NON-INTERVENTIONAL STUDY REPORT

TITLE PAGE

Division: Research and Development

Information Type: Non-Interventional Study Report

Title:	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Compound Number:	GSK1437173A
Effective Date:	16 Jul 2026
Subject:	Effectiveness and safety of recombinant zoster vaccine in adults with psoriasis or psoriatic arthritis.
Author(s):	PPD
Indication Studied:	Prevention of herpes zoster in immunodeficient or immunosuppressed adults

STUDY INFORMATION

Title	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Report version identifier	216976
Date of last version of report	Final: 16 Jul 2026
EU PAS (ENCEPP) register number	EUPAS107230
Active substance	VZV glycoprotein E (gE)
Medicinal product	*Shingrix* (Recombinant Zoster Vaccine, RZV)
Product reference	EMA EU/1/18/1272/001-1 vial and 1 vial; EU/1/18/1272/002-10 vials and 10 vials FDA IND #013879
Procedure number	EMEA/H/C/004336
Marketing authorisation holder(s)	GlaxoSmithKline Biologicals S.A.
Joint PASS	No
Research question and objectives	Evaluate effectiveness (prevention of herpes zoster) and safety (risk of flares) of recombinant zoster vaccine among adults with psoriasis or psoriatic arthritis
Country(-ies) of study	United States
Author	PPD

MARKETING AUTHORISATION HOLDER(S)

Marketing authorisation holder(s)	GlaxoSmithKline Biologicals S.A. Rue de l'Institut, 89, 1330 Rixensart, Belgium
MAH contact person	PPD

STUDY DETAILS

UNIQUE IDENTIFIER	216976
TITLE	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
STUDY ACCOUNTABLE PERSON	PPD, NIS & Planning Study Delivery Lead
SCIENTIFIC LEAD	PPD, Global epidemology
CONTRIBUTING AUTHORS	Kaiser Permanente Southern California
ASSET ID	GSK1437173A
GSK ASSET	Recombinant Zoster Vaccine (Shingrix)
EFFECTIVE DATE	16 Jul 2026
INDICATION	Shingrix is indicated for the prevention of herpes zoster (HZ) and HZ-related complications, such as postherpetic neuralgia (PHN), in: • Adults 50 years of age or older; • Adults 18 years of age or older at increased risk of HZ (in the EU); and • Adults 18 years of age or older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy (in the US)

REPORT REVISION HISTORY

Date	Version	Change(s) since last version
16 Jul 2026	Original	N/A

SPONSOR SIGNATORY

Title: Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis

Compound Number: GSK1437173A

Elizabeth Chmielewski-Yee
Primary Author/NI Scientific Lead

Date (DD Month YYYY)

Huifeng Yun
Therapy Area Leader/+1 Manager

Date (DD Month YYYY)

Note: Not applicable if an eSignature process is used to get the sponsor approval.

INVESTIGATOR REPORT AGREEMENT PAGE

- I have read this report and confirm that to the best of my knowledge the study was carried out as described in this GSK report.
- I acknowledge that I was responsible for overall study conduct. I personally conducted or supervised the described clinical study.
- I ensured that all associates, colleagues, and employees assisting in the conduct of the study were informed about their obligations. Mechanisms were in place to ensure that site staff receive the appropriate information throughout the study.

Investigator Name:

Hung Fu Tseng

_____

Investigator Signature	Date (DD Month YYYY)

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LIST OF ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
AID	Autoimmune disease
AIDS	Acquired Immunodeficiency Syndrome
ASD	Absolute standardized difference
CSF	Cerebrospinal fluid
CI	Confidence interval
COVID-19	Coronavirus disease 2019
CVX	Vaccine administered code set
DMARD	Biologic disease-modifying anti-rheumatic drug
ED	Emergency Department
EnCePP	European Network of Centers for Pharmacoepidemiology and Pharmacovigilance
EHR	Electronic health record
EMA	European Medicines Agency
EU	European Union
EU PAS	European Union Electronic Register of Post-Authorisation Studies
FDA	Food and Drug Administration
GSK	GlaxoSmithKline Biologicals S.A.
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HR	Hazard ratio
HZ	Herpes zoster
ICD	International Classification of Diseases

IRB	Institutional Review Board
IRR	Incidence rate ratio
JAK	Janus Kinase
KPSC	Kaiser Permanente Southern California
MTX	Methotrexate
NB-UVB	Narrowband ultraviolet B
NSAID	Nonsteroidal Anti-Inflammatory Drug
OSM	Oral small molecule
PASS	Post-Authorization Safety Studies
PCV	Pneumococcal conjugate vaccine
PDT	Photodynamic therapy
PHI	Protected Health Information
CCI [redacted]	
PsA	Psoriatic arthritis
PsO	Psoriasis
PUVA	Psoralen and ultraviolet A
RZV	Recombinant zoster vaccine
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SCCS	Self-Controlled Case Series
SD	Standard Deviation
Tdap	Tetanus, Diphtheria, and Acellular Pertussis Vaccine
TNF	Tumor Necrosis Factor
U.S.	United States
UV	Ultraviolet
VE	Vaccine effectiveness

VZV	Varicella Zoster Virus
ZVL	Zoster Vaccine Live

TRADEMARK INFORMATION

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1. RESPONSIBLE PARTIES

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Epidemiology Head	PPD
Study Delivery Lead	PPD

2. SYNOPSIS

Title: Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis

Keywords

Herpes zoster, vaccine effectiveness, vaccine safety, recombinant zoster vaccine, psoriasis, psoriatic arthritis

Rationale and background

Studies have shown higher incidence of herpes zoster (HZ) in individuals with conditions/treatments associated with altered immune function, compared to the general population. Robust, real-world data on the effectiveness and safety of recombinant zoster vaccine (RZV) in such at-risk populations are needed to help inform patient and physician decision-making regarding vaccination against HZ. This observational study evaluated the vaccine effectiveness (VE) and safety of RZV in adults with psoriasis (PsO) or psoriatic arthritis (PsA) at Kaiser Permanente Southern California (KPSC).

Research questions and objectives

The primary and secondary VE objectives estimated the VE of 2 doses of RZV in preventing HZ in adults ≥18 years of age with PsO or PsA. One-dose VE was estimated, and the baseline characteristics of the RZV-vaccinated and unvaccinated cohorts were described as secondary VE objectives. The primary and secondary safety objectives assessed the incidence rate ratio of flares within 30 days following RZV vaccination compared to self-controlled comparison windows in adults ≥18 years of age with PsO or PsA with flares. CCI [redacted]
CCI [redacted]
CCI [redacted]

Study design

This study evaluated the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA at KPSC. Accrual occurred from 01 April 2018 up to 31 December 2023 with follow-up through 31 December 2024 for HZ outcomes, CCI [redacted]
CCI [redacted]. For VE objectives, an observational matched cohort design was used in which RZV vaccinated individuals were compared to matched RZV unvaccinated individuals. For safety objectives, a self-controlled case series design was used to evaluate the rate of flare within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows.

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 VE objectives, 2-dose and 1-dose RZV cohorts were constructed for each autoimmune condition (PsO, PsA). The VE analyses included eligible individuals who received 1 or 2 doses of RZV by the end of the accrual period and their unvaccinated matched counterparts.

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

Subjects and study size

The 2-dose VE analyses included 10,381 PsO (2,616 vaccinated and 7,765 unvaccinated) and 2,163 PsA (548 vaccinated and 1,615 unvaccinated) individuals. The 1-dose VE analyses included 5,171 PsO (1,300 vaccinated and 3,871 unvaccinated) and 1,067 PsA (268 vaccinated and 799 unvaccinated) individuals. The PsO safety cohort included 3,086 vaccinated individuals and the PsA safety cohort included 1,073 vaccinated individuals.

Variables and data sources

Individuals with at least 2 health care encounters with assigned International Classification of Diseases (ICD-10) codes for PsO or PsA in the year prior to and including the index date (for VE analyses, this was the date of the 2nd dose for 2-dose analyses and date of the 1st dose for 1-dose analyses with the same date was used for unvaccinated matched individuals; for safety analyses, this was the vaccination date of the first RZV dose) were identified from electronic health records (EHR). RZV was identified from EHR using vaccine administered code sets (CVX). The exposure for 2-dose VE analysis was defined as 2 doses of RZV administered at least 4 weeks apart. The primary outcome for VE analysis was HZ, identified by ICD-10 codes and antiviral prescriptions. 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 against HZ in adults (≥18 years) was 60.7% (95% confidence interval [CI]: 40.5%, 74.0%) and 80.5% (95% CI: 34.3%, 94.2%) for PsO and PsA patients, respectively. The adjusted VE of 1 dose of RZV against HZ in adults (≥18 years) was 30.6% (95% CI: -29.6%, 66.1%) for PsO patients, and could not be estimated in PsA patients due to small sample size. The rate of flares was comparable across the risk and comparison windows for recipients of RZV with PsO (incidence rate ratio [IRR]= 0.94, 95% CI: 0.58, 1.52) and PsA (IRR= 1.21, 95% CI: 0.69, 2.13).

Discussion

Previous work evaluating the effectiveness and safety of RZV has largely focused on immunocompetent adults and older populations. This study also addressed the younger, immunocompromised population by expanding inclusion criteria to include ≥18-year-olds with PsO and PsA using real-world data from a large integrated health care delivery network.

Conclusions

For adults with PsO and PsA, 2 doses of RZV conferred protection against HZ with no statistically significant elevated rate of flares observed in the 30 days following vaccination. Our findings support the recommendation to vaccinate adults with PsO and PsA with 2 doses of RZV.

Marketing authorization holder

GlaxoSmithKline Biologicals S.A.

Names and affiliations of principal investigators

Hung Fu Tseng, Kaiser Permanente Southern California

2.1. Abstract

In accordance with Regulation (EU) No 520/2012, an abstract of the final study report is required for Post-Authorization Efficacy Studies and Post-Authorization Safety Studies (PASS). The abstract is included in *Annex 2*.

3. AMENDMENTS AND UPDATES

None

4. MILESTONES

Milestone	Planned date	Actual Date	Comments
Start of data collection	23 October 2023	23 October 2023	
End of data collection	29 August 2025	22 August 2025	<<Text>>
Registration in the EU PAS register	<<Date>>	20 October 2023	<<Text>>
Final report of study results	26 June 2026	16 Jul 2026	<<Text>>

5. RATIONALE AND BACKGROUND

Herpes zoster (HZ), or shingles, is an often-painful vesicular rash caused by reactivation of varicella zoster virus (VZV) persisting latently in dorsal root ganglia [Gnann, 2002; Dworkin, 2007]. The pain from acute HZ can be disabling, and if complicated by the development of postherpetic neuralgia (PHN), can last for months or years. Before a vaccine was introduced, about one million episodes of HZ occurred in the United States (U.S.) annually [Harpaz, 2008]. Aside from increasing age and immunosuppression, other risk factors for this condition are not well known [Thomas, 2004], but some evidence suggests that sex, race/ethnicity, family history, and comorbidities may be associated with the occurrence of HZ [Kawai, 2017].

Studies have shown higher incidence of HZ in individuals with conditions/treatments associated with altered immune function, compared to the general population. Individuals with psoriasis (PsO) or psoriatic arthritis (PsA) have been reported to be at increased risk for developing HZ, compared with the general population; this increased risk persisted when immunosuppressive effects of systemic therapy were controlled for [Baumrin, 2019]. A U.S. study using claims data estimated the incidence of HZ among individuals aged ≥18 years with PsO to be approximately 8 per 1,000 person-years [Chen, 2014], two times higher than in the general U.S. population (3 to 4 per 1,000 person-years) [Insinga, 2005; Mullooly, 2005; Yawn, 2007]. Further, a U.S. study using nationwide inpatient data demonstrated an association between HZ-related hospitalizations and PsO (odds ratio: 1.4, 95% confidence interval [CI]: 1.1, 1.7) [Chovatiya, 2021]. Similarly, a U.S. study using linked insurance data reported higher age-specific incidence rates of HZ in individuals with PsA than in healthy individuals (incidence rates per 1,000 person-years in individuals with PsA vs. healthy individuals = 9.8 vs. 3.3, 8.5 vs. 3.9, and 13.2 vs. 5.8, for 31-40-year, 41-50-year, and 51-60-year age groups, respectively) [Yun, 2016]. Systemic therapies further increase the risk of HZ in individuals with PsO or PsA, although the risk may vary depending on disease severity and type of therapy [Baumrin, 2019]. Recent data have shown that biological therapies, especially anti-tumor necrosis

factor (TNF)-α inhibitors and combinations of anti-TNF-α agents, Janus kinase (JAK)-inhibitors, and conventional disease-modifying anti-rheumatic drugs (c-DMARDs), contribute to the increased risk of HZ in individuals with PsO or PsA [Winthrop, 2017a; Winthrop, 2017b; Zou, 2021; Chiu, 2022].

Recombinant zoster vaccine (SHINGRIX, RZV), is a subunit, adjuvanted vaccine approved by the U.S. Food and Drug Administration (FDA) in October 2017 for the prevention of HZ in adults ≥50 years of age. Two RZV doses are necessary with the second dose recommended 2-6 months after the first [Anderson, 2022]. If the second dose is administered <4 weeks after the first dose date, the Advisory Committee on Immunization Practices (ACIP) recommends repeating the second dose ≥4 weeks after the first. However, the first dose does not need to be repeated if ≥6 months have elapsed since the first dose. In July 2021, the FDA expanded the indication for use of RZV for the prevention of HZ in adults aged ≥18 years who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy [FDA, 2017]. For individuals who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule, the second dose may be administered 1-2 months after the first dose. The ACIP recommended RZV vaccination for the prevention of HZ and related complications in immunocompetent adults aged ≥50 years and adults aged ≥19 years who are or will be immunodeficient or immunosuppressed because of disease or therapy [Dooling, 2018; Anderson, 2022]. The expansion of RZV recommendations to these high-risk populations (i.e., patient populations for whom zoster vaccine live [ZVL] was largely contraindicated) helped address an unmet medical need for HZ prevention. Real-world, population-based data on RZV in these complex patient populations, including individuals with autoimmune diseases (AID), is needed to assess the vaccine effectiveness (VE) and safety of RZV.

GSK has previously conducted some clinical trials of RZV in patient populations at increased risk for HZ (i.e., those with hematopoietic stem cell transplant, solid tumors, hematologic malignancy, human immunodeficiency virus [HIV] and renal transplant). However, data on the effectiveness and safety of RZV in other populations at increased risk, including those with AID, especially those on newer immunomodulating agents, are limited. Robust, real-world data are needed to help inform patient and physician decision-making regarding vaccination against HZ in these at-risk populations.

Therefore, we conducted an observational study at Kaiser Permanente Southern California (KPSC), a large integrated U.S. health care system, to evaluate the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA.

6. RESEARCH QUESTION AND OBJECTIVE(S)

This study assessed VE and safety of RZV among individuals at KPSC with PsO or PsA. For VE, individuals who received RZV ("vaccinated") were compared to individuals who did not receive RZV ("unvaccinated"). For safety, the rate of flares in pre-defined risk windows were compared to comparison windows within RZV-vaccinated individuals. Individuals who had both PsO and PsA were included in both the PsO and PsA analyses. The study population is described in detail in Section 7.2.2.

6.1. Vaccine Effectiveness Objectives

Primary VE objective:

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsO.

Secondary VE objectives:

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsO or PsA.
2. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsA.
3. To estimate the VE of 1 dose of RZV in preventing HZ in Southern California adults with PsO or PsA, separately.
4. To describe baseline characteristics of individuals vaccinated with 2 doses of RZV compared to their unvaccinated matches in Southern California adults ≥18 years of age with PsO or PsA, separately.

Exploratory VE objective:

CCI [redacted]

6.2. Safety Objectives

Primary safety objective:

1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows, in Southern California adults ≥18 years of age with PsO.

Secondary safety objectives:

1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows, in Southern California adults ≥18 years of age with PsO or PsA.

2. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows, in Southern California adults ≥18 years of age with PsA.

7. RESEARCH METHODS

7.1. Study Design

7.1.1. Overview

This study examined the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA at KPSC. For effectiveness objectives, the vaccine accrual period for individuals aged 18-49 years extended from 01 April 2018 to 31 December 2023 with follow-up through 31 December 2024 for the HZ and CCI [redacted] CCI [redacted]. The accrual period for individuals aged ≥50 years was 01 April 2018 to 30 September 2022 with follow-up through 31 December 2024 and 30 June 2025 for HZ and CCI [redacted] outcomes, respectively. For the safety objectives, in individuals with PsO aged ≥50 years, the accrual period was 01 April 2018 to 30 June 2022. For the safety objectives, in individuals with PsA aged ≥50 years, the accrual period was 01 April 2018 to 31 December 2022. For the safety objectives, in individuals with PsO or PsA aged 18-49 years, the accrual period was 01 April 2018 to 31 December 2023. The variability in accrual periods is explained by the accrual period for individuals aged ≥50 years ending once the target sample size was met. The safety observation time was partitioned into a 30-day risk window right after each RZV dose, a 30-day pre-vaccination comparison window, and a 30-day post-vaccination comparison window.

Due to the coronavirus disease 2019 (COVID-19) pandemic indirectly impacting health care delivery and vaccine seeking behaviors, subjects were not accrued in the study from March through December 2020. VE and safety outcomes were still assessed during this period. The impact COVID-19 might have had on health care utilization was unlikely to differ among RZV-vaccinated and unvaccinated individuals or during risk and comparison windows, thus any outcome misclassification resulting from the impact of COVID-19 was expected to be non-differential.

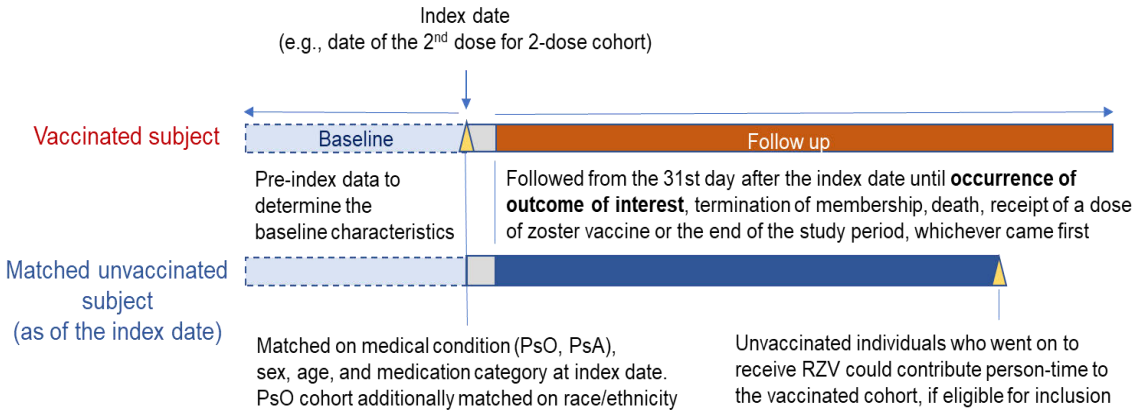
7.1.2. Vaccine Effectiveness

For the VE objectives, an observational, retrospective matched cohort design was used (Figure 1). For 2-dose VE objectives, the index date was defined as the date of receipt of the second dose of RZV (≥4 weeks after the first dose) for vaccinated individuals; the same date was assigned as the index date to their matched unvaccinated counterparts who had not been vaccinated as of the index date. Individuals ≥18 years of age who received a second dose of RZV were matched up to 1:3 without replacement to unvaccinated individuals on the following variables: age, sex, medical condition (PsO, PsA), and medication category at index date. PsO cohorts were additionally matched on race/ethnicity. For secondary VE objective 3 (1-dose VE objective), the date of the first dose of RZV was used as the index date.

Individuals were followed through the KPSC electronic health records (EHRs) from the 31st day after the index date until occurrence of outcome of interest, termination of membership, death, receipt of a dose of zoster vaccine (receipt of a third dose for 2-dose vaccinated individuals, receipt of a second dose for 1-dose vaccinated individuals, or receipt of a first dose for unvaccinated individuals or receipt of ZVL), or end of the study period, whichever came first. Individuals were followed from 31 days after index date to allow sufficient time for development of immunity in the vaccinated cohort and to avoid capture of pre-existing HZ episodes.

Primary analysis assessed 2-dose VE in individuals with PsO. Secondary analyses assessed 2-dose VE in individuals with PsO or PsA or individuals with PsA.. Analyses were performed overall and stratified by timing of the second dose of RZV (second dose given 4 weeks-6 months or >6 months after first dose), by age group (18-49 years or ≥50 years), by medication category, and by time elapsed since index date (in years). Additional secondary analyses examined 1-dose VE and described baseline characteristics of individuals in the vaccinated and unvaccinated cohorts. CCI [redacted]
CCI [redacted]

Figure 1 Matched Cohort Design Overview for VE Analysis



7.1.3. Safety

For safety objectives, a self-controlled case series (SCCS) analysis was conducted among individuals aged ≥18 years with PsO or PsA and flares who received ≥1 dose of RZV. The date of vaccination with the first dose of RZV was defined as Day 0. The observation time was partitioned into a 30-day risk window immediately following each RZV dose, a 30-day pre-vaccination comparison window, and a 30-day post-vaccination comparison window (details in Section 7.3.1.2). The rate of flare in the risk window was compared with that in the comparison window. There was a washout window before the date of vaccination. For the first dose, the wash out window was 60 days, and for the second dose, the washout window varied based on time between doses.

Given the complexity of accurately ascertaining disease flares, the EHRs were manually reviewed for these individuals to identify occurrence of flare rather than relying on administrative data. A flare was identified by documented contact with a health care provider, and new or worsening signs and/or symptoms suggestive of a flare, and a change in medication for flare (Appendix A). For primary analyses, the rate of flares in pre-defined risk windows compared to comparison windows was assessed for PsO. Secondary analyses assessed the rate of flares in individuals with PsO or PsA or individuals with PsA. Analyses for individuals with PsO or PsA were conducted overall and stratified by RZV dose, by age group (18-49 years or ≥50 years), and by medication category.

7.2. Study Population/Subjects and Setting

7.2.1. Study Setting

KPSC is one of the largest not-for-profit health plans and integrated health care systems in the U.S., providing an ideal environment for population-based research. KPSC's population includes at least 4.6 million members, of whom 2,075,288 were aged 18-49 years, and 1,632,097 were aged ≥50 years as of 01 January 2022. The diverse demographic makeup, including 260 different ethnicities and more than 150 different languages, closely mirrors the Southern California population [Koebnick, 2012]. Compared to the racial/ethnic distribution of the U.S. population, KPSC membership is composed of twice as many Asian/Pacific Islanders and 3 times as many Hispanic individuals.

KPSC facilities include hospitals and medical offices, all linked by an information infrastructure that supports both clinical practice and business needs. Health information from this infrastructure can be leveraged for research purposes. KPSC membership is known for its stability; >90% of members remain in the health plan after one year; and more than 75% remain after 3 years. The large, diverse, and stable population allows for rapid accrual of a large, representative cohort with the ability to evaluate long-term implications of immunization.

KPSC began administering ZVL in late 2006 when it was first recommended by the ACIP and the KPSC Regional Immunization Practice Committee. In 2017, the ACIP recommended RZV preferentially over ZVL. Since April 2018, RZV has been the preferred HZ vaccine for routine use and the standard of care for the prevention of HZ in adults aged ≥50 years at KPSC. With the FDA's expanded indication for RZV to include immunocompromised adults aged ≥18 years in July 2021, KPSC has expanded use of RZV to this population.

7.2.2. Study Population

To address VE related study objectives, two study cohorts were constructed, the 2-dose RZV cohort and 1-dose RZV cohort, for each condition (PsO and PsA). Individuals were eligible for the VE study cohort if the eligibility criteria detailed below were met.

The 2-dose RZV cohort included eligible individuals who received 2 doses of RZV separated by at least 4 weeks by the end of the accrual period. The index date was the vaccination date of the second RZV dose. RZV unvaccinated individuals who met the inclusion/exclusion criteria and were unvaccinated on the index date were randomly selected and up to 3:1 matched to the 2-dose RZV vaccinated individuals by age group (18-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, and 80+ years), sex, condition (PsO, PsA), and medication category at index date. The PsO cohort was additionally matched on race/ethnicity (White, Black, Hispanic, Asian, and Other), given its sufficient sample size. Individuals with both PsO and PsA were included in both the groups for matching. Matching for the PsO group and the PsA group was conducted separately. Vaccinated individuals with both PsO and PsA were matched to unvaccinated individuals with both conditions if sufficient matches were found. Otherwise, they were matched to unvaccinated individuals with PsO only in the PsO cohort and unvaccinated individuals with PsA only in the PsA cohort. For secondary objective 1 to estimate the VE of RZV among individuals with PsO or PsA, vaccinated individuals with PsO only and their matches were added to the PsA cohort. The index date for the 2-dose RZV unvaccinated match was the same as his/her matched 2-dose RZV vaccinated counterpart. Flow charts with inclusion/exclusion criteria applied for the 2-dose RZV cohort with PsO and the 2-dose RZV cohort with PsA are provided (Section 14, Figure 3 and Figure 4).

The 1-dose RZV cohort included eligible individuals who received 1 dose of RZV but did not receive a 2nd dose within 6 months after the 1st dose during the vaccine accrual period. Such individuals might have received a 2nd RZV dose more than 6 months after the 1st RZV dose or no subsequent RZV doses by the end of the accrual period. The index date was the vaccination date of the 1st dose of RZV. RZV unvaccinated individuals who met the eligibility criteria and were unvaccinated on the index date were randomly selected and up to 3:1 matched to the 1-dose RZV vaccinated individuals using the same matching algorithm described for the 2-dose RZV cohort above. An unvaccinated individual was allowed to be matched to both a vaccinated individual in the 2-dose RZV cohort and a vaccinated individual in the 1-dose RZV cohort. The index date for the 1-dose RZV unvaccinated match was the same as his/her matched 1-dose RZV vaccinated counterpart. Flow charts with inclusion/exclusion criteria applied for the 1-dose RZV cohort with PsO and the 1-dose RZV cohort with PsA are provided (Section 14, Figure 5 and Figure 6).

To address the safety objectives, individuals who received at least 1 dose of RZV were eligible for the safety cohort if the following eligibility criteria were met. The index date was the vaccination date of the 1st RZV dose.

7.2.2.1. Eligibility Criteria

Inclusion Criteria

VE Objectives

Individuals aged ≥18 years at index date with ≥1 year of continuous KPSC membership prior to the index date and until 31 days after index date (allowing for a 31-day gap in membership) with at least 2 health care encounters with assigned International Classification of Diseases, 10th Revision (ICD-10)codes for PsO or PsA in the year prior to and including the index date, as defined below, were included. This algorithm was selected based on the literature [Lee, 2021], and KPSC chart review indicated a high positive predictive value of this approach (100% for both PsO and PsA among 10 samples for each condition).

Safety Objectives

Individuals aged ≥18 years at index date who received ≥1 dose of RZV during the accrual period with ≥1 year of continuous KPSC membership prior to and including the index date (allowing for a 31-day gap in membership) with at least 2 health care encounters with assigned ICD-10 codes for PsO or PsA in the year prior to and including the index date, as defined below, were included.

Psoriasis (for primary VE objective 1, secondary VE objectives 1, 3, and 4, CCI [redacted]; for primary safety objective 1, secondary safety objective 1)

- L40.0: Psoriasis vulgaris
- L40.1: Generalized pustular psoriasis
- L40.2: Acrodermatitis continua
- L40.3: Pustulosis palmaris et plantaris
- L40.4: Guttate psoriasis
- L40.8: Other psoriasis
- L40.9: Psoriasis, unspecified

Psoriatic arthritis (for secondary VE objectives 1, 2, 3, and 4, CCI [redacted]; for secondary safety objectives 1 and 2)

- L40.50: Arthropathic psoriasis, unspecified
- L40.51: Distal interphalangeal psoriatic arthropathy
- L40.52: Psoriatic arthritis mutilans
- L40.53: Psoriatic spondylitis
- L40.59: Other psoriatic arthropathy

Individuals with both PsO and PsA were included in analyses for both conditions.

Exclusion Criteria

VE Objectives

For VE objectives, individuals with an HZ diagnosis in the 6 months prior to the index date were excluded to ensure that HZ diagnoses after the index date were new, rather than carried over from HZ episodes prior to the index date. Individuals with HZ occurring on or within 30 days after the index date for both vaccinated and unvaccinated groups were also excluded since it would be unclear if the HZ episode began before or after the index date and whether the length of time since vaccination (for RZV vaccinated individuals) was long enough to allow for sufficient development of immunity. Individuals who received a dose of zoster vaccine within 30 days after the index date or died during the 30 days after the index date were also excluded to prevent individuals from being censored before follow-up began.

Safety Objectives

Individuals who received a second RZV dose <4 weeks (28 days) after the first dose were excluded, because ACIP guidelines state that these individuals must repeat the second dose [Dooling, 2018].

