The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 112077 (Zoster-010)

Title: Immunogenicity and safety study of GSK Biologicals' herpes zoster vaccine 1437173A when combined with adjuvant (AS01B and AS01E) and administered twice in adults aged 50 years and older
GSK1437173A (gE/AS01B and gE/AS01E) (HZV): GSK Biologicals' recombinant herpes zoster (HZ) vaccine

Rationale: The aim of this study was to evaluate the safety and immunogenicity of Glycoprotein E (gE) adjuvanted with AS01 or unadjuvanted and Varicella-Zoster Virus (VZV) antigens in the overall study population aged 50 years and above vaccinated with HZV vaccine on a 0, 2-month schedule. This study comprised 2 main phases, a Primary vaccination phase (Month 0 to Month 3) followed by a Safety follow-up (SFU) phase (until Month 14).

Phase: II

Study Period: 12 January 2009 to:

- 02 July 2009 (LSLV Month 3)
- 16 December 2009 (LSLV Month 8)
- 02 July 2010 (LSLV Month 14)

Study Design: Observer blind, randomised, multicenter study with 4 parallel treatment groups (4:4:2:1)
For the safety follow-up part from Month 3 up to Month 14 the study remained blinded for the subjects, the investigator might become unblinded.

Centres: 12 centres (1 centre in Czech Republic, 4 centres in Spain and 7 centres in United States)

Indication: Primary immunisation of subjects aged 50 years and older against herpes zoster (HZ).

Treatment: The study groups were as follows:

- Control Group: Subjects in this group received 2 doses of Saline (placebo).
- HZV 3 Group: Subjects in this group received 2 doses of HZV formulation 3 vaccine.
- HZV 2 Group: Subjects in this group received 2 doses of HZV formulation 2 vaccine.
- HZV 1 Group: Subjects in this group received 2 doses of HZV formulation 1 vaccine.

All vaccines were administered intramuscularly in the upper deltoid region of the non-dominant arm on a 0, 2 month schedule.

Objectives:

- To compare gE and VZV-specific CD4* T cell-mediated and humoral immune responses to HZV formulations 1, 2 and 3 vaccines at Month 3 (one month following vaccinations at Months 0 and 2) in subjects aged 50 years and above (overall study population).

*cluster of differentiation 4

Primary Outcome/Efficacy Variable:
Immunogenicity:

- Frequencies of CD4 T-cells specific for gE and VZV-antigens, as determined by in vitro Intracellular Cytokine Staining (ICS), expressing at least 2 immunological activation markers (from among Interferon gamma (IFN-γ), Interleukin 2 (IL-2), Tumour Necrosis Factor alpha (TNF-α) and CD40 Ligand (CD40L)) 1 month after the second vaccination (Month 3)
- Anti-gE and anti-VZV antibody concentrations as determined by enzyme-linked immunosorbent assay (ELISA) 1 month after the second vaccination (Month 3)

Secondary Outcome/Efficacy Variable(s):
Immunogenicity:

- Frequencies of CD4 T cells specific for gE and VZV antigens, as determined by in vitro ICS, expressing at least 2 immunological activation markers (from among IFN-γ, IL-2, TNF-α and CD40L) at Months 0 and 2
- Frequencies of CD8 T cells specific for gE and VZV antigens, as determined by in vitro ICS, expressing at least 2 immunological activation markers (from among IFN-γ, IL-2, TNF-α and CD40L) at Months 0, 2 and 3 [£]
- Anti-gE and anti-VZV antibody concentrations as determined by ELISA at Months 0 and 2

Safety:

- Occurrence, intensity and relationship to vaccination of solicited local and general adverse events (AEs) during 7 days (Days 0-6) after each vaccination
- Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination
- Occurrence and relationship to vaccination of all serious adverse events (SAEs) starting at Day 0 and ending 12 months following the last vaccination

- Occurrence and relationship to vaccination of all New Onset of Autoimmune Disease (NOADs) starting at Day 0 and ending 12 months following the last vaccination
- Occurrence of suspected cases of HZ starting at Day 0 and ending 12 months following the last vaccination
- Haematological and biochemical parameters measured at Months 0, 2, and 3.

£ Analyses of CD8 T-cell responses were not performed

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort, Total Vaccinated Cohort for the Safety Follow-up (SFU) Month 14 and the According-to-Protocol (ATP) Cohort for immunogenicity.

- The Total Vaccinated Cohort included all subjects with at least one vaccine administration documented.
- The Total Vaccinated Cohort for the SFU Month 14 included all vaccinated subjects who were not withdrawn from the study during the period up to Month 3 nor from the SFU Month 8, and who signed the supplementary informed consent for participating to the End of study telephone contact.
- The ATP Cohort for analysis of immunogenicity included all evaluable subjects from Month 0 to Month 3. This included those subjects who met all eligibility criteria, complied with the procedures and intervals defined in the protocol, with no elimination criteria during this part of the study and for whom data related to immunogenicity outcome measures were available.

Analysis of Immunogenicity

The analysis of immunogenicity was performed on the ATP Cohort for immunogenicity.

Inferential analysis:

Cell mediated immune response:

Geometric means (GMs) of specific CD4+T frequencies and their 95% Confidence intervals (CIs) were tabulated for HZV1, HZV2 and HZV3 groups following both inductions with gE and VZV at Month 3 (1 month after 2 vaccinations). Geometric mean ratios of gE and VZV specific CD4+T frequencies were computed for comparison of interest (HZV1 and HZV2 over HZV3 and HZV1 over HZV2) with their 95% CIs at Month 3.

The following tests were performed at the 2.5% significance level (1-sided).

Humoral immune response:

Similar comparisons as described for the CMI immune response were performed for the humoral immune response. Geometric mean concentrations (GMCs) of anti-gE and anti-VZV antibodies and GM ratios for comparison were calculated together with 95% CIs. The significance level for the comparison of interest (HZV1 and HZV2 over HZV3 and HZV1 over HZV2) with their 95% CIs at Month 3 was set to 2.5% (1-sided).

Descriptive analysis:

Descriptive statistics of the frequencies of gE and VZV specific CD4+T secreting at least 2 different cytokines among IFN-γ, IL-2, TNF-α, and/or CD40L were tabulated by treatment group at Month 0, Month 2 and Month 3.

Seopositivity rates and Geometric mean concentrations (GMCs) for anti-gE and anti-VZV antibodies were computed with their 95% CI by ELISA for each group at pre-vaccination, Month 2 and Month 3.

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Analysis of Safety

The analysis of safety was performed on the Total Vaccinated Cohort and The Total Vaccinated Cohort for the SFU Month 14.

The percentages of subjects with solicited local and general AEs reported during the 7-day (Days 0-6) post vaccination period were tabulated by treatment group, after each dose and across doses with exact 95% CI. The same tabulation was performed for grade 3 solicited symptoms and for solicited general symptoms assessed by the investigator as related to vaccination.

The percentage of subjects with at least one report of an unsolicited AE reported within 30 days (Days 0-29) following vaccination was tabulated by treatment group according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The same tabulation was done for grade 3 unsolicited AEs and for those assessed by the investigator as related to vaccination.

The occurrence of NOADs, Cases of suspected HZ and SAEs were collected and summarized throughout the entire study period (Month 0 to Month 14).

