Clinical trial results:
Safety and Immunogenicity of Sanofi Pasteur Meningococcal (Groups A and C) Polysaccharide Vaccine versus Lanzhou Institute of Biological Products Meningococcal (Groups A and C) Polysaccharide Vaccine in Children 2-6 Years of Age in China

Summary

EudraCT number	2015-005189-48
Trial protocol	Outside EU/EEA
Global end of trial date	12 October 2011

Results information

Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	18 February 2016

Trial information

Trial identification

Sponsor protocol code	MPS01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01430611
WHO universal trial number (UTN)	U1111-1120-1190

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon Cedex 07, France, F-69367
Public contact	Medical Product Leader, Sanofi Pasteur SA, 33 4 37 66 96 18, philipp.oster@sanofipasteur.com
Scientific contact	Medical Product Leader, Sanofi Pasteur SA, 33 4 37 66 96 18, philipp.oster@sanofipasteur.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	31 August 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority in terms of seroconversion rate for serogroups A and C, 30 days after a single dose of Sanofi Pasteur Meningococcal (Groups A and C) Polysaccharide Vaccine versus Lanzhou Institute for Biological Products Meningococcal (Groups A and C) Polysaccharide Vaccine.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	23 August 2011
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	China: 665
Worldwide total number of subjects	665
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)	0
Children (2-11 years)	665
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:

The study subjects were enrolled from 23 August 2011 to 12 October 2011 at a single center in China.

Pre-assignment

Screening details:

A total of 665 of the 666 subjects who met all of the inclusion and none of the exclusion criteria that were randomized were vaccinated in this study.

Period 1

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

Blinding implementation details:

The trial was designed as a blind observer study. The vaccinator who administered the injections could not be blinded since the control vaccine differed front the investigational product. The staff members who collected safety data, Investigator, subjects, subjects' parents, laboratory personnel who analyzed the blood samples, and the Sponsor were all blinded to group assignment. If an emergency occurred, the Investigator could break the code using the decoding list as described in the protocol.

Arms

Are arms mutually exclusive?	Yes
Arm title	Meningo A+C® (Group 1)

Arm description:

Children aged 2 to 6 years received a single dose of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (Groups A and C) Polysaccharide Vaccine, manufactured by Sanofi Pasteur
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous in the anterolateral aspect of the upper arm, 1 injection on Day 0.

Arm title	Meng Ling Kang® (Group 2)

Arm description:

Children aged 2 to 6 years received a single dose of Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine.

Arm type	Active comparator
Investigational medicinal product name	Meningococcal (Groups A and C) Polysaccharide Vaccine, manufactured by Lanzhou Institute of Biologicals
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous in the anterolateral aspect of the upper arm, 1 injection on Day 0.

Number of subjects in period 1	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)
Started	332	333
Completed	315	318
Not completed	17	15
Consent withdrawn by subject	15	14
Adverse event, non-fatal	-	1
Lost to follow-up	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Meningo A+C® (Group 1)
Reporting group description:	
Children aged 2 to 6 years received a single dose of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine.	
Reporting group title	Meng Ling Kang® (Group 2)
Reporting group description:	
Children aged 2 to 6 years received a single dose of Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine.	

Reporting group values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)	Total
Number of subjects	332	333	665
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	332	333	665
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	3.2	3.1	
standard deviation	± 1.1	± 1	-
Gender categorical Units: Subjects			
Female	144	133	277
Male	188	200	388

End points

End points reporting groups

Reporting group title	Meningo A+C® (Group 1)
Reporting group description:	
Children aged 2 to 6 years received a single dose of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine.	
Reporting group title	Meng Ling Kang® (Group 2)
Reporting group description:	
Children aged 2 to 6 years received a single dose of Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine.	

Primary: Number of Subjects With Seroconversion Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Number of Subjects With Seroconversion Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine[1]
End point description:	
Seroconversion status was defined as antibody titers against meningococcal serogroups A and C, 30 days after vaccine administration ≥ 4-fold increase from pre-vaccination level measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).	
End point type	Primary
End point timeframe:	
Day 30 post-vaccination	

