

2. SYNOPSIS

Title: Non-interventional (observational) post-licensure study to assess the vaccine effectiveness and safety of recombinant zoster vaccine (RZV) in the rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) patient populations in adults 18 years of age and older

Keywords: Herpes zoster, vaccine effectiveness, vaccine safety, recombinant zoster vaccine, rheumatoid arthritis, inflammatory bowel disease

Rationale and background

Individuals with autoimmune disease (AID) are at higher risk of herpes zoster (HZ) compared to immunocompetent individuals. Studies have shown that the incidence rate of HZ among adults with rheumatoid arthritis (RA) is approximately twice the incidence rate of HZ among immunocompetent adults [Smitten, 2007; Yun, 2016]. Similarly, the incidence rate of HZ is higher among adults with inflammatory bowel disease (IBD), including ulcerative colitis (UC) or Crohn's disease (CD), than among immunocompetent adults [Gupta, 2006; Long, 2013; Yun, 2016; Khan, 2018]. Given the increased risk of HZ among those with AID, RZV may provide a substantial benefit to this at-risk population, but further studies are needed to examine its effectiveness and safety. In July 2021, the Food and Drug Administration (FDA) expanded the indication for RZV to include adults who are immunodeficient or immunosuppressed due to known disease or therapy [U.S. Food & Drug Administration, 2017]. This study aimed to provide vaccine effectiveness (VE) and safety data (risk of flare) in adult patients with RA and IBD, including UC or CD. The study was conducted at Kaiser Permanente Southern California (KPSC), an integrated health care system in the United States.

Research questions and objectives

The primary VE objectives were to estimate the 2-dose (4 weeks to 6 months apart) VE of RZV in preventing HZ in adults ≥ 18 years of age with RA or IBD, respectively. The primary safety objectives were to assess the risk of flares within 30 days following any RZV vaccination as compared to the risk in self-controlled comparison periods, in adults ≥ 18 years of age with RA or IBD, respectively. Secondary and exploratory objectives are detailed in Section 6.

Study design

This study examined the effectiveness and safety of RZV in adults with RA or IBD (UC or CD) at KPSC. The vaccine accrual period for the study extended from 04/2018 to 08/2023 with follow-up through 08/2024. For the primary VE objectives, an observational matched cohort design was used. Individuals ≥ 18 years of age who received 2 doses of RZV were up to 1:3 matched to RZV unvaccinated individuals by condition (RA, UC, CD), age, sex, race/ethnicity, and medication category. For the safety objectives, a self-controlled case series (SCCS) analysis was conducted among individuals aged ≥ 18 years with RA or IBD who received at least one dose of RZV.

Setting

Kaiser Permanente Southern California includes more than 4.6 million members. The demographic makeup of the KPSC membership closely mirrors the Southern California population.

To address primary VE objectives, 2-dose RZV cohorts were constructed for each autoimmune condition (RA and IBD). The primary VE analysis included eligible individuals who received 2 doses of RZV separated by 4 weeks to 6 months by the end of the accrual period and their unvaccinated matched counterparts.

To address the safety objectives, separate safety cohorts were constructed for RA and IBD and included individuals who received at least 1 dose of RZV.

Subjects and study size

The primary VE analyses included 7,565 RA (1,900 vaccinated and 5,665 unvaccinated) and 5,558 IBD (1,509 vaccinated and 4,049 unvaccinated) individuals. The RA safety cohort included 3,211 vaccinated individuals and the IBD safety cohort included 2,600 vaccinated individuals.

Variables and data sources

Individuals with at least 2 health care encounters with assigned ICD-10 codes for RA or IBD (UC or CD) in the year prior to and including the index date (date vaccine was received; same date was used for unvaccinated matched individuals) were identified from electronic health records (EHR). The primary exposure for VE analysis was 2 doses of RZV administered between 4 weeks and 6 months apart, identified from EHR codes. The primary outcome for VE analysis was HZ, identified by ICD-10 code and antiviral prescription. The primary outcome for safety analysis was clinically relevant flares identified from EHR by trained staff.

Results

The adjusted VE of 2 doses of RZV administered 4 weeks to 6 months apart against HZ in adults (≥ 18 years) was 57.2% (95% confidence interval [CI]: 39.0%, 69.9%) and 62.9% (95% CI: 34.3%, 79.1%) for RA and IBD patients, respectively. The risk of flares was comparable across the risk and comparison windows for recipients of RZV with RA (relative risk [RR]= 0.92, 95% CI: 0.70, 1.20) and IBD (RR= 0.80, 95% CI: 0.58, 1.12).

Discussion

Previous studies assessing the effectiveness and safety of RZV largely focused on older and immunocompetent adults. This study addressed an important gap in literature by expanding the inclusion criteria to include ≥ 18 -year-olds with RA and IBD using real-world data from a large integrated health care delivery network.

Conclusions

For adults with RA and IBD, 2 doses of RZV (4 weeks to 6 months apart) conferred protection against HZ with no elevated risk of flares observed following vaccination. Our findings support the recommendation to vaccinate adults with RA and IBD with 2 doses of RZV.

Marketing authorization holder

GlaxoSmithKline Biologicals S.A.

Names and affiliations of principal investigators

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