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# IMPACT OF REACTOGENICITY ON QUALITY OF LIFE AND PHYSICAL FUNCTIONING IN ADULTS ≥50 YEARS RECEIVING BOTH DOSES OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE


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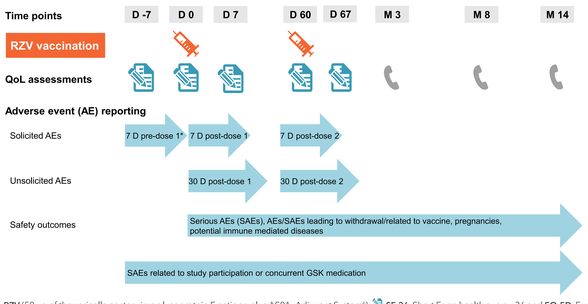
## BACKGROUND AND AIMS

- Herpes zoster (HZ) and its complications usually impact patients' quality of life (QoL) and daily life activities.[1,2]
- The adjuvanted recombinant zoster vaccine (RZV; *Shingrix*, GSK), administered as a 2-dose schedule 2–6 months apart, is highly efficacious in preventing HZ in adults aged ≥50 years.[3,4]
- The current study investigates whether the vaccinees' QoL and physical functioning (PF) are impacted by local and systemic reactions following RZV vaccination. We previously showed that the overall QoL and PF were not significantly affected by reactogenicity up to 7 days post-RZV dose 1.[5]
- Here we report the results from the same study post-RZV dose 2 and safety results from dose 1 up to study end.

## METHODS

### Phase III, single-arm, open-label, multicenter study (NCT02979639)




**RZV** (50 µg of the varicella-zoster virus glycoprotein E antigen plus AS01$_B$ Adjuvant System®); **SF-36**, Short Form health survey-36 and **EQ-5D**, Euro Quality of Life-5 Dimension, distributed at day **(D)** -7, month **(M)** 0 and M 2 and collected at D -7, D 7 and D 67; phone contact; *only systemic AEs.

### Quality of Life assessments

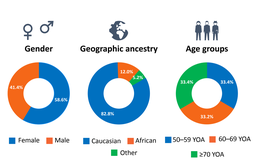
| | SF-36[7] | EQ-5D[8] |
|---|---|---|
| **Format** | 36 questions with 8 scales labeled as: Role Physical, Bodily Pain, Physical Functioning, General Health, Vitality, Social Function, Role Emotional and Mental Health. | Defines and combines health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression to generate health profiles providing a single index utility score. |
| **Scoring** | Higher SF-36 PF scores represent greater functioning/QoL. | EQ-5D utility scores; a higher score represents a better QoL. |
| **Statistical methodology** | The SF-36 PF scores were analyzed by age, gender, symptom type and reactogenicity grade.<br>A change from pre-vaccination of 3.3 in PF score is considered clinically relevant.[9] | Quality-adjusted life-year (QALY) loss (area-under-the-curve [AUC] method[10]). |
| **Reactogenicity grading** | **Grade 0**, no symptom reported;<br>**Grade 1**, mild solicited AE reported as maximum intensity;<br>**Grade 2**, moderate solicited AE reported as maximum intensity;<br>**Grade 3**, severe solicited AE reported as maximum intensity.<br>**Pain**: 0 (none); 1 (pain neither interfering with nor preventing every day activities); 2 (painful when limb was moved and interfered with every day activities); 3 (significant pain at rest that prevented every day activities).<br>**Swelling/erythema**: greatest surface diameter, 0 (<20 mm); 1 (≥20–≤50 mm); 2 (>50–≤100 mm); 3 (>100 mm).<br>**Fatigue, gastrointestinal symptoms, headache, myalgia, shivering**: 0 (none); 1 (event that was easily tolerated); 2 (event that interfered with every day activity); 3 (event that prevented every day activity).<br>**Fever**: 0 (<37.5 °C); 1 (37.5–38.0 °C); 2 (38.1–39.0 °C); 3 (>39.0 °C). | |

## RESULTS

### Study participants and demographics

**Total vaccinated cohort**

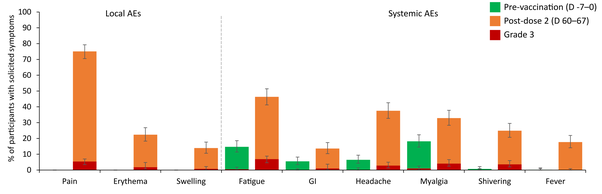
| Participants | Diary cards completed | Questionnaires completed | Mean age (±SD) years |
|---|---|---|---|
| N = received dose 1<br>N' = received dose 2 | N = 7 D post-dose 1<br>N' = 7 D post-dose 2 | [1]7 D post-dose 1<br>[2]7 D post-dose 2 | |
| N = 401 | N = 400 (99.8%) | [1]71.6%–99.5% | 64.6 (±8.8) |
| N' = 391 | N' = 389 (99.5%) | [2]74.4%–98.5% | |




**YOA**, years of age; **SD**, standard deviation. **Caucasian** = White-Caucasian/European heritage; **African** = African American/African heritage; **Other** = Asian/South-East Asian heritage, American Indian, Alasakan Native, White-Arabic/North African and unknown heritage.

