



Use of Recombinant Zoster Vaccine (RZV) in Immunocompromised Populations

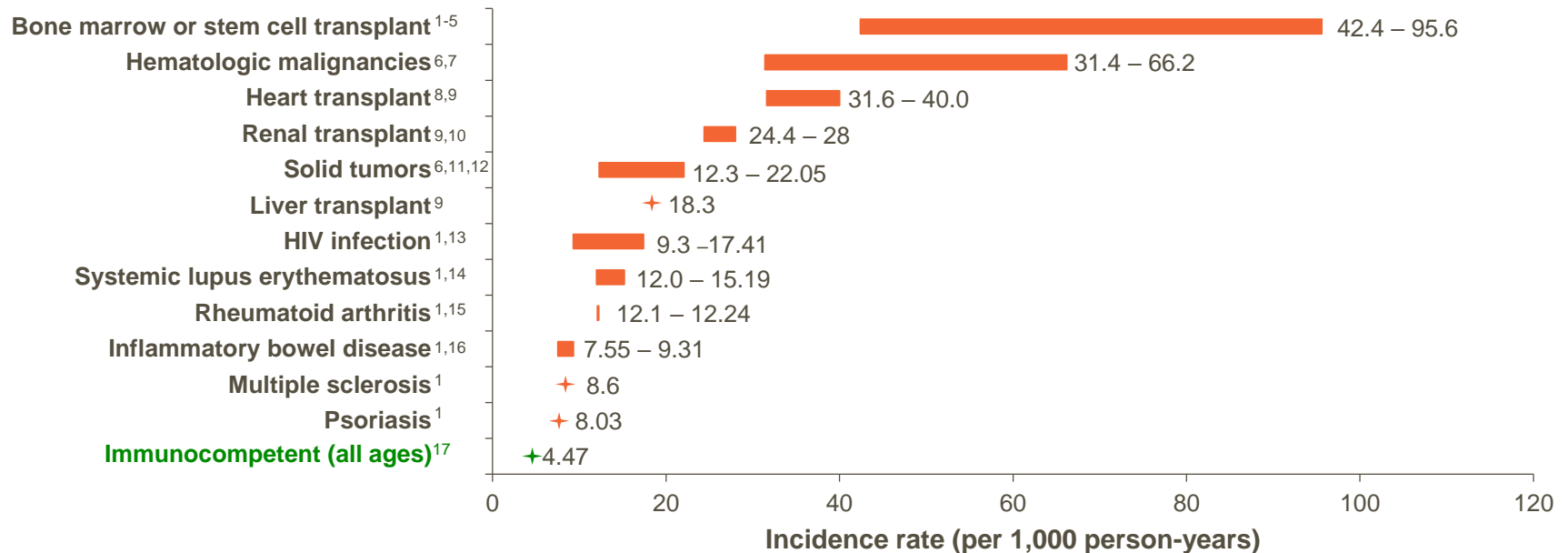
Robyn Widenmaier, Global Medical Portfolio Lead, Zoster Vaccine

ACIP Presentation
June 25, 2021

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



Incidence Rates of HZ in Adult Patients



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. Dagnev 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

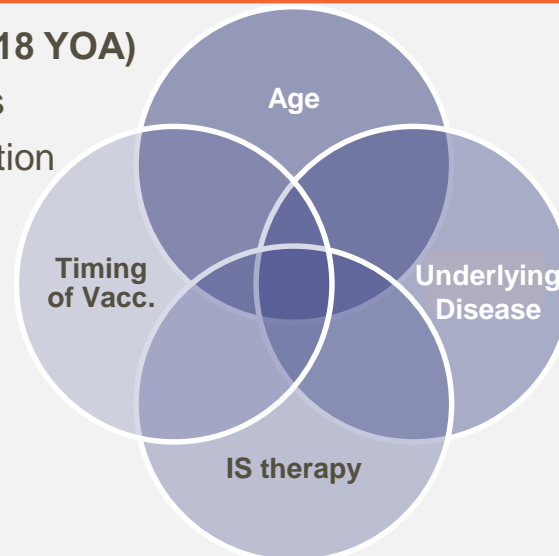
Addressing the Unmet Need



- RZV demonstrated >90% efficacy in **Immunocompetent Older Adults (≥50 YOA)**¹⁻²
- No safety concerns identified in clinical trials¹⁻²
- RZV was licensed by FDA on October 20, 2017³

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. Dagnev 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.

