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<b>Study No.:</b> 113630 (FLU D-PAN H1N1-022)
<b>Title:</b> Safety and immunogenicity study of GSK Biologicals' influenza vaccine GSK2340272A in adults aged 18 years and above. GSK2340272 (Flu): GlaxoSmithKline (GSK) Biologicals' A/California/7/2009 (H1N1)v-like adjuvanted vaccine.
<b>Rationale:</b> The aim of this study was to assess the safety and immunogenicity of 2 different vaccination schedules of Flu vaccine in adults aged 18 years and above. This summary presents results up to Day 42 on preliminary data and will be updated when additional data become available.
<b>Phase:</b> III
<b>Study Period:</b> 14 September 2009 to 03 November 2009 (data lock point Day 42)
<b>Study Design:</b> Open, randomised (1:1) study with 2 parallel groups. Subjects were stratified according to their age at study entry: 18-60 years and > 60 years of age.
<b>Centres:</b> 5 centres in France
<b>Indication:</b> Immunization against A/California/7/2009 (H1N1)v-like influenza.
<b>Treatment:</b> The study groups were as follows: <ul style="list-style-type: none"> <li>• Flu D21 Group: subjects received 2 doses of Flu vaccine, at Day 0 and Day 21.</li> <li>• Flu M6 Group: subjects received 1 dose of Flu vaccine at Day 0 and will receive 1 dose at Month 6.</li> </ul> Vaccines were administered intramuscularly in the deltoid region of the non-dominant arm (first dose) and of the dominant arm (second dose).
<b>Objectives:</b> To demonstrate that vaccination with one dose of Flu vaccine results in an Haemagglutination Inhibition (HI) immune response to the vaccine-homologous virus that meets or exceeds the 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 Flu vaccine in adults within the 18 to 60 years and above 60 years age strata.
<b>Primary Outcome/Efficacy Variable:</b> <i>Immunogenicity</i> <ul style="list-style-type: none"> <li>• Humoral immune response in terms of HI antibodies in subjects receiving Flu vaccine: <ul style="list-style-type: none"> <li>- SCR* at 21 days after first dose of Flu vaccine (Day 21)</li> <li>- SPR** at 21 days after first dose of Flu vaccine (Day 21)</li> <li>- GMFR*** at 21 days after first dose of Flu vaccine (Day 21)</li> </ul> </li> </ul> <p>*SCR: defined as the proportion of subjects who have either a pre-vaccination reciprocal HI titre &lt; 10 and a post-vaccination reciprocal titre ≥ 40, or a pre-vaccination reciprocal HI titre ≥ 10 and at least a 4-fold increase in post-vaccination reciprocal titre against the vaccine virus. The CHMP criterion was fulfilled if the point estimate for SCR was &gt; 40% in subjects 18 to 60 years of age or &gt;30% for subjects above 60 years of age.</p> <p>**SPR: the proportion of subjects with H1N1 reciprocal HI titres ≥ 40 against the vaccine-homologous virus. The CHMP criterion was fulfilled if the post-vaccination point estimate for SPR was &gt; 70% in subjects 18 to 60 years of age or &gt;60% for subjects above 60 years of age.</p> <p>***GMFR [also called seroconversion factor (SCF)]: the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus. The criterion was fulfilled if the point estimate for GMFR was &gt; 2.5 in subjects 18 to 60 years of age or &gt;2 for subjects above 60 years of age.</p>
<b>Secondary Outcome/Efficacy Variable(s):</b> <i>Immunogenicity</i> <ul style="list-style-type: none"> <li>• Humoral immune response in terms of HI antibodies in subjects receiving 2 doses of Flu vaccine: <ul style="list-style-type: none"> <li>- Geometric Mean Titres (GMTs) and seropositivity rates at Day 0, 21, 42, 182<sup>#</sup>, 203<sup>†#</sup> and 364<sup>#</sup></li> <li>- SCR* at Day 21, 42, 182<sup>#</sup>, 203<sup>†#</sup> and 364<sup>#</sup></li> <li>- SPR* at Day 0, 21, 42, 182<sup>#</sup>, 203<sup>†#</sup> and 364<sup>#</sup></li> <li>- GMFR* at Day 21, 42, 182<sup>#</sup>, 203<sup>†#</sup> and 364<sup>#</sup></li> </ul> </li> </ul> <p>*See primary outcome variable section on criteria for evaluation for each age stratum.</p> <ul style="list-style-type: none"> <li>• Humoral immune response in terms of neutralizing antibodies in a subset of subjects against A/California/7/2009 (H1N1) v-like antigen.<sup>§</sup></li> </ul>

- GMTs at Day 0, 21, 42, 182, 203† and 364
- SCR\*\* at Day 21, 42, 182, 203† and 364

\*\*SCR is defined as the percentage of vaccinees that have a four-fold increase between pre- and post-vaccination titres.

#### Safety

- Solicited local and general symptoms.
  - Occurrence, intensity and duration of each solicited local symptom during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination. #
  - Occurrence, intensity, duration and relationship to vaccination of each solicited general symptom during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination. #
- Unsolicited adverse events (AEs).
  - Occurrence, intensity and relationship to vaccination of unsolicited AEs within 21 days after the first vaccination (for all subjects) and 63 days after the second vaccination [Day 0 - Day 20 and either 63 days after the second vaccination (Day 21- Day 84, Flu D21 Group only) or 30 days after the second vaccination (Day 182 - Day 212, Flu M6 Group only)], according to the Medical Dictionary for Regulatory Activities (MedDRA) classification. #
- Adverse events of specific interest (AESIs) or potential Immune-Mediated Diseases (pIMDs) and AEs of special interest‡%.
  - Occurrence and relationship to vaccination of AESIs/pIMDs and AEs of special interest during the entire study period (up to Day 364 for Flu D21 Group and up to Day 546 for Flu M6 Group). #
- Serious adverse events (SAEs).
  - Occurrence and relationship to vaccination of SAEs during the entire study (up to Day 364 for Flu D21 Group and up to Day 546 for Flu M6 Group). #
- Safety evaluation in terms of biochemical parameters.
  - The number and percentage of subjects with normal or abnormal values of biochemical parameters at Day 0, Day 21, Day 42, Day 182#, Day 203†# and Day 364#.

