These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor:	**Study Identifiers:**
Sanofi	U1111-1275-1617
Drug substance(s): DTwP-HepB-Hib-IPV	**Study code:** SH600004

Title of the study:

Immunogenicity and safety of SHAN6™ vaccine when administered as booster in healthy toddlers in India

Study center(s):

This study was conducted at 10 centers that enrolled subjects in India.

Study period:

Date first participant enrolled: 30/Jun/2020

Date last participant completed: 13/Apr/2021

Study Status: Completed

Phase of development: III

Objectives:

Primary objectives:

- Immunogenicity: to describe the immunogenicity profile, 28 days after the booster dose of SHAN6, in subjects (primed with either SHAN6 or Shan 5 + ShanIPV) when administered concomitantly with or without MMR vaccine.
- Safety: to describe the safety profile, 28 days after the booster dose of the SHAN6 vaccine.

Secondary immunogenicity objectives:

- To describe the immune response to co-administered MMR vaccine in terms of seroconversion, 28 days after MMR vaccination in the MMR sub-cohort
- To describe the Ab persistence of SHAN6 or Shan 5 + ShanIPV at 12-24 months of age following a 3-dose primary series (as part of SH600003 study) at 6-8, 10-12, and 14-16 weeks of age
- To describe the immunogenicity profile, 28 days after the booster dose of SHAN6 when administered concomitantly with or without MMR vaccine, in subjects primed with SHAN6 and in subjects primed with Shan 5 + ShanIPV

Methodology:

This was a multi-center, open label, randomized, 2-arm, Phase III study to be conducted in a maximum of 1200 toddlers, who were participants of the SH600003 study. Toddlers aged 12 to 24 months were randomized in a 1:1 ratio to the following groups:

- Group A (N=600): SHAN6 and MMR on Day 0 (V01)
- Group B (N=600): SHAN6 on Day 0 (V01) and MMR on Day 28 (V02).

According to the randomization ratio of 3:1 in the primary series, it was expected that 900 subjects had received SHAN6 and 300 subjects had received Shan 5 + ShanIPV in the primary series (as part of SH600003 study).

A subset of 600 subjects (approximately half of the expected enrolled subjects, 450 who received SHAN6 and 150 who received Shan 5 + ShanIPV) were expected to be randomized to have a blood sample before and after the SHAN6 dose for Ab testing, according to the vaccine they received in the primary series study. These subjects constituted the "immunogenicity cohort".

In addition, among the 600 subjects from the immunogenicity cohort, half of these (300 in total, 150 subjects each in Groups A and B) were expected to undergo anti-measles, anti-mumps and anti-rubella Ab testing. These subjects constituted the "MMR sub-cohort".

As MMR vaccine was administered on Day 28 in Group B subjects, half of the subjects from the MMR sub-cohort needed to attend V03 in order to provide a blood sample 28 days after the MMR vaccination.

The subjects and subjects' parent(s)/legally authorized representative(s) (LAR) had to come to the study site for 2 visits (Group A) or 3 visits (for the MMR sub-cohort in Group B).

Study personnel contacted the subject's parent(s)/LAR by telephone 3 days (+ 2 days) after vaccination (Day 3) to remind them to complete the DCs, to check whether the subject experienced any SAEs not yet reported, and to plan the next visit at the center.

All subjects in the immunogenicity cohort were to provide 2 or 3 blood samples on the following schedule:

- Pre-booster (baseline) blood sample on Day 0,
- Post-booster sample on Day 28 (+ 14 days) in Group A and Group B, and on Day 56 (+ 14 days) for the MMR sub-cohort in Group B.

Approximately 4 mL of blood was collected on Day 0 and Day 28 and approximately 1.5 mL of blood on Day 56.

All subjects were to be followed for safety from V01 to approximately 28 days after SHAN6 vaccination. All subjects were observed for 30 minutes after SHAN6 vaccination under the supervision of a responsible healthcare professional at each study site and any unsolicited systemic AEs occurring during that time was recorded as immediate unsolicited systemic AEs in the case report book. The subject's parent(s)/LAR had to record in the DCs information about solicited injection site and systemic reactions from Day 0 to Day 7 post-vaccination and unsolicited AEs from Day 0 to Day 28 post-vaccination. Information on SAEs and AESIs was collected throughout the duration of the study. Only related SAEs were to be reported after Day 28. No safety data (except related SAEs) were collected following MMR vaccination. The subject's parent(s)/LAR were asked to notify the site immediately about potential SAEs (including AESIs) at any time during the study. The completed DC was reviewed with the subject's parent(s)/LAR at V02.

No early safety data review was performed.

Number of participants:

Planned: 1200

Randomized: 676

Evaluated:

FAS(full analysis set) for immunogenicity cohort: 450

SafAS(safety analysis set): 676

Diagnosis and criteria for inclusion:

Healthy toddlers aged between 12-24 months who had received 3 doses of either SHAN6 or Shan 5 + ShanIPV at 6-8, 10-12, and 14-16 weeks of age and provided the pre- and post-dose blood sample by virtue of their participation in study SH600003, who had not received any vaccine containing D, T, wP, acellular pertussis, Hep B, Hib, IPV in second year of life and who had received their first dose of MMR vaccines at least 4 weeks before enrollment in the study but not 2 doses of MMR-containing vaccines, could be included in study SH600004.

Study Products:

Investigational medicinal product(s): SHAN6 hexavalent (DTwP-HepB-Hib-IPV) vaccine manufactured by SHIPL.

Formulation/Form & composition: Liquid, each multi-dose presentation (5 mL) of vaccine contains 10 doses of SHAN6.

Active substances per 0.5 mL:

- Diphteria toxoid: ≥ 30 IU
- Tetanus toxoid (TT): ≥ 60 IU
- wP: ≥ 4 IU
- HBs: 10 µg
- Purified capsular polysaccharide of Hib conjugated to 22-40 µg of TT: 12 µg
- IPV type 1 (Mahoney)
- IPV type 2 (MEF-1)
- IPV type 3 (Saukett)

Route(s) of administration: Intramuscular injection into the upper outer aspect of the thigh.