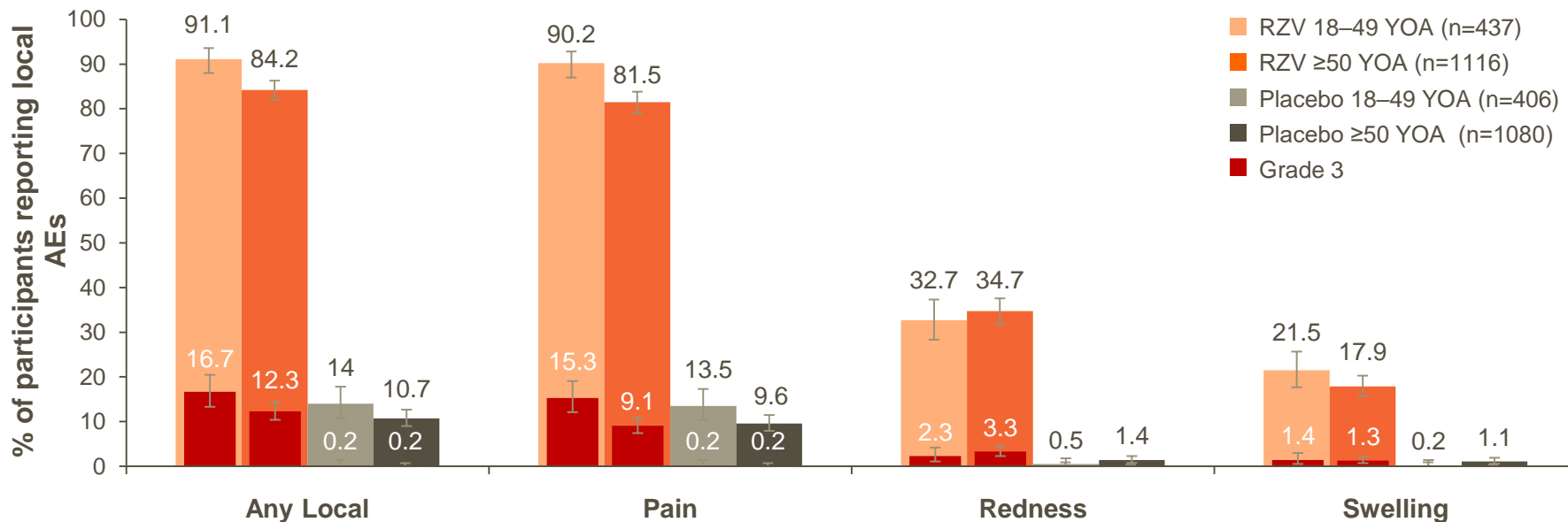


Pooled Reactogenicity in Immunocompromised Patients

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).

