The Adjuvanted Recombinant Zoster Vaccine (RZV) Confers Long-term Protection Against Herpes Zoster: Interim Results of an Extension Study (ZOSTER-049) of Two Clinical Trials (ZOE-50 and ZOE-70)

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Disclosures

- AH is employed by the GSK group of companies
- CB is a consultant for Aixial (on behalf of GSK); MS, PP are employees, AS is a former employee of the GSK group of companies and declare financial and non-financial relationships and activities; AS also holds GSK stock options or restricted shares; JD-D is board member, scientific research study investigator, advisor or review panel member for the GSK group of companies and MSD; GK is a consultant for Keyrus (on behalf of GSK); JCT and C-J Yu have no real or apparent conflicts of interest to disclose.
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- Zoster-049 study group (full list accessible via QR code at top)
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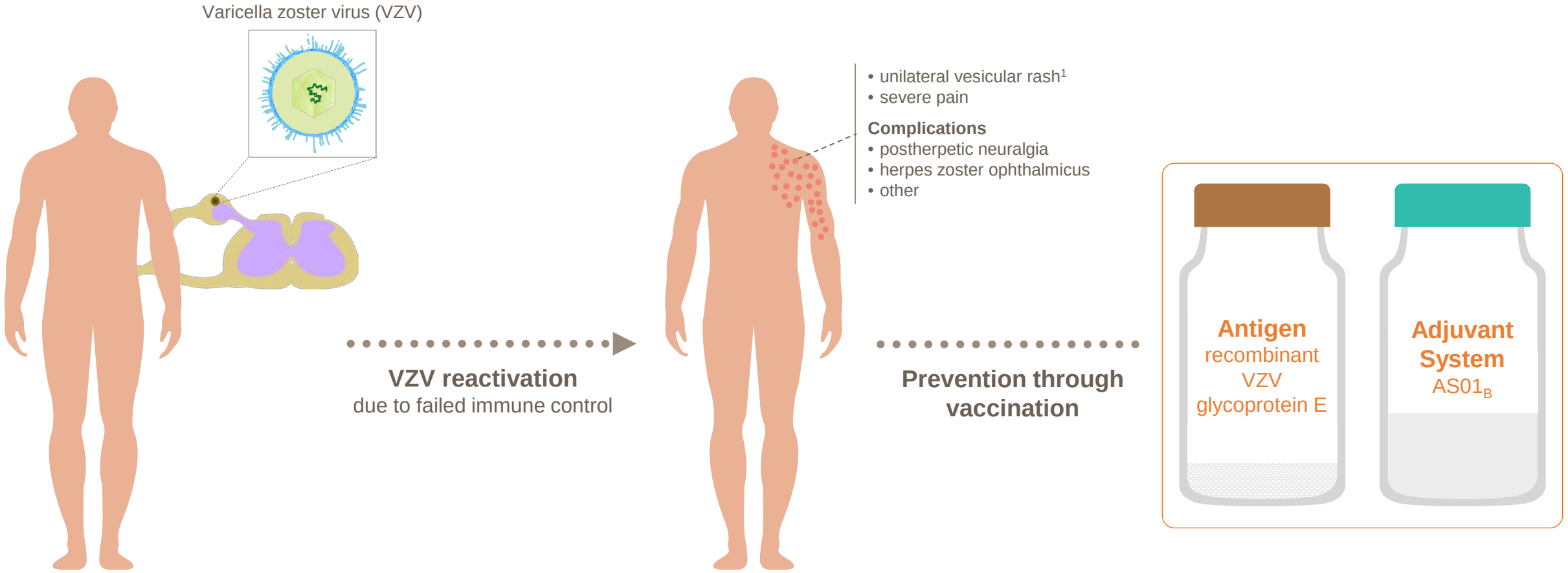
Background: herpes zoster (shingles) is caused by varicella zoster virus



