

**Clinical trial results:****A Phase 3, Multi-Center, Observer Blind, Controlled, Randomized Study to Compare the Immunogenicity and Safety of the Concomitant Administration of a Combined Tetanus, Reduced Diphtheria and Acellular Pertussis (Tdap) Vaccine (GSK Boostrix®) and Novartis (formerly Chiron) Meningococcal ACWY Conjugate Vaccine, With Either One Dose of Boostrix®, or One Dose of Novartis Meningococcal ACWY Conjugate Vaccine in Healthy Subjects Aged 11-25 Years**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2005-005519-12
Trial protocol	IT
Global end of trial date	08 May 2007

Results information

Result version number	v2 (current)
This version publication date	10 June 2016
First version publication date	07 December 2014
Version creation reason	• Correction of full data set re-QC of the study needed because of EudraCT system glitch and updates are required.

Trial information**Trial identification**

Sponsor protocol code	V59P11
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00329901
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines
Sponsor organisation address	Via Fiorentina, 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
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EMA paediatric investigation plan number(s)	EMA-000032-PIP01-07
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 December 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of a single dose of Tdap vaccine, separately but concomitantly administered with Chiron Men ACWY, is not inferior to that of a single dose of Tdap, concomitantly administered with a saline placebo

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for GCP, with applicable local regulations, including the European Directive 2001/20/EC, the US CFR Title 21, and the Japanese Ministry of Health, Labor, and Welfare, Novartis codes on the protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 2006
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	Italy: 1072
Worldwide total number of subjects	1072
EEA total number of subjects	1072

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)	106
Adolescents (12-17 years)	834
Adults (18-64 years)	132
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from 14 centers located in Italy.

Pre-assignment

Screening details:

A total of 1072 subjects were enrolled in the study, of which 1069 were vaccinated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tdap + MenACWY-CRM

Arm description:

Subjects received Tdap vaccine and MenACWY-CRM vaccine concomitantly, in separate arms.

Arm type	Experimental
Investigational medicinal product name	Tdap vaccine (GSK Boostrix vaccine)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose of the vaccine was administered by IM injection in the deltoid area.

Investigational medicinal product name	Novartis (formerly Chiron) Men ACWY Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose of the vaccine was administered by IM injection in the deltoid area.

Arm title	Tdap + Saline
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Arm description:

Subjects received Tdap vaccine and saline (placebo)concomitantly, in separate arms.

Arm type	Experimental
Investigational medicinal product name	saline placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose was administered by IM injection in the deltoid area.

Investigational medicinal product name	Tdap vaccine (GSK Boostrix vaccine)
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose of the vaccine was administered by IM injection in the deltoid area.

Arm title	MenACWY-CRM +Saline
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Arm description:

Subjects received MenACWY-CRM vaccine and saline (placebo) concomitantly, in separate arms.

Arm type	Experimental
Investigational medicinal product name	Novartis (formerly Chiron) Men ACWY Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose of the vaccine was administered by IM injection in the deltoid area.

Investigational medicinal product name	saline placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL dose was administered by IM injection in the deltoid area.

Number of subjects in period 1	Tdap + MenACWY-CRM	Tdap + Saline	MenACWY-CRM +Saline
Started	361	354	357
Completed	352	349	353
Not completed	9	5	4
Consent withdrawn by subject	4	3	2
Unable to classify	2	2	-
Lost to follow-up	2	-	1
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	Tdap + MenACWY-CRM
Reporting group description:	
Subjects received Tdap vaccine and MenACWY-CRM vaccine concomitantly, in separate arms.	
Reporting group title	Tdap + Saline
Reporting group description:	
Subjects received Tdap vaccine and saline (placebo)concomitantly, in separate arms.	
Reporting group title	MenACWY-CRM +Saline
Reporting group description:	
Subjects received MenACWY-CRM vaccine and saline (placebo) concomitantly, in separate arms.	

