1343. Persistence of Immune Response to an Adjuvanted Varicella-Zoster Virus Subunit Candidate Vaccine for up to Year 9 in Older Adults

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Background. In the ZOE-50 and ZOE-70 clinical trials, the candidate herpes-zoster subunit vaccine (HZ/su; 50µg varicella-zoster virus glycoprotein E [gE] and $AS01_B$ Adjuvant System) demonstrated high efficacy against HZ, with limited waning over 4 years and consistent efficacy across age cohorts. In adults ≥60 years of age, the immune responses elicited by 2 HZ/su doses administered 2 months apart persisted for at least 6 years.[1] Here we report immunogenicity and safety 9 years post-initial vaccination.

Methods. This Phase IIIB, open, long-term extension study (NCT02735915) followed 70 participants who received 2 HZ/su doses in the initial trial (NCT00434577). Blood samples to evaluate the persistence of cellular (intracellular cytokine staining) and humoral (ELISA) immune responses were taken at 9 years post-initial vaccination. Limited safety follow-up was performed (1 visit).

Results. All 70 participants (mean age at dose 1: 72.3 years; 61.4% female) were included in the according-to-protocol analysis. The fold increases over pre-vaccination in the frequency of gE-specific CD4+ T-cells expressing ≥2 activation markers plateaued after 4 years post-dose 1 (year 4: 3.4, year 5: 3.0, year 6: 3.4, year 9: 3.4). Anti-gE antibody geometric mean concentrations were also stable from year 4 onwards (Table 1) and remained above the pre-vaccination value of 1213.1mIU/mL. Cellular and humoral responses at year 9 were similar across age strata (60–69, ≥70 years). No vaccine-related serious adverse events nor suspected HZ episodes were reported.

Conclusion. In adults ≥60 years of age, HZ/su-induced cellular and humoral immune responses remained above pre-vaccination levels for at least 9 years post-initial vaccination, confirming immune persistence predictions[2] based on 6-year data.

Table 1

	Pre-vaccination (95% CI)	Year 4 (95% CI)	Year 5 (95% CI)	Year 6 (95% CI)	Year 9 (95% CI)
Anti-gE antibody GMC (mIU/mL)	1213.1 (983.8–1495.9)	9643.5 (8309.7–11191.3)	9124.1 (7805.1–10666.0)	8490.5 (7292.1–9885.7)	8931.2 (7625.7–10460.3)

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1344. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in Adults with Hematologic Malignancies: A Phase III, Randomized Clinical Trial

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Background. Hematologic malignancy (HM) patients receiving immunosuppressive cancer therapy (ICT) are at increased risk of herpes zoster (HZ). Currently, no HZ vaccine is indicated for immunocompromised patients. The HZ subunit vaccine candidate (HZ/su), containing recombinant varicella zoster virus glycoprotein E and $AS01_B$ Adjuvant System, showed >90% efficacy and an acceptable safety profile in immunocompetent adults in all age groups ≥50 years. Here we report HZ/su immunogenicity and safety in HM adults ≥18 years of age who completed or are undergoing ICT.

Methods. In this phase III, observer-blind, multicenter study (NCT01767467), participants were randomized 1:1 to receive HZ/su or placebo (2 doses, 1–2 months apart) ≥10 days pre- or post-ICT. Humoral and cell-mediated immunogenicity (CMI) were assessed. The co-primary immunogenicity objectives were to evaluate HZ/su vaccine response rate and compare the immune response to HZ/su and placebo in participants excluding those with non-Hodgkin B-cell lymphoma (NHBCL) or chronic lymphocytic leukemia (CLL) at 1 month post-dose 2 (M2). Solicited and unsolicited adverse events (AEs) were recorded for 7 and 30 days after each dose, respectively. Serious AEs (SAEs), disease-related events and potential immune-mediated diseases (pIMDs) were recorded throughout the study. Partial safety results up to 6 months post-dose 2 are shown (partially blinded, ongoing study).

Results. Of 562 participants (283 HZ/su 283; placebo 279), (mean age 57.3 [HZ/su 56.8; placebo 57.8] years), 415 were included in the according-to-protocol (ATP) cohort for humoral immunogenicity and 132 in the ATP sub-cohort for CMI. M2 immune responses were higher in the HZ/su group (Table 1). Both co-primary immunogenicity objectives were met (Figure 1). The most frequent local and general solicited AEs were pain and fatigue, reported by 48.2% and 47.8% of all participants (per-group data remain blinded). The frequency of unsolicited AEs, SAEs and pIMDs in the 2 groups was similar (Table 2).

Conclusion. HZ/su induced robust humoral and cellular immune responses at M2 in HM adults excluding NHBCL and CLL, who completed or are undergoing ICT. No safety concerns were observed up to 6 months post-dose 2.