VZV latent in ganglia

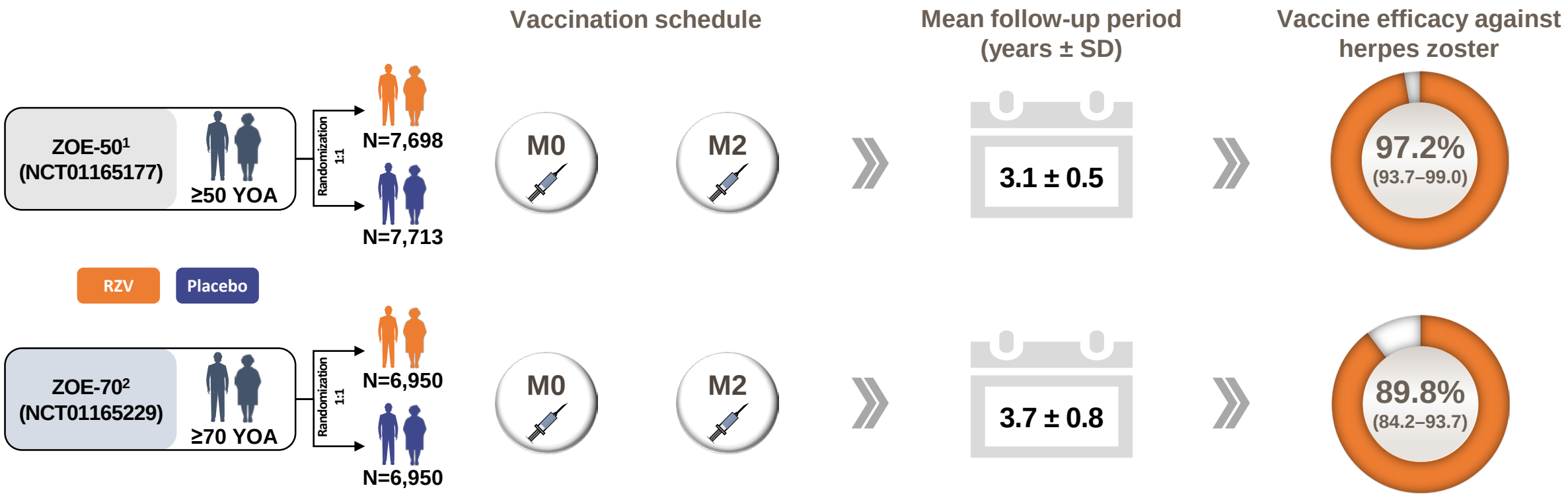
Acute herpes zoster (HZ)

Adjuvanted Recombinant Zoster Vaccine (RZV)

AS01$_B$, adjuvant system containing 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL, 50 µg), *Quillaja saponaria* Molina, fraction 21 (QS-21, 50 µg) and liposome.