Reporting group values	Tdap + MenACWY-CRM	Tdap + Saline	MenACWY-CRM +Saline
Number of subjects	361	354	357
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)	36	39	31
Adolescents (12-17 years)	277	273	284
Adults (18-64 years)	48	42	42
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	14.4	14.1	14.3
standard deviation	± 3.4	± 3.2	± 3.2
Gender categorical			
Units: Subjects			
Female	189	164	165
Male	172	190	192

Reporting group values	Total		
Number of subjects	1072		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	106		
Adolescents (12-17 years)	834		
Adults (18-64 years)	132		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	518		
Male	554		

End points

End points reporting groups

Reporting group title	Tdap + MenACWY-CRM
Reporting group description: Subjects received Tdap vaccine and MenACWY-CRM vaccine concomitantly, in separate arms.	
Reporting group title	Tdap + Saline
Reporting group description: Subjects received Tdap vaccine and saline (placebo)concomitantly, in separate arms.	
Reporting group title	MenACWY-CRM +Saline
Reporting group description: Subjects received MenACWY-CRM vaccine and saline (placebo) concomitantly, in separate arms.	
Subject analysis set title	Enrolled Set
Subject analysis set type	Full analysis
Subject analysis set description: All subjects who had data in the demography panel; it was used for the analysis of demographics and all subject listings.	
Subject analysis set title	Immunogenicity PP
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the MITT population who received all the relevant doses of vaccine correctly, provided evaluable serum samples at the relevant time points and had no major protocol violation as defined prior to unblinding. A major deviation was defined as a protocol deviation that was considered to have a significant impact on the immunogenicity results of the subject.	
Subject analysis set title	Immunogenicity MITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomized subjects who actually received a study vaccination and provided at least one evaluable serum sample both before and after baseline.	
Subject analysis set title	Exposed
Subject analysis set type	Per protocol
Subject analysis set description: All enrolled subjects who actually received a study vaccination.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the Exposed population who provided postbaseline safety data.	

Primary: 1. Percentage of Subjects With an Immune Response Against Diphtheria, Tetanus and Pertussis, When Tdap is Concomitantly Administered With MenACWY-CRM Compared to Tdap Given Concomitantly With Saline Placebo

End point title	1. Percentage of Subjects With an Immune Response Against Diphtheria, Tetanus and Pertussis, When Tdap is Concomitantly Administered With MenACWY-CRM Compared to Tdap Given Concomitantly With Saline Placebo ^[1]
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End point description:

To demonstrate that the immunogenicity of one injection of Tdap vaccine, concomitantly administered with MenACWY-CRM vaccine, is not inferior to that of one injection of Tdap vaccine, concomitantly administered with saline placebo, in terms of:

- the percentage of subjects with antibody levels against diphtheria toxin ≥ 1.0 IU/mL and against tetanus toxin ≥ 1.0 IU/mL and
- the percentage of subjects with at least 4 fold increase in antibody levels against pertussis toxin (PT), filamentous hemagglutinin (FHA) and pertactin (PRN) at 1 month after immunization, as measured by enzyme linked immunosorbent assay (ELISA).

End point type	Primary
End point timeframe:	
1 month after vaccination (Day 29)	

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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	Tdap + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	345		
Units: Percentages of subjects				
number (confidence interval 95%)				
Day 1 (diphtheria)	4 (2 to 7)	5 (3 to 7)		
Day 29 (diphtheria)	94 (91 to 96)	85 (80 to 88)		
Day 1 (tetanus)	25 (20 to 30)	36 (31 to 42)		
Day 29 (tetanus)	100 (99 to 100)	99 (98 to 100)		
Day 29 (PT) 4-fold increase (N=286, 287)	76 (70 to 80)	81 (76 to 85)		
Day 29 (FHA) 4-fold increase (N=286, 287)	83 (78 to 87)	86 (82 to 90)		
Day 29 (PRN) 4-fold increase (N=285, 287)	84 (79 to 88)	91 (87 to 94)		