Duration of treatment/participation:

The duration of the subject's participation in the trial was approximately 28 days (+ 14 days) for Group A and Group B, and 56 days (+ 14 days) for the MMR sub-cohort in Group B.

Criteria for evaluation:

Primary endpoints:

The primary endpoints for the evaluation of immunogenicity were assessed 28 days after the booster dose of the SHAN6 (Visit [V]02 [Day 28 + 14 days]):

- Seroprotection status for diphtheria (D), tetanus (T), Hep B, Hib (polyribosyl ribitol phosphate [PRP]) and poliovirus antigens with the following definitions:
    - Anti-D and anti-T antibody (Ab) titers ≥ 0.01 international unit (IU)/mL
    - Anti-hepatitis B surface (HBs) Ab titers ≥ 10 mIU/mL
    - Anti-PRP Ab titers ≥ 0.15 µg/mL
    - Anti-polio 1, 2, and 3 Ab titers ≥ 8 (1/dil)
- Ab titers above the following cut-off for each valence:
    - Anti-D and anti-T Ab concentrations ≥ 0.01 IU/mL, ≥ 0.1 IU/mL, and ≥ 1.0 IU/mL
    - Anti-HBs Ab concentrations ≥ 10 mIU/mL and ≥ 100 mIU/mL
    - Anti-PRP Ab titers ≥ 0.15 µg/mL and ≥ 1.0 µg/mL
    - Anti-polio 1, 2 and 3 Ab titers ≥ 8 (1/dil)
- Pertussis antigens vaccine response status for anti-pertussis toxin (PT), anti-filamentous hemagglutinin (FHA), anti-pertactin (PRN), and anti-fimbriae (FIM) Abs defined as follows:
    - If the pre-booster vaccination concentration was < 4 x lower limit of quantitation (LLOQ), then the post-booster vaccination concentration was ≥ 4 x the pre-booster concentration or
    - If the pre-booster vaccination concentration was ≥ 4 x LLOQ, then the post-booster vaccination concentration was ≥ 2 x the pre-booster concentration.

      Note: Pre-booster vaccination concentrations < LLOQ were converted to LLOQ for purposes of calculating this booster response
- Pertussis antigens vaccine seroconversion status for anti-PT, anti-FHA, anti-PRN and anti-FIM Abs defined as follows: a ≥ 4-fold rise in the respective PT, FHA, PRN, FIM Ab concentration between pre-booster and post-booster
- Ab concentrations/titers for each valence
- Ratio (post/pre-injection) of individual Ab concentrations/titers for each valence

The primary safety endpoints were:

- Occurrence of any unsolicited systemic adverse events (AEs) reported in the 30 minutes after study vaccine dose, as applicable
- Occurrence of solicited (ie, pre-listed in the subject's diary card [DC] and in the electronic case report form) injection site reactions and systemic reactions occurring up to 7 days after study vaccine dose, as applicable
- Occurrence of unsolicited (spontaneously reported) AEs up to 28 days after study vaccine dose, as applicable

Occurrence of serious adverse events (SAEs), including adverse events of special interest (AESIs), throughout the trial period

Secondary immunogenicity endpoints:

The following secondary immunogenicity endpoints were assessed at baseline (V01, Day 0) and 28 days after the booster dose of SHAN6 or MMR (V02 [Day 28 + 14 days] or V03 [Day 56 + 14 days]):

- Anti-measles, anti-mumps, and anti-rubella Abs ≥ LLOQ
- Seroprotection status for D, T, Hep B, Hib (PRP) and poliovirus antigens with the following definitions:
    - Anti-D and anti-T Ab titers ≥ 0.01 IU/mL
    - Anti-HBs Ab titers ≥ 10 mIU/mL
    - Anti-PRP Ab titers ≥ 0.15 µg/mL
    - Anti-polio 1, 2, and 3 Ab titers ≥ 8 (1/dil)
- Ab titers above the following cut-off for each valence:
    - Anti-D and anti-T Ab concentrations ≥ 0.01 IU/mL, ≥ 0.1 IU/mL, and ≥ 1.0 IU/mL
    - Anti-HBs Ab concentrations ≥ 10 mIU/mL and ≥ 100 mIU/mL
    - Anti-PRP Ab titers ≥ 0.15 µg/mL and ≥ 1.0 µg/mL
    - Anti-polio 1, 2 and 3 Ab titers ≥ 8 (1/dil)
- Ab concentrations/titers for each valence

The following secondary immunogenicity endpoints were assessed at 28 days after the booster dose of SHAN6 (V02 [Day 28 + 14 days]) or MMR (V02 [Day 28 + 14days] or V03 [Day 56 + 14 days]):

- Pertussis antigens vaccine response status for anti-PT, anti-FHA, anti-PRN, and anti-FIM Abs defined as follows:
    - If the pre-booster vaccination concentration was < 4 x LLOQ, then the post-booster vaccination concentration was ≥ 4 x the pre-booster concentration or
    - If the pre-booster vaccination concentration was ≥ 4 x LLOQ, then the post-booster vaccination concentration was ≥ 2 x the pre-booster concentration

      Note: If the pre-booster concentration was ≤LLOQ then this value was transformed to LLOQ
- Pertussis antigens vaccine seroconversion status for anti-PT, anti-FHA, anti-PRN, and anti-FIM Abs defined as follows: a ≥ 4-fold rise in the respective PT, FHA, PRN, FIM Ab concentration between pre-booster and post-booster
- For MMR antigens: ≥ 2-fold rise and ≥ 4-fold rise in the respective anti-measles, anti-mumps and anti-rubella Abs concentration between pre-booster and post-booster
- Ratio (post/pre-injection) of individual Ab concentrations/titers for each valence

Statistical methods:

The statistical analyses were performed on safety and immunogenicity data collected during the study. All analyses were descriptive; no hypotheses were tested.

