# Clinical trial results:
# Phase III randomized, open, controlled study to evaluate the immune response to the hepatitis B antigen of the RTS,S/AS01E candidate vaccine, when administered as primary vaccination integrated into an EPI regimen to infants living in sub-Saharan Africa.

## Summary

| | |
|---|---|
| EudraCT number | 2011-001508-37 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 09 February 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 17 August 2017 |
| First version publication date | 17 August 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 113681 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01345240 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

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

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Interim |
| Date of interim/final analysis | 09 February 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 09 February 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate in terms of antibody (ab) response to the HBs antigen, the non-inferiority (noninf) of RTS,S/AS01E (RTSS) to a primary vaccination regimen of a licensed hepatitis B vaccine (Engerix-B) integrated into an expanded program on immunization (EPI) regimen.

Protection of trial subjects:

The vaccinees were observed closely for at least 60 minutes following the administration of all vaccines used in the study, with appropriate medical treatment readily available in case of an anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 November 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 51 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Burkina Faso: 508 |
| Country: Number of subjects enrolled | Ghana: 197 |
| Worldwide total number of subjects | 705 |
| 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) | 705 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |

| | |
|---|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study was conducted in 4 phases, a Primary Vaccination Phase (up to Month (M) 3), a Safety Follow-Up Phase (M3-8), a First Immunogenicity Follow-Up (FU) Phase (M8-26), and a Second Immunogenicity FU Phase (M26 to study end at M51).

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | RTS,S Regimen A Group |

Arm description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candidate Plasmodium falciparum malaria vaccine |
| Investigational medicinal product code | RTS,S/AS02D |
| Other name | |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh

| | |
|---|---|
| Investigational medicinal product name | Engerix-B Junior |
| Investigational medicinal product code | HBV Paediatric 10 |
| Other name | Engerix-B |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| | |
|---|---|
| Investigational medicinal product name | Infanrix-Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

| | |
|---|---|
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

3-dose orally

| | |
|---|---|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| | |
|---|---|
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

2-dose orally

| | |
|---|---|
| Investigational medicinal product name | Measles and yellow fever vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1-dose intramuscular injection in the deltoid

| | |
|---|---|
| **Arm title** | RTS,S Regimen B Group |

Arm description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candidate Plasmodium falciparum malaria vaccine |
| Investigational medicinal product code | RTS,S/AS02D |
| Other name | |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh

| | |
|---|---|
| Investigational medicinal product name | Engerix-B Junior |
| Investigational medicinal product code | HBV Paediatric 10 |
| Other name | Engerix-B |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

| | |
|---|---|
| Dosage and administration details:<br>3-dose intramuscular injection in the thigh. | |
| Investigational medicinal product name | Infanrix-Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the deltoid. | |
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details:<br>3-dose orally | |
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the thigh. | |
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details:<br>2-dose orally | |
| Investigational medicinal product name | Measles and yellow fever vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>1-dose intramuscular injection in the deltoid | |
| **Arm title** | RTS,S Regimen C Group |

Arm description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Candidate Plasmodium falciparum malaria vaccine |
| Investigational medicinal product code | RTS,S/AS02D |
| Other name | |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the thigh | |
| Investigational medicinal product name | Engerix-B Junior |
| Investigational medicinal product code | HBV Paediatric 10 |
| Other name | Engerix-B |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the thigh. | |
| Investigational medicinal product name | Infanrix-Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the deltoid. | |
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details:<br>3-dose orally | |
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>3-dose intramuscular injection in the thigh. | |
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details:<br>2-dose orally | |
| Investigational medicinal product name | Measles and yellow fever vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details:<br>1-dose intramuscular injection in the deltoid | |
| **Arm title** | Engerix B Regimen A Group |

Arm description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Engerix-B Junior |
| Investigational medicinal product code | HBV Paediatric 10 |
| Other name | Engerix-B |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| | |
|---|---|
| Investigational medicinal product name | Infanrix-Hib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

| | |
|---|---|
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

3-dose orally

| | |
|---|---|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| | |
|---|---|
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

2-dose orally

| | |
|---|---|
| Investigational medicinal product name | Measles and yellow fever vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1-dose intramuscular injection in the deltoid

| | |
|---|---|
| **Arm title** | Engerix B Regimen B Group |

Arm description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Arm type | Active comparator |
|---|---|
| Investigational medicinal product name | Engerix-B Junior |
| Investigational medicinal product code | HBV Paediatric 10 |
| Other name | Engerix-B |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| Investigational medicinal product name | Infanrix-Hib |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

| Investigational medicinal product name | Polio Sabin |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

3-dose orally

| Investigational medicinal product name | Synflorix |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3-dose intramuscular injection in the thigh.

| Investigational medicinal product name | Rotarix |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

