SAFETY PROFILE OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE (RZV) IN IMMUNOCOMPROMISED POPULATIONS: AN OVERVIEW OF 6 TRIALS

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BACKGROUND AND AIM

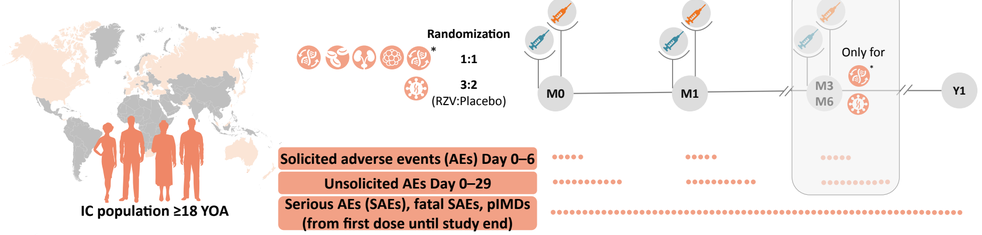
- Immunocompromised (IC) populations are at increased risk of herpes zoster (HZ) and its related complications.
- RZV demonstrated >68% efficacy against HZ in autologous hematopoietic stem cell transplant (auHSCT) recipients ≥18 years of age (YOA).[1]

Aim of the overview:
We present the pooled safety data across 6 clinical trials in IC populations

- **auHSCT** recipients, phase III, NCT01610414
- Hematologic malignancy (**HM**) patients, phase III, NCT01767467
- Renal transplant (**RT**) recipients, phase III, NCT02058589
- Patients with solid tumors (**ST**), phase II/III, NCT01798056
- * **auHSCT*** recipients, phase I/IIa, NCT00920218
- Human immunodeficiency virus (**HIV**)-infected adults, phase I/IIa, NCT01165203

METHODS

- **All 6 studies were randomized, observer-blinded, placebo-controlled.**
- **Reactogenicity data are pooled across the 6 studies and other safety data are presented by study.**



, RZV; , Placebo; **M**, month; **Y1**, 1 year post-last dose; **pIMDs**, potential immune mediated diseases. **Note:** HIV-infected adults received the second dose at 2 months post-first dose. auHSCT* participants received 3 doses at M0, M1 and M3. In the auHSCT study, follow-up was driven by HZ case accrual and ranged from 12 months to 4 years after the last dose, with a median of 29 months. Although fatal SAEs and related SAEs were collected until the end of study, for the purpose of this poster we are only presenting approximately 1 year data across studies.

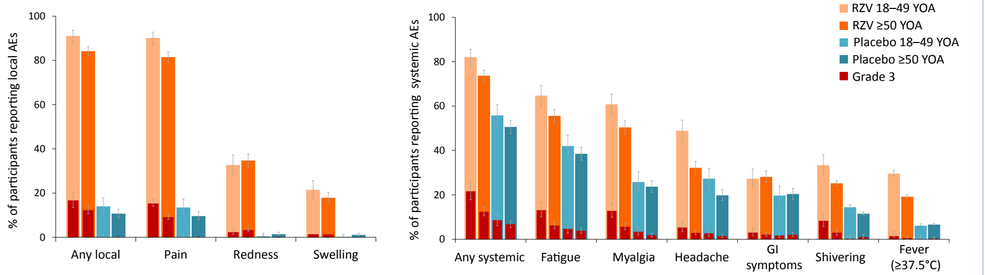
All data are presented by age group: 18–49 YOA and ≥50 YOA across the different IC populations.

