LONG-TERM IMMUNOLOGICAL PERSISTENCE OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE: CLINICAL DATA AND MATHEMATICAL MODELING

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Disclosures

- GlaxoSmithKline Biologicals SA was the funding source and involved in all the stages of the study conduct and analysis and the development of this presentation.
- Anne Schuind is an employee of the GSK Group of Companies and holds shares/stock options as part of her remuneration.
- Shingrix is a registered trademark of the GSK group of companies.

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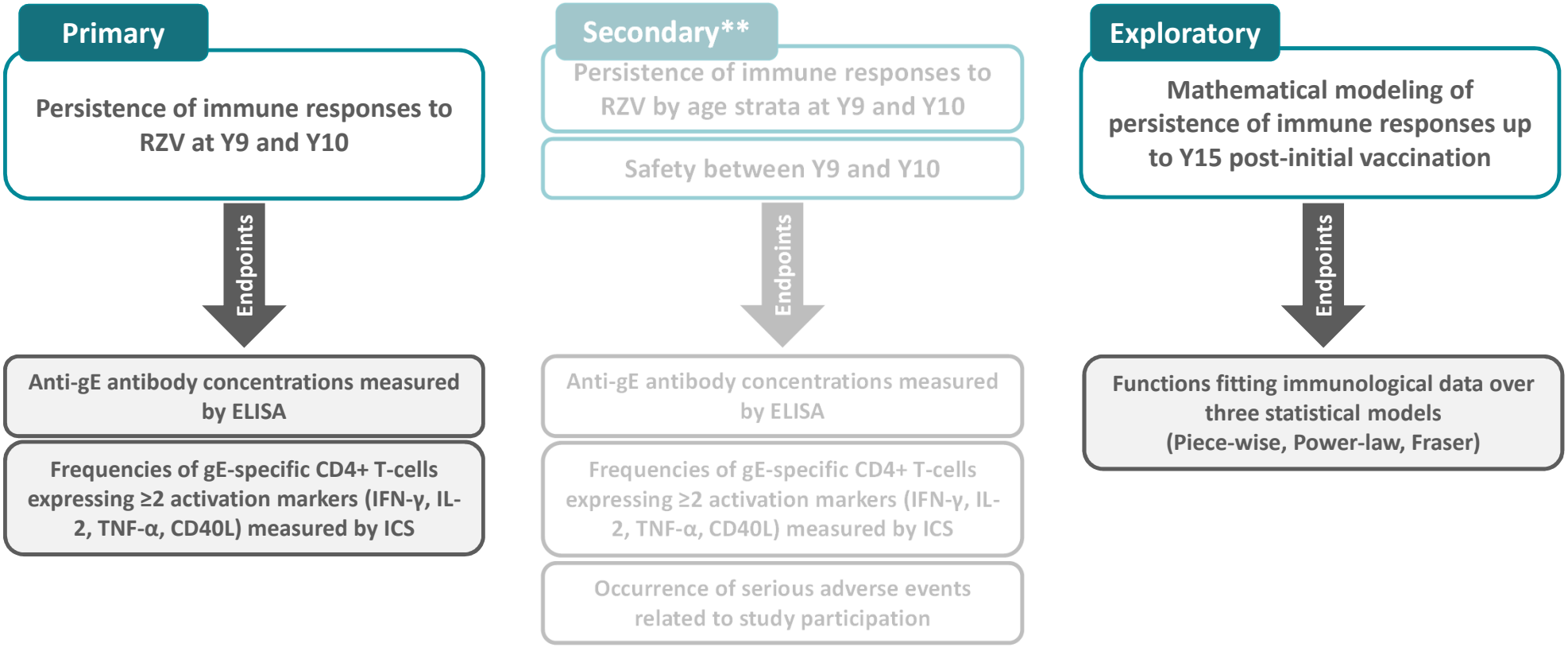
Background and aims