The proportion of subjects with haematology and biochemistry parameters below, within or above normal ranges was tabulated by treatment group at Month 0, Month 2 and Month 3.

Study Population: Male or female 50 years of age or above at the time of the first vaccination. Female subjects were to be of non-childbearing potential or if she is of childbearing potential, she must practice adequate contraception for 30 days prior to vaccination, have a negative pregnancy test and continue such precautions for 2 months after completion of the vaccination series. Subject must not have received any previous vaccination against HZ or varicella nor have any history of

HZ. Written informed consent was obtained from all subjects before any study procedure.				
Number of Subjects: Month 0-Month 3	Control Group	HZV 3 Group	HZV 2 Group	HZV 1 Group
Planned, N	36	72	144	144
Randomized, N (Total Vaccinated Cohort)	38	73	149	150
Completed to Month 3, n (%)	38 (100)	72 (98.6)	143 (96.0)	142 (94.7)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	1 (1.4)	6 (4.0)	8 (5.3)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	2 (1.3)	2 (1.3)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	1(1.4)	4 (2.7)	6 (4.0)
Number of Subjects: Month 0 - Month 8	Control Group	HZV 3 Group	HZV 2 Group	HZV 1 Group
Planned, N	36	72	144	144
Randomized, N (Total Vaccinated Cohort)	38	73	149	150
Completed to Month 8, n (%)	38 (100)	70 (95.9)	142 (95.3)	141 (94.0)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	3 (4.1)	7 (4.7)	9 (6.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	1 (1.4)	1 (0.7)	2 (1.3)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	2 (2.7)	6 (4.0)	7 (4.7)
Number of Subjects: Month 8 - Month 14	Control Group	HZV 3 Group	HZV 2 Group	HZV 1 Group
Planned, N	36	72	144	144
Entered, N (Total Vaccinated Cohort SFU Month 14)	34	65	130	126
Completed to Month 14, n (%)	33 (97.1)	63 (96.9)	129 (99.2)	126 (100)
Total Number Subjects Withdrawn, n (%)	1 (2.9)	2 (3.1)	1 (0.8)	0 (0.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	1 (1.5)	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 (2.9)	1(1.5)	1(0.8)	0 (0.0)
Demographics	Control Group	HZV 3 Group	HZV 2 Group	HZV 1 Group
N (Total Vaccinated Cohort)	38	73	149	150
Females: Males	22:16	40:33	89:60	81:69
Mean Age, years (SD)	65.0 (9.03)	65.1 (8.72)	65.1 (9.89)	65.0 (8.86)
White - Caucasian / European heritage, n (%)	38 (100)	72 (98.6)	145 (97.3)	141 (94.0)

Primary Efficacy Results: Fold increase in frequency of gE-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L for HZV 1 and HZV 2 over HZV 3 Groups (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean gE-specific Frequency			Fold increase over HZV formulation 3			p-value for ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	124	387.35	343.65	434.64	2.33	1.79	3.03	<.0001
	HZV 2	124	378.43	335.28	425.13	2.27	1.74	2.96	<.0001
	HZV 3	64	166.50	129.31	208.02	-	-	-	-
PII(M3)*	HZV 1	121	2048.74	1784.77	2348.01	5.21	3.89	6.98	<.0001
	HZV 2	124	1580.65	1373.74	1814.94	4.02	3.00	5.40	<.0001
	HZV 3	64	392.88	299.84	503.61	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in frequency of gE-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L for HZV 1 Group over HZV 2 Group (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean gE-specific Frequency			Fold increase over HZV formulation 2			p-value for ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	124	387.35	343.65	434.64	1.02	0.87	1.21	0.7835
	HZV 2	124	378.43	335.28	425.13	-	-	-	-

PII(M3)*	HZV 1	121	2048.74	1784.77	2348.01	1.30	1.07	1.58	0.0094
	HZV 2	124	1580.65	1373.74	1814.94	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Descriptive statistics of the frequency of gE-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L upon in vitro stimulation with gE-antigen (ATP Cohort for immunogenicity)

Group	Timing	N	Mean	SD	Median
Control	PRE	35	210.18	363.37	126.0
	PI(M2)	33	185.59	310.06	125.0
	PII(M3)*	32	231.82	411.84	113.3
HZV 3	PRE	65	130.98	115.90	106.7
	PI(M2)	70	189.46	188.80	146.7
	PII(M3)*	70	570.36	610.10	367.8
HZV 2	PRE	132	196.52	217.94	150.1
	PI(M2)	126	463.79	386.94	386.7
	PII(M3)*	126	2172.37	1805.51	1634.5
HZV 1	PRE	133	173.48	203.54	110.9
	PI(M2)	127	430.50	323.88	333.3
	PII(M3)*	125	2582.80	2154.92	1973.3

N = number of subjects with available results
SD = Standard Deviation
PRE = pre-vaccination blood sample at Month 0
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in frequency of VZV-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L for HZV 1 and HZV 2 over HZV 3 groups (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean VZV-specific Frequency			Fold increase over HZV formulation 3			p-value for ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	124	446.87	401.35	495.89	1.12	0.93	1.36	0.2192
	HZV 2	122	425.29	380.88	473.15	1.07	0.89	1.29	0.4821
	HZV 3	63	397.45	339.16	462.17	-	-	-	-
PII(M3)*	HZV 1	121	1009.42	889.88	1142.20	2.12	1.67	2.69	<.0001
	HZV 2	123	775.20	679.50	881.44	1.63	1.28	2.07	<.0001
	HZV 3	64	476.91	386.56	581.42	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in frequency of VZV-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L for HZV 1 Group over HZV 2 Group (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean VZV-specific Frequency			Fold increase over HZV formulation 2			p-value for ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	124	446.87	401.35	495.89	1.05	0.90	1.22	0.5199
	HZV 2	122	425.29	380.88	473.15	-	-	-	-
PII(M3)*	HZV 1	121	1009.42	889.88	1142.20	1.30	1.09	1.56	0.0042
	HZV 2	123	775.20	679.50	881.44	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Descriptive statistics of the frequency of VZV-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L upon in vitro stimulation with VZV-antigen (ATP Cohort for immunogenicity)

Group	Timing	N	Mean	SD	Median
Control	PRE	35	533.97	422.46	413.3
	PI(M2)	33	491.12	330.34	466.7
	PII(M3)*	32	457.43	275.25	433.3
HZV 3	PRE	65	352.71	283.42	280.0
	PI(M2)	68	410.69	356.65	326.7
	PII(M3)*	70	523.12	396.01	473.3
HZV 2	PRE	131	457.28	402.04	347.0
	PI(M2)	124	595.10	588.51	400.0
	PII(M3)*	126	1093.08	927.18	800.0
HZV 1	PRE	133	482.63	512.05	346.7
	PI(M2)	127	574.54	586.85	420.2
	PII(M3)*	125	1270.79	1106.45	866.7

