Immunogenicity and Safety of Shingrix in Adults Previously Vaccinated With a Live-Attenuated Herpes Zoster Vaccine (Zoster-048 Study)

ACIP – June 21, 2017

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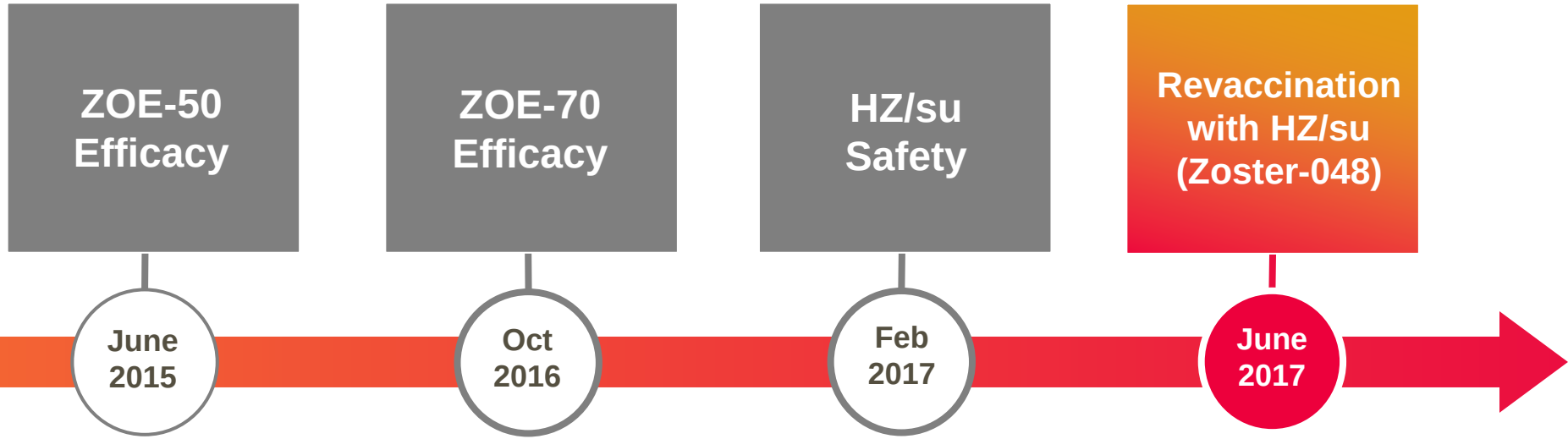
Today's Presentation



HZ/su, herpes zoster subunit vaccine; ZOE, zoster efficacy trials.

Agenda

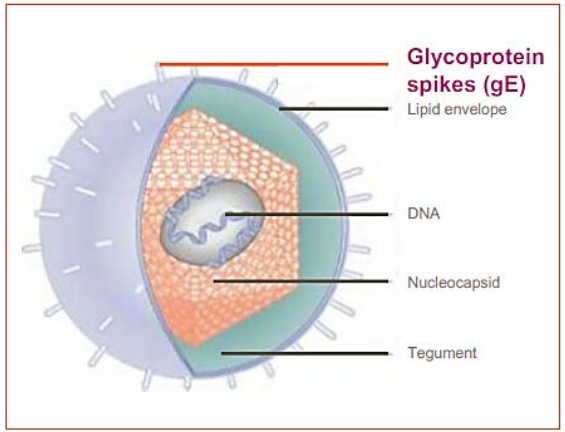
1. Context and Rationale
2. Objectives and Study Design (Zoster-048)
3. Results (Zoster-048)
4. Summary

HZ/su Vaccine Composition

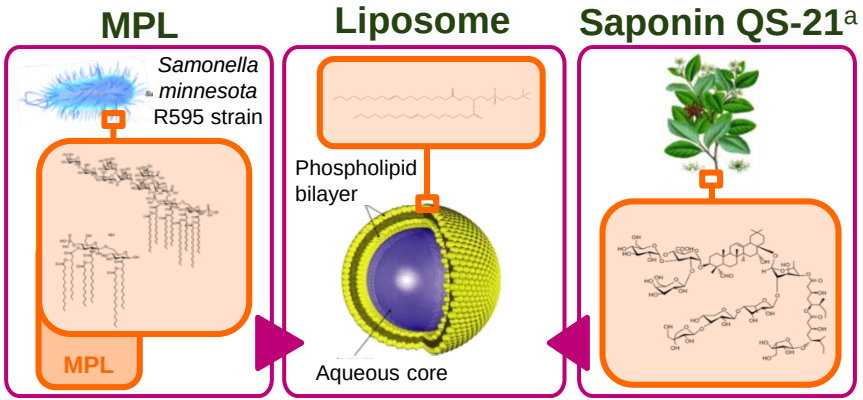
Context and rationale

Vaccine
Non-live

Antigen
Glycoprotein E (gE) - 50 µg



Adjuvant System
$AS01_B$ (MPL and QS-21[a]) - 50 µg each



[a]QS-21 (Quillaja saponaria Molina, fraction 21; licensed by GSK from Antigenics LLC, a wholly owned subsidiary of Agenus Inc, a Delaware, USA corporation). HZ/su, Herpes zoster subunit vaccine; MPL, monophosphoryl lipid A.

