Use of Recombinant Zoster Vaccine (RZV) in Immunocompromised Populations

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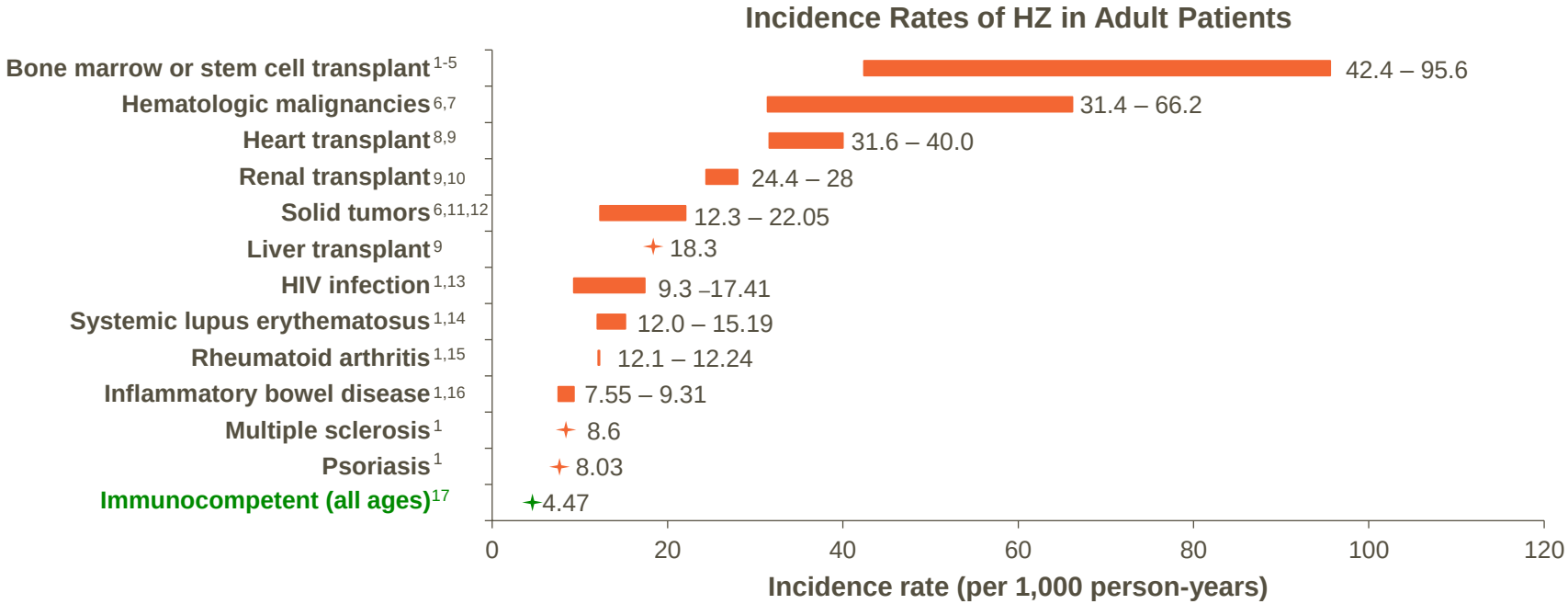
ACIP Presentation
June 25, 2021

Unmet Need: Patients With Immunocompromising Conditions Have a Higher Risk of HZ



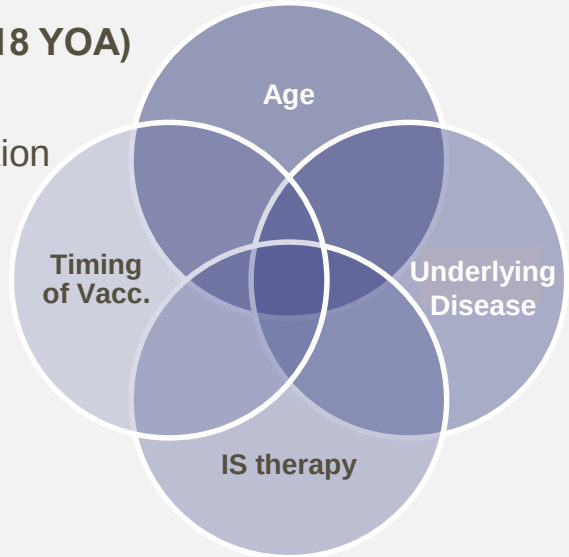
HIV, human immunodeficiency virus; HZ, herpes zoster.

1. Chen SY, et al. *Infection*. 2014;42(2):325-334. 2. Zhang D, et al. *Adv Therapy*. 2017 Jul 1;34(7):1610-21. 3. Sahoo F, et al. *Biol Blood Marrow Transplant*. 2017;23(3):505-11. 4. Winston DJ, et al. *Lancet*. 2018;391(10135):2116-27. 5. Bastidas A, et al. *JAMA*. 2019;322(2):123-33. 6. Habel LA, et al. *Cancer Epidemiol Biomarkers Prev*. 2013;22(1):82-90. 7. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000. 8. Koo S, et al. *Transpl Infect Dis*. 2014;16(1):17-25. 9. Pergam SA, et al. *Transpl Infect Dis*. 2011;13(1):15-23. 10. Arness T, et al. *Transpl Infect Dis*. 2008;10(4):260-268. 11. Mao J, et al. *Medicine (Baltimore)*. 2017;96(48):e8746.12. Tseng HF, et al. *Clin Infect Dis*. 2014;59(7):913-919.13. Blank LJ, et al. *J Acquir Immune Defic Syndr*. 2012;61(2):203-207. 14. Chakravarty EF. *Rheum Dis Clin North Am*. 2017;43(1):111-121. 15. Veetil BM, et al. *Arthritis Care Res (Hoboken)*. 2013 Jun;65(6):854-61. 16. Khan N, et al. *Clin Gastroenterol Hepatol*. 2018;16(12):1919-27.e3. 17. Johnson et al. *BMC Infect Dis* (2015);15:502

