Megan Riley, PhD[2]; Kenneth E. Schmader, MD[5]; Shelly McNeil, FRCPC, MD[6]; Anne Schuind, MD[2]; Desmond Curran, PhD[2]; [1]Dalhousie University; Canadian Centre for Vaccinology, Halifax, Nova Scotia, Canada; [2]GSK, Rockville, Maryland; [3]GSK, Wavre, Belgium, Wavre, Brabant Wallon, Belgium; [4]University of Colorado Anschutz Medical Campus, Aurora, Colorado; [5]Duke University Medical Center and GRECC, Durham Veterans Affairs Medical Center, Durham, North Carolina [6]Canadian Center for Vaccinology (CCfV), IWK Health Centre, Nova Scotia Health Authority (NSHA), and Dalhousie University, Halifax, Nova Scotia (NS), Halifax, Nova Scotia, Canada

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.

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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

Stephen I. Pelton, MD[1]; Maarten Postma, Dr.[2]; Victoria Divino, PhD[3]; Drishti Shah, PhD[3]; Joaquin F. Mould-Quevedo, PhD[4]; Mitchell DeKoven, PhD[3]; Girishanthy Krishnarajah, PhD[4]; [1]Boston Medical Center, boston, Massachusetts; [2]University of Groningen, Groningen, Groningen, Netherlands; [3]IQVIA, Falls Church, Virginia; [4]Seqirus Vaccines Ltd., Summit, New Jersey

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.

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

Joon Hyung Kim, MD[1]; Robert Johnson, MD, FRCA[2]; Martina Kovac, MD[3]; Anthony L. Cunningham, MBBS, MD, FRACP, FRCPA[4]; Srikanth Emmadi, MSc[5]; Keith Sullivan, MD, FASTCT[6]; Alemnew F. Dagnew, MD[3]; Desmond Curran, PhD[1]; Anne Schuind, MD[1]; [1]GSK, Rockville, Maryland; [2]University of Bristol, Bristol, United Kingdom, Bristol, England, United Kingdom [3]GSK, Rockville, MD, United States, Rockville, Maryland; [4]The Westmead Institute for Medical Research, Westmead, NSW, Australia and University of Sydney, Sydney, NSW, Australia, Sydney, Westmead, New South Wales, Australia; [5]GSK, Wavre, Belgium, Wavre, Brabant Wallon, Belgium; [6]Duke University Medical Center, Durham, NC, United States, Durham, North Carolina

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).