2-dose orally

| Investigational medicinal product name | Measles and yellow fever vaccine |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1-dose intramuscular injection in the deltoid

| **Number of subjects in period 1** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group |
|---|---|---|---|
| Started | 142 | 142 | 141 |
| Completed | 140 | 128 | 131 |
| Not completed | 2 | 14 | 10 |
| Lost to follow-up | 1 | 12 | 8 |
| Serious Adverse Event | 1 | 2 | 2 |

| **Number of subjects in period 1** | Engerix B Regimen A Group | Engerix B Regimen B Group |
|---|---|---|
| Started | 141 | 139 |
| Completed | 131 | 132 |
| Not completed | 10 | 7 |
| Lost to follow-up | 8 | 6 |
| Serious Adverse Event | 2 | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | RTS,S Regimen A Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | RTS,S Regimen B Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | RTS,S Regimen C Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | Engerix B Regimen A Group |
|---|---|

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | Engerix B Regimen B Group |
|---|---|

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| **Reporting group values** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group |
|---|---|---|---|
| Number of subjects | 142 | 142 | 141 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: weeks | | | |
| arithmetic mean | 8.4 | 8.3 | 8.3 |
| standard deviation | ± 0.83 | ± 0.62 | ± 0.69 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 59 | 69 | 67 |
| Male | 83 | 73 | 74 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| African Heritage/African American | 142 | 142 | 141 |

| **Reporting group values** | Engerix B Regimen A Group | Engerix B Regimen B Group | Total |
|---|---|---|---|
| Number of subjects | 141 | 139 | 705 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: weeks | | | |
| arithmetic mean | 8.3 | 8.3 | |
| standard deviation | ± 0.74 | ± 0.74 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 81 | 63 | 339 |
| Male | 60 | 76 | 366 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| African Heritage/African American | 141 | 139 | 705 |

### End points reporting groups

| Reporting group title | RTS,S Regimen A Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | RTS,S Regimen B Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | RTS,S Regimen C Group |
|---|---|

Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | Engerix B Regimen A Group |
|---|---|

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Reporting group title | Engerix B Regimen B Group |
|---|---|

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Subject analysis set title | RTS,S Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in any of its formulations, Lot 1, 2 or 3, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Engerix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Subject analysis set title | Engerix B Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects in this group were subjects from the Engerix B Regimen A and Engerix B Regimen B groups were administered Engerix B™ as a 3-dose primary vaccination course, at Weeks 0, 4 and 8, followed by a booster dose, at Month 50. Subjects in this group were also administered, according to varied schedules, depending on the vaccination regimen they were allocated too in their respective group, doses Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™ and of vaccines against yellow fever and against measles. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Subject analysis set title | RTS,S Lot 1 Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 1 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regiment received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Engerix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Subject analysis set title | RTS,S Lot 2 Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 2 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regiment received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Engerix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| Subject analysis set title | RTS,S Lot 3 Group |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 3 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Engerix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

## Primary: Anti-Hepatitis B (HBs) antibody concentrations

| End point title | Anti-Hepatitis B (HBs) antibody concentrations[1] |
|---|---|

End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis, with study groups pooled by primary vaccine administered (RTS,S vs Engerix-B™).

| End point type | Primary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | RTS,S Group | Engerix B Group | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 397 | 253 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| mIU/mL | 6412.7 (5732.9 to 7173) | 377.4 (310.6 to 458.7) | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Anti-Hepatitis B (HBs) antibody concentrations.

| End point title | Anti-Hepatitis B (HBs) antibody concentrations.[2] |
|---|---|

End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis, with study groups pooled by RTS,S or Engerix-B™ vaccination regimen received.

| End point type | Primary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 140 | 123 | 134 | 135 |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| mIU/mL | 5467.6 (4493.8 to 6652.5) | 6989.9 (5747.5 to 8501) | 6998.7 (5779.1 to 8475.7) | 334.4 (253.4 to 441.4) |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 118 | | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| mIU/mL | 433.4 (329.5 to 570.1) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-Hepatitis B (HBs) antibody concentrations

| End point title | Anti-Hepatitis B (HBs) antibody concentrations |
|---|---|

End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis. Results presented are for the study groups receiving the RTS,S vaccine, pooled by vaccine lot, that is, for the RTS,S Lot 1, RTS,S Lot 2, and RTS,S Lot 3 groups, as defined below.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

| End point values | RTS,S Lot 1 Group | RTS,S Lot 2 Group | RTS,S Lot 3 Group | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 132 | 134 | 131 | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |

| | | | | |
|---|---|---|---|---|
| mIU/mL | 6214.3 (5115.6 to 7548.9) | 6826.1 (5569.4 to 8366.3) | 6209.2 (5144.2 to 7494.8) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-Hepatitis B (HBs) antibody concentrations.

| End point title | Anti-Hepatitis B (HBs) antibody concentrations.[3] |
|---|---|

