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Session: O-2. Adult Vaccines

Background. Herpes zoster can negatively impact older adults' health and quality of life. An adjuvanted recombinant zoster vaccine (RZV) has excellent vaccine efficacy (VE), including in older adults. Given that frailty is strongly associated with vulnerability to illness and adverse health outcomes, we studied how frailty impacts RZV VE, immunogenicity, reactogenicity, and safety.

Methods. In the ZOE-50 and ZOE-70 pivotal Phase 3 efficacy studies of RZV, 29,305 participants aged 50–96 received 2 doses of RZV vs. placebo in 1:1 randomization. In this secondary analysis (NCT03563183), a baseline frailty index (FI) was created retrospectively following previously validated methods using pre-existing comorbidities and patient reported outcomes. Participants were categorized as non-frail (FI≤ 0.08), pre-frail (FI=0.08–0.25) or frail (FI≥ 0.25) for stratified analyses.

Results. FI was calculated for 99.8% of participants included in this secondary analysis (n=26,976), and was balanced between RZV and placebo groups. 45.6% were pre-frail and 11.3% were frail. Mean age was 68.8 years; 58.1% were women. RZV VE against HZ was consistently above 90% for all frailty categories [non-frail: 95.8% (95%CI: 91.6–98.2), pre-frail: 90.4% (84.4–94.4), frail: 90.2% (75.4–97.0)]. The RZV group demonstrated robust antibody responses post-dose 2 across frailty categories. In the RZV group, the percentage of participants reporting solicited adverse events decreased with increasing frailty. Unsolicited medically attended visits and serious adverse events increased with frailty and were balanced between placebo and RZV groups.

Conclusion. The ZOE studies included older adults who were frail and pre-frail, and VE was high across frailty categories. Reactogenicity decreased with increasing frailty, and no safety concerns were identified in any frailty group.

Disclosures. **Melissa K. Andrew, MD, PhD, MSc(Ph)**, **GSK** (Grant/Research Support, Research Grant or Support) **Joon Hyung Kim, MD**, **GSK** (Employee, Shareholder) **Sean Matthews, MSc**, **GSK** (Consultant) **Christophe Dessart, MSc**, **GSK** (Employee) **myron J. levin, MD**, **Curevo** (Advisor or Review Panel member)**GlaxoSmithKline** (Grant/Research Support, Advisor or Review Panel member)**GlaxoSmithKline** (Grant/Research Support, Advisor or Review Panel member)**Merck Research Laboratories** (Advisor or Review Panel member, GlaxoSmithKline)**Merck Research Laboratories** (Advisor or Review Panel member)**Merck ResearchLaboratories** (Advisor or Review Panel member) **Lidia Oostvogels, MD**, **GSK** (Shareholder) **Megan Riley, PhD**, **GSK** (Employee) **Shelly McNeil, FRCPC, MD**, **GSK** (Grant/Research Support, Scientific Research Study Investigator, Research Grant or Support, Other Financial or Material Support, honoraria for talks) **Anne Schuind, MD**, **GSK** (Employee, Other Financial or Material Support, own GSK stock options or restricted shares as part of renumeration) **Desmond Curran, PhD**, **GSK** (Employee, Shareholder)

6. MF59 ASSURANCE 2: A Real-world Study to Estimate the Relative Vaccine Effectiveness of Adjuvanted Trivalent Influenza Vaccine Compared to Egg-based Trivalent High-dose Among U.S. Older Adults During 2018–19 Influenza Season

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Session: O-2. Adult Vaccines

Background. In the 2018–19 influenza season, influenza resulted in almost 280,000 hospitalizations and over 25,000 deaths in U.S. adults > 65 years. This study aimed to evaluate the relative vaccine effectiveness (rVE) of adjuvant trivalent influenza vaccine (aTIV) compared to high-dose trivalent influenza vaccine (TIV-HD), against influenza-related hospitalizations/emergency room (ER) visits, office visits and hospitalization/ER visit for cardio-respiratory disease (CRD) among older adults for the 2018–19 flu season.

Methods. A retrospective cohort analysis of older adults (> 65 years) was conducted using professional fee, prescription claims and hospital charge master data in the U.S. Baseline characteristics included age, gender, payer type, region, Charlson Comorbidity Index (CCI), comorbidities, indicators of frail health status, and pre-index hospitalization rates. Adjusted analyses were conducted through inverse probability of treatment weighting (IPTW) to control for selection bias. Poisson regression was used to estimate the adjusted pairwise rVE against influenza-related hospitalizations/ER visits and office visits and any hospitalization/ER visit for CRD (based on diagnoses codes). An unrelated outcome, urinary tract infection (UTI) hospitalization, was assessed.