7.3. Variables

7.3.1. Exposure

RZV doses were identified using CVX code 187: Zoster vaccine recombinant.

7.3.1.1. VE exposure

Although RZV should be administered as 2 doses separated by 2-6 months, ACIP guidance followed at KPSC specifies that a 2nd dose administered <4 weeks after the 1st dose should be repeated, but a 2nd dose administered ≥4 weeks after the 1st dose does not need to be repeated [Anderson, 2022]. Furthermore, due to variation in real-world practice, the 2nd dose may be given earlier than 2 months after the 1st dose or later than 6 months after the 1st dose. Additionally, as of 21 January 2022, ACIP guidelines indicate that the 2nd dose of RZV can be administered 1–2 months after the 1st dose for individuals who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule [Anderson, 2022]. Therefore, VE objectives refer to 2 doses of RZV given at least 4 weeks apart through the end of the study accrual, except where it was indicated otherwise.

The exposure for primary VE objective 1, secondary VE objectives 1, 2, and 4, and CCI was 2 doses of RZV administered ≥4 weeks apart during the study accrual period. The index date was the date of receipt of the second RZV dose.

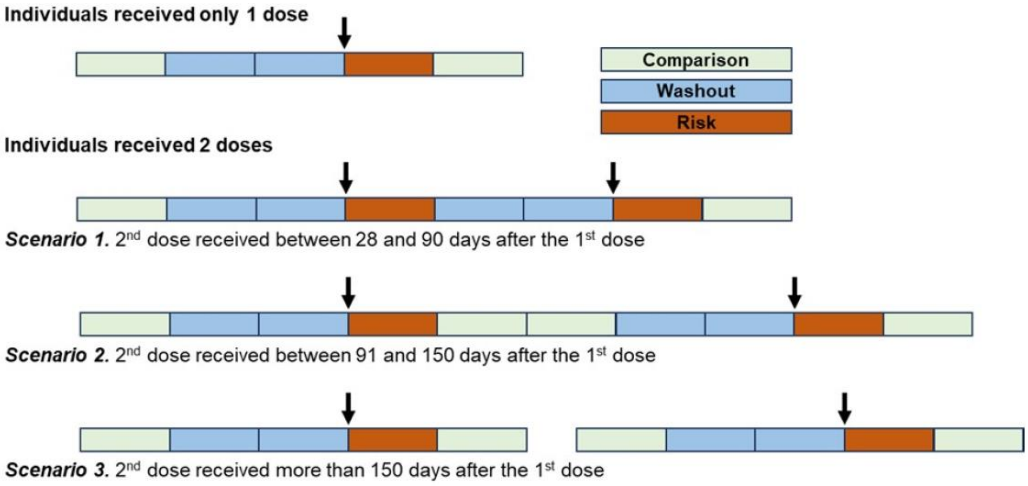
The exposure for secondary VE objective 3 was the first dose of RZV. The 1-dose VE was evaluated in individuals who received only 1 dose of RZV during the accrual period as well as those who received a second dose of RZV >6 months from the first dose during the accrual period, with 1-dose person-time having been censored upon receipt of a second RZV dose. Individuals who received a second RZV dose within 6 months of their first dose were not included in the 1-dose analysis due to the short follow-up period and lack of unvaccinated individuals for matching. The index date was the date of receipt of the first RZV dose.

7.3.1.2. Safety exposure

An SCCS design (Figure 2 below) was used. For patients receiving only 1 dose of RZV, the date of vaccination with the 1st dose of RZV was defined as Day 0, the risk window was defined as +1 to +30 days, and comparison windows were defined as -90 to -61 days and +31 to +60 days (Figure 2 below, Individuals received only 1 dose). The washout window was defined as -60 to -1 days. The 30-day risk window was determined based on prior literature, vaccine mode of action, and consultation with external physician experts (rheumatologists and dermatologists) [Sbidian, 2014; Didierlaurent, 2017; Winthrop, 2017a; Baumrin, 2019; Stevens, 2020; Dagnew, 2021; Gupta, 2022; Spinelli, 2022].

For individuals who received a 2nd dose of RZV between ≥4 weeks and 300 days of the 1st RZV dose, there were several scenarios for additional risk and comparison windows. If the 2nd dose was received between +28 to +90 days after the 1st dose, the risk window after the 1st dose was immediately followed by a washout window up to receipt of the 2nd dose (Figure 2 below, Scenario 1). In Scenario 1, the risk window after the 1st dose was between 28 and 30 days and the subsequent washout window was between 0 and 60 days. If the 2nd dose was received between +91 to +150 days after the 1st dose, the risk and comparison windows following the 1st dose were followed by a 60-day washout window immediately before the receipt of the 2nd dose (Figure 2 below, Scenario 2). In Scenario 2, the comparison window between 2 doses was between 1 and 60 days. If the 2nd dose were received between +151 days to +300 days after the 1st dose, the comparison window was -90 to -61 days prior to the 2nd dose and the washout window was -60 to -1 days prior to the 2nd dose (Figure 2 below, Scenario 3). The maximum follow-up window was set to 360 days after the 1st dose (maximum 300 days between first and second dose plus the 30-day risk window and the 30-day comparison window). Scenarios 1-3 in Figure 2 below represent the maximum time period between the 1st and 2nd dose.

Figure 2 SCCS Design Overview for Safety Analysis



7.3.2. Outcome

7.3.2.1. VE outcomes

HZ

The primary outcome was HZ, identified by ICD-10 code B02.xx in any health care setting (outpatient [including virtual visits], inpatient, Emergency Department [ED]) and a prescription for a non-topical antiviral (acyclovir, valacyclovir, famciclovir) in the 7 days before or after the HZ diagnosis code date, without a non-topical antiviral (acyclovir, valacyclovir, famciclovir) prescribed in the 183 days to 8 days prior to the HZ diagnosis code date [Langan, 2013; Tseng, 2020]. The first eligible HZ diagnosis after the index date was considered an incident HZ event.

CCI [redacted]

CCI

7.3.2.2. Safety outcomes

The outcome for primary and secondary safety objectives was flare, defined as new-onset flare or new-onset of disease worsening of PsO (primary safety objective 1, secondary safety objective 1) or PsA (secondary safety objectives 1 and 2). All individuals eligible for the safety objectives with health care encounters during pre-specified review windows (i.e., risk windows, comparison windows, and the 30 days after the end of risk or comparison windows) were identified for chart review. Among them, disease flare was assessed through EHR review by trained research associates and specialists (dermatologists and rheumatologists). Events were counted in the period in which the earliest symptom onset occurred. Cases with unclear signs and/or symptoms, dates of onset, or changes in medication for flare were reviewed by a dermatology or rheumatology specialist. The criteria for clinically relevant flare are described in Appendix A.

7.3.3. Other variable definitions

Other variables identified from the EHR and considered in analyses when appropriate as covariates, included:

- Demographic variables: age at index date, sex, race/ethnicity
- Health care utilization (number of outpatient [including virtual visits]/ED/inpatient encounters) in the year prior to the index date
- Comorbidities (kidney disease, heart disease, lung disease, liver disease, diabetes, other AID, severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2 infection]/COVID-19 diagnosis) in the year prior to the index date
- Immunocompromised status (HIV/acquired immunodeficiency syndrome [AIDS], leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications) assessed at index date

- History of ZVL or varicella vaccination prior to the index date based on dates of vaccinations in the EHR
- History of HZ prior to the index date identified using ICD-10 codes (B02.xx) and ICD-9 codes (053.xx) from hospital, outpatient (including virtual visits), and ED settings
- Concomitant vaccinations defined as receipt of vaccines such as influenza vaccine, pneumococcal conjugate vaccine (PCV)/pneumococcal polysaccharide vaccine (PPSV), tetanus, diphtheria, and acellular pertussis (Tdap) vaccine, or COVID-19 vaccine at the time (same date) of either the 1st or 2nd dose of RZV
- Medication category as detailed in Appendix B
- Membership history: length of continuous membership (allowing 31 days gap) prior to the index date.

7.3.3.1. Additional considerations

Other variables/confounders for safety objectives

The SCCS design inherently controls for fixed individual-level confounders. With comparison windows before and after the risk window, the design also controls for time-varying covariates such as age and seasonality.

Effect modifiers

We performed stratified analyses: (1) by time between first and second dose of RZV (4 weeks – 6 months, >6 months) for primary VE objective 1 and secondary VE objective 2; (2) by age (18–49 years, ≥50 years, 50–59 years, 60–69 years, and 70+ years) for primary VE objective 1 and secondary VE objective 2, and primary safety objective 1 and secondary safety objective 2; and (3) by medication category at baseline (primary VE objective 1 and secondary VE objective 2, and primary safety objective 1 and secondary safety objective 2).

7.4. Data sources

The KPSC EHR system was the data source for extracting information on exposures, outcomes, and covariates. Kaiser Permanente Health Connect is the largest civilian EHR system available in the U.S. In addition to supporting patient care, this robust system facilitates research, providing access to the EHR for the KPSC vaccine research team. Up-to-date details of patient care were available and accessible to researchers. Data regarding demographics, services, and diagnoses were tracked from the outpatient, ED, and hospital settings.

Pharmacy and vaccination utilization were linked through patients' unique medical record numbers. As KPSC is a pre-paid health care system, recommended vaccines such as RZV were provided to KPSC members at no charge and could be obtained at no-cost nurse visits or on a walk-in basis without appointment, which was an incentive for members to receive immunizations within the system. Vaccinations received outside of the health plan with appropriate documentation were also recorded in KPSC databases.

KPSC members had very strong motivation to use services internally. For outside providers to be reimbursed by the health plan for covered emergent or contract care, claims must be submitted with documentation of the episode of care, which was integrated into administrative data systems. Thus, the capture of care should have been very comprehensive. Care received at KPSC was updated and available to researchers in near real time. Claims data are typically over 90% complete after 3 months.

7.5. Bias

Some of the potential limitations of this study included residual confounding, misclassification, and misdiagnosis of HZ. These limitations are discussed in detail in Section 10.2.

7.6. Study size

Based on our power calculation for the primary VE objective, in a cohort study with a 1:3 matching ratio and an average 4.1 years of follow-up, and a censoring rate of 7% per year in the RZV vaccinated group (due to termination of membership, death, or receipt of an additional dose of zoster vaccine) and 25% per year in the RZV unvaccinated group (due to termination of membership, death, or receipt of zoster vaccine), the number of vaccinated subjects needed to detect a VE of 60% with 80% power and a type 1 error rate of 5% was 624, assuming that the incidence of HZ in the unvaccinated population was 12 cases per 1,000 person-years.

Our SCCS design required at least 49 events in the comparison window to achieve 80% power of detecting an increased flare rate of incidence rate ratio (IRR) =1.8 with a type 1 error rate of 5%, assuming the length of comparison window was twice of the length of risk window. With the same assumptions made, this design required 34 events in the comparison window to detect an increased flare rate of IRR=2.

The 2-dose RZV cohorts for PsO and PsA had 2,616 and 548 vaccinated patients, respectively. For the safety objectives, 42 and 26 events were recorded in the comparison windows for PsO and PsA, respectively.

7.7. Data analysis

Only descriptive analyses were performed when the number of cases was too small (<5 cases in the vaccinated cohort) to produce meaningful results for any study objective.

7.7.1. Primary analysis

7.7.1.1. Main analytical approach

For the VE analyses, the number and characteristics of vaccinated and unvaccinated individuals in each cohort were described and compared. Categorical variables were presented as absolute numbers and percentages with p-values using the Pearson χ^2 test or Fisher's exact test, as appropriate. For continuous variables such as age in years, mean with standard deviation (SD) and median with interquartile range were calculated, with p-values using the two-sample t-test or Wilcoxon rank-sum test, as appropriate. Absolute standardized differences (ASD) were calculated to assess the balance of covariates [Austin, 2011]. Potential confounders were determined by scientific relevance and association with exposure (ASD >0.1). Immunocompromised status and history of HZ, which were considered important risk factors, were kept in the adjusted model regardless of their association with exposure.

For the primary VE objective, the number of incident HZ cases and the number of person-years of follow-up were assessed for 2-dose RZV vaccinated individuals and unvaccinated matched individuals in the PsO cohort. The incidence of HZ was calculated by dividing the number of incident HZ cases by the total number of person-years. Unadjusted and adjusted hazard ratios (HRs) and 95% CIs comparing HZ incidence rates in the 2-dose RZV cohort and the matched unvaccinated cohort were estimated by Cox stratified proportional hazards regression models without and with adjusting for potential confounders described above. VE analyses in PsO patients were stratified by time between first and second dose (4 weeks to 6 months, >6 months), age group at index date (18-49 years, ≥50 years, further divided in 50-59, 60-69, and ≥70 years), medication category, and year after index date. For stratified analyses, subgroups were recategorized in post-hoc analyses when sample size in a subgroup was small. Estimates of VE (%) were calculated as (1 –HR) × 100 when the HR was less than or equal to 1, and ([1/HR] – 1) × 100 when the HR was greater than 1. In addition to assessing the VE of 2 doses of RZV, the cumulative incidence of HZ was estimated by the Kaplan–Meier method. Vaccinated and unvaccinated cumulative incidence estimates were plotted, and the difference between the two curves was tested by the log-rank test.

For the primary safety analyses, characteristics of individuals with PsO or PsA who met inclusion criteria were described. Incidence rates for PsO or PsA flare during risk windows and comparison windows were calculated by dividing the number of flares by person-time. The IRR (95% CI) for flare comparing risk and comparison windows overall and by 1st dose and 2nd dose were estimated using conditional Poisson regression [Whitaker, 2006]. Analyses were also stratified by age (18-49 years, ≥50 years) and by medication category at baseline. To describe the secular patterns, incidence of flare by day from Day -90 to Day 60 of Dose 1 and Dose 2 were plotted.

7.7.1.2. Data handling conventions/data transformations

Coding for exposures and outcomes is described in Section 7.3

7.7.1.3. Sensitivity analyses

Sensitivity analyses were conducted among the 2-dose RZV cohort with PsO, but without PsA. We calculated HZ incidence, unadjusted and adjusted HRs and 95% CIs, unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the analysis of primary VE objective 1.

For 2-dose vaccinated individuals with index dates between March 2020 and December 2020 who are not accrued for the analysis of primary VE objective 1, we described their demographic and clinical baseline characteristics and incidence of HZ.

7.7.2. Secondary analysis/CCI [redacted]

Secondary VE objectives 1-3: Analyses for secondary VE objectives 1-3 used similar methods as for the primary VE analyses in 2-dose RZV populations that were diagnosed with either PsO or PsA or were diagnosed with PsA, or 1-dose RZV recipients with either PsO or PsA (separately), respectively.

Secondary VE objective 4: Baseline characteristics of the 2-dose vaccinated and unvaccinated populations were described and compared as described above for both the PsO and PsA cohorts, separately.

CCI [redacted]

Secondary safety objective 1-2: Analyses for secondary safety objectives 1-2 used similar methods as for the primary safety analyses in RZV-vaccinated populations that were diagnosed with either PsO or PsA or were diagnosed with PsA, respectively.

7.7.3. Amendments to statistical plan

An amendment to planned analysis was that strata (e.g., medication categories) with small sample sizes may be combined into one stratum to produce meaningful estimates. In post-hoc analysis, medication categories and years since vaccination were combined due to small sample size.

7.8. Quality control and quality assurance

KPSC followed the Department of Research and Evaluation's Analytical Research Project Standard Operating Procedures, including data extraction, data analysis, communication, and documentation. The program for identifying the study cohorts as well as the program for identifying all outcomes were validated by double programming. Other programs developed for study purposes, including programs for data lock and programs for identifying covariates were reviewed by a second programmer. Statistical Analysis Systemprograms used for the analysis were reviewed by a second statistician. Statistical analyses (results tables) were discussed in the multisite meetings with GSK prior to study report finalization. KPSC provided a quality control checklist of data management and statistical analysis validation signed and dated by programmers and statisticians.

8. PROTECTION OF HUMAN SUBJECTS

8.1. Ethical approval and subject consent

This study complied with all applicable laws regarding subject privacy. No direct subject contact or primary collection of individual human subject data occurred. Study results were in tabular form and presented as aggregate analyses that omitted subject identification. Any publications and reports did not include subject identifiers. The study was IRB-approved and the requirement for informed consent was waived due to minimal risk to study subjects.

8.2. Subject confidentiality

In the U.S., Federal Policy for the Protection of Human Subjects is codified by the Department of Health and Human Services 45 Code of Federal Regulations Part 46 which outlines the basic regulations governing the protection of human subjects in research, including requirements for assuring compliance by research institutions, requirements for obtaining and documenting informed consent, and requirements for IRB membership, function, operations, review of research, and record keeping.

The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule governs the use and disclosure of protected health information (PHI) from covered entities. Throughout the course of the study, no human subjects were contacted or enrolled, and no PHI was disclosed; however, PHI was accessed through the EHR. This information was only accessed by those authorized to do so and was not shared with GSK or anyone outside of the KPSC study team. The KPSC team obtained IRB approval to use PHI for research activities. Since this access to PHI presented no more than minimal risk to individuals, and the research could not be practically done if required to obtain written authorization for usage, KPSC obtained a waiver for written HIPAA authorization for research involving use of the EHR to conduct the study.

Additionally, all investigators and project managers were trained in the protection of human research participants, Good Pharmacoepidemiology Practices, and HIPAA. The KPSC Department of Research and Evaluation had policies in place to govern the conduct and administration of research at KPSC. These policies supported compliance with federal and state regulatory requirements. Policies included conflict of interest, misconduct, sensitive data, and system access control. Policies were in place to ensure compliance with the Sunshine Act. All KPSC staff underwent annual compliance training and certification. The Principles of Responsibility was KPSC's code of conduct that addressed such issues as protection of confidential information and anti-bribery and corruption.

9. RESULTS

9.1. Participants

The 2-dose RZV cohort with PsO (Section 14, Figure 3) was assessed in the analyses associated with the primary VE objective, as well as secondary VE objectives 1 and 4, and the CCI [redacted]. In the primary VE objective, 2,616 RZV-vaccinated and 7,765 matched unvaccinated individuals with PsO were evaluated for HZ diagnosis during the study period (Section 14, Table 5). Of those with PsO who were RZV-vaccinated and unvaccinated, 257 (9.8%) and 693 (8.9%), respectively, also had PsA diagnoses. In the 2-dose cohort, 2,101 (80.3%) of RZV-vaccinated individuals with PsO received their second dose between 4 weeks and 6 months following the first. The 1-dose RZV cohort with PsO was assessed in the analysis associated with secondary VE objective 3 and consisted of 1,300 RZV-vaccinated and 3,871 matched unvaccinated individuals (Section 14, Figure 5) with 115 (8.8%) and 324 (8.4%) also diagnosed with PsA, respectively. The 2-dose RZV cohort with PsA (Section 14, Figure 4) was assessed in the analyses associated with secondary VE objectives 1, 2, and 4, and the CCI [redacted] CCI [redacted]. In the 2-dose cohort with PsA, 548 RZV-vaccinated and 1,615 matched unvaccinated individuals were evaluated for HZ diagnosis during the study period (Section 14, Table 6). Of those with PsA who were RZV-vaccinated and unvaccinated, 258 (47.1%) and 753 (46.6%), respectively, also had PsO diagnoses. In the 2-dose cohort, 437 (79.7%) of RZV-vaccinated individuals with PsA received their second dose between 4 weeks and 6 months following the first. The 1-dose RZV cohort with PsA was assessed in the analysis associated with the secondary VE objective 2 and consisted of 268 RZV-vaccinated and 799 matched unvaccinated individuals with 122 (45.5%) and 364 (45.6%) also diagnosed with PsO, respectively (Section 14, Figure 6).

The PsO and PsA safety cohorts (Section 14, Figure 11; Section 14, Figure 12) consisted of 3,086 and 1,073 RZV-vaccinated individuals, respectively. The two cohorts were assessed for the occurrence of flares during the risk and comparison windows to address the safety objective.

9.2. Descriptive data including baseline characteristics

PsO VE Cohorts

There was a total of 10,381 individuals that contributed person-time to the 2-dose PsO VE cohort, including 2,616 RZV-vaccinated and 7,765 matched unvaccinated individuals (Section 14, Table 1). In this cohort, the average age was 69.5 (SD 9.46) years with 73.3% of study participants falling between 60 and 79 years of age; 51.8% were female, and 58.1% were non-Hispanic White. RZV-vaccinated individuals had a greater proportion with frequent outpatient visits (≥11 visits, 81.1% vs. 76.8%; ASD 0.109) and a lower proportion with ED visits (>0 visits, 25.2% vs. 30.2%; ASD 0.116). The distribution of baseline comorbidities was similar (ASD <0.1) across vaccinated and unvaccinated individuals. RZV-vaccinated individuals had a higher proportion with previous ZVL/varicella vaccination (45.6% vs. 31.6%, ASD 0.323), compared to unvaccinated individuals.

Due to the healthcare impact of the COVID-19 pandemic, individuals with an index date between March and December 2020 were not accrued. Excluded from the 2-dose PsO VE cohort for this reason were 351 individuals with PsO (Section 14, Table 14). The characteristics of this cohort generally appeared similar to those individuals included in the final analysis.

In the 1-dose RZV cohort with PsO, the mean age was 68.7 (SD 10.17) years, 49.4% were female, and 52.2% were non-Hispanic White (Section 14, Table 3). RZV-vaccinated individuals had a smaller proportion with frequent outpatient visits (≥11 visits, 71.4% vs. 76.9%; ASD 0.156) and a higher proportion with previous ZVL/varicella vaccination (39.8% vs. 31.0%, ASD 0.199), compared to unvaccinated individuals. The frequency of other baseline comorbidities was similar (ASD <0.1) across vaccinated and unvaccinated individuals.

PsA VE Cohorts

In the 2-dose PsA VE cohort, there were 548 RZV-vaccinated and 1,615 matched unvaccinated individuals (Section 14, Table 2). In this cohort, the average age was 65.7 (SD 9.46) years with 68.2% of study participants falling between 60 and 79 years of age; 53.0% were female, and 56.9% were non-Hispanic White. RZV-vaccinated individuals had a greater proportion with frequent outpatient visits (≥11 visits, 88.3% vs. 82.5%; ASD 0.166) and a greater proportion with previous ZVL/varicella vaccination (28.8% vs. 20.7%, ASD 0.240), compared to unvaccinated individuals. The distribution of other baseline comorbidities across vaccinated and unvaccinated individuals was similar (ASD <0.1).

In the 1-dose RZV cohort with PsA, the mean age was 63.5 (SD 10.35) years, 56.6% were female, and 57.0% were non-Hispanic White (Section 14, Table 4). There were differences in race/ethnicity in the RZV-vaccinated and unvaccinated groups (ASD 0.129). As compared to the unvaccinated group, the RZV-vaccinated group had a smaller proportion with frequent outpatient visits (≥11 visits, 79.1% vs. 84.2%; ASD 0.165), a greater proportion with ED visits (>0 visits, 30.6% vs. 24.9%; ASD 0.148), and a greater proportion with hospitalizations (>0 visits, 11.9% vs. 8.4%; ASD 0.118). Apart from a greater proportion with liver disease in RZV-vaccinated individuals (12.3% vs 8.8%; ASD 0.116), the proportion with other baseline comorbidities was similar (ASD <0.1) across vaccinated and unvaccinated individuals. The RZV-vaccinated group had a higher proportion with previous ZVL/varicella vaccination (23.5% vs. 19.0%, ASD 0.130), compared to the unvaccinated group. RZV-vaccinated individuals who received 1 dose also had a larger proportion of members with KPSC membership >5 years compared to unvaccinated individuals (69.0% vs. 77.0%; ASD 0.190).

PsO Safety Cohort

In the PsO safety cohort (N=3,086), the mean age was 69.6 years (SD 9.49) years, 51.1% were female, 57.8% were non-Hispanic White, and 56.8% were on category 1 medications (Section 14, Table 15). Only 1.2% of individuals who received RZV were between 18 and 49 years of age. Of the PsO cohort, 8.8% were diagnosed with both PsO and PsA. The majority (77.3%) of the cohort received 2 doses of RZV. Nearly a quarter (22.5%) of individuals received their index dose in June.

PsA Safety Cohort

In the PsA safety cohort (N=1,073), the mean age was 65.8 years (SD 9.46) years, 55.2% were female, 54.1% were non-Hispanic White, and 40.9% were on category 3 medications (Section 14, Table 16). Of the PsA cohort, nearly half (44.3%) were diagnosed with both PsO and PsA. The majority (81.4%) of the cohort received 2 doses of RZV. Nearly two-thirds (65.7%) of individuals with PsA received their index doses between June and October.

9.3. Outcome data

VE outcomes

Among PsO patients who received 2 doses of RZV, 35 HZ cases were identified during the study period with an incidence of 4.0 (95% CI: 2.9, 5.6) per 1,000 person-years compared to 176 HZ cases among unvaccinated PsO patients with an incidence of 12.0 (95% CI: 10.3, 13.9) per 1,000 person-years (Section 14, Table 5). In patients who were diagnosed with only PsO, 31 HZ cases were identified with an incidence of 4.0 (95% CI: 2.8, 5.6) per 1,000 person-years among vaccinated compared to 159 HZ cases among unvaccinated PsO patients with an incidence of 12.0 (95% CI: 10.3, 14.0) per 1,000 person-years (Section 14, Table 7). Among PsA patients who received 2 doses of RZV, 9 HZ cases were identified with an incidence of 5.3 (95% CI: 2.8, 10.2) per 1,000 person-years compared to 44 HZ cases among unvaccinated PsA patients with an incidence of 15.3 (95% CI: 11.4, 20.6) per 1,000 person-years (Section 14, Table 6). In patients with

either PsO or PsA, there were 40 HZ cases identified with an incidence of 4.2 (95% CI: 3.1, 5.7) per 1,000 person-years among vaccinated compared to 199 HZ cases among unvaccinated patients with either PsO or PsA with an incidence of 12.3 (95% CI: 10.7, 14.2) per 1,000 person-years (Section 14, Table 7). CCI [redacted] CCI [redacted] CCI [redacted] (Section 14, Table 10, Table 11, Table 12, Table 13).

In PsO patients who received 1 dose of RZV, 11 HZ cases were identified during the study period with an incidence of 6.9 (95% CI: 3.8, 12.5) per 1,000 person-years compared to 53 HZ cases among unvaccinated PsO patients with an incidence of 13.1 (95% CI: 10.0, 17.2) per 1,000 person-years (Section 14, Table 8). Among PsA patients who received 1 dose of RZV, 0 HZ cases were identified compared to 12 HZ cases among unvaccinated PsA patients with an incidence of 14.3 (95% CI: 8.1, 25.3) per 1,000 person-years (Section 14, Table 9).

Safety outcomes

In the PsO safety cohort, 30 flare cases were identified in the risk window with an incidence of 66.82 (95% CI: 46.72, 95.57) per 1,000 person-years, compared to 42 flare cases in the comparison window with an incidence of 67.16 (95% CI: 49.63, 90.88) per 1,000 person-years (Section 14, Table 17). In the PsA safety cohort, 25 flare cases were identified in the risk window with an incidence of 156.74 (95% CI: 105.91, 231.97) per 1,000 person-years compared to 26 flare cases in the comparison window with an incidence of 117.31(95% CI: 79.87, 172.29) per 1,000 person-years (Section 14, Table 19). In patients with either PsO or PsA, there were 55 flare cases identified in the risk window with an incidence of 96.77 (95% CI: 74.30, 126.05) per 1,000 person-years compared to 67 flare cases in the comparison window with an incidence of 84.84 (95% CI: 66.77, 107.79) per 1,000 person-years (Section 14, Table 18).

9.4. Results of primary analyses

For the **primary VE objective** evaluating 2 doses of RZV in adults (≥18 years) with PsO, the unadjusted and adjusted VE was 61.9% (95% CI: 43.4%, 74.3%) and 60.7% (95% CI: 40.5%, 74.0%), respectively (Section 14, Table 5). In individuals who received their RZV doses 4 weeks to 6 months apart, adjusted VE was 63.6% (95% CI: 41.2%, 77.5%), while the adjusted VE in those who received their second RZV dose >6 months after the first was 46.2% (95% CI: -26.7%, 78.8%). While VE could not be calculated for all age groups due to an insufficient number of cases, adjusted VEs of 73.9% (95% CI: 37.3%, 89.1%) and 48.0% (95% CI: 14.1%, 68.6%) were observed in individuals aged 60-69 and ≥70 years, respectively. Post-hoc analysis was conducted on combined medication categories with adjusted VEs of 52.8% (95% CI: 17.7%, 73.0%) and 67.3% (95% CI: 38.1%, 82.7%) for categories 1-2 and 3-5, respectively. The cumulative incidence of HZ was lower in the RZV-vaccinated cohort compared to unvaccinated individuals (p<0.0001; Section 14, Figure 7). The adjusted VE against HZ was 71.0% (95% CI: 36.2%, 86.8%) in the 1st year after the index date (Section 14, Table 5, Figure 9). The adjusted VE dropped to 30.7% (95% CI: -32.4%, 67.5%) in the following year and increased to 69.4% (95% CI: 26.8%, 87.2%) in year 3. The adjusted VE for 1-

<3 years after index date (post-hoc analysis) was 55.4% (95% CI: 22.4%, 74.4%; Section 14, Figure 10). The CI was wide for subsequent years (3-<7 in post-hoc analysis) due to smaller sample size.