The per protocol analysis set (PPAS), as the main population, and the full analysis set (FAS) were used for the immunogenicity analyses; the safety analysis set (SafAS) was used for the safety analyses.

Immunogenicity endpoints (analyses) were summarized according to the concomitant MMR injection (MMR on Day 0, ie, Group A, or no MMR on Day 0, ie, Group B).

For the main immunogenicity parameters, 95% confidence intervals (CIs) of point estimates were calculated using the normal approximation for quantitative data and the exact binomial distribution (Clopper-Pearson method) for proportions. The primary immunogenicity endpoints were summarized among the subjects from the immunogenicity cohort according to the following parameters:

- Percentage of subjects with titers above predefined cut-off as per primary endpoints
- Percentage of subjects with ≥ 4-fold rise (seroconversion status) and vaccine response in anti-pertussis Abs (anti-PT, anti-FIM, anti-PRN, and anti-FHA) concentration
- Geometric mean of concentration (GMC)/geometric mean of titer for each valence, adjusted GMCs for PT, FIM, PRN, and FHA
- Geometric mean ratio of individual Ab concentration/titers

Immunogenicity endpoints on MMR were summarized according to the following parameters, in the MMR sub-cohort:

- Percentage of subjects with titers above predefined cut-off as per secondary endpoints
- Percentage of subjects with ≥ 2-fold rise and ≥ 4-fold rise in anti-measles, anti-mumps, and anti-rubella Abs concentration

- GMC/geometric mean of titer for each valence (anti-measles, anti-mumps, and anti-rubella)
- Geometric mean ratio of individual Ab concentration/titers

For Ab persistence and booster assessment, the same parameters and statistical approach as the one described for the primary analysis were used.

For each safety criterion, the percentage of subjects with the criterion (ie, occurrence of adverse reactions/AEs) was computed with its 95% CI (binomial distribution, Clopper-Pearson method).

All safety endpoints (analysis) were described in all included subjects and according to the concomitant MMR injection (MMR on Day 0, ie, Group A, or no MMR on Day 0, ie, Group B).

Table S1: Precision around expected estimates for booster immune response against diphtheria, tetanus, *Haemophilus influenzae* type B, and poliomyelitis

	Expected in each booster vaccine group	
Seroprotection rate (%)	**CI for N=300**	**CI for N=250**
95%	(91.9; 97.2)	(91.8; 97.5)
99%	(97.1; 99.8)	(97.1; 99.9)
100%	(98.8; 100)	(98.5; 100)

CI: confidence interval

Table S2: Precision around expected estimates for antibody persistence pre-booster according to the previous vaccines received

	Expected in each primary series vaccine group		**If lower sample size**
Seroprotection rate (%)	**CI for N=450**	**CI for N=150**	**CI for N=100**
95%	(85.0; 92.6)	(84.0; 94.3)	(82.4; 95.1)
99%	(92.7; 96.9)	(90.6; 98.1)	(88.7; 98.4)
100%	(99.2; 100)	(97.6; 100)	(96.4; 100)

CI: confidence interval

Table S3: Precision around expected estimates for immune response assessment against measles, mumps, and rubella

Seroprotection rate (%)	**CI for N=150**	**CI for N=100**
95%	(90.6; 98.1)	(88.7; 98.4)
99%	(94.3; 99.6)	(93.0; 99.8)
100%	(97.6; 100)	(96.4; 100)

CI: confidence interval

The estimates for anti-MMR immune response assessment were calculated based on the assumption that a seroconversion rate could be defined according to the selected assay and based on an expected number of subjects per the booster phase group (SHAN6 + MMR on Day 0 or Day 28).

Summary Results:

Demographic and Other Baseline Characteristics:

A total of 676 subjects were enrolled: 336 subjects were enrolled in Group A (SHAN6 and MMR on Day 0), and 340 subjects were enrolled in Group B (SHAN6 on Day 0 and MMR on Day 28). Baseline demographic characteristics were similar between the 2 vaccine groups in terms of gender repartition, age, and weight at inclusion. Overall, the male/female ratio was 1.05, the mean (standard deviation [SD]) age at inclusion was 16.9 (1.75) months, and the mean (SD) weight at inclusion was 10.3 (1.46) kg.

No differences were observed between vaccine groups in terms of medical and vaccination history. All subjects had had their first dose of measles/measles, rubella/MMR vaccine administered before Day 0.

Immunogenicity:

Primary objective: immunogenicity profile, 28 days after the booster dose of SHAN6, in subjects (primed with either SHAN6 or Shan 5 + ShanIPV) when administered concomitantly with or without MMR vaccine

Binary endpoints

At V01, the percentages of subjects with titers meeting the different thresholds were similar between vaccine groups for all antigens. The percentages of subjects meeting the different thresholds increased between V01 and V02 and were generally similar between vaccine groups at V02. The binary endpoints are summarized in Table S4.

Table S4: Summary of binary endpoints – Pre-dose and post-dose – PPAS

			Group A: SHAN6 and MMR at D0 (N=84)			**Group B: SHAN6 at D0; MMR at D28 (N=81)**		
Antigen	**Timepoint**	**Criteria**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Anti-D (DTP-ECL - IU/mL)	**Pre-dose (V01)**	**>= 0.01 IU/mL**	84/84	100	(95.7; 100.0)	80/81	98.8	(93.3; 100.0)
		>= 0.1 IU/mL	67/84	79.8	(69.6; 87.7)	61/81	75.3	(64.5; 84.2)
		>= 1.0 IU/mL	Nov-84	13.1	(6.7; 22.2)	Oct-81	12.3	(6.1; 21.5)
	Post-dose (V02)	**Seroprotection (ie. >= 0.01 IU/mL)**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
		>= 0.1 IU/mL	84/84	100	(95.7; 100.0)	79/81	97.5	(91.4; 99.7)
		>= 1.0 IU/mL	83/84	98.8	(93.5; 100.0)	72/81	88.9	(80.0; 94.8)