Statistical analyses

Statistical analysis title	Non-inferiority of anti-diphtheria immune response
Statistical analysis description:	
Non-inferiority of anti-diphtheria immune response following concomitant administration of Tdap with MenACWY-CRM as compared to Tdap given with placebo saline.	
Comparison groups	Tdap + MenACWY-CRM v Tdap + Saline
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Parameter estimate	Vaccine group difference
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	14

Notes:

[2] - The immune response to Tdap + MenACWY-CRM was considered non-inferior to that of Tdap+saline if for all five antigens (diphtheria, tetanus, PT, FHA, PRN) the lower limit of the 95% CI of the difference [(Tdap + MenACWY-CRM) minus(Tdap + saline)] was greater than -10, at 1 month (Day 29) after vaccination.

Statistical analysis title	Non-inferiority of anti-tetanus immune response
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Statistical analysis description:

Non-inferiority of anti-tetanus immune response following concomitant administration of Tdap with

MenACWY-CRM compared to Tdap given concomitantly with saline placebo.

Comparison groups	Tdap + MenACWY-CRM v Tdap + Saline
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Notes:

[3] - The immune response to Tdap + MenACWY-CRM was considered non-inferior to that of Tdap+saline if for all five antigens (diphtheria, tetanus, PT, FHA, PRN) the lower limit of the 95% CI of the difference [(Tdap + MenACWY-CRM) minus (Tdap + saline)] was greater than -10, at 1 month (Day 29) after vaccination.

Statistical analysis title	Non-inferiority of antiPT antigen immune response
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Statistical analysis description:

Non-inferiority of anti-PT antigen immune response following concomitant administration of Tdap with MenACWY as compared to Tdap given concomitantly with saline placebo.

Comparison groups	Tdap + MenACWY-CRM v Tdap + Saline
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Parameter estimate	Vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	1

Notes:

[4] - The immune response to Tdap + MenACWY-CRM was considered non-inferior to that of Tdap+saline if for all five antigens (diphtheria, tetanus, PT, FHA, PRN) the lower limit of the 95% CI of the difference [(Tdap + MenACWY-CRM) minus(Tdap + saline)] was greater than -10, at 1 month (Day 29) after vaccination.

Statistical analysis title	Non-inferiority of antiFHA antigen immune response
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Statistical analysis description:

Non-inferiority of anti-FHA antigen immune response following concomitant administration of Tdap with MenACWY as compared to Tdap given concomitantly with saline placebo.

Comparison groups	Tdap + MenACWY-CRM v Tdap + Saline
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
Parameter estimate	Vaccine group difference
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	3

Notes:

[5] - The immune response to Tdap + MenACWY-CRM was considered non-inferior to that of Tdap+saline if for all five antigens (diphtheria, tetanus, PT, FHA, PRN) the lower limit of the 95% CI of the difference [(Tdap + MenACWY-CRM) minus(Tdap + saline)] was greater than -10, at 1 month (Day 29) after vaccination.

Statistical analysis title	Non-inferiority of antiPRN antigen immune response
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Statistical analysis description:

Non-inferiority of anti-PRN antigen immune response following concomitant administration of Tdap with MenACWY as compared to Tdap given concomitantly with saline placebo.

Comparison groups	Tdap + MenACWY-CRM v Tdap + Saline
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[6]
Parameter estimate	Vaccine group difference
Point estimate	-7

Confidence interval

level	95 %
sides	2-sided
lower limit	-13
upper limit	-2

Notes:

[6] - The immune response to Tdap + MenACWY-CRM was considered non-inferior to that of Tdap+saline if for all five antigens (diphtheria, tetanus, PT, FHA, PRN) the lower limit of the 95% CI of the difference [(Tdap + MenACWY-CRM) minus(Tdap + saline)] was greater than -10, at 1 month (Day 29) after vaccination.