N = number of subjects with available results
SD = Standard Deviation
PRE = pre-vaccination blood sample at Month 0
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in anti-gE antibody concentrations for HZV 1 and HZV 2 groups over HZV 3 group (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean of Anti-gE concentration			Fold increase over HZV formulation 3			p-value for Ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	133	24516.93	21111.30	28471.94	2.51	1.94	3.24	<.0001
	HZV 2	133	19349.33	16662.13	22469.90	1.98	1.53	2.55	<.0001
	HZV 3	70	9772.12	7951.21	12010.04	-	-	-	-
PII(M3)*	HZV 1	132	68689.13	60569.84	77896.81	4.72	3.81	5.85	<.0001
	HZV 2	132	48973.99	43186.55	55537.00	3.36	2.72	4.17	<.0001
	HZV 3	70	14554.57	12243.09	17302.44	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in anti-gE antibody concentrations for HZV 1 Group over HZV 2 Group (ATP Cohort for immunogenicity)

Timing	Group	N	Geometric Mean of Anti-gE concentration			Fold increase over HZV formulation 2			p-value for Ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	133	24516.93	21111.30	28471.94	1.27	1.03	1.57	0.0284
	HZV 2	133	19349.33	16662.13	22469.90	-	-	-	-
PII(M3)*	HZV 1	132	68689.13	60569.84	77896.81	1.40	1.17	1.68	0.0002
	HZV 2	132	48973.99	43186.55	55537.00	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3

*Primary outcome measure

Primary Efficacy Results: Seropositivity rates and GMCs of anti-gE antibody (ATP cohort for immunogenicity)

			≥ 18 mIU/mL				GMC (mIU/mL)		
					95% CI			95% CI	
Group	Timing	N	n	%	LL	UL	value	LL	UL
Control	PRE	37	37	100	90.5	100	1907.7	1374.9	2646.9
	PI(M2)	37	37	100	90.5	100	2022.3	1484.6	2754.7
	PII(M3)*	36	36	100	90.3	100	1987.0	1405.8	2808.6
HZV 3	PRE	71	71	100	94.9	100	1640.3	1307.9	2057.3
	PI(M2)	70	70	100	94.9	100	10022.8	7593.7	13228.7
	PII(M3)*	70	70	100	94.9	100	14627.6	11347.9	18855.1
HZV 2	PRE	137	137	100	97.3	100	1526.7	1306.6	1783.8
	PI(M2)	134	134	100	97.3	100	19962.3	16894.4	23587.3
	PII(M3)*	133	133	100	97.3	100	49531.5	44269.3	55419.2
HZV 1	PRE	140	140	100	97.4	100	1398.3	1212.6	1612.5
	PI(M2)	133	133	100	97.3	100	23942.4	20536.9	27912.6
	PII(M3)*	132	132	100	97.2	100	68798.2	61596.8	76841.5

GMC = geometric mean antibody concentrations calculated on all subjects
N= number of subjects with available results
n/%= number/percentage of subjects with concentration above the specified range
95% CI= exact 95% confidence interval; LL = lower limit, UL = upper limit
PRE = pre-vaccination blood sample at Month 0
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in anti-VZV antibody concentrations for HZV 1 and HZV 2 groups over HZV 3 group (ATP Cohort for immunogenicity)

Timing	Treatment	N	Geometric Mean of Anti-VZV concentration			Fold increase over HZV formulation 3			p-value for Ratio
			value	95% CI		value	95% CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	109	5018.13	4438.87	5672.99	1.91	1.55	2.34	<.0001
	HZV 2	110	4294.16	3800.75	4851.62	1.63	1.33	2.00	<.0001
	HZV 3	61	2630.81	2230.70	3102.69	-	-	-	-
PII(M3)*	HZV 1	114	11906.52	10644.58	13318.08	3.21	2.64	3.90	<.0001
	HZV 2	117	9067.17	8118.32	10126.91	2.44	2.01	2.97	<.0001
	HZV 3	55	3711.18	3162.20	4355.47	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Fold increase in anti-VZV antibody concentrations for HZV 1 Group over HZV 2 Group (ATP Cohort for immunogenicity)

Timing	Treatment	N	Geometric Mean of Anti-VZV concentration			Fold increase over HZV formulation 2			p-value for Ratio
			value	95%CI		value	95%CI		
				LL	UL		LL	UL	
PI(M2)	HZV 1	109	5018.13	4438.87	5672.99	1.17	0.98	1.39	0.0776
	HZV 2	110	4294.16	3800.75	4851.62	-	-	-	-
PII(M3)*	HZV 1	114	11906.52	10644.58	13318.08	1.31	1.12	1.54	0.0008
	HZV 2	117	9067.17	8118.32	10126.91	-	-	-	-

N = number of subjects with available results
95% CI = 95% Confidence intervals, LL = lower limit, UL = upper limit
PI(M2) = Post Dose 1 blood sample at Month 2

PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

Primary Efficacy Results: Seropositivity rates and GMCs of anti-VZV antibodies (ATP cohort for immunogenicity)

			≥ 25 mIU/mL				GMC (mIU/mL)*		
					95% CI			95% CI	
Group	Timing	N	n	%	LL	UL	value	LL	UL
Control	PRE	37	37	100	90.5	100	1505.5	1191.7	1901.9
	PI(M2)	37	37	100	90.5	100	1365.5	1074.4	1735.4
	PII(M3)*	36	36	100	90.3	100	1423.2	1097.8	1845.0
HZV 3	PRE	71	71	100	94.9	100	1289.6	1100.3	1511.6
	PI(M2)	70	70	100	94.9	100	2392.8	2074.8	2759.5
	PII(M3)*	70	70	100	94.9	100	2786.4	2445.1	3175.3
HZV 2	PRE	137	137	100	97.3	100	1215.9	1077.4	1372.2
	PI(M2)	134	134	100	97.3	100	3125.6	2902.8	3365.5
	PII(M3)*	133	133	100	97.3	100	4565.4	4357.0	4783.7
HZV 1	PRE	140	140	100	97.4	100	1175.8	1051.0	1315.5
	PI(M2)	133	133	100	97.3	100	3355.1	3110.6	3618.9
	PII(M3)*	132	132	100	97.2	100	4972.8	4802.7	5148.8

GMC = geometric mean antibody concentrations calculated on all subjects
N= number of subjects with available results
n/%= number/percentage of subjects with concentration above the specified range
95% CI= exact 95% confidence interval; LL = lower limit, UL = upper limit
PRE = pre-vaccination blood sample at Month 0
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3
*Primary outcome measure

