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EFFICACY AND SAFETY OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE IN ADULTS WITH PRE-EXISTING POTENTIAL IMMUNE MEDIATED DISEASES: A POOLED POST-HOC ANALYSIS ON TWO PARALLEL RANDOMIZED TRIALS

Alemnew F. Dagnew[1], Debora Rausch[2], Caroline Hervé[3], Toufik Zahaf[4], Anne Schuind1 on behalf of the ZOE-50/70 study groups

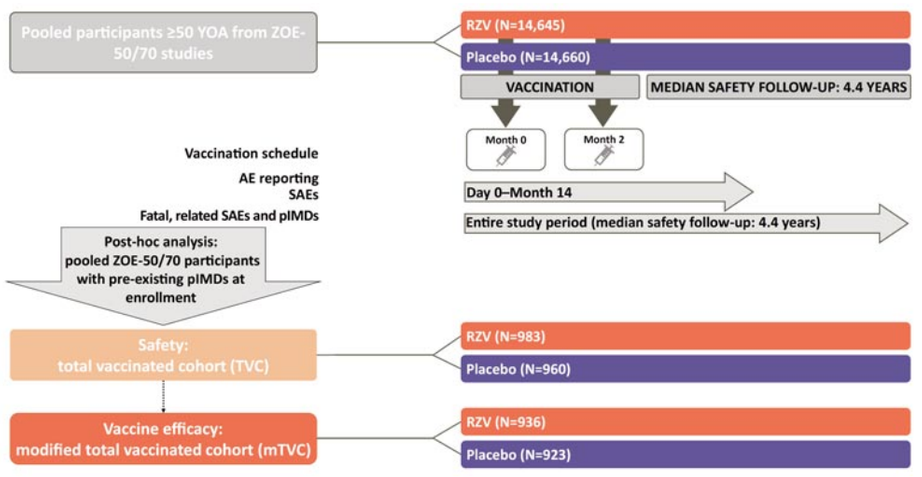
[1]GSK, Rockville,MD, USA; [2]GSK, Philadelphia, PA, USA; [3]GSK,Wavre, Belgium; [4]GSK, Rixensart, Belgium

BACKGROUND & OBJECTIVES

- Herpes zoster (HZ) is a painful, dermatomal rash which most often occurs in adults ≥50 years of age (YOA) due to reactivation of latent varicella-zoster virus.[1]
- The adjuvanted recombinant zoster vaccine (RZV; Shingrix, GSK) demonstrated high vaccine efficacy (VE) against HZ and postherpetic neuralgia in 2 large-scale clinical trials, ZOE-50 (NCT01165177)[2] and ZOE-70 (NCT01165229).[3]
- As shown in a previous publication, during the entire study period, rates of exacerbation of a pre-existing (at study entry) disease or a new onset of a different potential immune mediated disease (pIMD) were similar between RZV and placebo recipients.[4]
- Here we report a post-hoc analysis of RZV efficacy against HZ and occurrence of serious adverse events (SAEs) in the ZOE-50/70 population with pre-existing pIMDs.