†This only applies to subjects enrolled in the Flu M6 Group.

# This CTRS presents the data up to Day 42. The study is ongoing and the CTRS will be updated for results from later time points with availability of the data.

§ Not available at the time of writing this summary.

% AEs of special interest were not yet collected at the time of writing this summary as the protocol amendment to include those AEs happened after completion of Day 42 analyses.

#### Statistical Methods:

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

- The Total Vaccinated cohort included all subjects with at least 1 vaccine administration documented.
- The ATP cohort for immunogenicity included all eligible subjects, who met all inclusion criteria and had no exclusion criteria, who received at least 1 dose of study vaccine, had not received a vaccine not specified or forbidden in the protocol and for whom assay results were available for antibodies against H1N1 antigen.

#### Analysis of immunogenicity

The analysis was based on the ATP cohort for immunogenicity.

The HI immune response to the vaccine homologous virus was described per age stratum by estimating the following parameters (with 95% confidence intervals [CIs]): GMT and SPR on Days 0, 21 and 42, SCR and SCF on Days 21 and 42. The H1 immune response was described for pooled groups at Day 21 and per treatment group at Day 42.

#### Analysis of safety

The analysis was based on the Total Vaccinated cohort.

The incidence of solicited local and general symptom occurring during the 7 days after the first vaccination was tabulated with exact 95% CIs for the pooled groups (Flu D21 and Flu M6 Groups) and per age stratum.

The incidence of solicited local and general symptom occurring during the 7 days after each vaccination was also tabulated with exact 95% CIs for the Flu D21 group and per age stratum.

For pooled groups and for Flu D21 Group, the same calculations were performed for symptoms of any intensity, those with Grade 3 intensity and for solicited general symptoms assessed by the investigator as related to vaccination. The duration of the symptoms was also computed.

The percentage of subjects with at least one report of an unsolicited adverse event classified by MedDRA and reported up to 42 days after first dose was tabulated for each treatment group (i.e., after 2 doses in Flu D21 Group, after 1 dose in Flu

M6 Group) and per age stratum. The same tabulation was performed for Grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigators to be possibly related to vaccination. SAEs, AESIs/pIMDs and AEs of special interest were summarized up to Day 42. The number and proportion of subjects with normal or abnormal values for each biochemistry parameter were tabulated for the Flu D21 Group at each scheduled time point, up to Day 42 and for the pooled groups at Day 0 and Day 21.

**Study Population:** Male or female subjects aged 18 years or above at the time of first vaccination were enrolled in the study if results from a baseline medical assessment by history and physical were satisfactory and that subject had a stable health status. If the subject was female and of childbearing potential, she had to be abstinent or to have used contraceptive precautions for 30 days prior to vaccination; she had to have a negative pregnancy test at study entry and had to agree to continue contraceptive precautions for 2 months after completion of the vaccination series. Written informed consent was obtained from the subject prior to study entry.

Number of Subjects:	Flu D21 Group		Flu M6 Group	
	18-60 years	>60 years	18-60 years	>60 years
Planned, N	150		150	
Randomised, N (Total Vaccinated cohort)	93	91	70	52
Completed, n (%) (Day 42)	92 (98.9)	88 (96.7)	68 (97.1)	52 (100)
Total Number Subjects Withdrawn, n (%)	1 (1.1)	3 (3.3)	2 (2.9)	0(0.0)
Withdrawn due to Adverse Events n (%)	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
Withdrawn for other reasons n (%)	1 (1.1)	3 (3.3)	2 (2.9)	0(0.0)
Demographics	Flu D21 Group		Flu M6 Group	
	18-60 years	>60 years	18-60 years	>60 years
N (Total Vaccinated cohort)	93	91	70	52
Females: Males	50:43	42:49	37:33	26:26
Mean Age, years (SD)	39 (12.17)	66.8 (5.50)	40.8 (12.61)	66.1 (4.08)
White - Caucasian / European heritage, n (%)	86 (92.5)	88 (96.7)	64 (91.4)	50 (96.2)

**Primary Efficacy Results:** Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/2009 at Day 21 (ATP cohort for immunogenicity at Day 21)

					SCR			
					95% CI			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Pooled groups	18-60	PI(D21)	160	154	96.3	92.0	98.6
		>60	PI(D21)	136	121	89.0	82.5	93.7

18-60 = Subjects aged between and including 18 years to 60 years

>60 = Subjects aged more than 60 years

Seroconversion defined as:

For initially seronegative subjects, antibody titre  $\geq$  1:40 after vaccination

For initially seropositive subjects, antibody titre after vaccination  $\geq$  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

**Primary Efficacy Results:** Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 21)

					SPR			
					95% CI			
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/2009	Pooled groups	18-60	PRE	160	23	14.4	9.3	20.8
			PI(D21)	160	156	97.5	93.7	99.3
		>60	PRE	136	7	5.1	2.1	10.3
			PI(D21)	136	125	91.9	86.0	95.9

