype-specific Pneumococcal IgG antibody GMC at baseline for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. Evaluable immunogenicity population consisted of eligible participants in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Primary

End point timeframe:

Baseline

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	87	115	177
Units: mcg/ml				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 88, 87, 115, 172)	0.01 (0.01 to 0.02)	0.01 (0.01 to 0.02)	0.02 (0.01 to 0.02)	0.06 (0.05 to 0.08)
Serotype 6B (n= 86, 64, 100, 177)	0.12 (0.1 to 0.15)	0.16 (0.12 to 0.22)	0.27 (0.21 to 0.35)	1.3 (1.08 to 1.55)
Serotype 9V (n= 88, 84, 113, 177)	0.1 (0.08 to 0.12)	0.1 (0.08 to 0.13)	0.17 (0.13 to 0.21)	0.66 (0.56 to 0.77)
Serotype 14 (n= 88, 87, 115, 177)	0.16 (0.12 to 0.22)	0.04 (0.03 to 0.05)	0.03 (0.02 to 0.04)	0.36 (0.26 to 0.5)
Serotype 18C (n= 88, 87, 114, 172)	0.04 (0.03 to 0.06)	0.02 (0.01 to 0.02)	0.02 (0.02 to 0.03)	0.12 (0.1 to 0.16)
Serotype 19F (n= 88, 85, 115, 169)	0.11 (0.09 to 0.14)	0.09 (0.07 to 0.12)	0.13 (0.1 to 0.17)	0.71 (0.57 to 0.89)
Serotype 23F (n= 85, 75, 102, 174)	0.07 (0.06 to 0.09)	0.08 (0.06 to 0.11)	0.17 (0.12 to 0.23)	0.88 (0.74 to 1.04)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the Third Dose in Group 1

End point title	Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the Third Dose in Group 1[3]

End point description:

Serotype-specific Pneumococcal IgG antibody GMC one month after the third dose in Group 1 for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all with subjects available data for the specified blood draw. Evaluable immunogenicity population consisted of eligible participants in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

1 month after third dose of Prevenar in Group 1

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 analysed to report data for Group 1 only.

End point values	Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 88)	6.38 (5.56 to 7.33)			

Serotype 6B (n= 87)	2.88 (2.33 to 3.56)			
Serotype 9V (n= 88)	4.18 (3.51 to 4.98)			
Serotype 14 (n= 88)	11.16 (9.12 to 13.66)			
Serotype 18C (n= 88)	4.6 (3.8 to 5.57)			
Serotype 19F (n= 88)	3.6 (2.75 to 4.72)			
Serotype 23F (n= 88)	2.45 (1.97 to 3.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise (GMFR) of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 1 .

End point title	Geometric Mean Fold Rise (GMFR) of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 1 .[4]

End point description:

End point description: GMFRs for the 7 pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) from pre-vaccination to post-vaccination were computed using the logarithmically transformed assay results. CIs for GMFR are back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers. Evaluable immunogenicity population consisted of eligible subjects in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

Pre-vaccination to 1 month after third dose of Prevenar in Group 1

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 analysed to report data for Group 1 only.

End point values	Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 88)	453.17 (344.56 to 596.01)			
Serotype 6B (n= 85)	23.1 (18.15 to 29.4)			
Serotype 9V (n= 88)	43.38 (33.42 to 56.32)			
Serotype 14 (n= 88)	69.9 (45.95 to 106.35)			
Serotype 18C (n= 88)	106.74 (76.83 to 148.31)			

Serotype 19F (n= 88)	32.52 (23.39 to 45.21)			
Serotype 23F (n= 85)	34.01 (24.98 to 46.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the Second Dose in Group 2

End point title	Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the Second Dose in Group 2[5]

End point description:

Serotype-specific Pneumococcal IgG antibody GMC 1 month after the second dose in Group 2 for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all participants with available data for the specified blood draw. Evaluable immunogenicity population consisted of eligible subjects in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

1 month after second dose of Prevenar in Group 2

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 analysed to report data for Group 2 only.

End point values	Group 2			
Subject group type	Reporting group			
Number of subjects analysed	87			
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 87)	8.46 (7.36 to 9.72)			
Serotype 6B (n= 85)	2.67 (2.06 to 3.46)			
Serotype 9V (n= 87)	4.71 (3.91 to 5.66)			
Serotype 14 (n= 87)	8.05 (6.71 to 9.68)			
Serotype 18C (n= 87)	4.93 (4 to 6.08)			
Serotype 19F (n= 87)	3.03 (2.27 to 4.04)			
Serotype 23F (n= 87)	2.66 (2.1 to 3.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 2

End point title	GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 2[6]

End point description:

GMFRs for the 7 pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) from pre-vaccination to post-vaccination were computed using the logarithmically transformed assay results. CIs for GMFR are back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers. Evaluable immunogenicity population consisted of eligible subjects in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

Pre vaccination to 1 month after second dose of Prevenar in Group 2

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 analysed to report data for Group 2 only.

