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| Study No.: 113866 (FLU D-PAN H1N1-AS03-033) |
| Title: Safety and immunogenicity study of GSK Biologicals' influenza vaccine GSK2340272A in adults aged 18 to 60 years. GSK2340272A (Flu 1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain adjuvanted with AS03. |
| Rationale: The aim of the study was to assess the safety and immunogenicity of Flu 1 vaccine as compared to GSK2340269A. GSK2340269A (Flu 2): GSK Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain without adjuvant. This summary presents results up to Day 42 and will be updated when additional data become available. |
| Phase: III |
| Study Period: 07 October 2009 to 10 December 2009 (data lock point Day 42) |
| Study Design: Randomised (1:1) observer-blind study with 2 parallel groups. Subjects were further stratified by age (18-40 years, 41-50 years and 51-60 years in the ratio 2:1:1) |
| Centres: 1 centre in Belgium. |
| Indication: Immunization against A/California/7/2009 (H1N1)v-like influenza in male and female subjects aged 18 to 60 years. |
| Treatment: Study groups were as follows: <ul style="list-style-type: none"> • Flu 1 Group: subjects received two doses of Flu 1 vaccine. • Flu 2 Group: subjects received two doses of Flu 2 vaccine. Vaccines were given intramuscularly in the deltoid region of the non-dominant arm at Day 0 and of the dominant arm at Day 21. |
| Objectives: To assess the haemagglutination-inhibition (HI) immune response to the vaccine homologous virus induced by vaccination with 2 doses of the Flu 1 or the Flu 2 vaccine in terms of European Medicines Agency (EMA) (Committee for Medicinal Products for Human Use [CHMP]) guidance targets for pandemic vaccine seroconversion rate (SCR), seroprotection rate (SPR), and geometric mean fold rise (GMFR) at 21 days after the first dose of H1N1 vaccine in adults 18 to 60 years of age. |
| Primary Outcome/Efficacy Variable: <i>Humoral immune response in terms of vaccine HI antibodies in subjects from each vaccine group against A/California/7/2009 (H1N1)v-like virus</i> The following parameters were calculated with 95% confidence intervals (CIs): <ul style="list-style-type: none"> • SCR* at 21 days after the first dose of study vaccine (Day 21) • SPR** at 21 days after the first dose of H1N1 study vaccine (Day 21) • GMFR*** at 21 days after the first dose of H1N1 study vaccine (Day 21). *SCR was defined as the percentage of vaccinees that had either a pre-vaccination titre < 1:10 and a post-vaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre. The CHMP criterion was fulfilled if the point estimate for SCR was > 40% in subjects 18 to 60 years of age. **SPR was defined as the percentage of vaccinees with a serum HI titre ≥ 1:40, that usually is accepted as indicating protection. The CHMP criterion was fulfilled if the post-vaccination time point estimate for SPR was > 70% in subjects 18 to 60 years of age. ***GMFR, also called seroconversion factor (SCF) was defined as the fold increase in serum HI geometric mean titres (GMTs) post-vaccination compared to pre-vaccination. The criterion was fulfilled if the point estimate for SCF was > 2.5 in subjects 18 to 60 years of age. |
| Secondary Outcome/Efficacy Variable(s): <i>Humoral immune response in terms of H1N1 HI antibodies in subjects from each vaccine group against A/California/7/2009 (H1N1)v-like virus,</i> The following parameters were calculated with 95% CIs: <ul style="list-style-type: none"> • GMTs and seropositivity rates on Days 0, 21, 42, 182[#], and 364[#] • SCR* on Days 42, 182[#] and 364[#] • SPR* on Days 0, 42, 182[#] and 364[#] |

- SCF* on Days 42, 182[#] and 364[#].

* Criteria for evaluation were the same as those presented in the primary outcome section
The same analyses as above were performed for each age stratum.

Humoral immune response in terms of neutralising antibodies against A/California/7/2009 (H1N1)v-like (in a subset of half of the subjects randomly selected)

The following parameters were calculated with 95% CIs: §

- GMTs of serum neutralising antibody titres on Days 0, 21, 42, 182 and 364
- SCRs* on Days 21, 42, 182 and 364.

*SCR was defined as the percentage of vaccinees that had a 4-fold increase between pre- and post-vaccination titres.

Safety:

- Occurrence, duration and intensity of each solicited local symptom within 7 days (Day 0 to Day 6) after each vaccination.
- Occurrence, duration, intensity and relation to vaccination of each solicited general symptom within seven days (Day 0 to Day 6) after each vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited adverse events (AEs) within 21 days after the first vaccination (Day 0 to Day 20), and 63 days after the second vaccination[#] (Day 21 to Day 83), according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence and relationship to vaccination of AEs of specific interest (AESIs) / potential Immune-Mediated Disease (pIMDs) and serious adverse events (SAEs) during the entire study period (up to Day 364) [#].

[#]At the time of writing this summary, data were available up to Day 42 only. This summary will be updated when additional results become available.

§ Not available at the time of writing this summary.

Statistical Methods:

Analyses were performed on the Total Vaccinated cohort and the According-To-Protocol (ATP) cohort of immunogenicity.

- The Total Vaccinated cohort included all vaccinated subjects.
- The ATP cohort of immunogenicity included all evaluable subjects (i.e., those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study), who received 2 vaccine doses and for whom assay results were available for antibodies against H1N1 antigen for the blood sample taken 21 days after each vaccine dose.

Analysis of immunogenicity:

The analysis was done on the ATP cohort of immunogenicity.

Point estimate for SCR, SPR, SCF and the associated 95% CIs was computed on Day 21 after the first dose. If the point estimate for SCR \geq 40% and SPR \geq 70%, the CHMP criteria for SCR and SPR are met, and if the SCF is greater 2.5, the study primary objectives are met.

The analysis of immunogenicity was done as a descriptive analysis of the humoral immune response in adults 18 to 60 years of age and for each age group (18-40 years, 41-50 years and 51-60 years). For the humoral immune response in terms of H1N1 HI antibodies (with 95% CIs), the following parameters were calculated:

- GMTs of H1N1 HI antibody titres at Day 0, 21 and 42
- SCR at Days 21 and 42
- SCF at Days 21 and 42
- SPR at Days 0, 21 and 42

Analysis of safety:

The analysis was based on the Total Vaccinated cohort.

The incidence of solicited local and general symptoms occurring during the 7 days after each vaccination was tabulated with exact 95% CI for each treatment group. The same calculations were performed for Grade 3 symptoms, as well as for solicited general symptoms assessed by the investigator as related to vaccination. All solicited local AEs were deemed causally related to vaccination.

The percentage of subjects with at least one report of an unsolicited AE classified by MedDRA Preferred Term up to 42 days after first dose was tabulated with exact 95% CI for each treatment group. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigators as possibly related to vaccination.

SAEs and AESIs/ pIMDs were collected and summarized through the entire follow-up period[#].

[#]At the time of writing this summary, data were available up to Day 42 only. This summary will be updated when additional results become available.

Study Population: Healthy male or female adults 18 to 60 years of age at the time of first vaccination. Women were to be of non-childbearing potential or if of childbearing potential, had to practice adequate contraception for 30 days prior to vaccination, to have a negative pregnancy test, and to continue such precautions during the entire treatment period and for 2 months after completion of the vaccination series. A written informed consent was obtained from the subjects prior to study entry.

| Number of Subjects: | Flu 1 Group | | | Flu 2 Group | | |
|---|----------------|----------------|----------------|----------------|----------------|----------------|
| | 18-40Y | 41-50Y | 51-60Y | 18-40Y | 41-50Y | 51-60Y |
| Planned, N | 64 | | | 64 | | |
| Randomised, N (Total Vaccinated cohort) | 32 | 16 | 17 | 33 | 17 | 16 |
| Completed to Day 42, n (%) | 32 (100) | 16 (100) | 17 (100) | 33 (100) | 17 (100) | 16 (100) |
| Total Number Subjects Withdrawn, n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Withdrawn due to Adverse Events n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Withdrawn due to Lack of Efficacy n (%) | Not Applicable | Not Applicable | Not Applicable | Not applicable | Not Applicable | Not Applicable |
| Withdrawn for other reasons n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Demographics | Flu 1 Group | | | Flu 2 Group | | |
| | 18-40Y | 41-50Y | 51-60Y | 18-40Y | 41-50Y | 51-60Y |
| N (Total Vaccinated cohort) | 32 | 16 | 17 | 33 | 17 | 16 |
| Females: Males | 22:10 | 12:4 | 9:8 | 18:15 | 11:6 | 6:10 |
| Mean Age, years (SD) | 23.9 (4.75) | 46.1 (2.31) | 54.8 (2.63) | 26.2 (5.45) | 44.9 (2.69) | 56.5 (2.97) |
| White-Caucasian/European heritage, n(%) | 32 (100) | 16 (100) | 17 (100) | 33 (100) | 16 (94.1) | 16 (100) |