18-60 = Subjects aged between and including 18 years to 60 years

>60 = Subjects aged more than 60 years

N = Number of subjects with available results

n/% = Number/percentage of seroprotected subjects (HI titre $\geq$ 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											
<b>Primary Efficacy Results:</b> Seroconversion factor (SCF) for HI antibody titre (ATP cohort for immunogenicity at day 21)											
					<b>SCF</b>						
					<b>95% CI</b>						
Antibodies against	Group	Sub-group	Timing	N	Value	LL	UL				
Flu A/CAL/7/2009	Pooled Groups	18-60	PI(D21)	160	45.0	37.2	54.5				
		>60	PI(D21)	136	23.4	19.1	28.7				
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with pre- and post-vaccination results available SCF = Seroconversion Factor or geometric mean ratio (mean[log <sub>10</sub> (POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= Post-dose 1, Day 21											
<b>Secondary Outcome Variable(s):</b> Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)											
					<b><math>\geq</math> 1:10</b>		<b>GMT</b>				
					<b>95% CI</b>		<b>95% CI</b>				
Antibody against	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/CAL/7/2009	Flu D21 Group	18-60	PRE	87	30	34.5	24.6	45.4	8.9	7.2	11.0
			PI(D21)	87	87	100	95.8	100	459.8	374.2	565.1
			PII(D42)	87	87	100	95.8	100	771.8	660.5	901.7
		>60	PRE	83	26	31.3	21.6	42.4	7.3	6.3	8.5
			PI(D21)	83	83	100	95.7	100	168.2	129.0	219.3
			PII(D42)	83	83	100	95.7	100	400.9	329.3	488.2
	Flu M6 Group	18-60	PRE	67	25	37.3	25.8	50.0	9.3	7.4	11.8
			PI(D21)	67	65	97.0	89.6	99.6	366.1	266.7	502.7
			PI(D42)	67	65	97.0	89.6	99.6	297.6	218.6	405.2
		>60	PRE	48	20	41.7	27.6	56.8	8.0	6.6	9.8
			PI(D21)	48	48	100	92.6	100	187.5	136.6	257.4
			PI(D42)	48	48	100	92.6	100	132.6	94.3	186.6
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with available results 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 PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42											
<b>Secondary Outcome Variable(s):</b> Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)											
					<b>SCR</b>						
					<b>95% CI</b>						
Antibodies against	Group	Sub-group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/2009	Flu D21 Group	18-60	PI(D21)	87	87	100	95.8	100			
			PII(D42)	87	86	98.9	93.8	100			
		>60	PI(D21)	83	74	89.2	80.4	94.9			
			PII(D42)	83	82	98.8	93.5	100			
	Flu M6 Group	18-60	PI(D21)	67	62	92.5	83.4	97.5			
			PI(D42)	67	61	91.0	81.5	96.6			

		>60	PI(D21)	48	43	89.6	77.3	96.5
			PI(D42)	48	39	81.3	67.4	91.1
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years Seroconversion defined as: For initially seronegative subjects, antibody titre $\geq$ 1:40 after vaccination For initially seropositive subjects, antibody titre after vaccination $\geq$ 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 PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42								
<b>Secondary Outcome Variable(s):</b> Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/2009 (ATP cohort for immunogenicity at Day 42)								
					<b>SPR</b>			
					<b>95% CI</b>			
<b>Antibodies against</b>	<b>Group</b>	<b>Sub-group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/2009	Flu D21 Group	18-60	PRE	87	11	12.6	6.5	21.5
			PI(D21)	87	87	100	95.8	100
			PII(D42)	87	87	100	95.8	100
		>60	PRE	83	6	7.2	2.7	15.1
			PI(D21)	83	75	90.4	81.9	95.7
			PII(D42)	83	83	100	95.7	100
	Flu M6 Group	18-60	PRE	67	10	14.9	7.4	25.7
			PI(D21)	67	63	94.0	85.4	98.3
			PI(D42)	67	64	95.5	87.5	99.1
		>60	PRE	48	1	2.1	0.1	11.1
			PI(D21)	48	46	95.8	85.7	99.5
			PI(D42)	48	43	89.6	77.3	96.5
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years N = Number of subjects with available results n/% = Number/percentage of seroprotected subjects (HI titre $\geq$ 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 PI(D42)= Post-dose 1, Day 42 PII(D42)= Post-dose 2, Day 42								
<b>Secondary Outcome Variable(s):</b> Seroconversion factor (SCF) for HI antibody titre (ATP cohort for immunogenicity at Day 42)								
					<b>SCF</b>			
					<b>95% CI</b>			
<b>Antibodies against</b>	<b>Group</b>	<b>Sub-group</b>	<b>Timing</b>	<b>N</b>	<b>Value</b>	<b>LL</b>	<b>UL</b>	
Flu A/CAL/7/2009	Flu D21 Group	18-60	PI(D21)	87	51.6	40.7	65.5	
			PII(D42)	87	86.7	68.6	109.5	
		>60	PI(D21)	83	23.0	17.7	29.9	
			PII(D42)	83	54.9	43.4	69.3	
	Flu M6 Group	18-60	PI(D21)	67	39.2	28.3	54.2	
			PI(D42)	67	31.9	23.4	43.4	
		>60	PI(D21)	48	23.3	16.6	32.7	
			PI(D42)	48	16.5	11.8	23.0	
18-60 = Subjects aged between and including 18 years to 60 years >60 = Subjects aged more than 60 years								