Secondary: 2. Percentage of Subjects With Anti-diphtheria and Anti-tetanus Concentrations \geq 0.1 IU/mL When Tdap is Administered Concomitantly With MenACWY-CRM Vaccine Compared to Tdap Given Concomitantly With Saline Placebo

End point title	2. Percentage of Subjects With Anti-diphtheria and Anti-tetanus Concentrations \geq 0.1 IU/mL When Tdap is Administered Concomitantly With MenACWY-CRM Vaccine Compared to Tdap Given Concomitantly With Saline Placebo ^[7]
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End point description:

The percentage of subjects with anti-diphtheria and anti-tetanus concentrations \geq 0.1 IU/mL (as measured by ELISA) following concomitant administration of Tdap vaccine with MenACWY-CRM vaccine as compared to when Tdap was given concomitantly with saline placebo.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	Tdap + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	345		
Units: Percentages of subjects				
number (confidence interval 95%)				
Day 1 (diphtheria)	55 (50 to 60)	63 (57 to 68)		
Day 29 (diphtheria)	100 (99 to 100)	100 (98 to 100)		
Day 1 (tetanus)	97 (95 to 99)	97 (95 to 99)		
Day 29 (tetanus)	100 (99 to 100)	100 (99 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Geometric Mean Concentrations of Antibodies Against Diphtheria, Tetanus and Pertussis Antigens After Concomitant Administration of Tdap With MenACWYCRM Compared to Tdap Given Concomitantly With Saline Placebo

End point title	3. Geometric Mean Concentrations of Antibodies Against Diphtheria, Tetanus and Pertussis Antigens After Concomitant Administration of Tdap With MenACWYCRM Compared to Tdap Given Concomitantly With Saline Placebo ^[8]
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End point description:

The geometric mean concentrations (GMCs) of antibodies against diphtheria, tetanus and pertussis (PT, FHA and PRN) antigens in subjects, as measured by ELISA, following concomitant administration of Tdap with MenACWY-CRM as compared to when Tdap given concomitantly with saline placebo.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	Tdap + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	345		
Units: Concentrations of antibodies				
geometric mean (confidence interval 95%)				
Day 1 (diphtheria)	0.11 (0.085 to 0.14)	0.12 (0.096 to 0.16)		
Day 29 (diphtheria)	7.96 (6.19 to 10)	2.77 (2.15 to 3.57)		
Day 1 (tetanus)	0.62 (0.5 to 0.76)	0.75 (0.61 to 0.92)		
Day 29 (tetanus)	12 (9.84 to 14)	15 (13 to 18)		
Day 1 (PT) (N=286,287)	2.68 (1.97 to 3.66)	2.85 (2.1 to 3.86)		
Day 29 (PT) (N=286,287)	62 (52 to 74)	79 (66 to 93)		
Day 1 (FHA) (N=286,287)	15 (13 to 18)	17 (14 to 20)		

Day 29 (FHA) (N=286,287)	186 (165 to 209)	219 (194 to 246)		
Day 1 (PRN) (N=285,287)	6.45 (5.18 to 8.03)	8.7 (7.01 to 11)		
Day 29 (PRN) (N=285,287)	157 (131 to 189)	254 (211 to 304)		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Geometric Mean Ratios of Antibody Concentrations Against Diphtheria, Tetanus and Pertussis Antigens When Tdap is Administered Concomitantly With MenACWYCRM Vaccine Compared to Tdap Given Concomitantly With Saline Placebo

End point title	4. Geometric Mean Ratios of Antibody Concentrations Against Diphtheria, Tetanus and Pertussis Antigens When Tdap is Administered Concomitantly With MenACWYCRM Vaccine Compared to Tdap Given Concomitantly With Saline Placebo ^[9]
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End point description:

The geometric mean ratios (GMRs- day 29/day 1) of post-vaccination versus prevaccination antibody concentrations against diphtheria, tetanus and pertussis (PT, FHA and PRN) antigens following concomitant administration of Tdap vaccine with MenACWYCRM vaccine as compared to when Tdap was given concomitantly with saline placebo.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	Tdap + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	345		
Units: Ratios of Antibody Concentrations				
geometric mean (confidence interval 95%)				
diphtheria	72 (58 to 91)	22 (18 to 28)		
tetanus	19 (14 to 25)	20 (15 to 26)		
PT (N=286,287)	23 (18 to 30)	28 (21 to 36)		
FHA (N=286,287)	12 (10 to 14)	13 (11 to 15)		
PRN (N=285,287)	24 (20 to 30)	29 (24 to 35)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentage of Subjects With Serum Bactericidal Antibody Titers $\geq 1:4$ and $\geq 1:8$, When MenACWY-CRM is Concomitantly Administered With Tdap Vaccine