Zoster-048

Context and rationale

- Live-attenuated zoster vaccine (ZVL) has been licensed since 2006 and is recommended by ACIP for the prevention of HZ in immunocompetent adults ≥60 years of age
- Approximately 31% of US adults ≥60 years of age have been vaccinated for HZ[1]
- Vaccination with ZVL as the current standard offers protection against HZ (VE=51% in adults ≥60 years of age)[2] and this protection wanes over time[3]
- The Zoster-048 study was designed to generate immunogenicity and safety data in persons who received ZVL at least 5 years prior, to help inform immunization policy decision-making

HZ, herpes zoster; VE, vaccine efficacy; ZVL, live-attenuated zoster vaccine (Zostavax®).

1. CDC. Vaccination coverage among adults in the United States, NHIS, 2015. https://cdc.gov/vaccines. Accessed June 7, 2017.
2. 2016 Zostavax PI. **3.** Morrison VA, et al. *Clin Infect Dis*. 2015;60:900-999.

Objectives and Study Design

Zoster-048

Brief Overview of Zoster-048

Prospective, group-matched, non-randomized trial

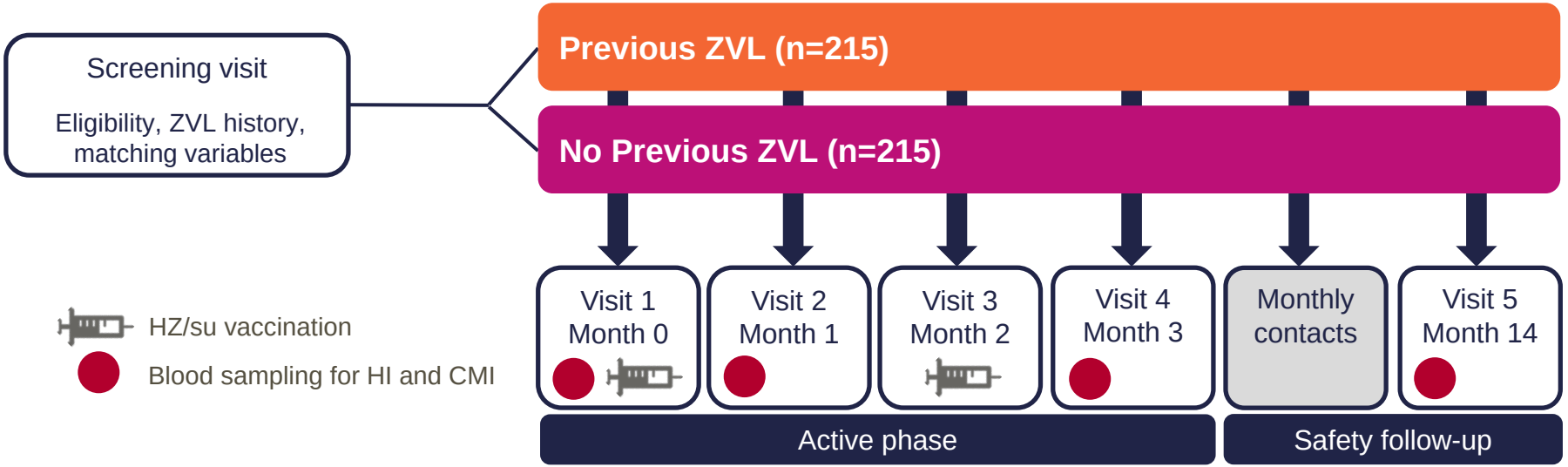
	Previous ZVL	No Previous ZVL
Experimental design	Phase III, prospective, group-matched, non-randomized, open label, multicenter study in US	
HZ vaccination history	ZVL ≥5 years prior	No previous HZ vaccine
Age range	≥65 years of age	
Co-primary objectives	• **Compare anti-gE antibody concentrations 1 month post-dose 2 (non-inferiority)[a]** • **Safety and reactogenicity up to 1 month post dose 2**	
Secondary objectives	• Humoral immune response and cell-mediated immunity at baseline, 1 month post-dose 1, and 1 and 12 months post-dose 2 • Safety up to 12 months post-dose 2 (ongoing)	

[a]Non-inferiority: upper limit of two-sided 95% CI of adjusted geometric mean concentration ratio (No Previous ZVL over Previous ZVL 1 month post-dose 2) is below 1.5 for anti-gE antibodies.

Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).
CI, confidence internal; gE, glycoprotein E; HZ, herpes zoster.