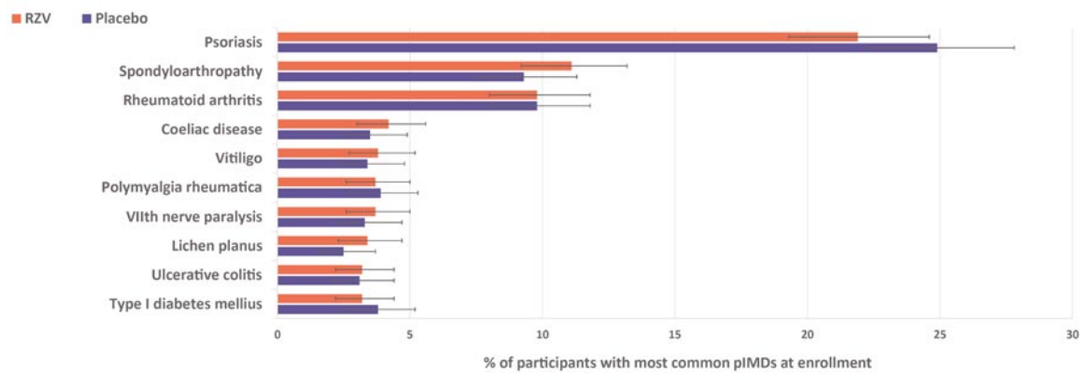
METHODS

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



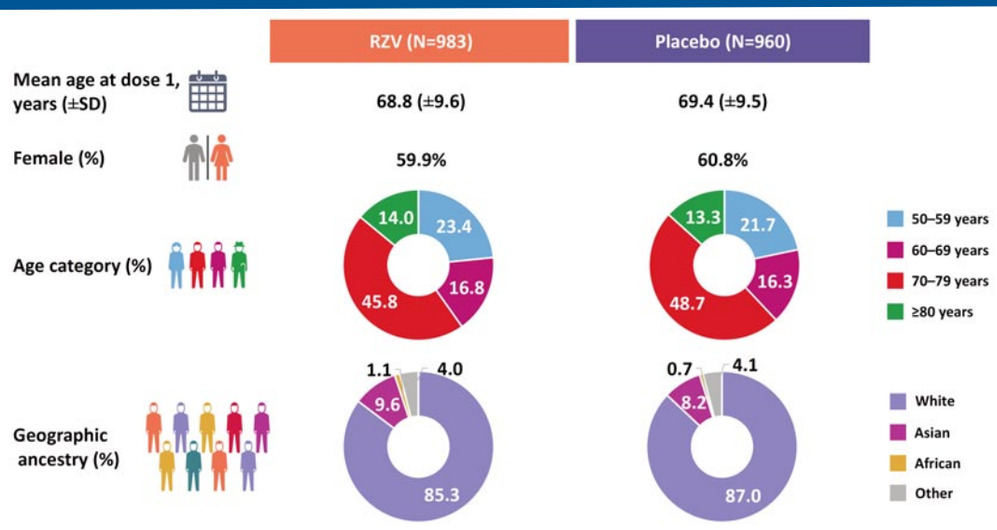
RESULTS

The 10 most common pIMDs in both groups at enrollment (TVC)



Note: Participants with pre-existing pIMDs were identified by querying the global medical history of the participants included in TVC with acustomized Medical Dictionary for Regulatory Activities (**MedDRA**) query for pIMDs.[6]

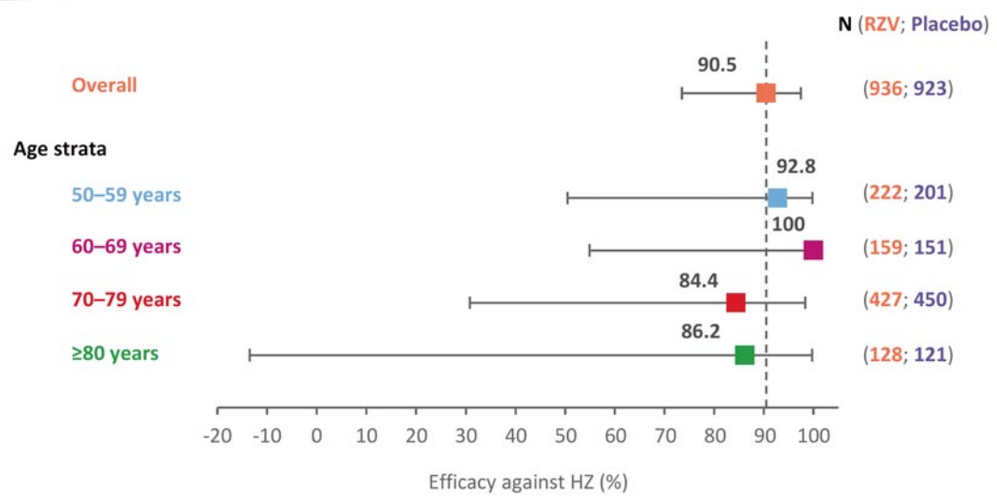
Demographic characteristics were balanced between groups (TVC)



SD, standard deviation. **White**, includes White-Caucasian/European and White Arabic/ North African; **Asian**, includes Asian-East-Asian and Asian-Japanese; **African**, includes African/African-American.