18-40Y = subjects aged 18 to 40 years
41-50Y = subjects aged 41 to 50 years
51-60Y = subjects aged 51 to 60 years

Primary Efficacy Results: Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab for subjects aged between and including 18-60 years (ATP cohort of immunogenicity)

| | | | | | SCR | | | |
|-----------------------|----------|-----------|----------|------|------|------|--------|------|
| | | | | | | | 95% CI | |
| Strain | Group | Sub-group | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PI(D21) | 35 | 31 | 88.6 | 73.3 | 96.8 |
| | | | PII(D42) | 35 | 35 | 100 | 90.0 | 100 |
| | | S+ | PI(D21) | 29 | 29 | 100 | 88.1 | 100 |
| | | | PII(D42) | 29 | 29 | 100 | 88.1 | 100 |
| | | Total | PI(D21)* | 64 | 60 | 93.8 | 84.8 | 98.3 |
| | PII(D42) | | 64 | 64 | 100 | 94.4 | 100 | |
| | Flu 2 | S- | PI(D21) | 43 | 27 | 62.8 | 46.7 | 77.0 |
| | | | PII(D42) | 43 | 36 | 83.7 | 69.3 | 93.2 |
| | | S+ | PI(D21) | 20 | 17 | 85.0 | 62.1 | 96.8 |
| | | | PII(D42) | 20 | 18 | 90.0 | 68.3 | 98.8 |
| Total | | PI(D21)* | 63 | 44 | 69.8 | 57.0 | 80.8 | |
| | PII(D42) | 63 | 54 | 85.7 | 74.6 | 93.3 | | |

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination

S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination

Seroconversion defined as:

For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination

For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre

N = Number of subjects with pre- and post-vaccination results available

n (%) = Number (percentage) of seroconverted subjects

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

PI(D21)= post-dose 1, Day 21

PII(D42)=post-dose 2, Day 42

* Primary results

Primary Efficacy Results: Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) for all subjects aged between and including 18-60 years (ATP cohort of immunogenicity)

| | | | | | SPR | | | |
|-----------------------|-------|-----------------|----------|----|-----|------|--------|------|
| | | | | | | | 95% CI | |
| Strain | Group | Pre-vacc status | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PRE | 35 | 0 | 0.0 | 0.0 | 10.0 |
| | | | PI(D21) | 35 | 31 | 88.6 | 73.3 | 96.8 |
| | | | PII(D42) | 35 | 35 | 100 | 90.0 | 100 |
| | | S+ | PRE | 29 | 7 | 24.1 | 10.3 | 43.5 |
| | | | PI(D21) | 29 | 29 | 100 | 88.1 | 100 |
| | | | PII(D42) | 29 | 29 | 100 | 88.1 | 100 |
| | | Total | PRE | 64 | 7 | 10.9 | 4.5 | 21.2 |
| | | | PI(D21)* | 64 | 60 | 93.8 | 84.8 | 98.3 |
| | | | PII(D42) | 64 | 64 | 100 | 94.4 | 100 |
| | Flu 2 | S- | PRE | 43 | 0 | 0.0 | 0.0 | 8.2 |
| | | | PI(D21) | 43 | 27 | 62.8 | 46.7 | 77.0 |
| | | | PII(D42) | 43 | 36 | 83.7 | 69.3 | 93.2 |
| | | S+ | PRE | 20 | 6 | 30.0 | 11.9 | 54.3 |
| | | | PI(D21) | 20 | 19 | 95.0 | 75.1 | 99.9 |
| | | | PII(D42) | 20 | 20 | 100 | 83.2 | 100 |
| | | Total | PRE | 63 | 6 | 9.5 | 3.6 | 19.6 |
| | | | PI(D21)* | 63 | 46 | 73.0 | 60.3 | 83.4 |
| | | | PII(D42) | 63 | 56 | 88.9 | 78.4 | 95.4 |

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
N = Number of subjects with available results
n (%) = Number (percentage) of seroprotected subjects (HI titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination, Day 0
PI(D21)= Post-dose 1, Day 21
PII(D42)= Post-dose 2, Day 42
* Primary results

Primary Efficacy Results: Geometric mean fold rise (GMFR) for HI antibody titre against Flu A/CAL/7/09.HA1 Ab (H1N1) for subjects in the age group 18-60 years (ATP cohort of immunogenicity)

| | | | | | GMFR | | |
|-------------------------------|-------|-----------|----------|----|--------|------|-------|
| | | | | | 95% CI | | |
| Vaccine strain | Group | Sub-group | Timing | N | Value | LL | UL |
| Flu A/CAL/7/09.HA1 Ab (1/DIL) | Flu 1 | S- | PI(D21) | 35 | 47.1 | 30.8 | 72.0 |
| | | | PII(D42) | 35 | 105.0 | 80.4 | 137.1 |
| | | S+ | PI(D21) | 29 | 41.3 | 28.6 | 59.8 |
| | | | PII(D42) | 29 | 45.5 | 32.2 | 64.1 |
| | | Total | PI(D21)* | 64 | 44.4 | 33.6 | 58.7 |
| | | | PII(D42) | 64 | 71.9 | 57.0 | 90.7 |
| | Flu 2 | S- | PI(D21) | 43 | 12.0 | 7.6 | 18.9 |
| | | | PII(D42) | 43 | 21.4 | 14.8 | 30.9 |
| | | S+ | PI(D21) | 20 | 10.4 | 5.9 | 18.3 |
| | | | PII(D42) | 20 | 12.0 | 7.6 | 18.9 |
| | | Total | PI(D21)* | 63 | 11.4 | 8.1 | 16.3 |
| | | | PII(D42) | 63 | 17.8 | 13.3 | 23.8 |

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
N = Number of subjects with pre- and post-vaccination results available
GMFR = geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21)= Post-dose 1, Day 21
PII(D42)= Post-dose 2, Day 42