- Herpes zoster (HZ) results from reactivation of latent varicella-zoster virus (VZV) and occurs most frequently in older adults[1,2]
- The adjuvanted recombinant zoster vaccine (RZV, *Shingrix*, GSK) has been licensed for the prevention of HZ in adults ≥50 years of age (YOA) since 2017
  - Composition of RZV: VZV gE+AS01$_B$[3]
- The 2-dose schedule RZV has demonstrated ≥90% efficacy against HZ across all age strata (50–59, 60–69 and 70+)[4] that is sustained over 4 years of follow-up
- In adults ≥60 YOA robust immune responses were elicited after 2-dose RZV, which persisted above pre-vaccination levels up to 9 years post-initial vaccination[5]

Here we present persistence of humoral and cellular immunity up to 10 years and mathematical modeling to predict immune persistence up to 15 years post-initial vaccination in the same population

1. Yawn and Gilden Neurology 2013;81:928–30; **2**. Kawai and Yawn Mayo Clin Proc 2017;92:1806–21; **3**. Lecrenier et al. Expert Rev Vaccines 2018;17:619–34; **4**. Cunningham et al. J Infect Dis 2018;217:1750–60; **5**. Schwarz et al. Hum Vaccin Immunother 2018;14:1370–7. **gE**, glycoprotein E.