### Reactogenicity and safety outcomes

- Pain (75.1%, local) and fatigue (46.3%, systemic) were the most frequent solicited AEs.
- Grade 3 solicited AEs were reported by 7.2% (local) and 11.1% (systemic) of participants.
- 127 (31.7%) participants reported unsolicited AE, of whom 25 (6.2%) reported grade 3 unsolicited AEs.
- 21 SAEs were reported by 14 (3.5%) participants up to 12 M post-RZV dose 2. No SAE was considered related to vaccination.

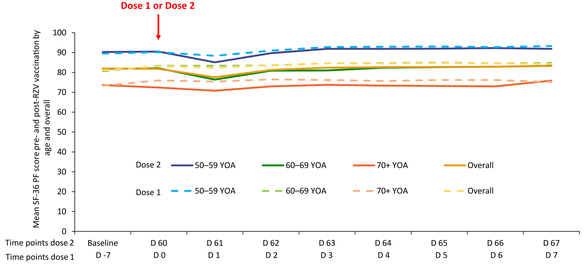



**GI**, gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain).

### QoL results

#### SF-36 -physical functioning

**Mean SF-36 PF score was only affected for 1–2 days post-RZV dose 2.**

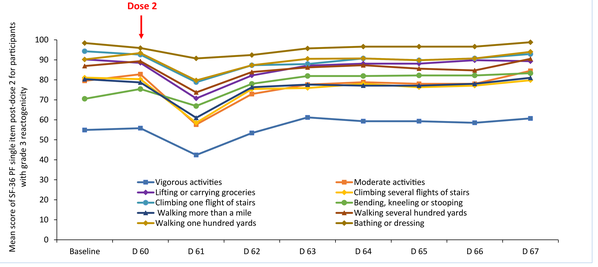



**A mean SF-36 PF score change of -0.4 points was observed from the mean baseline score during the 7 days post-RZV dose 2, indicating that PF was not clinically meaningfully[9] impacted. However, the mean SF-36 PF scores showed a transient clinically meaningful change, in particular in participants with grade 3 reactogenicity.**

| Time points | Participant's reactogenicity grade post-dose 2 | | | By symptoms | | | Overall |
|---|---|---|---|---|---|---|---|
| | 0<br>N=63 | 1 or 2<br>N=267 | 3<br>N=61 | None<br>N=59 | Local<br>N=302 | Systemic<br>N=245 | N=391 |
| **Pre-RZV dose 2** | | | | | | | |
| Baseline* | 78.5 | 82.6 | 82.8 | 79.0 | 82.7 | 83.5 | 82.0 |
| D 60 | 79.6 | 81.9 | 83.4 | 79.2 | 82.3 | 83.1 | 81.8 |
| **Post-RZV dose 2** | | | | | | | |
| D 61 | 83.9 | 78.2 | 68.0 | 83.3 | 76.4 | 75.6 | 77.6 |
| D 62 | 82.6 | 81.5 | 78.9 | 82.2 | 81.2 | 81.7 | 81.3 |
| D 63 | 82.4 | 82.5 | 82.2 | 81.9 | 82.9 | 83.3 | 82.4 |
| D 64 | 82.0 | 82.8 | 82.8 | 81.7 | 83.2 | 83.8 | 82.7 |
| D 65 | 82.1 | 83.1 | 82.3 | 82.0 | 83.3 | 83.9 | 82.8 |
| D 66 | 81.8 | 83.2 | 82.6 | 81.5 | 83.3 | 84.3 | 82.9 |
| D 67 | 83.2 | 82.9 | 85.5 | 82.6 | 83.3 | 84.1 | 83.3 |
| **Mean change from baseline** | | | | | | | |
| | 3.2 | -0.7 | -2.4 | 2.2 | -0.8 | -1.2 | -0.4 |

**N**, number of participants for each category. *Baseline is calculated as the mean of the D -7, D 0 (pre-RZV dose 1) and D 60 (pre-RZV dose 2) assessments. The mean change from baseline is calculated based only on participants who had both pre-vaccination and post-dose 2 data available.

