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

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BACKGROUND AND AIM

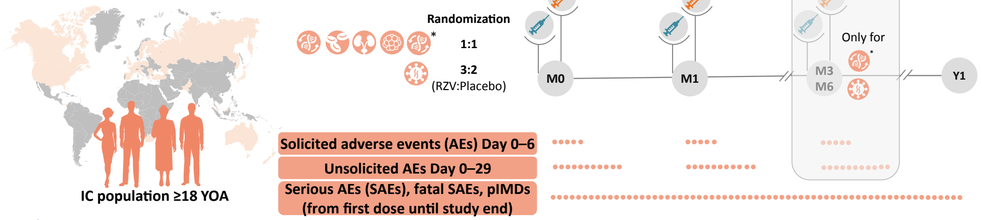
- Immunocompromised (IC) populations are at increased risk of herpes zoster (HZ) and its related complications.
- RZV demonstrated >68% efficacy against HZ in autologous hematopoietic stem cell transplant (auHSCT) recipients ≥18 years of age (YOA).[1]

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.

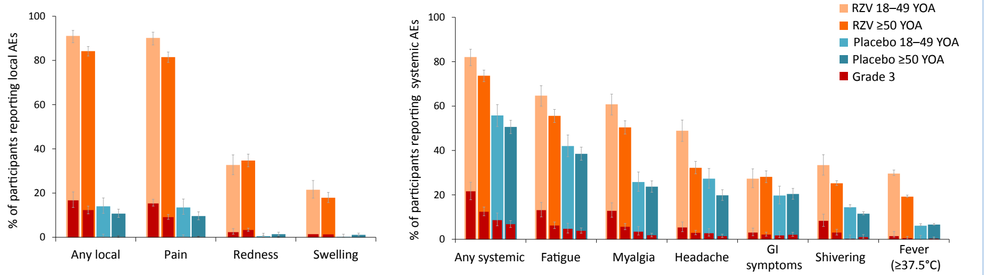
All data are presented by age group: 18–49 YOA and ≥50 YOA across the different IC populations.

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.

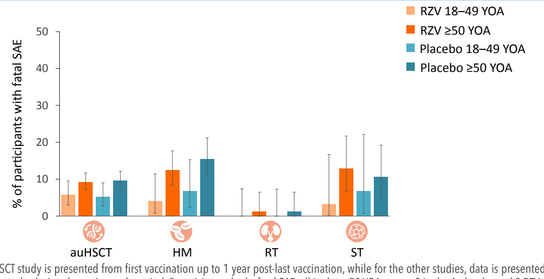
RESULTS

- **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.**

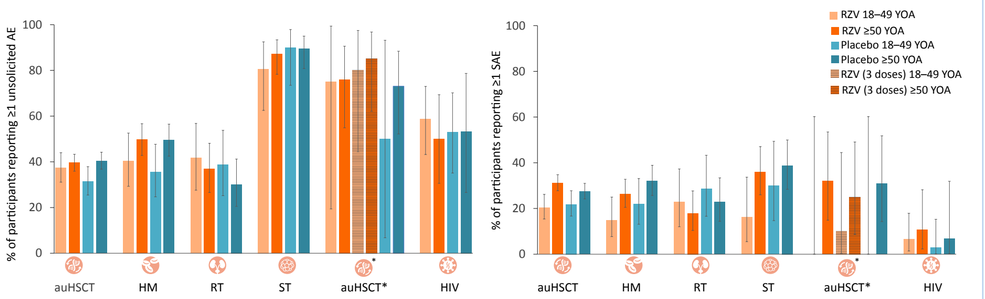


Fatal SAE data for auHSCT study is presented from first vaccination up to 1 year post-last vaccination, while for the other studies, data is presented for the whole study period. In the auHSCT* study, during the entire study period, 8 participants had a fatal SAE, all in the ≥50 YOA group: 2 in the 1 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

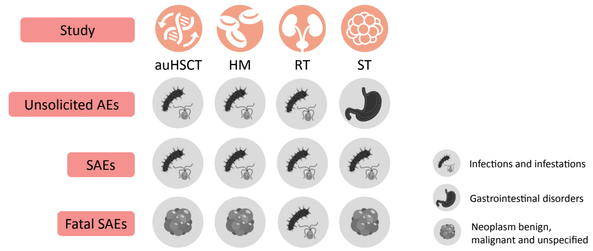
- The percentage of study participants reporting ≥1 pIMD was comparable between RZV and Placebo recipients.

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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