For the **primary safety objective**, the rate of flares was comparable across the risk and comparison windows (IRR=0.94, 95% CI: 0.58, 1.52) for recipients of RZV with PsO (Section 14, Table 17). The rate of flares within the risk windows following the 1st dose (IRR=0.90, 95% CI: 0.50, 1.62) and 2nd dose (IRR= 1.01, 95% CI: 0.54, 1.90) were comparable to the rate of flares in their respective comparison windows. IRR in individuals diagnosed with PsO was comparable across age groups and medication categories, where there were sufficient cases for analysis. A combined comparison window was used for IRR calculations, but incidence rate of flares for the pre- and post-comparison windows are provided in Section 14, Figure 13 and Figure 14.

9.5. Results of secondary analyses/CCI [redacted]

VE Objectives

For **secondary VE objective 1** evaluating 2 doses of RZV in adults (≥18 years) with either PsO or PsA, the adjusted VE in prevention of HZ was 61.3% (95% CI: 42.7%, 73.9%; Section 14, Table 7). For **secondary VE objective 2**, the adjusted VE of 2 doses of RZV in prevention of HZ was 80.5% (95% CI: 34.3%, 94.2%) in adults with PsA (Section 14, Table 6). VE in PsA patients was mostly represented by individuals who received their second RZV dose within 4 weeks to 6 months of the first, who were aged ≥50 years, and who were managed with category 3-5 medications, with adjusted VEs of 80.4% (95% CI: 25.1%, 94.9%), 80.5% (95% CI: 34.3%, 94.2%), and 81.6% (95% CI: 29.1%, 95.2%), respectively. The cumulative incidence of HZ in RZV-vaccinated individuals with PsA was significantly lower than those who were unvaccinated (p=0.0019; Section 14, Figure 8).

For **secondary VE objective 3**, the adjusted VE of 1 dose of RZV in prevention of HZ was 30.6% (95% CI: -29.6%, 66.1%) in adults diagnosed with PsO (Section 14, Table 8). In adults diagnosed with PsA, there were no cases of HZ identified in those who received 1 dose of RZV, thus the presumed VE of 100% lacked precision and a 95% CI could not be calculated. The comparison of baseline characteristics (**secondary VE objective 4**) between individuals who were vaccinated with 2 doses of RZV and their unvaccinated matches in the PsO and PsA cohorts is detailed in Section 9.3 and in Section 14, Table 1 and Table 2.

CCI [redacted]

Safety objectives

For **secondary safety objective 1**, the rates of flares in individuals diagnosed with either PsO or PsA were comparable across the risk and comparison windows (IRR=1.11, 95% CI: 0.77, 1.60; Section 14, Table 18). For **secondary safety objective 2**, the rate of flares in individuals diagnosed with PsA was comparable across the risk and comparison windows (IRR=1.21, 95% CI: 0.69, 2.13; Section 14, Table 19). The IRR of flares in individuals diagnosed with PsA was comparable across the risk and comparison windows for different age groups and medication categories, where there were sufficient cases for analysis. The rate of flares within the risk windows following the 1st dose (IRR=1.15, 95% CI: 0.58, 2.29) and 2nd dose (IRR= 1.32, 95% CI: 0.65, 2.68) were comparable to the rate of flares in their respective comparison windows. A combined comparison window was used for IRR calculations, but incidence rate of flares for the pre- and post-comparison windows are provided in Section 14, Figure 15 and Figure 16.

9.6. Adverse events/adverse reactions

This study was based on retrospective, observational data previously collected for other purposes e.g., routine healthcare encounters. As such, there was no requirement for the collection and reporting of Individual Case Safety Reports. Although the study was based on human review of unstructured data, the nature of the secondary data protocol driven data collection and analysis did not allow for reporting of serious and non-serious adverse events, pregnancy exposures, or incidents related to any GSK product during the conduct of this research.

10. DISCUSSION

10.1. Key results

This study provides real-world data to assess the VE and safety of RZV among adults aged ≥18 years with PsO and PsA. For adults with PsO, 2 doses of RZV conferred protection against HZ with a VE of 60.7% (95% CI: 40.5%, 74.0%) and no elevated rate of flares was observed during the 30-day risk window following vaccination. Similarly, for adults with PsA, 2 doses of RZV conferred protection against HZ with a VE of 80.5% (95% CI: 34.3%, 94.2%) and no elevated rate of flares observed during the 30-day risk window following vaccination. Previous studies assessing the effectiveness of RZV largely focused on generally immunocompetent populations and those that examine immunosuppressed populations have focused on older individuals, mostly aged ≥50 years [Zeevaert, 2023; Constenla, 2025]. Thus, data on the effectiveness and safety of RZV in other populations at increased risk, including those with autoimmune diseases and those receiving newer immunomodulating agents, are limited. This study addresses important gaps by focusing on individuals deemed at elevated risk of HZ, specifically with PsO or PsA diagnoses, and by including all eligible individuals aged ≥18 years.

The overall 2-dose RZV VE for the PsO and PsA populations was 60.7% and 80.5% in our study, respectively. While the observed VE was lower than the vaccine efficacy in randomized controlled trials and VE in observational studies reported for immunocompetent older adults, this is within range of the few studies published that have evaluated VE in PsO and PsA patients. In a study using Optum's deidentified Clinformatics® Data Mart Database datasets from January 2018 to December 2021, the VE of 2 doses of RZV against HZ was 77.2% (95% CI: 66.4%, 84.5%), 65.6% (95% CI: 37.3%, 81.2%), and 74.8% (95% CI: 65.1%, 81.7%) in individuals aged ≥50 years with PsO, PsA, and PsO or PsA, respectively [Constenla, 2025]. In other individuals with autoimmune diseases within KSPC, including those aged ≥50 years with rheumatoid arthritis and inflammatory bowel disease, VE was 60.7% (95% CI: 41.0%, 73.8%) and 65.1% (95% CI: 24.8%, 83.8%), respectively [Rayens, 2025; Tseng, 2025]. CCI [redacted] CCI [redacted] CCI [redacted] In our study of PsO patients, the VE of 2 doses of RZV in the 1st year after vaccination was 71.0% (95% CI: 36.2%, 86.8%), followed by 30.7% (95% CI: -32.4%, 67.5%) in the 2nd year and 69.4% (95% CI: 26.8%, 87.2%) in the 3rd year. Our VE estimates by year were likely unstable due to small numbers of individuals, since in post-hoc analysis, VE appeared stable throughout the follow-up period, with 71.0% (95% CI: 36.2%, 86.8%), 55.4% (95% CI: 22.4%, 74.4%), and 53.2% (95% CI: (-63.3%, 92.0%) for years <1, 1-<3, and 3-<7, respectively. With an observed of VE 30.6% (95% CI: -29.6%, 66.1%), we had insufficient power to demonstrate protection of a single dose of RZV against HZ in the PsO cohort. Further, we could not calculate 1-dose RZV VE against HZ in the PsA cohort due to small sample size.

The risk of disease flare after RZV has not been well-documented especially for younger populations (aged 18-49 years) that are immunocompromised and/or diagnosed with autoimmune diseases. We observed no statistically significant increased rate of flares among PsO or PsA patients during the 30-day risk window following vaccination in our study, although we were not separately able to calculate IRR for individuals aged 18-49 years due to insufficient sample size.

10.2. Limitations

A potential limitation of this study was that there could be differences between vaccinated and unvaccinated individuals that were difficult to control and measure despite matching on key variables and adjusting for several covariates including demographic characteristics, health care utilization, and comorbidities. The effect of residual confounding may have impacted VE or safety estimates. Proxy measures may not completely and accurately capture disease severity (medication category) and healthcare utilization (captured from one year prior to index date). For the safety objectives, the SCCS design should have minimized confounding by implicitly controlling for time-fixed confounders. During the initial months of the vaccine accrual period, RZV vaccination at KPSC was prioritized for individuals ages 60 years and older. However, this should not have biased results since individuals were matched on age for the VE analysis and age is implicitly controlled for in the SCCS analysis.

Despite high validity of diagnostic algorithms, misclassification of HZ status could occur inherently in EHR studies using automated data, but we do not expect differential misclassification between exposure groups. Misclassification of individuals with PsO and PsA was also possible. However, these definitions for PsO and PsA were selected based on prior knowledge, current literature [Lee, 2021], and KPSC chart review indicating a high positive predictive value.

It was unknown if RZV vaccination led to modified or atypical HZ presentations that were more likely to be underdiagnosed or misdiagnosed. If these cases were never diagnosed or were diagnosed as other conditions, they would not be identified through ICD-10 codes for HZ. This would lead to a potential overestimation of VE. It was also possible that there was differential misclassification of HZ due to differential health care seeking behaviors, but to address this, prior health care utilization was included as a covariate.

Some of the secondary and CCI [redacted] objective analyses, including subgroup analyses, yielded wide CIs potentially due to the small sample size, limiting our ability to draw robust conclusions for certain subgroups. This was true especially for the 18–49-year age group.

10.3. Interpretation of results

Our findings suggest that vaccination with 2 doses of RZV is protective against HZ for individuals with PsO and PsA aged 18 years and older. For both PsO and PsA patients, RZV is not associated with increased rate of disease flare within 30 days after vaccination.

10.4. Generalisability

This was a large study, composed of a diverse population that is representative of the Southern California region. Study results should be generalizable to similar clinical practice and care settings. Results may not be generalizable to individuals who receive care in different types of health systems in the U.S., for example, uninsured populations, or in other countries.

11. OTHER INFORMATION

Not applicable

12. CONCLUSIONS

For adults with PsO or PsA, 2 doses of RZV administered ≥4 weeks apart conferred protection against HZ. RZV vaccination was not associated with elevated rate of flares within 30 days following vaccination in either the PsO or PsA cohorts. A single dose of RZV was not as effective as 2 doses against HZ in the PsO cohort. VE estimates were robust for the ≥50-year-old PsO and PsA patients. For the 18–49-year age group, the sample size was too small to draw a definite conclusion. For the first 3 years after 2-dose vaccination, RZV continued to offer protection against HZ for PsO patients.

13. REFERENCES

Anderson, T. C., N. B. Masters, A. Guo, et al. "Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged >/=19 Years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022." MMWR Morb Mortal Wkly Rep.(2022). 71(3): 80-84.

Austin, P. C. "An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies." Multivariate Behav Res.(2011). **46**(3): 399-424.

Baumrin, E., A. Van Voorhees, A. Garg, et al. "A systematic review of herpes zoster incidence and consensus recommendations on vaccination in adult patients on systemic therapy for psoriasis or psoriatic arthritis: From the Medical Board of the National Psoriasis Foundation." J Am Acad Dermatol.(2019). 81(1): 102-110.

Chen, S. Y., J. A. Suaya, Q. Li, et al. "Incidence of herpes zoster in patients with altered immune function." Infection.(2014). 42(2): 325-334.

Chiu, H. Y., Y. T. Hung, S. W. Huang, et al. "Comparative risk of herpes zoster in patients with psoriatic disease on systemic treatments: a systematic review and network meta-analysis." Ther Adv Chronic Dis.(2022). 13: 20406223221091188.

Chovatiya, R. and J. I. Silverberg. "Association of herpes zoster and chronic inflammatory skin disease in US inpatients." J Am Acad Dermatol.(2021). 85(6): 1437-1445.

Constenla, D., G. Lonnet, E. Aris, et al. "Real-world effectiveness of the adjuvanted recombinant zoster vaccine in >/=50-year-old adults with autoimmune diseases." J Infect Dis.(2025).

Dagnew, A. F., D. Rausch, C. Herve, et al. "Efficacy and serious adverse events profile of the adjuvanted recombinant zoster vaccine in adults with pre-existing potential immune-mediated diseases: a pooled post hoc analysis on two parallel randomized trials." Rheumatology (Oxford).(2021). 60(3): 1226-1233.

Didierlaurent, A. M., B. Laupeze, A. Di Pasquale, et al. "Adjuvant system AS01: helping to overcome the challenges of modern vaccines." Expert Rev Vaccines.(2017). 16(1): 55-63.

Dooling, K. L., A. Guo, M. Patel, et al. "Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines." MMWR Morb Mortal Wkly Rep.(2018). 67(3): 103-108.

Dworkin, R. H., R. W. Johnson, J. Breuer, et al. "Recommendations for the management of herpes zoster." Clin Infect Dis.(2007). 44 Suppl 1: S1-26.

FDA (2017, 23 May 2023). "SHINGRIX." Retrieved 6 March, 2024, from https://www.fda.gov/vaccines-blood-biologics/vaccines/shingrix.

Gnann, J. W., Jr. and R. J. Whitley. "Clinical practice. Herpes zoster." N Engl J Med.(2002). 347(5): 340-346.

Gupta, S., R. J. Arasaratnam, E. B. Solow, et al. "A Medical Records Review Study Assessing Safety of Zoster Vaccine Recombinant, Adjuvanted in Patients With Rheumatic Disease." J Clin Rheumatol.(2022). 28(2): e528-e531.

Harpaz, R., I. R. Ortega-Sanchez, J. F. Seward, et al. "Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP)." MMWR Recomm Rep.(2008). 57(RR-5): 1-30; quiz CE32-34.

Insinga, R. P., R. F. Itzler, J. M. Pellissier, et al. "The incidence of herpes zoster in a United States administrative database." J Gen Intern Med.(2005). 20(8): 748-753.

Kawai, K. and B. P. Yawn. "Risk Factors for Herpes Zoster: A Systematic Review and Meta-analysis." Open Forum Infect Dis.(2017). 4(1): S313–S31421.

Koebnick, C., A. M. Langer-Gould, M. K. Gould, et al. "Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data." Perm J.(2012). 16(3): 37-41.

Langan, S. M., L. Smeeth, D. J. Margolis, et al. "Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study." PLoS Med.(2013). 10(4): e1001420.

Lee, H., M. He, S. K. Cho, et al. "Validation of claims-based algorithms to identify patients with psoriasis." Pharmacoepidemiol Drug Saf.(2021). 30(7): 868-874.

Mullooly, J. P., K. Riedlinger, C. Chun, et al. "Incidence of herpes zoster, 1997-2002." Epidemiol Infect.(2005). 133(2): 245-253.

Rayens, E., L. S. Sy, L. Qian, et al. "Effectiveness and safety of the recombinant zoster vaccine in individuals >/=50 years of age with rheumatoid arthritis: a matched cohort and self-controlled case series study." Ann Rheum Dis.(2025). 84(6): 960-969.

Sbidian, E., P. Eftekahri, M. Viguier, et al. "National survey of psoriasis flares after 2009 monovalent H1N1/seasonal vaccines." Dermatology.(2014). 229(2): 130-135.

Spinelli, F. R., E. G. Favalli, C. Garufi, et al. "Low frequency of disease flare in patients with rheumatic musculoskeletal diseases who received SARS-CoV-2 mRNA vaccine." Arthritis Res Ther.(2022). 24(1): 21.

Stevens, E., M. E. Weinblatt, E. Massarotti, et al. "Safety of the Zoster Vaccine Recombinant Adjuvanted in Rheumatoid Arthritis and Other Systemic Rheumatic Disease Patients: A Single Center's Experience With 400 Patients." ACR Open Rheumatol.(2020). 2(6): 357-361.

Thomas, S. L. and A. J. Hall. "What does epidemiology tell us about risk factors for herpes zoster?" Lancet Infect Dis.(2004). 4: 26-33.

Tseng, H. F., K. Bruxvoort, B. Ackerson, et al. "The Epidemiology of Herpes Zoster in Immunocompetent, Unvaccinated Adults >/=50 Years Old: Incidence, Complications, Hospitalization, Mortality, and Recurrence." J Infect Dis.(2020). 222(5): 798-806.

Tseng, H. F., L. S. Sy, E. Rayens, et al. "Effectiveness and safety of the recombinant zoster vaccine in adults aged >/=50 years with inflammatory bowel disease." Hum Vaccin Immunother.(2025). 21(1): 2576981.

Whitaker, H. J., C. P. Farrington, B. Spiessens, et al. "Tutorial in biostatistics: the self-controlled case series method." Stat Med.(2006). 25(10): 1768-1797.

Winthrop, K. L. "The emerging safety profile of JAK inhibitors in rheumatic disease." Nat Rev Rheumatol.(2017a). 13(5): 320.

Winthrop, K. L., J. R. Curtis, S. Lindsey, et al. "Herpes Zoster and Tofacitinib: Clinical Outcomes and the Risk of Concomitant Therapy." Arthritis Rheumatol.(2017b). 69(10): 1960-1968.

Yawn, B. P., P. Saddier, P. C. Wollan, et al. "A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction." Mayo Clin Proc.(2007). 82(11): 1341-1349.

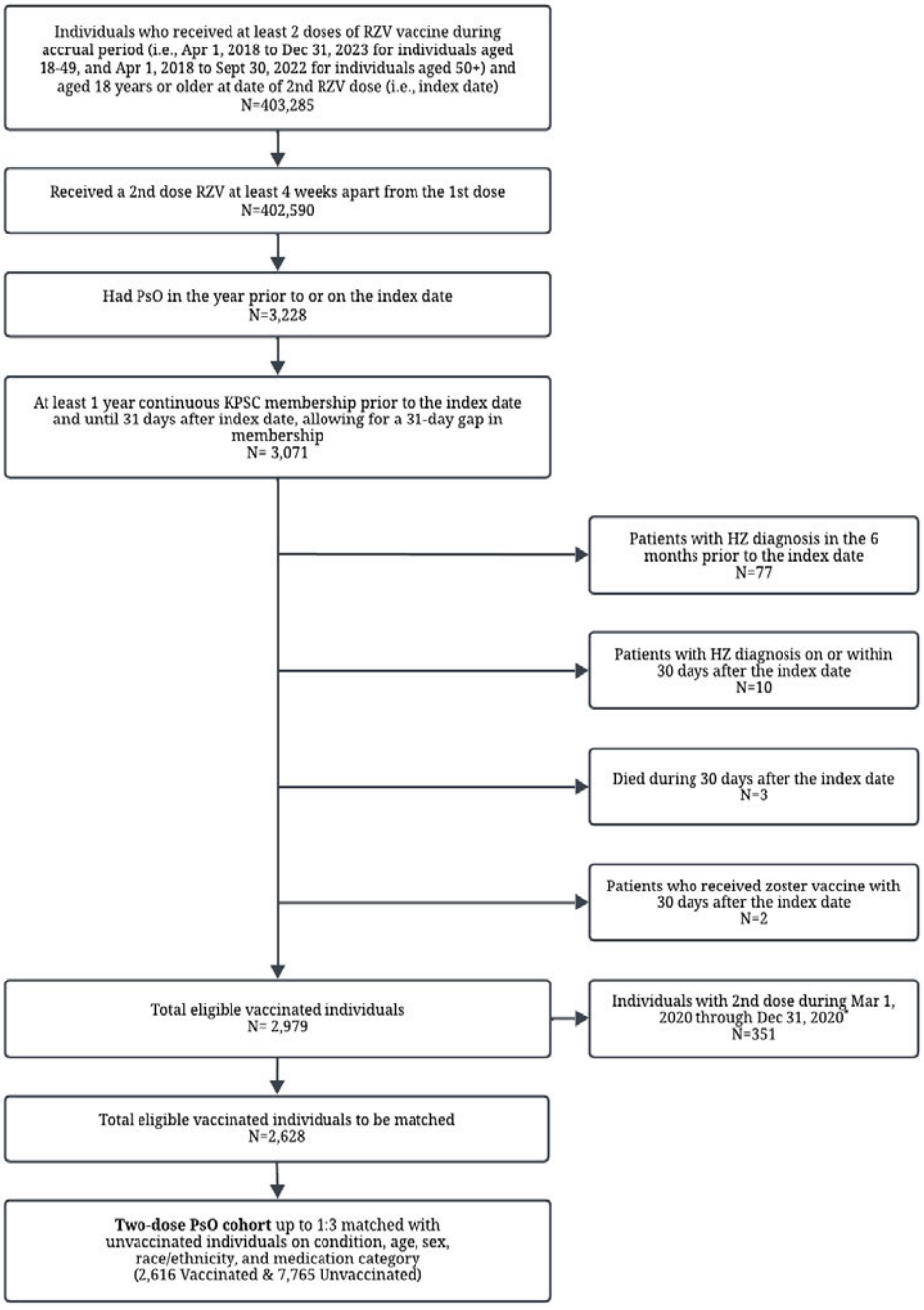
Yun, H., S. Yang, L. Chen, et al. "Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases: Implications for Vaccination." Arthritis Rheumatol.(2016). 68(9): 2328-2337.

Zeevaert, R., N. Thiry, C. Maertens de Noordhout, et al. "Efficacy and safety of the recombinant zoster vaccine: A systematic review and meta-analysis." Vaccine X.(2023). 15: 100397.

Zou, A., Y. Chen, N. Shi, et al. "Risk of herpes zoster associated with biological therapies for psoriasis and psoriatic arthritis: A systematic review and meta-analysis." Medicine (Baltimore).(2021). 100(40): e27368.

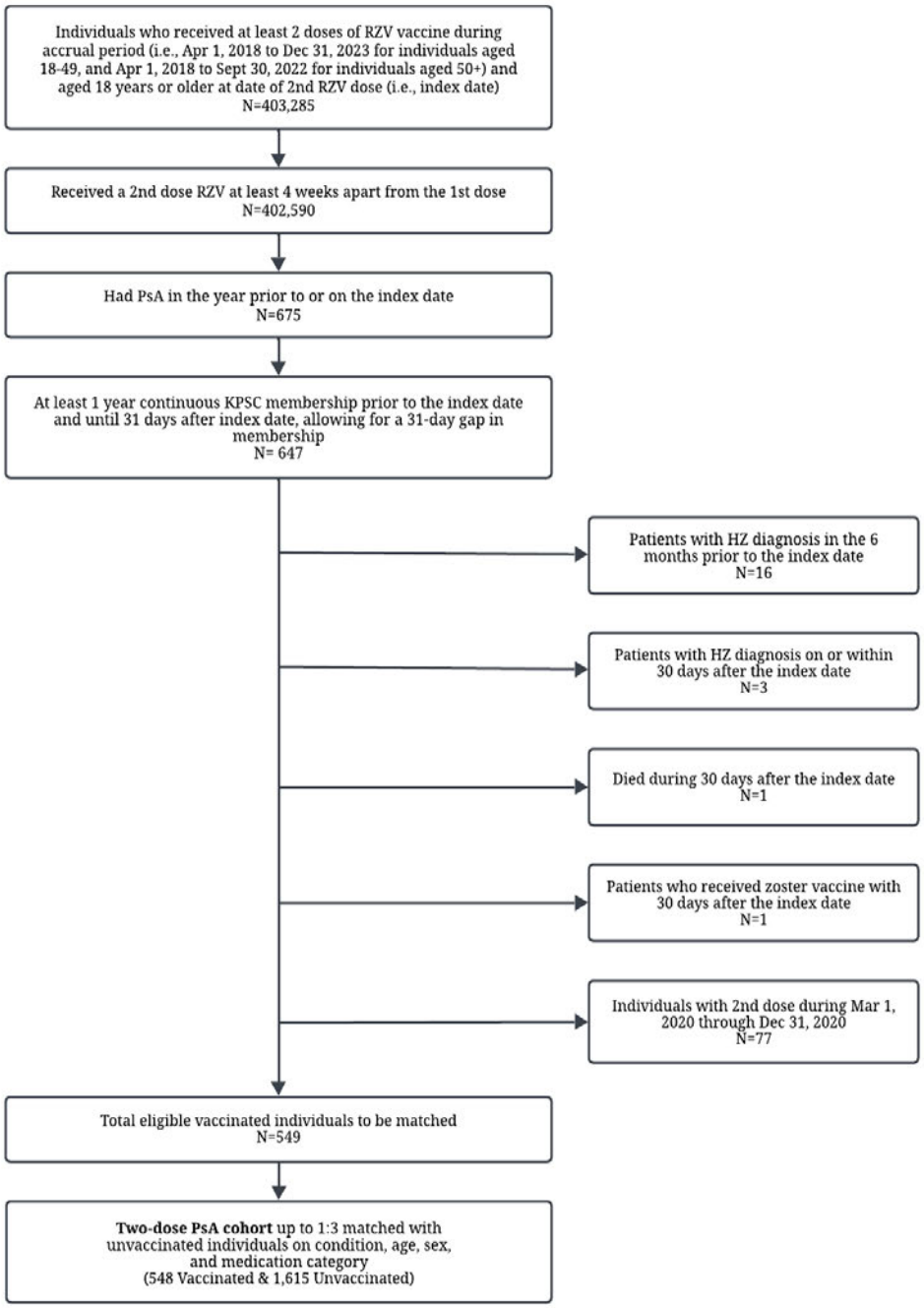
14. TABLES AND FIGURES

Figure 3 VE Flow chart for 2-dose RZV cohort with PsO



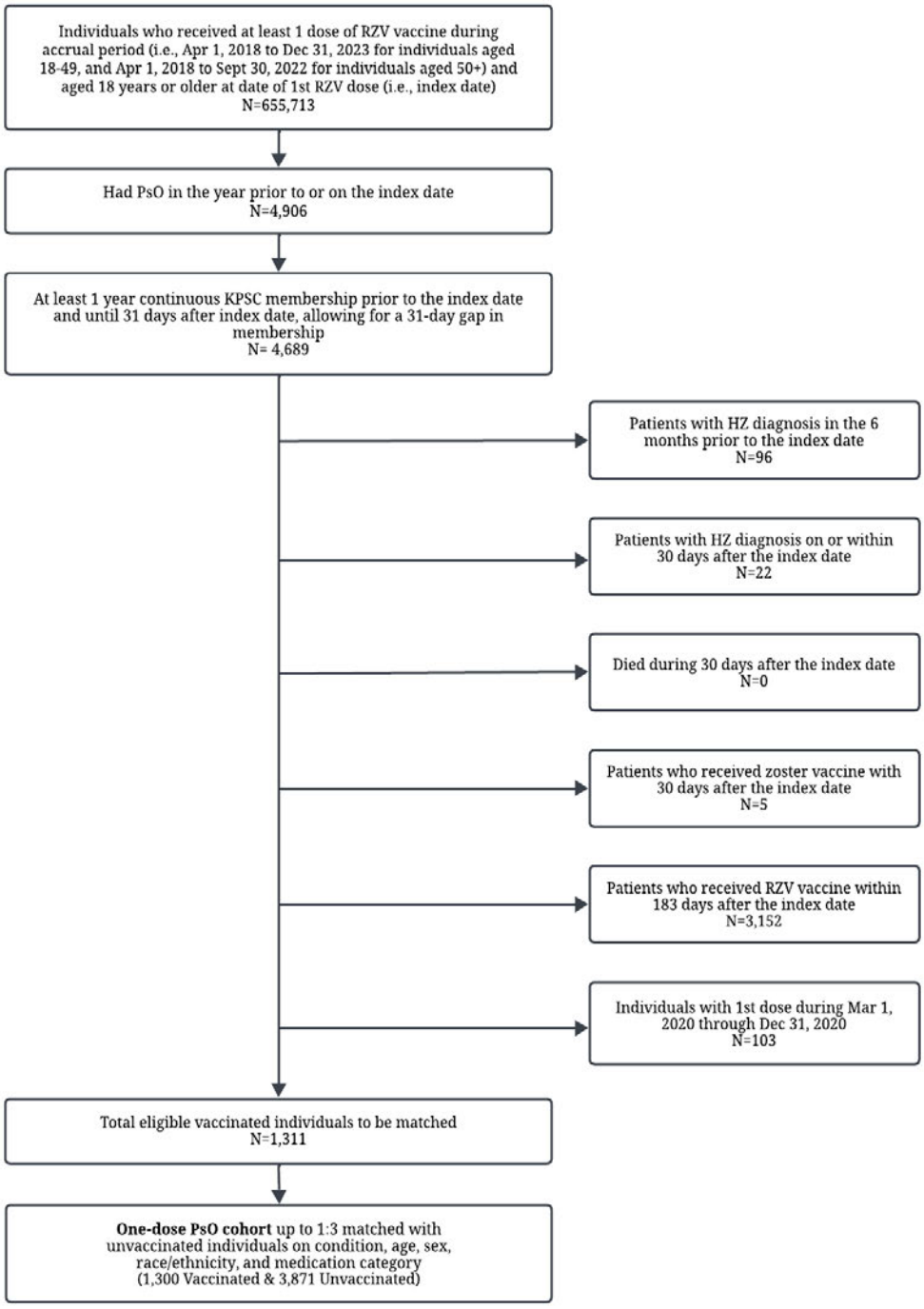
Abbreviations: HZ, herpes zoster; KPSC, Kaiser Permanente Southern California; N, number; PsO, psoriasis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness

Figure 4 VE flow chart for 2-dose RZV cohort with PsA



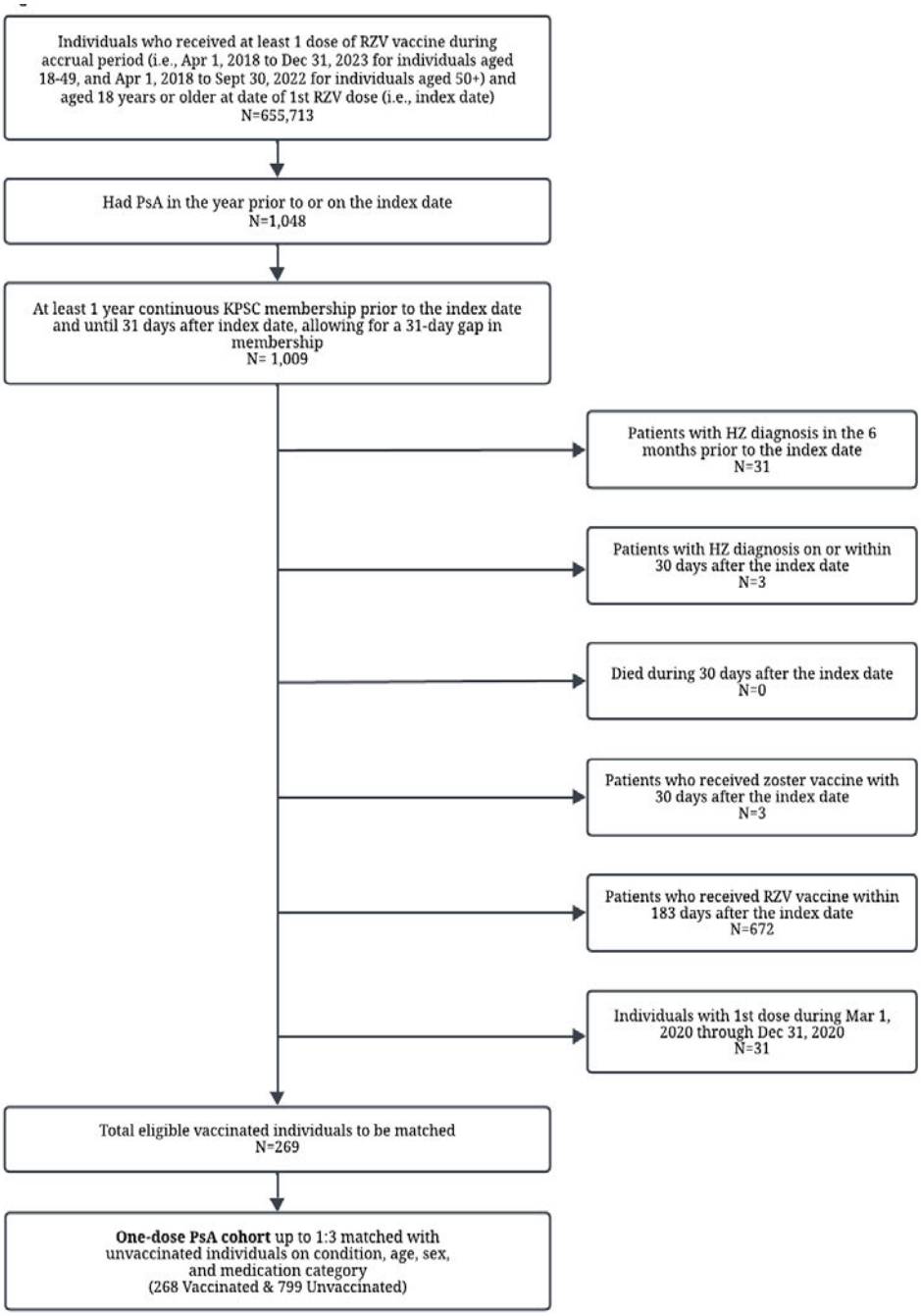
Abbreviations: HZ, herpes zoster; KPSC, Kaiser Permanente Southern California; N, number; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness

Figure 5 VE flow chart for 1-dose RZV cohort with PsO



Abbreviations: HZ, herpes zoster; KPSC, Kaiser Permanente Southern California; N, number; PsO, psoriasis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness

Figure 6 VE flow chart for 1-dose RZV cohort with PsA



Abbreviations: HZ, herpes zoster; KPSC, Kaiser Permanente Southern California; N, number; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness

Table 1 Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsO in VE analysis

	Vaccinated N=2616	Unvaccinated N=7765	Total N=10381	p value	ASD
Age at index date, years				0.426	0.016
mean (SD)	69.7 (9.08)	69.5 (9.58)	69.5 (9.46)		
median	70	70	70		
Q1, Q3	65.0, 75.0	63.0, 75.0	63.0, 75.0		
range	19.0, 95.0	23.0, 102.0	19.0, 102.0		
Age at index date, years, n (%)				1.000	0.007
18-29	2 (0.1%)	5 (0.1%)	7 (0.1%)		
30-39	5 (0.2%)	15 (0.2%)	20 (0.2%)		
40-49	10 (0.4%)	28 (0.4%)	38 (0.4%)		
50-59	343 (13.1%)	1020 (13.1%)	1363 (13.1%)		
60-69	886 (33.9%)	2631 (33.9%)	3517 (33.9%)		
70-79	1028 (39.3%)	3058 (39.4%)	4086 (39.4%)		
≥80	342 (13.1%)	1008 (13.0%)	1350 (13.0%)		
Sex, n (%)				0.928	0.002
Female	1357 (51.9%)	4020 (51.8%)	5377 (51.8%)		
Male	1259 (48.1%)	3745 (48.2%)	5004 (48.2%)		
Race/Ethnicity, n (%)				0.992	0.012
White	1513 (57.8%)	4522 (58.2%)	6035 (58.1%)		
Black	87 (3.3%)	247 (3.2%)	334 (3.2%)		
Hispanic	615 (23.5%)	1824 (23.5%)	2439 (23.5%)		
Asian	343 (13.1%)	1005 (12.9%)	1348 (13.0%)		
Other	58 (2.2%)	167 (2.2%)	225 (2.2%)		
Medication category, n (%)				0.893	0.018
Category 1	1437 (54.9%)	4290 (55.2%)	5727 (55.2%)		
Category 2	53 (2.0%)	140 (1.8%)	193 (1.9%)		
Category 3	763 (29.2%)	2272 (29.3%)	3035 (29.2%)		
Category 4+5	363 (13.9%)	1063 (13.7%)	1426 (13.7%)		
PsO, n (%)				0.168	0.031
PsO only	2359 (90.2%)	7072 (91.1%)	9431 (90.8%)		
PsO+PsA	257 (9.8%)	693 (8.9%)	950 (9.2%)		
Number of outpatient visits[a], n (%)				<0.001	0.109
0-4	52 (2.0%)	232 (3.0%)	284 (2.7%)		

	Vaccinated N=2616	Unvaccinated N=7765	Total N=10381	p value	ASD
5-10	443 (16.9%)	1566 (20.2%)	2009 (19.4%)		
≥11	2121 (81.1%)	5967 (76.8%)	8088 (77.9%)		
Number of ED visits[a], n (%)				<0.001	0.116
0	1957 (74.8%)	5417 (69.8%)	7374 (71.0%)		
1	378 (14.4%)	1285 (16.5%)	1663 (16.0%)		
≥2	281 (10.7%)	1063 (13.7%)	1344 (12.9%)		
Number of hospitalization[a], n (%)				<0.001	0.095
0	2324 (88.8%)	6708 (86.4%)	9032 (87.0%)		
1	215 (8.2%)	695 (9.0%)	910 (8.8%)		
≥2	77 (2.9%)	362 (4.7%)	439 (4.2%)		
Baseline Comorbidities[a], n (%)					
Kidney disease	477 (18.2%)	1598 (20.6%)	2075 (20.0%)	0.010	0.059
Heart disease	313 (12.0%)	1018 (13.1%)	1331 (12.8%)	0.130	0.035
Lung disease	588 (22.5%)	1719 (22.1%)	2307 (22.2%)	0.718	0.008
Liver disease	238 (9.1%)	684 (8.8%)	922 (8.9%)	0.653	0.010
Diabetes	894 (34.2%)	2820 (36.3%)	3714 (35.8%)	0.048	0.045
Other autoimmune diseases[b]	115 (4.4%)	342 (4.4%)	457 (4.4%)	0.986	0.000
SARS-CoV-2/COVID-19 dx	207 (7.9%)	596 (7.7%)	803 (7.7%)	0.694	0.009
Immunocompromised status[c] at index date, n (%)				0.283	0.024
Yes	571 (21.8%)	1618 (20.8%)	2189 (21.1%)		
No	2045 (78.2%)	6147 (79.2%)	8192 (78.9%)		
History of ZVL/varicella vaccination[d], n (%)				<0.001	0.323
No	1423 (54.4%)	5314 (68.4%)	6737 (64.9%)		
Yes, ≤ 5 years	228 (8.7%)	701 (9.0%)	929 (8.9%)		
Yes, > 5 years	965 (36.9%)	1750 (22.5%)	2715 (26.2%)		
History of HZ[d], n (%)				0.992	0.000
Yes	359 (13.7%)	1065 (13.7%)	1424 (13.7%)		
No	2257 (86.3%)	6700 (86.3%)	8957 (86.3%)		
Length of continuous membership[d], years, n (%)				0.024	0.062
≤5	489 (18.7%)	1626 (20.9%)	2115 (20.4%)		
6-10	474 (18.1%)	1444 (18.6%)	1918 (18.5%)		
≥11	1653 (63.2%)	4695 (60.5%)	6348 (61.2%)		

	Vaccinated N=2616	Unvaccinated N=7765	Total N=10381	p value	ASD
Concomitant vaccination[e], n (%)				N/A	N/A
Yes	994 (38.0%)	N/A	N/A		
No	1622 (62.0%)	N/A	N/A		
Time between first and second doses, n (%)				N/A	N/A
4 weeks - 6 months	2101 (80.3%)	N/A	N/A		
>6 months[f]	515 (19.7%)	N/A	N/A		

Abbreviations: AIDS, acquired immunodeficiency syndrome; ASD, absolute standardized difference; COVID-19, coronavirus disease 2019; Dx, diagnosis; ED, emergency department; HIV, human immunodeficiency virus; HZ, herpes zoster; n, number; N/A, not applicable; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Defined in the one year prior to index date
b. Multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease.
c. HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications.
d. Defined based on all available medical records prior to index date
e. Among subjects with concomitant vaccines: influenza vaccine (50.0%), COVID-19 vaccine (5.7%), PCV13/PPSV23 (27.0%), Tdap (33.7%), and other (7.5%); 66.2% concomitant with 1st dose and 51.5% concomitant with 2nd dose.
f. Among individuals who received the 2nd dose more than 6 months after the 1st dose, the range of time between two doses was from 6.0 to 48.3 months with a median of 10.5 months.

Table 2 Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsA in VE analysis

	Vaccinated N=548	Unvaccinated N=1615	Total N=2163	p value	ASD
Age at index date, years				0.380	0.051
mean (SD)	66.0 (9.29)	65.6 (9.51)	65.7 (9.46)		
median	66	66	66		
Q1, Q3	60.0, 72.0	60.0, 72.0	60.0, 72.0		
range	29.0, 93.0	25.0, 92.0	25.0, 93.0		
Age at index date, years, n (%)				1.000	0.023
18-29	1 (0.2%)	2 (0.1%)	3 (0.1%)		
30-39	3 (0.5%)	9 (0.6%)	12 (0.6%)		
40-49	7 (1.3%)	19 (1.2%)	26 (1.2%)		
50-59	123 (22.4%)	366 (22.7%)	489 (22.6%)		
60-69	225 (41.1%)	667 (41.3%)	892 (41.2%)		
70-79	148 (27.0%)	437 (27.1%)	585 (27.0%)		
≥80	41 (7.5%)	115 (7.1%)	156 (7.2%)		
Sex, n (%)				0.870	0.008
Female	292 (53.3%)	854 (52.9%)	1146 (53.0%)		
Male	256 (46.7%)	761 (47.1%)	1017 (47.0%)		
Race/Ethnicity, n (%)				0.667	0.076

	Vaccinated N=548	Unvaccinated N=1615	Total N=2163	p value	ASD
White	314 (57.3%)	916 (56.7%)	1230 (56.9%)		
Black	13 (2.4%)	44 (2.7%)	57 (2.6%)		
Hispanic	132 (24.1%)	415 (25.7%)	547 (25.3%)		
Asian	67 (12.2%)	166 (10.3%)	233 (10.8%)		
Other	22 (4.0%)	74 (4.6%)	96 (4.4%)		
Medication category, n (%)				0.962	0.026
Category 1	52 (9.5%)	147 (9.1%)	199 (9.2%)		
Category 2	47 (8.6%)	129 (8.0%)	176 (8.1%)		
Category 3	228 (41.6%)	681 (42.2%)	909 (42.0%)		
Category 4+5	221 (40.3%)	658 (40.7%)	879 (40.6%)		
PsA, n (%)				0.854	0.009
PsA only	290 (52.9%)	862 (53.4%)	1152 (53.3%)		
PsA+PsO	258 (47.1%)	753 (46.6%)	1011 (46.7%)		
Number of outpatient visits[a], n (%)				0.006	0.166
0-4	4 (0.7%)	22 (1.4%)	26 (1.2%)		
5-10	60 (10.9%)	260 (16.1%)	320 (14.8%)		
≥11	484 (88.3%)	1333 (82.5%)	1817 (84.0%)		
Number of ED visits[a], n (%)				0.301	0.078
0	412 (75.2%)	1159 (71.8%)	1571 (72.6%)		
1	82 (15.0%)	275 (17.0%)	357 (16.5%)		
≥2	54 (9.9%)	181 (11.2%)	235 (10.9%)		
Number of hospitalization[a], n (%)				0.189	0.096
0	492 (89.8%)	1428 (88.4%)	1920 (88.8%)		
1	45 (8.2%)	129 (8.0%)	174 (8.0%)		
≥2	11 (2.0%)	58 (3.6%)	69 (3.2%)		
Baseline Comorbidities[a], n (%)					
Kidney disease	100 (18.2%)	259 (16.0%)	359 (16.6%)	0.229	0.059
Heart disease	55 (10.0%)	149 (9.2%)	204 (9.4%)	0.575	0.028
Lung disease	113 (20.6%)	297 (18.4%)	410 (19.0%)	0.250	0.056
Liver disease	58 (10.6%)	154 (9.5%)	212 (9.8%)	0.476	0.035
Diabetes	195 (35.6%)	532 (32.9%)	727 (33.6%)	0.258	0.056
Other autoimmune diseases[b]	46 (8.4%)	142 (8.8%)	188 (8.7%)	0.775	0.014
SARS-CoV-2 /COVID-19 dx	47 (8.6%)	144 (8.9%)	191 (8.8%)	0.809	0.012
Immunocompromised status[c] at index date, n (%)				0.907	0.006
Yes	350 (63.9%)	1027 (63.6%)	1377 (63.7%)		
No	198 (36.1%)	588 (36.4%)	786 (36.3%)		
History of ZVL/varicella vaccination[d], n (%)				<0.001	0.240
No	390 (71.2%)	1281 (79.3%)	1671 (77.3%)		
Yes, ≤ 5 years	29 (5.3%)	104 (6.4%)	133 (6.1%)		
Yes, > 5 years	129 (23.5%)	230 (14.2%)	359 (16.6%)		
History of HZ[d], n (%)				0.306	0.050
Yes	85 (15.5%)	222 (13.7%)	307 (14.2%)		
No	463 (84.5%)	1393 (86.3%)	1856 (85.8%)		

	Vaccinated N=548	Unvaccinated N=1615	Total N=2163	p value	ASD
Length of continuous membership[b], years, n (%)				0.860	0.027
≤5	119 (21.7%)	369 (22.8%)	488 (22.6%)		
6-10	106 (19.3%)	308 (19.1%)	414 (19.1%)		
≥11	323 (58.9%)	938 (58.1%)	1261 (58.3%)		
Concomitant vaccination[e], n (%)				N/A	N/A
Yes	218 (39.8%)	N/A	N/A		
No	330 (60.2%)	N/A	N/A		
Time between first and second doses, n (%)				N/A	N/A
4 weeks - 6 months	437 (79.7%)	N/A	N/A		
>6 months[f]	111 (20.3%)	N/A	N/A		

Abbreviations: AIDS, acquired immunodeficiency syndrome; ASD, absolute standardized difference; COVID-19, coronavirus disease 2019; Dx, diagnosis; ED, emergency department; HIV, human immunodeficiency virus; HZ, herpes zoster; n, number; N/A, not applicable; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Defined in the one year prior to index date

b. Multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease.

c. HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications.

d. Defined based on all available medical records prior to index date

e. Among subjects with concomitant vaccines: influenza vaccine (47.7%), COVID-19 vaccine (11.5%), PCV13/PPSV23 (24.8%), Tdap (29.8%), and other (8.3%); 64.2% concomitant with 1st dose and 50.9% concomitant with 2nd dose.

f. Among individuals who received the 2nd dose more than 6 months after the 1st dose, the range of time between two doses was from 6.1 to 47.8 months with a median of 12.0 months

Table 3 Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsO in VE analysis

	Vaccinated N=1300	Unvaccinated N=3871	Total N=5171	p value	ASD
Age at index date, years				0.556	0.016
mean (SD)	68.8 (10.07)	68.7 (10.20)	68.7 (10.17)		
median	70	70	70		
Q1, Q3	62.0, 75.0	62.0, 75.0	62.0, 75.0		
range	22.0, 100.0	18.0, 101.0	18.0, 101.0		
Age at index date, years, n (%)				1.000	0.003
18-29	3 (0.2%)	9 (0.2%)	12 (0.2%)		
30-39	2 (0.2%)	6 (0.2%)	8 (0.2%)		
40-49	13 (1.0%)	39 (1.0%)	52 (1.0%)		
50-59	225 (17.3%)	667 (17.2%)	892 (17.3%)		
60-69	406 (31.2%)	1214 (31.4%)	1620 (31.3%)		
70-79	479 (36.8%)	1425 (36.8%)	1904 (36.8%)		
≥80	172 (13.2%)	511 (13.2%)	683 (13.2%)		

	Vaccinated N=1300	Unvaccinated N=3871	Total N=5171	p value	ASD
Sex, n (%)				0.957	0.002
Female	642 (49.4%)	1915 (49.5%)	2557 (49.4%)		
Male	658 (50.6%)	1956 (50.5%)	2614 (50.6%)		
Race/Ethnicity, n (%)				0.999	0.008
White	676 (52.0%)	2024 (52.3%)	2700 (52.2%)		
Black	50 (3.8%)	149 (3.8%)	199 (3.8%)		
Hispanic	358 (27.5%)	1060 (27.4%)	1418 (27.4%)		
Asian	168 (12.9%)	500 (12.9%)	668 (12.9%)		
Other	48 (3.7%)	138 (3.6%)	186 (3.6%)		
Medication category, n (%)				0.977	0.014
Category 1	744 (57.2%)	2228 (57.6%)	2972 (57.5%)		
Category 2	40 (3.1%)	110 (2.8%)	150 (2.9%)		
Category 3	349 (26.8%)	1036 (26.8%)	1385 (26.8%)		
Category 4+5	167 (12.8%)	497 (12.8%)	664 (12.8%)		
PsO, n (%)				0.594	0.017
PsO only	1185 (91.2%)	3547 (91.6%)	4732 (91.5%)		
PsO+PsA	115 (8.8%)	324 (8.4%)	439 (8.5%)		
Number of outpatient visits[a], n (%)				<0.001	0.156
0-4	84 (6.5%)	138 (3.6%)	222 (4.3%)		
5-10	288 (22.2%)	757 (19.6%)	1045 (20.2%)		
≥11	928 (71.4%)	2976 (76.9%)	3904 (75.5%)		
Number of ED visits[a], n (%)				0.729	0.026
0	915 (70.4%)	2703 (69.8%)	3618 (70.0%)		
1	208 (16.0%)	655 (16.9%)	863 (16.7%)		
≥2	177 (13.6%)	513 (13.3%)	690 (13.3%)		
Number of hospitalization[a], n (%)				0.359	0.047
0	1129 (86.8%)	3360 (86.8%)	4489 (86.8%)		
1	121 (9.3%)	331 (8.6%)	452 (8.7%)		
≥2	50 (3.8%)	180 (4.6%)	230 (4.4%)		
Baseline Comorbidities[a], n (%)					
Kidney disease	237 (18.2%)	771 (19.9%)	1008 (19.5%)	0.184	0.043
Heart disease	141 (10.8%)	506 (13.1%)	647 (12.5%)	0.036	0.069
Lung disease	289 (22.2%)	872 (22.5%)	1161 (22.5%)	0.825	0.007
Liver disease	132 (10.2%)	347 (9.0%)	479 (9.3%)	0.201	0.041
Diabetes	472 (36.3%)	1415 (36.6%)	1887 (36.5%)	0.873	0.005
Other autoimmune diseases[b]	61 (4.7%)	180 (4.6%)	241 (4.7%)	0.950	0.002
SARS-CoV-2 /COVID-19 dx	97 (7.5%)	302 (7.8%)	399 (7.7%)	0.691	0.013
Immunocompromised status[c] at index date, n (%)				0.463	0.024
Yes	256 (19.7%)	799 (20.6%)	1055 (20.4%)		
No	1044 (80.3%)	3072 (79.4%)	4116 (79.6%)		
History of ZVL/varicella vaccination[d], n (%)				<0.001	0.199
No	783 (60.2%)	2670 (69.0%)	3453 (66.8%)		
Yes, ≤ 5 years	139 (10.7%)	395 (10.2%)	534 (10.3%)		

	Vaccinated N=1300	Unvaccinated N=3871	Total N=5171	p value	ASD
Yes, > 5 years	378 (29.1%)	806 (20.8%)	1184 (22.9%)		
History of HZ[d], n (%)				0.484	0.022
Yes	175 (13.5%)	492 (12.7%)	667 (12.9%)		
No	1125 (86.5%)	3379 (87.3%)	4504 (87.1%)		
Length of continuous membership[d], years, n (%)				0.658	0.030
≤5	285 (21.9%)	896 (23.1%)	1181 (22.8%)		
6-10	246 (18.9%)	726 (18.8%)	972 (18.8%)		
≥11	769 (59.2%)	2249 (58.1%)	3018 (58.4%)		
Concomitant vaccinatione, n (%)				N/A	N/A
Yes	431 (33.2%)	N/A	N/A		
No	869 (66.8%)	N/A	N/A		

Abbreviations: AIDS, acquired immunodeficiency syndrome; ASD, absolute standardized difference; COVID-19, coronavirus disease 2019; Dx, diagnosis; ED, emergency department; HIV, human immunodeficiency virus; HZ, herpes zoster; n, number; N/A, not applicable; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Defined in the one year prior to index date

b. Multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease.

c. HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications.

d. Defined based on all available medical records prior to index date

e. Among subjects with concomitant vaccines: influenza vaccine (47.7%), COVID-19 vaccine (11.5%), PCV13/PPSV23 (24.8%), Tdap (29.8%), and other (8.3%); 64.2% concomitant with 1st dose and 50.9% concomitant with 2nd dose.

Table 4 Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsA in VE analysis

	Vaccinated N=268	Unvaccinated N=799	Total N=1067	p value	ASD
Age at index date, years				0.575	0.057
mean (SD)	64.0 (10.27)	63.4 (10.38)	63.5 (10.35)		
median	64.5	63	64		
Q1, Q3	57.0, 70.0	57.0, 70.0	57.0, 70.0		
range	28.0, 92.0	18.0, 96.0	18.0, 96.0		
Age at index date, years, n (%)				1.000	0.025
18-29	2 (0.7%)	6 (0.8%)	8 (0.7%)		
30-39	2 (0.7%)	6 (0.8%)	8 (0.7%)		
40-49	9 (3.4%)	27 (3.4%)	36 (3.4%)		
50-59	77 (28.7%)	231 (28.9%)	308 (28.9%)		
60-69	104 (38.8%)	312 (39.0%)	416 (39.0%)		
70-79	58 (21.6%)	174 (21.8%)	232 (21.7%)		
≥80	16 (6.0%)	43 (5.4%)	59 (5.5%)		
Sex, n (%)				0.920	0.007
Female	151 (56.3%)	453 (56.7%)	604 (56.6%)		

	Vaccinated N=268	Unvaccinated N=799	Total N=1067	p value	ASD
Male	117 (43.7%)	346 (43.3%)	463 (43.4%)		
Race/Ethnicity, n (%)				0.513	0.129
White	145 (54.1%)	463 (57.9%)	608 (57.0%)		
Black	PPD				
Hispanic	82 (30.6%)	208 (26.0%)	290 (27.2%)		
Asian	27 (10.1%)	73 (9.1%)	100 (9.4%)		
Other	PPD				
Medication category, n (%)				0.996	0.018
Category 1	24 (9.0%)	72 (9.0%)	96 (9.0%)		
Category 2	29 (10.8%)	82 (10.3%)	111 (10.4%)		
Category 3	117 (43.7%)	351 (43.9%)	468 (43.9%)		
Category 4+5	98 (36.6%)	294 (36.8%)	392 (36.7%)		
PsA, n (%)				0.992	0.001
PsA only	146 (54.5%)	435 (54.4%)	581 (54.5%)		
PsA+PsO	122 (45.5%)	364 (45.6%)	486 (45.5%)		
Number of outpatient visits[a], n (%)				0.040	0.165
0-4	11 (4.1%)	14 (1.8%)	25 (2.3%)		
5-10	45 (16.8%)	112 (14.0%)	157 (14.7%)		
≥11	212 (79.1%)	673 (84.2%)	885 (82.9%)		
Number of ED visits[a], n (%)				0.096	0.148
0	186 (69.4%)	600 (75.1%)	786 (73.7%)		
1	50 (18.7%)	135 (16.9%)	185 (17.3%)		
≥2	32 (11.9%)	64 (8.0%)	96 (9.0%)		
Number of hospitalizations[a], n (%)				0.219	0.118
0	236 (88.1%)	732 (91.6%)	968 (90.7%)		
1	22 (8.2%)	47 (5.9%)	69 (6.5%)		
≥2	10 (3.7%)	20 (2.5%)	30 (2.8%)		
Baseline Comorbidities[a], n (%)					
Kidney disease	35 (13.1%)	105 (13.1%)	140 (13.1%)	0.973	0.002
Heart disease	27 (10.1%)	65 (8.1%)	92 (8.6%)	0.328	0.068
Lung disease	52 (19.4%)	147 (18.4%)	199 (18.7%)	0.715	0.026
Liver disease	33 (12.3%)	70 (8.8%)	103 (9.7%)	0.088	0.116
Diabetes	90 (33.6%)	251 (31.4%)	341 (32.0%)	0.510	0.046
Other autoimmune diseases[b]	28 (10.4%)	78 (9.8%)	106 (9.9%)	0.745	0.023
SARS-CoV-2/COVID-19 dx	29 (10.8%)	78 (9.8%)	107 (10.0%)	0.618	0.035
Immunocompromised status[c] at index date, n (%)				0.426	0.056
Yes	171 (63.8%)	488 (61.1%)	659 (61.8%)		
No	97 (36.2%)	311 (38.9%)	408 (38.2%)		
History of ZVL/varicella vaccination[d], n (%)				0.166	0.130
No	205 (76.5%)	647 (81.0%)	852 (79.9%)		
Yes, ≤ 5 years	16 (6.0%)	49 (6.1%)	65 (6.1%)		
Yes, > 5 years	47 (17.5%)	103 (12.9%)	150 (14.1%)		

	Vaccinated N=268	Unvaccinated N=799	Total N=1067	p value	ASD
History of HZ[d], n (%)				0.523	0.045
Yes	39 (14.6%)	104 (13.0%)	143 (13.4%)		
No	229 (85.4%)	695 (87.0%)	924 (86.6%)		
Length of continuous membership[d], years, n (%)				0.024	0.190
≤5	83 (31.0%)	184 (23.0%)	267 (25.0%)		
6-10	45 (16.8%)	169 (21.2%)	214 (20.1%)		
≥11	140 (52.2%)	446 (55.8%)	586 (54.9%)		
Concomitant vaccination[e], n (%)				N/A	N/A
Yes	118 (44.0%)	N/A	N/A		
No	150 (56.0%)	N/A	N/A		

Abbreviations: AIDS, acquired immunodeficiency syndrome; ASD, absolute standardized difference; COVID-19, coronavirus disease 2019; Dx, diagnosis; ED, emergency department; HIV, human immunodeficiency virus; HZ, herpes zoster; n, number; N/A, not applicable; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Defined in the one year prior to index date

b. Multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease.

c. HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications.

d. Defined based on all available medical records prior to index date

e. Among subjects with concomitant vaccines: influenza vaccine (47.7%), COVID-19 vaccine (11.5%), PCV13/PPSV23 (24.8%), Tdap (29.8%), and other (8.3%); 64.2% concomitant with 1st dose and 50.9% concomitant with 2nd dose.

