ORAL ABSTRACTS

127. Efficacy, Immunogenicity and Safety of an Investigational Subunit Adjuvanted Herpes Zoster Vaccine in Adults Aged 60 Years and Older: Results From the ZOE-50 and ZOE-70 Efficacy Studies

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Background. The recombinant herpes zoster (HZ) subunit vaccine candidate (HZ/su) had >90% efficacy (VE) against HZ in older adults in two phase 3 clinical trials (ZOE-50, ZOE-70 [NCT01165177, NCT01165229]). Here we report HZ/su VE against HZ and postherpetic neuralgia (PHN), immunogenicity and safety data in adults ≥60 years of age (YOA) from these studies (VE ≥60 YOA [ZOE-50], immunogenicity/safety 69–69 YOA [ZOE-50], immunogenicity/safety ≥70 YOA [pooled ZOE-50/70]).

Methods. Subjects were randomized 1:1 to receive 2 intramuscular doses of HZ/su vaccine (containing 50 µg varicella-zoster virus glycoprotein E [gE] and $AS01_B$ Adjuvant System) or placebo (saline solution) 2 months (M) apart. We report VE in reducing HZ and PHN compared to placebo, humoral immune responses (assessed by anti-gE ELISA prior to vaccination and 1, 12, 24 and 36 M post-dose 2 [subset of subjects]) and safety (solicited [diary card subset of subjects] and unsolicited adverse events [AEs] collected for 7 and 30 days after each dose, respectively; medically attended AEs [MAEs] for 6 M after dose 2; fatal events, serious AEs [SAEs] related to vaccination/study participation and potential immune-mediated diseases [pIMDs] until study end [all subjects]).

Table 1. VE against HZ and PHN (mTVC)

	YOA	HZ/su			Placebo			VE, % (95% CI)
		N	n	Incidence	N	n	Incidence	
HZ VE	≥60	3852	3	0.2	3890	123	10.2	97.6 (92.7–99.6)
	60–69	2141	2	0.3	2166	75	10.8	97.4 (90.1–99.7)
	≥70*	8250	25	0.8	8346	284	9.3	91.3 (86.8–94.5)
PHN VE	≥60	3849	0	0.0	3890	10	0.7	100.0 (55.2–100.0)
	60–69	2140	0	0.0	2166	2	0.2	100.0 (-442.8–100.0)
	≥70*	8250	4	0.1	8346	36	1.2	88.8 (68.7–97.1)

VE, vaccine efficacy; PHN, postherpetic neuralgia; mTVC, modified total vaccinated cohort (subjects who received 2 doses and did not develop a confirmed case of HZ within 1 month after dose 2); YOA, years of age; N, number of subjects in the mTVC; n, number of subjects with ≥1 confirmed HZ episode or ≥1 PHN; CI, confidence interval. HZ cases were confirmed by the real-time polymerase-chain reaction (PCR) assay or by the ascertainment committee. Incidences are expressed as number of subjects with ≥1 confirmed HZ episode or ≥1 PHN per 1000 person-years. *Results for subjects ≥60 YOA and 60–69 YOA are from the ZOE-50 study and for subjects ≥70 YOA, from the pooled ZOE-50/ZOE-70 analysis.