Addressing the Unmet Need

Addressing the Unmet Need in Immunocompromised (IC) Adults (≥18 YOA)

- IC populations are very heterogeneous, both across and within groups
- Not feasible to define every possible IC condition/medication combination
- Immune responses and vaccine safety in IC populations are primarily influenced by:
  - Age
  - Underlying disease
  - Immunosuppressive therapy (IS)
  - Timing of vaccination (before, during, after therapy)



IC, immunocompromised; IS, immunosuppressive; RZV, recombinant zoster vaccine; Vacc, vaccination; YOA, years of age

1. Lal et al. *N Engl J Med* 2015;372:2087-96. 2. Cunningham et al. *N Engl J Med* 2016;375:1019-32. 3. Shingrix Prescribing information: US FDA; [revised March 2021]. Available from: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Shingrix/pdf/SHINGRIX.PDF

Addressing the Unmet Need

RZV Clinical Development Program in IC Populations

Phase III

Autologous Hematopoietic Stem Cell Transplant (auHSCT)[1]
Efficacy, Immunogenicity, Safety
N=1846

Hematologic Malignancies (HM)[2]
Immunogenicity, Safety, Post-hoc Efficacy
N=562

Solid Tumors (ST)[3]*
Immunogenicity, Safety
N=232

Renal Transplant (RT)[4]
Immunogenicity, Safety
N=264

Phase I/II

Human Immunodeficiency Virus (HIV)[5]
Immunogenicity, Safety
N=123

Autologous Hematopoietic Stem Cell Transplant (auHSCT)[6]
Immunogenicity, Safety
N=89

*Phase II/III study.
IC, immunocompromised; RZV, recombinant zoster vaccine.

1. Bastidas, et al. *JAMA*. 2019;322(2):123-133. 2. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000. 3. Vink P, et al. *Cancer*. 2019;125(8):1301-1312. 4. Vink P, et al. *Clin Infect Dis*. 2020;70(2):181-190. 5. Berkowitz EM, et al. *J Infect Dis*. 2015;211(8):1279-1287. 6. Stadtmauer EA, et al. *Blood*. 2014;124(19):2921-2929.

Addressing the Unmet Need

RZV Phase III Clinical Development in IC Populations

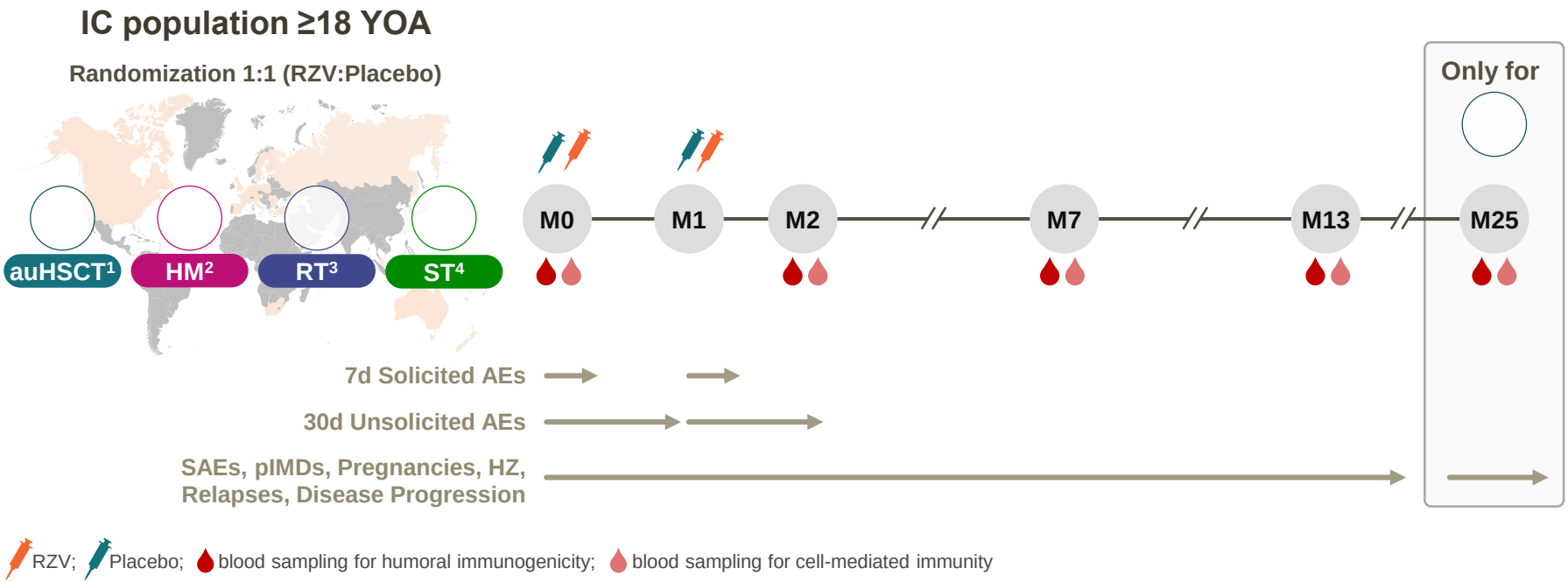
Phase III

Underlying Disease	Autologous Hematopoietic Stem Cell Transplant (auHSCT)[1]	Hematologic Malignancies (HM)[2]	Solid Tumors (ST)[3]*	Renal Transplant (RT)[4]
Age	18+ (18-49, 50+)	18+ (18-49, 50+)	18+ (18-49, 50+)	18+ (18-49, 50+)
Immunosuppressive (IS) Treatment	Pre-HSCT conditioning, Post-HSCT therapy (+/- antivirals)	IS chemotherapy per SOC	IS chemotherapy per SOC	Chronic IS per SOC
Timing of Vaccination	50-70d post-auHSCT	During Chemo (+/- 10d) After Chemo (10d–6mo)	PreChemo† OnChemo†	>4-18 mo post-allograft
Endpoints	Efficacy, Immunogenicity, Safety	Immunogenicity, Safety, (Post-hoc Efficacy)	Immunogenicity, Safety	Immunogenicity, Safety

*Phase II/III study. †Dose 1 given either 8-30 days before the start of a cycle (PreChemo group) or at the start of a cycle (OnChemo group).
Chemo, chemotherapy; d, day; IS, immunosuppressive; Mo, month; RZV, recombinant zoster vaccine; SOC, standard of care.