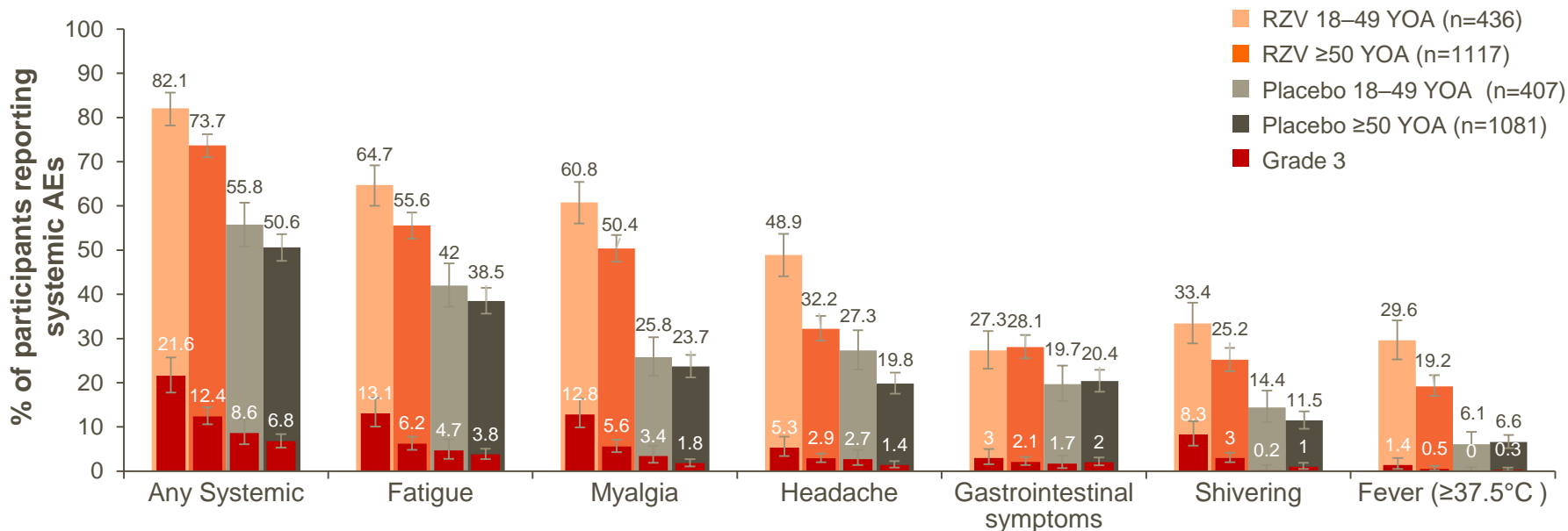
For the systemic AEs fatigue, headache (all, related), myalgia, shivering, and fever (all, related) were reported with higher incidences in the RZV 18-49 YOA group than in the RZV ≥50 YOA group. AE, adverse event; RZV, recombinant zoster vaccine; TVC, total vaccinated cohort; YOA, years of age.

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 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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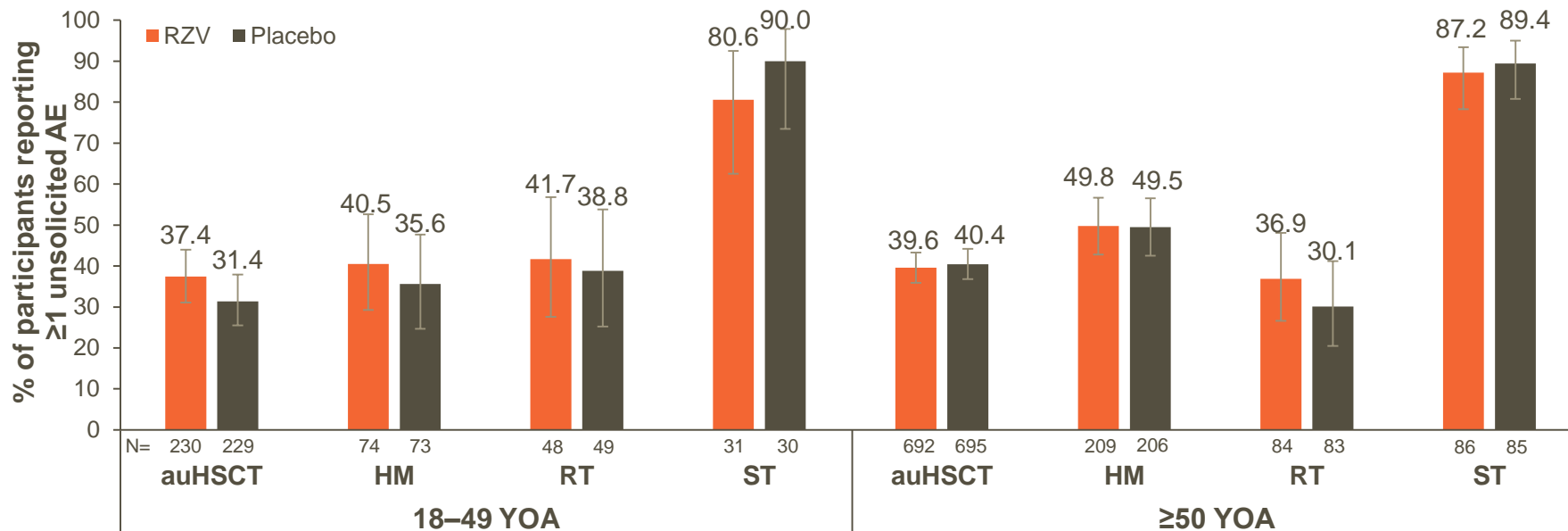
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October 21-25, 2020. <https://idweek.org>