Table 5 Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsO

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Overall	2616	35	8678.6	4.0 (2.9, 5.6)	7765	176	14685.2	12.0 (10.3, 13.9)	0.381 (0.257, 0.566)	0.393 (0.260, 0.595)	61.9% (43.4%, 74.3%)	60.7% (40.5%, 74.0%)
Time between first and second doses												
4 weeks to 6 months	2101	25	7007.5	3.6 (2.4, 5.3)	6232	139	11808.4	11.8 (10.0, 13.9)	0.365 (0.231, 0.577)	0.364 (0.225, 0.588)	63.5% (42.3%, 76.9%)	63.6% (41.2%, 77.5%)
>6 months	515	10	1671.0	6.0 (3.2, 11.1)	1533	37	2876.7	12.9 (9.3, 17.8)	0.437 (0.200, 0.959)	0.538 (0.212, 1.364)	56.3% (4.1%, 80.0%)	46.2% (-26.7%, 78.8%)
Age at index date, years												
18-49	17	0	33.6	0	48	1	115.3	8.7 (1.2, 61.6)	N/A	N/A	N/A	N/A
≥50	2599	35	8645.0	4.0 (2.9, 5.6)	7717	175	14569.9	12.0 (10.4, 13.9)	0.383 (0.258, 0.569)	0.396 (0.262, 0.600)	61.7% (43.1%, 74.2%)	60.4% (40.0%, 73.8%)
50-59	343	0	1001.9	0	1020	16	2207.7	7.2 (4.4, 11.8)	N/A	N/A	N/A	N/A
60-69	886	10	2929.1	3.4 (1.8, 6.3)	2631	60	4949.4	12.1 (9.4, 15.6)	0.283 (0.128, 0.629)	0.261 (0.109, 0.627)	71.7% (37.1%, 87.2%)	73.9% (37.3%, 89.1%)
≥70	1370	25	4713.9	5.3 (3.6, 7.8)	4066	99	7412.7	13.4 (11.0, 16.3)	0.502 (0.315, 0.799)	0.520 (0.314, 0.859)	49.8% (20.1%, 68.5%)	48.0% (14.1%, 68.6%)

HZ	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Medication category												
Category 1	1437	21	4821.1	4.4 (2.8, 6.7)	4290	95	8171.4	11.6 (9.5, 14.2)	0.431 (0.257, 0.723)	0.479 (0.274, 0.837)	56.9% (27.7%, 74.3%)	52.1% (16.3%, 72.6%)
Category 2	53	0	189.2	0	140	2	321.6	6.2 (1.6, 24.9)	N/A	N/A	N/A	N/A
Category 3	763	11	2506.1	4.4 (2.4, 7.9)	2272	54	4175.4	12.9 (9.9, 16.9)	0.344 (0.168, 0.704)	0.330 (0.158, 0.690)	65.6% (29.6%, 83.2%)	67.0% (31.0%, 84.2%)
Cat 4+5	363	3	1162.2	2.6 (0.8, 8.0)	1063	25	2016.8	12.4 (8.4, 18.3)	N/A	N/A	N/A	N/A
Medication category, combined[b]												
Cat 1-2	1490	21	5010.3	4.2 (2.7, 6.4)	4430	97	8493.0	11.4 (9.4, 13.9)	0.422 (0.252, 0.707)	0.472 (0.270, 0.823)	57.8% (29.3%, 74.8%)	52.8% (17.7%, 73.0%)
Cat 3-5	1126	14	3668.3	3.8 (2.3, 6.4)	3335	79	6192.2	12.8 (10.2, 15.9)	0.333 (0.179, 0.618)	0.327 (0.173, 0.619)	66.7% (38.2%, 82.1%)	67.3% (38.1%, 82.7%)
Year after index date												
0-<1	2616	8	2330.8	3.4 (1.7, 6.9)	7765	70	5840.9	12.0 (9.5, 15.1)	0.309 (0.148, 0.646)	0.290 (0.132, 0.638)	69.1% (35.4%, 85.2%)	71.0% (36.2%, 86.8%)
1-<2	2480	12	2407.8	5.0 (2.8, 8.8)	5234	41	4395.6	9.3 (6.9, 12.7)	0.631 (0.318, 1.254)	0.693 (0.325, 1.479)	36.9% (-20.3%, 68.2%)	30.7% (-32.4%, 67.5%)
2-<3	2333	8	1841.8	4.3 (2.2, 8.7)	3734	42	2663.7	15.8 (11.7, 21.3)	0.308 (0.136, 0.695)	0.306 (0.128, 0.732)	69.2% (30.5%, 86.4%)	69.4% (26.8%, 87.2%)
3-<4	1320	2	1018.7	2.0	1658	16	1096.6	14.6	N/A	N/A	N/A	N/A

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
				(0.5, 7.9)				(8.9, 23.8)				
4-<5	775	4	749.9	5.3 (2.0, 14.2)	644	6	509.7	11.8 (5.3, 26.2)	N/A	N/A	N/A	N/A
5-<6	613	1	309.6	3.2 (0.5, 22.9)	350	1	167.6	6.0 (0.8, 42.4)	N/A	N/A	N/A	N/A
6-<7	90	0	20.0	0	51	0	11.0	0	N/A	N/A	N/A	N/A
Year after index date, combined[b]												
0-<1	2616	8	2330.8	3.4 (1.7, 6.9)	7765	70	5840.9	12.0 (9.5, 15.1)	0.309 (0.148, 0.646)	0.290 (0.132, 0.638)	69.1% (35.4%, 85.2%)	71.0% (36.2%, 86.8%)
1-<3	2480	20	4249.6	4.7 (3.0, 7.3)	5234	83	7059.4	11.8 (9.5, 14.6)	0.451 (0.268, 0.761)	0.446 (0.256, 0.776)	54.9% (23.9%, 73.2%)	55.4% (22.4%, 74.4%)
3-<7	1320	7	2098.2	3.3 (1.6, 7.0)	1658	23	1784.9	12.9 (8.6, 19.4)	0.315 (0.105, 0.946)	0.468 (0.080, 2.728)	68.5% (5.4%, 89.5%)	53.2% (-63.3%, 92.0%)

Abbreviations: Cat, category; CI, confidence interval; ED, emergency department; HZ, herpes zoster; n, number; N/A, not applicable; PsO, psoriasis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Adjusted for covariates immunocompromised status, history of HZ, number of outpatient visits, number of ED visits, and history of ZVL/varicella vaccination.

b. Conducted as a post-hoc analysis.

Table 6 Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsA

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Overall	548	9	1701.7	5.3 (2.8, 10.2)	1615	44	2868.2	15.3 (11.4, 20.6)	0.224 (0.079, 0.632)	0.195 (0.058, 0.657)	77.6% (36.8%, 92.1%)	80.5% (34.3%, 94.2%)
Time between first and second doses												
4 weeks to 6 months	437	6	1375.0	4.4 (2.0, 9.7)	1286	40	2309.3	17.3 (12.7, 23.6)	0.184 (0.056, 0.603)	0.196 (0.051, 0.749)	81.6% (39.7%, 94.4%)	80.4% (25.1%, 94.9%)
>6 months	111	3	326.7	9.2 (3.0, 28.5)	329	4	558.8	7.2 (2.7, 19.1)	N/A	N/A	N/A	N/A
Age at index date, years												
18-49	11	0	22.8	0	30	0	62.8	0	N/A	N/A	N/A	N/A
≥50	537	9	1678.9	5.4 (2.8, 10.3)	1585	44	2805.3	15.7 (11.7, 21.1)	0.224 (0.079, 0.632)	0.195 (0.058, 0.657)	77.6% (36.8%, 92.1%)	80.5% (34.3%, 94.2%)
Medication category												
Category 1	52	2	142.5	14.0 (3.5, 56.1)	147	5	263.0	19.0 (7.9, 45.7)	N/A	N/A	N/A	N/A
Category 2	47	1	151.9	6.6 (0.9, 46.7)	129	3	199.7	15.0 (4.8, 46.6)	N/A	N/A	N/A	N/A
Category 3	228	5	726.2	6.9 (2.9, 16.5)	681	16	1170.4	13.7 (8.4, 22.3)	0.465 (0.133, 1.631)	0.941 (0.161, 5.509)	53.5% (-38.7%, 86.7%)	5.9% (-81.8%, 83.9%)

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Cat 4+5	221	1	681.2	1.5 (0.2, 10.4)	658	20	1235.1	16.2 (10.4, 25.1)	N/A	N/A	N/A	N/A
Medication category, combined[b]												
Cat 1-2	99	3	294.4	10.2 (3.3, 31.6)	276	8	462.7	17.3 (8.6, 34.6)	N/A	N/A	N/A	N/A
Cat 3-5	449	6	1407.4	4.3 (1.9, 9.5)	1339	36	2405.5	15.0 (10.8, 20.7)	0.199 (0.061, 0.656)	0.184 (0.048, 0.709)	80.1% (34.4%, 93.9%)	81.6% (29.1%, 95.2%)

Abbreviations: Cat, category; CI, confidence interval; HZ, herpes zoster; n, number; N/A, not applicable; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Adjusted for covariates race/ethnicity, immunocompromised status, history of HZ, number of outpatient visits, and history of ZVL/varicella vaccination.
b. Conducted as a post-hoc analysis.

Table 7 Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsO or PsA, or PsO only

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Among individuals with PsO or PsA	2906	40	9546.8	4.2 (3.1, 5.7)	8627	199	16130.4	12.3 (10.7, 14.2)	0.374 (0.257, 0.545)	0.387 (0.261, 0.573)	62.6% (45.5%, 74.3%)	61.3% (42.7%, 73.9%)
Among individuals with PsO only	2359	31	7847.3	4.0 (2.8, 5.6)	7072	159	13262.0	12.0 (10.3, 14.0)	0.385 (0.254, 0.584)	0.389 (0.251, 0.604)	61.5% (41.6%, 74.6%)	61.1% (39.6%, 74.9%)

Abbreviations: CI, confidence interval; ED, emergency department; HZ, herpes zoster; n, number; PsO, psoriasis; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Adjusted for covariates immunocompromised status, history of HZ, number of outpatient visits, number of ED visits, and history of ZVL/varicella vaccination.

Table 8 Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsO

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Overall	1300	11	1590.0	6.9 (3.8, 12.5)	3871	53	4044.2	13.1 (10.0, 17.2)	0.531 (0.272, 1.036)	0.694 (0.339, 1.421)	46.9% (-3.5%, 72.8%)	30.6% (-29.6%, 66.1%)
Year after index date												
0-<1	1300	7	961.1	7.3 (3.5, 15.3)	3871	36	2560.0	14.1 (10.1, 19.5)	0.507 (0.223, 1.150)	0.676 (0.276, 1.656)	49.3% (-13.0%, 77.7%)	32.4% (-39.6%, 72.4%)
1-<2	624	3	385.5	7.8 (2.5, 24.1)	1509	9	921.6	9.8 (5.1, 18.8)	N/A	N/A	N/A	N/A
2-<3	239	0	142.2	0	564	2	357.9	5.6 (1.4, 22.3)	N/A	N/A	N/A	N/A
3-<4	73	0	51.8	0	202	3	130.8	22.9 (7.4, 71.1)	N/A	N/A	N/A	N/A
4-<5	41	1	35.2	28.4 (4.0, 201.5)	80	3	53.7	55.8 (18.0, 173.1)	N/A	N/A	N/A	N/A
5-<6	26	0	12.1	0	33	0	18.2	0	N/A	N/A	N/A	N/A

Abbreviations: CI, confidence interval; HZ, herpes zoster; n, number; N/A, not applicable; PsO, psoriasis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; ZVL, zoster vaccine live

a. Adjusted for covariates immunocompromised status, history of HZ, number of outpatient visits, and history of ZVL/varicella vaccination.

Table 9 Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsA

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted	Unadjusted	Adjusted
Overall	268	0	318.5	0	799	12	836.7	14.3 (8.1, 25.3)	N/A	N/A	N/A	N/A

Abbreviations: CI, confidence interval; HZ, herpes zoster; n, number; N/A, not applicable; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness

CCI

CCI

CCI

Table 14 Baseline characteristics and HZ incidence of 2-dose RZV vaccinated individuals with PsO, index date between March 2020 and December 2020 (not accrued)

	Not accrued N=351
Age at index date, years	
mean (sd)	70.7 (8.53)
median	70
Q1, Q3	66.0, 76.0
range	50.0, 96.0
Age at index date, years, n (%)	
18-49	0 (0.0%)
50-59	33 (9.4%)
60-69	126 (35.9%)
70-79	141 (40.2%)
≥80	51 (14.5%)
Sex, n (%)	
Female	162 (46.2%)
Male	189 (53.8%)
Race/Ethnicity, n (%)	
White	219 (62.4%)
Black	PPD
Hispanic	62 (17.7%)
Asian	53 (15.1%)
Other	PPD
Medication category, n (%)	
Category 1	194 (55.3%)
Category 2	5 (1.4%)
Category 3	100 (28.5%)
Category 4+5	52 (14.8%)
PsO, n (%)	
PsO only	315 (89.7%)
PsO+PsA	36 (10.3%)
Number of outpatient visits[a], n (%)	
0-4	15 (4.3%)
5-10	58 (16.5%)
≥11	278 (79.2%)
Number of ED visits[a], n (%)	
0	273 (77.8%)
1	47 (13.4%)
≥2	31 (8.8%)
Number of hospitalization[a], n (%)	
0	312 (88.9%)
1	23 (6.6%)
≥2	16 (4.6%)

	Not accrued N=351
Baseline Comorbidities[a], n (%)	
Kidney disease	62 (17.7%)
Heart disease	36 (10.3%)
Lung disease	91 (25.9%)
Liver disease	29 (8.3%)
Diabetes	138 (39.3%)
Other autoimmune diseases[b]	14 (4.0%)
SARS-CoV-2 infection/COVID-19 diagnosis	3 (0.9%)
Immunocompromised status[c] at index date, n (%)	
Yes	76 (21.7%)
No	275 (78.3%)
History of ZVL/varicella vaccination[d], n (%)	
No	151 (43.0%)
Yes, ≤ 5 years	42 (12.0%)
Yes, > 5 years	158 (45.0%)
History of HZ[d], n (%)	
Yes	37 (10.5%)
No	314 (89.5%)
Length of continuous membership[d], years, n (%)	
≤5	63 (17.9%)
6-10	56 (16.0%)
≥11	232 (66.1%)
Concomitant vaccination[e], n (%)	
Yes	146 (41.6%)
No	205 (58.4%)
HZ cases during the follow up	
Number of cases	4
Number of person-years	1321.4
Incidence per 1000 person-years (95% CI)	3.0 (1.1, 8.1)

Abbreviations: AIDS, acquired immunodeficiency syndrome; COVID-19, coronavirus disease 2019; ED, emergency department; HIV, human immunodeficiency virus; HZ, herpes zoster; n, number; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis; ZVL, zoster vaccine live

a. Defined in the one year prior to index date

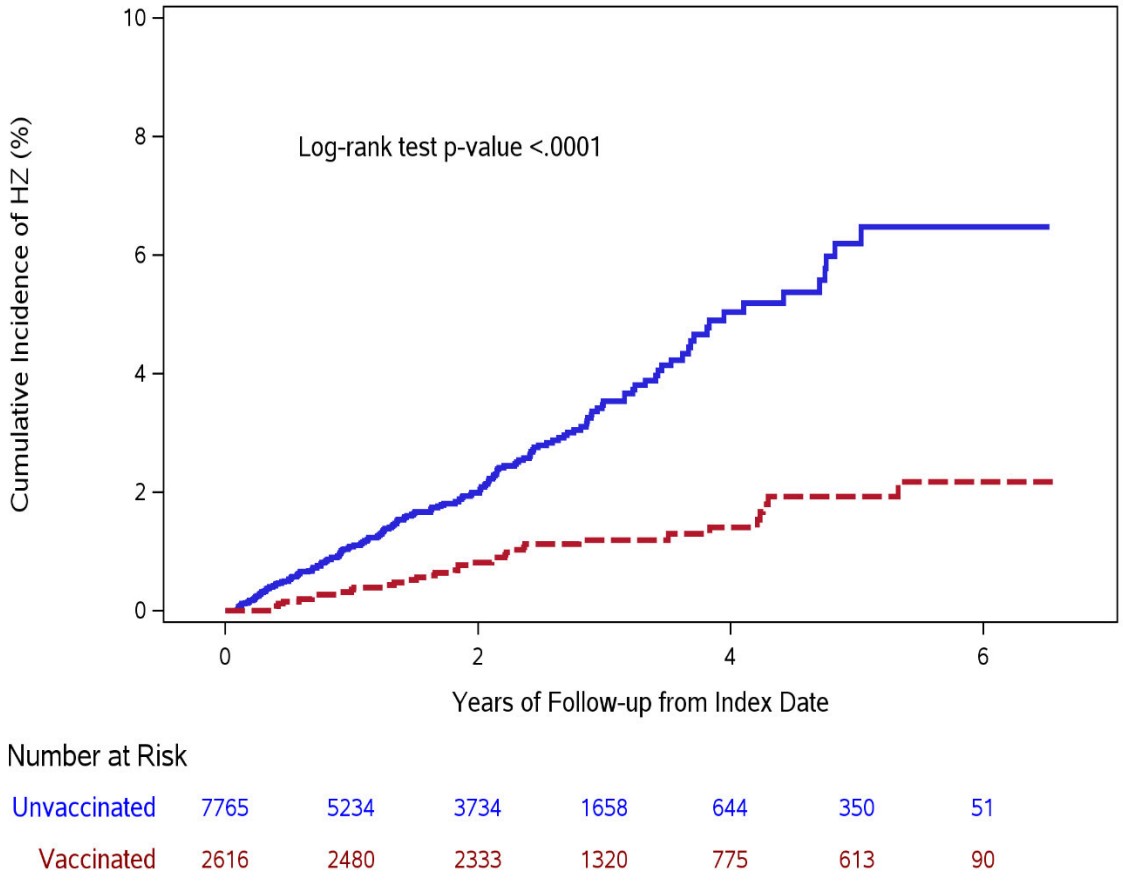
b. Multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease.

c. HIV/AIDS, leukemia/lymphoma, congenital/other immunodeficiencies, asplenia/hyposplenia, hematopoietic stem cell transplant/solid organ transplant, and receipt of immunosuppressive medications.

d. Defined based on all available medical records prior to index date

e. Among subjects with concomitant vaccines: influenza vaccine (52.7%), COVID-19 vaccine (0.0%), PCV13/PPSV23 (30.8%), Tdap (30.8%), and other (6.8%); 67.1% concomitant with 1st dose and 46.6% concomitant with 2nd dose.

Figure 7 **Cumulative incidence estimates of HZ by RZV vaccination status in 2-dose RZV cohort with PsO**

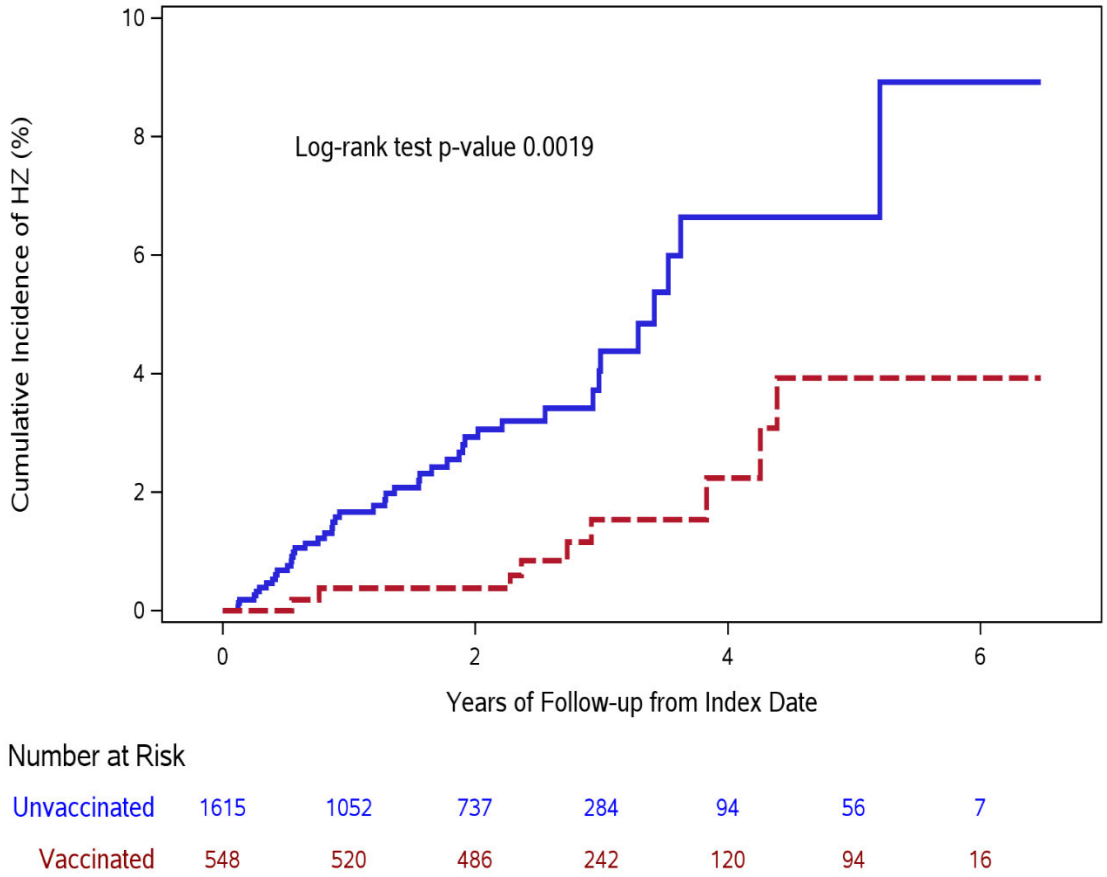


Number at Risk

Unvaccinated	7765	5234	3734	1658	644	350	51
Vaccinated	2616	2480	2333	1320	775	613	90

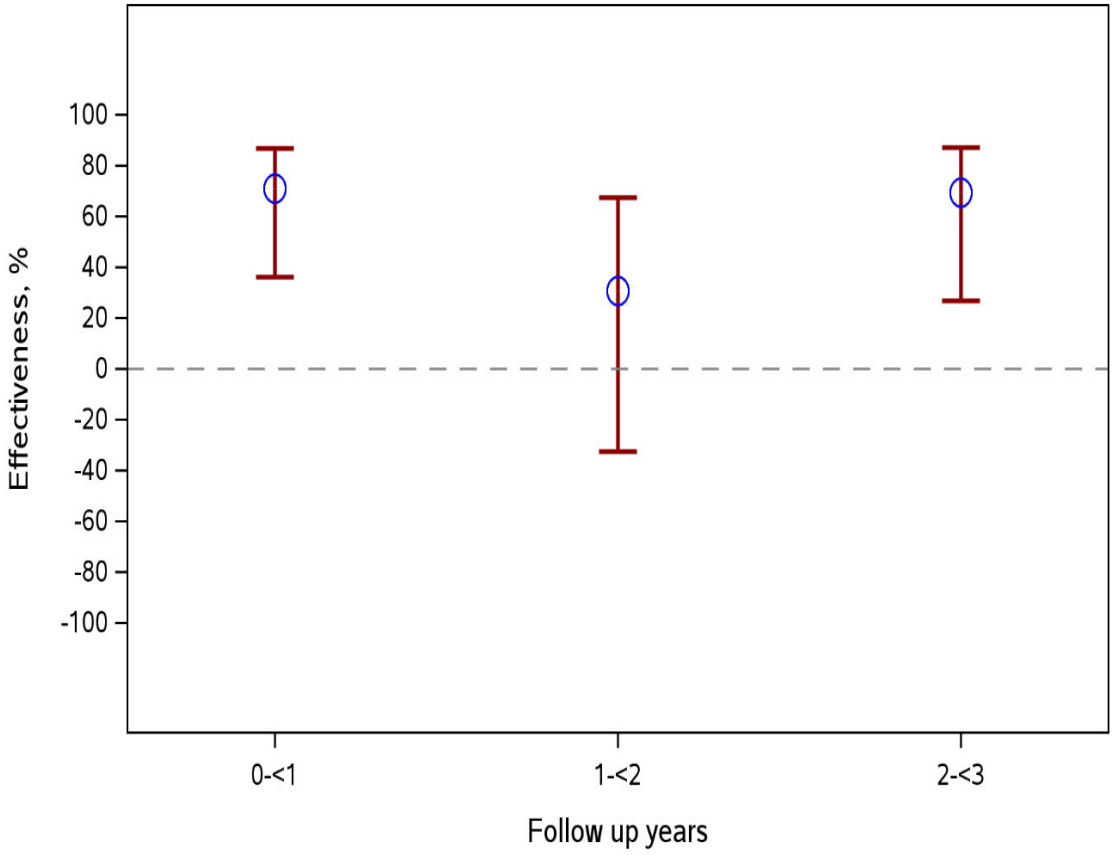
Abbreviations: HZ, herpes zoster; PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 8 **Cumulative incidence estimates of HZ by RZV vaccination status in 2-dose RZV cohort with PsA**



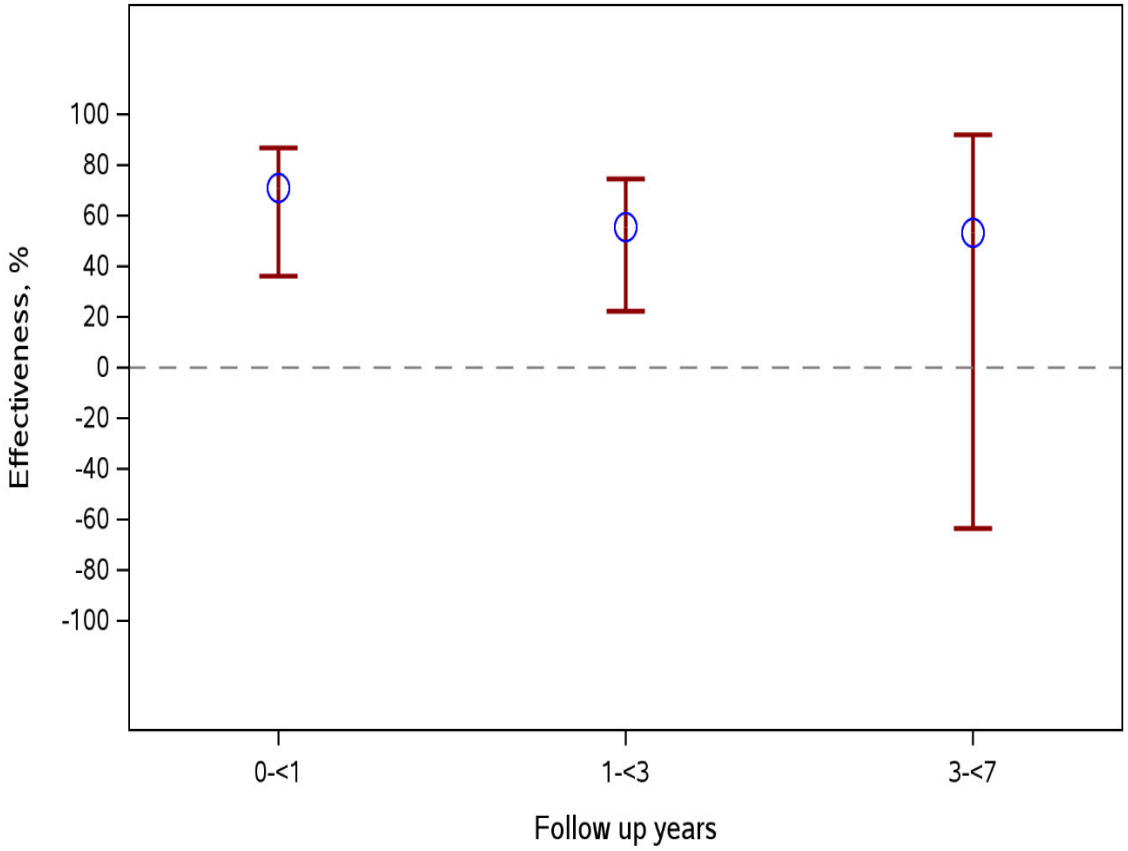
Abbreviations: HZ, herpes zoster; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine

Figure 9 **Effectiveness of 2 doses of RZV in preventing HZ by year after vaccination among individuals with PsO**