End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 10 mIU/mL.

| End point type | Secondary |
|---|---|

End point timeframe:

At Months 14 and 26, aka at 12 and 24 months post Dose 3 of RTS,S vaccine or Engerix-B™

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Engerix B Regimen A Group | Engerix B Regimen B Group | RTS,S Lot 1 Group | RTS,S Lot 2 Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 127 | 114 | 133 | 118 |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs – At Month 14 | 119.5 (91 to 157) | 137.5 (103.3 to 183.2) | 1530.1 (1259.4 to 1859.1) | 2430.9 (1975.7 to 2991) |
| Anti-HBs – At Month 26 | 68.8 (50.7 to 93.3) | 71 (51.6 to 97.8) | 1092.6 (867.4 to 1376.3) | 1896 (1487.2 to 2417.3) |

| End point values | RTS,S Lot 3 Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 129 | | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs – At Month 14 | 2189.1 (1840.3 to 2603.9) | | | |
| Anti-HBs – At Month 26 | 1849.8 (1478.9 to 2313.6) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1).

| End point title | Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1). |
|---|---|

End point description:

Anti-HBs RF1 antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 33 EL.U/mL.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 123 | 135 | 135 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 268.7 (226.8 to 318.3) | 327.1 (272.2 to 393.1) | 335.5 (283.2 to 397.5) | 25.5 (22.8 to 28.7) |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 117 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 28.7 (24.6 to 33.4) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-circumsporozoite protein (anti-CS) antibody concentrations

| End point title | Anti-circumsporozoite protein (anti-CS) antibody concentrations |
|---|---|

End point description:

Anti-CS antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 0.5 EL.U/mL. The table shows results with study groups pooled by vaccination regimen received.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 141 | 123 | 136 | 135 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 142.2 (116.4 to 173.7) | 188.5 (156.5 to 227) | 205.5 (167.3 to 252.5) | 99999 (99999 to 99999) |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 118 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 0.3 (0.3 to 0.4) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-circumsporozoite protein (anti-CS) antibody concentrations .

| End point title | Anti-circumsporozoite protein (anti-CS) antibody concentrations .[4] |
|---|---|

End point description:

Anti-CS antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to (>=) 0.5 EL.U/mL.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 14, aka at 12 months post Dose 3 of RTS,S vaccine or Engerix-B™.

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | Engerix B Regimen A Group | Engerix B Regimen B Group | RTS,S Lot 1 Group | RTS,S Lot 2 Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 85 | 76 | 91 | 82 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 0.3 (0.3 to 0.3) | 0.3 (0.3 to 0.4) | 5.7 (4.2 to 7.7) | 6.8 (5 to 9.4) |

| **End point values** | RTS,S Lot 3 Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 96 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 7.5 (5.3 to 10.6) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.

| End point title | Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.[5] |
|---|---|

End point description:

Antibody concentrations were measured by GSK assay, and expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The cut-off of the assay, by GSK assay, was greater than or equal to (>=) 0.2 µg/mL. This corresponds to a cut-off value of 0.35µg/mL by enzyme-linked immunosorbent assay (ELISA). This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of Synflorix™

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 141 | 135 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| ANTI-1 | 3.1 (2.8 to 3.6) | 3.6 (3.1 to 4.2) | | |
| ANTI-4 | 3.5 (3 to 4) | 4.2 (3.5 to 4.9) | | |
| ANTI-5 | 5.1 (4.5 to 5.8) | 6.5 (5.6 to 7.4) | | |
| ANTI-6B | 1.1 (0.8 to 1.3) | 1.2 (1 to 1.6) | | |
| ANTI-7F | 4.4 (3.9 to 4.9) | 4.9 (4.3 to 5.7) | | |
| ANTI-9V | 2.8 (2.4 to 3.3) | 3.7 (3.3 to 4.2) | | |
| ANTI-14 | 5.8 (5 to 6.7) | 5.7 (4.7 to 7) | | |
| ANTI-18C | 3.4 (2.8 to 4.1) | 6.2 (5.1 to 7.5) | | |
| ANTI-19F | 4.2 (3.4 to 5.2) | 5.1 (4.1 to 6.4) | | |
| ANTI-23F | 1.3 (1.1 to 1.6) | 1.5 (1.1 to 1.9) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.

| End point title | Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.[6] |
|---|---|

End point description:

Antibody concentrations were measured by GSK assay, and expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The cut-off of the assay, by GSK assay, was greater than or equal to (>=) 0.2 µg/mL. This corresponds to a cut-off value of 0.35µg/mL by enzyme-linked immunosorbent assay (ELISA).