Anti-T (DTP-ECL - IU/mL)	**Pre-dose (V01)**	**>= 0.01 IU/mL**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
		>= 0.1 IU/mL	84/84	100	(95.7; 100.0)	78/81	96.3	(89.6; 99.2)
		>= 1.0 IU/mL	26/84	31	(21.3; 42.0)	30/81	37	(26.6; 48.5)
	Post-dose (V02)	**Seroprotection (ie. >= 0.01 IU/mL)**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
		>= 0.1 IU/mL	84/84	100	(95.7; 100.0)	80/81	98.8	(93.3; 100.0)
		>= 1.0 IU/mL	84/84	100	(95.7; 100.0)	78/81	96.3	(89.6; 99.2)
Anti-PT (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	71/84	84.5	(75.0; 91.5)	72/81	88.9	(80.0; 94.8)
	Post-dose (V02)	**>= 2 EU/mL**	82/84	97.6	(91.7; 99.7)	79/81	97.5	(91.4; 99.7)
	Post-dose (V02) / pre (V01)	**Vaccine response***	76/84	90.5	(82.1; 95.8)	71/81	87.7	(78.5; 93.9)
		Seroconversion, (ie. >= 4-fold rise)	66/84	78.6	(68.3; 86.8)	68/81	84	(74.1; 91.2)
Anti-FIM (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	84/84	100	(95.7; 100.0)	79/81	97.5	(91.4; 99.7)
	Post-dose (V02)	**>= 2 EU/mL**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
	Post-dose (V02) / pre (V01)	**Vaccine response***	82/84	97.6	(91.7; 99.7)	75/81	92.6	(84.6; 97.2)
		Seroconversion, (ie. >= 4-fold rise)	79/84	94	(86.7; 98.0)	74/81	91.4	(83.0; 96.5)
Anti-PRN (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	61/84	72.6	(61.8; 81.8)	60/81	74.1	(63.1; 83.2)
	Post-dose (V02)	**>= 2 EU/mL**	84/84	100	(95.7; 100.0)	77/81	95.1	(87.8; 98.6)
	Post-dose (V02) / pre (V01)	**Vaccine response***	80/84	95.2	(88.3; 98.7)	69/81	85.2	(75.6; 92.1)
		Seroconversion, (ie. >= 4-fold rise)	77/84	91.7	(83.6; 96.6)	70/81	86.4	(77.0; 93.0)

Anti-FHA (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	79/84	94	(86.7; 98.0)	75/81	92.6	(84.6; 97.2)
	Post-dose (V02)	**>= 2 EU/mL**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
	Post-dose (V02) / pre (V01)	**Vaccine response***	80/84	95.2	(88.3; 98.7)	72/81	88.9	(80.0; 94.8)
		Seroconversion, (ie. >= 4-fold rise)	74/84	88.1	(79.2; 94.1)	69/81	85.2	(75.6; 92.1)
Anti-PRP (RIA - µg/mL)	**Pre-dose (V01)**	**>= 0.15 µg/mL**	83/84	98.8	(93.5; 100.0)	80/81	98.8	(93.3; 100.0)
		>= 1 µg/mL	75/84	89.3	(80.6; 95.0)	68/81	84	(74.1; 91.2)
	Post-dose (V02)	**Seroprotection (ie. >= 0.15 µg/mL)**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
		>= 1 µg/mL	84/84	100	(95.7; 100.0)	80/81	98.8	(93.3; 100.0)
Anti-HBs (ELISA - mIU/mL)	**Pre-dose (V01)**	**>= 10 mIU/mL**	81/84	96.4	(89.9; 99.3)	77/81	95.1	(87.8; 98.6)
		>= 100 mIU/mL	76/84	90.5	(82.1; 95.8)	64/81	79	(68.5; 87.3)
	Post-dose (V02)	**Seroprotection (ie. >= 10 mIU/mL)**	84/84	100	(95.7; 100.0)	80/81	98.8	(93.3; 100.0)
		>= 100 mIU/mL	83/84	98.8	(93.5; 100.0)	76/81	93.8	(86.2; 98.0)
Anti-Polio 1 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
Anti-Polio 2 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	84/84	100	(95.7; 100.0)	79/81	97.5	(91.4; 99.7)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)

Anti-Polio 3 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	84/84	100	(95.7; 100.0)	81/81	100	(95.5; 100.0)

n: number of subjects experiencing the endpoint listed in the first three columns

M: number of subjects with available data for the relevant endpoint

* Vaccine response is defined as:

If the pre-booster vaccination concentration was < 4xLLOQ, then the post-booster vaccination concentration was >= 4x the pre-booster concentration

If the pre-booster vaccination concentration was >= 4xLLOQ, then the post-booster vaccination concentration was >= 2x the pre-booster concentration

Note: Pre-booster vaccination concentrations <LLOQ were converted to LLOQ for purposes of calculating this booster response

Source: Modified from Section 8, Table 9.19

The trends described in the PPAS for binary endpoints were also observed in the FAS for immunogenicity cohort (Table S5). However, the vaccine response to pertussis antigens tended to be lower in the FAS for immunogenicity cohort compared with the PPAS.