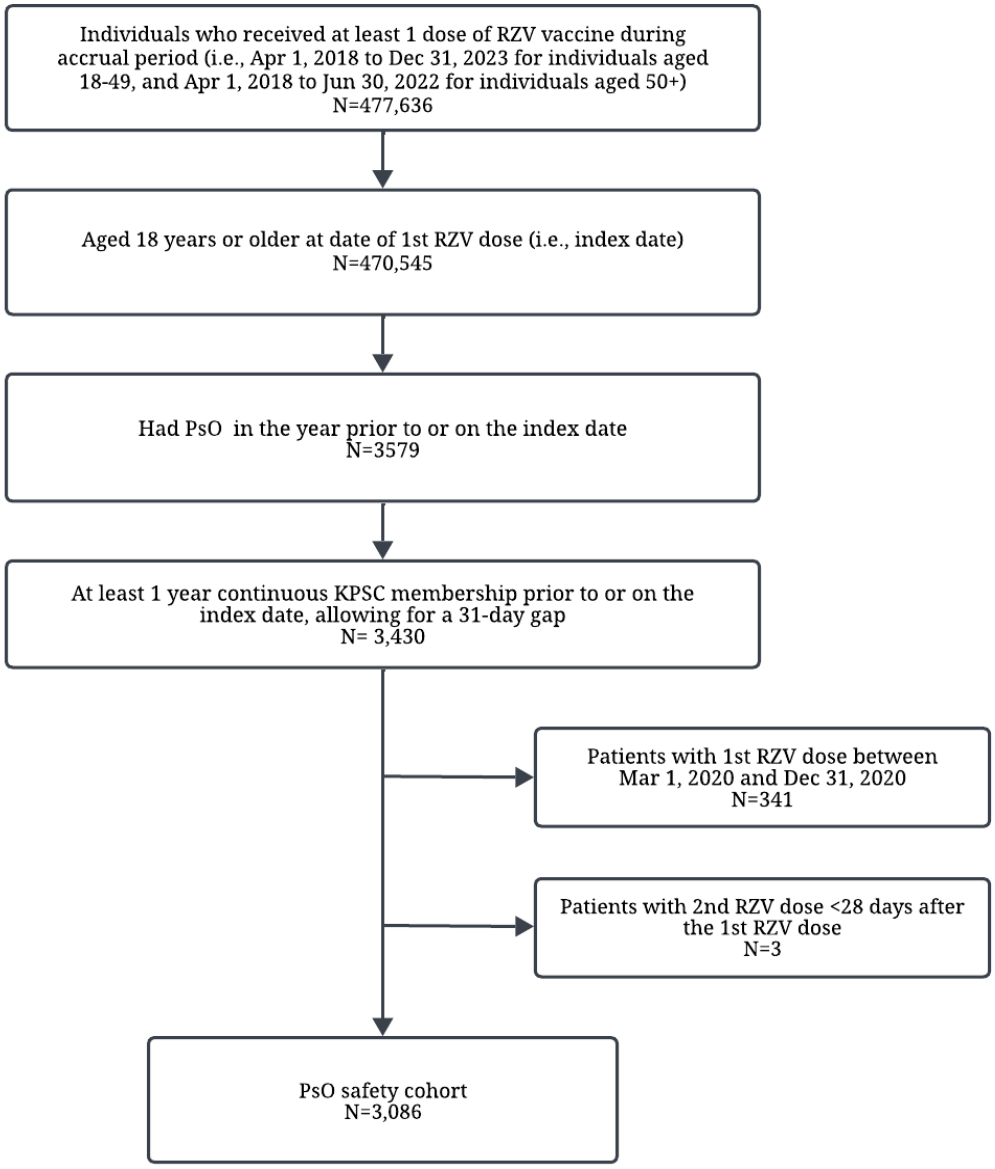
Abbreviations: HZ, herpes zoster; PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 10 Effectiveness of 2 doses of RZV in preventing HZ by year (combined) after vaccination among individuals with PsO



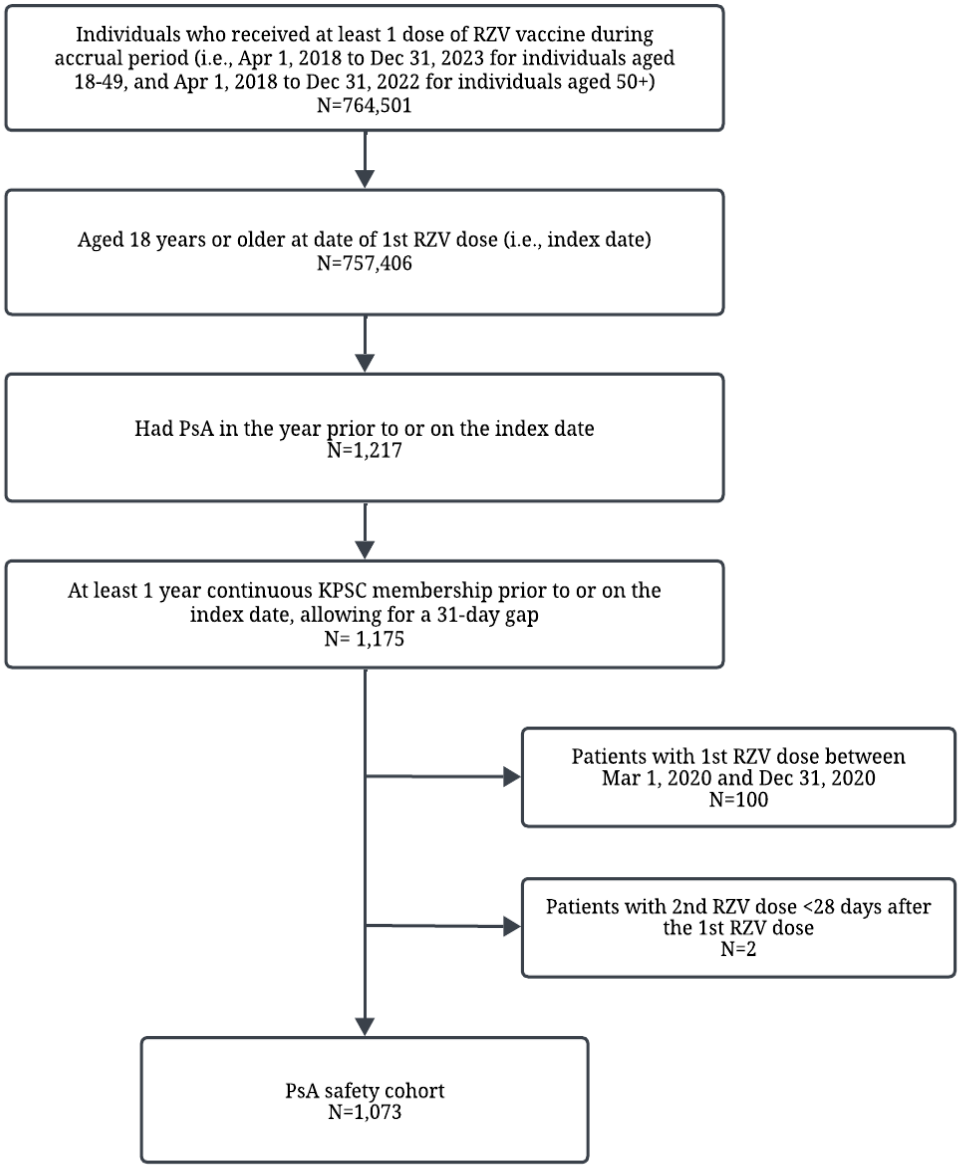
Abbreviations: HZ, herpes zoster; PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 11 Safety flow chart for RZV recipients with PsO



Abbreviations: KPSC, Kaiser Permanente Southern California; PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 12 Safety flow chart for RZV recipients with PsA



Abbreviations: KPSC, Kaiser Permanente Southern California; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine

Table 15 Baseline characteristics of RZV recipients with PsO in safety analysis

	Vaccinated N=3086
Age at index date, years	
mean (SD)	69.6 (9.49)
median	70
Q1, Q3	64.0, 76.0
range	19.0, 100.0
Age at index date, years, n (%)	
18-49	36 (1.2%)
50-59	427 (13.8%)
60-69	986 (32.0%)
70-79	1212 (39.3%)
≥80	425 (13.8%)
Sex, n (%)	
Female	1578 (51.1%)
Male	1508 (48.9%)
Race/Ethnicity, n (%)	
White	1784 (57.8%)
Black	98 (3.2%)
Hispanic	697 (22.6%)
Asian	416 (13.5%)
Other	91 (2.9%)
Medication category, n (%)	
Category 1	1753 (56.8%)
Category 2	64 (2.1%)
Category 3	849 (27.5%)
Category 4	410 (13.3%)
Category 5	10 (0.3%)
PsO, n (%)	
PsO only	2813 (91.2%)
PsO+PsA	273 (8.8%)
Number of RZV doses, n (%)	
One dose	700 (22.7%)
Two doses	2386 (77.3%)
Concomitant vaccination[a], n (%)	
Yes	1033 (33.5%)
No	2053 (66.5%)
Year of the index dose, n (%)	
2018	387 (12.5%)
2019	1017 (33.0%)
2020	156 (5.1%)
2021	622 (20.2%)
2022	886 (28.7%)

	Vaccinated N=3086
2023	18 (0.6%)
Month of the index dose, n (%)	
January	219 (7.1%)
February	220 (7.1%)
March	212 (6.9%)
April	195 (6.3%)
May	309 (10.0%)
June	694 (22.5%)
July	223 (7.2%)
August	206 (6.7%)
September	231 (7.5%)
October	258 (8.4%)
November	173 (5.6%)
December	146 (4.7%)

Abbreviations: COVID-19, coronavirus disease 2019; n, number; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis

a. Among subjects with concomitant vaccines: influenza vaccine (50.0%), COVID-19 vaccine (6.9%), PCV13/PPSV23 (25.2%), Tdap (28.1%), and other (7.6%); 70.2% concomitant with 1st dose and 40.4% concomitant with 2nd dose.

Table 16 Baseline characteristics of RZV recipients with PsA in safety analysis

	Vaccinated N = 1073
Age at index date, years	
mean (SD)	65.8 (9.46)
median	66
Q1, Q3	59.0, 72.0
range	28.0, 92.0
Age at index date, years, n (%)	
18-49	23 (2.1%)
50-59	260 (24.2%)
60-69	415 (38.7%)
70-79	292 (27.2%)
≥80	83 (7.7%)
Sex, n (%)	
Female	592 (55.2%)
Male	481 (44.8%)
Race/Ethnicity, n (%)	
White	581 (54.1%)
Black	28 (2.6%)
Hispanic	290 (27.0%)
Asian	131 (12.2%)
Other	43 (4.0%)

	Vaccinated N = 1073
Medication category, n (%)	
Category 1	94 (8.8%)
Category 2	96 (8.9%)
Category 3	439 (40.9%)
Category 4	424 (39.5%)
Category 5	20 (1.9%)
PsA, n (%)	
PsA only	598 (55.7%)
PsA+PsO	475 (44.3%)
Number of RZV doses, n (%)	
One dose	200 (18.6%)
Two doses	873 (81.4%)
Concomitant vaccinationa, n (%)	
Yes	464 (43.2%)
No	609 (56.8%)
Year of the index dose, n (%)	
2018	60 (5.6%)
2019	152 (14.2%)
2020	30 (2.8%)
2021	152 (14.2%)
2022	668 (62.3%)
2023	11 (1.0%)
Month of the index dose, n (%)	
January	41 (3.8%)
February	47 (4.4%)
March	37 (3.4%)
April	40 (3.7%)
May	43 (4.0%)
June	141 (13.1%)
July	142 (13.2%)
August	154 (14.4%)
September	139 (13.0%)
October	129 (12.0%)
November	87 (8.1%)
December	73 (6.8%)

Abbreviations: COVID-19, coronavirus disease 2019; n, number; PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine; SD, standard deviation; Tdap, tetanus, diphtheria, and acellular pertussis

a. Among subjects with concomitant vaccines: influenza vaccine (47.6%), COVID-19 vaccine (12.1%), PCV13/PPSV23 (30.4%), Tdap (26.9%), and other (5.8%); 76.9% concomitant with 1st dose and 34.3% concomitant with 2nd dose.

Table 17 Incidence and incidence rate ratio of PsO flare after RZV among individuals with PsO

	Risk Window			Comparison Window			Incidence Rate Ratio[a] (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall	30	448.94	66.82 (46.72, 95.57)	42	625.35	67.16 (49.63, 90.88)	0.94 (0.58, 1.52)
RZV dose							
First	16	253.21	63.19 (38.71, 103.14)	42	625.35	67.16 (49.63, 90.88)	0.90 (0.50, 1.62)
Second	14	195.73	71.53 (42.36, 120.77)	34	511.26	66.50 (47.52, 93.07)	1.01 (0.54, 1.90)
Age at index date, years							
18-49[b]	2	4.76	419.83 (105.00, 1678.65)	2	7.31	273.60 (68.43, 1093.95)	N/A
≥50	28	444.17	63.04 (43.53, 91.30)	40	618.04	64.72 (47.47, 88.23)	0.93 (0.57, 1.53)
Medication category, n (%)							
Category 1	8	251.92	31.76 (15.88, 63.50)	12	352.56	34.04 (19.33, 59.93)	1.02 (0.40, 2.60)
Category 2b	2	8.38	238.57 (59.67, 953.91)	3	12.58	238.52 (76.93, 739.54)	N/A
Category 3	12	126.24	95.06 (53.98, 167.38)	17	175.27	96.99 (60.30, 156.02)	0.85 (0.40, 1.81)
Category 4	8	61.07	130.99 (65.51, 261.93)	10	82.83	120.73 (64.96, 224.39)	1.18 (0.44, 3.14)
Category 5	0	1.31	0.00	0	2.11	0.00	N/A

Abbreviations: CI, confidence interval; N/A, not applicable; PsO, psoriasis; RZV, recombinant zoster vaccine

a. Time-varying covariate season (i.e., Mar-May, June-Aug, Sept-Nov, Dec-Feb) was adjusted in the analysis.

b. Only descriptive analysis was conducted due to the small number of events (<5 in the risk window).

Table 18 Incidence and incidence rate ratio of PsO or PsA flare after RZV among individuals with PsO or PsA

	Risk Window			Comparison Window			Incidence Rate Ratio[a] (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall	55	568.33	96.77 (74.30, 126.05)	67	789.76	84.84 (66.77, 107.79)	1.11 (0.77, 1.60)
RZV dose							
First	29	318.8	90.97 (63.21, 130.90)	67	789.76	84.84 (66.77, 107.79)	1.07 (0.68, 1.68)
Second	26	249.53	104.20 (70.94, 153.03)	56	652.31	85.85 (66.07, 111.55)	1.19 (0.74, 1.92)

Abbreviations: CI, confidence interval; PsA, psoriatic arthritis; PsO, psoriasis; RZV, recombinant zoster vaccine

a. Time-varying covariate season (i.e., Mar-May, June-Aug, Sept-Nov, Dec-Feb) was adjusted in the analysis.

Table 19 Incidence and incidence rate ratio of PsA flare after RZV among individuals with PsA

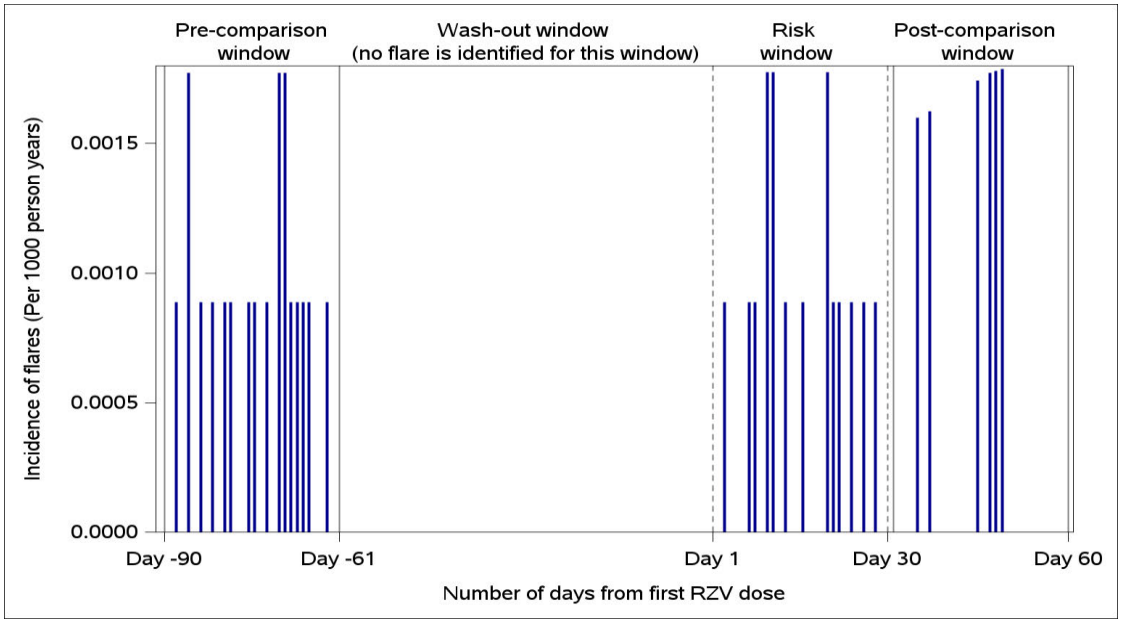
	Risk Window			Comparison Window			Incidence Rate Ratio[a] (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall	25	159.50	156.74 (105.91, 231.97)	26	221.64	117.31 (79.87, 172.29)	1.21 (0.69, 2.13)
RZV dose							
First	13	88.01	147.70 (85.77, 254.37)	26	221.64	117.31 (79.87, 172.29)	1.15 (0.58, 2.29)
Second	12	71.48	167.87 (95.34, 295.60)	23	189.12	121.62 (80.82, 183.01)	1.32 (0.65, 2.68)
Age at index date, years							
18-49	1	3.12	320.39 (45.13, 2274.51)	0	5.10	0.00	N/A
≥50	24	156.38	153.48 (102.87, 228.98)	26	216.53	120.07 (81.75, 176.35)	1.15 (0.65, 2.04)
Medication category, n (%)							
Category 1	2	13.63	146.69 (36.69, 586.52)	0	18.84	0.00	N/A
Category 2[b]	2	14.05	142.34 (35.60, 569.15)	1	20.54	48.69 (6.86, 345.68)	N/A
Category 3	11	65.26	168.54 (93.34, 304.34)	15	90.50	165.74 (99.92, 274.92)	0.94 (0.41, 2.12)
Category 4	10	63.92	156.45 (84.18, 290.77)	10	87.93	113.72 (61.19, 211.36)	1.33 (0.53, 3.32)
Category 5	0	2.63	0.00	0	3.82	0.00	N/A

Abbreviations: CI, confidence interval; N/A, not applicable; PsA, psoriatic arthritis; RZV, recombinant zoster vaccine

a. Time-varying covariate season (i.e., Mar-May, June-Aug, Sept-Nov, Dec-Feb) was adjusted in the analysis.

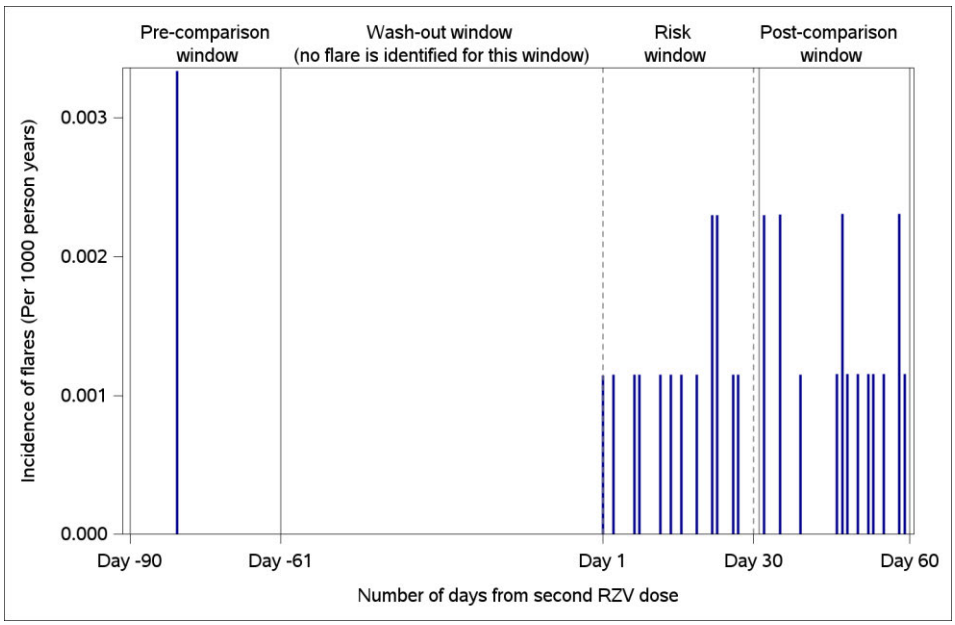
b. Only descriptive analysis was conducted due to the small number of events (<5).

Figure 13 Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsO



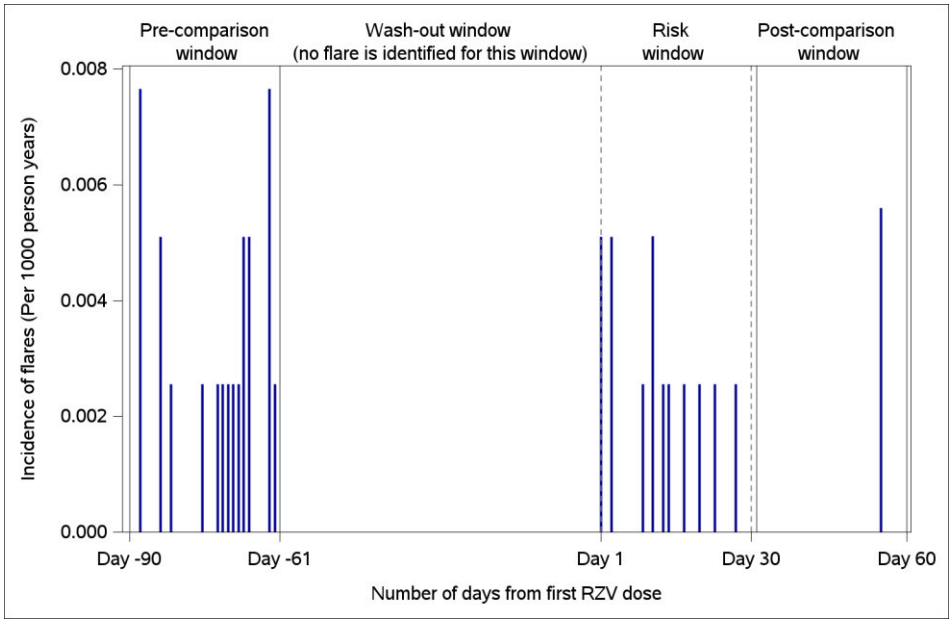
Abbreviations: PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 14 Incidence of flare by day during the risk and comparison windows of second dose among RZV recipients with PsO



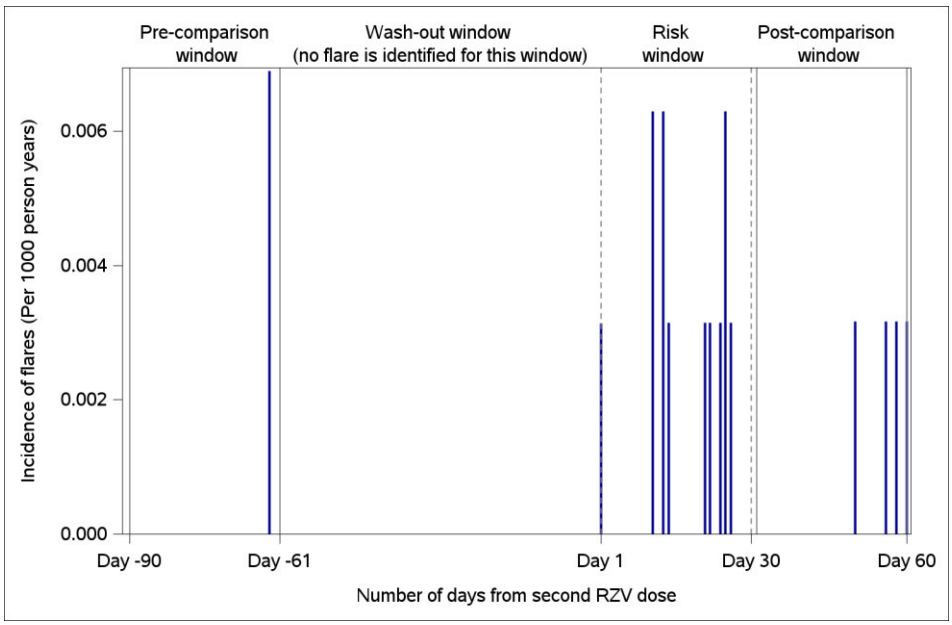
Abbreviations: PsO, psoriasis; RZV, recombinant zoster vaccine

Figure 15 Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsA



Abbreviations: PsA, psoriatic arthritis; RZV, recombinant zoster vaccine

Figure 16 Incidence of flare by day during the risk and comparison windows of second dose among RZV recipients with PsA



Abbreviations: PsA, psoriatic arthritis; RZV, recombinant zoster vaccine

ANNEX 1 LIST OF STAND-ALONE DOCUMENTS

No.	Document Reference No	Date	Title
1.	TMF-16226474	23 June 2023	Protocol
2.	TMF-17314342	09 November 2023	Statistical Analysis Plan
3.	TMF-17314342	27 August 2025	Sub-Amendment 01

Appendix A: Definition of clinically relevant flare

The definitions below were used for chart reviews to identify medically attended PsO/PsA flares for the safety objectives (assess the rate of PsO/PsA flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows).

Flare was defined as clinically relevant new-onset flare or new-onset disease worsening of PsO (primary safety objective 1, secondary safety objectives 2 & 3, CCI [redacted] CCI [redacted] or PsA (secondary safety objective 1 & 4, CCI [redacted] These definitions were selected in consultation with rheumatology and dermatology experts, recognizing that new-onset disease worsening could be difficult to differentiate from flare. Trained research associates and PsO/PsA specialists reviewed all potential flare events to identify a new onset or worsening of flare as meeting the criteria listed below:

1. Contact with health care provider via documented email, phone call, telehealth visit, in-person office visit, Emergency Department visit, urgent care visit, or inpatient visit

AND

2. New or worsening signs and/or symptoms suggestive of a flare (≥1 of the signs or symptoms for each condition [i.e., for PsO, A and/or C; for PsA, B and/or C]):

   A. For PsO only:

   1. Pain in the location of prior involvement, severe itching/sensation, patches/plaques, inflamed/red skin, soreness, skin flaking/thickening/scarring, nail involvement, skin lesions.

   2. Shift to a higher Body Surface Area involvement category (mild <3%, moderate 3- 10%, severe >10%)

   B. For PsA only:

   1. Peripheral arthritis (joint pain, swelling, tenderness or stiffness), joint damage (actively inflamed joints, joint deformities, restricted motion, ankylosis, or unstable joints), axial disease, extra-articular manifestations (enthesitis, dactylitis, tendonitis, nail disease, uveitis, iritis, or inflammatory bowel disease [Crohn's disease or ulcerative colitis]).

2. Shift to a higher visual analog score category (mild 1-3, moderate 4-6, severe 7-10)

C. For both PsO and PsA: Provider mention of flare, worsening of disease, aggravation, recurrence, relapse, deterioration, complaints, exacerbation, acute onset, sudden onset/change, change from baseline/previously controlled, or disease progression

AND

1. Change in medication for flare[1]:

Medication regimen change/escalation algorithm for flare (applies to both PsO and PsA unless otherwise indicated)

a. Intra-articular corticosteroid joint injection(s) (PsA only), or

b. Initiation of systemic (oral, intramuscular, or intravenous) corticosteroid (e.g., prednisone) (PsA only), or

c. Increase in dose of baseline systemic corticosteroid (e.g., prednisone 5 mg daily to prednisone 40 mg daily with taper) (PsA only), or

d. Initiation of intralesional or intramuscular corticosteroid (e.g., triamcinolone) (PsO only), or

e. Switch in MTX from oral route to subcutaneous, or

f. Increase in dose and/or frequency of administration of any medication in current baseline regimen, or

g. Addition of another medication to current medication regimen (e.g., adding a DMARD to current regimen of ibuprofen, adding golimumab to current regimen of MTX), or

h. Switch of a current medication to another medication, in the same or different category (e.g., MTX + TNF-α inhibitor to MTX + tofacitinib; MTX + TNF- α inhibitor to MTX + a different TNF-α inhibitor)

Chart review was performed among individuals eligible for the safety analysis. Trained research associates reviewed medical records from health care encounters during risk windows, comparison windows, and the 30 days after a risk or comparison window (while masked to the precise window) for evidence of clinically relevant flare. They identified new or worsening signs and/or symptoms suggestive of a flare and captured the date of onset of new or worsening signs and/or symptoms. They determined whether a change in medication was made for flare by a provider. Cases with unclear sign and/or symptoms, date of onset, or change in medication for flare were reviewed by a PsO or PsA specialist.