| * Primary results | | | | | | | | | | | | |
|--|--------|-----------------|-----------------|----------|--------|------|------|--------|-------|--------|--------|--------|
| Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) by pre-vaccination status for all subjects aged between and including 18-60 years (ATP cohort of immunogenicity) | | | | | | | | | | | | |
| | | | | | ≥ 1:10 | | | GMT | | | | |
| | | | | | | | | 95% CI | | 95% CI | | |
| Antibody | Group | Pre-vacc status | Timing | N | n | % | LL | UL | value | LL | UL | |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PRE | 35 | 0 | 0.0 | 0.0 | 10.0 | 5.0 | 5.0 | 5.0 | |
| | | | PI(D21) | 35 | 35 | 100 | 90.0 | 100 | 235.4 | 153.8 | 360.1 | |
| | | | PII(D42) | 35 | 35 | 100 | 90.0 | 100 | 525.0 | 402.2 | 685.5 | |
| | | S+ | PRE | 29 | 29 | 100 | 88.1 | 100 | 20.9 | 14.9 | 29.2 | |
| | | | PI(D21) | 29 | 29 | 100 | 88.1 | 100 | 863.0 | 651.4 | 1143.2 | |
| | | | PII(D42) | 29 | 29 | 100 | 88.1 | 100 | 949.4 | 748.2 | 1204.8 | |
| | | Total | PRE | 64 | 29 | 45.3 | 32.8 | 58.3 | 9.6 | 7.6 | 12.0 | |
| | | | PI(D21) | 64 | 64 | 100 | 94.4 | 100 | 424.0 | 312.4 | 575.5 | |
| | | | PII(D42) | 64 | 64 | 100 | 94.4 | 100 | 686.7 | 567.0 | 831.7 | |
| | Flu 2 | S- | PRE | 43 | 0 | 0.0 | 0.0 | 8.2 | 5.0 | 5.0 | 5.0 | |
| | | | PI(D21) | 43 | 38 | 88.4 | 74.9 | 96.1 | 59.8 | 37.8 | 94.6 | |
| | | | PII(D42) | 43 | 42 | 97.7 | 87.7 | 99.9 | 106.9 | 73.9 | 154.7 | |
| | | S+ | PRE | 20 | 20 | 100 | 83.2 | 100 | 25.9 | 16.8 | 39.7 | |
| | | | PI(D21) | 20 | 20 | 100 | 83.2 | 100 | 269.4 | 136.7 | 530.9 | |
| | | | PII(D42) | 20 | 20 | 100 | 83.2 | 100 | 309.1 | 174.1 | 548.7 | |
| Total | | PRE | 63 | 20 | 31.7 | 20.6 | 44.7 | 8.4 | 6.7 | 10.6 | | |
| | | PI(D21) | 63 | 58 | 92.1 | 82.4 | 97.4 | 96.4 | 64.0 | 145.3 | | |
| | | PII(D42) | 63 | 62 | 98.4 | 91.5 | 100 | 149.7 | 108.0 | 207.7 | | |
| <p>S- = seronegative subjects (antibody titre < 1:10) prior to vaccination S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with pre-vaccination results available n (%) = number (percentage) of subjects with titre within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE =Pre-vaccination, Day 0 PI(D21) = Post-dose 1, Day 21 PII(D42) = Post-dose 2, Day 42</p> | | | | | | | | | | | | |
| Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) by pre-vaccination status for the subjects aged between and including 18-40 years and 41-60 years (ATP cohort of immunogenicity) | | | | | | | | | | | | |
| | | | | | ≥ 1:10 | | | GMT | | | | |
| | | | | | | | | 95% CI | | 95% CI | | |
| Antibody | Group | Sub-group | Pre-vacc status | Timing | N | n | % | LL | UL | value | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | 18-40Y | S- | PRE | 15 | 0 | 0.0 | 0.0 | 21.8 | 5.0 | 5.0 | 5.0 |
| | | | | PI(D21) | 15 | 15 | 100 | 78.2 | 100 | 452.7 | 281.3 | 728.5 |
| | | | | PII(D42) | 15 | 15 | 100 | 78.2 | 100 | 686.0 | 476.7 | 987.3 |
| | | | S+ | PRE | 17 | 17 | 100 | 80.5 | 100 | 27.6 | 16.1 | 47.3 |
| | | | | PI(D21) | 17 | 17 | 100 | 80.5 | 100 | 1044.0 | 776.7 | 1403.4 |
| | | | | PII(D42) | 17 | 17 | 100 | 80.5 | 100 | 1132.6 | 874.0 | 1467.8 |
| | | Total | PRE | 32 | 17 | 53.1 | 34.7 | 70.9 | 12.4 | 8.2 | 18.7 | |
| | | | PI(D21) | 32 | 32 | 100 | 89.1 | 100 | 705.7 | 523.8 | 950.7 | |
| | | | PII(D42) | 32 | 32 | 100 | 89.1 | 100 | 895.4 | 714.7 | 1121.8 | |
| | 41-60Y | S- | PRE | 20 | 0 | 0.0 | 0.0 | 16.8 | 5.0 | 5.0 | 5.0 | |
| | | | PI(D21) | 20 | 20 | 100 | 83.2 | 100 | 144.1 | 79.6 | 260.9 | |
| | | | PII(D42) | 20 | 20 | 100 | 83.2 | 100 | 429.6 | 293.7 | 628.6 | |

| | | | | | | | | | | | | |
|-------|--------|----------|----------|----------|------|------|------|-------|-------|-------|-------|--------|
| | Flu 2 | 18-40Y | S+ | PRE | 12 | 12 | 100 | 73.5 | 100 | 14.0 | 11.7 | 16.9 |
| | | | | PI(D21) | 12 | 12 | 100 | 73.5 | 100 | 658.9 | 376.7 | 1152.4 |
| | | | | PII(D42) | 12 | 12 | 100 | 73.5 | 100 | 739.5 | 469.2 | 1165.3 |
| | | | Total | PRE | 32 | 12 | 37.5 | 21.1 | 56.3 | 7.4 | 6.1 | 8.9 |
| | | | | PI(D21) | 32 | 32 | 100 | 89.1 | 100 | 254.8 | 156.7 | 414.4 |
| | | | | PII(D42) | 32 | 32 | 100 | 89.1 | 100 | 526.7 | 393.1 | 705.6 |
| | | | S- | PRE | 18 | 0 | 0.0 | 0.0 | 18.5 | 5.0 | 5.0 | 5.0 |
| | | | | PI(D21) | 18 | 17 | 94.4 | 72.7 | 99.9 | 98.8 | 49.8 | 196.0 |
| | | | | PII(D42) | 18 | 18 | 100 | 81.5 | 100 | 131.8 | 75.3 | 230.6 |
| | S+ | PRE | | 13 | 13 | 100 | 75.3 | 100 | 32.2 | 17.7 | 58.5 | |
| | | PI(D21) | | 13 | 13 | 100 | 75.3 | 100 | 365.8 | 146.6 | 913.0 | |
| | | PII(D42) | | 13 | 13 | 100 | 75.3 | 100 | 429.1 | 205.8 | 894.6 | |
| | Total | PRE | 31 | 13 | 41.9 | 24.5 | 60.9 | 10.9 | 7.2 | 16.5 | | |
| | | PI(D21) | 31 | 30 | 96.8 | 83.3 | 99.9 | 171.1 | 96.7 | 302.8 | | |
| | | PII(D42) | 31 | 31 | 100 | 88.8 | 100 | 216.2 | 134.8 | 346.8 | | |
| | 41-60Y | S- | PRE | 25 | 0 | 0.0 | 0.0 | 13.7 | 5.0 | 5.0 | 5.0 | |
| | | | PI(D21) | 25 | 21 | 84.0 | 63.9 | 95.5 | 41.7 | 22.5 | 77.0 | |
| | | | PII(D42) | 25 | 24 | 96.0 | 79.6 | 99.9 | 91.9 | 54.8 | 154.2 | |
| | | S+ | PRE | 7 | 7 | 100 | 59.0 | 100 | 17.2 | 9.6 | 30.8 | |
| | | | PI(D21) | 7 | 7 | 100 | 59.0 | 100 | 152.6 | 49.3 | 472.5 | |
| | | | PII(D42) | 7 | 7 | 100 | 59.0 | 100 | 168.1 | 62.7 | 450.9 | |
| Total | | PRE | 32 | 7 | 21.9 | 9.3 | 40.0 | 6.5 | 5.3 | 8.1 | | |
| | | PI(D21) | 32 | 28 | 87.5 | 71.0 | 96.5 | 55.4 | 32.0 | 95.7 | | |
| | | PII(D42) | 32 | 31 | 96.9 | 83.8 | 99.9 | 104.9 | 67.4 | 163.2 | | |

18-40Y = Subjects aged between and including 18 years to 40 years

41-60Y = Subjects aged between and including 41 years to 60 years

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination

S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination

GMT = geometric mean antibody titre calculated on all subjects

N = number of subjects with pre-vaccination results available

n (%) = number (percentage) of subjects with titre within the specified range

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

PRE =Pre-vaccination, Day 0

PI(D21) = Post-dose 1, Day 21

PII(D42) = Post-dose 2, Day 42

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) by pre-vaccination status for the subjects aged between and including 41-50 years and 51-60 years (ATP cohort of immunogenicity)

| Antibody | Group | Sub-group | Pre-vacc status | Timing | N | ≥ 1:10 | | | | GMT | | |
|-----------------------|--------|-----------|-----------------|----------|----|--------|------|--------|-------|-------|--------|--------|
| | | | | | | n | % | 95% CI | | value | 95% CI | |
| | | | | | | | | LL | UL | | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | 41-50Y | S- | PRE | 12 | 0 | 0.0 | 0.0 | 26.5 | 5.0 | 5.0 | 5.0 |
| | | | | PI(D21) | 12 | 12 | 100 | 73.5 | 100 | 213.5 | 113.8 | 400.3 |
| | | | | PII(D42) | 12 | 12 | 100 | 73.5 | 100 | 427.2 | 297.6 | 613.3 |
| | | | S+ | PRE | 4 | 4 | 100 | 39.8 | 100 | 12.9 | 7.6 | 21.9 |
| | | | | PI(D21) | 4 | 4 | 100 | 39.8 | 100 | 698.1 | 224.0 | 2175.3 |
| | | | | PII(D42) | 4 | 4 | 100 | 39.8 | 100 | 587.0 | 228.9 | 1505.2 |
| | | Total | PRE | 16 | 4 | 25.0 | 7.3 | 52.4 | 6.3 | 5.0 | 8.1 | |
| | | | PI(D21) | 16 | 16 | 100 | 79.4 | 100 | 287.1 | 164.1 | 502.1 | |
| | | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 | 462.5 | 340.9 | 627.5 | |
| | 51-60Y | S- | PRE | 8 | 0 | 0.0 | 0.0 | 36.9 | 5.0 | 5.0 | 5.0 | |
| | | | PI(D21) | 8 | 8 | 100 | 63.1 | 100 | 79.9 | 23.4 | 273.5 | |
| | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 | 433.4 | 168.0 | 1117.9 | |