Results. During 2018–19 flu season, following IPTW analyses, 561,315 recipients of aTIV and 1,672,779 of TIV-HD were identified. After IPTW adjustment and Poisson regression, aTIV was more effective in reducing influenza-related office visits compared to TIV-HD (6.6%; 95% CI: 2.8%-10.3%). aTIV was statistically comparable to TIV-HD (2.0%; 95% CI: -3.7%-7.3%) for prevention of influenza-related hospitalizations/ER visits but more effective than TIV-HD (2.6%; 95% CI: 2.0%-3.2%) in reducing hospitalizations/ER visits for CRD. No treatment effect was identified for control condition (UTI hospitalization).

Conclusion. In adjusted analyses, aTIV reduced influenza-related office visits and CRD hospitalizations/ER visits compared to TIV-HD. aTIV and TIV-HD demonstrated comparable reductions in influenza-related hospitalizations/ER visits.

Disclosures. **Stephen I. Pelton, MD**, **Merck vaccine** (Consultant, Grant/Research Support)**Pfizer** (Consultant, Grant/Research Support)**Sanofi Pasteur** (Consultant, Other Financial or Material Support, DSMB)**Seqirus Vaccine Ltd.** (Consultant) **Maarten Postma, Dr.**, **IQVIA** (Consultant) **Victoria Divino, PhD**, **Seiqrus Vaccines Ltd.** (Consultant) **Drishti Shah, PhD**, **Seqirus Vaccines Ltd.** (Consultant) **Joaquin F. Mould-Quevedo, PhD**, **Seqirus Vaccines Ltd.** (Employee, Shareholder) **Mitchell DeKoven, PhD**, **Seqirus Vaccines Ltd.** (Consultant) **Girishanthy Krishnarajah, PhD**, **Seqirus Vaccines Ltd.** (Employee, Shareholder)

7. Can Recombinant Zoster Vaccine Administration Decrease the Use of Herpes Zoster-related Pain Medication Across Randomized Controlled Studies?

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Session: O-2. Adult Vaccines

Background. Older and immunocompromised adults are at increased risk for herpes zoster (HZ) and often experience persistent, severe HZ-related pain, impacting their quality of life and activities of daily living. High vaccine efficacy (VE) of the adjuvanted recombinant zoster vaccine (RZV) in preventing HZ and reducing severe and clinically significant HZ-related pain has been shown in adults ≥ 50 years of age (YOA; ZOE-50 study; NCT01165177), ≥ 70 YOA (ZOE-70; NCT01165229) and ≥ 18 YOA undergoing autologous hematopoietic stem cell transplantation (ZOE-HSCT; NCT01610414).

Methods. In patients with confirmed HZ from the above phase III, randomized, placebo-controlled studies, we analyzed VE of RZV in reducing the duration of clinically significant HZ-related pain and in reducing the use and duration of HZ-related pain medication. Pain was assessed by the Zoster Brief Pain Inventory (ZBPI). Use of all HZ-related medication was recorded.

Results. VE in reducing the duration of clinically significant HZ-related pain (ZBPI pain score ≥3) during HZ episodes was 38.5% (p-value: 0.0099) in RZV-vaccinated patients from the ZOE-HSCT study compared to placebo. A similar trend (not statistically significant) was observed in the ZOE-50 (VE: 26.9%; p-value: 0.4318) and ZOE-70 (VE: 28.4%; p-value: 0.1877) studies. VE in reducing the use (**Table 1**) and duration (**Table 2**) of HZ-related pain medication was 39.6% (p-value: 0.0083) and 49.3%(p-value: 0.0404), respectively, in the ZOE-70 study; corresponding positive VE estimates were also seen in the ZOE-50 and ZOE-HSCT studies. Non-opioids were used by 61.2%, 44.3% and 22.1% of patients in the ZOE-50, ZOE-70 and ZOE-HSCT studies, respectively; weak opioids by 18.6%, 13.0% and 10.8% of patients, and strong opioids by 8.0%, 2.0% and 5.3% of patients (**Table 3**).

Table 1. Reduction in the use of HZ-related pain medication in patients with confirmed HZ

	RZV					Placebo							
Study	N	n+	n	Pain med use (%)	95% CI	N	n+	n	Pain med use (%)	95% CI	VE (%)	95% CI	p-value
ZOE-50	9	13	6	66.67	(29.93, 92.51)	254	529	190	74.80	(69.00, 80.02)	11.69	(-19.40, 53.58)	0.6972
ZOE-70	23	31	10	43.48	(23.19, 65.51)	223	631	160	71.75	(65.35, 77.56)	39.60	(10.79, 64.75)	0.0083
ZOE-HSCT*	49	65	32	65.31	(50.36, 78.33)	135	262	94	69.63	(61.13, 77.24)	6.21	(-15.84, 27.82)	0.5937

*This analysis excluded pain medication linked to a confirmed HZ case after the start of relapse treatment; **CI**, confidence interval; **med**, medication; **HZ**, herpes zoster; **N**, number of patients with at least one confirmed HZ episode; **n+**, number of pain medications in each group (all confirmed HZ episodes considered); **n**, number of patients with at least one pain medication in each group (all confirmed HZ episodes considered); **RZV**, recombinant zoster vaccine; **VE**, vaccine efficacy (adjusted by age strata in the ZOE-50 and ZOE-70 studies).