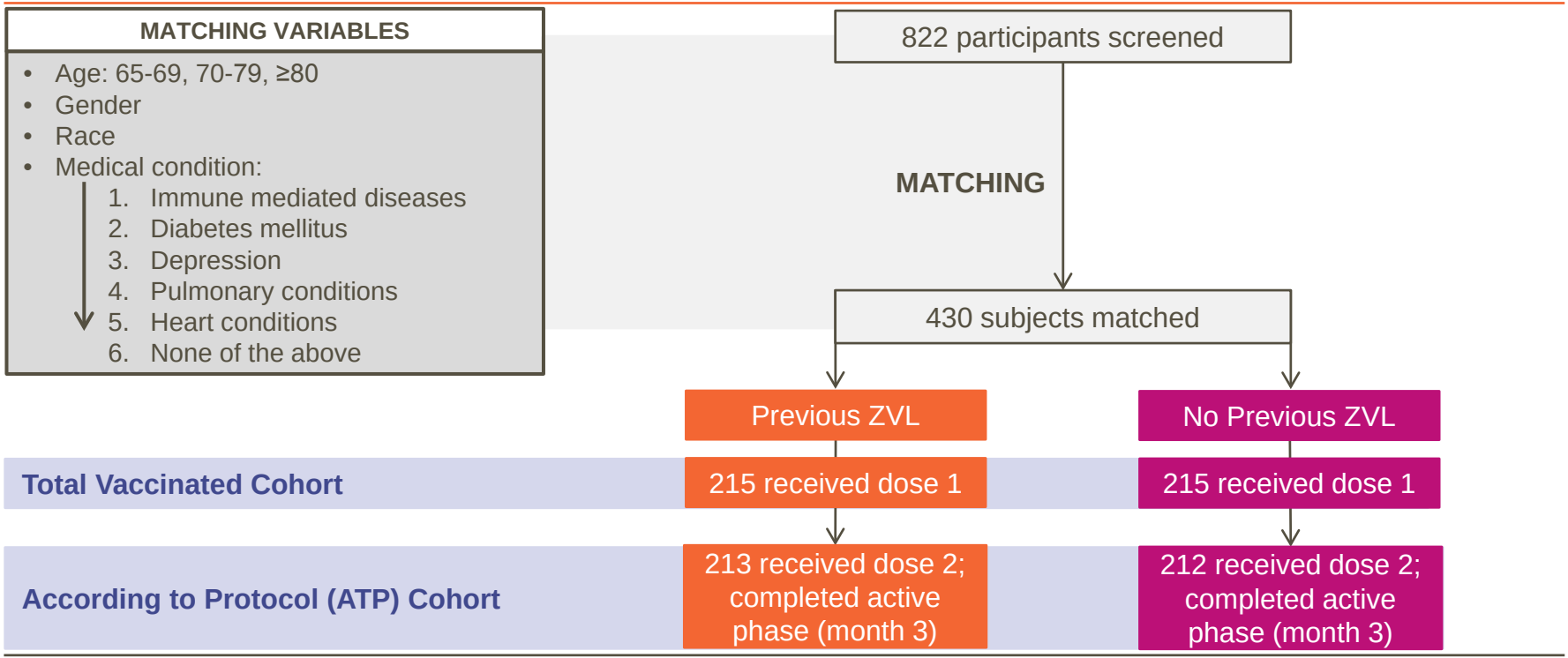
Zoster-048 Study Design

Prospective, group-matched, non-randomized trial



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).
HZ/su, Herpes zoster subunit vaccine; HI, humoral immune response; CMI, cell-mediated immunity.

Zoster-048 Participant Enrollment



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).

Results

Zoster-048; Active phase month 3 data

Summary of Demographic Characteristics

Total vaccinated cohort

Characteristics	Parameters or Categories	Previous ZVL n=215		No Previous ZVL n=215		Total N=430	
		Value or n	%	Value or n	%	Value or n	%
Age (years) at vaccination dose 1	Mean	71.1	-	70.8	-	**70.9**	-
	SD	4.5	-	4.6	-	4.6	-
	Median	70.0	-	70.0	-	70.0	-
	Minimum	65	-	65	-	65	-
	Maximum	87	-	85	-	87	-
Gender	Female	109	50.7	111	51.6	220	**51.2**
	Male	106	49.3	104	48.4	210	**48.8**
Geographic Ancestry	White—Caucasian / European Heritage	215	100	215	100	430	**100**
	Other	0	0.0	0	0.0	0	0.0
Time (years) since previous ZVL vaccination	Mean	**6.7**	-	-	-	-	-
	SD	1.11	-	-	-	-	-

Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).
SD, standard deviation.

Primary Endpoint Met

Non-inferiority of Previous ZVL to No Previous ZVL demonstrated for humoral immune response to HZ/su

Previous ZVL				No Previous ZVL				Adjusted GMC ratio (No Previous ZVL/ Previous ZVL)		
		95% CI				95% CI			95% CI	
n	Adjusted GMC	LL	UL	n	Adjusted GMC	LL	UL	Value	LL	UL
204	48589.4	42649.4	55356.6	204	50522.9	44347.4	57558.4	1.04	0.92	1.17

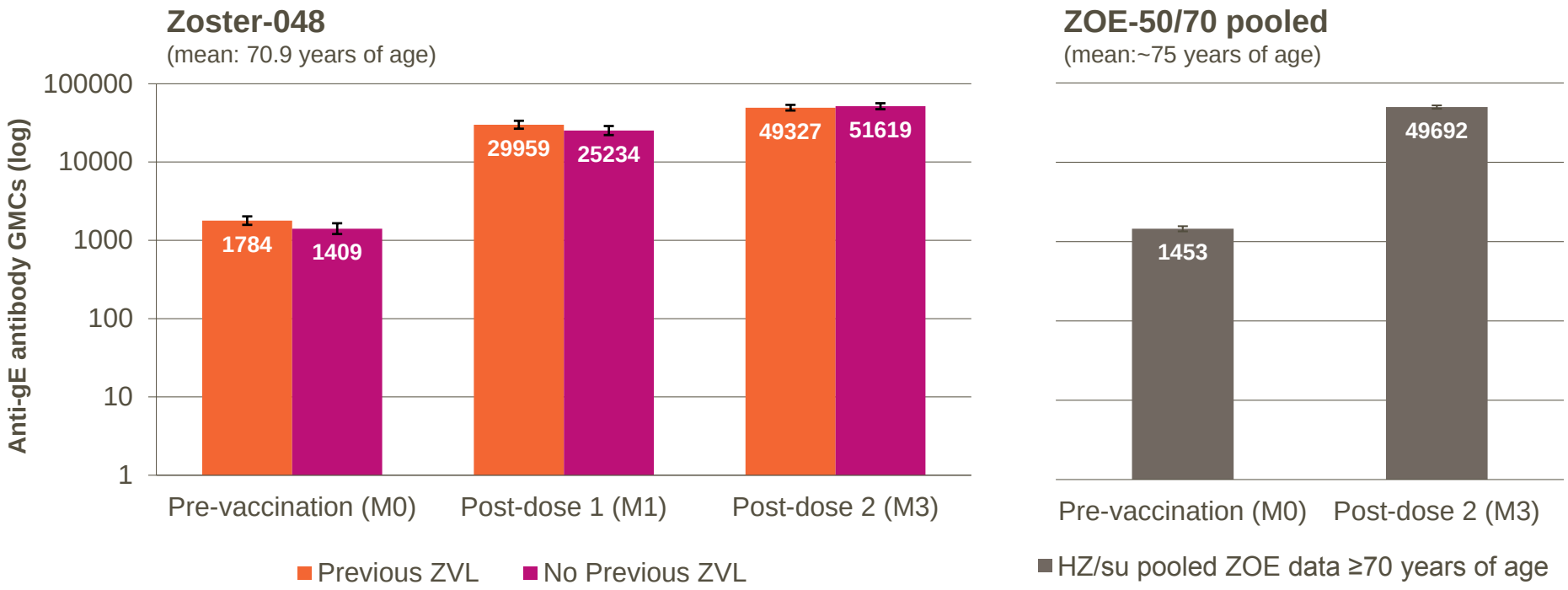
Adjusted ratios of No Previous ZVL over Previous ZVL anti-gE antibody ELISA GMCs at one month post-dose 2 (ATP cohort for immunogenicity)