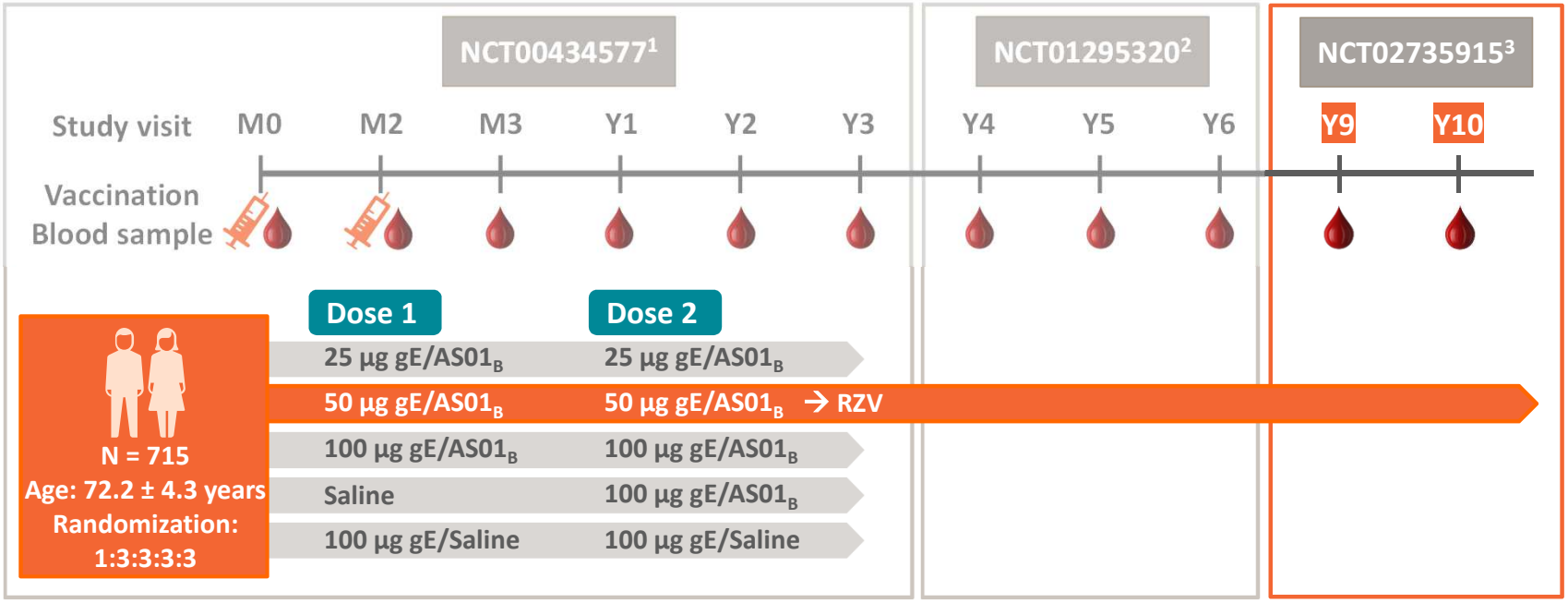
Study objectives and endpoints*



IFN-γ, interferon-gamma; **IL-2**, interleukin 2; **TNF-α**, tumor necrosis factor-alpha; **CD40L**, CD40 ligand; **ELISA**, enzyme-linked immunosorbent assay; **ICS**, intracellular cytokine staining; **Y**, year. *selected study objectives are listed; **data not shown here; **Note**: Y9 and Y10 post-dose 1 from initial vaccination.

Study design: phase IIIB, open-label, extension trial in Europe*

Evaluation of immunological persistence

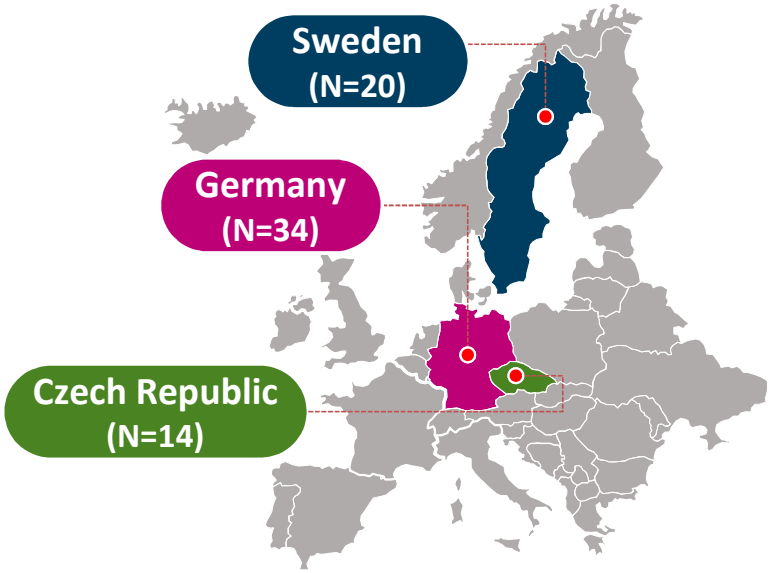


- **Mathematical modeling – based on data collected from adults who received 2 doses of RZV in the parent study and were willing to participate in the follow-up studies**

1. Chlibek et al. Vaccine 2014;32:1745–53 ; **2**. Chlibek et al. Vaccine 2016;34:863–8; **3**. Schwarz et al. Hum Vaccin Immunother 2018;14:1370–7. **N**, number of adults enrolled in initial study; *only study interventions relevant for the results presented here are depicted

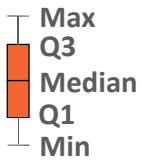
Demographic characteristics

According-to-protocol cohort for persistence N=68		
	Age at primary vaccination mean ± SD (years)	72.2 ± 4.3
+ 10 years	Age at Y10 visit mean ± SD (years)	82.6 ± 4.4
	Sex, N (%) (male)	26 (38.2)
	White-Caucasian/ European heritage, N (%)	68 (100)