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

		Control Group					HZV 3 Group					HZV 2 Group					HZV 1 Group				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Intensity	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																					
Pain	Any	38	1	2.6	0.1	13.8	73	8	11.0	4.9	20.5	149	89	59.7	51.4	67.7	150	112	74.7	66.9	81.4
	Grade 3	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	1	0.7	0.0	3.7	150	0	0.0	0.0	2.4
Redness	Any	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	15	10.1	5.7	16.1	150	26	17.3	11.6	24.4
	> 100 mm	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	2	1.3	0.2	4.8	150	2	1.3	0.2	4.7
Swelling	Any	38	0	0.0	0.0	9.3	73	1	1.4	0.0	7.4	149	9	6.0	2.8	11.2	150	8	5.3	2.3	10.2
	> 100 mm	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	1	0.7	0.0	3.7	150	0	0.0	0.0	2.4
Dose 2																					
Pain	Any	37	2	5.4	0.7	18.2	72	9	12.5	5.9	22.4	143	82	57.3	48.8	65.6	143	106	74.1	66.1	81.1
	Grade 3	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0	143	1	0.7	0.0	3.8	143	6	4.2	1.6	8.9
Redness	Any	37	0	0.0	0.0	9.5	72	3	4.2	0.9	11.7	143	19	13.3	8.2	20.0	143	37	25.9	18.9	33.9
	> 100 mm	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0	143	1	0.7	0.0	3.8	143	1	0.7	0.0	3.8
Swelling	Any	37	0	0.0	0.0	9.5	72	2	2.8	0.3	9.7	143	20	14.0	8.8	20.8	143	18	12.6	7.6	19.2
	> 100 mm	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0	143	0	0.0	0.0	2.5	143	1	0.7	0.0	3.8
Across Doses																					
Pain	Any	38	3	7.9	1.7	21.4	73	14	19.2	10.9	30.1	149	104	69.8	61.7	77.0	150	125	83.3	76.4	88.9
	Grade 3	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	2	1.3	0.2	4.8	150	6	4.0	1.5	8.5
Redness	Any	38	0	0.0	0.0	9.3	73	3	4.1	0.9	11.5	149	26	17.4	11.7	24.5	150	44	29.3	22.2	37.3
	> 100 mm	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	3	2.0	0.4	5.8	150	2	1.3	0.2	4.7
Swelling	Any	38	0	0.0	0.0	9.3	73	3	4.1	0.9	11.5	149	25	16.8	11.2	23.8	150	23	15.3	10.0	22.1
	> 100 mm	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9	149	1	0.7	0.0	3.7	150	1	0.7	0.0	3.7

N= number of subjects with at least one administered 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 symptom regardless of intensity grade

Grade 3 pain = Pain that prevented normal activity

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

		Control Group					HZV 3 Group				
					95 % CI					95 % CI	
Symptom	Intensity/ Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	38	3	7.9	1.7	21.4	73	10	13.7	6.8	23.8
	Grade 3	38	0	0.0	0.0	9.3	73	1	1.4	0.0	7.4
	Related	38	3	7.9	1.7	21.4	73	9	12.3	5.8	22.1
Gastrointestinal	Any	38	1	2.6	0.1	13.8	73	1	1.4	0.0	7.4
	Grade 3	38	1	2.6	0.1	13.8	73	0	0.0	0.0	4.9
	Related	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
Headache	Any	38	2	5.3	0.6	17.7	73	8	11.0	4.9	20.5
	Grade 3	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	Related	38	1	2.6	0.1	13.8	73	5	6.8	2.3	15.3
Myalgia	Any	38	1	2.6	0.1	13.8	73	8	11.0	4.9	20.5
	Grade 3	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	Related	38	1	2.6	0.1	13.8	73	6	8.2	3.1	17.0
Fever (axillary)	> 37.5°C	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	> 39.0°C	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	Related	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
Dose 2											
Fatigue	Any	37	5	13.5	4.5	28.8	72	10	13.9	6.9	24.1
	Grade 3	37	1	2.7	0.1	14.2	72	1	1.4	0.0	7.5
	Related	37	3	8.1	1.7	21.9	72	9	12.5	5.9	22.4
Gastrointestinal	Any	37	2	5.4	0.7	18.2	72	4	5.6	1.5	13.6
	Grade 3	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0
	Related	37	1	2.7	0.1	14.2	72	3	4.2	0.9	11.7
Headache	Any	37	3	8.1	1.7	21.9	72	5	6.9	2.3	15.5
	Grade 3	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0
	Related	37	1	2.7	0.1	14.2	72	5	6.9	2.3	15.5
Myalgia	Any	37	2	5.4	0.7	18.2	72	8	11.1	4.9	20.7
	Grade 3	37	1	2.7	0.1	14.2	72	0	0.0	0.0	5.0
	Related	37	2	5.4	0.7	18.2	72	8	11.1	4.9	20.7
Fever (axillary)	> 37.5°C	37	1	2.7	0.1	14.2	72	0	0.0	0.0	5.0
	> 39.0°C	37	0	0.0	0.0	9.5	72	0	0.0	0.0	5.0
	Related	37	1	2.7	0.1	14.2	72	0	0.0	0.0	5.0
Across Doses											
Fatigue	Any	38	7	18.4	7.7	34.3	73	16	21.9	13.1	33.1
	Grade 3	38	1	2.6	0.1	13.8	73	2	2.7	0.3	9.5
	Related	38	6	15.8	6.0	31.3	73	14	19.2	10.9	30.1
Gastrointestinal	Any	38	3	7.9	1.7	21.4	73	5	6.8	2.3	15.3
	Grade 3	38	1	2.6	0.1	13.8	73	0	0.0	0.0	4.9
	Related	38	1	2.6	0.1	13.8	73	3	4.1	0.9	11.5
Headache	Any	38	4	10.5	2.9	24.8	73	10	13.7	6.8	23.8
	Grade 3	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	Related	38	2	5.3	0.6	17.7	73	8	11.0	4.9	20.5
Myalgia	Any	38	2	5.3	0.6	17.7	73	12	16.4	8.8	27.0
	Grade 3	38	1	2.6	0.1	13.8	73	0	0.0	0.0	4.9
	Related	38	2	5.3	0.6	17.7	73	11	15.1	7.8	25.4
Fever (axillary)	> 37.5°C	38	1	2.6	0.1	13.8	73	0	0.0	0.0	4.9
	> 39.0°C	38	0	0.0	0.0	9.3	73	0	0.0	0.0	4.9
	Related	38	1	2.6	0.1	13.8	73	0	0.0	0.0	4.9
		HZV 2 Group					HZV 1 Group				