Efficacy results (mTVC)

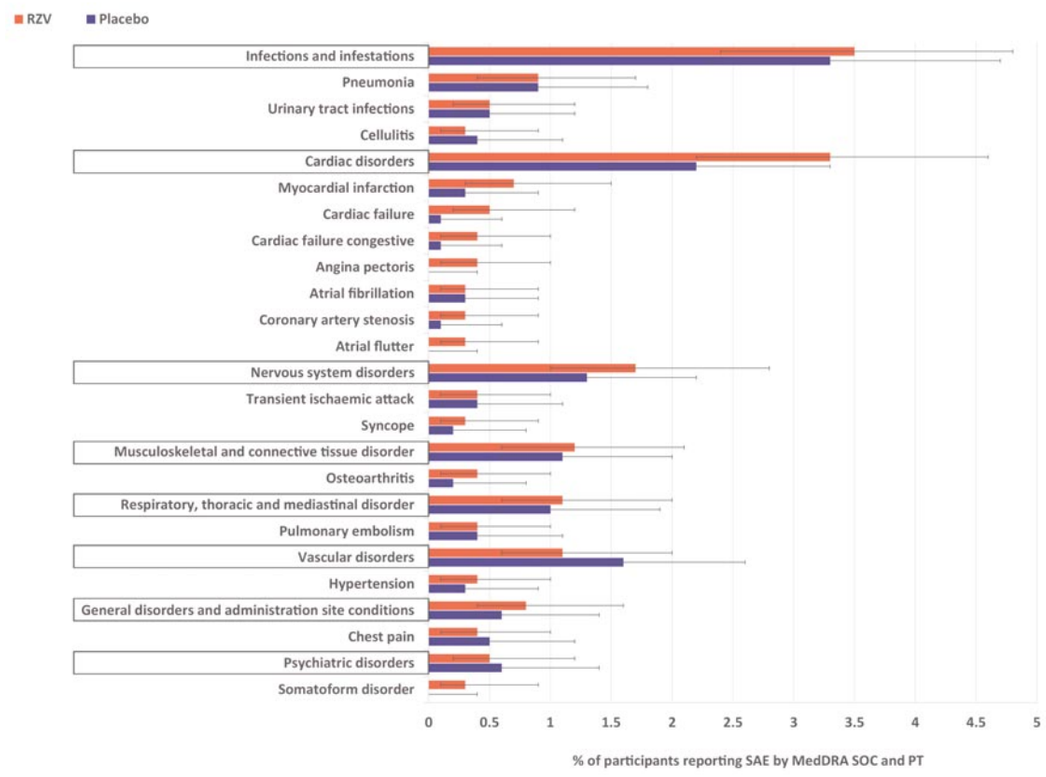
- ***Efficacy in peventing HZ in pooled ZOE-50/70 participants with a pIMD at enrollment was 90.5% (95% confidence interval [CI]: 73.5–97.5%).***
- ***RZV showed similar VE against HZ irrespective of age strata, in pooled ZOE-50/70 participants with pre-existing pIMDs at enrollment.***



Note: Error bars represent CIs. Vertical dashed line represents the overall VE against HZ (90.5%) evaluated in the pooled population from ZOE-50/70 with pre-existing pIMDs at enrollment. VE was calculated by means of the Poisson method. All efficacy estimates were adjusted by region; overall efficacy estimates were also adjusted by age strata.

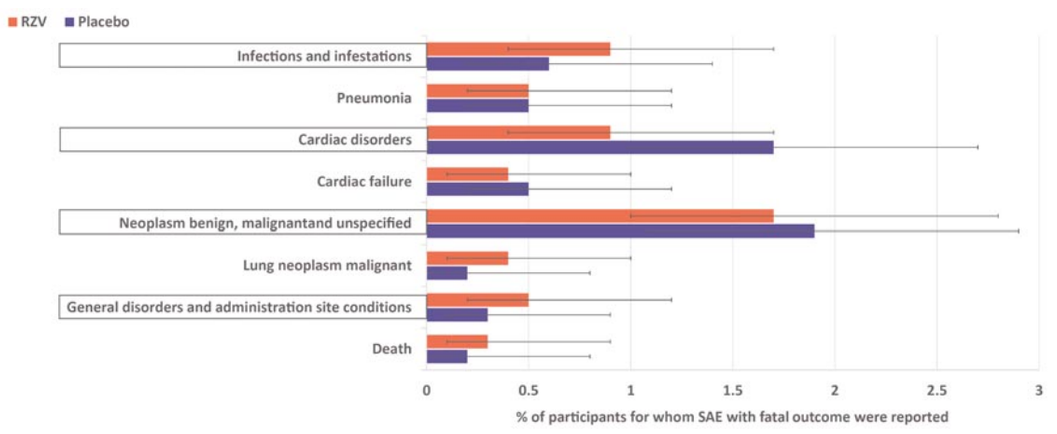
Safety results (TVC)

- ***One year post-last RZV dose, SAEs were reported by 144 (14.6%) RZV and 112 (11.7%) placebo recipients. The most common reported SAEs by MedDRA SOC and PT are presented below.***



SOC, system organ class; **PT**, preferred term. **Note**: Per PT, only SAEs reported by ≥0.3% of RZV recipients are presented here. The framed SAE category represent SOC.