<p>N = Number of subjects with pre- and post-vaccination results available  SCF = Seroconversion Factor or 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  PI(D42)= Post-dose 1, Day 42  PII(D42)= Post-dose 2, Day 42</p>											
<p><b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups)</p>											
		<b>Pooled Groups</b>									
		<b>18-60 years</b>					<b>&gt;60 years</b>				
					<b>95 % CI</b>					<b>95 % CI</b>	
<b>Symptom</b>	<b>Intensity</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
<b>Dose 1</b>											
Pain	Any	162	154	95.1	90.5	97.8	142	106	74.6	66.7	81.6
	Grade 3	162	0	0.0	0.0	2.3	142	2	1.4	0.2	5.0
Redness	Any	162	18	11.1	6.7	17.0	142	9	6.3	2.9	11.7
	> 100 mm	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
Swelling	Any	162	17	10.5	6.2	16.3	142	7	4.9	2.0	9.9
	> 100 mm	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
<p>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 local symptoms regardless of their intensity grade  Grade 3 pain= Significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school</p>											
<p><b>Secondary Outcome Variable(s):</b> Number of days with local symptoms during the solicited post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups)</p>											
<b>Solicited symptom</b>	<b>Group</b>	<b>Sub-group</b>			<b>N</b>		<b>Mean</b>		<b>Median</b>		
Pain	Pooled Groups	18-60			154		3.3		3.0		
		>60			106		2.9		3.0		
Redness	Pooled Groups	18-6			18		2.6		2.0		
		>60			9		2.6		2.0		
Swelling	Pooled Groups	18-60			17		2.8		3.0		
		>60			7		2.7		2.0		
<p>N = number of doses with the symptom</p>											
<p><b>Secondary Outcome Variable(s):</b> 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 D21 Goup)</p>											
		<b>Flu D21 Group</b>									
		<b>18-60 years</b>					<b>&gt;60 years</b>				
					<b>95 % CI</b>					<b>95 % CI</b>	
<b>Symptom</b>	<b>Intensity</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
<b>Dose 1</b>											
Pain	Any	92	87	94.6	87.8	98.2	90	71	78.9	69.0	86.8
	Grade 3	92	0	0.0	0.0	3.9	90	2	2.2	0.3	7.8
Redness	Any	92	10	10.9	5.3	19.1	90	8	8.9	3.9	16.8
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	11	12.0	6.1	20.4	90	6	6.7	2.5	13.9
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
<b>Dose 2</b>											
Pain	Any	90	80	88.9	80.5	94.5	84	62	73.8	63.1	82.8
	Grade 3	90	2	2.2	0.3	7.8	84	0	0.0	0.0	4.3
Redness	Any	90	6	6.7	2.5	13.9	84	11	13.1	6.7	22.2
	> 100 mm	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
Swelling	Any	90	8	8.9	3.9	16.8	84	10	11.9	5.9	20.8
	> 100 mm	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3

Across doses											
Pain	Any	92	91	98.9	94.1	100	90	78	86.7	77.9	92.9
	Grade 3	92	2	2.2	0.3	7.6	90	2	2.2	0.3	7.8
Redness	Any	92	14	15.2	8.6	24.2	90	17	18.9	11.4	28.5
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
Swelling	Any	92	15	16.3	9.4	25.5	90	15	16.7	9.6	26.0
	> 100 mm	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
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 local symptoms regardless of their intensity grade Grade 3 pain= Significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school											
<b>Secondary Outcome Variable(s):</b> Number of days with local symptoms during the solicited post-vaccination period following each dose and overall (Total Vaccinated cohort – Flu D21 Group)											
Solicited symptom	Dose	Group		Sub-group			N	Mean	Median		
Pain	Dose 1	Flu D21 Group		18-60			87	3.3	3.0		
				>60			71	3.0	3.0		
	Dose 2	Flu D21 Group		18-60			80	3.0	3.0		
				>60			62	3.3	3.0		
Overall/dose	Flu D21 Group		18-60			167	3.1	3.0			
			>60			133	3.2	3.0			
Redness	Dose 1	Flu D21 Group		18-6			10	2.5	2.5		
				>60			8	2.5	2.0		
	Dose 2	Flu D21 Group		18-60			6	2.8	2.5		
				>60			11	2.5	1.0		
Overall/dose	Flu D21 Group		18-60			16	2.6	2.5			
			>60			19	2.5	2.0			
Swelling	Dose 1	Flu D21 Group		18-60			11	2.4	2.0		
				>60			6	2.2	2.0		
	Dose 2	Flu D21 Group		18-60			8	2.5	2.0		
				>60			10	3.2	3.0		
Overall/dose	Flu D21 Group		18-60			19	2.4	2.0			
			>60			16	2.8	2.5			
N = number of doses with the symptom											
<b>Secondary Outcome Variable(s):</b> Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups)											
		Pooled Groups									
		18-60 years					>60 years				
					95 % CI					95 % CI	
Symptom	Intensity/ Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	162	67	41.4	33.7	49.4	142	44	31.0	23.5	39.3
	Grade 3	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6
	Related	162	56	34.6	27.3	42.4	142	34	23.9	17.2	31.8
Headache	Any	162	56	34.6	27.3	42.4	142	29	20.4	14.1	28.0
	Grade 3	162	1	0.6	0.0	3.4	142	1	0.7	0.0	3.9
	Related	162	43	26.5	19.9	34.0	142	23	16.2	10.6	23.3
Joint pain at other location	Any	162	31	19.1	13.4	26.0	142	27	19.0	12.9	26.4
	Grade 3	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
	Related	162	26	16.0	10.8	22.6	142	20	14.1	8.8	20.9
Muscle aches	Any	162	66	40.7	33.1	48.7	142	41	28.9	21.6	37.1
	Grade 3	162	0	0.0	0.0	2.3	142	1	0.7	0.0	3.9