1. Centers for Disease Control and Prevention. MMWR. 2008 May;57(RR-5):1–30.

Background: ZOE-50 and ZOE-70 parent studies

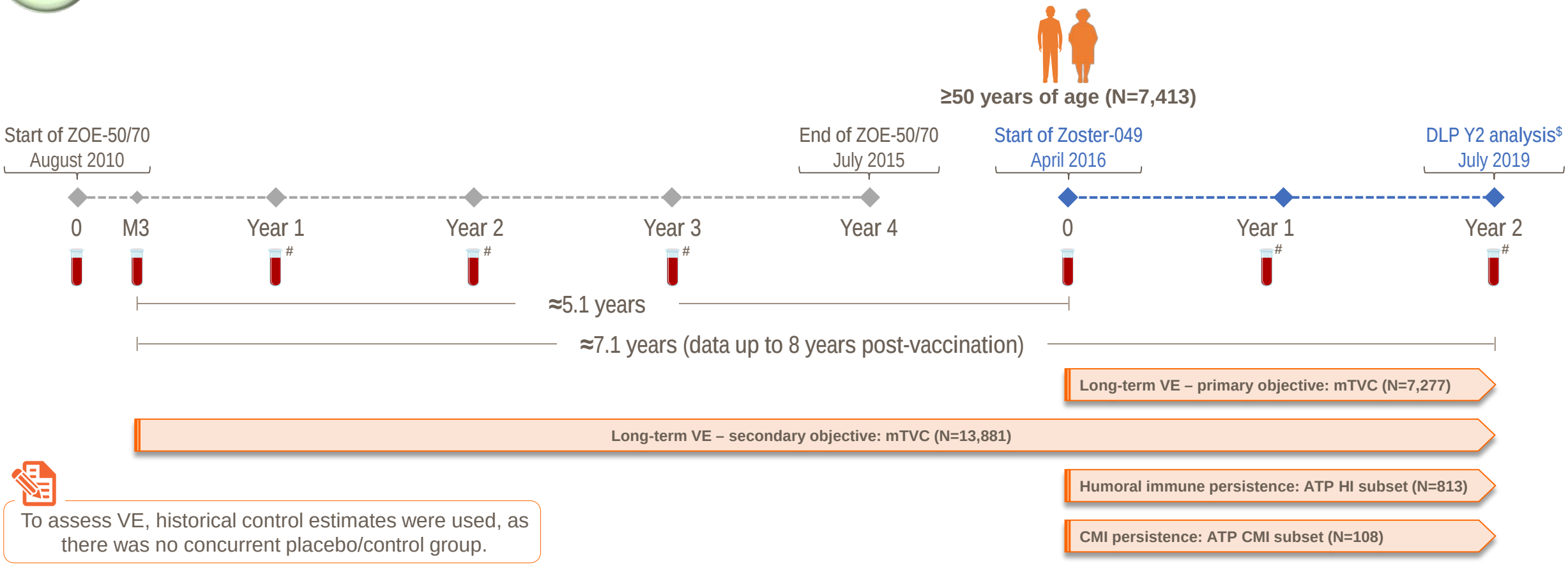


RZV was efficacious, highly immunogenic, and had a clinically acceptable safety profile

1. Lal H, et al. *N Engl J Med.* 2015;372(22):2087–96. **2.** Cunningham AL, et al. *N Engl J Med.* 2016;375(11):1019–32.
💉 vaccination with RZV/placebo; **RZV,** adjuvanted recombinant zoster vaccine; **YOA**, years of age; **SD**, standard deviation; **M**, month; **N**, number of participants.
Values in parentheses represent 95% confidence intervals.

Zoster-049 (NCT02723773): phase IIIb, open-label, multi-center, long-term FU study

AIM We report interim results of the extension study (Zoster-049) after at least 2 years of follow-up (starting and ending ≈5.1 and 7.1 years, respectively, following initial vaccination)



To assess VE, historical control estimates were used, as there was no concurrent placebo/control group.