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	308		
Units: Number of subjects				
number (not applicable)				
Serogroup A	295	301		
Serogroup C	288	292		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Post-vaccination Titer ≥ 1:8 for Serogroup A Before and Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Percentage of Subjects with Post-vaccination Titer ≥ 1:8 for Serogroup A Before and Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Meningococcal Group A antibodies were measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	308		
Units: Percentage of subjects				
number (not applicable)				
Serogroup A (pre-vaccination)	12.5	8.8		
Serogroup A (post-vaccination)	98	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Post-vaccination Titer ≥ 1:8 for Serogroup C Before and Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Percentage of Subjects With Post-vaccination Titer ≥ 1:8 for Serogroup C Before and Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Meningococcal Group C antibodies were measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	308		
Units: Percentage of subjects				
number (not applicable)				
Serogroup C (pre-vaccination)	25	26		
Serogroup C (post-vaccination)	97	96.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Serogroup A and C Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Geometric Mean Titers of Serogroup A and C Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Meningococcal Group A and C antibodies were measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	333		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serogroup A (pre-vaccination)	1.75 (1.52 to 2)	1.45 (1.29 to 1.63)		
Serogroup A (post-vaccination)	207 (182 to 236)	223 (201 to 248)		
Serogroup C (pre-vaccination)	3.57 (3.2 to 3.97)	3.65 (3.28 to 4.07)		
Serogroup C (post-vaccination)	181 (158 to 208)	192 (168 to 220)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Serogroup A Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Geometric Mean Titers of Serogroup A Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Meningococcal Group A antibodies were measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	308		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serogroup A (pre-vaccination)	1.71 (1.49 to 1.97)	1.44 (1.27 to 1.63)		
Serogroup A (post-vaccination)	203 (178 to 233)	225 (202 to 250)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Serogroup C Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Geometric Mean Titers of Serogroup C Antibodies Following Vaccination With Either Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Meningococcal Group C antibodies were measured by 2,3,5 triphenyltetrazolium chloride (TTC) serum bactericidal assay using baby rabbit complement (SBA-BR).

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	308		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serogroup C (pre-vaccination)	3.66 (3.27 to 4.1)	3.64 (3.25 to 4.07)		
Serogroup C (post-vaccination)	179 (155 to 206)	191 (167 to 220)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting A Solicited Injection Site or Systemic Reactions Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point title	Number of Subjects Reporting A Solicited Injection Site or Systemic Reactions Following Vaccination of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine or Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine

End point description:

Solicited Injection site: Pain, Erythema, and Swelling. Solicited Systemic reactions: Fever (Temperature), Headache, Malaise, and Myalgia. Grade 3 Injection site: Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, ≥30 mm. Grade 3 Systemic reactions: Fever, temperature >39°C; Headache, Malaise, and Myalgia, Significant, preventing daily activity.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	332		
Units: Number of subjects				
number (not applicable)				
Injection site Pain	82	71		
Grade 3 Injection site Pain	1	0		
Injection site Erythema	44	32		
Grade 3 Injection site Erythema	1	0		
Injection site Swelling	20	17		
Grade 3 Injection site Swelling	0	1		
Fever	46	39		
Grade 3 Fever	1	0		
Headache	27	20		

Grade 3 Headache	0	0		
Malaise	32	33		
Grade 3 Malaise	0	0		
Myalgia	29	42		
Grade 3 Myalgia	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 30 post-vaccination.

Adverse event reporting additional description:

A Group 2 subject received the wrong vaccine and was included in the Full Analysis Set for Group 2 (classification per vaccine randomized to) and also Group 1 Safety Analysis Set (SafAS, classification according to vaccine actually received). For the solicited injection site and systemic reactions, the total (N) is the number with available data.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	Meningo A+C® (Group 1)

Reporting group description:

Children aged 2 to 6 years received a single dose of Sanofi Pasteur Meningococcal A+C Polysaccharide Vaccine.

Reporting group title	Meng Ling Kang® (Group 2)

Reporting group description:

Children aged 2 to 6 years received a single dose of Lanzhou Institute of Biological Products Meningococcal A+C Polysaccharide Vaccine.

Serious adverse events	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 333 (0.60%)	1 / 332 (0.30%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 333 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	1 / 333 (0.30%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Meningo A+C® (Group 1)	Meng Ling Kang® (Group 2)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 333 (24.62%)	71 / 332 (21.39%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	27 / 331 (8.16%)	20 / 331 (6.04%)	
occurrences (all)	27	20	
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	82 / 331 (24.77%)	71 / 331 (21.45%)	
occurrences (all)	82	71	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	44 / 331 (13.29%)	32 / 331 (9.67%)	
occurrences (all)	44	32	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	20 / 331 (6.04%)	17 / 331 (5.14%)	
occurrences (all)	20	17	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	46 / 330 (13.94%)	39 / 330 (11.82%)	
occurrences (all)	46	39	
Malaise			
alternative assessment type: Systematic			

subjects affected / exposed[6]	32 / 331 (9.67%)	33 / 331 (9.97%)	
occurrences (all)	32	33	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 333 (5.11%)	29 / 332 (8.73%)	
occurrences (all)	17	32	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[7]	29 / 331 (8.76%)	42 / 331 (12.69%)	
occurrences (all)	29	42	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	56 / 333 (16.82%)	46 / 332 (13.86%)	
occurrences (all)	60	48	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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