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REACTOGENICITY PROFILE OF ADJUVANTED RECOMBINANT ZOSTER VACCINE AFTER DOSE 2 ACCORDING TO THE INTENSITY OF THE SAME EVENT EXPERIENCED AFTER DOSE 1

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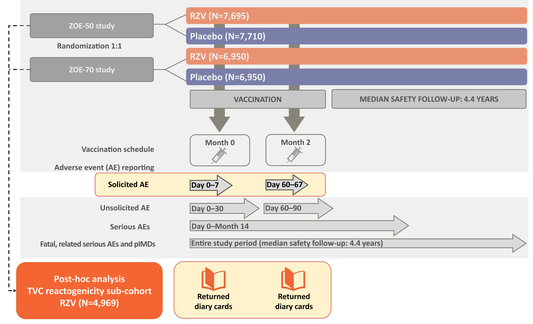
BACKGROUND AND AIMS

- In 2 large clinical trials, ZOE-50 (NCT01165177)[1] and ZOE-70 (NCT01165229)[2], 2 doses of the adjuvanted recombinant zoster vaccine (RZV; *Shingrix*, GSK) showed high efficacy against herpes zoster (HZ) and postherpetic neuralgia.
- The incidence of reported solicited events was higher for RZV compared to placebo recipients.[3]
- Reactogenicity may contribute to a person's willingness to be vaccinated and if a vaccine recipient knows what to expect after dose 1, this might contribute to higher compliance with dose 2 and might further enhance protection provided by RZV.
- Here we present a post-hoc analysis assessing the intensity of an event after RZV dose 2 reported to the same event's intensity after RZV dose 1.

METHODS

Phase III, observer-blind, placebo-controlled multicenter trials



N, number of participants with available results; RZV (50 µg varicella-zoster virus glycoprotein E antigen plus AS01$_B$ Adjuvant System[4]) or **placebo** (saline solution); **pIMDs**, potential immune mediated diseases; **TVC**, total vaccinated cohort included participants with at least 1 administered RZV dose.
Note: For this post-hoc analysis, ZOE-50 and ZOE-70 data from participants having completed the diary cards for both RZV doses were pooled (TVC reactogenicity sub-cohort). The participants did not receive both doses of RZV if they had a confirmed HZ episode between RZV dose 1 and 30 days after RZV dose 2.

Grading of solicited events

- In the current analysis, the intensity of each solicited event after dose 2 was stratified by the intensity of the same event after dose 1.

	Grade 0	Grade 1	Grade 2	Grade 3
Injection-site events				
Pain	None	Any pain neither interfering with nor preventing everyday activities	Painful when limb was moved and interfered with everyday activities	Significant pain at rest that prevented everyday activities
Redness / Swelling	∅<20 mm	∅20–50 mm	∅>50–100 mm	∅>100 mm
General events				
GI / Myalgia / Fatigue / Headache / Shivering	None	Event that was easily tolerated	Event that interfered with everyday activity	Event that prevented everyday activity
Fever	<37.5 °C	37.5–38.0 °C	38.1–39.0 °C	>39.0 °C

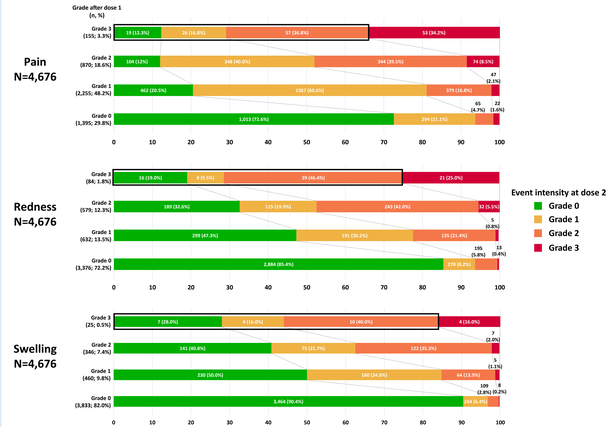
GI, gastrointestinal symptoms including nausea, vomiting, diarrhea and/or abdominal pain.

RESULTS

- Amongst participants who experienced a Grade 3 AE after dose 1, 63.5% to 67.6% of the participants experienced the same event at lower intensity (≤Grade 2) after dose 2.
- Amongst participants who experienced Grade 0 AE after dose 1, the proportion of participants who experienced Grade 0 (of the same set of events) after dose 2 ranged from 69.9% to 71.3%.