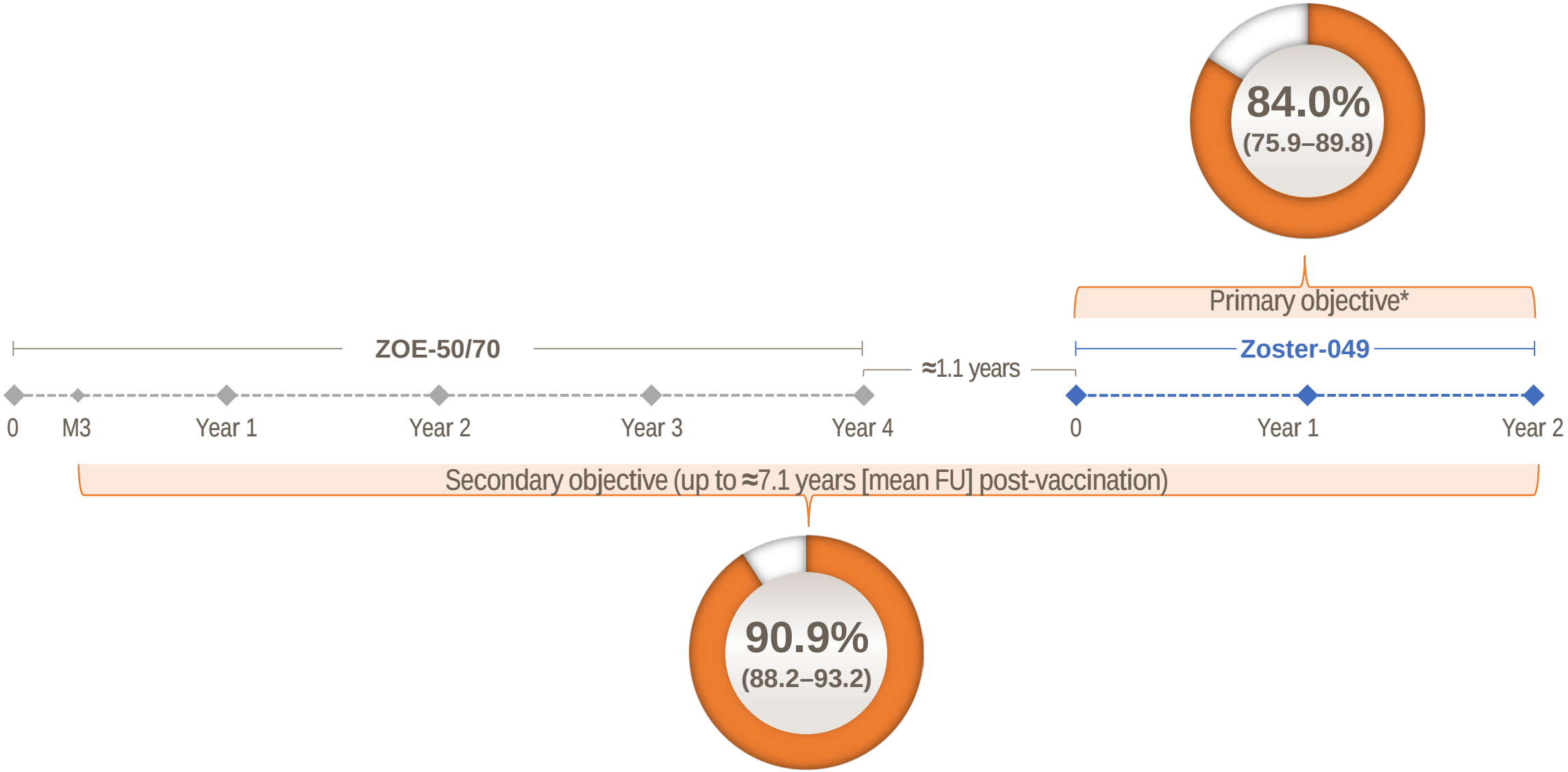
blood sampling; **FU,** follow-up; **N**, maximum number of participants; **M3**, one month post-second RZV dose; **Y**, year; **DLP**, data lock point; **VE**, vaccine efficacy against herpes zoster; **mTVC**, modified total vaccinated cohort including participants who received both RZV doses and did not develop a confirmed HZ episode for 1 month after second dose in the ZOE-50/70 studies; **ATP HI subset**, according-to-protocol subset of ZOE-50/70 for humoral immunity persistence; **ATP CMI subset**, according-to-protocol subset of ZOE-50 for cell-mediated immunity persistence. #sample collected only from the HI and CMI subsets. $DLP set when the last participant had reached 2 years of follow-up. All data in the database up to that time point was included in the analysis.

Demographic characteristics: are similar across cohorts

	Participants, N	Mean age*, years ± SD	Gender, %	Geographical ancestry, %
Modified total vaccinated cohort	7,277	67.2 ± 9.4	♂ 39.3 ♀ 60.7	76.5 White; 18.7 Asian; 0.9 African; 4.0 Other
ATP HI subset	813	66.1 ± 9.0	♂ 39.2 ♀ 60.8	71.5 White; 25.4 Asian; 1.0 African; 1.9 Other
ATP CMI subset	108	62.6 ± 8.2	♂ 48.1 ♀ 51.9	69.4 White; 28.7 Asian; 1.9 African