1. Bastidas, et al. *JAMA*. 2019;322(2):123-133. 2. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000. 3. Vink P, et al. *Cancer*. 2019;125(8):1301-1312. 4. Vink P, et al. *Clin Infect Dis*. 2020;70(2):181-190.

RZV Multicenter Studies in IC Populations Were Randomized, Observer-blinded, Placebo-controlled



AE, adverse event; auHSCT, autologous hematopoietic stem cell transplant; HM, hematologic malignancies, HZ, herpes zoster; IC, immunocompromised; M, month; pIMD, potential immune-mediated disease; RT, renal transplant; RZV, recombinant zoster vaccine; SAE, serious adverse event; ST, solid tumor; YOA, years of age.

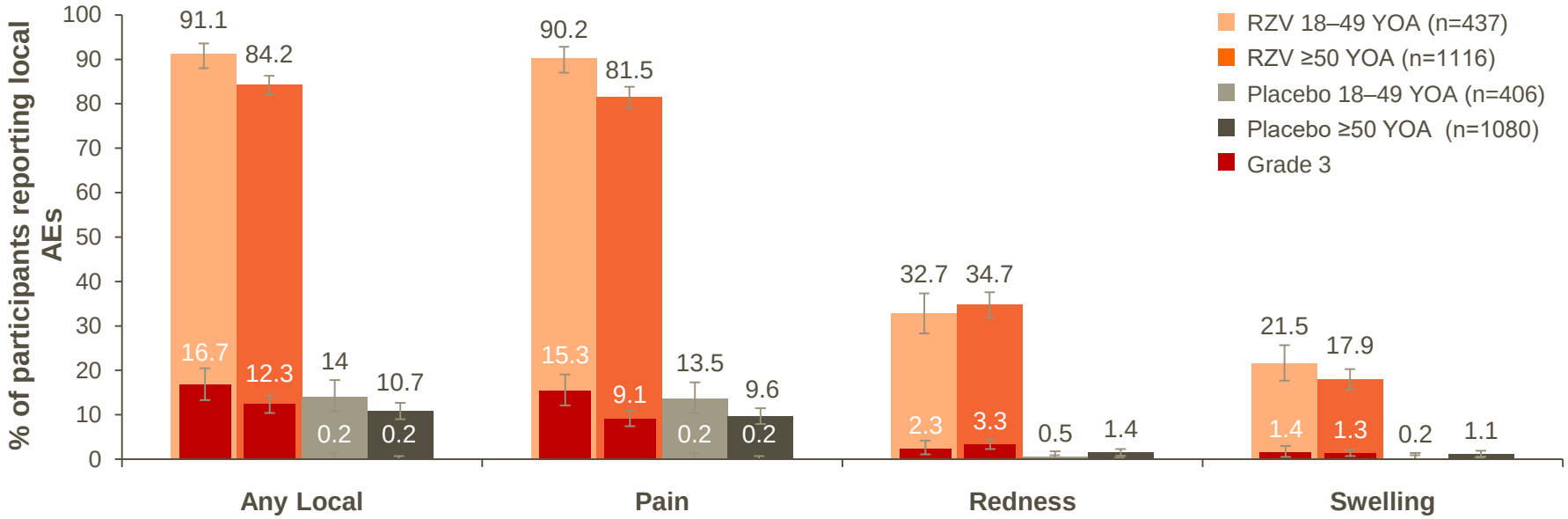
1. Data on File, ZOSTER-002 Clinical study report. Available on https://www.gsk-studyregister.com/study/115523 2. Data on File, ZOSTER-039 Clinical study report. Available on https://www.gsk-studyregister.com/study/116428 3. Data on File, ZOSTER-041 Clinical study report. Available on https://www.gsk-studyregister.com/study/116886 4. Data on File, ZOSTER-028 Clinical study report. Available on https://www.gsk-studyregister.com/study/116427

Pooled Reactogenicity in Immunocompromised Patients

Fauqued ML, et al. Safety Profile of the Adjuvanted Recombinant Zoster Vaccine (RZV) in Immunocompromised Populations: an Overview of 6 Trials. Presented at: IDWeek 2020 (virtual event). October 21 25, 2020. https://idweek.org

Percentage of Participants With Solicited Local AEs

Reported across 6 pooled studies – 7 days post-vaccination; Overall – TVC



Solicited local AEs were mostly mild/moderate in intensity and lasted a median of 3 days. Grade 3 solicited local AEs had a median duration of 1-2 days.

Graph reproduced from Fauqued ML , 2020. Presented at IDWeek 2020

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.

AE, adverse event; RZV, recombinant zoster vaccine; TVC, total vaccinated cohort; YOA, years of age.