| | | | | | | | | | | | | | | |
|--|--------|----------|-------|----------|----|----------|------|------|------|-------|-------|---------|------|-------|
| | | | S+ | PRE | 8 | 8 | 100 | 63.1 | 100 | 14.6 | 11.5 | 18.6 | | |
| | | | | PI(D21) | 8 | 8 | 100 | 63.1 | 100 | 640.1 | 278.0 | 1473.7 | | |
| | | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 | 829.9 | 432.1 | 1594.0 | | |
| | | | Total | PRE | 16 | 8 | 50.0 | 24.7 | 75.3 | 8.6 | 6.3 | 11.7 | | |
| | | | | PI(D21) | 16 | 16 | 100 | 79.4 | 100 | 226.2 | 95.3 | 536.6 | | |
| | | | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 | 599.7 | 352.3 | 1020.8 | | |
| | | | Flu 2 | 41-50Y | S- | PRE | 11 | 0 | 0.0 | 0.0 | 28.5 | 5.0 | 5.0 | 5.0 |
| | | | | | | PI(D21) | 11 | 11 | 100 | 71.5 | 100 | 102.8 | 40.7 | 259.9 |
| | | | | | | PII(D42) | 11 | 11 | 100 | 71.5 | 100 | 160.1 | 76.1 | 336.6 |
| | S+ | PRE | | | 5 | 5 | 100 | 47.8 | 100 | 18.6 | 7.3 | 47.5 | | |
| | | PI(D21) | | | 5 | 5 | 100 | 47.8 | 100 | 184.1 | 32.5 | 1043.8 | | |
| | | PII(D42) | | | 5 | 5 | 100 | 47.8 | 100 | 196.9 | 42.2 | 918.2 | | |
| | Total | PRE | | | 16 | 5 | 31.3 | 11.0 | 58.7 | 7.5 | 5.1 | 11.2 | | |
| | | PI(D21) | | | 16 | 16 | 100 | 79.4 | 100 | 123.3 | 59.5 | 255.5 | | |
| | | PII(D42) | | | 16 | 16 | 100 | 79.4 | 100 | 170.8 | 94.4 | 308.8 | | |
| | 51-60Y | S- | | PRE | 14 | 0 | 0.0 | 0.0 | 23.2 | 5.0 | 5.0 | 5.0 | | |
| | | | | PI(D21) | 14 | 10 | 71.4 | 41.9 | 91.6 | 20.5 | 10.4 | 40.5 | | |
| | | | | PII(D42) | 14 | 13 | 92.9 | 66.1 | 99.8 | 59.5 | 29.3 | 120.4 | | |
| | | S+ | | PRE | 2 | 2 | 100 | 15.8 | 100 | 14.0 | 14.0 | 14.0 | | |
| | | | | PI(D21) | 2 | 2 | 100 | 15.8 | 100 | 95.5 | 0.1 | 67258.1 | | |
| | | | | PII(D42) | 2 | 2 | 100 | 15.8 | 100 | 113.1 | 1.4 | 9248.7 | | |
| | | Total | | PRE | 16 | 2 | 12.5 | 1.6 | 38.3 | 5.7 | 4.7 | 6.9 | | |
| | | | | PI(D21) | 16 | 12 | 75.0 | 47.6 | 92.7 | 24.8 | 12.9 | 47.9 | | |
| | | | | PII(D42) | 16 | 15 | 93.8 | 69.8 | 99.8 | 64.4 | 34.6 | 120.0 | | |

41-50Y = Subjects aged between and including 41 years to 50 years
51-60Y = Subjects aged between and including 51 years to 60 years
S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE =Pre-vaccination, Day 0
PI(D21) = Post-dose 1, Day 21
PII(D42) = Post-dose 2, Day 42

Secondary Outcome Variable(s): Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab for subjects aged between and including 18-40 years (ATP cohort of immunogenicity)

| | | | | | SCR | | | |
|-----------------------|-------|-----------|----------|----|-----|------|--------|------|
| | | | | | | | 95% CI | |
| Strain | Group | Sub-group | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PI(D21) | 15 | 15 | 100 | 78.2 | 100 |
| | | | PII(D42) | 15 | 15 | 100 | 78.2 | 100 |
| | | S+ | PI(D21) | 17 | 17 | 100 | 80.5 | 100 |
| | | | PII(D42) | 17 | 17 | 100 | 80.5 | 100 |
| | | Total | PI(D21) | 32 | 32 | 100 | 89.1 | 100 |
| | | | PII(D42) | 32 | 32 | 100 | 89.1 | 100 |
| | Flu 2 | S- | PI(D21) | 18 | 14 | 77.8 | 52.4 | 93.6 |
| | | | PII(D42) | 18 | 15 | 83.3 | 58.6 | 96.4 |
| | | S+ | PI(D21) | 13 | 11 | 84.6 | 54.6 | 98.1 |
| | | | PII(D42) | 13 | 12 | 92.3 | 64.0 | 99.8 |
| | | Total | PI(D21) | 31 | 25 | 80.6 | 62.5 | 92.5 |
| | | | PII(D42) | 31 | 27 | 87.1 | 70.2 | 96.4 |

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
Seroconversion defined as:

For initially seronegative subjects, antibody titre $\geq 1:40$ after vaccination
 For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
 N = Number of subjects with pre- and post-vaccination results available
 n/% = Number/percentage of seroconverted subjects
 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
 PI(D21)= post-dose 1, Day 21
 PII(D42)= post-dose 2, Day 42

Secondary Outcome Variable(s): Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab for subjects aged between and including 41-50 years (ATP cohort of immunogenicity)

| | | | | | SCR | | | |
|-----------------------|-------|-----------|----------|----|-----|------|--------|------|
| | | | | | n | % | 95% CI | |
| Strain | Group | Sub-group | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PI(D21) | 12 | 12 | 100 | 73.5 | 100 |
| | | | PII(D42) | 12 | 12 | 100 | 73.5 | 100 |
| | | S+ | PI(D21) | 4 | 4 | 100 | 39.8 | 100 |
| | | | PII(D42) | 4 | 4 | 100 | 39.8 | 100 |
| | | Total | PI(D21) | 16 | 16 | 100 | 79.4 | 100 |
| | | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 |
| | Flu 2 | S- | PI(D21) | 11 | 8 | 72.7 | 39.0 | 94.0 |
| | | | PII(D42) | 11 | 11 | 100 | 71.5 | 100 |
| | | S+ | PI(D21) | 5 | 4 | 80.0 | 28.4 | 99.5 |
| | | | PII(D42) | 5 | 4 | 80.0 | 28.4 | 99.5 |
| | | Total | PI(D21) | 16 | 12 | 75.0 | 47.6 | 92.7 |
| | | | PII(D42) | 16 | 15 | 93.8 | 69.8 | 99.8 |

S- = seronegative subjects (antibody titre $< 1:10$) prior to vaccination
 S+ = seropositive subjects (antibody titre $\geq 1:10$) prior to vaccination
 Seroconversion defined as:
 For initially seronegative subjects, antibody titre $\geq 1:40$ after vaccination
 For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
 N = Number of subjects with pre- and post-vaccination results available
 n/% = Number/percentage of seroconverted subjects
 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
 PI(D21)= post-dose 1, Day 21
 PII(D42)= post-dose 2, Day 42

