PERSISTENCE OF IMMUNE RESPONSE AND SAFETY OF AN ADJUVANTED RECOMBINANT ZOSTER VACCINE IN OLDER ADULTS PREVIOUSLY VACCINATED WITH A LIVE-ATTENUATED HERPES ZOSTER VACCINE: END-OF-STUDY RESULTS OF A PHASE III, GROUP-MATCHED CLINICAL TRIAL

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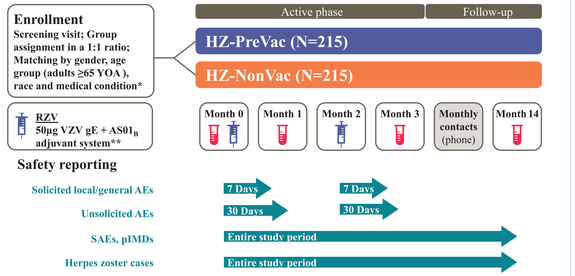
BACKGROUND

- Herpes zoster (HZ), caused by reactivation of latent varicella-zoster virus (VZV), typically manifests as a dermatomal rash, and can result in complications such as postherpetic neuralgia. HZ risk increases with age likely due to age-related decline of immunity.
- At the time of this study start, Zoster Vaccine Live (ZVL; containing live-attenuated VZV) was recommended in the US in adults ≥60 years of age (YOA). The efficacy of ZVL is lower in older age groups i.e.: 51.3% in ≥60 YOA, 37.6% in ≥70 YOA and 18% in ≥80 YOA adults.[1,2] The efficacy of ZVL declines from 51.3% to 21.1% by years 7–11 post-vaccination, in adults ≥60 YOA.[3]
- The adjuvanted Recombinant Zoster Vaccine (RZV; containing VZV glycoprotein E and $AS01_B$ adjuvant system) demonstrated efficacy against HZ of >90% sustained over 4 years of follow-up, across all age groups (≥50 YOA, ≥70 YOA, ≥80 YOA).[4-6]
- The Advisory Committee on Immunization Practices (ACIP) recommends RZV for adults ≥50 YOA and also the revaccination of previous ZVL recipients with RZV.[7] RZV is now approved in several countries worldwide.[8-10]
- Here, we present immunogenicity and safety of RZV up to 12 months post-dose 2 in adults ≥65 YOA that (1) have either been vaccinated with ZVL at least 5 years before (HZ-PreVac) or (2) have never received ZVL (HZ-NonVac).

METHODS

Study design

Figure 1. Phase III, multi-center, open-label study (NCT02581410)



, vaccination; , blood sampling; **N**, number of participants vaccinated; **AE**, adverse event; **SAE**, serious AE; **pIMD**, potential immune-mediated disease.

* Matching by medical condition was performed in a hierarchical manner: (1) immune-mediated diseases, (2) diabetes mellitus, (3) current depression, (4) pulmonary conditions, (5) heart conditions, (6) none of the above.

**contains 50 µg of MPL (3-*O*-desacyl-4'-monophosphoryl lipid A), 50 µg of QS-21 (*Quillaja saponaria* Molina, fraction 21) and liposome.

RESULTS

Study participants and demographics

Figure 2. CONSORT diagram

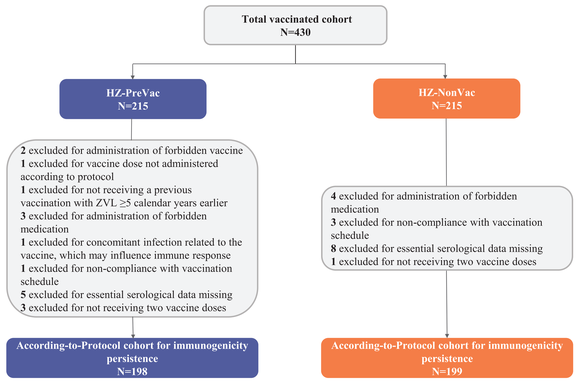
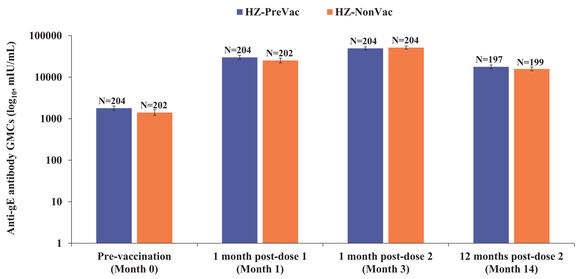


Table 1. Summary of demographic characteristics for the According-to-Protocol cohort for immunogenicity persistence

Characteristics	HZ-PreVac N=198	HZ-NonVac N=199
Mean age (years) at vaccination dose 1	71.2	70.7
Gender (male/female)	97/101	98/101
Geographic ancestry	100% White-Caucasian/European heritage	

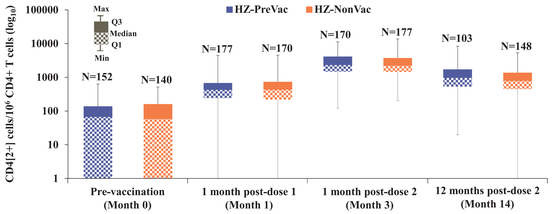
Immunogenicity

Figure 3. Similar anti-gE antibody geometric mean concentrations (GMCs) prior to and following RZV vaccination between study groups (adapted ATP cohort for immunogenicity)



ATP, according-to-protocol; **N**, number of participants with available results; **IU**, international unit; **Error bars** represent 95% confidence intervals; **Note**: Adapted ATP cohort for Immunogenicity denotes that for each time point presented, the corresponding ATP cohort for immunogenicity was used.

