Megan Riley, PhD
Kenneth E. Schmader, MD
Shelly McNeil, FRCPC, MD
Anne Schuind, MD
Desmond Curran, PhD
Dalhousie University; Canadian Centre for Vaccinology, Halifax, Nova Scotia, Canada; GSK, Rockville, Maryland; GSK, Waver, Belgium, Waver, Brabant Wallon, Belgium; University of Colorado Anschutz Medical Campus, Aurora, Colorado; Duke University Medical Center and GSK, Durham, Durham, North Carolina; Canadian Center for Vaccinology (CCV), IWK Health Centre, Nova Scotia Health Authority (NSHA), and Dalhousie University, Halifax, Nova Scotia (NS), Halifax, Nova Scotia.

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, 29,365 participants aged 50-96 received 2 doses of RZV vs. placebo in 1.0 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 normal (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. Unrelated 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 (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

Abstract

Introduction. In the 2018-19 influenza season, influenza resulted in approximately 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 adjuvanted 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 diagnosis 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 conditions (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 J. Pelton, MD, Merck vaccine (Consultant, Grant/Research Support), Pfizer (Consultant, Grant/Research Support). Sanofi Pasteur (Consultant, Other Financial or Material Support, DMSB), Seqirus Vaccine Ltd. (Consultant), Maartens Postma, Dr, IQVIA (Consultant); Victoria Dinovio, PhD, Seqirus Vaccines Ltd. (Consultant), Bristhi Shah, PhD, Seqirus Vaccines Ltd. (Consultant), F. Mould-Quevedo, PhD, Seqirus Vaccines Ltd. (Employee, Shareholder), Mitchell DeKoven, PhD, Seqirus Vaccines Ltd. (Consultant), Girishanthi Krishnarajah, PhD, Seqirus Vaccines Ltd. (Employee, Shareholder)

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

Abstract

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 (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 medication, using the ZOE-HSCT 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 duration (Table 2) and use (Table 1) 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-ops 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).

Conclusion. In the use of HZ-related pain medication in patients with confirmed HZ.

Disclosures. Stephen J. Pelton, MD, Merck vaccine (Consultant, Grant/Research Support), Pfizer (Consultant, Grant/Research Support). Sanofi Pasteur (Consultant, Other Financial or Material Support, DMSB), Seqirus Vaccine Ltd. (Consultant), Maartens Postma, Dr, IQVIA (Consultant); Victoria Dinovio, PhD, Seqirus Vaccines Ltd. (Consultant), Bristhi Shah, PhD, Seqirus Vaccines Ltd. (Consultant), F. Mould-Quevedo, PhD, Seqirus Vaccines Ltd. (Employee, Shareholder), Mitchell DeKoven, PhD, Seqirus Vaccines Ltd. (Consultant), Girishanthi Krishnarajah, PhD, Seqirus Vaccines Ltd. (Employee, Shareholder)

Abstract

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 (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 medication, using the ZOE-HSCT 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 duration (Table 2) and use (Table 1) 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-ops 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).
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-+ 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)

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

| Medication class | ZOE-50 study | ZOE-70 study | ZOE-mTVC study* |
|------------------|--------------|--------------|-----------------|
|                   | (N=254) | (N=283) | (N=254) |
| Antibacterials    | 0.0% | 0.0% | 0.0% |
| Antifungals       | 0.0% | 0.0% | 0.0% |
| Antidepressants   | 0.0% | 0.0% | 0.0% |
| Anticonvulsants   | 0.0% | 0.0% | 0.0% |
| Antihypertensives | 0.0% | 0.0% | 0.0% |
| Antihyperlipidemics | 0.0% | 0.0% | 0.0% |
| Antibiotics       | 0.0% | 0.0% | 0.0% |
| Antineoplastics   | 0.0% | 0.0% | 0.0% |
| Antivirals        | 0.0% | 0.0% | 0.0% |
| Antipsychotics    | 0.0% | 0.0% | 0.0% |
| Antiretrovirals   | 0.0% | 0.0% | 0.0% |
| Antitumourals     | 0.0% | 0.0% | 0.0% |
| Antiulcer         | 0.0% | 0.0% | 0.0% |
| Other             | 0.0% | 0.0% | 0.0% |

*This analysis evaluated past medication related to a confirmed HZ case after the start of vaccine treatment. All groups received RZV, herpes zoster; N, number of patients with at least one confirmed HZ case in the mTVC group (number percentage) of patients with at least one event in the specified medication class. Medication classes include those with <1% prevalence (N=7,277 or 6,972).