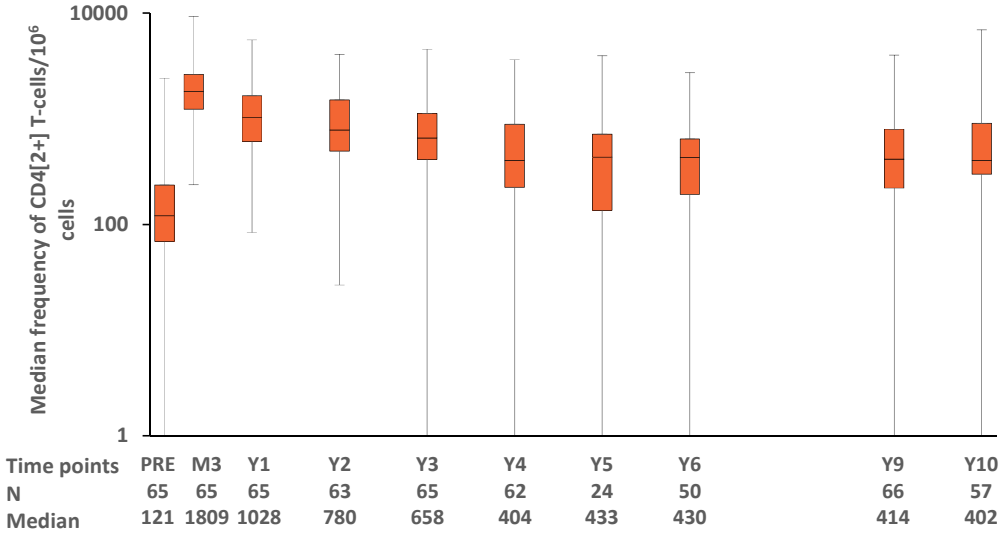


N, number of adults; **SD**, standard deviation.

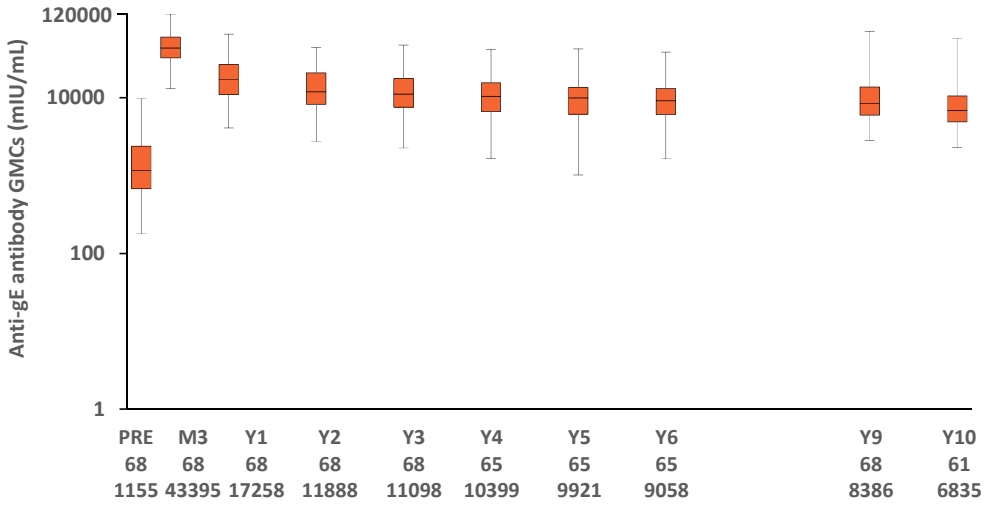
Immune responses persisted up to Y10 post-initial vaccination



Cell-mediated immune responses remained 3.3-fold above pre-initial vaccination levels



Humoral immune responses remained 5.9-fold above pre-initial vaccination levels



According-to-protocol cohort for persistence. PRE, before vaccination in the initial study; **GMC**, geometric mean concentration; **N**, number of adults with available results; **Q1**, first quartile; **Q3**, third quartile; **Min**, minimum; **Max**, maximum.