UL of 95% CI <1.5
Non inferiority is reached

Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). ATP, according-to-protocol; CI, confidence interval; ELISA, enzyme-linked immunosorbent assay; gE, glycoprotein E; adjusted GMC, geometric mean antibody concentration adjusted for group-matching; HZ/su, herpes zoster subunit vaccine; LL, lower limit; UL, upper limit.

Month 3 Humoral Immune Responses Similar Between Groups and Consistent With ZOE Trials

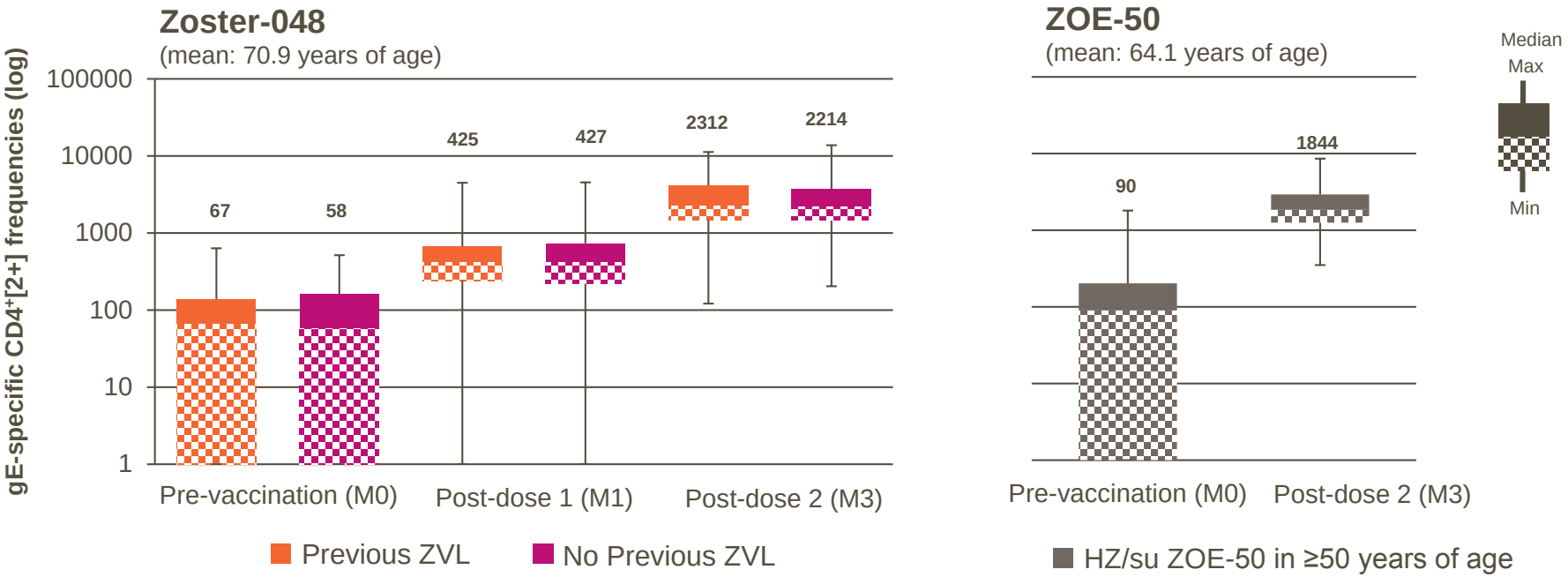
Geometric mean concentrations of anti-gE antibody



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). gE, glycoprotein E; GMC, geometric mean concentration; M, month; ZOE-50/70, zoster efficacy trials.