Secondary Outcome Variable(s): Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab for subjects aged between and including 51-60 years (ATP cohort of immunogenicity)

| | | | | | SCR | | | |
|-----------------------|-------|-----------|----------|----|-----|------|--------|------|
| | | | | | n | % | 95% CI | |
| Strain | Group | Sub-group | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | S- | PI(D21) | 8 | 4 | 50.0 | 15.7 | 84.3 |
| | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 |
| | | S+ | PI(D21) | 8 | 8 | 100 | 63.1 | 100 |
| | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 |
| | | Total | PI(D21) | 16 | 12 | 75.0 | 47.6 | 92.7 |
| | | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 |
| | Flu 2 | S- | PI(D21) | 14 | 5 | 35.7 | 12.8 | 64.9 |
| | | | PII(D42) | 14 | 10 | 71.4 | 41.9 | 91.6 |
| | | S+ | PI(D21) | 2 | 2 | 100 | 15.8 | 100 |
| | | | PII(D42) | 2 | 2 | 100 | 15.8 | 100 |
| | | Total | PI(D21) | 16 | 7 | 43.8 | 19.8 | 70.1 |
| | | | PII(D42) | 16 | 12 | 75.0 | 47.6 | 92.7 |

S- = seronegative subjects (antibody titre $< 1:10$) prior to vaccination
 S+ = seropositive subjects (antibody titre $\geq 1:10$) prior to vaccination
 Seroconversion defined as:
 For initially seronegative subjects, antibody titre $\geq 1:40$ after vaccination

| <p>For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= post-dose 1, Day 21 PII(D42)= post-dose 2, Day 42</p> | | | | | | | | | |
|--|----------|-----------|-----------------|----------|------|---------------|------|------|------|
| <p>Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) for the subjects aged between and including 18-40 years and 41-60 years (ATP cohort of immunogenicity)</p> | | | | | | | | | |
| | | | | | | SPR | | | |
| | | | | | | 95% CI | | | |
| Strain | Group | Sub-group | Pre-vacc status | Timing | N | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | 18-40Y | S- | PRE | 15 | 0 | 0.0 | 0.0 | 21.8 |
| | | | | PI(D21) | 15 | 15 | 100 | 78.2 | 100 |
| | | | | PII(D42) | 15 | 15 | 100 | 78.2 | 100 |
| | | | S+ | PRE | 17 | 7 | 41.2 | 18.4 | 67.1 |
| | | | | PI(D21) | 17 | 17 | 100 | 80.5 | 100 |
| | | | | PII(D42) | 17 | 17 | 100 | 80.5 | 100 |
| | | Total | PRE | 32 | 7 | 21.9 | 9.3 | 40.0 | |
| | | | PI(D21) | 32 | 32 | 100 | 89.1 | 100 | |
| | | | PII(D42) | 32 | 32 | 100 | 89.1 | 100 | |
| | | 41-60Y | S- | PRE | 20 | 0 | 0.0 | 0.0 | 16.8 |
| | | | | PI(D21) | 20 | 16 | 80.0 | 56.3 | 94.3 |
| | | | | PII(D42) | 20 | 20 | 100 | 83.2 | 100 |
| | S+ | | PRE | 12 | 0 | 0.0 | 0.0 | 26.5 | |
| | | | PI(D21) | 12 | 12 | 100 | 73.5 | 100 | |
| | | | PII(D42) | 12 | 12 | 100 | 73.5 | 100 | |
| | Total | PRE | 32 | 0 | 0.0 | 0.0 | 10.9 | | |
| | | PI(D21) | 32 | 28 | 87.5 | 71.0 | 96.5 | | |
| | | PII(D42) | 32 | 32 | 100 | 89.1 | 100 | | |
| | Flu 2 | 18-40Y | S- | PRE | 18 | 0 | 0.0 | 0.0 | 18.5 |
| | | | | PI(D21) | 18 | 14 | 77.8 | 52.4 | 93.6 |
| | | | | PII(D42) | 18 | 15 | 83.3 | 58.6 | 96.4 |
| | | | S+ | PRE | 13 | 5 | 38.5 | 13.9 | 68.4 |
| | | | | PI(D21) | 13 | 12 | 92.3 | 64.0 | 99.8 |
| | | | | PII(D42) | 13 | 13 | 100 | 75.3 | 100 |
| Total | | PRE | 31 | 5 | 16.1 | 5.5 | 33.7 | | |
| | | PI(D21) | 31 | 26 | 83.9 | 66.3 | 94.5 | | |
| | | PII(D42) | 31 | 28 | 90.3 | 74.2 | 98.0 | | |
| 41-60Y | | S- | PRE | 25 | 0 | 0.0 | 0.0 | 13.7 | |
| | | | PI(D21) | 25 | 13 | 52.0 | 31.3 | 72.2 | |
| | | | PII(D42) | 25 | 21 | 84.0 | 63.9 | 95.5 | |
| | S+ | PRE | 7 | 1 | 14.3 | 0.4 | 57.9 | | |
| | | PI(D21) | 7 | 7 | 100 | 59.0 | 100 | | |
| | | PII(D42) | 7 | 7 | 100 | 59.0 | 100 | | |
| Total | PRE | 32 | 1 | 3.1 | 0.1 | 16.2 | | | |
| | PI(D21) | 32 | 20 | 62.5 | 43.7 | 78.9 | | | |
| | PII(D42) | 32 | 28 | 87.5 | 71.0 | 96.5 | | | |
| <p>18-40Y = Subjects aged between and including 18 years to 40 years 41-60Y = Subjects aged between and including 41 years to 60 years S- = seronegative subjects (antibody titre < 1:10) prior to vaccination S+ = seropositive subjects (antibody titre $\geq 1:10$) prior to vaccination N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titre $\geq 1:40$)</p> | | | | | | | | | |

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

PRE= Pre-vaccination, Day 0

PI(D21)= Post-dose 1, Day 21

PII(D42)= Post-dose 2, Day 42

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) for the subjects aged between and including 41-50 years and 51-60 years (ATP cohort of immunogenicity)

| Strain | Group | Sub-group | Pre-vacc status | Timing | N | SPR | | | |
|-----------------------|----------|-----------|-----------------|----------|------|------|------|------|------|
| | | | | | | n | % | LL | UL |
| Flu A/CAL/7/09.HA1 Ab | Flu 1 | 41-50Y | S- | PRE | 12 | 0 | 0.0 | 0.0 | 26.5 |
| | | | | PI(D21) | 12 | 12 | 100 | 73.5 | 100 |
| | | | | PII(D42) | 12 | 12 | 100 | 73.5 | 100 |
| | | | S+ | PRE | 4 | 0 | 0.0 | 0.0 | 60.2 |
| | | | | PI(D21) | 4 | 4 | 100 | 39.8 | 100 |
| | | | | PII(D42) | 4 | 4 | 100 | 39.8 | 100 |
| | | Total | PRE | 16 | 0 | 0.0 | 0.0 | 20.6 | |
| | | | PI(D21) | 16 | 16 | 100 | 79.4 | 100 | |
| | | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 | |
| | | 51-60Y | S- | PRE | 8 | 0 | 0.0 | 0.0 | 36.9 |
| | | | | PI(D21) | 8 | 4 | 50.0 | 15.7 | 84.3 |
| | | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 |
| | S+ | | PRE | 8 | 0 | 0.0 | 0.0 | 36.9 | |
| | | | PI(D21) | 8 | 8 | 100 | 63.1 | 100 | |
| | | | PII(D42) | 8 | 8 | 100 | 63.1 | 100 | |
| | Total | PRE | 16 | 0 | 0.0 | 0.0 | 20.6 | | |
| | | PI(D21) | 16 | 12 | 75.0 | 47.6 | 92.7 | | |
| | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 | | |
| | Flu 2 | 41-50Y | S- | PRE | 11 | 0 | 0.0 | 0.0 | 28.5 |
| | | | | PI(D21) | 11 | 8 | 72.7 | 39.0 | 94.0 |
| | | | | PII(D42) | 11 | 11 | 100 | 71.5 | 100 |
| | | | S+ | PRE | 5 | 1 | 20.0 | 0.5 | 71.6 |
| | | | | PI(D21) | 5 | 5 | 100 | 47.8 | 100 |
| | | | | PII(D42) | 5 | 5 | 100 | 47.8 | 100 |
| Total | | PRE | 16 | 1 | 6.3 | 0.2 | 30.2 | | |
| | | PI(D21) | 16 | 13 | 81.3 | 54.4 | 96.0 | | |
| | | PII(D42) | 16 | 16 | 100 | 79.4 | 100 | | |
| 51-60Y | | S- | PRE | 14 | 0 | 0.0 | 0.0 | 23.2 | |
| | | | PI(D21) | 14 | 5 | 35.7 | 12.8 | 64.9 | |
| | | | PII(D42) | 14 | 10 | 71.4 | 41.9 | 91.6 | |
| | S+ | PRE | 2 | 0 | 0.0 | 0.0 | 84.2 | | |
| | | PI(D21) | 2 | 2 | 100 | 15.8 | 100 | | |
| | | PII(D42) | 2 | 2 | 100 | 15.8 | 100 | | |
| Total | PRE | 16 | 0 | 0.0 | 0.0 | 20.6 | | | |
| | PI(D21) | 16 | 7 | 43.8 | 19.8 | 70.1 | | | |
| | PII(D42) | 16 | 12 | 75.0 | 47.6 | 92.7 | | | |