IC populations, study reference		TVC, N				Mean age, Years ± SD		Female, %	
		RZV		Placebo					
		18–49 YOA	≥50 YOA	18–49 YOA	≥50 YOA	RZV	Placebo	RZV	Placebo
	auHSCT	230	692	229	695	54.8 ± 11.7	55.1 ± 11.4	37.1	37.4
	HM	74	209	73	206	56.8 ± 15.5	57.8 ± 14.9	40.3	40.9
	RT	48	84	49	83	52.3 ± 12.5	52.4 ± 12.8	28.8	31.1
	ST	31	86	30	85	57.1 ± 10.8	58.5 ± 11.7	59.8	60.0
*	auHSCT*	N'=4	N'=25	-	-	57.5 ± 6.9	-	31.0	-
		N''=10	N''=20	N''=4	N''=26	53.1 ± 12.2	57.3 ± 8.6	40.0	36.7
	HIV	46	28	34	15	46.6 ± 10.7	45.1 ± 11.4	6.8	4.1

N, number of patients/subgroup receiving at least 1 dose of RZV or placebo (total vaccinated cohort [**TVC**]) in each study; **N'**, patients receiving 1 placebo dose followed by 2 RZV doses; **N''**, patients receiving 3 doses of either RZV or placebo; **SD**, standard deviation. Additional details on demographic characteristics are provided *via* QR code.

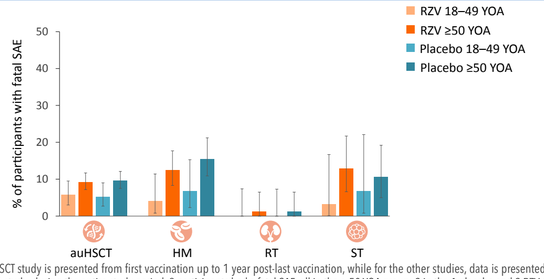
RESULTS

- **As expected, most solicited symptoms were more frequently reported in the RZV group than in the Placebo group.**
- **Pain, fatigue, headache, myalgia, shivering and fever were reported more frequently in the RZV 18–49 YOA *vs* RZV ≥50 YOA.**



Pooled TVC. **GI**, gastrointestinal. Grade 3 definitions are provided *via* QR code.

- **The percentage of study participants with fatal SAE was comparable between RZV and Placebo groups.**
- **Most of these fatal SAEs were related to the underlying diseases specific to each study population.**

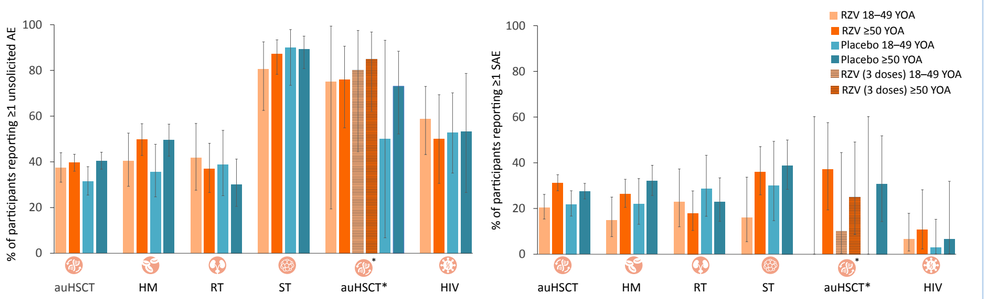


Fatal SAE data for auHSCT study is presented from first vaccination up to 1 year post-last vaccination, while for the other studies, data is presented for the whole study period. In the auHSCT* study, during the entire study period, 8 participants had a fatal SAE, all in the ≥50 YOA group: 2 in the 1 placebo and 2 RZV doses group, 3 in the 3 RZV doses group and 3 in Placebo group. In the HIV study, no fatal SAEs were reported.

pIMDs

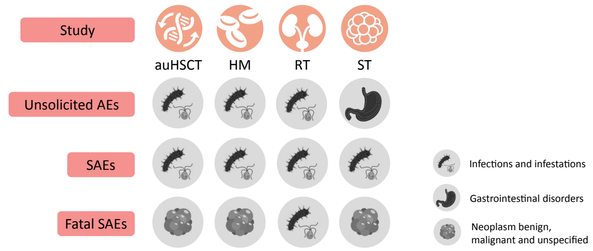
- The percentage of study participants reporting ≥1 pIMD was comparable between RZV and Placebo recipients.