	Related	162	56	34.6	27.3	42.4	142	35	24.6	17.8	32.6
Shivering	Any	162	31	19.1	13.4	26.0	142	18	12.7	7.7	19.3
	Grade 3	162	0	0.0	0.0	2.3	142	1	0.7	0.0	3.9
	Related	162	22	13.6	8.7	19.8	142	11	7.7	3.9	13.4
Sweating	Any	162	19	11.7	7.2	17.7	142	17	12.0	7.1	18.5
	Grade 3	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6
	Related	162	13	8.0	4.3	13.3	142	9	6.3	2.9	11.7
Temperature/ (Axillary)	≥37.5°C	162	3	1.9	0.4	5.3	142	2	1.4	0.2	5.0
	≥ 39.0°C	162	0	0.0	0.0	2.3	142	0	0.0	0.0	2.6
	Related	162	1	0.6	0.0	3.4	142	0	0.0	0.0	2.6

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 symptoms, regardless of their intensity grade or their relationship to vaccination

Grade 3= general symptom that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider

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

**Secondary Outcome Variable(s):** Number of days with general symptoms during the solicited post-vaccination period following first dose (Total Vaccinated cohort – Pooled Groups)

Solicited symptom	Group	Sub-group	N	Mean	Median
Fatigue	Pooled Groups	18-60	67	2.4	2.0
		>60	44	2.3	2.0
Headache	Pooled Groups	18-60	56	1.6	1.0
		>60	29	2.0	1.0
Joint pain at other location	Pooled Groups	18-60	31	2.1	2.0
		>60	27	3.0	2.0
Muscle aches	Pooled Groups	18-60	66	2.3	2.0
		>60	41	2.4	2.0
Sweating	Pooled Groups	18-60	19	1.7	1.0
		>60	17	2.1	1.0
Shivering	Pooled Groups	18-60	31	1.4	1.0
		>60	18	1.9	1.0
Temperature	Pooled Groups	18-60	3	1.3	1.0
		>60	3	1.0	1.0

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 D21 Group)

		Flu D21 Group									
		18-60 years					>60 years				
				95 % CI					95 % CI		
Symptom	Intensity/ Relationship	N	n	%	LL	UL	N	n	%	LL	UL
<b>Dose 1</b>											
Fatigue	Any	92	40	43.5	33.2	54.2	90	26	28.9	19.8	39.4
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	35	38.0	28.1	48.8	90	22	24.4	16.0	34.6
Headache	Any	92	34	37.0	27.1	47.7	90	20	22.2	14.1	32.2
	Grade 3	92	0	0.0	0.0	3.9	90	1	1.1	0.0	6.0
	Related	92	30	32.6	23.2	43.2	90	17	18.9	11.4	28.5
Joint pain at other location	Any	92	21	22.8	14.7	32.8	90	19	21.1	13.2	31.0
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	17	18.5	11.1	27.9	90	15	16.7	9.6	26.0
Muscle aches	Any	92	43	46.7	36.3	57.4	90	26	28.9	19.8	39.4
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0

	Related	92	36	39.1	29.1	49.9	90	23	25.6	16.9	35.8
Shivering	Any	92	17	18.5	11.1	27.9	90	12	13.3	7.1	22.1
	Grade 3	92	0	0.0	0.0	3.9	90	1	1.1	0.0	6.0
	Related	92	13	14.1	7.7	23.0	90	8	8.9	3.9	16.8
Sweating	Any	92	12	13.0	6.9	21.7	90	10	11.1	5.5	19.5
	Grade 3	92	1	1.1	0.0	5.9	90	0	0.0	0.0	4.0
	Related	92	9	9.8	4.6	17.8	90	6	6.7	2.5	13.9
Temperature/ (Axillary)	≥37.5°C	92	1	1.1	0.0	5.9	90	1	1.1	0.0	6.0
	≥ 39.0°C	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
<b>Dose 2</b>											
Fatigue	Any	90	48	53.3	42.5	63.9	84	27	32.1	22.4	43.2
	Grade 3	90	3	3.3	0.7	9.4	84	1	1.2	0.0	6.5
	Related	90	41	45.6	35.0	56.4	84	18	21.4	13.2	31.7
Headache	Any	90	41	45.6	35.0	56.4	84	19	22.6	14.2	33.0
	Grade 3	90	1	1.1	0.0	6.0	84	1	1.2	0.0	6.5
	Related	90	36	40.0	29.8	50.9	84	12	14.3	7.6	23.6
Joint pain at other location	Any	90	17	18.9	11.4	28.5	84	21	25.0	16.2	35.6
	Grade 3	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
	Related	90	13	14.4	7.9	23.4	84	17	20.2	12.3	30.4
Muscle aches	Any	90	38	42.2	31.9	53.1	84	25	29.8	20.3	40.7
	Grade 3	90	0	0.0	0.0	4.0	84	0	0.0	0.0	4.3
	Related	90	31	34.4	24.7	45.2	84	19	22.6	14.2	33.0
Shivering	Any	90	26	28.9	19.8	39.4	84	13	15.5	8.5	25.0
	Grade 3	90	1	1.1	0.0	6.0	84	1	1.2	0.0	6.5
	Related	90	24	26.7	17.9	37.0	84	9	10.7	5.0	19.4
Sweating	Any	90	19	21.1	13.2	31.0	84	13	15.5	8.5	25.0
	Grade 3	90	1	1.1	0.0	6.0	84	0	0.0	0.0	4.3
	Related	90	17	18.9	11.4	28.5	84	8	9.5	4.2	17.9
Temperature/ (Axillary)	≥37.5°C	90	6	6.7	2.5	13.9	84	5	6.0	2.0	13.3
	≥ 39.0°C	90	0	0.0	0.0	4.0	84	2	2.4	0.3	8.3
	Related	90	5	5.6	1.8	12.5	84	4	4.8	1.3	11.7
<b>Across doses</b>											
Fatigue	Any	92	59	64.1	53.5	73.9	90	39	43.3	32.9	54.2
	Grade 3	92	3	3.3	0.7	9.2	90	1	1.1	0.0	6.0
	Related	92	53	57.6	46.9	67.9	90	30	33.3	23.7	44.1
Headache	Any	92	53	57.6	46.9	67.9	90	30	33.3	23.7	44.1
	Grade 3	92	1	1.1	0.0	5.9	90	2	2.2	0.3	7.8
	Related	92	46	50.0	39.4	60.6	90	23	25.6	16.9	35.8
Joint pain at other location	Any	92	26	28.3	19.4	38.6	90	27	30.0	20.8	40.6
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	21	22.8	14.7	32.8	90	22	24.4	16.0	34.6
Muscle aches	Any	92	53	57.6	46.9	67.9	90	34	37.8	27.8	48.6
	Grade 3	92	0	0.0	0.0	3.9	90	0	0.0	0.0	4.0
	Related	92	46	50.0	39.4	60.6	90	29	32.2	22.8	42.9
Shivering	Any	92	34	37.0	27.1	47.7	90	22	24.4	16.0	34.6
	Grade 3	92	1	1.1	0.0	5.9	90	2	2.2	0.3	7.8
	Related	92	29	31.5	22.2	42.0	90	15	16.7	9.6	26.0
Sweating	Any	92	24	26.1	17.5	36.3	90	19	21.1	13.2	31.0
	Grade 3	92	2	2.2	0.3	7.6	90	0	0.0	0.0	4.0
	Related	92	19	20.7	12.9	30.4	90	13	14.4	7.9	23.4
Temperature/ (Axillary)	≥37.5°C	92	7	7.6	3.1	15.1	90	5	5.6	1.8	12.5
	≥ 39.0°C	92	0	0.0	0.0	3.9	90	2	2.2	0.3	7.8
	Related	92	5	5.4	1.8	12.2	90	4	4.4	1.2	11.0