Table S5: Summary of binary endpoints – Pre-dose and post-dose – FAS for immunogenicity cohort

			Group A: SHAN6 and MMR at D0 (N=224)			**Group B: SHAN6 at D0; MMR at D28 (N=226)**		
Antigen	**Timepoint**	**Criteria**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Anti-D (DTP-ECL - IU/mL)	**Pre-dose (V01)**	**>= 0.01 IU/mL**	222/223	99.6	(97.5; 100.0)	223/226	98.7	(96.2; 99.7)
		>= 0.1 IU/mL	179/223	80.3	(74.4; 85.3)	174/226	77	(70.9; 82.3)
		>= 1.0 IU/mL	44/223	19.7	(14.7; 25.6)	31/226	13.7	(9.5; 18.9)
	Post-dose (V02)	**Seroprotection (ie. >= 0.01 IU/mL)**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
		>= 0.1 IU/mL	220/220	100	(98.3; 100.0)	217/219	99.1	(96.7; 99.9)
		>= 1.0 IU/mL	192/220	87.3	(82.1; 91.4)	178/219	81.3	(75.5; 86.2)
Anti-T (DTP-ECL - IU/mL)	**Pre-dose (V01)**	**>= 0.01 IU/mL**	224/224	100	(98.4; 100.0)	226/226	100	(98.4; 100.0)
		>= 0.1 IU/mL	217/224	96.9	(93.7; 98.7)	221/226	97.8	(94.9; 99.3)
		>= 1.0 IU/mL	99/224	44.2	(37.6; 51.0)	106/226	46.9	(40.3; 53.6)
	Post-dose (V02)	**Seroprotection (ie. >= 0.01 IU/mL)**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)

		>= 0.1 IU/mL	220/220	100	(98.3; 100.0)	218/219	99.5	(97.5; 100.0)
		>= 1.0 IU/mL	219/220	99.5	(97.5; 100.0)	216/219	98.6	(96.0; 99.7)
Anti-PT (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	195/224	87.1	(81.9; 91.2)	208/226	92	(87.7; 95.2)
	Post-dose (V02)	**>= 2 EU/mL**	216/220	98.2	(95.4; 99.5)	215/218	98.6	(96.0; 99.7)
	Post-dose (V02) / pre (V01)	**Vaccine response***	167/220	75.9	(69.7; 81.4)	157/218	72	(65.6; 77.9)
		Seroconversion, (ie. >= 4-fold rise)	140/220	63.6	(56.9; 70.0)	147/218	67.4	(60.8; 73.6)
Anti-FIM (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	222/224	99.1	(96.8; 99.9)	222/226	98.2	(95.5; 99.5)
	Post-dose (V02)	**>= 2 EU/mL**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
	Post-dose (V02) / pre (V01)	**Vaccine response***	179/220	81.4	(75.6; 86.3)	177/219	80.8	(75.0; 85.8)
		Seroconversion, (ie. >= 4-fold rise)	167/220	75.9	(69.7; 81.4)	170/219	77.6	(71.5; 83.0)
Anti-PRN (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	172/224	76.8	(70.7; 82.1)	170/226	75.2	(69.1; 80.7)
	Post-dose (V02)	**>= 2 EU/mL**	220/220	100	(98.3; 100.0)	215/219	98.2	(95.4; 99.5)
	Post-dose (V02) / pre (V01)	**Vaccine response***	175/220	79.5	(73.6; 84.7)	170/219	77.6	(71.5; 83.0)
		Seroconversion, (ie. >= 4-fold rise)	171/220	77.7	(71.6; 83.0)	166/219	75.8	(69.6; 81.3)
Anti-FHA (DTP-ECL – EU/mL)	**Pre-dose (V01)**	**>= 2 EU/mL**	214/224	95.5	(91.9; 97.8)	215/226	95.1	(91.5; 97.5)
	Post-dose (V02)	**>= 2 EU/mL**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
	Post-dose (V02) / pre (V01)	**Vaccine response***	172/220	78.2	(72.1; 83.5)	177/219	80.8	(75.0; 85.8)

		Seroconversion, (ie. >= 4-fold rise)	162/220	73.6	(67.3; 79.3)	171/219	78.1	(72.0; 83.4)
Anti-PRP (RIA - µg/mL)	**Pre-dose (V01)**	**>= 0.15 µg/mL**	220/224	98.2	(95.5; 99.5)	223/225	99.1	(96.8; 99.9)
		>= 1 µg/mL	197/224	87.9	(82.9; 91.9)	196/225	87.1	(82.0; 91.2)
	Post-dose (V02)	**Seroprotection (ie. >= 0.15 µg/mL)**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
		>= 1 µg/mL	220/220	100	(98.3; 100.0)	218/219	99.5	(97.5; 100.0)
Anti-HBs (ELISA - mIU/mL)	**Pre-dose (V01)**	**>= 10 mIU/mL**	218/224	97.3	(94.3; 99.0)	218/226	96.5	(93.1; 98.5)
		>= 100 mIU/mL	191/224	85.3	(79.9; 89.6)	191/226	84.5	(79.1; 89.0)
	Post-dose (V02)	**Seroprotection (ie. >= 10 mIU/mL)**	220/220	100	(98.3; 100.0)	218/219	99.5	(97.5; 100.0)
		>= 100 mIU/mL	217/220	98.6	(96.1; 99.7)	213/219	97.3	(94.1; 99.0)
Anti-Polio 1 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	224/224	100	(98.4; 100.0)	225/225	100	(98.4; 100.0)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
Anti-Polio 2 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	224/224	100	(98.4; 100.0)	222/224	99.1	(96.8; 99.9)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)
Anti-Polio 3 (MIT-1/dil)	**Pre-dose (V01)**	**>= 8 (1/dil)**	224/224	100	(98.4; 100.0)	225/225	100	(98.4; 100.0)
	Post-dose (V02)	**Seroprotection (ie. >= 8 (1/dil))**	220/220	100	(98.3; 100.0)	219/219	100	(98.3; 100.0)

n: number of subjects experiencing the endpoint listed in the first three columns

M: number of subjects with available data for the relevant endpoint

* Vaccine response is defined as:

If the pre-booster vaccination concentration was < 4xLLOQ, then the post-booster vaccination concentration was >= 4x the pre-booster concentration

If the pre-booster vaccination concentration was >= 4xLLOQ, then the post-booster vaccination concentration was >= 2x the pre-booster concentration

Note: Pre-booster vaccination concentrations <LLOQ were converted to LLOQ for purposes of calculating this booster response

Source: Modified from Section 8, Table 9.20

Geometric means

At V01, GMCs were generally similar between vaccine groups for each antigen. The GMCs increased between V01 and V02 and were generally similar between vaccine groups at V02. Geometric mean concentrations are summarized in Table S6.