Month 3 Cellular Immune Responses Similar Between Groups and Consistent With ZOE-50 Trial

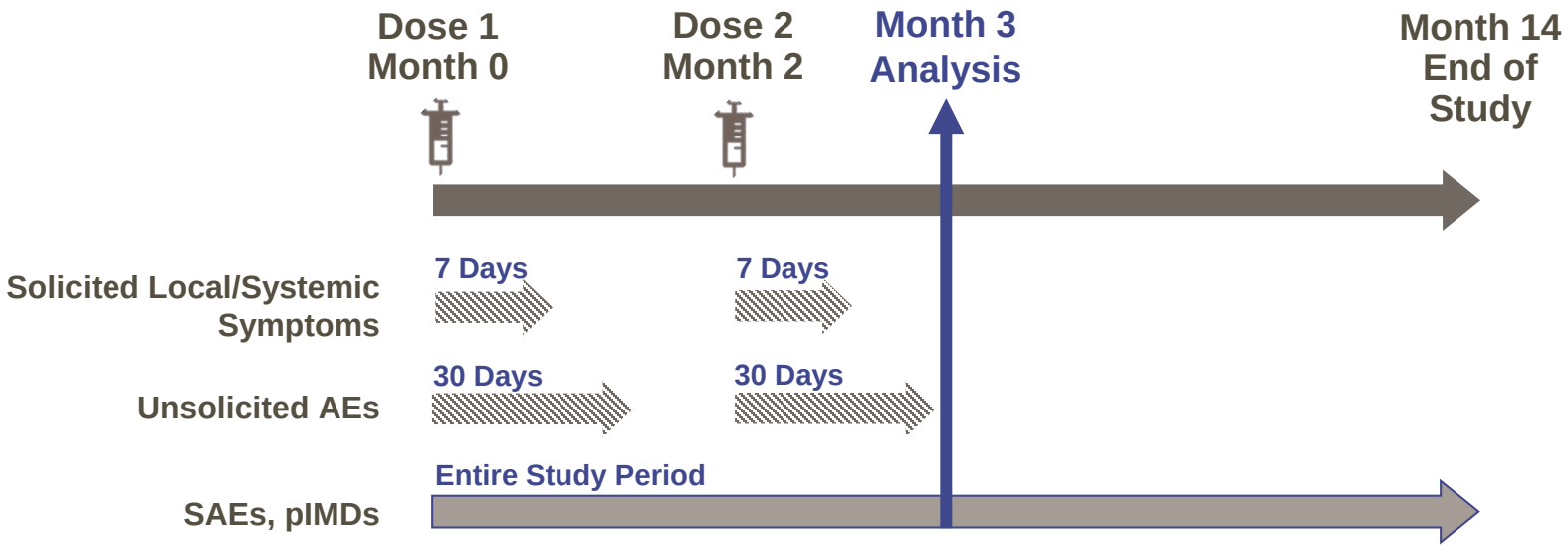
gE-specific CD4⁺[2+] frequencies



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). CD4⁺[2+], CD4+ T-cells secreting at least two activation markers (IFN-γ, IL-2, TNF-α, CD40L);
gE, glycoprotein E; M, month; Q1, Quartile 1=25th percentile; Q3, Quartile 3=75th percentile; ZOE-50, zoster efficacy trial ≥50 years of age.

Overview of Safety Reporting

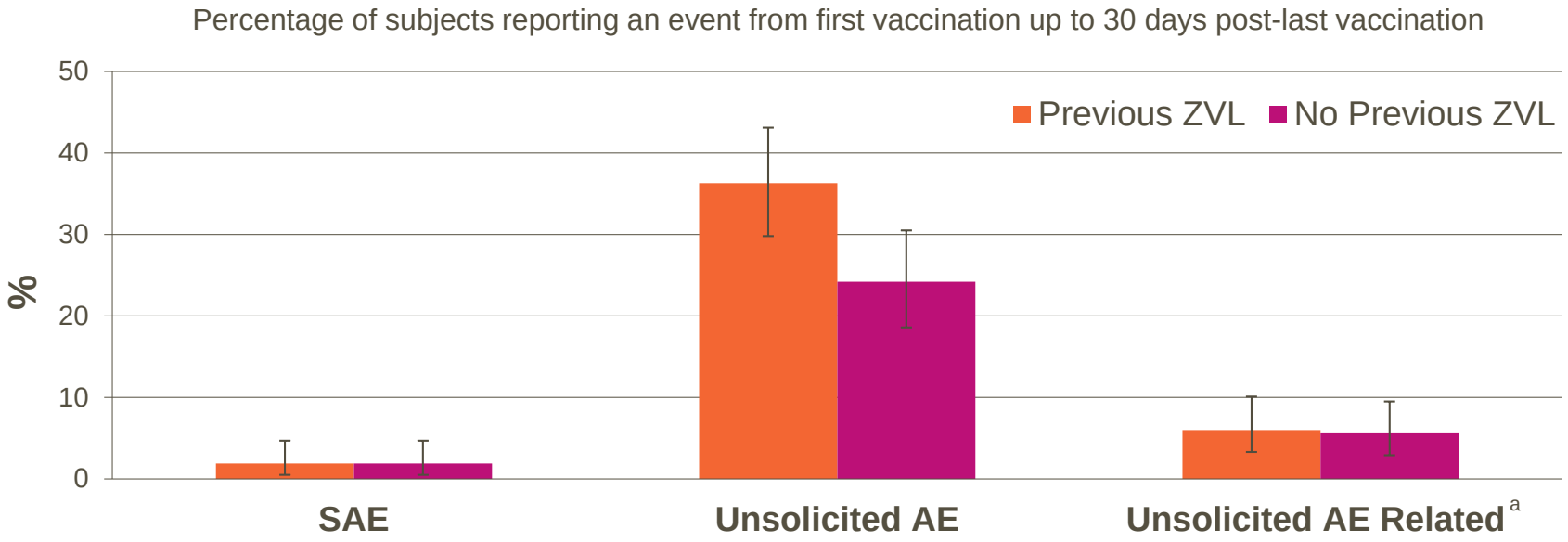
Zoster-048 study ongoing; 3-month analysis



AE, adverse event; pIMD, potential Immune-Mediated Disease; SAE, serious adverse event.