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 symptoms, regardless of their intensity grade or their relationship to vaccination  
Grade 3= general symptom that prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider  
Related= general symptom assessed by the investigator as causally related to the study vaccination

**Secondary Outcome Variable(s):** Number of days with general symptoms during the solicited post-vaccination period following each dose and overall (Total Vaccinated cohort – Flu D21 Group)

Solicited symptom	Dose	Group	Sub-group	N	Mean	Median
Fatigue	Dose 1	Flu D21 Group	18-60	40	2.2	2.0
			>60	26	2.5	2.0
	Dose 2	Flu D21 Group	18-60	48	2.1	2.0
			>60	27	2.8	2.0
	Overall/dose	Flu D21 Group	18-60	88	2.2	2.0
			>60	53	2.7	2.0
Headache	Dose 1	Flu D21 Group	18-60	34	1.5	1.0
			>60	20	2.0	1.0
	Dose 2	Flu D21 Group	18-60	41	2.2	2.0
			>60	19	2.2	2.0
	Overall/dose	Flu D21 Group	18-60	75	1.9	1.0
			>60	39	2.1	2.0
Joint pain at other location	Dose 1	Flu D21 Group	18-60	21	2.0	2.0
			>60	19	2.9	2.0
	Dose 2	Flu D21 Group	18-60	17	2.2	2.0
			>60	21	2.6	2.0
	Overall/dose	Flu D21 Group	18-60	38	2.1	2.0
			>60	40	2.7	2.0
Muscle aches	Dose 1	Flu D21 Group	18-60	43	2.1	2.0
			>60	26	2.4	2.0
	Dose 2	Flu D21 Group	18-60	38	2.2	2.0
			>60	25	2.6	2.0
	Overall/dose	Flu D21 Group	18-60	81	2.2	2.0
			>60	51	2.5	2.0
Sweating	Dose 1	Flu D21 Group	18-60	12	1.8	1.5
			>60	10	2.4	2.0
	Dose 2	Flu D21 Group	18-60	19	2.1	2.0
			>60	13	1.9	1.0
	Overall/dose	Flu D21 Group	18-60	31	2.0	2.0
			>60	23	2.1	2.0
Shivering	Dose 1	Flu D21 Group	18-60	17	1.3	1.0
			>60	12	2.1	1.0
	Dose 2	Flu D21 Group	18-60	26	1.5	1.0
			>60	13	1.6	2.0
	Overall/dose	Flu D21 Group	18-60	43	1.4	1.0
			>60	25	1.8	1.0
Temperature	Dose 1	Flu D21 Group	18-60	1	1.0	1.0
			>60	1	1.0	1.0
	Dose 2	Flu D21 Group	18-60	6	1.5	1.0
			>60	5	1.0	1.0
	Overall/dose	Flu D21 Group	18-60	7	1.4	1.0
			>60	6	1.0	1.0