41-50Y = Subjects aged between and including 41 years to 50 years

51-60Y = Subjects aged between and including 51 years to 60 years

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination

S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination

N = Number of subjects with available results

n/% = Number/percentage of seroprotected subjects (HI titre ≥ 1:40)

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

PRE= Pre-vaccination, Day 0

| PI(D21)= Post-dose 1, Day 21 PII(D42)= Post-dose 2, Day 42 | | | | | | | |
|---|-------|-----------|----------|----|---------------|------|-------|
| Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibody titre against Flu A/CAL/7/09.HA1 Ab (H1N1) for subjects in the age group 18-40 years (ATP cohort of immunogenicity) | | | | | | | |
| | | | | | GMFR | | |
| | | | | | 95% CI | | |
| Vaccine strain | Group | Sub-group | Timing | N | Value | LL | UL |
| Flu A/CAL/7/09.HA1 Ab (1/DIL) | Flu 1 | S- | PI(D21) | 15 | 90.5 | 56.3 | 145.7 |
| | | | PII(D42) | 15 | 137.2 | 95.3 | 197.5 |
| | | S+ | PI(D21) | 17 | 37.8 | 21.8 | 65.5 |
| | | | PII(D42) | 17 | 41.0 | 24.0 | 70.0 |
| | | Total | PI(D21) | 32 | 56.9 | 38.9 | 83.4 |
| | | | PII(D42) | 32 | 72.2 | 49.3 | 105.9 |
| | Flu 2 | S- | PI(D21) | 18 | 19.8 | 10.0 | 39.2 |
| | | | PII(D42) | 18 | 26.4 | 15.1 | 46.1 |
| | | S+ | PI(D21) | 13 | 11.3 | 5.3 | 24.5 |
| | | | PII(D42) | 13 | 13.3 | 7.3 | 24.3 |
| | | Total | PI(D21) | 31 | 15.7 | 9.6 | 25.6 |
| | | | PII(D42) | 31 | 19.8 | 13.2 | 29.7 |
| S- = seronegative subjects (antibody titre < 1:10) prior to vaccination S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination N = Number of subjects with pre- and post-vaccination results available GMFR = geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= Post-dose 1, Day 21 PII(D42)= Post-dose 2, Day 42 | | | | | | | |
| Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibody titre against Flu A/CAL/7/09.HA1 Ab (H1N1) for subjects in the age group 41-50 years (ATP cohort of immunogenicity) | | | | | | | |
| | | | | | GMFR | | |
| | | | | | 95% CI | | |
| Vaccine strain | Group | Sub-group | Timing | N | Value | LL | UL |
| Flu A/CAL/7/09.HA1 Ab (1/DIL) | Flu 1 | S- | PI(D21) | 12 | 42.7 | 22.8 | 80.1 |
| | | | PII(D42) | 12 | 85.4 | 59.5 | 122.7 |
| | | S+ | PI(D21) | 4 | 54.0 | 17.2 | 169.0 |
| | | | PII(D42) | 4 | 45.4 | 21.0 | 98.2 |
| | | Total | PI(D21) | 16 | 45.3 | 27.8 | 73.6 |
| | | | PII(D42) | 16 | 72.9 | 52.9 | 100.6 |
| | Flu 2 | S- | PI(D21) | 11 | 20.6 | 8.1 | 52.0 |
| | | | PII(D42) | 11 | 32.0 | 15.2 | 67.3 |
| | | S+ | PI(D21) | 5 | 9.9 | 1.9 | 51.7 |
| | | | PII(D42) | 5 | 10.6 | 2.5 | 44.7 |
| | | Total | PI(D21) | 16 | 16.4 | 7.9 | 33.9 |
| | | | PII(D42) | 16 | 22.7 | 11.9 | 43.1 |
| S- = seronegative subjects (antibody titre < 1:10) prior to vaccination S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination N = Number of subjects with pre- and post-vaccination results available GMFR = geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= Post-dose 1, Day 21 PII(D42)= Post-dose 2, Day 42 | | | | | | | |
| Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibody titre against Flu A/CAL/7/09.HA1 Ab (H1N1) for subjects in the age group 51-60 years (ATP cohort of immunogenicity) | | | | | | | |
| | | | | | GMFR | | |
| | | | | | 95% CI | | |
| Vaccine strain | Group | Sub-group | Timing | N | Value | LL | UL |

| | | | | | | | |
|----------------------------------|-------|----------|----------|------|------|------|--------|
| Flu A/CAL/7/09.HA1 Ab (1/DIL) | Flu 1 | S- | PI(D21) | 8 | 16.0 | 4.7 | 54.7 |
| | | | PII(D42) | 8 | 86.7 | 33.6 | 223.6 |
| | | S+ | PI(D21) | 8 | 43.7 | 20.0 | 95.7 |
| | | | PII(D42) | 8 | 56.7 | 29.4 | 109.4 |
| | | Total | PI(D21) | 16 | 26.4 | 13.2 | 52.9 |
| | | | PII(D42) | 16 | 70.1 | 41.9 | 117.4 |
| | Flu 2 | S- | PI(D21) | 14 | 4.1 | 2.1 | 8.1 |
| | | | PII(D42) | 14 | 11.9 | 5.9 | 24.1 |
| | | S+ | PI(D21) | 2 | 6.8 | 0.0 | 4804.2 |
| | | | PII(D42) | 2 | 8.1 | 0.1 | 660.6 |
| Total | | PI(D21) | 16 | 4.4 | 2.4 | 8.0 | |
| | | PII(D42) | 16 | 11.3 | 6.1 | 20.9 | |

S- = seronegative subjects (antibody titre < 1:10) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 1:10) prior to vaccination
N = Number of subjects with pre- and post-vaccination results available
GMFR = geometric mean ratio (mean[log10(POST/PRE)])
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21)= Post-dose 1, Day 21
PII(D42)= Post-dose 2, Day 42

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

| | | Flu 1 Group | | | | | Flu 2 Group | | | | |
|---------------------|-----------|-------------|----|------|---------|------|-------------|----|------|---------|------|
| | | | | | 95 % CI | | | | | 95 % CI | |
| Symptom | Intensity | N | n | % | LL | UL | N | n | % | LL | UL |
| Dose 1 | | | | | | | | | | | |
| Pain | Any | 65 | 60 | 92.3 | 83.0 | 97.5 | 66 | 16 | 24.2 | 14.5 | 36.4 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| Redness | Any | 65 | 4 | 6.2 | 1.7 | 15.0 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | > 100 mm | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| Swelling | Any | 65 | 8 | 12.3 | 5.5 | 22.8 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | > 100 mm | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| Dose 2 | | | | | | | | | | | |
| Pain | Any | 64 | 57 | 89.1 | 78.8 | 95.5 | 64 | 11 | 17.2 | 8.9 | 28.7 |
| | Grade 3 | 64 | 1 | 1.6 | 0.0 | 8.4 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| Redness | Any | 64 | 6 | 9.4 | 3.5 | 19.3 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | > 100 mm | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| Swelling | Any | 64 | 6 | 9.4 | 3.5 | 19.3 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | > 100 mm | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| Across doses | | | | | | | | | | | |
| Pain | Any | 65 | 62 | 95.4 | 87.1 | 99.0 | 66 | 21 | 31.8 | 20.9 | 44.4 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| Redness | Any | 65 | 9 | 13.8 | 6.5 | 24.7 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | > 100 mm | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| Swelling | Any | 65 | 11 | 16.9 | 8.8 | 28.3 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | > 100 mm | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |

N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
95% confidence interval; LL = lower limit, UL = upper limit
Any= occurrence of any local symptom regardless of intensity grade
Grade 3 pain= significant pain at rest that prevented normal activities

Secondary Outcome Variable(s): Number of days with any local symptoms during the solicited post-vaccination period (Total Vaccinated cohort)

| Solicited symptom | Dose | Group | N | Mean | Median |
|-------------------|--------|-------|----|------|--------|
| Pain | Dose 1 | Flu 1 | 60 | 3.4 | 3.0 |
| | | Flu 2 | 16 | 1.8 | 2.0 |

| | | | | | |
|----------|--------------|-------|-----|-----|-----|
| | Dose 2 | Flu 1 | 57 | 3.2 | 3.0 |
| | | Flu 2 | 11 | 1.7 | 2.0 |
| | Across doses | Flu 1 | 117 | 3.3 | 3.0 |
| | | Flu 2 | 27 | 1.7 | 2.0 |
| Redness | Dose 1 | Flu 1 | 4 | 2.0 | 2.0 |
| | Dose 2 | Flu 1 | 6 | 3.0 | 2.5 |
| | Across doses | Flu 1 | 10 | 2.6 | 2.0 |
| Swelling | Dose 1 | Flu 1 | 8 | 1.9 | 1.5 |
| | Dose 2 | Flu 1 | 6 | 2.3 | 2.0 |
| | Across doses | Flu 1 | 14 | 2.1 | 2.0 |

N = number of doses with the symptom

Secondary Outcome Variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

| | | Flu 1 Group | | | | | Flu 2 Group | | | | |
|------------------------------|----------------------------|-------------|----|------|---------|------|-------------|----|------|---------|------|
| | | | | | 95 % CI | | | | | 95 % CI | |
| Symptom | Intensity/ Relationship | N | n | % | LL | UL | N | n | % | LL | UL |
| Dose 1 | | | | | | | | | | | |
| Fatigue | Any | 65 | 31 | 47.7 | 35.1 | 60.5 | 66 | 22 | 33.3 | 22.2 | 46.0 |
| | Grade 3 | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| | Related | 65 | 28 | 43.1 | 30.8 | 56.0 | 66 | 18 | 27.3 | 17.0 | 39.6 |
| Headache | Any | 65 | 25 | 38.5 | 26.7 | 51.4 | 66 | 16 | 24.2 | 14.5 | 36.4 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | Related | 65 | 22 | 33.8 | 22.6 | 46.6 | 66 | 11 | 16.7 | 8.6 | 27.9 |
| Joint pain at other location | Any | 65 | 13 | 20.0 | 11.1 | 31.8 | 66 | 4 | 6.1 | 1.7 | 14.8 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 12 | 18.5 | 9.9 | 30.0 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| Muscle aches | Any | 65 | 17 | 26.2 | 16.0 | 38.5 | 66 | 6 | 9.1 | 3.4 | 18.7 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 16 | 24.6 | 14.8 | 36.9 | 66 | 5 | 7.6 | 2.5 | 16.8 |
| Shivering | Any | 65 | 9 | 13.8 | 6.5 | 24.7 | 66 | 6 | 9.1 | 3.4 | 18.7 |
| | Grade 3 | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 9 | 13.8 | 6.5 | 24.7 | 66 | 6 | 9.1 | 3.4 | 18.7 |
| Sweating | Any | 65 | 9 | 13.8 | 6.5 | 24.7 | 66 | 9 | 13.6 | 6.4 | 24.3 |
| | Grade 3 | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 8 | 12.3 | 5.5 | 22.8 | 66 | 9 | 13.6 | 6.4 | 24.3 |
| Temperature/(Axillary) | ≥37.5°C | 65 | 2 | 3.1 | 0.4 | 10.7 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| | ≥39°C | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | Related | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| Dose 2 | | | | | | | | | | | |
| Fatigue | Any | 64 | 28 | 43.8 | 31.4 | 56.7 | 64 | 15 | 23.4 | 13.8 | 35.7 |
| | Grade 3 | 64 | 2 | 3.1 | 0.4 | 10.8 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 27 | 42.2 | 29.9 | 55.2 | 64 | 13 | 20.3 | 11.3 | 32.2 |
| Headache | Any | 64 | 21 | 32.8 | 21.6 | 45.7 | 64 | 10 | 15.6 | 7.8 | 26.9 |
| | Grade 3 | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 20 | 31.3 | 20.2 | 44.1 | 64 | 9 | 14.1 | 6.6 | 25.0 |
| Joint pain at other location | Any | 64 | 12 | 18.8 | 10.1 | 30.5 | 64 | 1 | 1.6 | 0.0 | 8.4 |
| | Grade 3 | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 12 | 18.8 | 10.1 | 30.5 | 64 | 1 | 1.6 | 0.0 | 8.4 |
| Muscle aches | Any | 64 | 22 | 34.4 | 22.9 | 47.3 | 64 | 3 | 4.7 | 1.0 | 13.1 |
| | Grade 3 | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 22 | 34.4 | 22.9 | 47.3 | 64 | 1 | 1.6 | 0.0 | 8.4 |
| Shivering | Any | 64 | 12 | 18.8 | 10.1 | 30.5 | 64 | 2 | 3.1 | 0.4 | 10.8 |
| | Grade 3 | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |

| | | | | | | | | | | | |
|------------------------------|---------|----|----|------|------|------|----|----|------|------|------|
| | Related | 64 | 12 | 18.8 | 10.1 | 30.5 | 64 | 2 | 3.1 | 0.4 | 10.8 |
| Sweating | Any | 64 | 8 | 12.5 | 5.6 | 23.2 | 64 | 4 | 6.3 | 1.7 | 15.2 |
| | Grade 3 | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 8 | 12.5 | 5.6 | 23.2 | 64 | 4 | 6.3 | 1.7 | 15.2 |
| Temperature/(Axillary) | ≥37.5°C | 64 | 1 | 1.6 | 0.0 | 8.4 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | ≥39°C | 64 | 0 | 0.0 | 0.0 | 5.6 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| | Related | 64 | 1 | 1.6 | 0.0 | 8.4 | 64 | 0 | 0.0 | 0.0 | 5.6 |
| Across doses | | | | | | | | | | | |
| Fatigue | Any | 65 | 38 | 58.5 | 45.6 | 70.6 | 66 | 30 | 45.5 | 33.1 | 58.2 |
| | Grade 3 | 65 | 2 | 3.1 | 0.4 | 10.7 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| | Related | 65 | 35 | 53.8 | 41.0 | 66.3 | 66 | 27 | 40.9 | 29.0 | 53.7 |
| Headache | Any | 65 | 37 | 56.9 | 44.0 | 69.2 | 66 | 22 | 33.3 | 22.2 | 46.0 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | Related | 65 | 35 | 53.8 | 41.0 | 66.3 | 66 | 18 | 27.3 | 17.0 | 39.6 |
| Joint pain at other location | Any | 65 | 22 | 33.8 | 22.6 | 46.6 | 66 | 5 | 7.6 | 2.5 | 16.8 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 21 | 32.3 | 21.2 | 45.1 | 66 | 3 | 4.5 | 0.9 | 12.7 |
| Muscle aches | Any | 65 | 32 | 49.2 | 36.6 | 61.9 | 66 | 9 | 13.6 | 6.4 | 24.3 |
| | Grade 3 | 65 | 1 | 1.5 | 0.0 | 8.3 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 31 | 47.7 | 35.1 | 60.5 | 66 | 6 | 9.1 | 3.4 | 18.7 |
| Shivering | Any | 65 | 17 | 26.2 | 16.0 | 38.5 | 66 | 7 | 10.6 | 4.4 | 20.6 |
| | Grade 3 | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 17 | 26.2 | 16.0 | 38.5 | 66 | 7 | 10.6 | 4.4 | 20.6 |
| Sweating | Any | 65 | 15 | 23.1 | 13.5 | 35.2 | 66 | 12 | 18.2 | 9.8 | 29.6 |
| | Grade 3 | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 1 | 1.5 | 0.0 | 8.2 |
| | Related | 65 | 15 | 23.1 | 13.5 | 35.2 | 66 | 12 | 18.2 | 9.8 | 29.6 |
| Temperature/(Axillary) | ≥37.5°C | 65 | 3 | 4.6 | 1.0 | 12.9 | 66 | 2 | 3.0 | 0.4 | 10.5 |
| | ≥39°C | 65 | 0 | 0.0 | 0.0 | 5.5 | 66 | 0 | 0.0 | 0.0 | 5.4 |
| | Related | 65 | 2 | 3.1 | 0.4 | 10.7 | 66 | 2 | 3.0 | 0.4 | 10.5 |