End point values	Group 2			
Subject group type	Reporting group			
Number of subjects analysed	87			
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 87)	705.95 (540.5 to 922.05)			
Serotype 6B (n= 63)	16.64 (11.17 to 24.79)			
Serotype 9V (n= 84)	44.72 (34.22 to 58.44)			
Serotype 14 (n= 87)	217.21 (152.52 to 309.33)			
Serotype 18C (n= 87)	317.9 (219.65 to 460.1)			
Serotype 19F (n= 85)	33.66 (24.28 to 46.65)			
Serotype 23F (n= 75)	30.77 (21.3 to 44.45)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the First Dose in Group 3

End point title	Antibody Concentrations to the 7 Pneumococcal Serotypes Contained in Prevenar at 1 Month After the First Dose in Group 3[7]

End point description:

Serotype-specific Pneumococcal IgG antibody GMC one month after the first dose in Group 3 for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all participants with available data for the specified blood draw. Evaluable immunogenicity population consisted of eligible subjects in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

1 month after first dose of Prevenar in Group 3

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 analysed to report data for Group 3 only.

End point values	Group 3			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 115)	8.44 (7.25 to 9.81)			
Serotype 6B (n= 113)	1.92 (1.51 to 2.42)			
Serotype 9V (n= 115)	4.77 (4.09 to 5.56)			
Serotype 14 (n= 115)	3.37 (2.74 to 4.16)			
Serotype 18C (n= 115)	5.72 (4.82 to 6.77)			
Serotype 19F (n= 113)	1.96 (1.55 to 2.49)			
Serotype 23F (n= 115)	2.83 (2.26 to 3.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 3

End point title	GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values in Group 3[8]

End point description:

GMFRs for the 7 pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) from pre-vaccination to post-vaccination were computed using the logarithmically transformed assay results. CIs for GMFR are back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers. Evaluable immunogenicity population consisted of eligible subjects in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

Pre-vaccination to 1 month after first dose of Prevenar in Group 3

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 analysed to report data for Group 3 only.

End point values	Group 3			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 115)	476.49 (363.31 to 624.93)			
Serotype 6B (n= 99)	7.06 (5.5 to 9.05)			
Serotype 9V (n= 113)	28.11 (22.18 to 35.63)			
Serotype 14 (n= 115)	108.18 (78.76 to 148.6)			
Serotype 18C (n= 114)	236.39 (182.65 to 305.93)			
Serotype 19F (n= 113)	15.13 (11.02 to 20.77)			
Serotype 23F (n= 102)	17.64 (13.43 to 23.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Concentrations Against the 7 Pneumococcal Serotypes Contained in Prevenar at 12 Months After the Last Dose

End point title	Antibody Concentrations Against the 7 Pneumococcal Serotypes Contained in Prevenar at 12 Months After the Last Dose

End point description:

Serotype-specific Pneumococcal IgG antibody GMC 12 months after the last dose for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. Evaluable immunogenicity population consisted subjects who had received all, assigned vaccination(s), had blood drawn within required time frame for 12 month follow-up blood draw visit, had at least 1 valid and determinate assay result, had received no prohibited vaccines, and had no major protocol violations.

End point type	Secondary

End point timeframe:

12 months after the last dose

End point values	Group 1 Follow up period	Group 2 Follow up period	Group 3 Follow up period	Group 4 Follow up period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	79	111	162
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 4 (n=81, 79, 111, 162)	0.78 (0.62 to 0.98)	0.65 (0.52 to 0.82)	0.96 (0.8 to 1.14)	1.27 (1.11 to 1.45)
Serotype 6B (n=81, 78, 109, 161)	3.22 (2.41 to 4.29)	2.31 (1.77 to 3.03)	2.38 (1.89 to 3)	4.2 (3.49 to 5.04)
Serotype 9V (n=81, 79, 111, 162)	1.26 (1 to 1.59)	0.98 (0.79 to 1.21)	1.44 (1.2 to 1.71)	2.23 (1.94 to 2.56)
Serotype 14 (n=81, 79, 111, 162)	1.84 (1.4 to 2.41)	2.18 (1.62 to 2.94)	2.61 (2.09 to 3.27)	5.19 (4.25 to 6.33)
Serotype 18C (n=81, 79, 111, 162)	0.87 (0.69 to 1.1)	0.71 (0.59 to 0.85)	0.98 (0.84 to 1.15)	1.46 (1.24 to 1.72)
Serotype 19F (n=80, 76, 109, 156)	1.25 (0.95 to 1.64)	1.29 (0.85 to 1.95)	1.39 (1.03 to 1.88)	2.85 (2.28 to 3.56)
Serotype 23F (n=81, 78, 110, 162)	1.38 (1.07 to 1.77)	1.2 (0.91 to 1.59)	1.79 (1.45 to 2.21)	2.49 (2.13 to 2.92)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values at 12 Months After the Last Dose