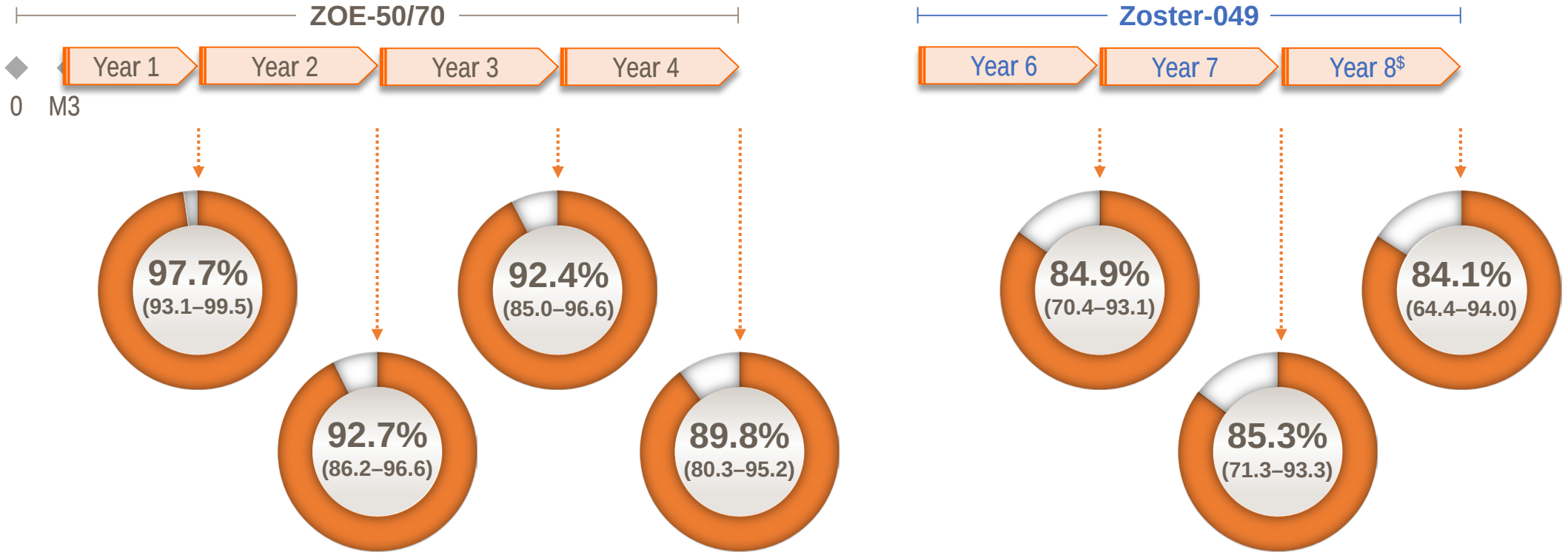
ATP HI subset, according-to-protocol subset of ZOE-50/70 for humoral immunity persistence; **ATP CMI subset**, according-to-protocol subset of ZOE-50 for cell-mediated immunity persistence; **White**, Caucasian/ European and Arabic/ North African heritages; **Asian**, Central, East, South East Asian and Japanese heritages. ***mean age at first vaccination in ZOE-50/70 trials.

VE against HZ: remained high up to ≈7.1 years (mean) post-vaccination (mTVC)