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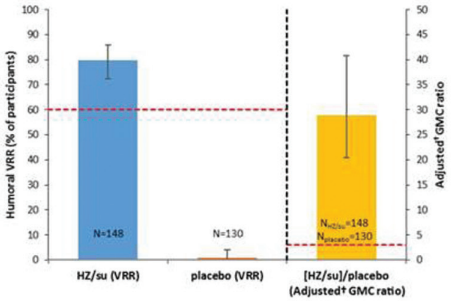
Table 1. Humoral and cellular immune responses at 1 month post-dose 2

	Population	HZ/su N	HZ/su Value	placebo N	placebo Value	Adjusted† GMC ratio [HZ/su]/placebo
Humoral immunogenicity (ATP cohort for humoral immunogenicity)						
VRR, % (95% CI)	All excluding NHBCL and CLL	148	79.7 (72.3*–85.9)	130	0.8 (0.0–4.2)	–
	All excluding NHBCL	184	68.5 (61.2–75.1)	165	0.6 (0.0–3.3)	
	All	217	65.0 (58.2–71.3)	198	0.5 (0.0–2.8)	
Adjusted† GMC, mIU/mL (95% CI)	All excluding NHBCL and CLL	148	22719.0 (16296.3–31673.1)	130	786.6 (711.0–870.2)	28.9 (20.4*–40.9)
Cellular immunogenicity (ATP sub-cohort for CMI)						
VRR, % (95% CI)	All	43	83.7 (69.3–93.2)	44	6.8 (1.4–18.7)	–
Frequency of gE-specific CD4[2+] T-cells, Median (Min [Q_1; Q_3] Max)	All	53	3081.9 (1.0 [1766.2; 7413.6] NP)	50	99.1 (1.0 [1.0; 268.3] NP)	–

ATP, according to protocol; **CMI,** cell-mediated immunogenicity; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; , **GMC,** (anti-glycoprotein E [gE] antibodies) geometric mean concentration; †, adjusted for baseline values; **N,** number of participants with available results; **%,** percentage of participants; **All,** all participants; **NHBCL,** participants with non-Hodgkin B-cell lymphoma; **CLL,** participants with chronic lymphocytic leukemia; **CI,** confidence interval; **IU,** international units; **CD4[2+],** CD4+ T-cells producing at least two of the four activation markers assessed (IFN-γ, IL2, TNFα, and CD40 Ligand) upon in vitro stimulation with the antigen; **Min/Max**, minimum/maximum; Q_1/Q_3, 1st/3rd quartiles; **NP**, data not published due to risk of unblinding.
*, co-primary immunogenicity objectives (criteria: [i] lower limit [LL] of 95% CI for HZ/su humoral VRR ≥60%, [ii] LL of 95% CI for adjusted GMC [HZ/su]/placebo ratio ≥3, in participants excluding those with NHBCL and CLL) were met.
VRR, vaccine response rate: **humoral,** for initially seronegative participants, antibody concentration at post-vaccination ≥4-fold the cut-off for anti-gE (97 mIU/ml); for initially seropositive participants, antibody concentration at post-vaccination ≥4-fold the pre-vaccination antibody concentration; **CMI,** for participants with pre-vaccination T cell frequencies below the threshold, ≥2-fold increase as compared to the threshold (320 Events/10^6 CD4+ T cells); for participants with pre-vaccination T cell frequencies above the threshold, ≥2-fold increase as compared to pre-vaccination T cell frequencies.

Figure 1. Humoral immune responses at 1 month post-dose 2 (ATP cohort for humoral immunogenicity) and co-primary immunogenicity objectives



ATP, according-to-protocol; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; **GMC,** (anti-glycoprotein E[gE] antibodies) geometric mean concentration; **N,** number of participants with available results; **error bars,** 95% confidence interval (CI); **†,** adjusted for baseline values.
red dashed lines, confirmatory co-primary immunogenicity objectives (criteria: [i] lower limit [LL] of 95% CI for HZ/su humoral VRR ≥60%, [ii] LL of 95% CI for [HZ/su]/placebo adjusted GMC ratio ≥3 in all participants excluding those with non-Hodgkin B-cell lymphoma [NHBCL] and chronic lymphocytic leukemia [CLL]). **VRR,** vaccine response rate: for initially seronegative participants, antibody concentration at post-vaccination ≥4-fold the cut-off for anti-gE (4x97 mIU/ml); for initially seropositive participants, antibody concentration at post-vaccination ≥4-fold the pre-vaccination antibody concentration.
This graph presents data for **all participants excluding NHBCL and CLL**.

Table 2. Frequency of adverse events (total-vaccinated cohort)

AE reporting period	HZ/su (N=283) % [95% CI] All	HZ/su (N=283) % [95% CI] Grade 3	HZ/su (N=283) % [95% CI] Related	placebo (N=279) % [95% CI] All	placebo (N=279) % [95% CI] Grade 3	placebo (N=279) % [95% CI] Related
Unsolicited AEs Days 0–29 post each dose	46.6 (40.7–52.6)	8.8 (5.8–12.8)	6.4 (3.8–9.9)	45.9 (39.9–51.9)	9.7 (6.5–13.8)	1.8 (0.6–4.1)
SAEs From dose 1 to 6 Months post dose 2	17.7 (13.4–22.6)	–	NP	21.5 (16.8–26.8)	–	NP
pIMDs From dose 1 to 6 Months post dose 2	0.7 (0.1–2.5)	–	N/A	0.4 (0.0–2.0)	–	N/A

AE, adverse event; **SAE,** serious AE; **pIMD,** potential immune-mediated disease; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; **N**, number of participants with ≥1 administered dose; **%,** percentage of participants who reported at least one symptom; **CI**, confidence interval; **All**, all AEs/pIMDs; **Grade 3**, severe AEs (>100 mm [redness, swelling], prevent normal everyday activities [other symptoms]); **Related**, AEs considered by the investigator as causally related to vaccination (all local solicited AEs are considered related to vaccination); **N/A**, not applicable (for this phase of analysis); **NP**, data not published due to risk of unblinding. Per-group **solicited AEs** data is not published due to risk of unblinding.

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1345. A Replication-Defective Herpes Simplex Virus (HSV)-2 Vaccine, HSV529, is Safe and Well-Tolerated in Adults with or without HSV Infection and Induces Significant HSV-2-Specific Antibody Responses in HSV Seronegative Individuals

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