Across studies, the percentage of adults reporting ≥1 unsolicited AE or ≥1 SAE was similar between RZV and Placebo groups, regardless of age.



TVC. SAE data for auHSCT study is presented from first vaccination up to 1 year post-last vaccination, while for the other studies, data is presented for the whole study period.

Overall, the majority of reported unsolicited AEs, SAEs and fatal SAEs by Medical Dictionary for Regulatory Activities System Organ Class (MedDRA SOC) were in line with the respective study population's underlying diseases and therapies. The most frequently reported AE by MedDRA SOC for each phase III study is presented below.



Data were calculated for the auHSCT, HM, RT and ST studies. In the auHSCT* and HIV studies due to the small sample size the data is limited. The top 3 most reported unsolicited AEs, SAEs and fatal SAEs by age group are available *via* QR code.

CONCLUSIONS

- Reactogenicity symptoms were more frequent after RZV than Placebo and in younger age groups. The majority of symptoms were mild to moderate in intensity and short in duration.
- The frequency of unsolicited AEs and SAEs (including vaccination-related by investigator assessment) were similar between the RZV and the Placebo groups. Most of the reported AEs and SAEs (including fatal SAEs) were in the context of underlying diseases and therapies.
- Overall, the safety data presented here together with the efficacy in auHSCT recipients[1] and the immunogenicity data across populations (see immunogenicity data in presentation #4, Adult Vaccines Session) support a favorable benefit-risk profile of vaccination with RZV in IC adults.

The **extensive safety data** summarized here provides useful medical information for the prevention of HZ in a **broad range of populations with an impaired immune system** due to **underlying diseases or therapy**.

Reference: 1. Bastidas et al, JAMA. 2019;322(2):123–33.

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Disclosures: MLF, MC, PB, JJFG, FTS are employed by the GSK group of companies and declare financial and non-financial relationships and activities. AB, AFD and AS were employees of GSK group of companies at the time this study was designed, initiated and/or conducted and data was interpreted. AB, AFD, AS and FTS hold shares in the GSK group of companies. JJFG reports personal fees during the conduct of the study and outside the submitted work from the GSK group of companies.

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SUPPLEMENTARY MATERIALS

Demographic characteristics

IC populations, study reference	Gender (Male, Female)		Race (White, Black, Other)	
	RZV	Placebo	RZV	Placebo
auHSCT	37.1 / 62.9	37.4 / 62.6	19.9 / 1.6 / 78.5	18.9 / 2.7 / 78.4
HM	40.3 / 59.7	40.9 / 59.1	26.8 / 0.4 / 72.8	29.8 / 0.4 / 69.8
RT	28.8 / 71.2	31.1 / 68.9	29.5 / 2.3 / 68.2	24.2 / 0.8 / 75.0
ST	40.2 / 59.8	40.0 / 60.0	12.0 / 1.9 / 86.1	15.9 / 1.9 / 82.2
auHSCT* (2 doses)	31.0 / 69.0		96.6 / 3.4	
auHSCT* (3 doses)	40.0 / 60.0	36.7 / 63.3	83.3 / 10.0 / 6.7	23.3 / 73.3 / 3.3
HIV	6.8 / 93.2	4.1 / 95.9	89.2 / 2.7 / 8.1	10.2 / 85.7 / 4.1