Unsolicited Adverse Events (AEs)



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

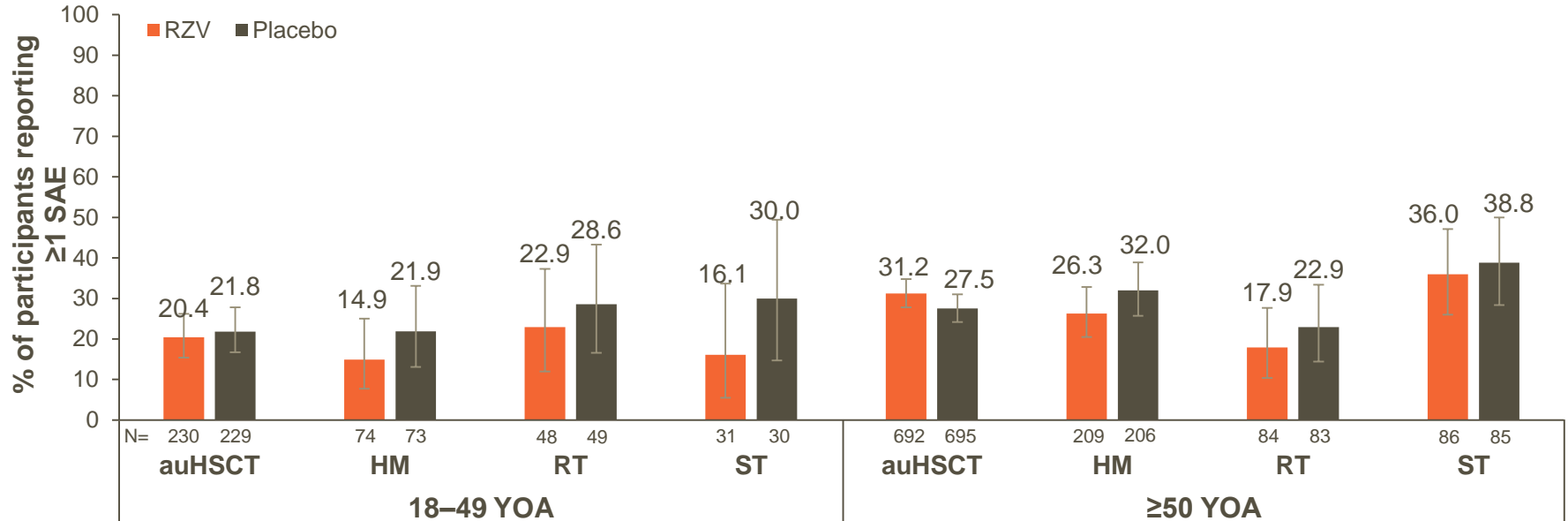


Across studies, the percentage of adults reporting ≥ 1 unsolicited AE was similar between RZV and placebo groups

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. 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>