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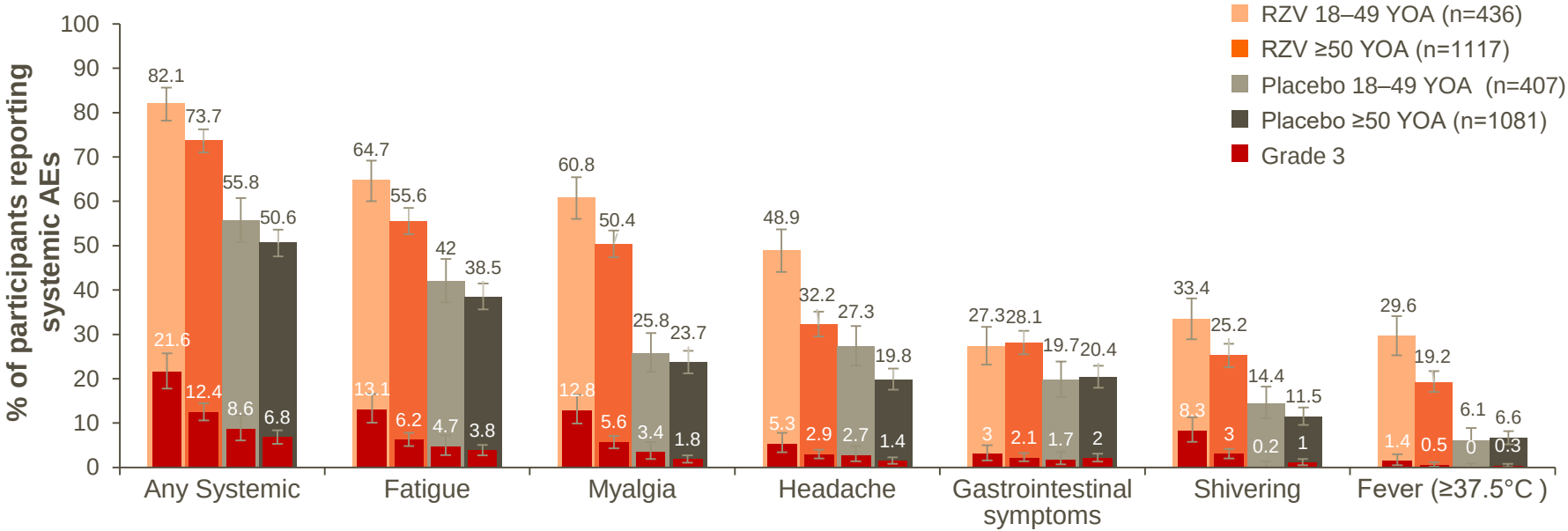
Percentage of Participants With Solicited General AEs

Reported across 6 pooled studies – 7 days post-vaccination; Overall – TVC



Solicited general AEs were mostly mild/moderate and lasted ≤3 days. Grade 3 solicited general AEs lasted ≤2 days (median duration)

Graph reproduced from Fauqued ML , 2020. Presented at IDWeek 2020

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).

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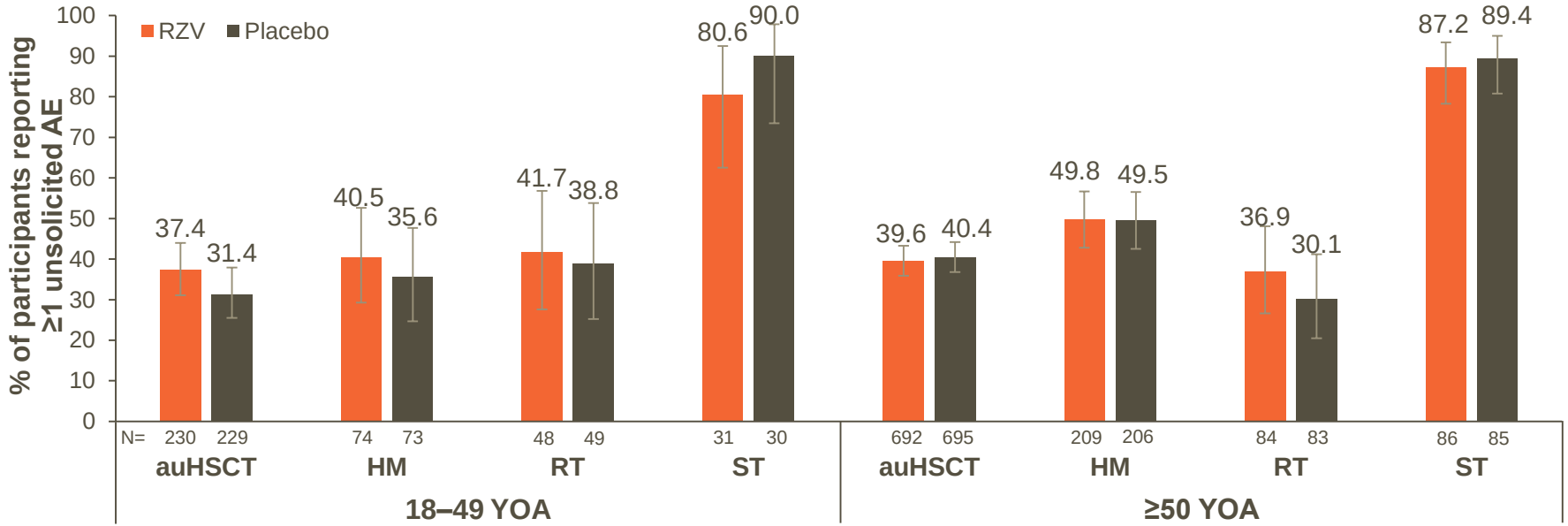
Unsolicited Adverse Events (AEs)

Percentage of participants reporting ≥1 unsolicited AE 30 days post-vaccination per study – TVC



Across studies, the percentage of adults reporting ≥1 unsolicited AE was similar between RZV and placebo groups