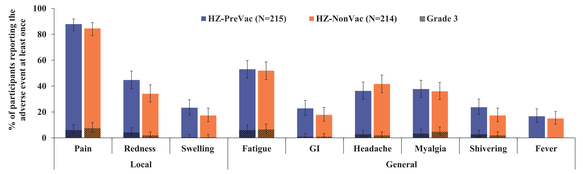
Figure 4. Similar gE-specific CD4[2+] T cell levels prior to and following RZV vaccination between study groups (adapted ATP cohort for immunogenicity)



ATP, according-to-protocol; **CD4[2+] T cells**, CD4+ T cells expressing at least 2 of the 4 activation markers assessed (interferon-γ, interleukin-2, tumor necrosis factor-α, CD40 ligand); N, number of participants with available results; **Min/Max**, minimum/maximum; **Q1**, Quartile 1; **Q3**, Quartile 3 ; **Note**: Adapted ATP cohort for Immunogenicity denotes that for each time point presented, the corresponding ATP cohort for immunogenicity was used.

Safety and reactogenicity

Figure 5. Similar incidence of local and general solicited adverse events (all grades and grade 3) between study groups (TVC)



TVC, total vaccinated cohort; **N**, number of participants with at least one documented dose; **Grade 3**, severe symptom (significant pain at rest; prevents normal every day activities [pain]; diameter >100 mm [redness, swelling]; oral temperature >39.0 °C [fever], prevents normal activity [other symptoms]); **GI**, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain); **Fever**, temperature ≥37.5 °C. **Error bars** represent exact 95% confidence intervals.

- Incidence of unsolicited adverse events was higher in HZ-PreVac group. Medical review of unsolicited adverse events did not reveal any medically relevant differences between study groups.
- Comparable incidence of serious adverse events and potential immune-mediated diseases between groups. Up to study end, no serious adverse events and no potential immune-mediated diseases were considered causally related to vaccination by the investigator.
- There were no confirmed HZ cases during the study.

Table 2. Incidence of unsolicited adverse events (AEs), serious AEs (SAEs) and potential immune-mediated diseases (pIMDs) (TVC)

AE (overall/participant)		Reporting Period	HZ-PreVac (N=215)	HZ-NonVac (N=215)
			n (% [95% CI])	n (% [95% CI])
Unsolicited AE	All	Days 0–29	81 (**37.7** [31.2–44.5])	54 (**25.1** [19.5–31.5])
	Related		13 (**6.0** [3.3–10.1])	13 (**6.0** [3.3–10.1])
SAE	All	From Day 0 to study end	18 (**8.4** [5.0–12.9])	22 (**10.2** [6.5–15.1])
pIMD	All		2 (**0.9** [0.1–3.3])	4 (**1.9** [0.5–4.7])

TVC, total vaccinated cohort; **N**, number of participants with at least one administered dose; **n/%**, number/percentage of participants reporting the outcome of interest at least once; **95% CI**, exact 95% confidence interval; **Related**, AEs assessed by the investigator to be causally related to vaccination.

CONCLUSIONS

- RZV induced strong humoral and cellular immune responses at similar levels in all participants, whether they had been vaccinated with ZVL ≥5 years earlier or had never received ZVL.
- Humoral and cellular immune responses persisted above pre-vaccination levels at least up to 12 months post-dose 2 in both study groups.
- No clinically significant differences were observed in the RZV reactogenicity and safety profile regardless of previous ZVL vaccination.

References
1. Oxman MN et al. N Engl J Med 2005;352(22):2271–84
2. Gabutti G et al. J Prev Med Hyg 2014;55(4):130–36
3. Morrison VA et al. Clin Infect Dis 2015;60(6):900–09
4. Lal H et al. N Engl J Med 2015;372:2087–96
5. Cunningham AL et al. N Engl J Med 2016;375:1019–32
6. Lecrenier N et al. Expert Rev of Vaccines 2018;17(7):619–34
7. Dooling KL et al. Morb Mortal Wkly Rep 2018;67:103–08
8. FDA. Shingrix Prescribing Information. Available at: https://www.fda.gov/downloads/Biologics-BloodVaccines/Vaccines/ApprovedProducts/UCM581605.pdf. Accessed 07 Sep 2018
9. Health Canada. Summary Basis of Decision. Available at: https://hpr-rps.hres.ca/reg-content/summary-basis-decision-detailTwo.php?linkID=SBD00377. Accessed 07 Sep 2018
10. EMA. Shingrix. Summary of product characteristics. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/004336/WC500246550.pdf. Accessed 07 Sep 2018

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POSTER No.1956

Persistence of Immune Response and Safety of an Adjuvanted Recombinant Zoster Vaccine in Older Adults Previously Vaccinated with a Live-Attenuated Herpes Zoster Vaccine: End-of-Study Results of a Phase III, Group-Matched Clinical Trial

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7. GSK, Rockville, Maryland, US.

CONFLICT OF INTEREST

AS, HL, TM, TCH, LC, LO, CH, KG and MD are/were employees of the GSK group of companies. LO is employee of CureVac AG as of March 1st 2018 and is an inventor on a patent application related to the vaccine used in this study. HL is employee of Pfizer and receives salary and stock, as compensation from Pfizer Inc. AS, TM, TCH, HL and LC also hold/held shares in the GSK group of companies as part of their employee remuneration. GC is/was a board member in the GSK group of companies. GK and TCH are/were GSK consultants and received consultant fees. TCH is an inventor on a patent application related to the vaccine used in this study. NPK received research support from GSK group of companies during the conduct of this study, as well as grants from Sanofi Pasteur, Merck& Co, Pfizer Inc., Protein Science (now S-P), MedImmune and Dynavax for work outside of this study.

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