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

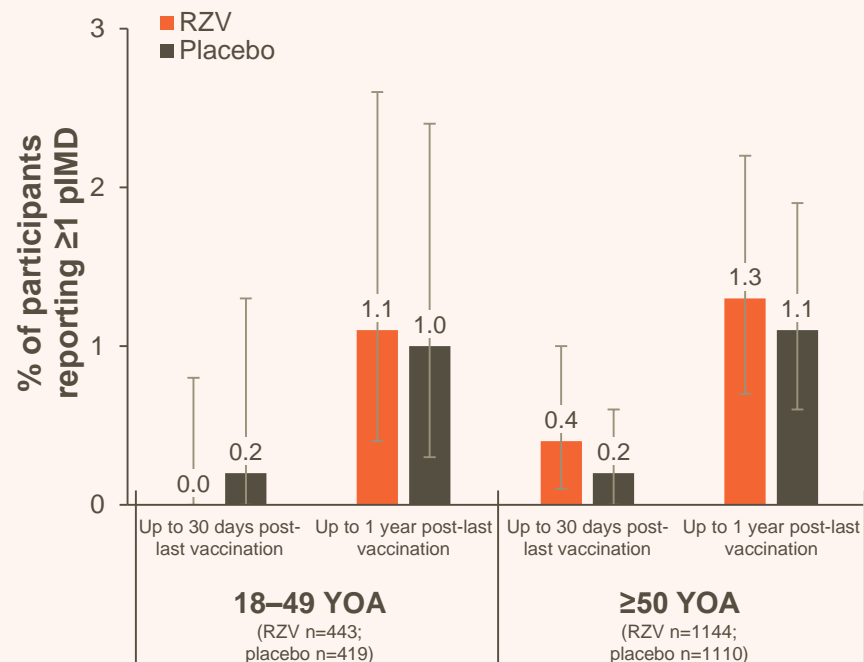
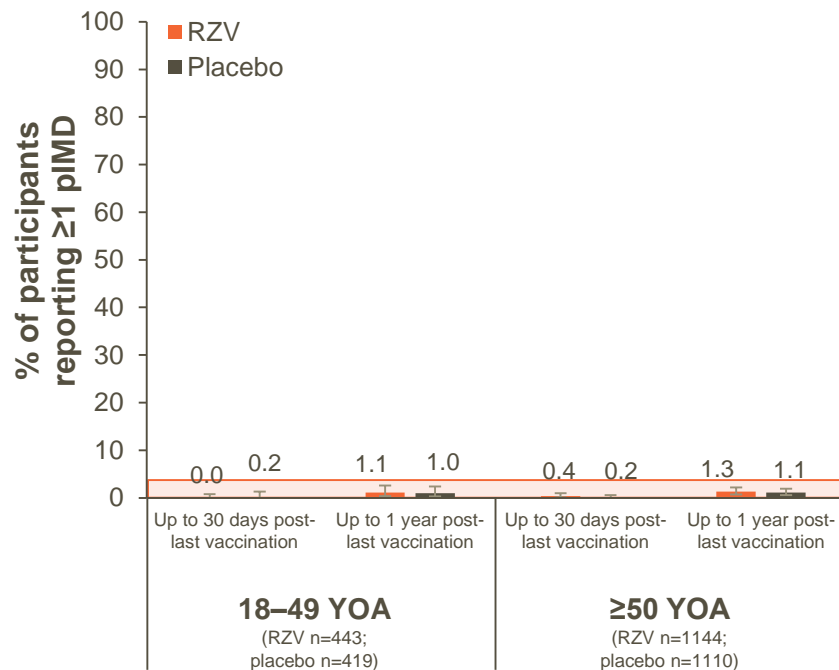
Error bars represent 95% CI. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.** auHSCT, autologous hematopoietic stem cell transplant; CI, confidence interval; HM, hematological malignancies; RT, renal transplant; RZV, recombinant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

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Potential immune mediated diseases (pIMDs)



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



Safety: Underlying Disease-related Events



auHSCT¹ HM²

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



RT³

- 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.

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>



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. Dagnev 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).