- ***One year post-last RZV dose, SAEswith fatal outcomewere reported for 12 (1.2%) RZV and 9 (0.9%) placebo recipients.****
- ***During the entire study period, SAEs with fatal outcome were recorded for 50 (5.1%) RZV and 63 (6.6%) placebo recipients. Themost common SAEs with fatal outcomes reported during the entire study period are presented below.***



Note: Per PT, only SAEs reported by ≥0.3% of RZV recipients are presented here. The framed SAE category represent SOC. *Within 1 year post-last vaccination, none of the events were reported by ≥0.3% of RZV recipients. RZV = 1 of each of the following events: acute myocardial infarction, myocardial infarction, large intestinal obstruction, sudden death, neutropenic sepsis, pneumonia, skull fracture, ovarian cancer, prostate cancer, rectal adenocarcinoma, cerebrovascular accident, pneumonia aspiration, and 2 pancreatic carcinomas. Placebo = 1 of each of the following events: acute myocardial infarction, chronic hepatic failure, large cell lung cancer, metastases to central nervous system, cerebrovascular accident, azotaemia, pulmonary fibrosis, and 2 pancreatic carcinomas.

Plain Language Summary

What is the context?

- Initial infection with varicella zoster virus causes varicella (chickenpox). After the varicella infection disappears, the virus stays dormant in the body and may reactivate later in life causing shingles (also called herpes zoster), typically characterized by a painful rash.
- Shingles generally affects adults over 50 years old due to age-related decline in immunity. Several autoimmune diseases, resulting from an abnormal functioning of the immune system, were found to further increase the risk for shingles.

What is new?

- In two large clinical trials, the adjuvanted recombinant zoster vaccine (*Shingrix*, GSK) wasfound to protect against shingles in adults over 50 years old. In the pooled population fromthese trials, around 6.6% had at least 1 potential immune mediated disease when entering the study. Additional analyses were performed to evaluate the impact of pre-existingpotential immune mediated diseases on the safety and efficacy of Shingrix.
- The most frequently reported potential immune mediated diseases were psoriasis, spondyloarthropathy, rheumatoid arthritis, and coeliac disease. In participants with preexisting conditions *Shingrix* was protective and the safety profile was similar in the vaccine and placebo groups.

What is the impact?

- *Shingrix* showed high efficacy against herpes zoster in the population with a pre-existing potential immune mediated disease.Hence,patientswith these medical conditionsmay benefit from this vaccine.

CONCLUSIONS

- **The number of pooled ZOE-50/70 participants with pre-existing pIMD at enrollment was substantial and therefore allowed for the estimation of VE against HZ and occurrence of SAEs in this population subset.**
- **Post-hoc analysis of the ZOE-50/70 studies showed that RZV is highly efficacious in the prevention of HZ in adults ≥50 YOA with a pre-existing pIMD at enrollment.**
- **Additionally, for this subset, the occurrence of SAEs and SAEs with fatal outcome was similar between RZV and placebo groups.**
- **Study limitations:**
  - **The ZOE-50/70 studies were not powered to assess VE or safety in subsets such as study participants with pre-existing pIMDs.**
  - **Persons with pre-existing pIMD who were undergoing immunosuppressive treatment were not enrolled in the ZOE-50/70 studies.**

Funding: GlaxoSmithKline Biologicals SA funded the study and the development of the abstract and poster.

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

Disclosures: TZ is an employee of the GSK group of companies, AFD, DR, CH and AS were employees of the GSK group of companies during the conduct of the study. AFD, DR, CH, TZ and AS hold shares in the GSK group of companies. The authors declare no other financial or non-financial relationships or activities.

Acknowledgments: Maria C Maior (Modis c/o GSK) provided writing support and Janne Tys (Business & Decision Life Sciences c/o GSK) coordinated poster development and editorial support.

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Presenter:
Emma Bandy
emma.k.bandy@gsk.com