Table 2. Reduction in the duration of HZ-related pain medication use in patients with confirmed HZ

	RZV			Placebo					
Study	N	n	T (days)	N	n	T (days)	VE (%)	95% CI	p-value
ZOE-50	9	6	159	254	190	14524	24.72	(-73.67, 67.37)	0.5056
ZOE-70	23	10	1108	223	160	31949	49.25	(2.92, 73.47)	0.0404
ZOE-HSCT*	49	32	1917	135	94	15465	22.45	(-15.85, 48.09)	0.2144

*This analysis excluded pain medication linked to a confirmed HZ case after the start of relapse treatment; **CI**, confidence interval; **HZ**, herpes zoster; **N**, number of patients with at least one confirmed HZ episode; **n**, number of patients with at least one day of HZ-related pain medication use; **RZV**, recombinant zoster vaccine; **T**, sum of follow-up period (for subjects without clinically significant pain T is 1, for subjects with clinically significant pain T is the duration of clinically significant pain); **VE**, vaccine efficacy (adjusted by age strata and region in the ZOE-50 and ZOE-70 studies).

Table 3. HZ-related medication types in patients with confirmed HZ

Medication class	ZOE-50 study						ZOE-70 study						ZOE-HSCT study*					
	RZV (N=9)		Placebo (N=254)		Total (N=263)		RZV (N=23)		Placebo (N=223)		Total (N=246)		RZV (N=49)		Placebo (N=135)		Total (N=184)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Non-opioids†	6	66.7	155	61.0	161	61.2	6	26.1	103	46.2	109	44.3	22	44.9	62	45.9	84	45.7
Weak opioids†	0	0	49	19.3	49	18.6	2	8.7	30	13.5	32	13.0	6	12.2	34	25.2	40	21.7
Strong opioids†	0	0	21	8.3	21	8.0	0	0	5	2.2	5	2.0	5	10.2	12	8.9	17	9.2
Corticosteroids	3	33.3	21	8.3	24	9.1	1	4.3	10	4.5	11	4.5	2	4.1	14	10.4	16	8.7
Antidepressants	0	0	17	6.7	17	6.5	1	4.3	18	8.1	19	7.7	3	6.1	13	9.6	16	8.7
Psychiatric medications	0	0	55	21.7	55	20.9	3	13.0	35	15.7	38	15.4	8	16.3	42	31.1	50	27.2
Anesthetics	0	0	15	5.9	15	5.7	0	0	11	4.9	11	4.5	0	0	7	5.2	7	3.8
Antihistamines	0	0	10	3.9	10	3.8	1	4.3	9	4.0	10	4.1	1	2.0	11	8.1	12	6.5
GI medications	1	11.1	24	9.4	25	9.5	0	0	6	2.7	6	2.4	2	4.1	2	1.5	4	2.2
Antibiotics	1	11.1	37	14.6	38	14.4	2	8.7	32	14.3	34	13.8	5	10.2	14	10.4	19	10.3
Muscle relaxants	0	0	1	0.4	1	0.4	0	0	2	0.9	2	0.8	0	0	0	0	0	0
Other medications	3	33.3	54	21.3	57	21.7	3	13.0	42	18.8	45	18.3	6	12.2	19	14.1	25	13.6

*This analysis excluded pain medication linked to a confirmed HZ case after the start of relapse treatment; **GI**, gastro-intestinal; **HZ**, herpes zoster; **N**, number of patients with at least one confirmed HZ episode; **n (%)**, number (percentage) of patients with at least one event in the specified category; **RZV**, recombinant zoster vaccine.
†Based on the World Health Organization's pain relief ladder (WHO's Pain Relief Ladder, 2019. Available at: www.who.int/cancer/palliative/painladder/en/): non-opioids (e.g. nonsteroidal anti-inflammatory drugs and paracetamol [acetaminophen]), weak opioids (e.g. codeine) and strong opioids (e.g. morphine, oxycodone), each with or without adjuvant therapies (e.g. corticosteroids or psychiatric medication).

Conclusion. In addition to a high VE in preventing HZ in these studies, we also observed an attenuation of HZ-related pain, and thus lower use and duration of pain medication in breakthrough cases after RZV vaccination, thereby potentially improving patient quality of life.