Table S6: Summary of geometric means – Pre-dose and post-dose – PPAS

		Group A: SHAN6 and MMR at D0 (N=84)			Group B: SHAN6 at D0; MMR at D28 (N=81)		
Antigen	**Timepoint**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**
Anti-D (DTP-ECL - IU/mL)	**Pre-dose (V01)**	84	0.263	(0.203; 0.342)	81	0.242	(0.180; 0.325)
	Post-dose (V02)	84	6.48	(5.35; 7.86)	81	5.25	(3.86; 7.14)
	Ratio V02/V01	84	24.6	(19.5; 31.1)	81	21.7	(15.7; 30.1)
Anti-T (DTP-ECL - IU/mL)	**Pre-dose (V01)**	84	0.854	(0.674; 1.08)	81	0.832	(0.656; 1.05)
	Post-dose (V02)	84	17.4	(15.5; 19.4)	81	14.3	(11.3; 18.1)
	Ratio V02/V01	84	20.3	(15.7; 26.4)	81	17.2	(12.4; 23.8)
Anti-PT (DTP-ECL – EU/mL)	**Pre-dose (V01)**	84	15.8	(11.1; 22.5)	81	14.3	(10.5; 19.4)
	Post-dose (V02)	84	154	(112; 210)	81	129	(93.4; 178)
	Ratio V02/V01	84	9.7	(7.21; 13.1)	81	9.02	(6.65; 12.2)
Anti-FIM (DTP-ECL – EU/mL)	**Pre-dose (V01)**	84	125	(99.3; 157)	81	103	(77.2; 138)
	Post-dose (V02)	84	1992	(1689; 2350)	81	1738	(1333; 2267)
	Ratio V02/V01	84	16	(12.7; 20.0)	81	16.8	(12.5; 22.7)
Anti-PRN (DTP-ECL – EU/mL)	**Pre-dose (V01)**	84	4.33	(3.38; 5.57)	81	4.27	(3.26; 5.60)
	Post-dose (V02)	84	81.6	(63.1; 105)	81	59.6	(42.1; 84.3)

	Ratio V02/V01	84	18.8	(15.0; 23.7)	81	14	(9.76; 20.0)
Anti-FHA (DTP-ECL – EU/mL)	**Pre-dose (V01)**	84	7.99	(6.38; 10.0)	81	7.61	(6.00; 9.66)
	Post-dose (V02)	84	106	(86.7; 128)	81	90.3	(70.1; 116)
	Ratio V02/V01	84	13.2	(10.8; 16.2)	81	11.9	(9.20; 15.3)
Anti-PRP (PRP-RIA - µg/mL)	**Pre-dose (V01)**	84	5.94	(4.32; 8.16)	81	6.91	(4.72; 10.1)
	Post-dose (V02)	84	128	(104; 156)	81	127	(98.1; 164)
	Ratio V02/V01	84	21.5	(15.0; 30.8)	81	18.4	(12.1; 27.9)
Anti-HBs (ELISA - mIU/mL)	**Pre-dose (V01)**	84	503	(354; 716)	81	335	(225; 497)
	Post-dose (V02)	84	14140	(10337; 19342)	81	8821	(5729; 13583)
	Ratio V02/V01	84	28.1	(21.4; 36.8)	81	26.4	(17.8; 39.2)
Anti-Polio 1 (MIT-1/dil)	**Pre-dose (V01)**	84	783	(628; 977)	81	613	(504; 746)
	Post-dose (V02)	84	2908	(2405; 3516)	81	2269	(1853; 2780)
	Ratio V02/V01	84	3.71	(2.88; 4.79)	81	3.7	(2.83; 4.84)
Anti-Polio 2 (MIT-1/dil)	**Pre-dose (V01)**	84	167	(137; 205)	81	139	(105; 185)
	Post-dose (V02)	84	2337	(1898; 2878)	81	1704	(1296; 2241)
	Ratio V02/V01	84	14	(10.9; 17.9)	81	12.2	(8.93; 16.7)
Anti-Polio 3 (MIT-1/dil)	**Pre-dose (V01)**	84	751	(594; 950)	81	626	(480; 816)
	Post-dose (V02)	84	6062	(4952; 7420)	81	6586	(5251; 8260)
	Ratio V02/V01	84	8.07	(5.76; 11.3)	81	10.5	(7.70; 14.4)

M: number of subjects with available data for the relevant endpoint
Source: Modified from Section 8, Table 9.21

The trends described in the PPAS for GMCs were also observed in the FAS for immunogenicity cohort (Table S7). However, post-dose GMCs and/or post-dose/pre-dose ratios tended to be lower than in the PPAS for most antigens.

Table S7: Summary of geometric means – Pre-dose and post-dose – FAS for immunogenicity cohort