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 133 | 126 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| ANTI-1 | 4.5 (3.8 to 5.4) | 5.4 (4.5 to 6.4) | | |
| ANTI-4 | 6.1 (5.1 to 7.2) | 6.8 (5.7 to 8) | | |
| ANTI-5 | 6.5 (5.5 to 7.8) | 7.6 (6.4 to 9.1) | | |

| | | | | |
|---|---|---|---|---|
| ANTI-6B | 4.7 (4 to 5.5) | 4.1 (3.5 to 4.9) | | |
| ANTI-7F | 7.1 (6.2 to 8.2) | 7.2 (6.3 to 8.2) | | |
| ANTI-9V | 6 (5.1 to 7.1) | 5.7 (4.9 to 6.6) | | |
| ANTI-14 | 9 (7.6 to 10.7) | 9 (7.4 to 10.8) | | |
| ANTI-18C | 13.7 (11.5 to 16.3) | 14.5 (12.3 to 17.2) | | |
| ANTI-19F | 6 (4.9 to 7.4) | 7.2 (5.8 to 8.8) | | |
| ANTI-23F | 4.1 (3.4 to 5.1) | 3.9 (3.2 to 4.8) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.

| End point title | Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.[7] |
|---|---|

End point description:

The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Streptococcus pneumoniae opsonophagocytic activity was presented as the dilution of serum (opsonic titer) able to sustain 50 % killing of live pneumococci under the assay conditions, expressed as geometric mean titers (GMTs). The cut-off of the assay was an opsonic dilution >= 8. This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month (1M) post Dose 3 of Synflorix™

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 133 | 124 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| ANTI-1 | 48.9 (34.6 to 68.9) | 65 (45 to 93.7) | | |
| ANTI-4 | 768.3 (617.6 to 955.8) | 810.9 (676.5 to 972) | | |
| ANTI-5 | 77.6 (61.9 to 97.3) | 93.8 (73.6 to 119.6) | | |
| ANTI-6B | 444.4 (295 to 669.5) | 389.3 (250.1 to 606.1) | | |
| ANTI-7F | 3774 (3232.7 to 4405.8) | 3947.4 (3338.3 to 4667.7) | | |
| ANTI-9V | 1257.7 (977.3 to 1618.7) | 1469.3 (1180.4 to 1828.8) | | |

| | | | | |
|---|---|---|---|---|
| ANTI-14 | 1426.3 (1136 to 1790.9) | 1269 (965.1 to 1668.6) | | |
| ANTI-18C | 192.6 (139.2 to 266.4) | 249.7 (185 to 337) | | |
| ANTI-19F | 159.3 (109.9 to 231) | 228.8 (160.4 to 326.3) | | |
| ANTI-23F | 760.9 (476.3 to 1215.5) | 735.6 (456.3 to 1185.9) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.

| End point title | Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.[8] |
|---|---|

End point description:

The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Streptococcus pneumoniae opsonophagocytic activity was presented as the dilution of serum (opsonic titer) able to sustain 50 % killing of live pneumococci under the assay conditions, expressed as geometric mean titers (GMTs). The cut-off of the assay was an opsonic dilution >= 8.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 130 | 121 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-1 | 649.9 (464.7 to 908.9) | 840.1 (603.4 to 1169.7) | | |
| Opsono-4 | 2347.1 (1847.4 to 2982) | 2527.8 (2064.1 to 3095.7) | | |
| Opsono-5 | 324.2 (244.1 to 430.5) | 392.8 (291.3 to 529.6) | | |
| Opsono-6B | 955.3 (761.4 to 1198.6) | 828.2 (652.7 to 1050.9) | | |
| Opsono-7F | 9167.3 (7979.2 to 10532.3) | 7794.6 (6577.6 to 9236.8) | | |
| Opsono-9V | 3035.3 (2523.3 to 3651.3) | 3164.6 (2669.8 to 3751.1) | | |
| Opsono-14 | 1975.7 (1565.8 to 2493) | 1865 (1463.9 to 2375.9) | | |

| | | | | |
|---|---|---|---|---|
| Opsono-18C | 1694.1 (1188.6 to 2414.7) | 1548.7 (1096.3 to 2188) | | |
| Opsono-19F | 344.5 (223 to 532.3) | 469.7 (320 to 689.4) | | |
| Opsono-23F | 3199.8 (2543.7 to 4025.1) | 3198.1 (2526.5 to 4048.4) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-protein D (PD) antibody concentrations

| End point title | Anti-protein D (PD) antibody concentrations[9] |
|---|---|

End point description:

Anti-PD antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off of the assay was the seropositivity cut-off value of greater than or equal to 100 EL.U/mL. This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka at one month post Dose 3 of Synflorix™

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 141 | 134 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 2435.3 (2204.3 to 2690.6) | 2956.7 (2647.5 to 3302.1) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-protein D (PD) antibody concentrations

| End point title | Anti-protein D (PD) antibody concentrations[10] |
|---|---|

End point description:

Anti-PD antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off

of the assay was the seropositivity cut-off value of greater than or equal to 100 EL.U/mL.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | RTS,S Regimen A Group | Engerix B Regimen A Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 133 | 126 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| EL.U/mL | 2648.3 (2194.2 to 3196.4) | 2819.1 (2391.1 to 3323.7) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against acellular B-pertussis (BPT)

| End point title | Concentrations of antibodies against acellular B-pertussis (BPT) |
|---|---|

End point description:

The antibodies against BPT assessed were against pertussis toxoid (anti-PT), against filamentous haemagglutinin (anti-FHA), and against pertactin (anti-PRN). Concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off of the assay was the seropositivity cut-off value of greater than or equal to (>=) 5 EL.U/mL.

| End point type | Secondary |
|---|---|

End point timeframe:

At Day 0 and at Month 3 (one month post Dose 3 of Infanrix™-Hib)

| **End point values** | RTS,S Group | Engerix B Group | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 401 | 253 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT – At Day 0 | 3.8 (3.6 to 4.1) | 4.3 (3.9 to 4.8) | | |
| Anti-PT – At Month 3 | 105.9 (99.2 to 113.1) | 114.2 (104.8 to 124.5) | | |
| Anti-FHA – At Day 0 | 13.9 (12.7 to 15.2) | 15.7 (14.1 to 17.5) | | |

| | | | | |
|---|---|---|---|---|
| Anti-FHA – At Month 3 | 271.1 (252.8 to 290.8) | 292.9 (268.9 to 319.1) | | |
| Anti-PRN – At Day 0 | 3.2 (3 to 3.4) | 3.2 (3 to 3.5) | | |
| Anti-PRN – At Month 3 | 164.1 (153.6 to 175.3) | 179.7 (164.4 to 196.5) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-Rotavirus (anti-RV) antibody concentrations

| End point title | Anti-Rotavirus (anti-RV) antibody concentrations[11] |
|---|---|

End point description:

Anti-Rotavirus (anti-RV) antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs). The cut-off of the assay was the seropositive cut-off value of greater than or equal to (>=) 20 units per milliliter (U/mL). This outcome measure was assessed in subjects who were administered Rotarix™ as part of an EPI regimen, with and without RTS,S vaccine co-administration. This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Rotarix™. Results presented are for the study groups pooled by RTS,S or Engerix-B™ vaccine co-administration, that is, for the RTS,S Regimen B and Engerix-B Regimen B groups.

| End point type | Secondary |
|---|---|

End point timeframe:

At Month 3, aka one month post Dose 2 of Rotarix™

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | RTS,S Regimen B Group | Engerix B Regimen B Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 116 | | |
| Units: U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| U/mL | 24.9 (19.3 to 32) | 27.6 (20.8 to 36.5) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited local symptoms

| End point title | Number of subjects with solicited local symptoms |
|---|---|

End point description:

Assessed solicited local symptoms were pain, redness and swelling at the site of injection. All solicited local symptoms assessed were considered by the investigator as causally related to the study vaccination. Analysis for this outcome was performed solely for the 7-days follow-up periods following

the primary vaccination with RTS,S vaccine or Engerix-B™ (at Day 0, and Months 1 and 2). Data presented are those for any occurrence of the assessed solicited local symptoms, that is, the occurrences of these symptoms regardless of their intensity grade.

| End point type | Secondary |
|---|---|

End point timeframe:

Within the 7-day follow-up period (Days 0-6) after administration of Dose (D) 1, 2 and 3, respectively, with RTS,S or Engerix-B™ vaccine

| **End point values** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Pain - Post D1 | 41 | 28 | 31 | 29 |
| Pain – Post D2 | 30 | 14 | 21 | 24 |
| Pain – Post D3 | 14 | 10 | 14 | 18 |
| Redness – Post D1 | 1 | 0 | 2 | 5 |
| Redness – Post D2 | 5 | 1 | 2 | 3 |
| Redness – Post D3 | 3 | 0 | 1 | 3 |
| Swelling – Post D1 | 5 | 2 | 6 | 10 |
| Swelling – Post D2 | 8 | 3 | 4 | 9 |
| Swelling – Post D3 | 7 | 2 | 6 | 11 |

| **End point values** | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Pain - Post D1 | 15 | | | |
| Pain – Post D2 | 9 | | | |
| Pain – Post D3 | 7 | | | |
| Redness – Post D1 | 1 | | | |
| Redness – Post D2 | 0 | | | |
| Redness – Post D3 | 0 | | | |
| Swelling – Post D1 | 4 | | | |
| Swelling – Post D2 | 4 | | | |
| Swelling – Post D3 | 3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited general symptoms

| End point title | Number of subjects with solicited general symptoms |
|---|---|