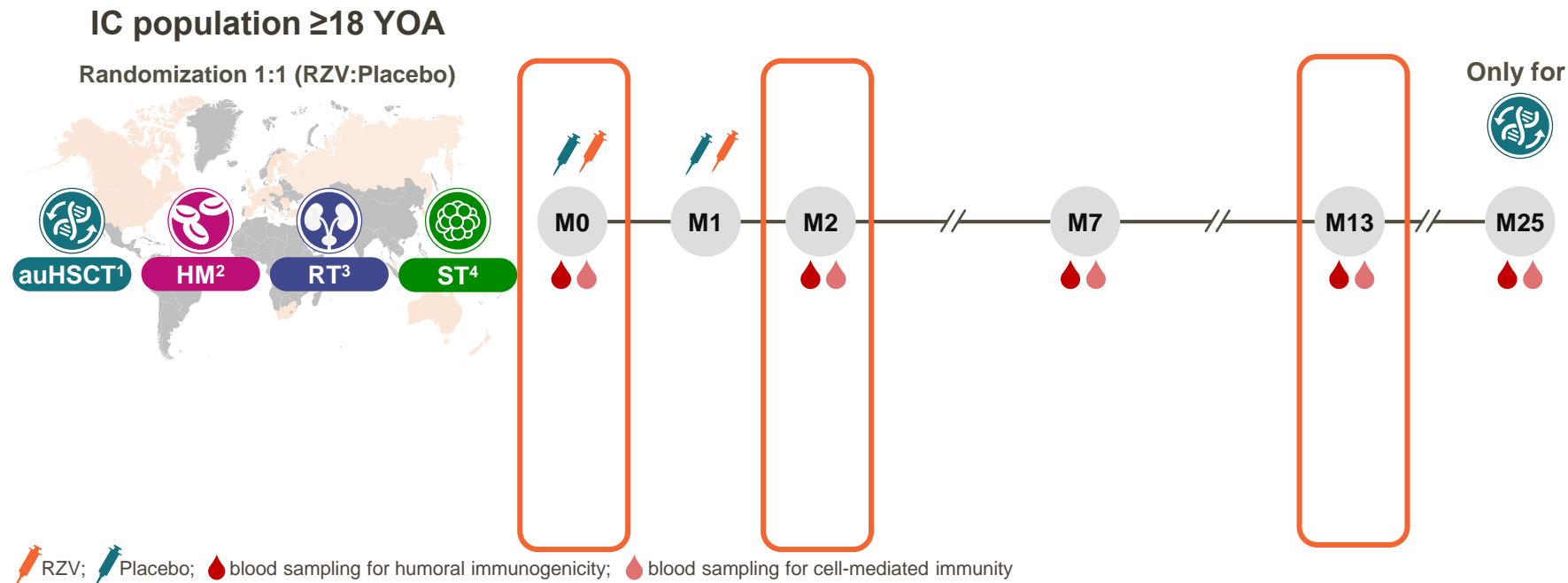
1. Bastidas et al. *JAMA*. 2019; 322(2):123-133. 2. Data on File, ZOSTER-002 Clinical study report. Available on <https://www.gsk-studyregister.com/study/115523> 3. Dagnew AF, et al. *Lancet Infect Dis*. 2019;19(9):988-1000.