					95 % CI					95 % CI	
Symptom	Intensity/ Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	149	32	21.5	15.2	28.9	150	42	28.0	21.0	35.9
	Grade 3	149	2	1.3	0.2	4.8	150	2	1.3	0.2	4.7
	Related	149	28	18.8	12.9	26.0	150	39	26.0	19.2	33.8
Gastrointestinal	Any	149	10	6.7	3.3	12.0	150	8	5.3	2.3	10.2
	Grade 3	149	2	1.3	0.2	4.8	150	0	0.0	0.0	2.4
	Related	149	7	4.7	1.9	9.4	150	7	4.7	1.9	9.4
Headache	Any	149	22	14.8	9.5	21.5	150	32	21.3	15.1	28.8
	Grade 3	149	0	0.0	0.0	2.4	150	1	0.7	0.0	3.7
	Related	149	14	9.4	5.2	15.3	150	29	19.3	13.3	26.6
Myalgia	Any	149	36	24.2	17.5	31.8	150	42	28.0	21.0	35.9
	Grade 3	149	0	0.0	0.0	2.4	150	2	1.3	0.2	4.7
	Related	149	29	19.5	13.4	26.7	150	40	26.7	19.8	34.5
Fever (axillary)	> 37.5°C	149	7	4.7	1.9	9.4	150	11	7.3	3.7	12.7
	> 39.0°C	149	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4
	Related	149	3	2.0	0.4	5.8	150	8	5.3	2.3	10.2
Dose 2											
Fatigue	Any	143	41	28.7	21.4	36.8	143	58	40.6	32.4	49.1
	Grade 3	143	3	2.1	0.4	6.0	143	7	4.9	2.0	9.8
	Related	143	34	23.8	17.1	31.6	143	56	39.2	31.1	47.7
Gastrointestinal	Any	143	12	8.4	4.4	14.2	143	12	8.4	4.4	14.2
	Grade 3	143	0	0.0	0.0	2.5	143	0	0.0	0.0	2.5
	Related	143	8	5.6	2.4	10.7	143	9	6.3	2.9	11.6
Headache	Any	143	25	17.5	11.6	24.7	143	42	29.4	22.1	37.6
	Grade 3	143	0	0.0	0.0	2.5	143	4	2.8	0.8	7.0
	Related	143	20	14.0	8.8	20.8	143	38	26.6	19.5	34.6
Myalgia	Any	143	33	23.1	16.4	30.9	143	49	34.3	26.5	42.7
	Grade 3	143	2	1.4	0.2	5.0	143	6	4.2	1.6	8.9
	Related	143	26	18.2	12.2	25.5	143	48	33.6	25.9	41.9
Fever (axillary)	> 37.5°C	143	14	9.8	5.5	15.9	143	21	14.7	9.3	21.6
	> 39.0°C	143	0	0.0	0.0	2.5	143	0	0.0	0.0	2.5
	Related	143	11	7.7	3.9	13.3	143	20	14.0	8.8	20.8
Across Doses											
Fatigue	Any	149	52	34.9	27.3	43.1	150	72	48.0	39.8	56.3
	Grade 3	149	5	3.4	1.1	7.7	150	9	6.0	2.8	11.1
	Related	149	45	30.2	23.0	38.3	150	71	47.3	39.1	55.6
Gastrointestinal	Any	149	18	12.1	7.3	18.4	150	17	11.3	6.7	17.5
	Grade 3	149	2	1.3	0.2	4.8	150	0	0.0	0.0	2.4
	Related	149	12	8.1	4.2	13.6	150	15	10.0	5.7	16.0
Headache	Any	149	37	24.8	18.1	32.6	150	56	37.3	29.6	45.6
	Grade 3	149	0	0.0	0.0	2.4	150	5	3.3	1.1	7.6
	Related	149	29	19.5	13.4	26.7	150	53	35.3	27.7	43.5
Myalgia	Any	149	49	32.9	25.4	41.0	150	62	41.3	33.4	49.7
	Grade 3	149	2	1.3	0.2	4.8	150	7	4.7	1.9	9.4
	Related	149	41	27.5	20.5	35.4	150	62	41.3	33.4	49.7
Fever (axillary)	≥ 37.5°C	149	18	12.1	7.3	18.4	150	25	16.7	11.1	23.6
	> 39.0°C	149	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4
	Related	149	13	8.7	4.7	14.5	150	23	15.3	10.0	22.1

N= number of subjects with at least one administered 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 ay solicited general symptom regardless of intensity grade or relationship to vaccination
Grade 3 = symptom that prevented normal activity

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

Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of New Onset of Autoimmune Disease (NOADs), from Day 0 up to Month 8 (Total Vaccinated Cohort)

NOADs	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any NOADs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of New Onset of Autoimmune Disease (NOADs), during the period after Month 8 up to the end of the study at Month 14 (Total Vaccinated Cohort SFU Month 14)

NOADs	Control Group N = 34	HZV 3 Group N = 65	HZV 2 Group N = 130	HZV 1 Group N = 126
Subjects with any NOADs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of HZ cases, from Day 0 up to Month 8 (Total Vaccinated Cohort)

HZ cases	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any HZ case, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of HZ cases, during the period after Month 8 up to the end of the study at Month 14 (Total Vaccinated Cohort SFU Month 14)

HZ cases	Control Group N = 34	HZV 3 Group N = 65	HZV 2 Group N = 130	HZV 1 Group N = 126
Subjects with any HZ case, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Variable(s): Distribution of haematology and biochemistry with respect to normal laboratory ranges (Total Vaccinated Cohort)

		Control Group									HZV 1 Group								
			Unknown		Below		Normal		Above			Unknown		Below		Normal		Above	
Parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
Alanine Aminotransferase	PRE	38	0	0.0	0	0.0	35	92.1	3	7.9	150	0	0.0	0	0.0	146	97.3	4	2.7
	PI(M2)	38	0	0.0	0	0.0	36	94.7	2	5.3	143	0	0.0	0	0.0	139	97.2	4	2.8
	PII(M3)	38	0	0.0	0	0.0	36	94.7	2	5.3	142	0	0.0	0	0.0	138	97.2	4	2.8
Aspartate Aminotransferase	PRE	38	0	0.0	0	0.0	38	100	0	0.0	150	0	0.0	0	0.0	148	98.7	2	1.3
	PI(M2)	38	0	0.0	0	0.0	38	100	0	0.0	143	0	0.0	0	0.0	139	97.2	4	2.8
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	0	0.0	0	0.0	139	97.9	3	2.1
Basophils	PRE	38	1	2.6	0	0.0	37	97.4	0	0.0	150	2	1.3	0	0.0	148	98.7	0	0.0
	PI(M2)	38	1	2.6	0	0.0	37	97.4	0	0.0	143	3	2.1	0	0.0	140	97.9	0	0.0
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	3	2.1	0	0.0	139	97.9	0	0.0
Calcium	PRE	38	0	0.0	0	0.0	38	100	0	0.0	150	0	0.0	0	0.0	150	100	0	0.0
	PI(M2)	38	0	0.0	0	0.0	38	100	0	0.0	143	0	0.0	2	1.4	137	95.8	4	2.8
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	0	0.0	1	0.7	140	98.6	1	0.7
Creatinine	PRE	38	0	0.0	0	0.0	36	94.7	2	5.3	150	0	0.0	0	0.0	144	96.0	6	4.0
	PI(M2)	38	0	0.0	0	0.0	37	97.4	1	2.6	143	0	0.0	0	0.0	138	96.5	5	3.5
	PII(M3)	38	0	0.0	0	0.0	37	97.4	1	2.6	142	0	0.0	0	0.0	135	95.1	7	4.9
Eosinophils	PRE	38	1	2.6	0	0.0	36	94.7	1	2.6	150	2	1.3	11	7.3	132	88.0	5	3.3
	PI(M2)	38	1	2.6	1	2.6	35	92.1	1	2.6	143	3	2.1	12	8.4	125	87.4	3	2.1
	PII(M3)	38	0	0.0	1	2.6	36	94.7	1	2.6	142	3	2.1	7	4.9	131	92.3	1	0.7
Fibrinogen	PRE	38	0	0.0	1	2.6	34	89.5	3	7.9	150	3	2.0	2	1.3	127	84.7	18	12.0
	PI(M2)	38	0	0.0	1	2.6	34	89.5	3	7.9	143	2	1.4	12	8.4	124	86.7	5	3.5
	PII(M3)	38	0	0.0	1	2.6	35	92.1	2	5.3	142	3	2.1	5	3.5	125	88.0	9	6.3
Hematocrit	PRE	38	1	2.6	2	5.3	35	92.1	0	0.0	150	2	1.3	12	8.0	135	90.0	1	0.7
	PI(M2)	38	1	2.6	2	5.3	35	92.1	0	0.0	143	3	2.1	12	8.4	126	88.1	2	1.4
	PII(M3)	38	0	0.0	4	10.5	34	89.5	0	0.0	142	3	2.1	12	8.5	126	88.7	1	0.7
Hemoglobin	PRE	38	1	2.6	1	2.6	36	94.7	0	0.0	150	2	1.3	6	4.0	141	94.0	1	0.7
	PI(M2)	38	1	2.6	1	2.6	35	92.1	1	2.6	143	3	2.1	9	6.3	129	90.2	2	1.4
	PII(M3)	38	0	0.0	2	5.3	35	92.1	1	2.6	142	3	2.1	10	7.0	127	89.4	2	1.4
Lactase Dehydrogenase	PRE	38	0	0.0	0	0.0	38	100	0	0.0	150	0	0.0	0	0.0	149	99.3	1	0.7
	PI(M2)	38	0	0.0	0	0.0	38	100	0	0.0	143	0	0.0	0	0.0	143	100	0	0.0