[1] Exclude medication changes for any reasons other than for flare, such as acute kidney injury or other adverse effects from prior medication.

Appendix B: Medication categories

Medication categories were used as an indicator for disease severity and risk for HZ to match vaccinated and unvaccinated individuals. The medication categories were developed based on consultation with KPSC and external experts (rheumatologists and dermatologists) to ensure matching based on differences in disease severity and risk of HZ.

Medication category was determined by the highest category of medication prescribed during the search periods specified below:

- Biologic disease-modifying anti-rheumatic drugs (DMARDs), intralesional/Intramuscular corticosteroids, psoralen and ultraviolet A (PUVA), photodynamic therapy (PDT), narrowband ultraviolet B (NB-UVB) (with or without tar), UV phototherapy (with or without tar), and excimer laser: 3 months before index date[2]
- Targeted synthetic DMARDs (JAK inhibitors): 3 months before index date to 1 month after index date[3]
- Nonsteroidal anti-inflammatory drugs (NSAIDs), topical medications, steroids, and conventional synthetic DMARDs: Medication prescribed/refilled within 6 months prior to index date AND medication duration covers the index date[4]

Individuals who met the criteria for both PsO and PsA were included in both the PsO and PsA cohorts. The most advanced medication category used for treatment of either condition was used for both cohorts. For example, if an individual identified as having both PsO and PsA was using a Category 2 medication for PsO (e.g., UV phototherapy) and a Category 4 medication for PsA (e.g., Orencia), then Category 4 was used for both PsO and PsA analyses.

[2] Some biologics were given as far apart as approximately every 8 weeks, thus the search period for biologics was 3 months before the index date.

[3] The search period for JAK inhibitors (a type of biologic) was extended to 1 month after the index date; because JAK inhibitors were associated with a significantly increased risk of HZ, providers might administer RZV prior to initiating treatment with a JAK inhibitor.

[4] While medications were typically dispensed as a ≤90-day supply, some medications were occasionally dispensed as a ≥100-day supply. To ensure identification of prescriptions covering the index date, medications prescribed/refilled within 6 months prior to the index date were searched to identify those medications with a duration covering the index date.

Table 20 Medication categories for PsO

Category 1 (least severe)	Topical medications (topical corticosteroids, calcineurin inhibitors, vitamin D analogues, tazarotene, salicylic acid, anthralin [dithranol], coal tar/liquor carbonis detergens [LCD], roflumilast [Zoryve], tapinarof [Vtama]), or no treatment from Category 2 to Category 5
Category 2	Psoralen and ultraviolet A (PUVA), photodynamic therapy (PDT), narrowband ultraviolet B (NB-UVB) (with or without tar), UV phototherapy (with or without tar), and excimer laser.
Category 3	**Conventional synthetic DMARDs:** Traditional DMARD: methotrexate (MTX) (Trexall, Xatmep, Otrexup, Rheumatrex, Rasuvo), cyclosporine, acitretin, apremilast (Otezla), azathioprine (Imuran, Azasan), hydroxyurea, mycophenolate mofetil (MMF), tacrolimus, leflunomide (Arava), thioguanine (6-TG, Tabloid, Lanvis) **Intralesional/IM corticosteroids:** triamcinolone (Kenalog, Aristocort-Forte, Aristospan, Cinacort Span, Triamcort, Triam-Forte)
Category 4	**Biologic DMARDs[a]:** TNF-α inhibitors: etanercept (Enbrel), infliximab and biosimilars (Avsola, Inflectra, Remicade, Renflexis), adalimumab and biosimilars (Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Humira, Hyrimoz, Idacio, Yusimry), certolizumab pegol (Cimzia), golimumab (Simponi, Simponi Aria) IL-12/IL-23 inhibitors: ustekinumab (Stelara) IL-17 inhibitors: secukinumab (Cosentyx), ixekizumab (Taltz), brodalumab (Siliq), bimekizumab (Bimzelx) IL-23 inhibitors: guselkumab (Tremfya), tildrakizumab-asmn (Ilumya), risankizumab-rzaa (Skyrizi)
Category 5 (most severe)	**Targeted synthetic DMARDs:** JAK inhibitors: tofacitinib (Xeljanz, Xeljanz XR), upadacitinib (Rinvoq), deucravacitinib (Sotyktu)

Abbreviations: ; DMARDs, disease-modifying anti-rheumatic drugs; HZ, herpes zoster; IL, interleukin; IM, intramuscular; IV, intravenous; JAK, Janus kinase; MTX, methotrexate; PO, oral; PsO, psoriasis; SC, subcutaneous; TNF, tumour necrosis factor

a. Biologics are administered as either SC or IV. Both SC or IV forms are available for golimumab (SC [Simponi] or IV [Simponi Aria]) and ustekinumab (Stelara). Infliximab and biosimilars are administered as IV only. All others are administered as SC.

Table 21 Medication categories for PsA

Category 1 (least severe)	Non-pharmacologic therapies, or no treatment from Category 2 to Category 5
Category 2	**NSAIDs:** Ibuprofen (Motrin, Advil), naproxen (Aleve, Anaprox, Mediproxen), indomethacin (Indocin, Tivorbex), meloxicam (Vivlodex, Mobic, Comfort Pac Meloxicam), celecoxib (Celebrex), nabumetone (Relafen), etodolac (Lodine), diclofenac (Xrylix, Voltaren, Solaraze, Flector, Zorvolex, Zipsor, Cambia), sulindac (Clinoril), salsalate (Disalcid), ketorolac (Toradol, Acular) **Low dose steroids (PO):** Methylprednisolone (Medrol), prednisolone, prednisone (<20 mg prednisone or equivalent)
Category 3	**Conventional synthetic DMARDs:** Oral small molecules (OSMs): MTX (Trexall, Xatmep, Otrexup, Rheumatrex, Rasuvo), sulfasalazine (Azulfidine), leflunomide (Arava), apremilast (Otezla) **High-dose systemic steroids:** hydrocortisone (IM/IV), methylprednisolone (Medrol [IM/IV], Solu-Medrol [IM/IV], Depo-Medrol [IM/IV]), prednisolone (IM/IV), triamcinolone (Kenalog, Aristocort-Forte, Aristospan, Cinacort Span, Triamcort, Triam-Forte) [IM/IV]), prednisone (PO) (≥20 mg prednisone or equivalent)
Category 4[a]	**Biologic DMARDsb:** TNF-α inhibitors: etanercept (Enbrel), infliximab and biosimilars (Avsola, Inflectra, Remicade, Renflexis), adalimumab and biosimilars (Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Humira, Hyrimoz, Idacio, Yusimry), certolizumab pegol (Cimzia), golimumab (Simponi, Simponi Aria) IL-12/IL-23 inhibitors: ustekinumab (Stelara) IL-17 inhibitors: secukinumab (Cosentyx), ixekizumab (Taltz) CTLA4-immunoglobulin: abatacept (Orencia) IL-23 inhibitors: guselkumab (Tremfya), risankizumab-rzaa (Skyrizi) and biosimilars (risankizumab-AbbVie, risankizumab-rzza)
Category 5[a]	**Targeted synthetic DMARDs**: JAK inhibitors: tofacitinib (Xeljanz, Xeljanz XR), upadacitinib (Rinvoq) and biosimilars (upadacitinib-AbbVie)

Abbreviations: CTLA-4, Cytotoxic T-lymphocyte associated protein 4; DMARDs, disease-modifying anti-rheumatic drugs; HZ, herpes zoster; IL, interleukin; IM, intramuscular; IV, intravenous; JAK, Janus kinase; MTX, methotrexate; NSAIDs, nonsteroidal anti-inflammatory drugs; PO, oral; PsA, psoriatic arthritis; SC, subcutaneous; TNF, tumour necrosis factor

a. For safety objectives, Categories 4 and 5 were combined into Category 4, indicating most severe disease, as use of JAK inhibitors (Category 5) was not indicative of more severe disease than use of Category 4 medications. For VE objectives, Categories 1 – 5 were used as listed, as the risk of HZ was greater in those treated with JAK inhibitors compared to the risk in those treated with medications in Category 4.
b. Biologics were administered either as SC or IV. Both SC or IV forms were available for abatacept (Orencia), ustekinumab (Stelara) and golimumab (SC [Simponi] or IV [Simponi Aria]). Infliximab and biosimilars were administered as IV only. All others were administered as SC.

NON-INTERVENTIONAL STUDY REPORT (ABSTRACT)

Title	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Date of the Abstract	16 Jul 2026
Name and affiliation of main author	PPD Kaiser Permanente Southern California
Keywords	Herpes zoster, vaccine effectiveness, vaccine safety, recombinant zoster vaccine, psoriasis, psoriatic arthritis
Marketing authorisation holder(s)	GlaxoSmithKline Biologicals S.A.
Names and affiliations of principal investigators	Hung Fu Tseng Kaiser Permanente Southern California

Rationale and background

Studies have shown higher incidence of herpes zoster (HZ) in individuals with altered immune function, compared to the general population. Real-world data on the effectiveness and safety of recombinant zoster vaccine (RZV) in such at-risk populations are needed to help inform patient and physician decision-making regarding vaccination against HZ.

Research questions and objectives

Primary and secondary VE objectives estimated the VE of 2 doses of RZV in preventing HZ in adults ≥18 years of age with PsO or PsA, separately and with either condition. One-dose VE was estimated, and the baseline characteristics of the RZV-vaccinated and unvaccinated cohorts were described as secondary objectives. The primary and secondary safety objectives assessed the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison windows. CCI
CCI

Study design

For VE objectives, an observational matched cohort design was used in which RZV vaccinated individuals were compared to matched RZV unvaccinated individuals. For safety objectives, a self-controlled case series design was used to evaluate the rate of flare. Accrual occurred from 01 April 2018 up to 31 December 2023 with follow-up through 31 December 2024 for HZ outcomes, and up to 30 June 2025 for CCI

Setting

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

Subjects and study size, including dropouts

The primary VE analyses included 10,391 PsO (2,616 vaccinated and 7,765 unvaccinated) and 2,163 PsA (548 vaccinated and 1,615 unvaccinated) individuals. The PsO and PsA safety cohorts included 3,086 and 1,073 vaccinated individuals, respectively.

Variables and data sources

Individuals with at least 2 previous encounters with assigned ICD-10 codes for PsO or PsA were identified from electronic health records (EHR). The primary exposure for VE analysis was 2 doses of RZV. 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 against HZ in adults (≥18 years) was 60.7 (95% confidence interval [CI]: 40.5%, 74.0%) and 80.5% (95% CI: 34.3%, 94.2%) for PsO and PsA patients, respectively. The rate of flares was comparable across the risk and comparison windows for recipients of RZV with PsO (incidence rate ratio [IRR]= 0.94, 95% CI: 0.58, 1.52) and PsA (IRR= 1.21, 95% CI: 0.69, 2.13).

Discussion

Previous work evaluating the effectiveness and safety of RZV has largely focused on immunocompetent adults and older populations. This study also addressed the younger, immunocompromised population by expanding inclusion criteria to include ≥18-year-olds with PsO and PsA using real-world data from a large integrated health care delivery network.

Conclusion

For adults with PsO and PsA, 2 doses of RZV conferred protection against HZ with no elevated rate of flares observed in the 30 days following vaccination. Our findings support the recommendation to vaccinate adults with PsO and PsA with 2 doses of RZV.

Signature Page for 216976 TMF-24134454 v1.0

Reason for signing: Approved	Name: PPD Role: Approver Date of signature: 13-Jul-2026 23:26:46 GMT+0000

Reason for signing: Approved	Name: PPD Role: Author Date of signature: 16-Jul-2026 18:16:45 GMT+0000

Signature Page for TMF-24134454 v1.0

Protocol

Study ID: 216976

Official Title of Study: Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis

Date of Document: 23 June 2023

TITLE PAGE

Division: Research and Development

Information Type: Non-Interventional PASS Protocol

Title	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Compound Number	GSK1437173A
Development Phase	IV
Effective Date	23 Jun 2023
Subject	Effectiveness and safety of recombinant zoster vaccine in adults with psoriasis and psoriatic arthritis
Author(s)	KPSC authors Hung-Fu Tseng, Principal Investigator Jennifer Ku, Co-Investigator Ana Florea, Co-Investigator Brad Ackerson, Co-Investigator Lina Sy, Co-Investigator Lei Qian, Co-Investigator/Biostatistician GSK authors PPD r, Epidemiology PPD, Real World Analytics PPD, PV Alliances PPD Study Delivery Lead PPD, Senior Medical Writer PPD
Indication Studied	Prevention of herpes zoster in immunodeficient or immunosuppressed adults

PASS INFORMATION

Title	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Protocol version identifier	216976 (EPI-ZOSTER-045 VE US)
Date of last version of protocol	Final: 23 Jun 2023
EU PAS (ENCEPP) register number	Study not registered
Active substance	VZV glycoprotein E (gE)
Medicinal product	*Shingrix* (Recombinant Zoster Vaccine, RZV)
Product reference	EMA EU/1/18/1272/001-1 vial and 1 vial; EU/1/18/1272/002-10 vials and 10 vials FDA IND #013879
Procedure number	EMEA/H/C/004336
Marketing authorisation holder(s)	GlaxoSmithKline Biologicals S.A. Rue de l'Institut, 89, 1330 Rixensart, Belgium
Joint PASS	No
Research question and objectives	Evaluate effectiveness (prevention of herpes zoster) and safety (risk of flares) of recombinant zoster vaccine among adults with psoriasis or psoriatic arthritis
Country of study	United States

Author	KPSC authors Jennifer Ku, Co-Investigator Hung-Fu Tseng, Principal Investigator Ana Florea, Co-Investigator Brad Ackerson, Co-Investigator Lina Sy, Co-Investigator Lei Qian, Co-Investigator/Biostatistician GSK authors PPD, Epidemiology PPD, Real World Analytics PPD, PV Alliances PPD, Study Delivery Lead PPD, Senior Medical Writer PPD

MARKETING AUTHORISATION HOLDER(S)

Marketing authorisation holder(s)	GlaxoSmithKline Biologicals S.A. Rue de l'Institut, 89, 1330 Rixensart, Belgium
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LIST OF ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
CI	Confidence interval
COVID-19	Coronavirus disease 2019
DMARDs	Biologic disease-modifying anti-rheumatic drugs
EHR	Electronic health records
EMA	European Medicines Agency
EUPAS register	European Union electronic Register of Post authorization Studies
FDA	U.S. Food and Drug Administration
GSK	GlaxoSmithKline
HIPAA	Health Insurance Portability and Accountability Act
HR	Hazard ratio
HZ	Herpes zoster
ICD-10	International Classification of Diseases, 10th edition
ICSR	Individual Case Safety Reporting
IRB	Institutional Review Board
IRR	Incidence rate ratio
JAK	Janus Kinase
KPSC	Kaiser Permanente Southern California
MTX	Methotrexate
OSM	Oral small molecule
PHN	Post-herpetic neuralgia
PsA	Psoriatic arthritis
PsO	Psoriasis

RZV	Recombinant zoster vaccine
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SCCS	Self-controlled case series
SCRI	Self-controlled risk interval
U.S.	United States
VE	Vaccine effectiveness
ZVL	Zoster Vaccine Live

TRADEMARK INFORMATION

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N/A

1. RESPONSIBLE PARTIES

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Ana Florea, Co-Investigator

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Lina Sy, Co-Investigator

Lei Qian, Co-Investigator/Biostatistician

GSK authors

PPD , Epidemiology

PPD , Real World Analytics

PPD , PV Alliances

PPD Study Delivery Lead

PPD Senior Medical Writer

PPD

1.1. SPONSOR SIGNATORY

Title:	Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
Compound Number:	GSK1437173A

Huifeng Yun	Date (DD Month YYYY)
Therapy Area Leader/+1 Manager	

Peggy Webster	Date (DD Month YYYY)
Qualified Person/Delegate	

Note: Not applicable if an eSignature process is used to get the sponsor approval.

1.2. SPONSOR INFORMATION PAGE

Study ID: 216976

Sponsor Legal Registered Address:

GlaxoSmithKline Research & Development Limited
980 Great West Road
Brentford
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Sponsor Contact Address

GlaxoSmithKline Research & Development Limited
14200 Shady Grove Rd
Rockville
MD 20850
USA

1.3. INVESTIGATOR PROTOCOL AGREEMENT PAGE

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receive the appropriate information throughout the study.

Investigator Name: Hung-Fu Tseng

Investigator Signature	Date (DD Month YYYY)

2. ABSTRACT

Title: Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis

Rationale and background

Studies have shown higher incidence of herpes zoster (HZ) in individuals with conditions/treatments associated with altered immune function, compared to the general population. Robust, real-word data on the effectiveness and safety of recombinant zoster vaccine (RZV) in such at-risk populations are needed to help inform patient and physician decision-making regarding vaccination against HZ. This observational study will evaluate the vaccine effectiveness (VE) and safety of RZV in adults with psoriasis (PsO) or psoriatic arthritis (PsA) at Kaiser Permanente Southern California (KPSC).

Research question and Objective(s)

The primary and secondary VE objectives will estimate the VE of 2 doses of RZV in preventing HZ in adults ≥18 years of age with PsO or PsA. One-dose VE will be estimated as a secondary objective. The primary and secondary safety objectives will assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in adults ≥18 years of age with PsO or PsA. An exploratory VE objective will also be evaluated.

Study Design

This study will examine the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA at KPSC. For VE objectives, an observational matched cohort design will be used in which RZV vaccinated individuals are compared to matched RZV unvaccinated individuals. For safety objectives, a self-controlled case series design will be used to evaluate the rate of flare within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods.

Population

The study will be conducted at KPSC, a large, integrated United States health care system with a diverse member population. Individuals aged ≥18 years with ≥1-year of continuous KPSC membership and ≥2 health care encounters with diagnosis codes for PsO or PsA in the year prior to and including the index date will be eligible for inclusion.

Variables

The exposure of interest will be RZV vaccination. Outcomes for the VE objectives will be HZ, post-herpetic neuralgia, disseminated HZ, and HZ-related meningoencephalitis. The outcome for the safety objectives will be flare, defined as new-onset flare or new-onset disease worsening of PsO or PsA.

Data sources

Study data will be obtained from KPSC's electronic health records.

Study size

For VE, we anticipate accruing approximately 2,402 eligible RZV 2-dose recipients for the PsO cohort, with a 1:3 matching ratio of RZV vaccinated to unvaccinated individuals. For safety, we anticipate accruing approximately 3,060 eligible individuals with PsO who have received ≥1 dose of RZV. The study is sufficiently powered to assess the primary VE and safety objectives.

Data analysis

For VE objectives, incidence rates of HZ will be assessed for the PsO and PsA cohort. VE will be calculated using hazard ratios, which will be estimated by Cox proportional hazards regression models.

For safety objectives, rates of PsO or PsA flare for risk periods and comparison periods will be calculated. Incidence rate ratio comparing the rate of flares in the risk and comparison periods will be estimated using conditional Poisson regression.

Milestones

RZV vaccination data will be accrued between April 2018 and December 2023, with follow-up through December 2024, followed by a 3-month data settling period by March 2025. The vaccine accrual period may end earlier once the target sample size is met. Chart reviews will be completed by July 2025, followed by data soft lock by August 2025. A final report will be completed by June 2026.

3. AMENDMENTS AND UPDATES

None

4. MILESTONES

Milestone	**Planned date**
Start of data collection (Receipt of 1st RZV dose)	April 2018
End of accrual period	December 2023
End of follow-up	December 2024
End of 3-month data settling period	March 2025
End of 6-month follow-up period for PHN	June 2025

Milestone	Planned date
Chart review completion	July 2025
Data soft lock	August 2025
Final results tables	February 2026
Final report	June 2026

5. RATIONALE AND BACKGROUND

Herpes Zoster (HZ), or shingles, is an often painful vesicular rash caused by reactivation of varicella zoster virus (VZV) persisting latently in dorsal root ganglia (Dworkin, 2007; Gnann, 2002). The pain from acute HZ can be disabling, and if complicated by the development of post-herpetic neuralgia (PHN), can last for months or years. Before a vaccine was introduced, about one million episodes of HZ occurred in the United States (U.S.) annually (Harpaz, 2008). Aside from increasing age and immunosuppression, other risk factors for this condition are not well known (Thomas, 2004, but some evidence suggests that sex, race/ethnicity, family history, and comorbidities may be associated with the occurrence of HZ (Kawai, 2017).

Studies have shown higher incidence of HZ in individuals with conditions/treatments associated with altered immune function, compared to the general population. Individuals with psoriasis (PsO) or psoriatic arthritis (PsA) have been reported to be at increased risk for developing HZ, compared with the general population; this increased risk persisted when immunosuppressive effects of systemic therapy were controlled for (Baumrin, 2019). A U.S. study using claims data estimated the incidence of HZ among individuals aged ≥18 years with PsO to be approximately 8 per 1,000 person-years (Chen, 2014), two times higher than in the general U.S. population (3 to 4 per 1,000 person-years) (Insinga, 2005; Mullooly, 2005; Yawn, 2007). Further, a U.S. study using nationwide inpatient data demonstrated an association between HZ-related hospitalizations and PsO (odds ratio: 1.4, 95% confidence interval [CI]:1.1-1.7) (Chovatiya, 2021). Similarly, a U.S. study using linked insurance data reported age-specific incidence rates of HZ in individuals with PsA (incidence rate per 1,000 person-years [PsA vs. healthy subjects] = 9.8 vs. 3.3, 8.5 vs. 3.9, and 13.2 vs. 5.8, for 31-40-year, 41-50-year, and 51-60-year age groups, respectively) (Yun, 2016). Systemic therapies further increase the risk of HZ in individuals with PsO or PsA, although the risk may vary depending on disease severity and type of therapy (Baumrin, 2019). Recent data have shown that biological therapies, especially anti-tumor necrosis factor (TNF)-α inhibitors and combinations of anti-TNF-α agents, Janus kinase (JAK)-inhibitors, and conventional disease-modifying antirheumatic drugs (c-DMARDs), contribute to the increased risk of HZ in individuals with PsO or PsA (Chiu, 2022; Winthrop, 2017; Winthrop, 2017; Zisman, 2016; Zou, 2021).

Recombinant zoster vaccine (SHINGRIX, RZV), is a subunit, adjuvanted vaccine approved by the U.S. Food and Drug Administration (FDA) in October 2017 for the prevention of HZ in adults ≥50 years of age. Two RZV doses are necessary with the second dose recommended 2-6 months after the first (Anderson, 2022). If the second

dose is administered ≤4 weeks after the first dose date, the Advisory Committee on Immunization Practices (ACIP) recommends repeating the second dose ≥4 weeks after the first. However, the first dose does not need to be repeated if ≥6 months have elapsed since the first dose. In July 2021, the FDA expanded the indication for use of RZV for the prevention of HZ in adults aged ≥18 years who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy (GlaxoSmithKline Biologicals, 2021). For individuals who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule, the second dose may be administered 1-2 months after the first dose. The ACIP recommended RZV vaccination for the prevention of HZ and related complications in immunocompetent adults aged ≥50 years and adults aged ≥19 years who are or will be immunodeficient or immunosuppressed because of disease or therapy (Anderson, 2022; Dooling, 2018). The expansion of RZV recommendations to these high-risk populations (i.e., patient populations for whom zoster vaccine live [ZVL] was largely contraindicated) help address an unmet medical need for HZ prevention. Real-world, population-based data on RZV in these complex patient populations, including individuals with autoimmune diseases, are needed to assess the vaccine effectiveness (VE) and safety of RZV.

GSK has conducted some clinical trials of RZV in patient populations at increased risk for HZ (i.e., those with hematopoietic stem cell transplant, solid tumors, hematologic malignancy, human immunodeficiency virus [HIV] and renal transplant). However, data on the effectiveness and safety of RZV in other populations at increased risk, including those with autoimmune diseases, especially those on newer immunomodulating agents, are limited. Robust, real-world data are needed to help inform patient and physician decision-making regarding vaccination against HZ in these at-risk populations. Therefore, we will conduct an observational study at Kaiser Permanente Southern California (KPSC), a large integrated U.S. health care system, to evaluate the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA.

6. RESEARCH QUESTION AND OBJECTIVE(S)

This study will assess VE and safety of RZV among individuals at KPSC with PsO or PsA. For VE, individuals who receive RZV ("vaccinated") will be compared to individuals who do not receive RZV ("unvaccinated"). For safety, the rate of flares in pre-defined risk periods will be compared to comparison periods within RZV vaccinated individuals. Individuals who have both PsO and PsA will be included in both the PsO and PsA analyses. The study population is described in detail in **Section 7.2.4** Study Population.

6.1. Vaccine Effectiveness Objectives

Primary VE objective:

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsO.

Secondary VE objectives:

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsO or PsA.
2. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥18 years of age with PsA.
3. To estimate the VE of 1 dose of RZV in preventing HZ in Southern California adults with PsO or PsA, separately.
4. To describe baseline characteristics of individuals vaccinated with 2 doses of RZV compared to their unvaccinated matches in Southern California adults ≥18 years of age with PsO or PsA, separately.

Exploratory VE objective:

CCI

[redacted]

6.2. Safety Objectives

Primary safety objective:

1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsO.

Secondary safety objectives:

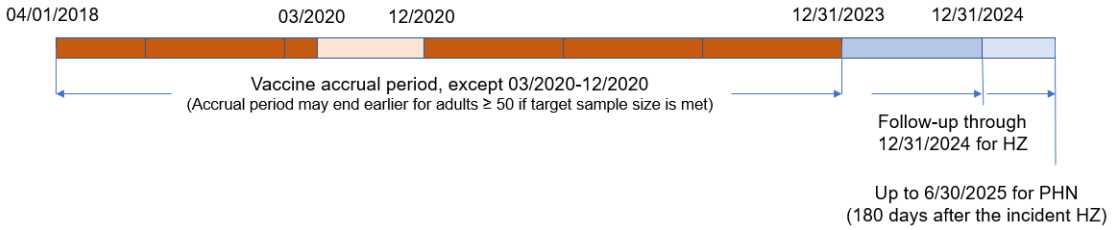
1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsO or PsA.
2. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsA.

7. RESEARCH METHODS

7.1. Study Design

7.1.1. Overview

This study will examine the effectiveness and safety of RZV in individuals aged ≥18 years with PsO or PsA at KPSC. The vaccine accrual period will extend from 04/01/2018 up to 12/31/2023 with follow-up through 12/31/2024 for HZ and safety outcomes, and through 06/30/2025 for PHN outcomes (180 days after the end of follow-up for incident HZ). The vaccine accrual period may end earlier once the target sample size is met.



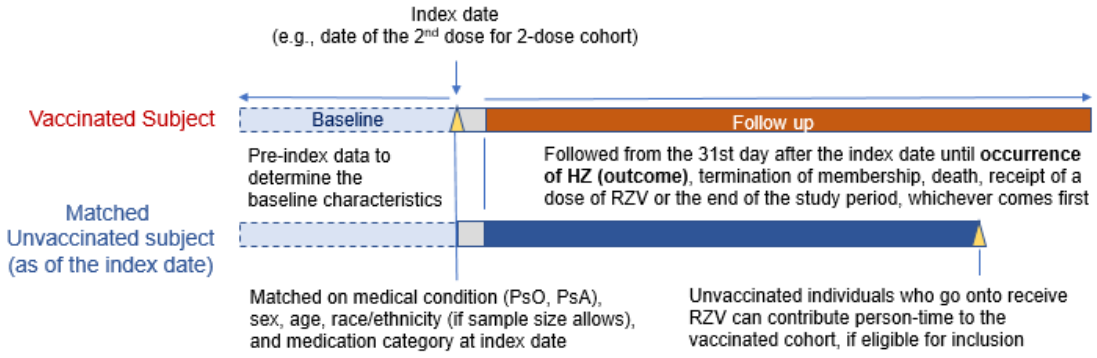
On March 4, 2020, the Governor of California declared a State of Emergency following the first official coronavirus disease 2019 (COVID-19) death in the state, followed by the enaction of a stay-at-home order on March 19, 2020 to slow the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We observed a significant drop in adult vaccinations during the early pandemic period. The COVID-19 pandemic may have indirectly impacted health care delivery and vaccine-seeking behaviors. To prevent potential selection bias, subjects with index dates from March 2020 to December 2020 (between the time of the stay-at-home order and the time of introduction of the first COVID-19 vaccine) will be excluded. VE and safety outcomes will continue to be ascertained during this period. KPSC was able to transition to virtual modalities in place of in-person visits for many conditions typically seen in outpatient settings (Robinson, 2020), and patients were still able to be evaluated for VE and safety outcomes via virtual visits (Xu, 2021). Further, the impact COVID-19 may have had on health care utilization was unlikely to differ among RZV vaccinated and unvaccinated individuals or during risk and comparison periods, thus any outcome misclassification resulting from the impact of COVID-19 is expected to be non-differential.