Error bars represent 95% CI. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.**
AE, adverse event; auHSCT, autologous hematopoietic stem cell transplant; CI, confidence interval; HM, hematological malignancies; RT, renal transplant; RZV, recombinant zoster vaccine; ST, solid tumors patients; TVC, total vaccinated cohort; YOA, years of age.
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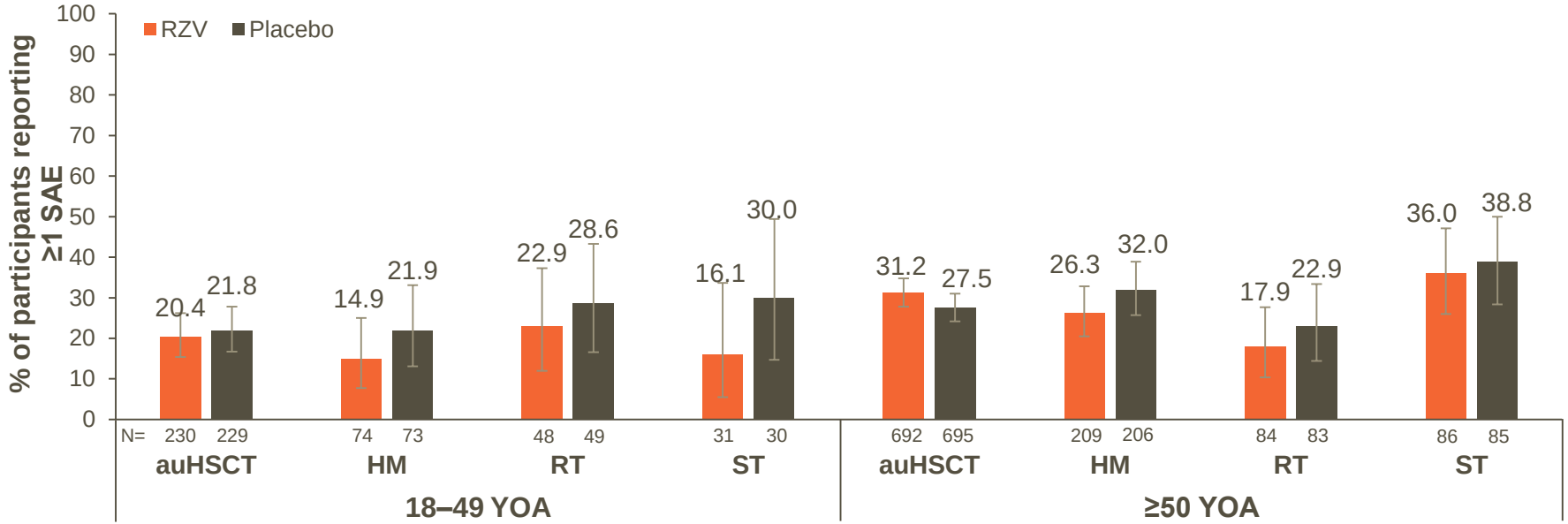
Serious Adverse Events (SAEs)

Percentage of participants reporting ≥1 SAE from dose 1 until 1-year post-last dose per study – TVC



The percentage of adults with ≥1 SAE, causally related SAEs, fatal SAEs and pIMDs was similar between RZV and placebo and between age groups

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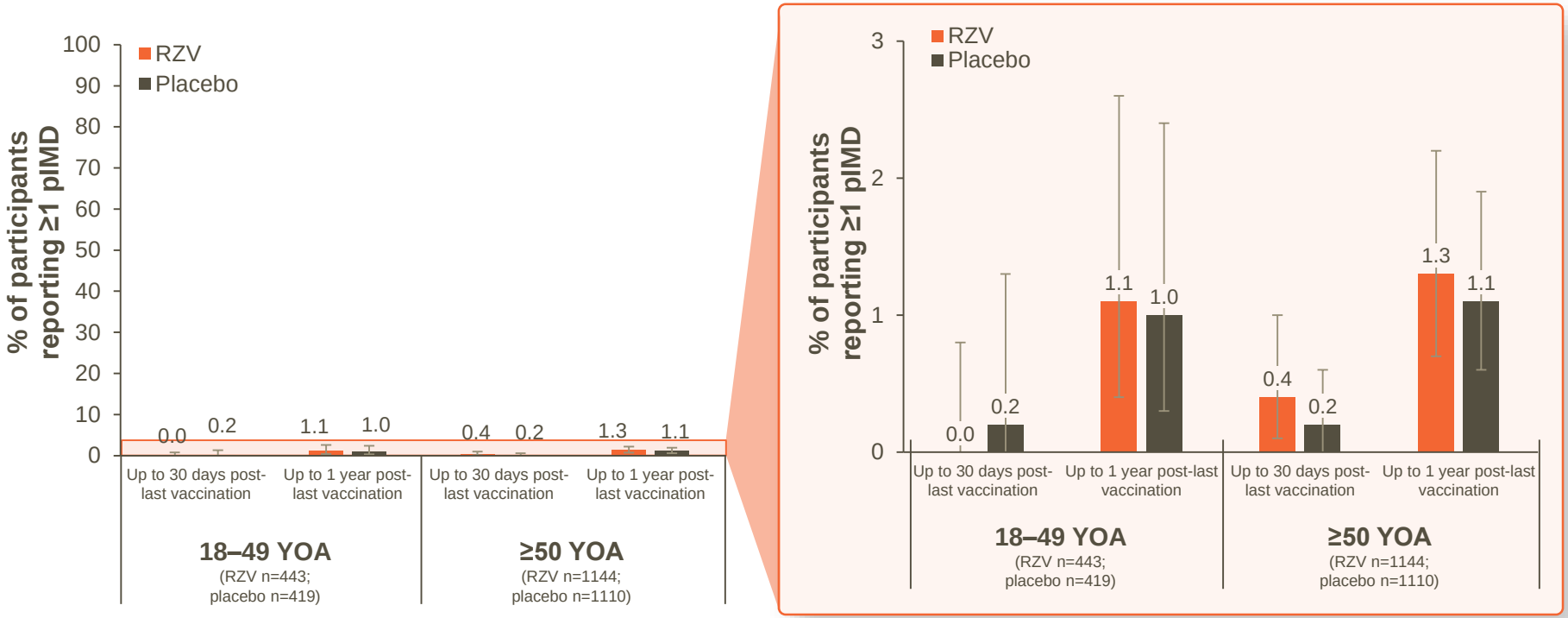
Potential immune mediated diseases (pIMDs)

Percentage of participants reporting ≥1 pIMD during selected study periods – TVC (pooled)



pIMD, potential immune mediated disease; TVC, total vaccinated cohort; YOA, years of age.
Data on file, 2021N477632.