Mathematical modeling

- 3 linear mixed models for repeated measurements were used to predict persistence of immune responses

Piece-wise linear model

Based on assumption that the immune response declines linearly over time at a slope varying between non-overlapping time intervals (M3–M12, M12–M26, M26–onwards for anti-gE and M3–M12, M12–M49, M49–onwards for gE-specific CD4[2+] T-cells)

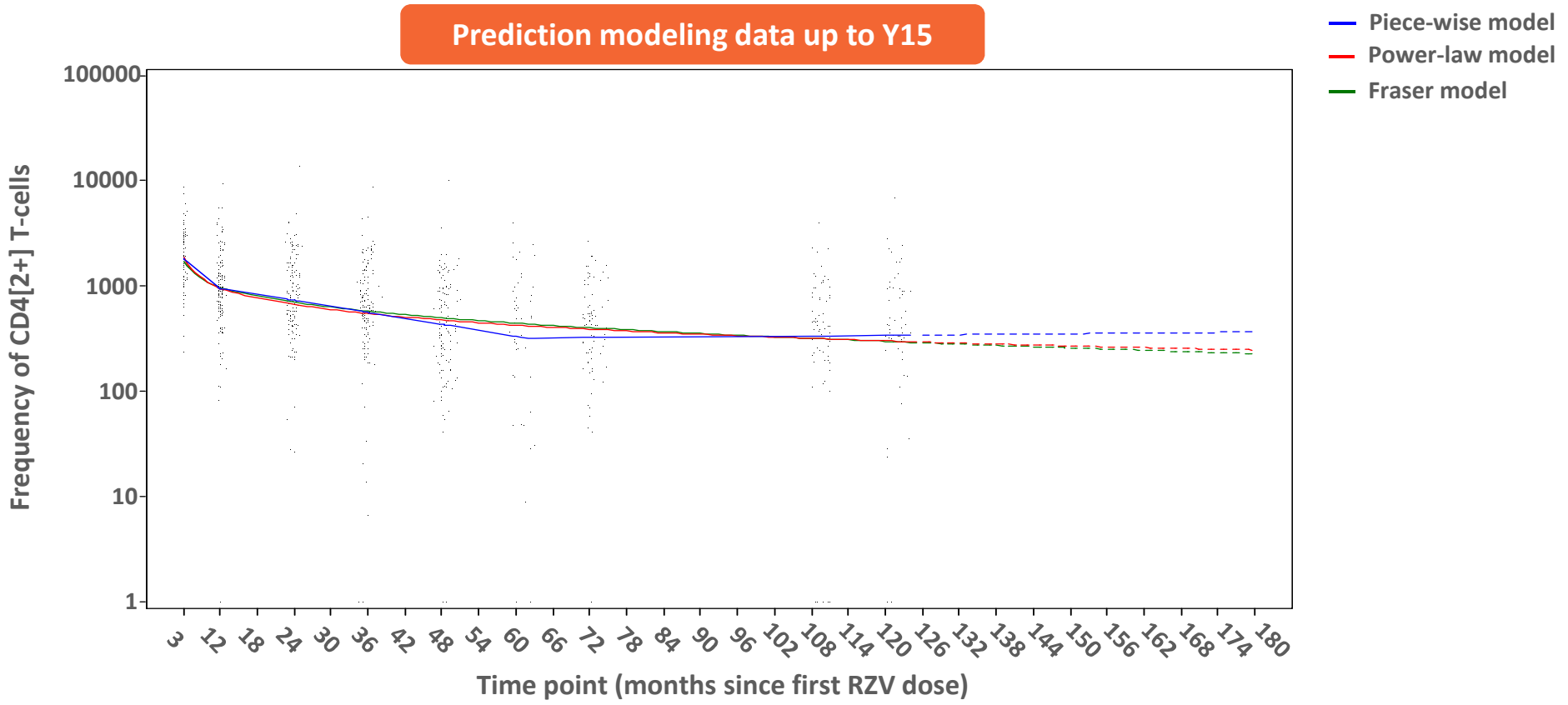
Power-law model

Based on assumption that the immune response declines over time following a logarithmic function