End point description:

Assessed solicited general symptoms were fever, irritability/fussiness, drowsiness, and loss of appetite. Fever was defined as axillary temperature higher than (>) 37.5 degrees Celsius (°C). Analysis for this outcome was performed solely for the 7-days follow-up periods following the primary vaccination with RTS,S vaccine or Engerix-B™ (at Day 0, and Months 1 and 2). Data presented are those for any occurrence of the assessed solicited general symptoms, that is, the occurrences of these symptoms regardless of their intensity grade or relationship to vaccination.

| End point type | Secondary |
|---|---|

End point timeframe:

Within the 7-day follow-up period (Days 0-6) after administration of Dose (D) 1, 2 and 3, respectively, with RTS,S or Engerix-B™ vaccine

| **End point values** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Fever – D1 | 44 | 20 | 16 | 23 |
| Fever – D2 | 30 | 14 | 18 | 20 |
| Fever – D3 | 38 | 20 | 26 | 16 |
| Irritability – D1 | 15 | 11 | 11 | 9 |
| Irritability – D2 | 13 | 7 | 12 | 10 |
| Irritability – D3 | 5 | 3 | 10 | 6 |
| Drowsiness – D1 | 2 | 1 | 3 | 3 |
| Drowsiness – D2 | 5 | 1 | 1 | 3 |
| Drowsiness – D3 | 3 | 0 | 2 | 1 |
| Loss of appetite – D1 | 4 | 1 | 2 | 4 |
| Loss of appetite – D2 | 3 | 1 | 1 | 3 |
| Loss of appetite – D3 | 2 | 0 | 1 | 1 |

| **End point values** | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Fever – D1 | 13 | | | |
| Fever – D2 | 5 | | | |
| Fever – D3 | 12 | | | |
| Irritability – D1 | 5 | | | |
| Irritability – D2 | 0 | | | |
| Irritability – D3 | 1 | | | |
| Drowsiness – D1 | 0 | | | |
| Drowsiness – D2 | 0 | | | |
| Drowsiness – D3 | 0 | | | |
| Loss of appetite – D1 | 0 | | | |
| Loss of appetite – D2 | 0 | | | |
| Loss of appetite – D3 | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with potential immune mediated disorders (pIMDs)

| End point title | Number of subjects with potential immune mediated disorders (pIMDs) |
|---|---|

End point description:

A potential immune mediated disorder (pIMD) was defined as an event about which concerns arose that vaccination may have interfered with immunological self-tolerance of the subjects. IMDs assessed included among others neuroinflammatory disorders (such as optic neuritis, multiple sclerosis, or encephalitis), musculoskeletal disorders (such as cutaneous lupus, rheumatoid arthritis, juvenile arthritis, or psoriatic arthropathy), gastrointestinal disorders (ulcerative colitis and ulcerative proctitis, celiac disease), metabolic diseases (such as autoimmune thyroiditis, or diabetes Mellitus Type 1, Addison's disease), skin disorders (such as psoriasis or vitiligo), and other disorders such as vasculitis, pernicious anemia, or, sarcoidosis.

| End point type | Secondary |
|---|---|

End point timeframe:

From Day 0 to Month 8.

| **End point values** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Subject | 0 | 0 | 0 | 0 |

| **End point values** | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Subject | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with potential immune mediated disorders (pIMDs)

| End point title | Number of subjects with potential immune mediated disorders (pIMDs) |
|---|---|

End point description:

A potential immune mediated disorder (pIMD) was defined as an event about which concerns arose that vaccination may have interfered with immunological self-tolerance of the subjects. IMDs assessed included among others neuroinflammatory disorders (such as optic neuritis, multiple sclerosis, or encephalitis), musculoskeletal disorders (such as cutaneous lupus, rheumatoid arthritis, juvenile arthritis, or psoriatic arthropathy), gastrointestinal disorders (ulcerative colitis and ulcerative proctitis, celiac disease), metabolic diseases (such as autoimmune thyroiditis, or diabetes Mellitus Type 1, Addison's disease), skin disorders (such as psoriasis or vitiligo), and other disorders such as vasculitis, pernicious anemia, or, sarcoidosis.

| End point type | Secondary |
|---|---|

End point timeframe:

From study start at Day 0 to Month 26

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Subject | 0 | 0 | 0 | 0 |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Subject | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Number of subjects with unsolicited adverse events (AEs) |
|---|---|

End point description:

An unsolicited AE was defined as an untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

| End point type | Secondary |
|---|---|

End point timeframe:

Within the 30-day follow-up periods (Days 0-29) after vaccination with RTS,S vaccine or Engerix-B™

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Subject | 121 | 115 | 120 | 120 |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Subject | 105 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

| End point title | Number of subjects with any and fatal serious adverse events (SAEs) |
|---|---|