Compared to MenACWY-CRM Given Concomitantly With Saline Placebo

End point title	5. Percentage of Subjects With Serum Bactericidal Antibody Titers $\geq 1:4$ and $\geq 1:8$, When MenACWY-CRM is Concomitantly Administered With Tdap Vaccine Compared to MenACWY-CRM Given Concomitantly With Saline Placebo ^[10]
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End point description:

The percentage of subjects with serum bactericidal antibody titers (hSBA) $\geq 1:4$ and $\geq 1:8$ against *Neisseria meningitidis* serogroups A,C,W and Y, following concomitant administration of MenACWY-CRM vaccine with Tdap vaccine as compared to when MenACWY-CRM was given concomitantly with saline placebo. The serum bactericidal antibodies directed against *N.meningitidis* serogroup A, C, W and Y, are measured by human complement Serum Bactericidal Assay (hSBA).

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

Notes:

[10] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	MenACWY-CRM +Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	126		
Units: Percentages of subjects				
number (confidence interval 95%)				
Day 1 (Men A) hSBA $\geq 1:4$	3 (1 to 7)	5 (2 to 10)		
Day 29 (Men A) hSBA $\geq 1:4$	79 (71 to 86)	83 (75 to 89)		
Day 1 (Men C) hSBA $\geq 1:4$ (N=118,124)	36 (28 to 46)	30 (22 to 39)		
Day 29 (Men C) hSBA $\geq 1:4$ (N=118,124)	94 (88 to 98)	90 (84 to 95)		
Day 1 (Men W) hSBA $\geq 1:4$ (N=116,124)	57 (47 to 66)	56 (47 to 65)		
Day 29 (Men W) hSBA $\geq 1:4$ (N=116,124)	97 (93 to 99)	97 (92 to 99)		
Day 1 (Men Y) hSBA $\geq 1:4$ (N=117,125)	47 (38 to 56)	42 (33 to 51)		
Day 29 (Men Y) hSBA $\geq 1:4$ (N=117,125)	96 (90 to 99)	97 (92 to 99)		
Day 1 (Men A) hSBA $\geq 1:8$	2 (0 to 6)	4 (1 to 9)		
Day 29 (Men A) hSBA $\geq 1:8$	74 (65 to 82)	80 (72 to 87)		
Day 1 (Men C) hSBA $\geq 1:8$ (N=118,124)	25 (17 to 33)	25 (18 to 34)		
Day 29 (Men C) hSBA $\geq 1:8$ (N=118,124)	92 (86 to 96)	88 (81 to 93)		
Day 1 (Men W) hSBA $\geq 1:8$ (N=116,124)	53 (43 to 62)	56 (46 to 65)		
Day 29 (Men W) hSBA $\geq 1:8$ (N=116,124)	96 (90 to 99)	97 (92 to 99)		
Day 1 (Men Y) hSBA $\geq 1:8$ (N=117,125)	38 (30 to 48)	38 (29 to 47)		
Day 29 (Men Y) hSBA $\geq 1:8$ (N=117,125)	93 (87 to 97)	94 (89 to 98)		

Statistical analyses

Secondary: 6. The hSBA Geometric Mean Titers Against N.Meningitidis Serogroups A,C,W and Y, When MenACWY-CRM is Concomitantly Administered With Tdap Vaccine Compared to MenACWY-CRM Given Concomitantly With Saline Placebo

End point title	6. The hSBA Geometric Mean Titers Against N.Meningitidis Serogroups A,C,W and Y, When MenACWY-CRM is Concomitantly Administered With Tdap Vaccine Compared to MenACWY-CRM Given Concomitantly With Saline Placebo ^[11]
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End point description:

The hSBA geometric mean titers (GMTs) against N.meningitidis serogroups A,C,W and Y, at baseline and at one month, following concomitant administration of MenACWYCRM vaccine with Tdap vaccine, as compared to when MenACWY-CRM was given concomitantly with saline placebo.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

Notes:

[11] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	MenACWY-CRM +Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	126		
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1 (Men A)	2.14 (1.99 to 2.31)	2.21 (2.05 to 2.38)		
Day 29 (Men A)	34 (23 to 50)	50 (34 to 74)		
Day 1 (Men C) (N=118,124)	4 (3.23 to 4.96)	3.92 (3.16 to 4.86)		
Day 29 (Men C) (N=118,124)	89 (58 to 136)	92 (60 to 140)		
Day 1 (Men W) (N=116,124)	11 (7.7 to 15)	9.49 (6.93 to 13)		
Day 29 (Men W) (N=116,124)	73 (54 to 98)	77 (57 to 103)		
Day 1 (Men Y) (N=117,125)	5.38 (4.2 to 6.89)	5 (3.91 to 6.39)		
Day 29 (Men Y) (N=117,125)	73 (54 to 98)	70 (52 to 94)		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Geometric Mean Ratios of hSBA Titers Against N.Meningitidis Serogroups A,C,W and Y, When MenACWY-CRM is Concomitantly Administered With Tdap Compared to MenACWY-CRM Given Concomitantly With Saline Placebo

End point title	7. Geometric Mean Ratios of hSBA Titers Against N.Meningitidis Serogroups A,C,W and Y, When MenACWY-CRM is Concomitantly Administered With Tdap Compared to MenACWY-CRM Given Concomitantly With Saline Placebo ^[12]
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End point description:

The geometric mean ratios (GMRs-day 29/day1)of post-vaccination versus prevaccination hSBA titers against N.meningitidis serogroups A,C,W and Y, when MenACWY-CRM vaccine is concomitantly administered with Tdap vaccine as compared to when MenACWY-CRM was given concomitantly with saline placebo.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

Notes:

[12] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	MenACWY-CRM +Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	126		
Units: Geometric Mean Ratios				
geometric mean (confidence interval 95%)				
Men A	16 (11 to 23)	23 (16 to 33)		
Men C (N=118,124)	22 (15 to 33)	23 (16 to 35)		
Men W (N=116,124)	6.9 (4.84 to 9.85)	8.09 (5.69 to 12)		
Men Y (N=117,125)	14 (9.41 to 19)	14 (9.79 to 20)		

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Percentage of Subjects With hSBA Seroresponse, When MenACWY-CRM is Concomitantly Administered With Tdap Compared to MenACWY-CRM Given Concomitantly With Saline Placebo

End point title	8. Percentage of Subjects With hSBA Seroresponse, When MenACWY-CRM is Concomitantly Administered With Tdap Compared to MenACWY-CRM Given Concomitantly With Saline Placebo ^[13]
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End point description:

The percentage of subjects showing an hSBA seroresponse against N.meningitidis serogroups A,C,W and Y, following concomitant administration of MenACWY-CRM vaccine with Tdap vaccine as compared to when MenACWY-CRM was given concomitantly with saline placebo.

Seroresponse to MenACWY-CRM is defined as a pre-vaccination hSBA titer < 1:4 to a post-vaccination hSBA titer of ≥ 1:8 or a pre-vaccination hSBA titer ≥ 1:4 to a postvaccinationtiter of at least four times the baseline hSBA titer.

End point type	Secondary
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End point timeframe:

1 month after vaccination (Day 29)

Notes:

[13] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	MenACWY-CRM +Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	126		
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	74 (65 to 82)	80 (72 to 87)		
Men C (N=118,124)	82 (74 to 89)	78 (70 to 85)		
Men W (N=116,124)	58 (48 to 67)	59 (50 to 68)		
Men Y (N=117,125)	70 (61 to 78)	70 (61 to 78)		

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of Subjects With Solicited Local and Systemic Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to When MenACWY-CRM is Concomitantly Administered With Saline Placebo.