Fraser model

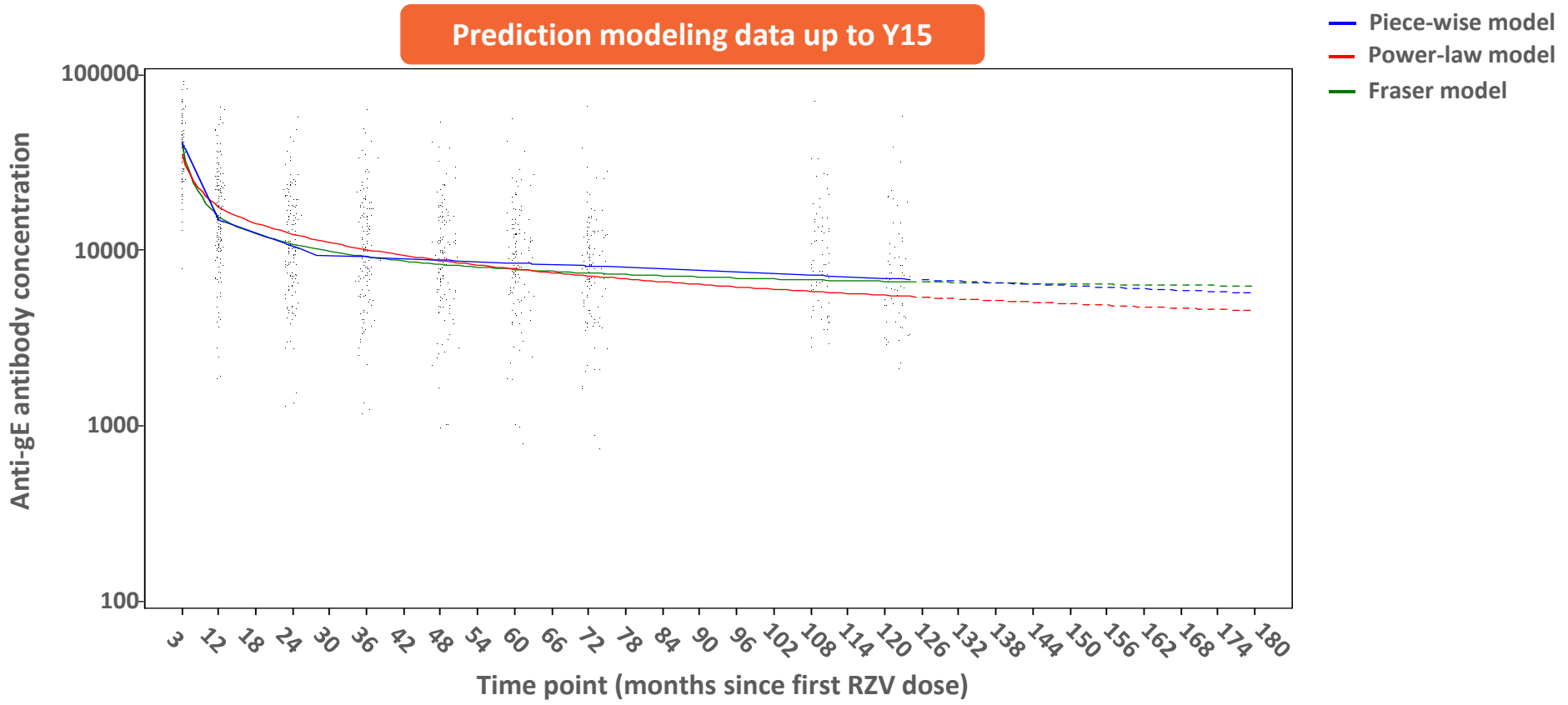
Modified Power-law model includes a constant in the logarithmic function

Cellular immune responses - predicted to remain above pre-vaccination levels for at least 15 years post-initial vaccination



According-to-protocol cohort for modeling.