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.

| End point type | Secondary |
|---|---|

End point timeframe:

Within the 30-day follow-up periods (Days 0-29) after vaccination with RTS,S vaccine or Engerix-B™

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Subject with SAE(s) | 1 | 3 | 3 | 1 |
| Subjects with fatal SAE(s) | 1 | 0 | 1 | 0 |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Subject with SAE(s) | 3 | | | |
| Subjects with fatal SAE(s) | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

| End point title | Number of subjects with any and fatal serious adverse events (SAEs) |
|---|---|

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.

| End point type | Secondary |
|---|---|

End point timeframe:

From Day 0 to Month 8

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Subjects with SAE(s) | 1 | 7 | 7 | 3 |
| Subjects with fatal SAE(s) | 1 | 2 | 2 | 0 |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Subjects with SAE(s) | 5 | | | |
| Subjects with fatal SAE(s) | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

| End point title | Number of subjects with any and fatal serious adverse events (SAEs) |
|---|---|

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.

| End point type | Secondary |
|---|---|

End point timeframe:

From Day 0 to Month 26

| End point values | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group | Engerix B Regimen A Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 142 | 142 | 141 | 141 |
| Units: Subject | | | | |
| Any SAEs - At Month 26 | 1 | 8 | 7 | 6 |
| Fatal SAEs - At Month 26 | 1 | 3 | 2 | 2 |

| End point values | Engerix B Regimen B Group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 139 | | | |
| Units: Subject | | | | |
| Any SAEs - At Month 26 | 6 | | | |
| Fatal SAEs - At Month 26 | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

Solicited local, general symptoms and Unsolicited AEs: Within the 30-day periods after primary vaccination. SAEs: Within the 30-day periods after primary vaccination and from Day 0 to Month 26.

| | |
|---|---|
| Assessment type | Systematic |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

## Reporting groups

| | |
|---|---|
| Reporting group title | RTS,S Regimen A Group |

Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Reporting group title | RTS,S Regimen B Group |

Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Reporting group title | RTS,S Regimen C Group |

Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Reporting group title | Engerix B Regimen B Group |

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| | |
|---|---|
| Reporting group title | Engerix B Regimen A Group |

Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

| **Serious adverse events** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | 7 / 142 (4.93%) | 7 / 141 (4.96%) |
| number of deaths (all causes) | 1 | 3 | 2 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Hypertrophic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 0 / 142 (0.00%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 0 / 142 (0.00%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | 1 / 142 (0.70%) | 2 / 141 (1.42%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malaria | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 0 / 142 (0.00%) | 1 / 141 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 0 / 142 (0.00%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 0 / 141 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 2 / 142 (1.41%) | 2 / 141 (1.42%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Trichomoniasis intestinal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 0 / 141 (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 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 1 / 142 (0.70%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | 0 / 142 (0.00%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | 0 / 142 (0.00%) | 0 / 141 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Engerix B Regimen B Group | Engerix B Regimen A Group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 139 (3.60%) | 3 / 141 (2.13%) | |
| number of deaths (all causes) | 1 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Hypertrophic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 139 (0.72%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 1 / 141 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaria | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Fungal infection | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 139 (0.72%) | 2 / 141 (1.42%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trichomoniasis intestinal | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 0 / 141 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | RTS,S Regimen A Group | RTS,S Regimen B Group | RTS,S Regimen C Group |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 129 / 142 (90.85%) | 123 / 142 (86.62%) | 128 / 141 (90.78%) |
| Nervous system disorders | | | |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 142 (5.63%) | 2 / 142 (1.41%) | 6 / 141 (4.26%) |
| occurrences (all) | 10 | 2 | 5 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 55 / 142 (38.73%) | 40 / 142 (28.17%) | 47 / 141 (33.33%) |
| occurrences (all) | 85 | 52 | 66 |
| Swelling | | | |
| subjects affected / exposed | 17 / 142 (11.97%) | 7 / 142 (4.93%) | 14 / 141 (9.93%) |
| occurrences (all) | 20 | 7 | 16 |
| Pyrexia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 81 / 142 (57.04%) | 49 / 142 (34.51%) | 50 / 141 (35.46%) |
| occurrences (all) | 116 | 56 | 66 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 8 / 142 (5.63%) | 10 / 142 (7.04%) | 11 / 141 (7.80%) |
| occurrences (all) | 8 | 10 | 12 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 19 / 142 (13.38%) | 8 / 142 (5.63%) | 20 / 141 (14.18%) |
| occurrences (all) | 19 | 8 | 20 |
| Psychiatric disorders | | | |
| Irritability / fussiness | | | |
| subjects affected / exposed | 28 / 142 (19.72%) | 18 / 142 (12.68%) | 27 / 141 (19.15%) |
| occurrences (all) | 33 | 21 | 33 |
| Infections and infestations | | | |
| Malaria | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 44 / 142 (30.99%) | 44 / 142 (30.99%) | 39 / 141 (27.66%) |
| occurrences (all) | 50 | 54 | 46 |
| Gastroenteritis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 42 / 142 (29.58%) | 47 / 142 (33.10%) | 51 / 141 (36.17%) |
| occurrences (all) | 55 | 58 | 71 |