Safety: Underlying Disease-related Events

auHSCT[1] HM[2]

- Proportion of patients with disease progressions or disease relapse were balanced between RZV and placebo groups.

RT[3]

- 4 biopsy-confirmed allograft rejections in the RZV group.
- 7 biopsy-confirmed allograft rejections in the placebo group.
- No impact on renal-allograft function based on serum creatinine levels.

Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.**
auHSCT, autologous hematopoietic stem cell transplant; HM, hematologic malignancies, RT, renal transplant; RZV, recombinant zoster vaccine.
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Vaccine Efficacy in Immunocompromised Patients

Pivotal Vaccine Efficacy: auHSCT
Post-hoc Vaccine Efficacy: HM

auHSCT, autologous hematopoietic stem cell transplant; HM, hematologic malignancies

1. Bastidas, et al. *JAMA*. 2019;322(2):123 133.
2. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988 1000.

Vaccine Efficacy in IC Patients

First or only episode of HZ – mTVC

	RZV			Placebo			VE (95% CI)	Median follow up
	N	n	HZ Incidence Rate (per 1000 person years)	N	n	HZ Incidence Rate (per 1000 person years)		
auHSCT[1,2]	**870**	**49**	**30**	**851**	**135**	**94.3**	**68.2 (55.6, 77.5)**	**21 months**
18-49	213	9	21.5	212	29	76	71.8 (38.7, 88.3)	
≥50	657	40	33	639	106	100.9	67.3 (52.6, 77.9)	
PHN	870	1	0.5	851	9	4.9	89.3 (22.5, 99.8)	
HM[3]*	**259**	**2**	**8.5**	**256**	**14**	**66.2**	**87.2 (44.3, 98.6)**	**11 months**

*Efficacy was evaluated in a post-hoc analysis.
Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.**
auHSCT, autologous hematopoietic stem cell transplant; CI, confidence interval; HM, hematologic malignancies; HZ, herpes zoster; IC, immunocompromised; mTVC, modified total vaccinated cohort; N, number of subjects included in each group; n, number of subjects having at least one confirmed HZ episode; VE, vaccine efficacy (Poisson method).
1. Bastidas et al. *JAMA*. 2019; 322(2):123-133. 2. Data on File, ZOSTER-002 Clinical study report. Available on https://www.gsk-studyregister.com/study/115523 3. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000.

Vaccine Immunogenicity

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3. Vink P, et al. *Cancer*. 2019;125(8):1301 1312.
4. Vink P, et al. *Clin Infect Dis*. 2020;70(2):181 190.
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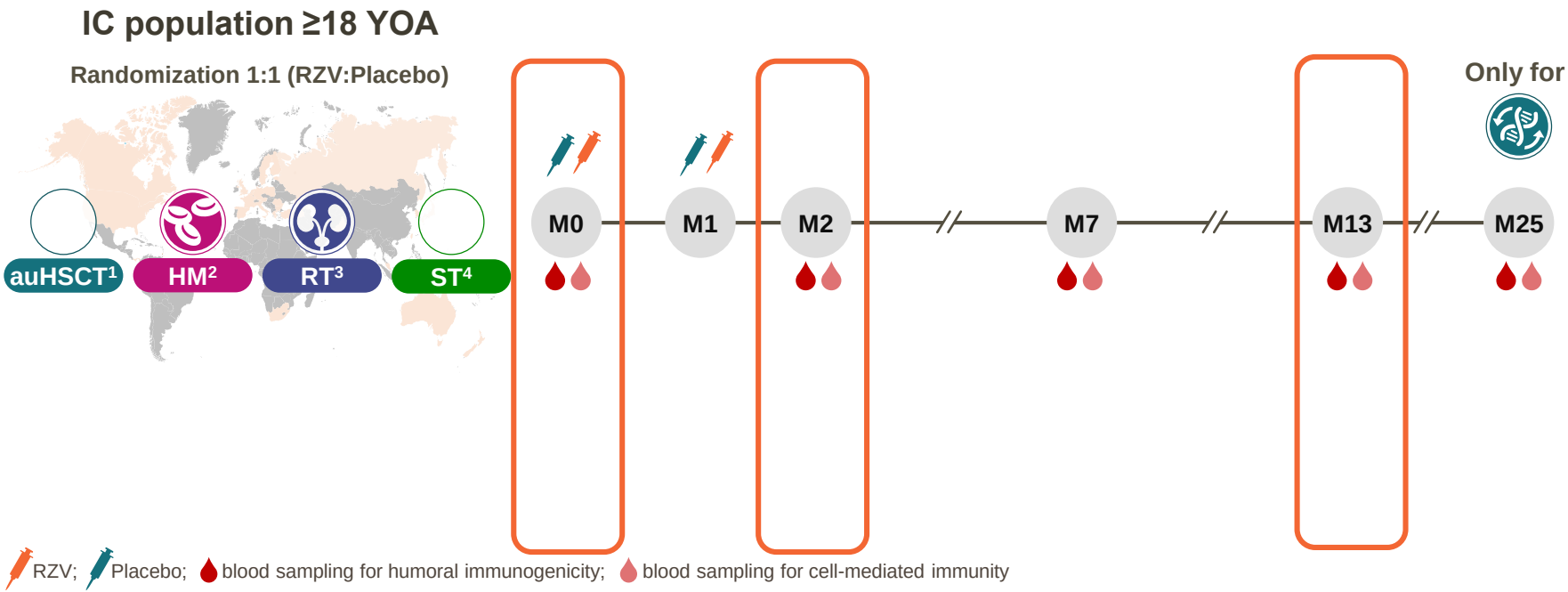
RZV Multicenter Studies in IC Populations Were Randomized, Observer-blinded, Placebo-controlled