**The decrease in mean SF-36 PF scores observed for participants who reported grade 3 reactogenicity was seen in days 1–2 post-RZV dose 2 and impacted activities such as walking and climbing stairs.**



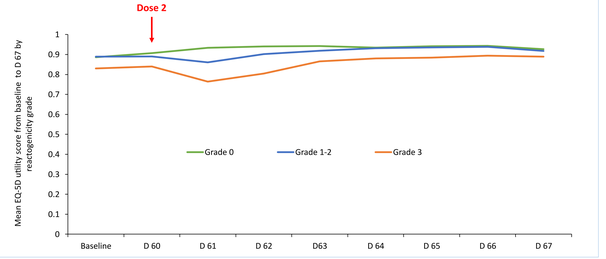

#### EQ-5D

**No QALY loss (represented by AUC) was observed overall over the 7 days post-RZV dose 2 (mean change observed: +0.113).**

| Reactogenicity | | Grade 0 (N=63) | Grade 1-2 (N=267) | Grade 3 (N=61) | All grades (N=391) |
|---|---|---|---|---|---|
| Pre-RZV dose 2 score (AUC) | Mean (±SD) | 6.323 (±0.744) | 6.293 (±0.774) | 5.889 (±1.165) | 6.235 (±0.853) |
| Post-RZV dose 2 score (AUC) | N'<br>Mean (±SD) | 61<br>6.553 (±0.677) | 266<br>6.392 (±0.777) | 61<br>5.980 (±1.015) | 388<br>6.353 (±0.821) |
| Change in AUC | N'<br>Mean (±SD)<br>SE | 61<br>0.184 (±0.434)<br>0.067 | 266<br>0.102 (±0.494)<br>0.032 | 61<br>0.091 (±0.685)<br>0.067 | 388<br>0.113 (±0.520) |

**N'**, number of participants with non-missing values; **SE**, standard error. AUC applied to D -7, D 0 and D 60 utility values for pre-vaccination and to D 61–67 utility values for post-vaccination. The change in AUC is calculated based only on participants who had both pre-vaccination and post-dose 2 data available.

**For participants experiencing grade 3 solicited AEs, a transient decrease in mean EQ-5D utility score was observed on D 61, but this had returned to pre-vaccination values by D 63.**




## CONCLUSIONS

- Overall, the QoL and PF of adults aged ≥50 years were not affected post-RZV dose 2, but a transient impact was observed, in particular in participants with grade 3 reactogenicity. These results are consistent with what was observed post-RZV dose 1 administration.[5]
- The reactogenicity profile is similar after either RZV dose;[5] both the safety and reactogenicity profile reported in this study are consistent with the known safety profile of the vaccine.[11]
- The transient impact of RZV vaccination on QoL and PF are greatly outweighed by the benefits of RZV vaccination.

## PLAIN LANGUAGE SUMMARY

### What is the context?

- About 30% of the global population will experience herpes zoster in their lifetime, and the risk of herpes zoster increases with age. Herpes zoster is associated with a significant burden of disease including pain and a decrease in quality of life.
- An adjuvanted recombinant zoster vaccine (*Shingrix*) is licensed for the prevention of herpes zoster, but it may cause adverse reactions that have the potential to impact quality of life and daily physical activities.
- We assessed if *Shingrix* impacts the quality of life and daily physical functioning of vaccinees.

### What is new?

- The impact of adverse reactions following *Shingrix* vaccination on quality of life was evaluated in adults aged ≥50 years from multiple locations across the United States.
- Overall, no reduction of physical functioning or quality of life was observed after vaccination. However, the quality of life of the participants experiencing high intensity reactions was transiently impacted over the first two days after the second vaccine dose.

### What is the impact?

- Patients at risk of herpes zoster as well as healthcare providers considering *Shingrix* vaccination may want to assess the benefits and the impact of vaccination on quality of life.
- Our study demonstrated that vaccine-related reactions following vaccination with two doses of *Shingrix* had a minimal impact on quality of life that was far lower than the decrease in quality of life associated with a herpes zoster episode.


**References**
**1.** Schmader et al, Clin J Pain 2007;23:490–6; **2.** Copland et al, J Pain 2004;5:344–56; **3.** Cunningham et al, N Engl J Med 2016;375:1019–32; **4.** Lal et al, N Engl J Med 2015;372:2087–96; **5.** Schmader et al, J Gerontol A Biol Sci Med 2019;74:1217–24; **6.** Lecrenier et al, Expert Rev Vaccines 2018;17:619–34; **7.** Ware and Kosinski, 2001; 2nd edition; Lincoln, RI: Quality Metric Incorporated; **8.** Kind, 1996; 2nd edition; Philadelphia: Lippincott-Raven Publishers; **9.** Angst et al, Arthritis Rheum 2001;45:384–91; **10.** Yeh, 2002; SUGI 27 Proceedings. Available at: http://www2.sas.com/proceedings/sugi27/p229-27.pdf [accessed July 2019]; **11.** Shingrix Prescribing Information. Available at: https://www.fda.gov/vaccines-blood-biologics/vaccines/shingrix [accessed August 2019].



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**Trademark statement**
Shingrix is a trademark of the GSK group of companies.



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