Vaccine Immunogenicity

1. Bastidas, et al. *JAMA*. 2019;322(2):123-133.
2. Dagnev 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

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

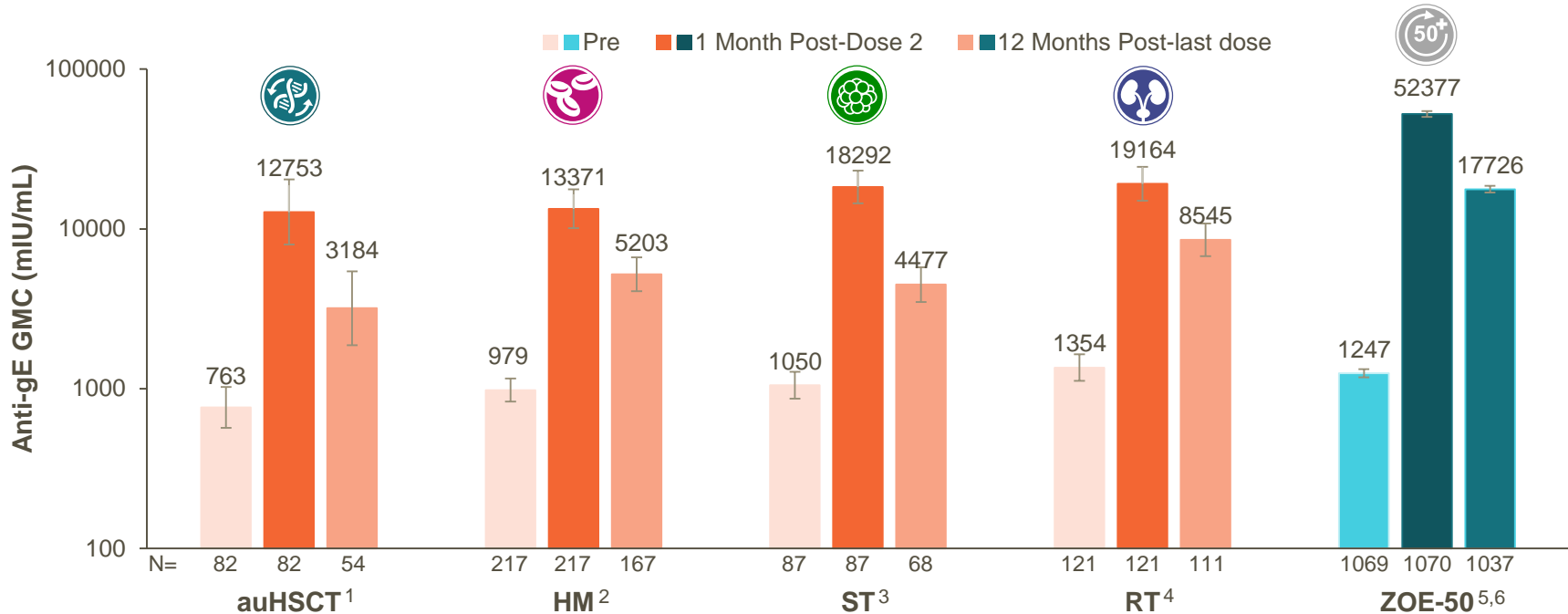


AE, adverse event; auHSCT, autologous hematopoietic stem cell transplant; HM, hematologic malignancies, HZ, herpes zoster; IC, immunocompromised; M, month; pIMD, potential immune-mediated disease; RT, renal transplant; RZV, recombinant zoster vaccine; SAE, serious adverse event; ST, solid tumor; YOA,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

RZV Humoral Mediated Immunity

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



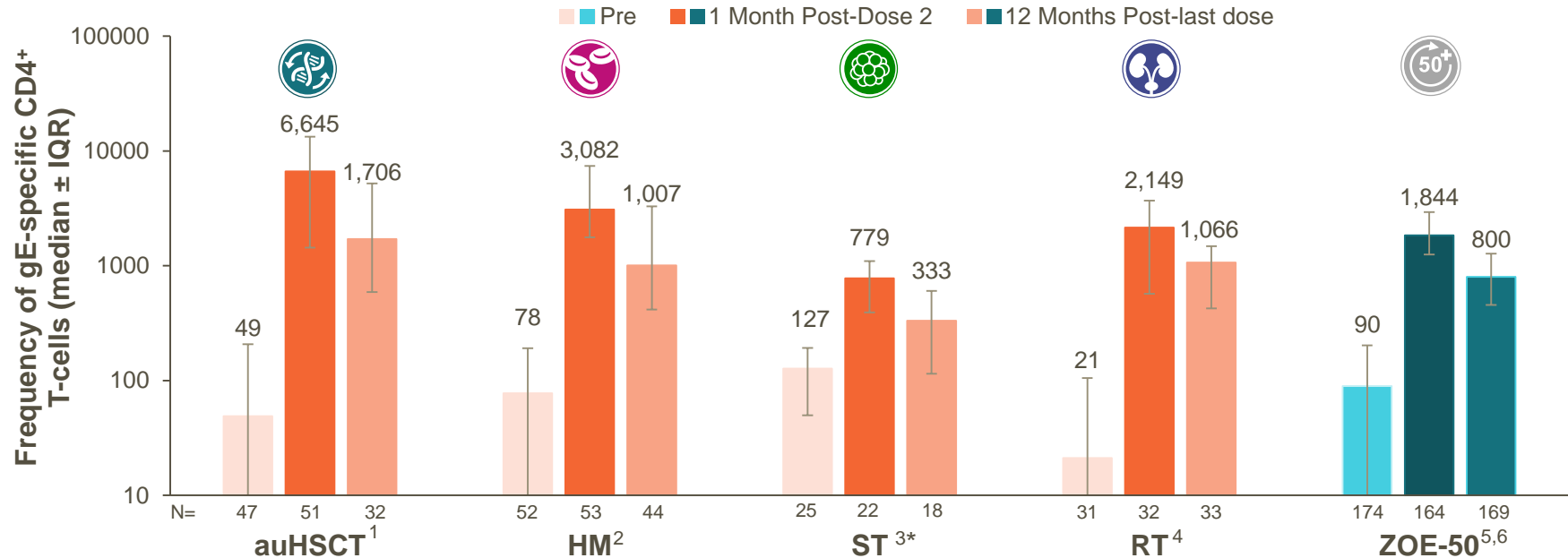
Error bars represent 95% CI. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.** auHSCT, autologous hematopoietic stem cell transplant; ATP, according to protocol; gE, glycoprotein E; GMC, geometric mean concentration; HM, 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. Dagnev 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).

auHSC¹, autologous hematopoietic stem cell transplant; ATP, according to protocol; gE, glycoprotein E; IQR, interquartile range; 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.