	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	0	0.0	0	0.0	141	99.3	1	0.7
Lymphocytes	PRE	38	1	2.6	1	2.6	35	92.1	1	2.6	150	2	1.3	2	1.3	146	97.3	0	0.0
	PI(M2)	38	1	2.6	0	0.0	37	97.4	0	0.0	143	3	2.1	2	1.4	137	95.8	1	0.7
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	3	2.1	3	2.1	136	95.8	0	0.0
Mean Corpuscular Volume	PRE	38	1	2.6	0	0.0	37	97.4	0	0.0	150	2	1.3	5	3.3	140	93.3	3	2.0
	PI(M2)	38	1	2.6	0	0.0	37	97.4	0	0.0	143	3	2.1	2	1.4	134	93.7	4	2.8
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	3	2.1	3	2.1	133	93.7	3	2.1
Monocytes	PRE	38	1	2.6	1	2.6	36	94.7	0	0.0	150	2	1.3	6	4.0	142	94.7	0	0.0
	PI(M2)	38	1	2.6	3	7.9	34	89.5	0	0.0	143	3	2.1	10	7.0	130	90.9	0	0.0
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	3	2.1	9	6.3	130	91.5	0	0.0
Neutrophils	PRE	38	1	2.6	0	0.0	37	97.4	0	0.0	150	2	1.3	3	2.0	142	94.7	3	2.0
	PI(M2)	38	1	2.6	1	2.6	36	94.7	0	0.0	143	3	2.1	3	2.1	136	95.1	1	0.7
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	3	2.1	4	2.8	135	95.1	0	0.0
Partial Thromboplastin Time	PRE	38	0	0.0	1	2.6	36	94.7	1	2.6	150	4	2.7	10	6.7	135	90.0	1	0.7
	PI(M2)	38	0	0.0	0	0.0	37	97.4	1	2.6	143	2	1.4	1	0.7	132	92.3	8	5.6
	PII(M3)	38	0	0.0	0	0.0	37	97.4	1	2.6	142	3	2.1	0	0.0	131	92.3	8	5.6
Platelets	PRE	38	2	5.3	0	0.0	35	92.1	1	2.6	150	2	1.3	3	2.0	144	96.0	1	0.7
	PI(M2)	38	1	2.6	1	2.6	36	94.7	0	0.0	143	3	2.1	3	2.1	137	95.8	0	0.0
	PII(M3)	38	1	2.6	0	0.0	37	97.4	0	0.0	142	7	4.9	4	2.8	131	92.3	0	0.0
Prothrombin Time	PRE	38	0	0.0	2	5.3	35	92.1	1	2.6	150	4	2.7	7	4.7	135	90.0	4	2.7
	PI(M2)	38	0	0.0	0	0.0	37	97.4	1	2.6	143	2	1.4	0	0.0	136	95.1	5	3.5
	PII(M3)	38	0	0.0	0	0.0	37	97.4	1	2.6	142	3	2.1	0	0.0	131	92.3	8	5.6
Red Blood Cells	PRE	38	1	2.6	0	0.0	37	97.4	0	0.0	150	2	1.3	7	4.7	141	94.0	0	0.0
	PI(M2)	38	1	2.6	1	2.6	36	94.7	0	0.0	143	3	2.1	8	5.6	131	91.6	1	0.7
	PII(M3)	38	0	0.0	2	5.3	36	94.7	0	0.0	142	3	2.1	7	4.9	131	92.3	1	0.7
Total Protein	PRE	38	0	0.0	0	0.0	38	100	0	0.0	150	0	0.0	0	0.0	149	99.3	1	0.7
	PI(M2)	38	0	0.0	0	0.0	38	100	0	0.0	143	0	0.0	1	0.7	142	99.3	0	0.0
	PII(M3)	38	0	0.0	0	0.0	38	100	0	0.0	142	0	0.0	0	0.0	142	100	0	0.0
White Blood Cells	PRE	38	1	2.6	0	0.0	37	97.4	0	0.0	150	2	1.3	1	0.7	145	96.7	2	1.3
	PI(M2)	38	1	2.6	1	2.6	35	92.1	1	2.6	143	3	2.1	6	4.2	133	93.0	1	0.7
	PII(M3)	38	0	0.0	0	0.0	37	97.4	1	2.6	142	3	2.1	6	4.2	132	93.0	1	0.7

		HZV 2 Group									HZV 3 Group								
			Unknown		Below		Normal		Above			Unknown		Below		Normal		Above	
Parameter	Timing	N	n	%	n	%	n	%	n	%	N	n	%	n	%	n	%	n	%
Alanine Aminotransferase	PRE	149	0	0.0	0	0.0	142	95.3	7	4.7	73	0	0.0	0	0.0	71	97.3	2	2.7
	PI(M2)	144	0	0.0	0	0.0	138	95.8	6	4.2	72	0	0.0	0	0.0	68	94.4	4	5.6
	PII(M3)	142	0	0.0	0	0.0	139	97.9	3	2.1	72	0	0.0	0	0.0	70	97.2	2	2.8
Aspartate Aminotransferase	PRE	149	0	0.0	0	0.0	146	98.0	3	2.0	73	0	0.0	0	0.0	71	97.3	2	2.7
	PI(M2)	144	0	0.0	0	0.0	140	97.2	4	2.8	72	1	1.4	0	0.0	67	93.1	4	5.6
	PII(M3)	142	0	0.0	0	0.0	140	98.6	2	1.4	72	0	0.0	0	0.0	70	97.2	2	2.8
Basophils	PRE	149	1	0.7	0	0.0	148	99.3	0	0.0	73	0	0.0	0	0.0	73	100	0	0.0
	PI(M2)	144	2	1.4	0	0.0	142	98.6	0	0.0	72	2	2.8	0	0.0	70	97.2	0	0.0
	PII(M3)	142	3	2.1	0	0.0	139	97.9	0	0.0	72	3	4.2	0	0.0	69	95.8	0	0.0
Calcium	PRE	149	0	0.0	0	0.0	144	96.6	5	3.4	73	0	0.0	0	0.0	73	100	0	0.0
	PI(M2)	144	0	0.0	1	0.7	136	94.4	7	4.9	72	1	1.4	0	0.0	71	98.6	0	0.0
	PII(M3)	142	0	0.0	0	0.0	138	97.2	4	2.8	72	0	0.0	1	1.4	71	98.6	0	0.0
Creatinine	PRE	149	0	0.0	0	0.0	142	95.3	7	4.7	73	0	0.0	0	0.0	70	95.9	3	4.1
	PI(M2)	144	0	0.0	0	0.0	138	95.8	6	4.2	72	1	1.4	0	0.0	67	93.1	4	5.6
	PII(M3)	142	0	0.0	0	0.0	134	94.4	8	5.6	72	0	0.0	0	0.0	68	94.4	4	5.6
Eosinophils	PRE	149	1	0.7	12	8.1	135	90.6	1	0.7	73	0	0.0	8	11.0	65	89.0	0	0.0
	PI(M2)	144	2	1.4	12	8.3	129	89.6	1	0.7	72	2	2.8	7	9.7	62	86.1	1	1.4
	PII(M3)	142	3	2.1	13	9.2	122	85.9	4	2.8	72	3	4.2	11	15.3	57	79.2	1	1.4
Fibrinogen	PRE	149	2	1.3	3	2.0	126	84.6	18	12.1	73	1	1.4	0	0.0	56	76.7	16	21.9
	PI(M2)	144	3	2.1	4	2.8	131	91.0	6	4.2	72	0	0.0	9	12.5	59	81.9	4	5.6
	PII(M3)	142	0	0.0	4	2.8	133	93.7	5	3.5	72	2	2.8	2	2.8	61	84.7	7	9.7