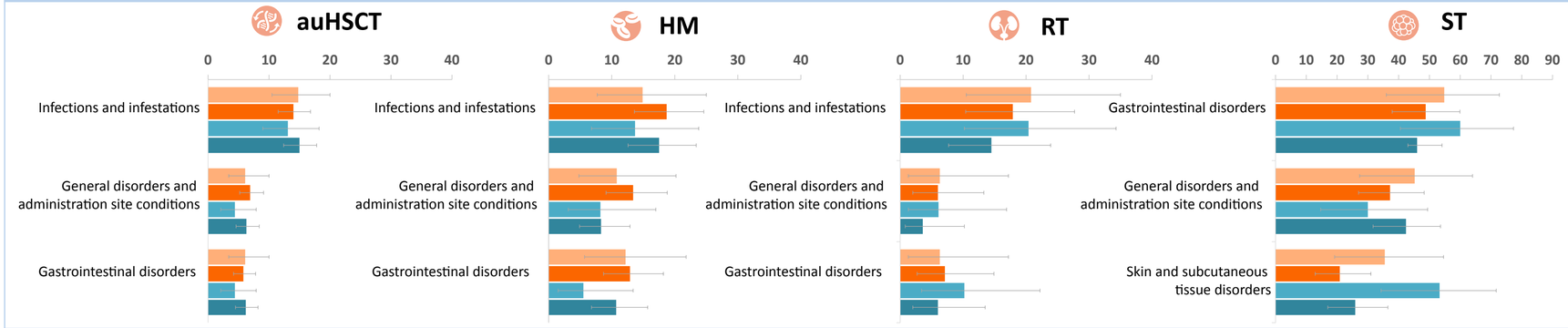
IC, immunocompromised; **RZV**, the adjuvanted recombinant zoster vaccine; **auHSCT**, autologous hematopoietic stem cell transplant recipients; **HM**, hematological malignancies patients; **RT**, renal transplant recipients; **ST**, solid tumors patients; **auHSCT***, HSCT phase I study; **HIV**, human immunodeficiency virus -infected adults. In the auHSCT* study, the 2 doses group received 1 placebo dose and 2 RZV doses and the 3 doses group received either 3 RZV either 3 placebo doses.

Solicited adverse events (AEs)

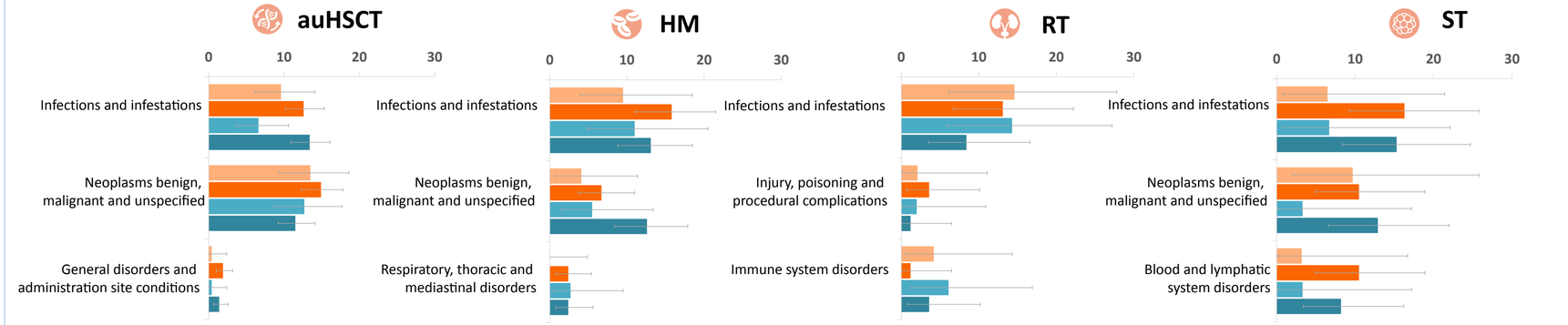
Grade 3 was defined as follows: pain that prevented normal activity; >100 mm diameter for redness and swelling; symptoms that prevented normal activity for headache, myalgia, fatigue and gastrointestinal symptoms; fever >39.0 °C (axillary/oral temperature). Among systemic AEs, fatigue, headache (all, related), myalgia, shivering, and fever (all, related) were reported more frequently in the RZV 18–49 YOA group than in the RZV ≥50 YOA group.