End point title	GMFR of Anti-Pneumococcal Antibody Levels to the 7 Pneumococcal Serotypes Contained in Prevenar Above Vaccination Baseline Values at 12 Months After the Last Dose

End point description:

GMFRs for the 7 pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) from pre-vaccination to 12- month follow-up were computed using the logarithmically transformed assay results. CIs for GMFR are back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers.Evaluable immunogenicity population consisted of eligible participants in the age range who had received all the assigned vaccination(s), had blood drawn within required time frames, had at least 1 valid and determinate assay result for the proposed analysis, had received no prohibited vaccines, and had no other major protocol violations.

End point type	Secondary

End point timeframe:

Pre-vaccination to 12 months after the last dose

End point values	Group 1 Follow up period	Group 2 Follow up period	Group 3 Follow up period	Group 4 Follow up period
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	79	111	162
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 4 (n= 81, 79, 111, 157)	52.86 (37.61 to 74.31)	50.54 (37.47 to 68.18)	52.19 (39.75 to 68.53)	21.01 (17.04 to 25.91)

Serotype 6B (n= 79, 58, 95, 161)	25.52 (18.57 to 35.07)	15.58 (10.18 to 23.83)	7.99 (5.98 to 10.67)	3.16 (2.7 to 3.7)
Serotype 9V (n= 81, 76, 109, 162)	12.73 (9.41 to 17.24)	8.97 (6.84 to 11.77)	8.4 (6.55 to 10.77)	3.35 (2.93 to 3.83)
Serotype 14 (n= 81, 79, 111, 162)	10.19 (6.84 to 15.19)	55.55 (37.23 to 82.87)	88.27 (63.53 to 122.63)	15.67 (11.43 to 21.47)
Serotype 18C (n= 81, 79, 110, 158)	19.75 (14 to 27.87)	45.07 (33.12 to 61.33)	41.14 (32.18 to 52.59)	11.43 (9.38 to 13.92)
Serotype 19F (n= 80, 74, 109, 150)	10.06 (6.85 to 14.77)	12.62 (8.67 to 18.39)	11.15 (7.87 to 15.8)	4.19 (3.19 to 5.51)
Serotype 23F (n= 79, 67, 97, 159)	18.8 (13.26 to 26.66)	13.5 (9.56 to 19.04)	11.39 (8.31 to 15.61)	2.86 (2.39 to 3.42)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through 12 months following last dose of Prevenar

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study. EU BR specific AE tables were generated using latest coding.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Group 1

Reporting group description:

Subjects 121 to <212 days of age and received 4 doses of Prevenar.

Reporting group title	Group 2

Reporting group description:

Subjects 212 days to <12 months of age (before the first birthday) and received 3 doses of Prevenar.

Reporting group title	Group 3

Reporting group description:

Subjects 12 to <24 months of age (before the second birthday) and received 2 doses of Prevenar.

Reporting group title	Group 4

Reporting group description:

Subjects 24 to <72 months of age (before the sixth birthday) and received 1 dose of Prevenar.

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	1 / 125 (0.80%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	0 / 125 (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

Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis shigella			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	1 / 125 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 180 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis shigella			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 100 (3.00%)	4 / 100 (4.00%)	3 / 125 (2.40%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 100 (2.00%)	4 / 100 (4.00%)	1 / 125 (0.80%)
occurrences (all)	2	4	2
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	0 / 125 (0.00%)
occurrences (all)	1	0	0
Dermatitis Allergic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	2 / 125 (1.60%)
occurrences (all)	0	0	2

Non-serious adverse events	Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 180 (0.56%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 180 (0.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences (all)	0		
Dermatitis Allergic			
subjects affected / exposed	0 / 180 (0.00%)		
occurrences (all)	0		

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