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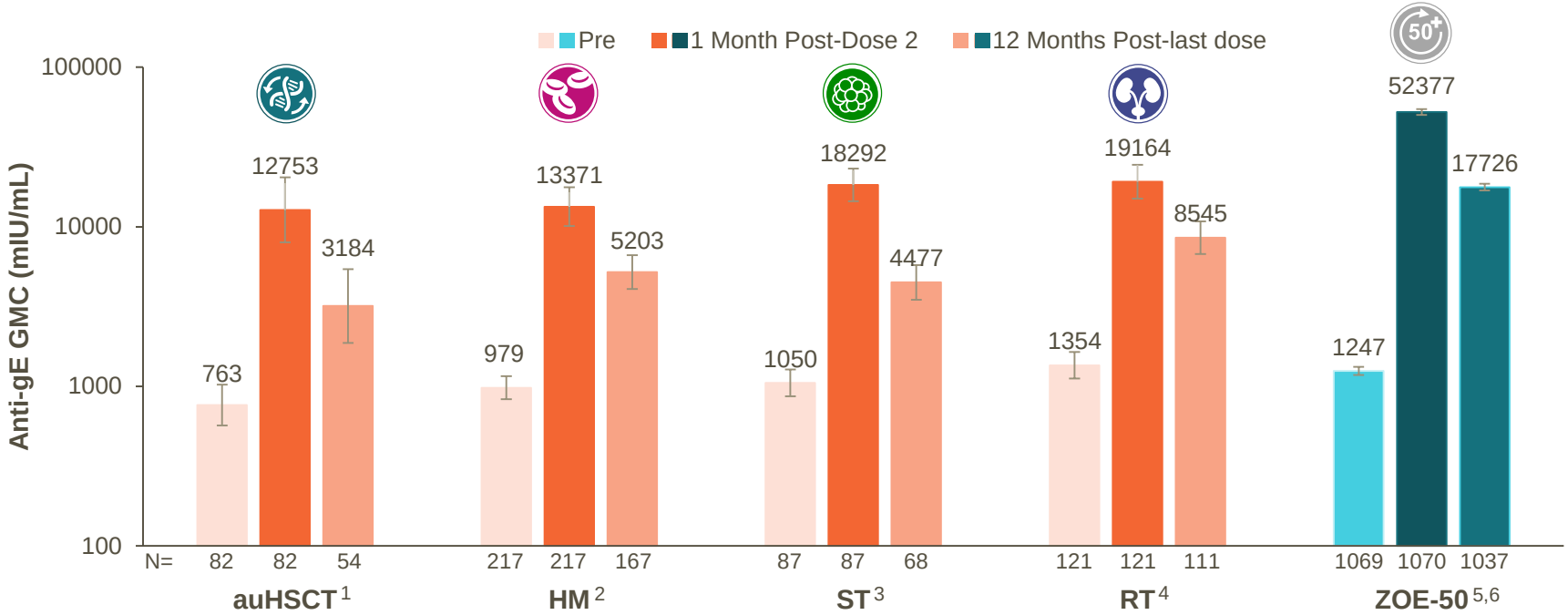
RZV Humoral Mediated Immunity

Anti-gE GMCs (ELISA) Pre-, 1 month post dose 2, and 12 months post last dose – ATP cohort for immunogenicity