AEs by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC)

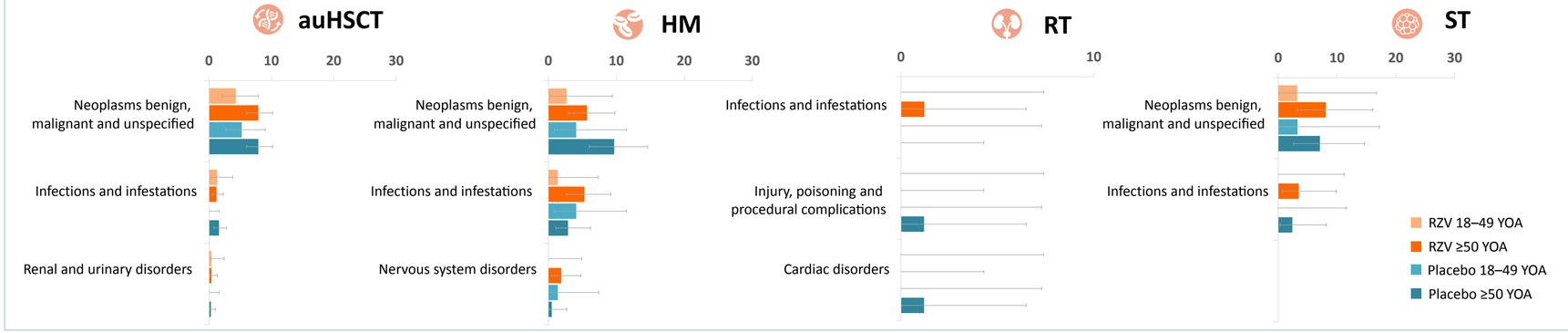
Unsolicited AEs by MedDRA SOC



Serious AEs (SAEs) by MedDRA SOC



Fatal SAEs by MedDRA SOC



SAFETY PROFILE OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE (RZV) IN IMMUNOCOMPROMISED POPULATIONS: AN OVERVIEW OF 6 TRIALS

ABSTRACT NO 907134

Background: Immunocompromised (IC) populations are at increased risk of herpes zoster (HZ) and its related complications. RZV demonstrated >68% efficacy against HZ in autologous hematopoietic stem cell transplant (HSCT) recipients ≥18 years of age (YOA). Here we present the safety data across 6 clinical trials in IC populations: autologous HSCT recipients, HIV-infected adults, renal transplant recipients, patients with solid tumor and patients with hematological malignancies.

Methods: All 6 studies (Table 1) enrolled IC adults ≥18 YOA in RZV and Placebo groups. Safety was evaluated in the total vaccinated cohort (TVC). Solicited adverse events (AEs) were collected for 7 days and unsolicited AEs for 30 days after each dose. Serious AEs (SAEs), and potential immune-mediated diseases (pIMDs) were collected from dose 1 until 1 year post-last dose or study end (for causally related [assessed by investigator] and fatal SAEs). Data are presented by age group: 18–49 YOA and ≥50 YOA. Reactogenicity data are pooled across the 6 studies and other safety data are presented by study.

Results: 1587 (RZV) and 1529 (Placebo) adults were included in the pooled TVC. Solicited AEs were more frequently reported in the RZV than Placebo group. Pain, fatigue, headache, myalgia, shivering and fever were reported more frequently in the RZV 18–49 YOA than in the RZV ≥50 YOA (Figure 1). Solicited AEs were mostly mild/moderate and lasted ≤3 days and grade 3 solicited AEs lasted ≤2 days (median duration). Across studies, the percentage of adults reporting ≥1 unsolicited AE was similar between RZV (18–49 YOA: 37.4–80.6%; ≥50 YOA: 36.9–87.2%) and Placebo (18–49 YOA: 31.4–90.0%; ≥50 YOA: 30.1–89.4%) (Figure 2). Overall, the percentage of adults with ≥1 SAE (Figure 3), causally related SAEs, fatal SAEs and pIMDs was similar between RZV and Placebo and between age groups. Overall, no safety concern was identified.