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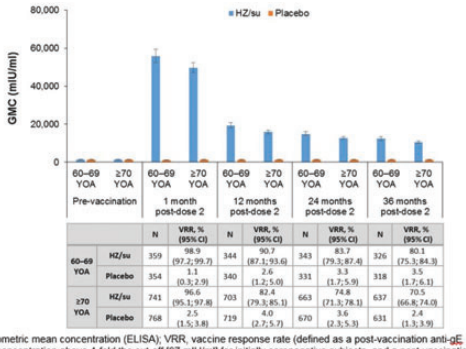
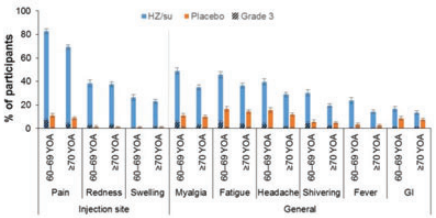
Results. A total of 4490 subjects 60–69 YOA (HZ/su: 2244; control: 2246), 8122 ≥60 YOA (4053; 4069) (ZOE-50) and 17531 ≥70 YOA (8758; 8773) (pooled ZOE-50/70) were vaccinated. VE against HZ in ZOE-50 was 97.6% (95% confidence interval: 92.7–99.6) in adults ≥60 YOA. VE in 60–69 YOA was 97.4% (ZOE-50) and in ≥70 YOA, 91.3% (pooled ZOE-50/70). VE against PHN was 100.0% (55.2–100.0) in adults ≥60 YOA (ZOE-50) and 88.8% in ≥70 YOA (pooled ZOE-50/70) (Table 1). Highest vaccine response rates and geometric mean concentrations of anti-gE antibodies in the HZ/su group were observed 1M post-dose 2. Immune responses persisted for 36M post-vaccination (Figure 1). HZ/su vaccine was more reactogenic than placebo, but reactions were mostly mild or moderate and transient (Figure 2). SAEs, fatal cases and pIMDs were equally distributed between HZ/su group and placebo.



		N	VRR, % (95% CI)	N	VRR, % (95% CI)	N	VRR, % (95% CI)	N	VRR, % (95% CI)
60–69 YOA	HZ/su	359	98.9 (97.2; 99.7)	344	90.7 (87.1; 93.6)	343	83.7 (79.3; 87.4)	326	80.1 (75.3; 84.3)
	Placebo	354	1.1 (0.3; 2.9)	340	2.6 (1.2; 5.0)	331	3.3 (1.7; 5.9)	318	3.5 (1.7; 6.1)
≥70 YOA	HZ/su	741	96.6 (95.1; 97.8)	703	82.4 (79.3; 85.1)	663	74.8 (71.3; 78.1)	637	70.5 (66.8; 74.0)
	Placebo	768	2.5 (1.5; 3.8)	719	4.0 (2.7; 5.7)	670	3.6 (2.3; 5.3)	631	2.4 (1.3; 3.9)

GMC, geometric mean concentration (ELISA); VRR, vaccine response rate (defined as a post-vaccination anti-gE antibody concentration above 4-fold the cut-off [97 mIU/ml] for initially seronegative subjects, and a post-vaccination antibody concentration above 4-fold the pre-vaccination antibody concentration for initially seropositive subjects); ATP, according-to-protocol; N, number of subjects with pre- and post-vaccination results available; CI, confidence interval. *for pre-vaccination and 1 month post-dose 2, ATP cohort for immunogenicity month 3; for 12, 24 and 36 months post-dose 2, ATP cohorts for immunogenicity at the respective timepoints. Results for subjects 60–69 YOA are from the ZOE-50 study, and for subjects ≥70 YOA, from the pooled ZOE-50/ZOE-70 analysis. Error bars depict 95% confidence intervals (CIs).

Figure 1. Anti-gE GMCs and VRRs by age group (adapted ATP cohort for immunogenicity-humoral*)



AE, adverse event; TVC, total vaccinated cohort; %, percentage of subjects reporting the symptom at least once; GI, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain); all symptoms, grades: 1 (mild), 2 (moderate) and 3 (severe: significant pain at rest, preventing normal everyday activities [pain], diameter >100 mm [redness, swelling], oral temperature >39.0°C [fever, oral temperature ≥37.5°C], preventing normal everyday activities [other symptoms]). Results for subjects 60–69 YOA are from the ZOE-50 study and for subjects ≥70 YOA, from the pooled ZOE-50/ZOE-70 analysis. Error bars depict 95% confidence intervals (CIs).

Figure 2. Incidence of solicited injection site and general AEs (TVC diary card)

Conclusion. In adults ≥60 YOA, HZ/su vaccine is efficacious against HZ and PHN, highly immunogenic and has a clinically acceptable safety profile.

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