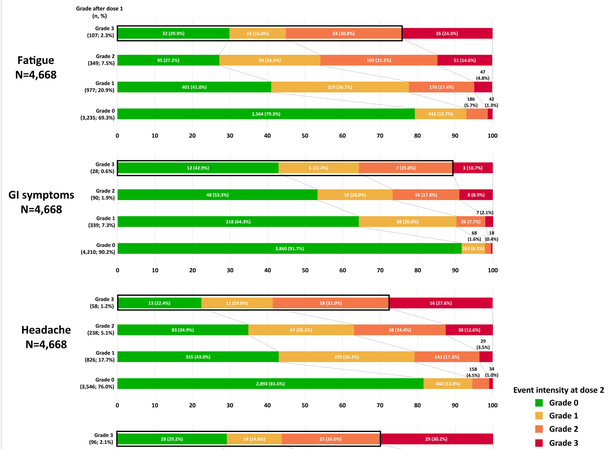
N, number of RZV vaccinees with both doses administered and corresponding event intensity after dose 1 and/or after dose 2; **n**, number of RZV vaccinees with events at specific grade. There were 9 events (4 for injection-site and 5 for general events) with missing grade after dose 1 and 6 events (3 for injection-site and 3 for general events) with missing grade after dose 2.
Note: Black rectangle indicates the proportion of participants who had a Grade 3 event after dose 1 and experienced a lower intensity for the same event after dose 2.

- Amongst participants who experienced a Grade 3 specific local AE after dose 1, 65.8% to 84.0% of the participants experienced the same event at lower intensity (≤Grade 2) after dose 2.
- Amongst participants who experienced Grade 0 local AE after dose 1, the proportion of participants who experienced Grade 0 of the same event after dose 2 ranged from 72.6% to 90.4%.



Missing grade events: pain (1 event after dose 1 and 2 events after dose 2), redness (5 events after dose 1 and 8 events after dose 2) and swelling (12 events after dose 1 and 10 events after dose 2).

- Amongst participants who experienced a Grade 3 specific systemic AE after dose 1, 69.8% to 89.3% of the participants experienced the same event at lower intensity (≤Grade 2) after dose 2.
- Amongst participants who experienced Grade 0 systemic AE after dose 1, the proportion of participants who experienced Grade 0 of the same event after dose 2 ranged from 79.3% to 91.7 %.



Missing grade events: GI symptoms (1 event after dose 1 and 1 event after dose 2) and fever (7 events after dose 1 and 6 events after dose 2).

RZV second dose compliance was high and comparable between RZV and Placebo groups (pooled TVC)

Reason	RZV (N=14,645)		Placebo (N=14,660)	
	n	(%)	n	(%)
Received both doses	13,915	95.0	14,079	96.0
Reason for not receiving dose 2				
Consent withdrawal, not due to an AE	240	1.6	212	1.4
Non-serious AE	155	1.1	57	0.4
Serious AE and/or pIMD	59	0.4	61	0.4
Lost to follow-up	39	0.3	44	0.3
Migrated / moved from the study area	16	0.1	8	0.1
Protocol violation	9	0.1	10	0.1
Suspected HZ episode	8	0.1	33	0.2
Other	204	1.4	156	1.1
Total	**730**	**5.0**	**581**	**4.0**

- Of the 432 RZV vaccinees from the reactogenicity sub-cohort who reported any grade 3 injection-site or general events after the first dose, 394 (91.2%) returned to receive their second dose.

CONCLUSIONS

- Vaccinees who did not experience a specific AE after dose 1, generally did not experience the same event after dose 2.
- Vaccinees who reported Grade 3 specific AEs after dose 1 were more likely to report the same AE at lower intensity after dose 2.
- The proportion of participants with a Grade 3 AE after dose 2, was higher in participants that reported the same AE after dose 1.
- Study limitations:
  - This is a post-hoc analysis that is not statistically powered and results should be interpreted with caution. Further, results are presented as proportion (%) of participants and thus need to be adjusted for the different size of the analyzed sub-sets.

PLAIN LANGUAGE SUMMARY

What is the context?

- Initial infection with the varicella-zoster virus causes chickenpox. After symptoms disappear, the virus remains dormant in the body and may reactivate later in life (usually in people over 50 years old) and can cause shingles (also called herpes zoster), characterized typically by a painful rash on one side of the body.
- Two large clinical trials in adults over 50 and 70 years of age showed that two doses of the recombinant zoster vaccine (*Shingrix*, GSK) is over 90% effective in preventing shingles and postherpetic neuralgia (a chronic pain that can persist for months or years after the rash has resolved).
- We measured the intensity of common side effects and looked for any differences after the administration of the first and second vaccine dose.

What is new?

- Participants who did not experience a certain side effect after the first dose, generally did not experience the side effect after the second dose either.
- Percentage of participants reporting a side effect at high intensity after their first dose and reporting the same side effect at lower intensity (or not at all) after their second dose:
  - Approximately 70% for side effects at the injection site
  - Approximately 65% for general side effects

What is the impact?

- Providing healthcare providers and patients with a greater understanding of the frequency and intensity of potential side effects after vaccination may support compliance with second dose administration.

References: 1. Lal et al, N Engl J Med 2015; 372:2087–96; **2.** Cunningham et al, N Engl J Med 2016; 375:1019–32; **3.** López-Fauqued et al, Vaccine 2019; 37:2482–93; **4.** Lecrenier et al, Expert Rev Vaccines 2018; 17:619–34.

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Trademark statement
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