N= number of subjects with at least one documented dose

n/%= number/percentage of subjects reporting at least once the symptom

95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Any= occurrence of any general symptom regardless of intensity grade and relationship to vaccination

Grade 3= general symptom that prevented normal activities

Related= general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Number of days with any general symptoms during the solicited post-vaccination period (Total Vaccinated cohort)

| Solicited symptom | Dose | Group | N | Mean | Median |
|------------------------------|--------------|-------|----|------|--------|
| Fatigue | Dose 1 | Flu 1 | 31 | 2.6 | 2.0 |
| | | Flu 2 | 22 | 3.0 | 2.0 |
| | Dose 2 | Flu 1 | 28 | 2.5 | 2.0 |
| | | Flu 2 | 15 | 2.5 | 2.0 |
| | Across doses | Flu 1 | 59 | 2.5 | 2.0 |
| | | Flu 2 | 37 | 2.8 | 2.0 |
| Headache | Dose 1 | Flu 1 | 25 | 2.3 | 2.0 |
| | | Flu 2 | 16 | 1.9 | 1.5 |
| | Dose 2 | Flu 1 | 21 | 2.0 | 1.0 |
| | | Flu 2 | 10 | 1.8 | 2.0 |
| | Across doses | Flu 1 | 46 | 2.2 | 2.0 |
| | | Flu 2 | 26 | 1.8 | 2.0 |
| Joint pain at other location | Dose 1 | Flu 1 | 13 | 1.8 | 1.0 |
| | | Flu 2 | 4 | 1.5 | 1.0 |
| | Dose 2 | Flu 1 | 12 | 1.9 | 2.0 |
| | | Flu 2 | 1 | 2.0 | 2.0 |

| | | | | | |
|--------------|--------------|-------|----|-----|-----|
| | Across doses | Flu 1 | 25 | 1.9 | 2.0 |
| | | Flu 2 | 5 | 1.6 | 1.0 |
| Muscle aches | Dose 1 | Flu 1 | 17 | 2.6 | 2.0 |
| | | Flu 2 | 6 | 2.0 | 2.0 |
| | Dose 2 | Flu 1 | 22 | 2.1 | 2.0 |
| | | Flu 2 | 3 | 1.3 | 1.0 |
| | Across doses | Flu 1 | 39 | 2.3 | 2.0 |
| | | Flu 2 | 9 | 1.8 | 2.0 |
| Sweating | Dose 1 | Flu 1 | 9 | 2.6 | 2.0 |
| | | Flu 2 | 9 | 2.8 | 2.0 |
| | Dose 2 | Flu 1 | 8 | 2.5 | 2.0 |
| | | Flu 2 | 4 | 2.3 | 2.0 |
| | Across doses | Flu 1 | 17 | 2.5 | 2.0 |
| | | Flu 2 | 13 | 2.6 | 2.0 |
| Shivering | Dose 1 | Flu 1 | 9 | 1.4 | 1.0 |
| | | Flu 2 | 6 | 2.7 | 1.5 |
| | Dose 2 | Flu 1 | 12 | 1.5 | 1.0 |
| | | Flu 2 | 2 | 2.0 | 2.0 |
| | Across doses | Flu 1 | 21 | 1.5 | 1.0 |
| | | Flu 2 | 8 | 2.5 | 1.5 |
| Temperature | Dose 1 | Flu 1 | 2 | 1.5 | 1.5 |
| | | Flu 2 | 2 | 1.5 | 1.5 |
| | Dose 2 | Flu 1 | 1 | 1.0 | 1.0 |
| | Across doses | Flu 1 | 3 | 1.3 | 1.0 |
| | | Flu 2 | 2 | 1.5 | 1.5 |

N = number of doses with the symptom

Secondary Outcome Variable(s): Number (%) of subjects with adverse events of specific interest (AESIs) / potential Immune-Mediated Disease (pIMDs) up to Day 42 (Total Vaccinated cohort)

| Most frequent AESIs/pIMDs | Flu 1 Group N = 65 | Flu 2 Group N = 66. |
|---|-------------------------------|--------------------------------|
| Subjects with any AESI(s), n (%) | 0 (0.0) | 0 (0.0) |
| Safety results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated cohort) | | |
| Most frequent adverse events - On-Therapy (occurring within Day 0-41 following vaccination) | Flu 1 Group N = 65 | Flu 2 Group N = 66 |
| Subjects with any AE(s), n (%) | 42 (64.6) | 33 (50.0) |
| Subjects with grade 3 AE(s), n (%) | 4 (6.2) | 4 (6.1) |
| Subjects with related AE(s), n (%) | 15 (23.1) | 11 (16.7) |
| Upper respiratory tract infection | 11 (16.9) | 6 (9.1) |
| Rhinitis | - | 6 (9.1) |
| Gastroenteritis | 4 (6.2) | 1 (1.5) |
| Nausea | 2 (3.1) | 3 (4.5) |
| Back pain | 2 (3.1) | 2 (3.0) |
| Headache | 3 (4.6) | 1 (1.5) |
| Influenza like illness | 2 (3.1) | 2 (3.0) |
| Arthralgia | 2 (3.1) | 1 (1.5) |
| Fatigue | - | 3 (4.5) |
| Malaise | 2 (3.1) | 1 (1.5) |
| Insomnia | 2 (3.1) | - |
| Productive cough | - | 2 (3.0) |
| Syncope | 2 (3.1) | - |
| Abdominal pain upper | - | 1 (1.5) |
| Decreased appetite | - | 1 (1.5) |
| Deep vein thrombosis | - | 1 (1.5) |
| Diarrhoea | - | 1 (1.5) |

| | | |
|---|------------------------------|------------------------------|
| Dizziness | - | 1 (1.5) |
| Feeling hot | - | 1 (1.5) |
| Gastrointestinal disorder | - | 1 (1.5) |
| Injection site haemorrhage | - | 1 (1.5) |
| Injection site pain | - | 1 (1.5) |
| Injection site reaction | - | 1 (1.5) |
| Nasal congestion | - | 1 (1.5) |
| Open wound | - | 1 (1.5) |
| Oropharyngeal pain | - | 1 (1.5) |
| Palpitations | - | 1 (1.5) |
| Procedural pain | - | 1 (1.5) |
| Pruritus | - | 1 (1.5) |
| Pruritus generalised | - | 1 (1.5) |
| Rash | - | 1 (1.5) |
| Sensation of heaviness | - | 1 (1.5) |
| Tendonitis | - | 1 (1.5) |
| Tonsillitis | - | 1 (1.5) |
| Tooth abscess | - | 1 (1.5) |
| Toothache | - | 1 (1.5) |
| Wound | - | 1 (1.5) |
| -: adverse event absent or not meeting the selected rule: more than 30 patients per treatment group and ≤ 3 groups: display the most frequent 10 adverse events in each group Grade 3= event that prevented normal activities Related= event assessed by the investigator as causally related to the study vaccination | | |
| Safety results: Number (%) of subjects with serious adverse events up to Day 42 (Total Vaccinated cohort) | | |
| Serious adverse event, n (%) [n considered by the investigator to be related to study medication] | | |
| All SAEs | Flu 1 Group N= 65 | Flu 2 Group N= 66 |
| Subjects with any SAE(s), n (%) [n assessed by the investigator as related] | 0 (0.0) [0] | 0 (0.0) [0] |
| Fatal SAEs | Flu 1 Group N= 65 | Flu 2 Group N= 66 |
| Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related] | 0 (0.0) [0] | 0 (0.0) [0] |

Conclusion:

21 days after the first dose, the seroconversion rate for HI antibodies against Flu A/CAL/7/09.HA1 Ab (H1N1) was 93.8% in Flu 1 Group and 69.8% in Flu 2 Group. At this time point, 93.8% of the subjects in Flu 1 Group and 73.0% of the subjects in Flu 2 Group had HI antibody titres commonly accepted as indicating seroprotection and the SCF values were 44.4 and 11.4, respectively.

Up to Day 42, 42 (64.6%) subjects in Flu 1 Group and 33 (50.0%) subjects in Flu 2 Group reported at least one unsolicited AE. No SAE was reported up to Day 42.

Publications: None

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