		Group A: SHAN6 and MMR at D0 (N=224)			Group B: SHAN6 at D0; MMR at D28 (N=226)		
Antigen	**Timepoint**	**M**	**GM**	**(95% CI)**	**M**	**GM**	**(95% CI)**
Anti-D (DTP-ECL - IU/mL)	**Pre-dose (V01)**	223	0.32	(0.268; 0.382)	226	0.269	(0.225; 0.322)
	Post-dose (V02)	220	4.52	(3.90; 5.24)	219	4.28	(3.60; 5.09)
	Ratio V02/V01	219	13.8	(11.2; 17.0)	219	15.7	(12.5; 19.6)
Anti-T (DTP-ECL - IU/mL)	**Pre-dose (V01)**	224	0.994	(0.841; 1.18)	226	1.03	(0.883; 1.21)
	Post-dose (V02)	220	12.7	(11.4; 14.1)	219	12.9	(11.4; 14.6)
	Ratio V02/V01	220	12.7	(10.3; 15.7)	219	12.1	(9.77; 15.1)
Anti-PT (DTP-ECL – EU/mL)	**Pre-dose (V01)**	224	17.3	(14.2; 21.0)	226	18	(15.1; 21.4)
	Post-dose (V02)	220	112	(92.6; 135)	218	93.9	(76.9; 115)
	Ratio V02/V01	220	6.55	(5.33; 8.05)	218	5.27	(4.26; 6.53)
Anti-FIM (DTP-ECL – EU/mL)	**Pre-dose (V01)**	224	171	(144; 203)	226	129	(106; 157)
	Post-dose (V02)	220	1706	(1517; 1919)	219	1438	(1247; 1658)
	Ratio V02/V01	220	9.85	(8.08; 12.0)	219	11.1	(8.86; 13.8)
Anti-PRN (DTP-ECL – EU/mL)	**Pre-dose (V01)**	224	7.22	(5.82; 8.96)	226	6.65	(5.34; 8.28)
	Post-dose (V02)	220	89.1	(77.7; 102)	219	75	(64.0; 87.8)
	Ratio V02/V01	220	12	(9.79; 14.6)	219	11.1	(8.94; 13.9)
Anti-FHA (DTP-ECL – EU/mL)	**Pre-dose (V01)**	224	11.1	(9.31; 13.2)	226	10.5	(8.82; 12.4)

	Post-dose (V02)	220	91.6	(81.2; 103)	219	93.9	(83.2; 106)
	Ratio V02/V01	220	8.2	(6.87; 9.79)	219	9.09	(7.64; 10.8)
Anti-PRP (PRP-RIA - µg/mL)	**Pre-dose (V01)**	224	8.72	(6.81; 11.2)	225	10.5	(8.11; 13.5)
	Post-dose (V02)	220	119	(103; 137)	219	141	(122; 162)
	Ratio V02/V01	220	13.4	(10.4; 17.3)	218	12.9	(9.83; 17.0)
Anti-HBs (ELISA - mIU/mL)	**Pre-dose (V01)**	224	406	(332; 497)	226	390	(315; 483)
	Post-dose (V02)	220	8084	(6569; 9948)	219	7705	(6080; 9765)
	Ratio V02/V01	220	20	(15.8; 25.3)	219	19.9	(15.6; 25.5)
Anti-Polio 1 (MIT-1/dil)	**Pre-dose (V01)**	224	734	(643; 838)	225	659	(580; 749)
	Post-dose (V02)	220	2244	(1992; 2528)	219	1892	(1678; 2133)
	Ratio V02/V01	220	3.06	(2.58; 3.63)	218	2.92	(2.47; 3.46)
Anti-Polio 2 (MIT-1/dil)	**Pre-dose (V01)**	224	185	(159; 216)	224	173	(148; 202)
	Post-dose (V02)	220	1661	(1423; 1938)	219	1455	(1243; 1703)
	Ratio V02/V01	220	8.71	(6.95; 10.9)	217	8.53	(6.92; 10.5)
Anti-Polio 3 (MIT-1/dil)	**Pre-dose (V01)**	224	807	(690; 943)	225	824	(705; 964)
	Post-dose (V02)	220	5131	(4486; 5868)	219	5729	(5035; 6518)
	Ratio V02/V01	220	6.31	(5.12; 7.77)	218	7.1	(5.76; 8.75)

M: number of subjects with available data for the relevant endpoint

Source: Modified from Section 8, Table 9.22

Secondary objective: immune response to co-administered measles, mumps, and rubella vaccine in terms of seroconversion

At V01, the percentages of subjects with anti-measles, anti-mumps, and anti-rubella ≥ LLOQ were high (≥ 88.1%) and similar in both vaccine groups. The geometric means for MMR antigens

were similar in both vaccine groups. Twenty-eight days after injection, subjects showed an immune response to the measles and mumps antigens of the MMR vaccine, independently of the concomitant administration with SHAN6. The post-dose/pre-dose ratios were similar between vaccine groups: 2.34 (95% CI: 1.87; 2.94) in Group A and 2.64 (95% CI: 2.15; 3.24) in Group B for measles, 7.45 (95% CI: 5.44; 10.2) in Group A and 6.25 (95% CI: 4.51; 8.65) in Group B for mumps, and 1.35 (95% CI: 0.981; 1.85) in Group A and 1.23 (95% CI: 0.918; 1.64) in Group B for rubella.

Secondary objective: antibody persistence of SHAN6 or Shan 5 + ShanIPV at 12-24 months of age following a 3-dose primary series

The percentages of subjects with titers ≥ 0.01 IU/mL for anti-D and anti-T, ≥ 0.15 µg/mL for anti-PRP, ≥ 10 mIU/mL for anti-HBs, and ≥ 8 (1/dil) for anti-polio 1, 2, and 3 at V01 were high (≥ 96.8%) and similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV for each antigen. The percentages of subjects with anti-PT, anti-PRN, and anti-FHA titers ≥ 2 EU/mL at

V01 were similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV; they ranged between 75.5% and 97.3%. The percentage of subjects with anti-FIM titers ≥ 2 EU/mL at V01 was slightly higher in subjects primed with SHAN6 (99.7% [95% CI: 98.4; 100.0]) than Shan 5 + ShanIPV (95.5% [95% CI: 89.8; 98.5]).

The geometric means at V01 were similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV for each antigen, except for anti-polio 3: the geometric mean was higher in subjects primed with SHAN6 (877 [1/dil] [95% CI: 774; 994]) than Shan 5 + ShanIPV (653 [1/dil] [95% CI: 519; 822]).