Conclusion: Reactogenicity symptoms were more frequent after RZV than placebo, and in younger age groups but no safety concern was identified. Most of the reported AEs and SAEs were in the context of underlying diseases and therapies. Overall our data support a favorable benefit-risk profile of vaccination with RZV in IC adults.

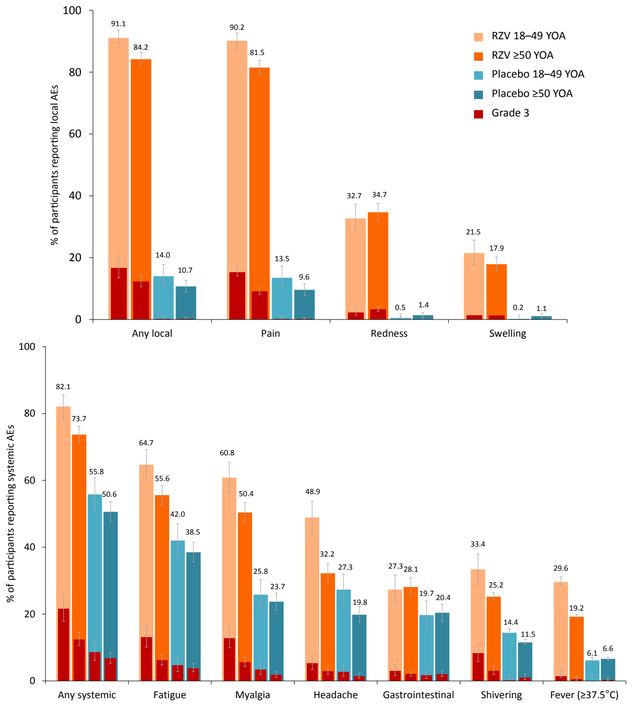
Funding: GlaxoSmithKline Biologicals SA

Table 1. Clinical trials with immunocompromised populations included in our analysis

Populations (reference used for the study)	Total Vaccinated Cohort				Study type and registration numbers	Vaccination schedule and doses administered/groups
	RZV		Placebo			
	18–49 YOA	≥50 YOA	18–49 YOA	≥50 YOA		
Autologous Hematopoietic Stem Cell Transplant recipients (**HSCT***)	N=10 N'=4	N=20 N'=25	N=4	N=26	Phase I/IIa, randomized, observer-blind, placebo controlled NCT00920218	3 doses (at months 0, 1 and 3): 3 RZV doses or 3 gE/AS01$_B$ doses or 1 placebo + 2 RZV doses or 3 placebo doses
HIV-infected adults (**HIV**)	N=46	N=28	N=34	N=15	Phase I/IIa, randomized, observer-blind, placebo controlled NCT01165203	3 doses (at months 0, 2 and 6): 3 RZV doses or 3 placebo doses
Autologous Hematopoietic Stem Cell Transplant recipients (**HSCT**)	N=230	N=692	N=229	N=695	Phase III, randomized, observer-blind, placebo-controlled efficacy study NCT01610414	2 doses (at months 0 and 1–2): 2 RZV doses or 2 placebo doses
Hematologic malignancy patients (**HM**)	N=74	N=209	N=73	N=206	Phase III, randomized, observer-blind, placebo-controlled study NCT01767467	2 doses (at months 0 and 1–2): 2 RZV doses or 2 placebo doses
Solid tumor patients on chemotherapy (**ST**)	N=31	N=86	N=30	N=85	Phase II/III, randomized, observer-blind, placebo-controlled study NCT01798056	2 doses (month 0 and 1–2): 2 RZV doses or 2 placebo doses
Renal transplant recipients (**RT**)	N=48	N=84	N=49	N=83	Phase III, randomized, observer-blind, placebo-controlled study. NCT02058589	2 doses (at months 0 and 1-2): 2 RZV doses or 2 placebo doses