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8. 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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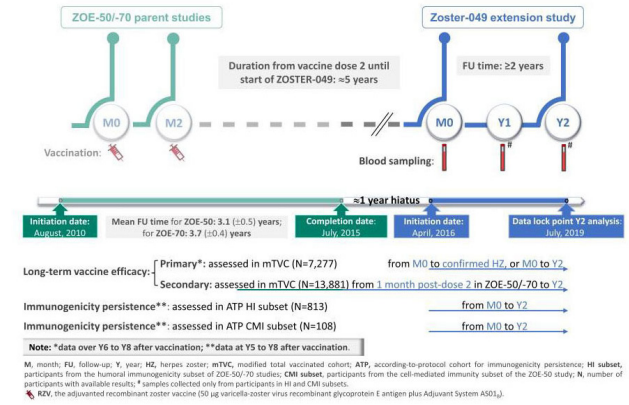
on behalf of the Zoster-049 study group

Session: O-2. Adult Vaccines

Background. Two large-scale phase 3 clinical trials (ZOE-50 [NCT01165177] and ZOE-70 [NCT01165229]) demonstrated that, in adults ≥ 50 years of age followed over a mean period of 3.1 and 3.7 years respectively, the adjuvanted recombinant zoster vaccine (RZV) was efficacious against herpes zoster (HZ), highly immunogenic and had a clinically acceptable safety profile. In this extension study (ZOSTER-049 [NCT02723773]), RZV-induced immunogenicity persistence and long-term vaccine efficacy (VE) against HZ were evaluated; we report interim results after at least 2 years of follow-up (starting and ending ≈5.1 and 7.1 years, respectively, after initial vaccination during the parent studies).

Methods. The study design is detailed in **Figure 1**. Primary objective: VE against HZ over the ZOSTER-049 study. Secondary objectives: VE against HZ from 1 month post-dose 2 in ZOE-50/-70 until the end of observation for year (Y)2 of ZOSTER-049, persistence of vaccine-induced humoral immunogenicity (HI) in terms of anti-gE antibody concentrations (by ELISA) and cell-mediated immune (CMI) response in terms of frequency of gE-specific CD4+ T-cells (by intracellular cytokine staining).

Figure 1. Study design of the extension study in relation to the parent studies. ZOSTER-049 study procedures, timing, endpoints and cohorts



Results. Of the 7,413 participants enrolled in ZOSTER-049, 7,277 were included in the VE analysis (**Figure 2**) and 6,972 reached Y2 of this study. The overall VE against HZ during at least 2 years of follow-up in ZOSTER-049 was 84.0% (95% confidence interval [CI]: 75.9–89.8%). From 1 month post-dose 2 in the ZOE-50/-70 studies until the end of observation for Y2 of ZOSTER-049, the overall VE was 90.9% (95% CI: 88.2–93.2%). Anti-gE antibody concentrations persisted ≈6 times above pre-vaccination levels up to Y8 after vaccination (**Figure 3A**) and the frequency of gE-specific CD4[2+] T-cells remained above baseline from Y6 to Y8 after vaccination (i.e. until the end of observation for Y2 of ZOSTER-049) (**Figure 3B**).

Figure 2. Demographic characteristics of participants included in the ZOSTER-049 study, for the analysis of vaccine efficacy against herpes zoster (mTVC)

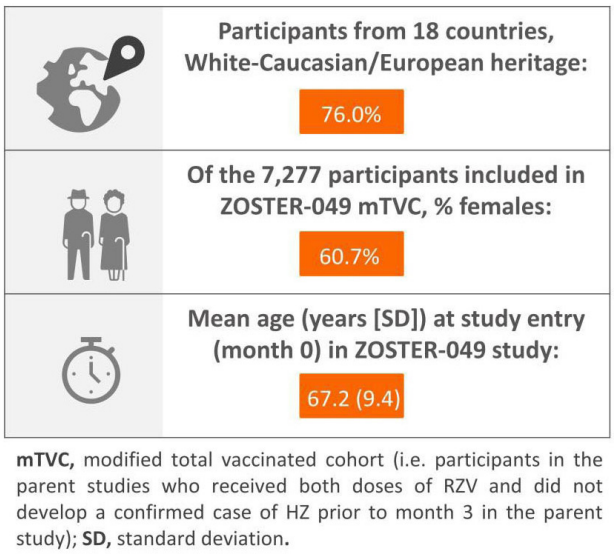


Figure 3. Long-term persistence of humoral immunogenicity (HI) and cell-mediated immune (CMI) responses up to year 8 post-vaccination dose 2 administered in the ZOE-50/-70 studies