End point title	9. Number of Subjects With Solicited Local and Systemic Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to When MenACWY-CRM is Concomitantly Administered With Saline Placebo. ^[14]
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End point description:

The number of subjects reporting solicited local and systemic reactions following concomitant administration of MenACWY-CRM vaccine and Tdap vaccine as compared to when MenACWY-CRM vaccine was concomitantly administered with saline placebo.

End point type	Secondary
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End point timeframe:

Day 1-7 after any vaccination

Notes:

[14] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	MenACWY-CRM +Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	357		
Units: Participants				
Local	278	179		
Injection site pain (MenACWY)	82	116		
Injection site erythema (MenACWY)	48	66		
Injection site induration (MenACWY)	41	59		
Injection site pain (Tdap or saline)	227	57		
Injection site erythema (Tdap or saline)	103	37		
Injection site induration (Tdap or saline)	110	23		
Systemic	198	171		
Chills	39	47		
Nausea	43	28		
Malaise	65	43		
Myalgia	118	79		

Arthralgia	57	40		
Headache	129	128		
Fever $\geq 38^{\circ}\text{C}$	11	14		
Other	42	33		
Stayed home due to reaction (N=358,357)	12	12		
Analgesic Antipyretic medication used	38	31		

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Number of Subjects With Solicited Local and Systemic Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to When Tdap is Concomitantly Administered With Saline Placebo

End point title	10. Number of Subjects With Solicited Local and Systemic Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to When Tdap is Concomitantly Administered With Saline Placebo ^[15]
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End point description:

The number of subjects reporting solicited local and systemic reactions following concomitant administration of MenACWY-CRM vaccine and Tdap vaccine as compared to when Tdap was concomitantly administered with saline placebo.

End point type	Secondary
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End point timeframe:

Day 1-7 after any vaccination

Notes:

[15] - 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: there was no statistical analyses for this endpoint.

End point values	Tdap + MenACWY-CRM	Tdap + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	353		
Units: Participants				
Local	278	282		
Injection site pain (Tdap)	227	246		
Injection site erythema (Tdap)	103	103		
Injection site induration (Tdap)	110	118		
Injection site pain (MenACWY or saline)	82	41		
Injection site erythema (MenACWY or saline)	48	34		
Injection site induration (MenACWY or saline)	41	27		
Systemic	198	202		
Chills	39	41		
Nausea	43	35		
Malaise	65	57		
Myalgia	118	127		
Arthralgia	57	60		
Headache	129	110		

Fever $\geq 38^{\circ}\text{C}$	11	7		
Other	42	39		
Stayed home due to reaction (N=358,357)	12	15		
Analgesic Antipyretic medication used	38	38		

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Number of Subjects With Unsolicited Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to MenACWY-CRM or Tdap Concomitantly Administered With Saline Placebo

End point title	11. Number of Subjects With Unsolicited Adverse Events When Tdap is Concomitantly Administered With MenACWY-CRM Compared to MenACWY-CRM or Tdap Concomitantly Administered With Saline Placebo
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End point description:

The number of subjects reporting any unsolicited adverse events (AEs) when Tdap is concomitantly administered with MenACWY-CRM as compared to when MenACWYCRM vaccine or Tdap vaccine was concomitantly administered with saline placebo.

End point type	Secondary
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End point timeframe:

Throughout the study (Day 1 to Day 181)