N = number of doses with the symptom

<b>Secondary Outcome Variable(s):</b> Number (%) of subjects with adverse events of specific interest or potential immune-mediated diseases reporting until Day 42 (Total Vaccinated cohort)																					
<b>Most frequent adverse events - On-Therapy (occurring within day 0-41 following vaccination)</b>		<b>Flu D21 Group</b>										<b>Flu M6 Group</b>									
		<b>18-60 years N = 93</b>					<b>&gt;60 years N = 91</b>					<b>18-60 years N = 70</b>				<b>&gt;60 years N = 52</b>					
Subjects with any AESI(s)/pIMDs, n (%)		0 (0.0)					0 (0.0)					0 (0.0)				0 (0.0)					
<b>Secondary Outcome Variable(s):</b> Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated cohort – Pooled Groups)																					
		<b>Pooled Groups</b>																			
		<b>18-60 years N = 163</b>										<b>&gt;60 years N = 143</b>									
		<b>Unknown</b>			<b>Below</b>		<b>Within</b>		<b>Above</b>			<b>Unknown</b>			<b>Below</b>		<b>Within</b>		<b>Above</b>		
<b>Laboratory parameter</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
ALAT	PRE	163	0	0.0	4	2.5	144	88.3	13	8.0	143	2	1.4	0	0.0	129	90.2	12	8.4		
	PI(D21)	161	1	0.6	3	1.9	143	88.8	12	7.5	140	0	0.0	0	0.0	123	87.9	14	10.0		
AP	PRE	163	1	0.6	7	4.3	150	92.0	3	1.8	143	0	0.0	5	3.5	135	94.4	3	2.1		
	PI(D21)	161	0	0.0	8	5.0	149	92.5	2	1.2	140	0	0.0	5	3.6	128	91.4	4	2.9		
ASAT	PRE	163	0	0.0	2	1.2	149	91.4	10	6.1	143	2	1.4	1	0.7	130	90.9	10	7.0		
	PI(D21)	161	1	0.6	0	0.0	147	91.3	11	6.8	140	1	0.7	1	0.7	125	89.3	10	7.1		
Bilirubin	PRE	163	1	0.6	0	0.0	153	93.9	7	4.3	143	2	1.4	0	0.0	137	95.8	4	2.8		
	PI(D21)	161	1	0.6	0	0.0	151	93.8	7	4.3	140	0	0.0	0	0.0	132	94.3	5	3.6		
Creatinine	PRE	163	0	0.0	5	3.1	149	91.4	7	4.3	143	0	0.0	2	1.4	120	83.9	21	14.7		
	PI(D21)	161	0	0.0	5	3.1	146	90.7	8	5.0	140	0	0.0	3	2.1	119	85.0	15	10.7		
BUN	PRE	163	2	1.2	1	0.6	153	93.9	5	3.1	143	1	0.7	3	2.1	110	76.9	29	20.3		
	PI(D21)	161	0	0.0	0	0.0	152	94.4	7	4.3	140	0	0.0	2	1.4	102	72.9	33	23.6		
<p>N = number of subjects with laboratory results for the specified visit and laboratory parameter  n/% = number/percentage of subjects in a given category  Unknown = value unknown for the specified time point and laboratory parameter  Below = value below the laboratory reference range defined for the specified time point and laboratory parameter  Within = value within the laboratory reference range defined for the specified time point and laboratory parameter  Above = value above the laboratory reference range defined for the specified time point and laboratory parameter  ALAT= Alanine aminotransferase  AP= Alkaline phosphatase  ASAT=Aspartate aminotransferase  BUN= Blood urea nitrogen</p>																					
<b>Secondary Outcome Variable(s):</b> Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated cohort – Flu D21 Group)																					
		<b>Flu D21 Group</b>																			
		<b>18-60 years N = 93</b>										<b>&gt;60 years N = 91</b>									
		<b>Unknown</b>			<b>Below</b>		<b>Within</b>		<b>Above</b>			<b>Unknown</b>			<b>Below</b>		<b>Within</b>		<b>Above</b>		
<b>Laboratory parameter</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
ALAT	PRE	93	0	0.0	4	4.3	83	89.2	4	4.3	91	2	2.2	0	0.0	83	91.2	6	6.6		
	PI(D21)	91	1	1.1	3	3.3	83	91.2	3	3.3	88	0	0.0	0	0.0	74	84.1	11	12.5		
	PI(D42)	92	0	0.0	3	3.3	84	91.3	5	5.4	86	0	0.0	0	0.0	79	91.9	6	7.0		
AP	PRE	93	1	1.1	3	3.2	85	91.4	2	2.2	91	0	0.0	2	2.2	86	94.5	3	3.3		
	PI(D21)	91	0	0.0	3	3.3	86	94.5	1	1.1	88	0	0.0	2	2.3	79	89.8	4	4.5		
	PI(D42)	92	0	0.0	2	2.2	88	95.7	2	2.2	86	0	0.0	2	2.3	82	95.3	1	1.2		
ASAT	PRE	93	0	0.0	1	1.1	87	93.5	3	3.2	91	2	2.2	1	1.1	81	89.0	7	7.7		
	PI(D21)	91	1	1.1	0	0.0	85	93.4	4	4.4	88	1	1.1	1	1.1	75	85.2	8	9.1		
	PI(D42)	92	0	0.0	0	0.0	88	95.7	4	4.3	86	0	0.0	0	0.0	79	91.9	6	7.0		

Bilirubin	PRE	93	0	0.0	0	0.0	86	92.5	5	5.4	91	2	2.2	0	0.0	88	96.7	1	1.1
	PI(D21)	91	1	1.1	0	0.0	86	94.5	3	3.3	88	0	0.0	0	0.0	83	94.3	2	2.3
	PII(D42)	92	0	0.0	0	0.0	89	96.7	3	3.3	86	0	0.0	0	0.0	84	97.7	1	1.2
Creatinine	PRE	93	0	0.0	1	1.1	86	92.5	4	4.3	91	0	0.0	1	1.1	75	82.4	15	16.5
	PI(D21)	91	0	0.0	2	2.2	83	91.2	5	5.5	88	0	0.0	0	0.0	73	83.0	12	13.6
	PII(D42)	92	0	0.0	5	5.4	84	91.3	3	3.3	86	0	0.0	2	2.3	75	87.2	8	9.3
BUN	PRE	93	2	2.2	1	1.1	87	93.5	1	1.1	91	1	1.1	1	1.1	67	73.6	22	24.2
	PI(D21)	91	0	0.0	0	0.0	87	95.6	3	3.3	88	0	0.0	1	1.1	60	68.2	24	27.3
	PII(D42)	92	3	3.3	0	0.0	84	91.3	5	5.4	86	2	2.3	0	0.0	66	76.7	17	19.8