Secondary objective: immunogenicity profile of SHAN6 when administered concomitantly or without measles, mumps, and rubella vaccine, in subjects primed with SHAN6 and in subjects primed with Shan 5 + ShanIPV

The percentages of subjects with titers meeting the seroprotection thresholds (≥ 0.01 IU/mL for D and T, ≥ 0.15 µg/mL for PRP, ≥ 10 mIU/mL for HBs, and ≥ 8 [1/dil] for polio 1, 2 and 3) post-dose were high (≥ 99.7%) and similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV for each antigen. The percentages of subjects with titers meeting higher thresholds (≥ 0.1 IU/mL and ≥ 1.0 IU/mL for D and T, ≥ 1 µg/mL for PRP, and ≥ 100 mIU/mL for HBs) were also similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV. The percentages of subjects with vaccine response against pertussis antigens post-dose were similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV; they ranged between 72.0% and 84.3%. The percentages of subjects with seroconversion against pertussis antigens post-dose were similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV; they ranged between 59.8% and 80.6%.

Post-dose geometric means were similar in subjects primed with SHAN6 and with Shan 5 + ShanIPV for each antigen, except for FHA: the geometric mean was lower in subjects primed with SHAN6 (86.9 EU/mL [95% CI: 78.8; 95.9]) than Shan 5 + ShanIPV (113 EU/mL [95% CI: 95.7; 134]).

Safety Results:

An overview of safety after vaccine injection for subjects in the SafAS is presented in Table S8.

No immediate unsolicited AEs were reported within 30 minutes after SHAN6 injection.

Solicited injection site reactions were reported within 7 days after SHAN6 injection in 136 (41.0%) subjects in Group A and 129 (38.6%) subjects in Group B. Most were of Grade 1 intensity. Grade 3 solicited injection site reactions were reported in 13 (3.9%) subjects in Group A and 12 (3.6%) subjects in Group B. Injection site tenderness was the most frequently observed injection site reaction within 7 days after SHAN6 injection, followed by injection site swelling and injection site erythema in both vaccine groups. Injection site tenderness was reported in 128 (38.6%) subjects in Group A and 121 (36.2%) subjects in Group B.

Solicited systemic reactions were reported within 7 days after vaccination (SHAN6 and MMR on Day 0 in Group A, SHAN6 on Day 0 in Group B) in 120 (36.6%) subjects in Group A and 109 (32.6%) subjects in Group B. Most were of Grade 1 intensity. Grade 3 solicited systemic reactions were reported in 3 (0.9%) subjects in Group A and 1 (0.3%) subject in Group B. Irritability was the most frequently observed solicited systemic reactions within 7 days after vaccine injection (71 [21.4%] subjects in Group A and 65 [19.5%] subjects in Group B), followed by fever (67 [20.2%] subjects in Group A and 58 [17.4%] subjects in Group B) and appetite loss (34 [10.2%] subjects in Group A and 29 [8.7%] subjects in Group B).

Unsolicited AEs were reported within 28 days after SHAN6 injection in 8 (2.4%) subjects in Group A and 5 (1.5%) subjects in Group B. One (0.3%) subject in Group A experienced an unsolicited adverse reaction reported as an SAE (febrile convulsion).

During the study, SAEs were reported in 2 (0.6%) subjects in Group A (febrile convulsions, also reported as AESIs) and no subjects in Group B. No AE leading to study discontinuation and no death were reported during the study.

Table S8: Safety overview after any vaccine injections – Safety Analysis Set

	Group A: SHAN6 and MMR at D0 (N=336)			**Group B: SHAN6 at D0; MMR at D28 (N=340)**			**All (N=676)**		
Period/ Subjects experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 28 days after injection									
Immediate unsolicited systemic AE	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
Immediate unsolicited systemic AR	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
Solicited reaction	162/332	48.8	(43.3; 54.3)	157/334	47.0	(41.6; 52.5)	319/666	47.9	(44.0; 51.8)
Solicited injection site reaction	136/332	41.0	(35.6; 46.5)	129/334	38.6	(33.4; 44.1)	265/666	39.8	(36.0; 43.6)
Solicited systemic reaction	120/332	36.1	(31.0; 41.6)	109/334	32.6	(27.6; 38.0)	229/666	34.4	(30.8; 38.1)
Unsolicited AE	8/336	2.4	(1.0; 4.6)	5/340	1.5	(0.5; 3.4)	13/676	1.9	(1.0; 3.3)
Unsolicited AR	1/336	0.3	(0.0; 1.6)	0/340	0.0	(0.0; 1.1)	1/676	0.1	(0.0; 0.8)
Unsolicited non-serious AE	6/336	1.8	(0.7; 3.8)	5/340	1.5	(0.5; 3.4)	11/676	1.6	(0.8; 2.9)
Unsolicited non-serious AR	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)

	Group A: SHAN6 and MMR at D0 (N=336)			Group B: SHAN6 at D0; MMR at D28 (N=340)			All (N=676)		
Unsolicited non-serious injection site AR	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
Unsolicited non-serious systemic AE	6/336	1.8	(0.7; 3.8)	5/340	1.5	(0.5; 3.4)	11/676	1.6	(0.8; 2.9)
Unsolicited non-serious systemic AR	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
SAE	2/336	0.6	(0.1; 2.1)	0/340	0.0	(0.0; 1.1)	2/676	0.3	(0.0; 1.1)
AESI	2/336	0.6	(0.1; 2.1)	0/340	0.0	(0.0; 1.1)	2/676	0.3	(0.0; 1.1)
Death	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
AE leading to study discontinuation*	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
During the study period									
SAE	2/336	0.6	(0.1; 2.1)	0/340	0.0	(0.0; 1.1)	2/676	0.3	(0.0; 1.1)
AESI	2/336	0.6	(0.1; 2.1)	0/340	0.0	(0.0; 1.1)	2/676	0.3	(0.0; 1.1)
Death	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)
AE leading to study discontinuation*	0/336	0.0	(0.0; 1.1)	0/340	0.0	(0.0; 1.1)	0/676	0.0	(0.0; 0.5)

n: number of subjects experiencing the endpoint listed in the first column
M: number of subjects with available data for the relevant endpoint
* Identified in the termination form as SAE or other AE
Source: Section 8, Table 9.63

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