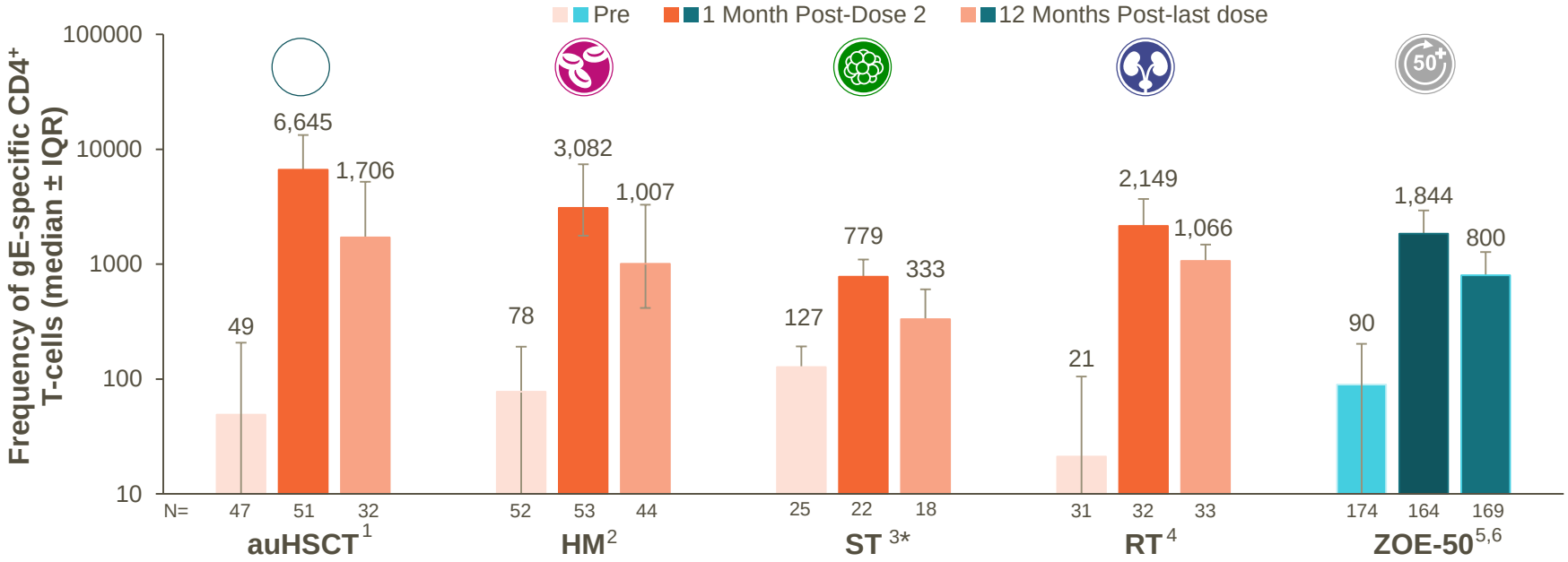


Error bars represent 95% CI. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.** auHSCT, autologous hematopoietic stem cell transplant; ATP, according to protocol; gE, glycoprotein E; GMC, geometric mean concentration; HM, hematologic malignancies; RT, renal transplant; RZV, recombinant zoster vaccine; ST, solid tumor; ZOE-50, Zoster Older adults Efficacy trial in ≥50 years of age.

1. Bastidas, et al. *JAMA*. 2019;322(2):123-133. 2. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000. 3. Vink P, et al. *Cancer*. 2019;125(8):1301-1312. 4. Vink P, et al. *Clin Infect Dis*. 2020;70(2):181-190. 5. Cunningham AL, et al. *J Infect Dis*. 2018;217(11):1750-1760. 6. Data on File, Study 110390 (ZOE-50) Clinical study report. Available on https://www.gsk-studyregister.com/study/110390.

RZV Cellular Mediated Immunity

Median Frequency for gE-specific CD4⁺ T-cells Pre-, 1 Month post dose 2, and 12 Months post last dose – ATP cohort for immunogenicity



Error bars represent 1st and 3rd IQR. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.**
*For ST study: on-chemo group (1st dose administered 8-30 days before chemotherapy and 2nd dose on the day of chemotherapy).
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Addressing the Unmet Need

RZV Clinical Development Program in IC Patients

auHSCT[1]

HM[2]

ST[3]

RT[4]

- Reactogenicity profile is expected based on clinical experience and nature of underlying conditions
- AEs, SAEs, pIMDs, relapses, disease progressions, and allograft rejections were balanced between the RZV and placebo groups
- Efficacy demonstrated in 2 populations: 68.2% (95% CI: 55.6-77.5) in auHSCT recipients and 87.2% (95% CI: 44.3-98.6) in HM* patients
- RZV is immunogenic even considering the impact of age, underlying disease, immunosuppressive treatment and immunization either before, during or after immunosuppressive treatments

RZV immunogenicity and safety data support a favorable benefit risk profile in IC adults ≥18 YOA, who are at an increased risk of HZ

*Efficacy was evaluated in a post-hoc analysis.
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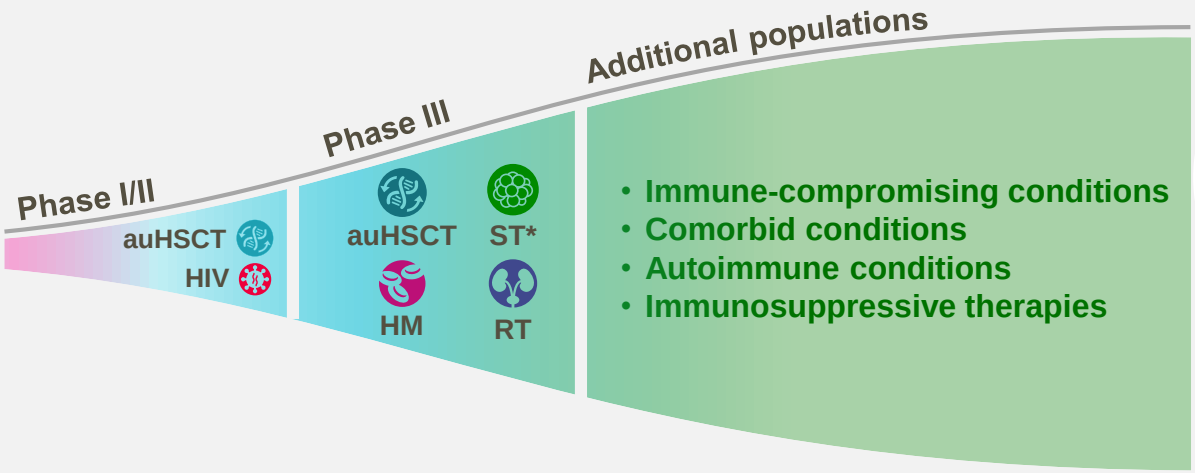

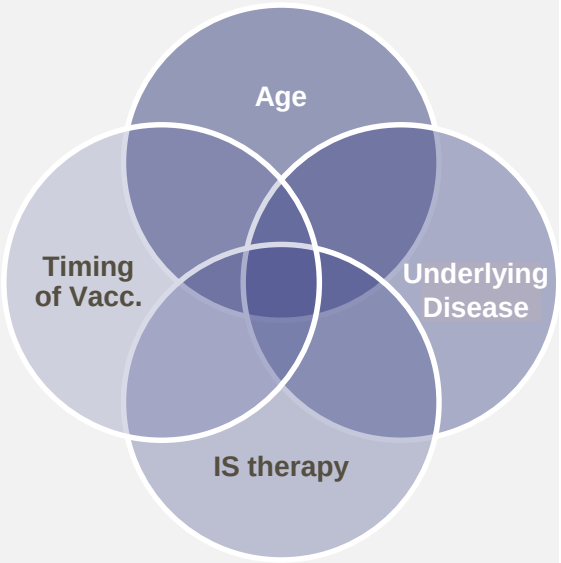

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Thank You