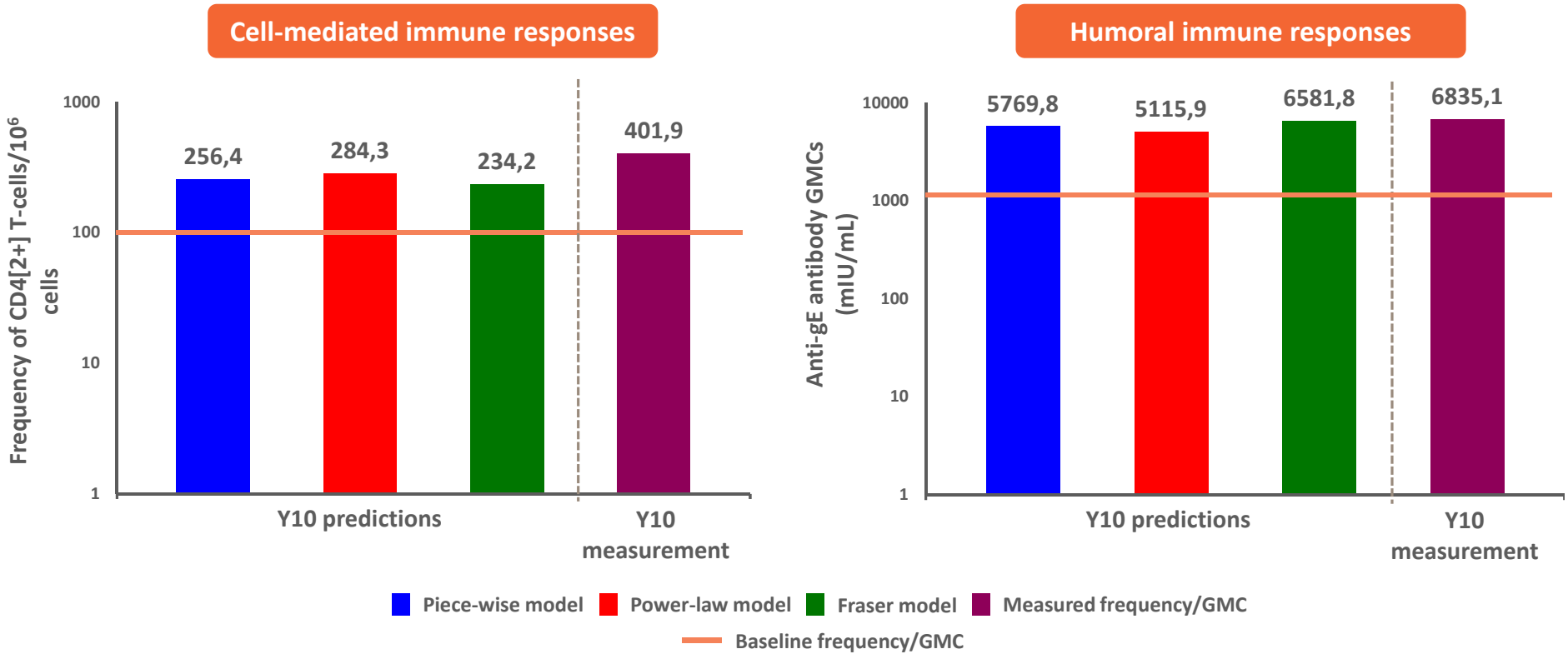
Humoral immune responses - predicted to remain above pre-vaccination levels for at least 15 years post-initial vaccination



According-to-protocol cohort for modeling.

Y10 measured cellular and humoral responses are similar to predicted values

Predictions of the Y10 immune response based on Y6 data using the 3 models[1,2]



According to protocol cohort for modeling. 1. Schwarz et al. Hum Vaccin Immunother 2018;14:1370–7; **2**. Lal et al. IDWeek 2015.

Conclusions

- In adults vaccinated at ≥60 YOA, humoral and cellular immune responses induced by 2 RZV doses remain above pre-vaccination levels up to 10 years post-initial vaccination (end of observation period)
- Mathematical modeling predicts that the vaccine-induced immune response will be maintained for at least 15 years post-initial vaccination
- Similar results were obtained in 3 different mathematical models (Piece-wise, Power-law and Fraser) predicting immunological persistence

Thank you