| | | | |
|---|---|---|---|
| Rhinitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 32 / 142 (22.54%) | 35 / 142 (24.65%) | 33 / 141 (23.40%) |
| occurrences (all) | 37 | 41 | 41 |
| Bronchitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 36 / 142 (25.35%) | 33 / 142 (23.24%) | 28 / 141 (19.86%) |
| occurrences (all) | 47 | 35 | 35 |
| Pharyngitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 23 / 142 (16.20%) | 13 / 142 (9.15%) | 15 / 141 (10.64%) |
| occurrences (all) | 24 | 15 | 19 |
| Otitis media | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 11 / 142 (7.75%) | 12 / 142 (8.45%) | 6 / 141 (4.26%) |
| occurrences (all) | 11 | 13 | 6 |
| Upper respiratory tract infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 15 / 142 (10.56%) | 8 / 142 (5.63%) | 12 / 141 (8.51%) |
| occurrences (all) | 17 | 9 | 15 |
| Respiratory tract infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 142 (4.23%) | 8 / 142 (5.63%) | 14 / 141 (9.93%) |
| occurrences (all) | 6 | 8 | 17 |
| Fungal skin infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | 7 / 142 (4.93%) | 6 / 141 (4.26%) |
| occurrences (all) | 1 | 7 | 6 |
| Bronchiolitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 9 / 142 (6.34%) | 5 / 142 (3.52%) | 5 / 141 (3.55%) |
| occurrences (all) | 8 | 5 | 5 |
| Pneumonia | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 142 (3.52%) | 14 / 142 (9.86%) | 4 / 141 (2.84%) |
| occurrences (all) | 5 | 15 | 4 |

| **Non-serious adverse events** | Engerix B Regimen B Group | Engerix B Regimen A Group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 114 / 139 (82.01%) | 132 / 141 (93.62%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 139 (0.00%) | 7 / 141 (4.96%) | |
| occurrences (all) | 0 | 5 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 25 / 139 (17.99%) | 48 / 141 (34.04%) | |
| occurrences (all) | 32 | 71 | |
| Swelling | | | |
| subjects affected / exposed | 10 / 139 (7.19%) | 23 / 141 (16.31%) | |
| occurrences (all) | 11 | 30 | |
| Pyrexia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 34 / 139 (24.46%) | 55 / 141 (39.01%) | |
| occurrences (all) | 37 | 65 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 7 / 139 (5.04%) | 9 / 141 (6.38%) | |
| occurrences (all) | 7 | 10 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 139 (4.32%) | 12 / 141 (8.51%) | |
| occurrences (all) | 6 | 13 | |
| Psychiatric disorders | | | |
| Irritability / fussiness | | | |
| subjects affected / exposed | 5 / 139 (3.60%) | 19 / 141 (13.48%) | |
| occurrences (all) | 6 | 25 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Malaria | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 44 / 139 (31.65%) | 48 / 141 (34.04%) | |
| occurrences (all) | 53 | 51 | |
| Gastroenteritis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 38 / 139 (27.34%) | 43 / 141 (30.50%) | |
| occurrences (all) | 47 | 57 | |
| Rhinitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 31 / 139 (22.30%) | 31 / 141 (21.99%) | |
| occurrences (all) | 36 | 36 | |
| Bronchitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 29 / 139 (20.86%) | 28 / 141 (19.86%) | |
| occurrences (all) | 37 | 31 | |
| Pharyngitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 17 / 139 (12.23%) | 14 / 141 (9.93%) | |
| occurrences (all) | 18 | 17 | |
| Otitis media | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 10 / 139 (7.19%) | 15 / 141 (10.64%) | |
| occurrences (all) | 11 | 19 | |
| Upper respiratory tract infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 7 / 139 (5.04%) | 8 / 141 (5.67%) | |
| occurrences (all) | 10 | 9 | |
| Respiratory tract infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 139 (4.32%) | 8 / 141 (5.67%) | |
| occurrences (all) | 7 | 9 | |
| Fungal skin infection | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 139 (2.88%) | 12 / 141 (8.51%) | |
| occurrences (all) | 4 | 12 | |
| Bronchiolitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 139 (2.88%) | 4 / 141 (2.84%) | |
| occurrences (all) | 4 | 4 | |
| Pneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 139 (1.44%) | 11 / 141 (7.80%) | |
| occurrences (all) | 2 | 11 | |

## 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