Hematocrit	PRE	149	1	0.7	9	6.0	135	90.6	4	2.7	73	0	0.0	1	1.4	71	97.3	1	1.4
	PI(M2)	144	2	1.4	11	7.6	126	87.5	5	3.5	72	1	1.4	4	5.6	65	90.3	2	2.8
	PII(M3)	142	3	2.1	10	7.0	126	88.7	3	2.1	72	4	5.6	6	8.3	61	84.7	1	1.4
Hemoglobin	PRE	149	1	0.7	7	4.7	137	91.9	4	2.7	73	0	0.0	1	1.4	70	95.9	2	2.7
	PI(M2)	144	2	1.4	7	4.9	134	93.1	1	0.7	72	1	1.4	3	4.2	66	91.7	2	2.8
	PII(M3)	142	3	2.1	5	3.5	133	93.7	1	0.7	72	3	4.2	3	4.2	65	90.3	1	1.4
Lactase Dehydrogenase	PRE	149	0	0.0	0	0.0	149	100	0	0.0	73	0	0.0	0	0.0	73	100	0	0.0
	PI(M2)	144	0	0.0	0	0.0	144	100	0	0.0	72	0	0.0	0	0.0	71	98.6	1	1.4
	PII(M3)	142	0	0.0	0	0.0	142	100	0	0.0	72	0	0.0	0	0.0	71	98.6	1	1.4
Lymphocytes	PRE	149	1	0.7	1	0.7	145	97.3	2	1.3	73	0	0.0	1	1.4	72	98.6	0	0.0
	PI(M2)	144	2	1.4	2	1.4	139	96.5	1	0.7	72	2	2.8	3	4.2	67	93.1	0	0.0
	PII(M3)	142	3	2.1	2	1.4	136	95.8	1	0.7	72	3	4.2	1	1.4	68	94.4	0	0.0
Mean Corpuscular Volume	PRE	149	1	0.7	1	0.7	145	97.3	2	1.3	73	0	0.0	2	2.7	69	94.5	2	2.7
	PI(M2)	144	2	1.4	1	0.7	139	96.5	2	1.4	72	1	1.4	3	4.2	67	93.1	1	1.4
	PII(M3)	142	3	2.1	1	0.7	137	96.5	1	0.7	72	4	5.6	4	5.6	63	87.5	1	1.4
Monocytes	PRE	149	1	0.7	4	2.7	144	96.6	0	0.0	73	0	0.0	2	2.7	71	97.3	0	0.0
	PI(M2)	144	2	1.4	9	6.3	133	92.4	0	0.0	72	2	2.8	6	8.3	64	88.9	0	0.0
	PII(M3)	142	3	2.1	13	9.2	126	88.7	0	0.0	72	3	4.2	8	11.1	61	84.7	0	0.0
Neutrophils	PRE	149	1	0.7	0	0.0	146	98.0	2	1.3	73	0	0.0	0	0.0	71	97.3	2	2.7
	PI(M2)	144	2	1.4	1	0.7	138	95.8	3	2.1	72	2	2.8	1	1.4	68	94.4	1	1.4
	PII(M3)	142	3	2.1	0	0.0	138	97.2	1	0.7	72	3	4.2	0	0.0	65	90.3	4	5.6
Partial Thromboplastin Time	PRE	149	2	1.3	5	3.4	137	91.9	5	3.4	73	1	1.4	1	1.4	70	95.9	1	1.4
	PI(M2)	144	3	2.1	1	0.7	129	89.6	11	7.6	72	0	0.0	0	0.0	64	88.9	8	11.1
	PII(M3)	142	0	0.0	0	0.0	136	95.8	6	4.2	72	2	2.8	0	0.0	68	94.4	2	2.8
Platelets	PRE	149	2	1.3	3	2.0	143	96.0	1	0.7	73	0	0.0	1	1.4	70	95.9	2	2.7
	PI(M2)	144	4	2.8	5	3.5	135	93.8	0	0.0	72	2	2.8	0	0.0	68	94.4	2	2.8
	PII(M3)	142	3	2.1	4	2.8	134	94.4	1	0.7	72	4	5.6	1	1.4	66	91.7	1	1.4
Prothrombin Time	PRE	149	2	1.3	2	1.3	137	91.9	8	5.4	73	1	1.4	3	4.1	67	91.8	2	2.7
	PI(M2)	144	3	2.1	1	0.7	132	91.7	8	5.6	72	0	0.0	0	0.0	67	93.1	5	6.9
	PII(M3)	142	0	0.0	0	0.0	137	96.5	5	3.5	72	2	2.8	0	0.0	68	94.4	2	2.8
Red Blood Cells	PRE	149	1	0.7	4	2.7	142	95.3	2	1.3	73	0	0.0	2	2.7	68	93.2	3	4.1
	PI(M2)	144	2	1.4	10	6.9	131	91.0	1	0.7	72	1	1.4	3	4.2	66	91.7	2	2.8
	PII(M3)	142	3	2.1	8	5.6	131	92.3	0	0.0	72	4	5.6	2	2.8	64	88.9	2	2.8
Total Protein	PRE	149	0	0.0	0	0.0	148	99.3	1	0.7	73	0	0.0	0	0.0	73	100	0	0.0
	PI(M2)	144	0	0.0	0	0.0	144	100	0	0.0	72	0	0.0	0	0.0	72	100	0	0.0
	PII(M3)	142	0	0.0	0	0.0	142	100	0	0.0	72	0	0.0	0	0.0	72	100	0	0.0
White Blood Cells	PRE	149	1	0.7	0	0.0	140	94.0	8	5.4	73	0	0.0	1	1.4	70	95.9	2	2.7
	PI(M2)	144	2	1.4	0	0.0	139	96.5	3	2.1	72	2	2.8	1	1.4	67	93.1	2	2.8
	PII(M3)	142	3	2.1	2	1.4	137	96.5	0	0.0	72	3	4.2	2	2.8	64	88.9	3	4.2

N = total number of subjects with available results
n/% = number/percentage of subjects in the appropriate category
PRE = pre-vaccination blood sample at Month 0
PI(M2) = Post Dose 1 blood sample at Month 2
PII(M3) = Post Dose 2 blood sample at Month 3