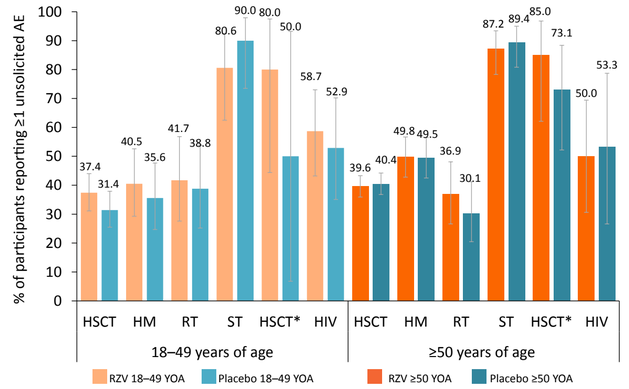
N, number of patients/subgroup receiving at least 1 dose of RZV or placebo (total vaccinated cohort [TVC]) in each study; **N'**, number of patients receiving 1 placebo dose followed by 2 RZV doses whom were additionally included into the RZV group in the pooled TVC; **YOA**, years of age; **RZV**, adjuvanted recombinant zoster vaccine; **HIV**, human immunodeficiency virus; **gE/AS01E**, glycoprotein E/ Adjuvant System containing MPL, QS-21 and liposome (25 µg MPL and 25 µg QS-21). All studies are registered on clinicaltrials.gov.

Figure 1. Percentage of participants with solicited local and systemic AEs, reported across 6 pooled studies (7 days post-vaccination, overall/participant, pooled total vaccinated cohort)



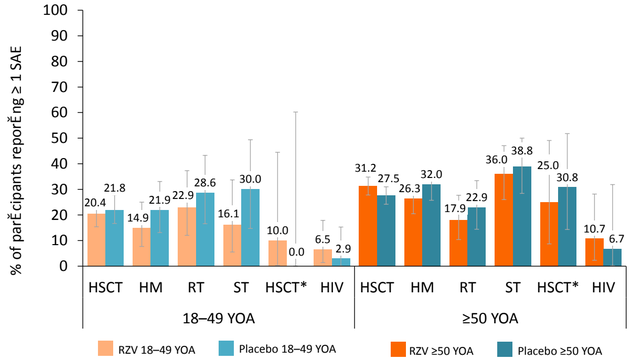
AE, adverse event; **RZV**, adjuvanted recombinant zoster vaccine; **YOA**, years of age. Grade 3 was defined as follows: pain that prevented normal activity; >100 mm diameter for redness and swelling; symptoms that prevented normal activity for headache, myalgia, fatigue and gastrointestinal symptoms; fever >39.0°C (axillary/oral temperature).
For the systemic AEs fatigue, headache (all, related), myalgia, shivering, and fever (all, related) were reported with higher incidences in the RZV 18–49 YOA group than in the RZV ≥50 YOA group.

Figure 2. Percentage of participants reporting ≥1 unsolicited AE 30 days post-vaccination per study (total vaccinated cohort)



AE, adverse event; **HSCT**, autologous hematopoietic stem cell transplant recipients; **HM**, hematological malignancies patients; **RT**, renal transplant recipients; **ST**, solid tumors patients; **HSCT***, HSCT phase 1 study; **HIV**, human immunodeficiency virus; **RZV**, adjuvanted recombinant zoster vaccine; **YOA**, years of age.

Figure 3. Percentage of participants reporting ≥1 SAE from dose 1 until 1 year post-last dose per study (total vaccinated cohort)



SAE, serious adverse event; **HSCT**, autologous hematopoietic stem cell transplant recipients; **HM**, hematological malignancies patients; **RT**, renal transplant recipients; **ST**, solid tumors patients; **HSCT***, HSCT phase 1 study; **HIV**, human immunodeficiency virus; **RZV**, adjuvanted recombinant zoster vaccine; **YOA**, years of age.