Safety Reporting up to 30 Days Post-Last Vaccination

Total vaccinated cohort

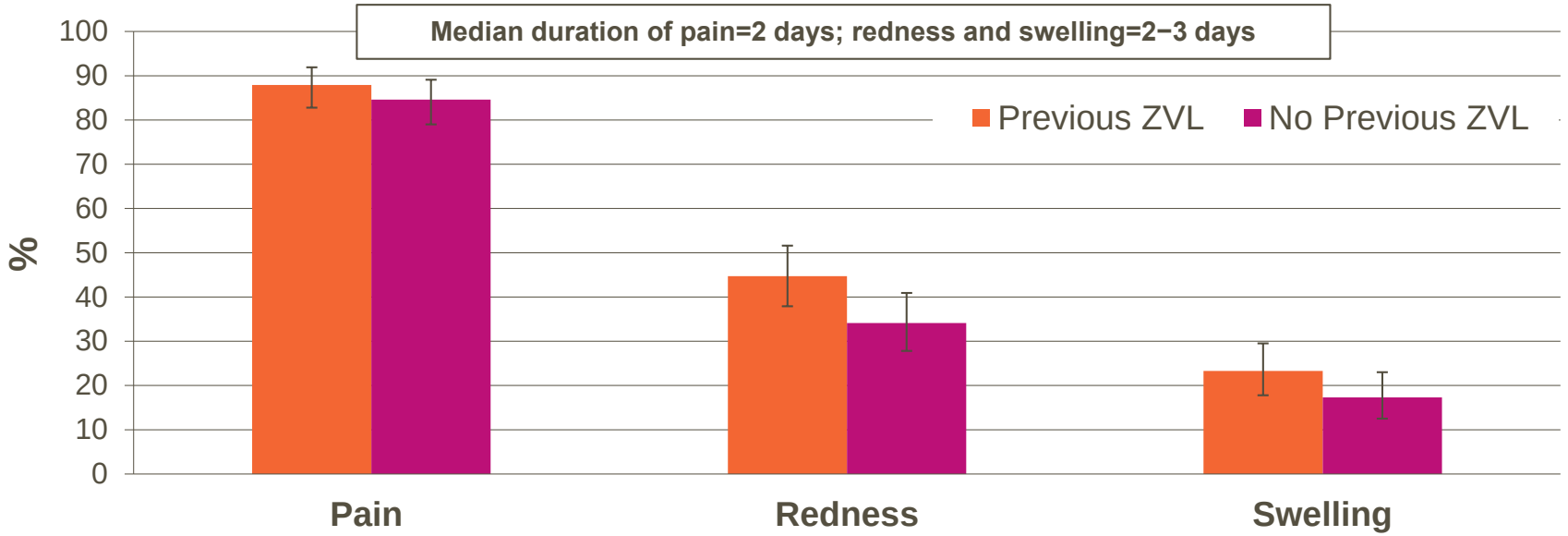


No pIMDs or related SAEs were reported from first vaccination up to 30 days post last vaccination

[a]According to the investigator AE is considered as potentially related to HZ/su vaccination.
Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). AE, adverse event; HZ/su, herpes zoster subunit vaccine; pIMD, potential Immune-Mediated disease; SAE, serious adverse event.

Solicited Local Symptoms Within 7 Days Post-Vaccination

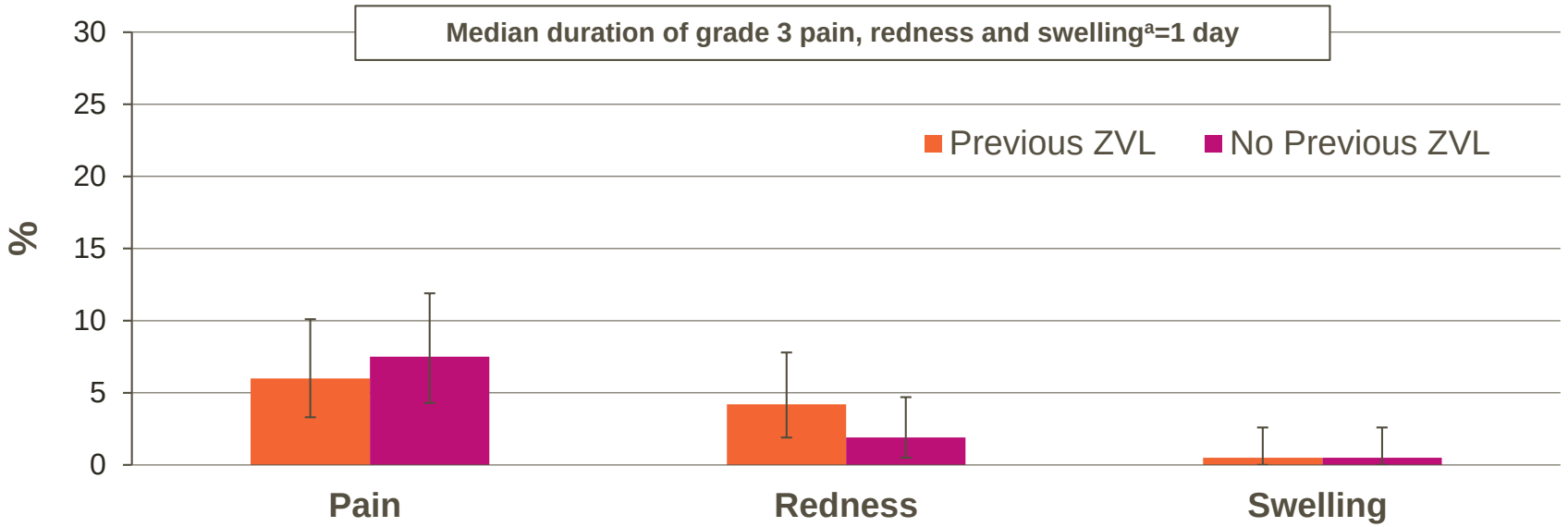
Any grade *overall by subject in total vaccinated cohort*



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).