Safety Results: Percentage of subjects reporting the occurrence of unsolicited AEs within the 30-day (Days 0-29) post-vaccination period (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within Days 0-29 following vaccination)	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any AE(s), n (%)	6 (15.8)	18 (24.7)	37 (24.8)	46 (30.7)
Subjects with Grade 3 AE(s), n (%)	1 (2.6)	1 (1.4)	3 (2.0)	5 (3.3)
Subjects with related AE(s), n (%)	0 (0.0)	2 (2.7)	15 (10.1)	24 (16.0)
Chills	-	-	3 (2.0)	8 (5.3)
Rash	-	-	-	4 (2.7)
Injection site pruritus	-	-	4 (2.7)	3 (2.0)
Nasopharyngitis	1 (2.6)	1 (1.4)	4 (2.7)	3(2.0)

Back pain	-	2 (2.7)	4 (2.7)	-
Malaise	-	-	3 (2.0)	3 (2.0)
Viral infection	1 (2.6)	1 (1.4)	-	3 (2.0)
Tremor	-	-	-	3 (2.0)
Toothache	-	2 (2.7)	-	-
Injection site haematoma	-	2 (2.7)	-	-
Influenza	-	2 (2.7)	-	-
Bradycardia	-	1 (1.4)	-	-
Coronary artery occlusion	-	1 (1.4)	-	-
Conjunctival irritation	-	1 (1.4)	-	-
Diarrhoea	1 (2.6)	-	-	-
Dyspepsia	1 (2.6)	-	-	-
Influenza like illness	-	1 (1.4)	-	-
Bile duct obstruction	-	1 (1.4)	-	-
Cholelithiasis	1 (2.6)	1 (1.4)	-	-
Bronchitis	-	1 (1.4)	-	-
Escherichia sepsis	-	1 (1.4)	-	-
Oral herpes	-	1 (1.4)	-	-
Sinusitis	-	1 (1.4)	-	-
Osteoarthritis	1 (2.6)	1 (1.4)	-	-
Headache	1 (2.6)	1 (1.4)	-	-
Sciatica	-	1 (1.4)	-	-
Renal failure acute	-	1 (1.4)	-	-
Cough	-	1 (1.4)	-	-
Rhinalgia	-	1 (1.4)	-	-
Rhinorrhoea	-	1 (1.4)	-	-

Counting rule applied: As there were more than 30 subjects per treatment group and > 3 groups, only the 5 most frequent events in each treatment group are to be listed.
-: Implies that adverse event was absent or was reported in the particular group but did not fall within the pre-defined counting rule of 5 most frequent events for that group.
Grade 3 = event which 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 Month 3 (Total Vaccinated Cohort)

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]

All SAEs	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	2 (5.3) [0]	3 (4.1) [0]	4 (2.7) [0]	4 (2.7) [0]
Cholelithiasis	1 (2.6) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Hiatus hernia	1 (2.6) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Abdominal pain	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Coronary artery occlusion	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Transient ischaemic attack	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Bile duct obstruction	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Escherichia sepsis	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Renal failure acute	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Upper gastrointestinal haemorrhage	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Ileus	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Depression	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Osteoarthritis	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Myocardial ischaemia	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Pancreatic mass	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Ileus	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Myocardial infarction	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Pulmonary embolism	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]

Fatal SAEs	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Myocardial infarction	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Safety results: Number (%) of subjects with serious adverse events during the period after Month 3 up to Month 8 (Total Vaccinated Cohort)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	1 (2.6) [0]	4 (5.5) [0]	2 (1.3) [0]	2 (1.3) [0]
Hiatus hernia	1 (2.6) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Bladder cancer	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Haematoma	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Multiple myeloma	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Appendicitis	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Subileus	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]
Chest pain	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Atrial fibrillation	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Bradycardia	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Sick sinus syndrome	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]
Fatal SAEs	Control Group N = 38	HZV 3 Group N = 73	HZV 2 Group N = 149	HZV 1 Group N = 150
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with serious adverse events during the period after Month 8 up to the End of study telephone contact (Month 14) (Total Vaccinated Cohort SFU Month 14)				
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]				
All SAEs	Control Group N = 34	HZV 3 Group N = 65	HZV 2 Group N = 130	HZV 1 Group N = 126
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	1 (2.9) [0]	3 (4.6) [0]	1 (0.8) [0]	4 (3.2) [0]
Osteoarthritis	1 (2.9) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Diverticulitis	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Hernia	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Acute myocardial infarction	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Renal failure	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Femur fracture	0 (0.0) [0]	0 (0.0) [0]	1 (0.8) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.8) [0]
Respiratory failure	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.8) [0]
Cerebrovascular disorder	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.8) [0]
Bladder cancer	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.8) [0]
Fatal SAEs	Control Group N = 34	HZV 3 Group N = 65	HZV 2 Group N = 130	HZV 1 Group N = 126
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Acute myocardial infarction	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Renal failure	0 (0.0) [0]	1 (1.5) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
One month after the second dose vaccination, at Month 3, the median frequencies of gE-specific CD4+ T-cells secreting at

least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L was 113.3 in the Control Group, 367.8 in the HZV 3 Group, 1634.5 in the HZV 2 Group and 1973.3 in the HZV 1 Group.
At Month 3, the median frequencies of VZV-specific CD4+ T-cells secreting at least 2 different immunological activation markers among IFN-γ, IL-2, TNF-α and CD40L was 433.3 in the Control Group, 473.3 in the HZV 3 Group, 800.0 in the HZV 2 Group and 866.7 in the HZV 1 Group.
One month post second dose vaccination, the GMCs of anti-gE antibody (mIU/mL) were 1987.0 in the Control Group, 14627.6 in the HZV 3 Group, 49531.5 in the HZV 2 Group and 68798.2 in the HZV 1 Group.
At the same time point, the GMCs anti-VZV antibody (mIU/mL) were 1423.2 in the Control Group, 2786.4 in the HZV 3 Group, 4565.4 in the HZV 2 Group and 4972.8 in the HZV 1 Group.
Within the 30-day (Days 0-29) follow-up period, at least one unsolicited AE was reported for 6 (15.8%), 18 (24.7%), 37 (24.8%) and 46 (30.7%) subjects in the Control, HZV 3, HZV 2 and HZV 1 Groups, respectively.
Up to Month 3, at least one SAE was reported for 2 (5.3%) subjects in the Control Group, 3 (4.1%) subjects in the HZV 3 Group, 4 (2.7%) subjects in the HZV 2 Group and 4 (2.7%) in the HZV 1 Group. One fatal SAE (myocardial infarction) was reported for 1 subject in the HZV 1 Group.
After Month 3 up to Month 8, at least one SAE was reported for 1 (2.6%) subject in the Control Group, 4 (5.5%) subjects in the HZV 3 Group, 2 (1.3%) subjects in the HZV 2 Group and 2 (1.3%) in the HZV 1 Group. One fatal SAE (cardiac failure) was reported for 1 subject in the HZV 3 Group.
After Month 8 up to Month 14, at least one SAE was reported for 1 (2.9%) subject in the Control Group, 3 (4.6%) subjects in the HZV 3 Group, 1 (0.8%) subject in the HZV 2 Group and 4 (3.2%) subjects in the HZV 1 Group. Two fatal SAEs (acute myocardial infarction and renal failure) were reported for one subject in the HZV 3 Group.
None of these SAEs were assessed by the investigator as related to the study vaccination.

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