End point values	Tdap + MenACWY-CRM	Tdap + Saline	MenACWY-CRM +Saline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	353	357	
Units: Participants				
Any AE (Day 1 to 29)	43	31	48	
Possibly/probably related AE (Day 1 to 29)	8	6	6	
Serious AEs (Day 1 to 29)	0	0	0	
Possibly/probably related SAE(Day 1 to 29)	0	0	0	
AE's leading to discontinuation (Day 1 to 29)	0	0	0	
Death (Day 1 to 29)	0	0	0	
Any AE (Day 30 to 181)	42	36	39	
Possibly/probably related AE (Day 30 to 181)	0	0	0	
Serious AEs (Day 30 to 181)	1	2	0	
Possibly/probably related SAE (Day 30 to 181)	0	0	0	
AE's leading to discontinuation (Day 30 to 181)	0	0	0	
Death (Day 30 to 181)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All SAEs were collected throughout the study (Day 1-181). All solicited events were collected from Day 1-7 post vaccination; unsolicited adverse events were collected from Day 1-181. Solicited events after day 7 were counted as unsolicited events.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Tdap + MenACWYCRM
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Reporting group description:

Subjects received Tdap vaccine and MenACWY-CRM vaccine concomitantly, in separate arms

Reporting group title	Tdap + Saline
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Reporting group description:

Subjects received Tdap vaccine and saline (placebo) concomitantly, in separate arms

Reporting group title	MenACWY-CRM + Saline
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Reporting group description:

Subjects received MenACWY-CRM vaccine and saline (placebo) concomitantly, in separate arms

Serious adverse events	Tdap + MenACWYCRM	Tdap + Saline	MenACWY-CRM + Saline
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 359 (0.28%)	2 / 353 (0.57%)	0 / 357 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Heat stroke			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 359 (0.28%)	0 / 353 (0.00%)	0 / 357 (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
Gastrointestinal disorders			
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 359 (0.00%)	1 / 353 (0.28%)	0 / 357 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 359 (0.00%)	1 / 353 (0.28%)	0 / 357 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Tdap + MenACWYCRM	Tdap + Saline	MenACWY-CRM + Saline
Total subjects affected by non-serious adverse events			
subjects affected / exposed	296 / 359 (82.45%)	309 / 353 (87.54%)	232 / 357 (64.99%)
Nervous system disorders			
Headache			
subjects affected / exposed	131 / 359 (36.49%)	113 / 353 (32.01%)	136 / 357 (38.10%)
occurrences (all)	169	148	166
General disorders and administration site conditions			
Chills			
subjects affected / exposed	39 / 359 (10.86%)	41 / 353 (11.61%)	47 / 357 (13.17%)
occurrences (all)	41	44	51
Injection site erythema			
subjects affected / exposed	119 / 359 (33.15%)	110 / 353 (31.16%)	83 / 357 (23.25%)
occurrences (all)	156	140	109
Injection site induration			
subjects affected / exposed	125 / 359 (34.82%)	131 / 353 (37.11%)	72 / 357 (20.17%)
occurrences (all)	156	150	86
Injection site pain			
subjects affected / exposed	259 / 359 (72.14%)	262 / 353 (74.22%)	139 / 357 (38.94%)
occurrences (all)	315	296	188
Malaise			
subjects affected / exposed	67 / 359 (18.66%)	57 / 353 (16.15%)	43 / 357 (12.04%)
occurrences (all)	73	64	46
Pyrexia			
subjects affected / exposed	21 / 359 (5.85%)	14 / 353 (3.97%)	21 / 357 (5.88%)
occurrences (all)	28	17	25
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	44 / 359 (12.26%) 49	38 / 353 (10.76%) 41	31 / 357 (8.68%) 40
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	57 / 359 (15.88%) 60	60 / 353 (17.00%) 62	40 / 357 (11.20%) 45
Myalgia subjects affected / exposed occurrences (all)	119 / 359 (33.15%) 124	128 / 353 (36.26%) 135	80 / 357 (22.41%) 95

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2006	Amendment 1 issues dealt with: <ul style="list-style-type: none">- The addition of 6 new sites.- The extension of the enrollment period and therefore, the total duration of the study- The addition of a second location involved in the subjects enrollment at the site 04- The change of the corporate denominations of the sponsor
05 July 2006	Amendment 2 issues dealt with administrative change at the trial site number 11, it has been substituted with a new trial site name and address.
17 April 2007	Amendment 3 issues dealt with modification of study endpoints and expand analyses to address regulatory concerns.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/20164251>