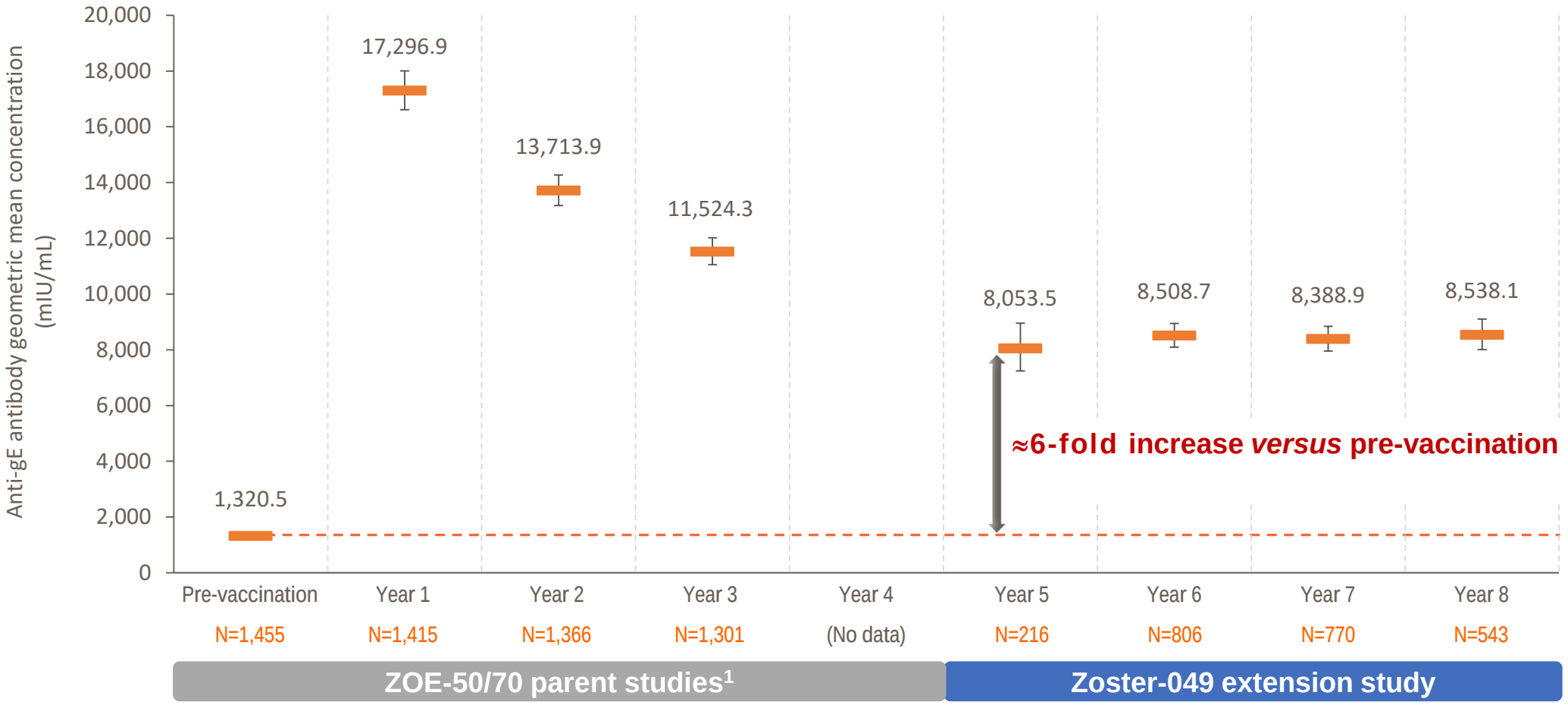
*data solely from Zoster-049 study. Values in parentheses depict 95% confidence intervals.

VE against HZ by year: remains >84% up to 8 years following the initial vaccination



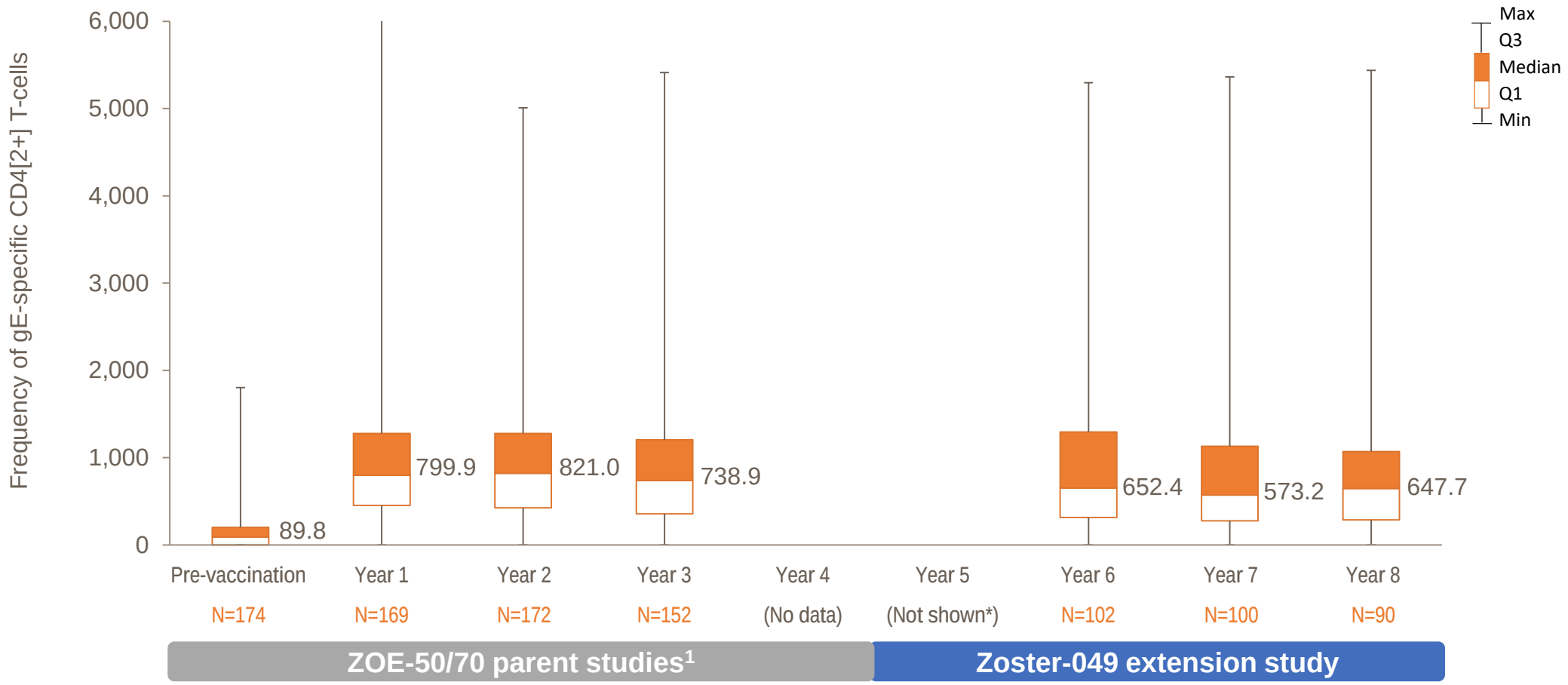
Analysis performed in the pooled ZOE-50/70 and Zoster-049 populations. **M3**, one month post-second RZV dose. $only data from those participants who reached Year 8 up to the data lock point of this interim analysis.