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Available on <https://www.gsk-studyregister.com/study/110390>

Addressing the Unmet Need



RZV Clinical Development Program in IC Patients



auHSCT¹



HM²



ST³



RT⁴

- 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.

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; HM, hematologic malignancies; HZ< herpes zoster; IC, immunocompromised; pIMD, potential immune-mediated disease; RT, renal transplant; RZV, recombinant zoster vaccine; SAE, serious adverse event; ST, solid tumor; YOA, years of age.

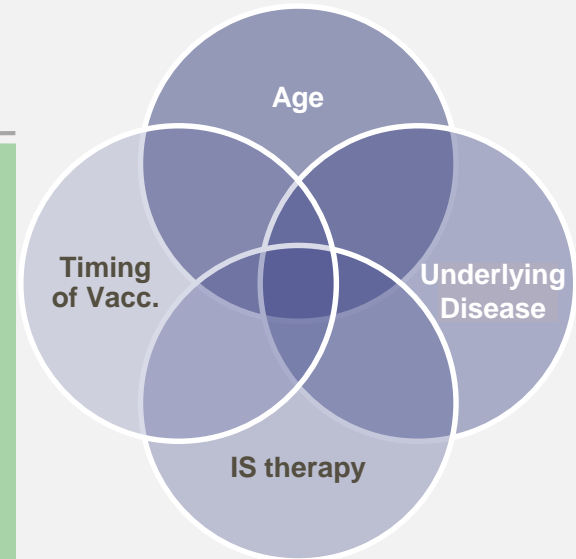
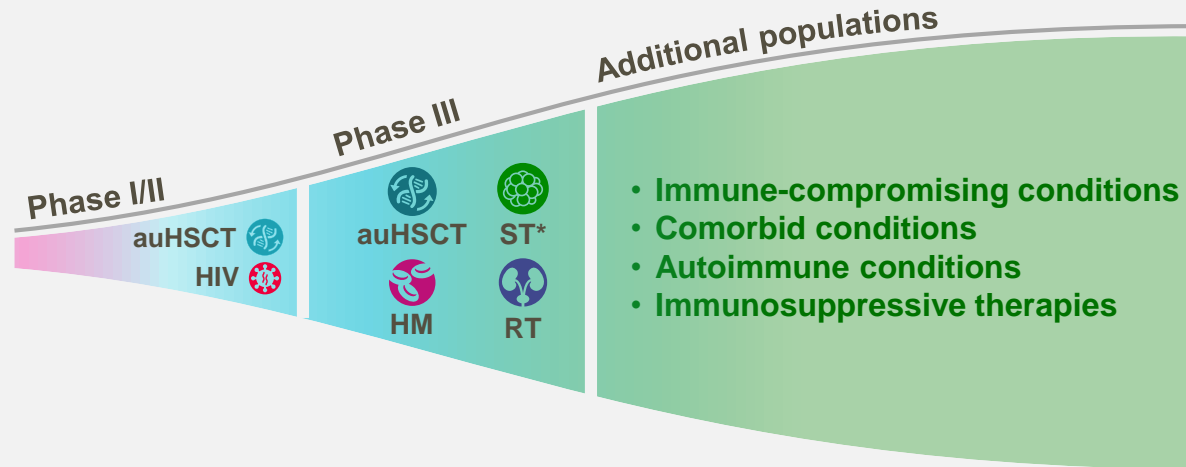
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Addressing the Unmet Need



Addressing the Unmet Need in IC Adults (≥ 18 YOA)¹⁻⁶

- IC populations are very heterogeneous, both across and within groups
- Not feasible to define every possible IC condition/medication combination



*Phase II/III study

IC, immunocompromised; IS, immunosuppressive; RZV, recombinant zoster vaccine; Vacc, vaccination; YOA, 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. Berkowitz EM, et al. *J Infect Dis*. 2015;211(8):1279-1287. 6. Stadtmauer EA, et al. *Blood*. 2014;124(19):2921-2929.



Thank You