Solicited Local Symptoms Within 7 Days Post-Vaccination

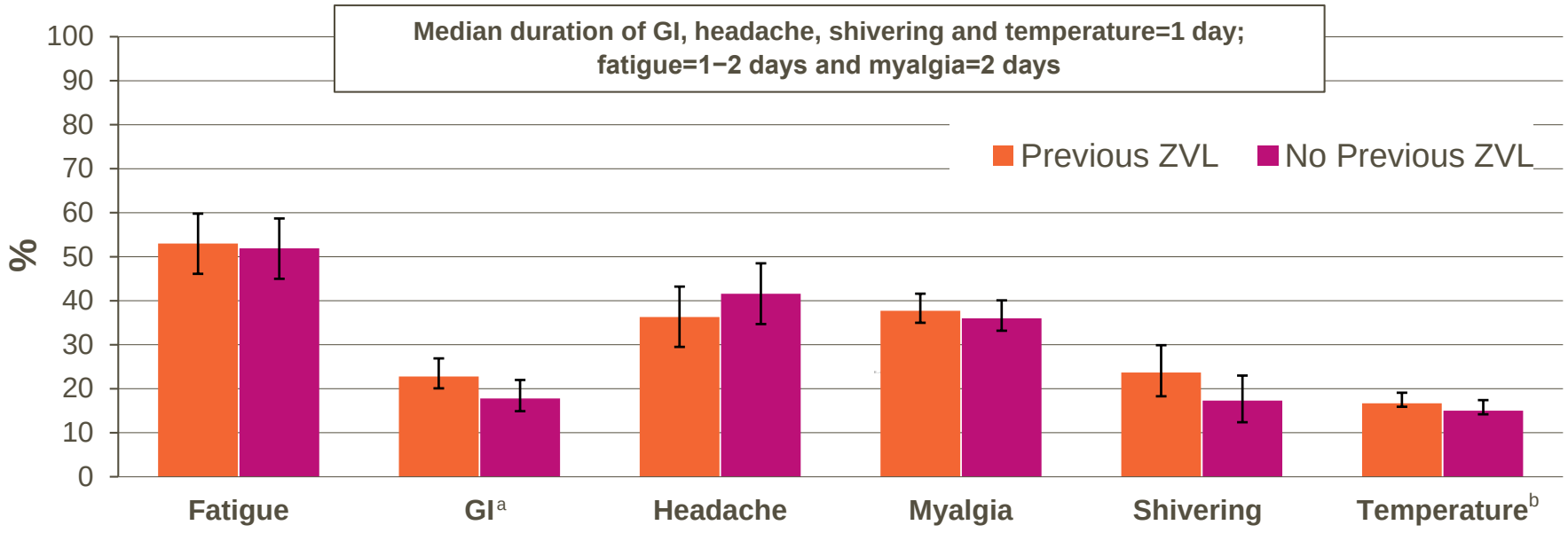
Grade 3 *overall by subject in total vaccinated cohort*



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier;
No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®).
[a]Redness/swelling at the injection site scored as grade 3 for those >100 mm. Pain was scored as grade 3 if preventing normal activity.

Solicited Systemic Symptoms Within 7 Days Post Vaccination

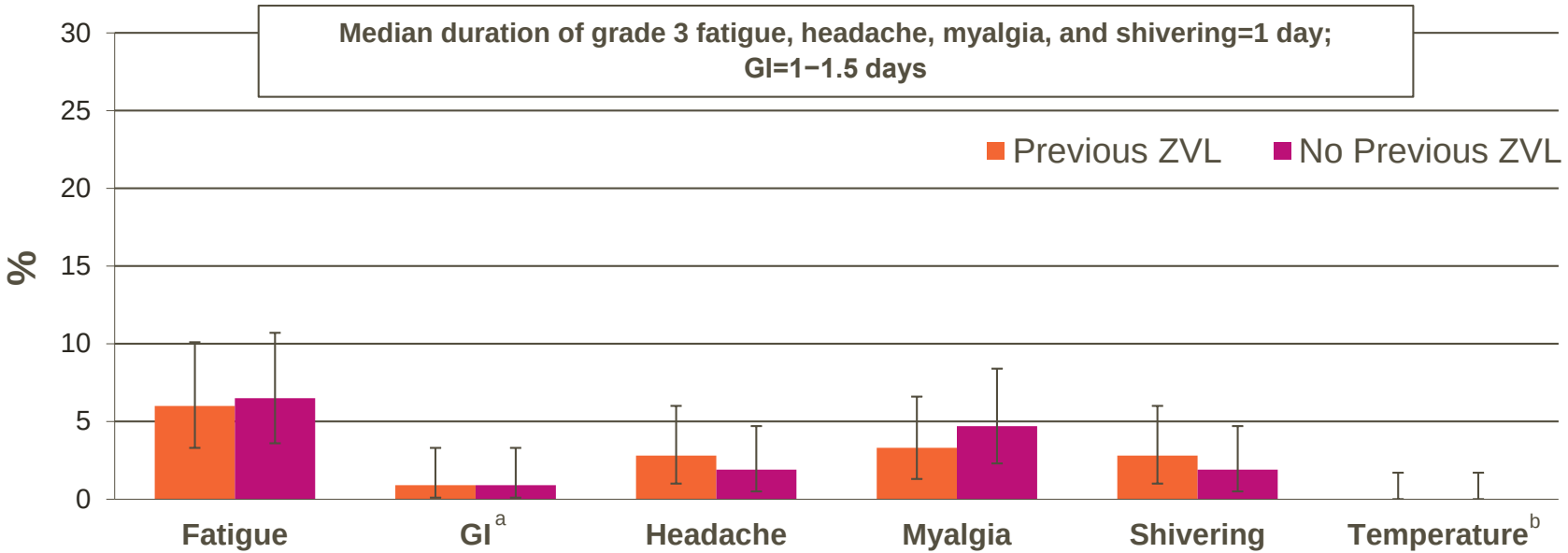
***Any grade** overall by subject in total vaccinated cohort*