Humoral immunity: plateau at ≈6-fold above the pre-vaccination level



1. Cunningham AL, et al. *N Engl J Med.* 2016;375(11):1019–32. **ATP HI subset**, according-to-protocol subset for humoral immunity persistence; **gE**, glycoprotein E; **N**, number of participants with available results; **mIU/mL,** milli international unit/milliliter. Error bars depict 95% confidence interval.

gE-specific CD4[2+] T-cells: remained above baseline from Y6 to Y8 after vaccination



1. Cunningham AL, et al. *N Engl J Med.* 2016;375(11):1019–32. **ATP CMI subset**, according-to-protocol subset for cell-mediated immunity persistence; **gE**, glycoprotein E; **Min**, minimum; **Q1,Q3**, quartile 1 and 3; **Max**, maximum. Maximum value at Year 1 is 6018.8; **CD4[2+]**, T-cells expressing ≥2 markers of the 4 assessed (interferon gamma, interleukin-2, tumour necrosis factor alpha, CD40 ligand). The frequency of gE-specific CD4[2+] T-cells was assessed per 10^6 total CD4 T-cells. *****Year 5 CMI results not shown because of insufficient samples (i.e. 3) for the analysis.

Safety profile: remains clinically acceptable and no safety signal was identified

Serious adverse events (SAEs) were consistent with the aging population of the study

No deaths or other SAE were considered as causally-related to vaccination

Two participants with a confirmed HZ case reported HZ-related complication

- 1 participant experienced postherpetic neuralgia
- 1 participant experienced disseminated HZ disease (>1 dermatome affected)

Safety was assessed in the total vaccinated cohort, that included all participants from the ZOE-50 and ZOE-70 studies who were enrolled in the Zoster-049 extension study.

Conclusions

- RZV demonstrated high (84.0%) efficacy against herpes zoster over approximately 2 years of follow-up in Zoster-049 study
- Vaccine efficacy was 84.1% at Year 8 following initial vaccination (end of observation period for the year 2 interim analysis of Zoster-049 study)
- Both humoral and cellular immune responses remained high and consistent from Year 5 until Year 8
- No safety signal was identified from Zoster-049 study start up to data lock point for this interim analysis

Key messages

- ✓ RZV remains efficacious against herpes zoster up to 7.1 years (mean) post-initial vaccination in adults ≥50 years of age
- ✓ Humoral and cell-mediated immune responses persist up to 8 years post-vaccination

- ➢ **RZV is able to confer long-lasting protection**
- ➢ **This extension study further supports the benefit of RZV vaccination**

Thank you