N = number of subjects with laboratory results for the specified visit and laboratory parameter

n/% = number/percentage of subjects in a given category

Unknown = value unknown for the specified time point and laboratory parameter

Below = value below the laboratory reference range defined for the specified time point and laboratory parameter

Within = value within the laboratory reference range defined for the specified time point and laboratory parameter

Above = value above the laboratory reference range defined for the specified time point and laboratory parameter

ALAT= Alanine aminotransferase

AP= Alkaline phosphatase

ASAT=Aspartate aminotransferase

BUN= Blood urea nitrogen

**Safety results:** Number (%) of subjects with unsolicited adverse events within the 42-day (Days 0-41) post vaccination period (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-41 following vaccination)	Flu D21 Group*		Flu M6 Group**	
	18-60 years N = 93	>60 years N = 91	18-60 years N = 70	>60 years N = 52
Subjects with any AE(s), n (%)	40 (43.0)	38 (41.8)	27 (38.6)	11 (21.2)
Subjects with Grade 3 AE(s), n (%)	6 (6.5)	6 (6.6)	6 (8.6)	1 (1.9)
Subjects with related AE(s), n (%)	11 (11.8)	15 (16.5)	5 (7.1)	2 (3.8)
Lymphadenopathy	-	-	-	1 (1.9)
Vertigo	3 (3.2)	-	-	-
Conjunctivitis	-	-	-	1 (1.9)
Abdominal pain	-	2 (2.2)	-	1 (1.9)
Diarrhoea	4 (4.3)	-	-	1 (1.9)
Fatigue	-	-	-	1 (1.9)
Influenza like illness	-	-	-	1 (1.9)
Injection site joint pain	-	-	-	1 (1.9)
Injection site pruritus	-	2 (2.2)	-	-
Bronchitis	-	2 (2.2)	-	-
Nasopharyngitis	9 (9.7)	3 (3.3)	2 (2.9)	1 (1.9)
Rhinitis	9 (9.7)	7 (7.7)	4 (5.7)	-
Joint injury	-	-	-	1 (1.9)
Joint sprain	-	-	-	1 (1.9)
Hepatic enzyme increased	-	2 (2.2)	-	-
Liver function test abnormal	-	2 (2.2)	-	-
Arthralgia	-	-	2 (2.9)	1 (1.9)
Back pain	-	3 (3.3)	-	1 (1.9)
Hypercreatinemia	-	2 (2.2)	-	-
Headache	-	-	2 (2.9)	1 (1.9)
Sciatica	-	-	-	1 (1.9)
Cough	-	-	-	1 (1.9)
Oropharyngeal pain	3 (3.2)	-	3 (4.3)	-

Dermatitis contact	-	-	-	1 (1.9)
Haematoma	-	-	-	1 (1.9)
*In Flu Day 21 Group: after 2 vaccine doses **In Flu M6 Group: after 1 vaccine dose -: adverse event absent or not meeting the selected rule: If more than 30 subjects per group and > 3 groups, then only the 5 most frequent adverse events in each group are to be listed. Grade 3= event that prevented normal activity Related= event assessed by the investigator as causally related to the study vaccination				
<b>Safety results:</b> Number (%) of subjects with serious adverse events until Day 42 (Total Vaccinated cohort)				
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>				
<b>All SAEs</b>	<b>Flu D21 Group</b>		<b>Flu M6 Group</b>	
	<b>18-60 years N = 93</b>	<b>&gt;60 years N = 91</b>	<b>18-60 years N = 70</b>	<b>&gt;60 years N = 52</b>
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	2 (2.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Hepatic enzyme increased	0 (0.0) [0]	1 (1.1) [1]	0 (0.0) [0]	0 (0.0) [0]
Lentigo maligna stage unspecified	0 (0.0) [0]	1 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Flu D21 Group</b>		<b>Flu M6 Group</b>	
	<b>18-60 years N = 93</b>	<b>&gt;60 years N = 91</b>	<b>18-60 years N = 70</b>	<b>&gt;60 years N = 52</b>
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

**Conclusion:**

21 days after Flu vaccine administration, SCR for HI antibodies against vaccine-homologous virus was of 96.3% in subjects aged 18-60 years and 89.0% in subjects above 60 years. At the same timepoint, SPR was of 97.5% for subjects aged 18-60 years and 91.9% in subjects above 60 years, and SCF was 45.0 in subjects aged 18-60 years and 23.4 in subjects above 60 years.

During the 42-day follow-up period after the first dose, 40 (43.0%) subjects of Flu D21 (18-60 years) Group, 38 (41.8%) subjects of Flu D21 (>60 years) Group, 27 (38.6%) subjects of Flu M6 (18-60 years) Group and 11 (21.2%) subjects of Flu M6 (>60 years) Group reported at least one unsolicited adverse event.

Up to Day 42, 2 subjects from the Flu D21 (>60 years) Group reported serious adverse events, one of which was assessed by the investigator as related to the study vaccination. No fatal SAE was reported during the study.

**Publications:** None

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