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). [a]Gastrointestinal symptoms included nausea, vomiting, diarrhea, and/or abdominal pain. [b]≥37.5°C (preferred route for recording temperature was oral).

Solicited Systemic Symptoms Within 7 Days Post-Vaccination

Grade 3 *overall by subject in total vaccinated cohort*



Previous ZVL, received live-attenuated zoster vaccine (Zostavax®) ≥5 years earlier; No Previous ZVL, never received live-attenuated zoster vaccine (Zostavax®). [a]Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. [b]Scored as grade 3 ≥39°C (preferred route for recording temperature was oral). All other symptoms were scored as 3 for preventing normal activity.

Summary

Zoster-048: Active phase month 3 data

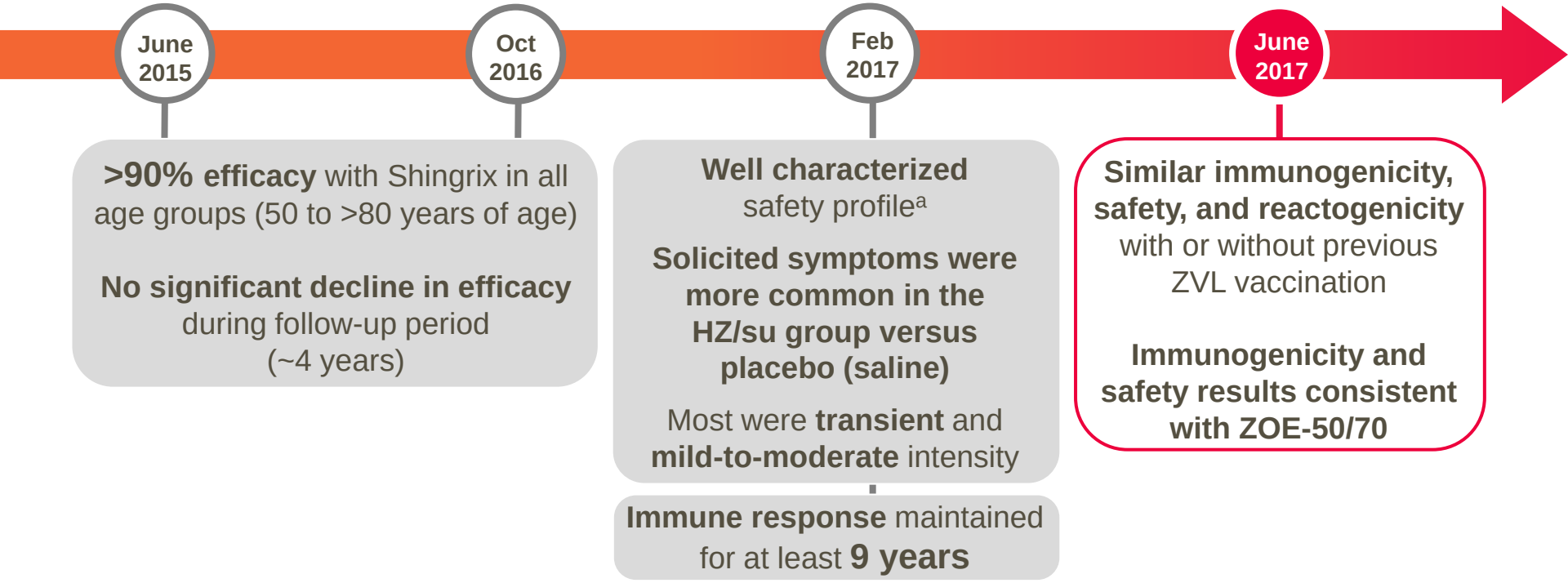
Zoster-048 Study Summary

Revaccination of previous ZVL recipients

- Shingrix (adjuvanted herpes zoster subunit vaccine) induced a strong immune response (humoral and cellular), consistent with ZOE trials, regardless of previous vaccination with ZVL (live-attenuated herpes zoster vaccine)
- No apparent safety differences observed between study groups within 30 days post dose 2 of Shingrix
- Solicited local and systemic symptoms were similar between study groups

Summary of Shingrix Clinical Data

ZOE-50, ZOE-70, and Zoster-048



[a]Large safety database (>14,645 subjects) available to evaluate safety of HZ/su candidate vaccine (gE + $AS01_B$) with more than 60,000 person years of active follow up.

Thank You