7.1.2. Vaccine Effectiveness Objectives

For the VE objectives, an observational matched cohort design will be used. For 2-dose VE objectives, the index date will be defined as the date of receipt of the second dose of RZV (≥4 weeks apart) for vaccinated individuals; the same date will be assigned as the index date to their matched unvaccinated counterparts who have not been vaccinated as of the index date. Individuals ≥18 years of age who receive a second dose of RZV will be matched without replacement to unvaccinated individuals on the following variables: medical condition (PsO, PsA), sex, age group (by decade, if sample size allows), and

medication category at index date (**Appendix 1**). Individuals may also be matched on race/ethnicity if sample size allows. For secondary VE objective 3 (secondary one-dose VE objective), the date of the first dose of RZV will be used as the index date. Unvaccinated and vaccinated individuals will be matched on exact combination of matching variables. Matching is described in detail in **Section 7.7.2** and the Statistical Analysis Plan.

Individuals will be followed through the KPSC electronic health records (EHR) from the 31st day after the index date until occurrence of HZ, termination of membership, death, receipt of a dose of RZV (receipt of a third dose for 2-dose vaccinated individuals, receipt of a second dose for 1-dose vaccinated individuals, or receipt of a first dose for unvaccinated individuals), or end of the study period, whichever comes first. Primary analysis will assess 2-dose VE in individuals with PsO. Secondary analyses will assess 2-dose VE in individuals with PsO or PsA. Analyses will be performed overall and stratified by timing of the second dose of RZV (second dose given ≤6 months or >6 months after first dose), by age group (18-49 years or ≥50 years), and by medication category. Additional secondary analyses will examine 1-dose VE. Additional exploratory analyses will also be conducted.



7.1.3. Safety Objectives

For safety objectives, a self-controlled case series (SCCS) analysis will be conducted among individuals aged ≥18 years with PsO or PsA who receive ≥1 dose of RZV. The date of vaccination with the first dose of RZV will be defined as Day 0. The observation time will be partitioned into a 30-day risk window right after each RZV dose, a 30-day pre-vaccination comparison window, and a 30-day post-vaccination comparison window. The incidence of flare in the risk window will be compared with that in the comparison window. There will be a washout period before the date of vaccination. For the first dose, the wash out period will be 60 days, and for the second dose, the washout period will vary based on time between doses. Please see **Section 7.3.3** for further details.

The SCCS method was developed to investigate associations between acute outcomes and transient exposures. It has been widely used in vaccine safety studies (Hechter, 2019; Tseng, 2017; Whitaker, 2006). By design, each individual serves as their own

comparator. All time-fixed (or near time-fixed) confounding factors, known and unknown, are controlled for implicitly. Additionally, with comparison periods within close proximity to the risk period (before and after the risk period), the design also controls for time-varying covariates such as age and seasonality. Further adjustment for seasonal confounding can be considered in the analysis model. Please see Statistical Analysis Plan for more details. These features of the SCCS method make it advantageous to use this method for the safety objectives rather than using a cohort design.

The SCCS design assumes that flare events: (1) are independent and do not influence the probability of subsequent flares; (2) do not influence the probability of RZV exposure; and (3) do not cause censoring or affect the observation period. Although some individual patients may be predisposed to frequent flares, the SCCS design allows individuals to have different risk levels of flares, that is, allowing events at different time points to be conditionally independent given the individual (Simpson, 2013). We also have chart review procedures in place, such as review of complex cases by specialists, to distinguish whether a flare is a new event or a continuation of a previous flare. Regarding flares influencing the probability of RZV exposure, it is possible that individuals are less likely to be vaccinated during a flare, and the incidence of flare may be lower just before vaccination (i.e., healthy vaccinee effect) (Baker, 2015). Therefore, we will exclude the time period immediately prior to vaccination from the analysis (i.e., washout period) to correct for the effect of event-dependent exposures (Whitaker, 2006). Lastly, individuals can continue to be followed after having a flare and flare is unlikely to lead to death (censoring event).

Given the complexity of accurately ascertaining disease flare, the EHR will be manually reviewed for these individuals to identify occurrence of flare rather than relying on administrative data. A flare will be identified by documented contact with a health care provider, and new or worsening signs and/or symptoms suggestive of a flare, and a change in medication for flare (**Appendix 2**). For primary analyses, the rate of flares in pre-defined risk periods compared to comparison periods will be assessed for PsO (**Section 7.3.3**). Secondary analyses will assess the rate of flares in individuals with PsO or PsA or individuals with PsA. Analyses for individuals with PsO and individuals with PsA will be conducted overall and stratified by age groups (18-49 years or ≥50 years) and by medication category.

7.2. Study Population and Setting

7.2.1. Study Setting

KPSC is one of the largest not-for-profit health plans and integrated health care systems in the U.S., providing an ideal environment for population-based research. KPSC's population includes >4.6 million members, of whom 2,075,288 are ages 18-49 years, and 1,632,097 are ages ≥50 years (as of January 1, 2022). The diverse demographic makeup, including 260 different ethnicities and more than 150 different languages, closely mirrors the Southern California population (Koebnick, 2012). Compared to the racial/ethnic distribution of the U.S. population, KPSC membership is composed of twice as many Asian/Pacific Islanders and three times as many Hispanic individuals.

KPSC facilities include hospitals and medical offices, all linked by an information infrastructure that supports both clinical practice and business needs. Health information from this infrastructure can be leveraged for research purposes. KPSC membership is known for its stability; >90% of members remain in the health plan after one year; and more than three-quarters remain after 3 years. The large, diverse, and stable population allows for rapid accrual of a large, representative cohort with the ability to evaluate long-term implications of immunization.

KPSC began administering ZVL in late 2006 when it was first recommended by the ACIP and KPSC Regional Immunization Practice Committee. In 2017, the ACIP recommended RZV preferentially over ZVL. Since April 2018, RZV has been the preferred HZ vaccine for routine use and the standard of care for the prevention of HZ in adults aged ≥50 years at KPSC. KPSC's routine RZV use has expanded to immunocompromised adults ≥18 years, with the FDA's expanded indication for RZV to include this population in July 2021.

7.2.2. Source Population

Demographic make-up and stability of KPSC membership

KPSC's member population is socioeconomically diverse and broadly representative of the racial/ethnic groups living in Southern California **(Table 1**). Members enroll through the Kaiser Foundation Health Plan for prepaid health care insurance, including pharmaceutical benefits, through group plans, individual plans, Medicare, Medicaid, and other low-income programs.

As of January 1, 2022, KPSC membership consisted of 3,707,385 members aged ≥18 years, of which 56% were between 18 and 49 years, and 44% aged ≥50 years (**Table 1**). Members were 52% female, and the racial/ethnic composition included Hispanic (40%), White (31%), Asian/Pacific Islander (11%), and Black (8%). Geographically, KPSC covers the entire Southern California region from Bakersfield to San Diego.

Table 1 Demographic distribution of KPSC members aged ≥18 years as of 01/01/2022

	Number (%)
Age (years)	
18-49	2,075,288 (56.0%)
50-59	613,626 (16.6%)
60-69	530,111 (14.3%)
70-79	335,710 (9.1%)
80+	152,650 (4.1%)
Sex	
Female	1,937,681 (52.3%)
Male	1,769,704 (47.7%)
Race/Ethnicity[1]	
Hispanic	1,486,297 (40.1%)
White	1,135,586 (30.6%)
Asian/Pacific islander	408,419 (11.0%)
Black	284,284 (7.7%)
Multiple/Other/Unknown	392,799 (10.6%)
Total	3,707,385

1. All categories other than Hispanic are non-Hispanic ethnicity.

Among 2,644,872 members enrolled in KPSC as of 01/01/2012, 35% of members aged 18-49 years, 51% of members aged 50-59 years, 60% of members aged 60-69 years, and 56% of members aged 70-79 years had retained KPSC membership for >10 years (**Table 2**).

Table 2 Length of KPSC membership among individuals aged ≥18 years as of 01/01/2012

	Membership length (years)			
Age (years) As of January 1, 2012	**0-5**	**>5-10**	**>10**	**Total**
18-49	725,034 (48.3%)	253,346 (16.9%)	522,778 (34.8%)	1,501,158 (100%)
50-59	155,032 (31.1%)	88,964 (17.9%)	253,849 (51.0%)	497,845 (100%)
60-69	92,534 (25.5%)	54,458 (14.0%)	216,234 (59.5%)	363,226 (100%)
70-79	38,875 (20.8%)	44,045 (23.6%)	103,978 (55.6%)	186,898 (100%)
80+	42,125 (44.0%)	31,506 (32.9%)	22,114 (23.1%)	95,745 (100%)
Total	1,053,600	472,319	1,118,953	2,644,872

KPSC members with PsO or PsA

Among individuals with PsO who were unvaccinated as of 01/01/2022, 49% were female, 42% were non-Hispanic White, and 62% were aged ≥50 years, while among

those with PsO who were vaccinated, 51% were female, 61% were non-Hispanic White, and 99.7% were aged ≥50 years (**Table 3**).

Of those with PsA who were unvaccinated as of 01/01/2022, 53% were female, 50% were non-Hispanic White and 66% were aged ≥50 years. Individuals with PsA who were vaccinated were 50% female, 60% non-Hispanic White, and 99.4% were aged ≥50 years. **Table 3** shows the characteristics of individuals with PsO and PsA by RZV vaccination status as of 1/1/2022 and is not indicative of the entire study population.

Table 3 Demographic characteristics of RZV unvaccinated and vaccinated individuals with PsO and PsA at KPSC as of 01/01/2022

	Psoriasis		Psoriatic arthritis	
	Unvaccinated[1]	**Vaccinated[2]**	**Unvaccinated[1]**	**Vaccinated[2]**
Age at index date (years)				
18-49	4,027 (38.4%)	7 (0.3%)	888 (34.0%)	3 (0.6%)
50-59	1,928 (18.4%)	308 (13.5%)	610 (23.4%)	89 (16.5%)
60-69	1,978 (18.9%)	773 (34.0%)	616 (23.6%)	228 (42.4%)
70-79	1,753 (16.7%)	870 (38.2%)	364 (13.9%)	181 (33.6%)
80+	808 (7.7%)	318 (14.0%)	133 (5.1%)	37 (6.9%)
Sex				
Female	5,183 (49.4%)	1,167 (51.3%)	1,378 (52.8%)	270 (50.2%)
Male	5,311 (50.6%)	1,109 (48.7%)	1,233 (47.2%)	268 (49.8%)
Race/Ethnicity[3]				
White	4,372 (41.7%)	1,376 (60.5%)	1,313 (50.3%)	322 (59.9%)
Hispanic	3,693 (35.2%)	476 (21.0%)	779 (29.8%)	107 (19.9%)
Asian	1,356 (12.9%)	294 (12.9%)	318 (12.2%)	74 (13.8%)
Black	433 (4.1%)	62 (2.7%)	66 (2.5%)	8 (1.5%)
Multiple/Other/Unknown	640 (6.1%)	68 (3.0%)	135 (5.2%)	27 (5.0%)
Charlson comorbidity index[4]				
0	4,293 (40.9%)	469 (20.6%)	972 (37.2%)	123 (22.9%)
1-2	4,175 (39.8%)	1,067 (46.9%)	1,097 (42.0%)	235 (43.7%)
3-4	1,403 (13.4%)	515 (22.6%)	400 (15.3%)	129 (24.0%)
≥5	623 (5.9%)	225 (9.9%)	142 (5.4%)	51 (9.5%)
Total	10,494	2,276	2,611	538

KPSC = Kaiser Permanente Southern California; PsO = Psoriasis; PsA = Psoriatic arthritis; RZV = Recombinant Zoster Vaccine

1. Index date was 1/1/2022. Included individuals had ≥1 year of KPSC membership prior to index date, had ≥2 diagnoses of the condition (PsO or PsA) in the year prior to index date, and never received RZV prior to 2022.
2. Index date was the date of the first RZV dose between 4/2018 and 12/2021. Included individuals had ≥1 year of KPSC membership prior to index date and had ≥2 diagnoses of the condition (PsO or PsA) in the year prior to index date.
3. All ethnic categories other than Hispanic are non-Hispanic.
4. Charlson comorbidity index is based on data in the 1 year prior to index date.

7.2.3. Study Period

The vaccine accrual period will extend from 04/01/2018 up to 12/31/2023 with follow-up through 12/31/2024 for HZ and safety outcomes, and through 06/30/2025 for PHN outcomes. The vaccine accrual period may end earlier once the target sample size is met, particularly for adults ≥50 years, and possibly if uptake in adults 18-49 years increases substantially upon implementation of alerts in the KPSC EHR. Implementation of EHR alerts is currently under discussion by KPSC's Regional Immunization Practice Committee.

7.2.4. Study Population

Inclusion criteria

Individuals will be included in the study if they meet the following criteria:

VE objectives

- Aged ≥18 years at index date
- ≥1-year of continuous KPSC membership prior to the index date and until 31 days after index date (allowing for a 31-day gap in membership)
- Meet criteria for PsO or PsA in the year prior to and including the index date as defined below

Safety objectives

- Received ≥1 dose of RZV during the accrual period
- Aged ≥18 years at index date (date of first RZV dose)
- ≥1-year continuous KPSC membership prior to and including index date (allowing for a 31-day gap in membership)
- Meet criteria for PsO or PsA in the year prior to and including the index date as defined below

Individuals with ≥2 health care encounters with International Classification of Diseases, Tenth Revision (ICD-10) codes for PsO or PsA in the year prior to and including the index date will be identified from the EHR, as listed below. Studies have shown that increasing the number of codes required in a given time window increased positive predictive values (Icen, 2008), and requiring ≥2 codes maximizes positive predictive value of our definition while maintaining appropriate sample size. These definitions for PsO and PsA were selected based on prior knowledge, current literature (Lee, 2021), and KPSC chart review indicating a high positive predictive value (100% for both PsO and PsA among 10 samples for each condition).

Psoriasis (for primary VE objective 1, secondary VE objectives 1, 3, and 4, exploratory VE objective 1; for primary safety objective 1, secondary safety objective 1)

- L40.0: Psoriasis vulgaris

- L40.1: Generalized pustular psoriasis
- L40.2: Acrodermatitis continua
- L40.3: Pustulosis palmaris et plantaris
- L40.4: Guttate psoriasis
- L40.8: Other psoriasis
- L40.9: Psoriasis, unspecified

Psoriatic arthritis (for secondary VE objectives 1, 2, 3, and 4, exploratory VE objective 1; for secondary safety objectives 1 and 2)

- L40.50: Arthropathic psoriasis, unspecified
- L40.51: Distal interphalangeal psoriatic arthropathy
- L40.52: Psoriatic arthritis mutilans
- L40.53: Psoriatic spondylitis
- L40.59: Other psoriatic arthropathy

Individuals with both PsO and PsA will be included in analyses for both conditions.

Exclusion criteria

For VE objectives, individuals with an HZ diagnosis in the 6 months prior to the index date will be excluded to ensure that HZ diagnoses after the index date are new, rather than carried over from HZ episodes prior to the index date. Individuals with HZ occurring on or within 30 days after the index date for both vaccinated and unvaccinated groups will also be excluded since it is unclear if the HZ episode began before or after the index date and whether the length of time since vaccination (for RZV vaccinated individuals) is long enough to allow for sufficient development of immunity. Individuals who receive RZV vaccine within 30 days after the index date or die during the 30 days after the index date will also be excluded to prevent individuals from being censored before follow-up begins.

For safety objectives, individuals who receive a second RZV dose <4 weeks (28 days) after the first dose will be excluded, since ACIP guidelines state that these individuals must repeat the second dose (Dooling, 2018).

7.3. Variables

7.3.1. Exposure definitions (VE and Safety)

RZV vaccination will be received as part of routine clinical care. We will identify RZV exposure (CVX 187; zoster vaccine recombinant (CDC, 2023) from the EHR, which is available and accessible in real-time, providing the ability to view vaccine details and collect patient immunization history at the point of care. All vaccinations are entered into

the EHR when they are given, with vaccine, dose, manufacturer, and lot number entered electronically or manually if scanning is not feasible at the time of vaccination. Vaccinations received outside of the KPSC system are recorded and incorporated into the KPSC EHR with appropriate documentation.

7.3.2. Exposure for VE Objectives

Following the ACIP guidelines, KPSC specifies that a second dose administered <4 weeks after the first dose should be repeated, but the vaccine series does not need to be restarted if >6 months have elapsed after the initial dose (Anderson, 2022). Furthermore, due to variations in real-world practice, the second dose may be administered earlier than 2 months after the first dose or later than 6 months after the first dose. Additionally, as of January 21, 2022, ACIP guidelines indicate that the second dose can be administered 1–2 months after the first dose for individuals who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule (Anderson, 2022).

The exposure for primary VE objective 1, secondary VE objectives 1, 2, and 4, and exploratory VE objective 1 is 2 doses of RZV administered ≥4 weeks apart during the study accrual period. The index date will be date of receipt of the second RZV dose.

The exposure for secondary VE objective 3 is the first dose of RZV. The 1-dose VE will be evaluated in individuals who receive only 1 dose of RZV during the accrual period as well as those who receive a second dose of RZV >6 months from the first dose during the accrual period, with 1-dose person-time being censored upon receipt of a second RZV dose. Individuals receiving a second RZV dose within 6 months of their first dose will not be included in the 1-dose analysis due to the short follow-up period and lack of unvaccinated individuals for matching. The index date will be date of receipt of the first RZV dose.

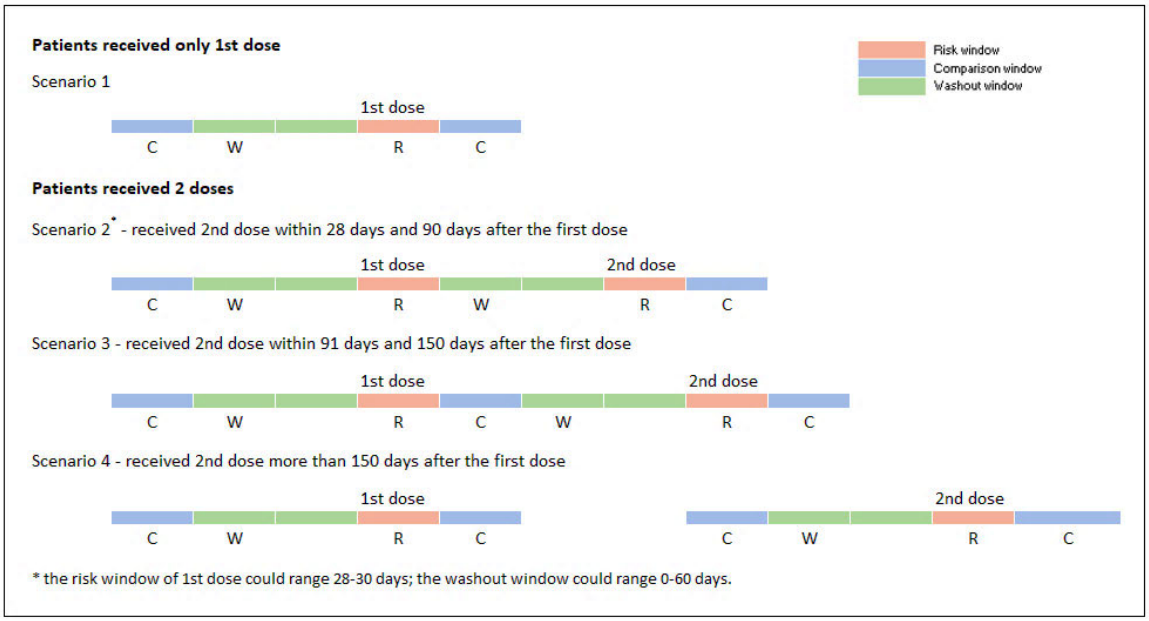
7.3.3. Exposure for Safety Objectives

An SCCS design will be used for safety objectives (**Figure 1**). For individuals who receive only one dose of RZV, the date of vaccination will be defined as Day 0, the risk period will be defined as +1 to +30 days, and comparison periods will be defined as -90 to -61 days and +31 to +60 days (**Scenario 1**). The washout period will be defined as -60 to -1 days. The 30-day risk period was determined based on prior literature (Baumrin, 2019; Dagnew, 2021; Gunes, 2015; Gupta, 2022; Leung, 2022; Sbidian, 2014; Spinelli, 2022; Stevens, 2020; Winthrop, 2022), vaccine mode of action (Didierlaurent, 2017), and consultation with subject matter experts (dermatologists and rheumatologists).

For individuals who receive a second dose of RZV between ≥4 weeks and 300 days after the first dose, there are several scenarios for additional risk and comparison periods. If the second dose is received between +28 to +90 days after the first dose, the risk period after the first dose will immediately be followed by a washout period up to receipt of the second dose (**Scenario 2**). If the second dose is received between +91 to +150 days after the first dose, the risk and comparison periods after the first dose will be followed by a washout period from +61 days until receipt of the second dose (**Scenario 3**). If the second

dose is received between +151 days to +300 days after the first dose (expected to be less common), there will be a comparison period -90 to -61 days prior to the second dose and a washout period -60 to -1 days prior to the second dose (**Scenario 4**). For all scenarios, the second dose will be followed by a 30-day risk period and a 30-day comparison period. The maximum follow-up period will be 360 days after the first dose (maximum 300 days between first and second dose plus the 30-day risk period and the 30-day comparison period).

Figure 1 SCCS design overview for safety analysis



A comparison period is placed before and after vaccination to control for time-varying covariates. The length of the comparison period can be double the length of the risk period because there are up to two comparison periods per risk period; incidence rate is estimated accounting for the length of the periods. The longer comparison periods increase statistical power.

7.3.4. Outcome Definitions

Chart review will be conducted for PHN and flares, but not for HZ, disseminated HZ, HZ-related meningoencephalitis, and hospitalized HZ, which will be ascertained from structured EHR data.

<u>Outcomes for VE objectives</u>

Herpes zoster

The primary outcome is HZ, identified by ICD-10 code B02.xx in any health care setting (outpatient [to include virtual visits], inpatient, emergency department) and by a prescription for a non-topical antiviral (acyclovir, valacyclovir, famciclovir) ±7 days from the HZ diagnosis code date, without a non-topical antiviral (acyclovir, valacyclovir,

famciclovir) prescribed in the 183 days to 8 days prior to the HZ diagnosis code date. (Langan, 2013; Tseng, 2020). The first eligible HZ diagnosis after the index date will be considered an incident HZ event.

Post-herpetic neuralgia

PHN will be defined as HZ-related pain persisting ≥3 months after HZ diagnosis. HZ-related pain will be defined as pain consistent with the HZ episode not explained by other obvious causes. Targeted chart review will be conducted to identify PHN from encounters within 3 to 6 months after HZ diagnosis. Given the potential for poor positive predictive value and negative predictive value for PHN using only automated data (based on prior work by the KPSC research team), all HZ cases with encounters during the ≥3 to 6-month period after HZ diagnosis will be reviewed to ascertain occurrence of PHN.

Disseminated herpes zoster

Disseminated HZ will be identified by ICD-10 code for disseminated zoster (B02.7) within ≤30 days following the incident HZ event date.

Herpes zoster-related meningoencephalitis

HZ-related meningoencephalitis will be identified based on ICD-10 codes and laboratory tests among individuals with HZ who are hospitalized ≤6 months after the incident HZ event date. HZ-related meningoencephalitis will be defined based on any of the following criteria: (1) ICD-10 codes for zoster encephalitis (B02.0) or zoster meningitis (B02.1) in the hospital setting; (2) an HZ diagnosis with a cerebrospinal fluid (CSF) test positive for varicella zoster virus (VZV); or (3) a herpes viral infection diagnosis (B00.xx) in the hospital setting with a CSF test positive for VZV.

Hospitalized HZ

Hospitalized HZ will be identified among incident HZ events with ICD-10 codes for HZ from inpatient encounters or emergency department-to-inpatient transfers.

Outcomes for safety objectives

The outcome for primary and secondary safety objectives is flare, defined as new-onset flare or new-onset of disease worsening of PsO (primary safety objective 1, secondary safety objective 1) or PsA (secondary safety objectives 1 and 2). All individuals eligible for the safety objectives with health care encounters during pre-specified review windows (i.e., risk windows, comparison windows, and the 30 days after the end of risk or comparison windows) will be identified for chart review. Among them, flare will be assessed through EHR review by trained research associates and specialists (dermatologists and rheumatologists). Events are counted in the period in which earliest symptom onset occurs. Cases with unclear sign and/or symptoms, date of onset, or change in medication for flare will be reviewed by a dermatology or rheumatology specialist. Clinically relevant flare is described in **Appendix 2**.

7.3.5. Confounders and Effect Modifiers

Other variables/confounders for VE objectives

Other variables will be identified from the EHR and considered in analyses when appropriate as covariates, including, but not limited to:

- Demographic variables: age at index date, sex, race/ethnicity
- Health care utilization: number of outpatient (including virtual) visits, emergency department, and inpatient encounters in the year prior to the index date
- Comorbidities: kidney disease, cardiovascular disease, pulmonary disease (i.e., chronic obstructive pulmonary disease or chronic bronchitis), liver disease, diabetes mellitus, other autoimmune diseases, immunocompromising conditions (i.e., HIV, cancer, transplant, immunosuppressive medications), and SARS-CoV-2 infection/COVID-19 diagnosis, in the year prior to the index date
- History of ZVL or varicella vaccination prior to the index date based on dates of vaccinations in the EHR
- History of HZ prior to the index date identified using ICD-10 codes (B02.xx) and ICD-9 codes (053.xx) from hospital, outpatient (including virtual), and emergency department settings
- Concomitant vaccinations at the time of exposure (e.g., receipt of influenza vaccine, pneumococcal vaccine, tetanus, diphtheria and pertussis vaccine, COVID-19 vaccine)
- Medication category as detailed in **Appendix 1**.

Other variables/confounders for safety objectives

The SCCS design inherently controls for fixed individual-level confounders. With comparison periods before and after the risk period, the design also controls for time-varying covariates such as age and seasonality.

Effect modifiers

We will perform stratified analyses: (1) by time between first and second dose of RZV (≤6 months, >6 months) for primary VE objective 1 and secondary VE objective 2; (2) by age (18-49 years, ≥50 years) for primary VE objective 1 and secondary VE objective 2, and primary safety objective 1 and secondary safety objective 2; and (3) by medication category at baseline (primary VE objective 1 and secondary VE objective 2, and primary safety objective 1 and secondary safety objective 2).

7.4. Data Sources

Kaiser Permanente Health Connect is the largest and most advanced civilian EHR system available in the U.S. In addition to supporting patient care, this robust system facilitates research, providing access to the EHR for the KPSC vaccine research team. Up-to-date details of patient care are available and accessible to researchers. Data regarding

demographics, services, and diagnoses are tracked from the outpatient (including virtual), emergency department, and hospital settings.

Pharmacy and vaccination utilization are linked through members' unique medical record numbers. As KPSC is a pre-paid health care system, recommended vaccines such as RZV are provided to KPSC members at no cost and can be obtained at no-cost nurse visits or on a walk-in basis without appointment. Thus, there is an incentive for members to receive immunizations within the system. Vaccinations received outside of the system with appropriate documentation are also recorded in the KPSC databases.

KPSC members have very strong motivation to use services internally. For outside providers to be reimbursed by the health plan for covered emergent or contract care, claims must be submitted with documentation of the episode of care, which is integrated into KPSC databases. Thus, the capture of care is considered to be very comprehensive. Care received at KPSC is updated and available to researchers in near real time. Claims data are over 90% complete after 3 months.

7.5. Study Size

We aim to include 2,402 individuals with PsO who receive 2 doses of RZV for the VE primary objective. The target sample size was determined based on predicted numbers of vaccinated individuals using January 2022 data given considerations of study timeline, statistical power, and availability of unvaccinated individuals. The target sample size was already reached as of 2022. The accrued PsO population mostly includes those aged ≥50 years (only 14 individuals aged 18-49 years by February 2023), thus this section provides estimates for this age group. However, accrual for individuals aged 18–49 years will extend through December 2023, which may expand the number of individuals included in this age group.

Table 4 describes the expected number of vaccinated individuals with PsO aged ≥50 years at KPSC that will be available for analyses for the VE and safety objectives. The total number of individuals aged ≥18 years at KPSC by the end of 2023 included in analyses will not exceed this target sample size. The number of vaccinated individuals with PsA aged ≥50 years at KPSC that will be available for analyses for the VE and safety objectives is described in **Appendix 3**.

Table 4 Sample size and average follow-up time per person (individuals with PsO aged ≥50 years)

	Average follow-up time by 12/2024 (years)[4]	2-dose PsO cohort	≥1-dose PsO cohort[3]
2018	6.3	157	414
2019	5.5	790	1,078
2020/1-2020/2[1]	4.9	155	168
2021	3.5	650	700
2022 (estimated)	2.5	650	700
Average follow up time (weighted)	4.1	N/A	N/A
Total sample size[2]	N/A	2,402	3,060

N/A = not applicable; PsO = psoriasis

1. Vaccine accrual period in 2020 shortened due to impact of COVID-19 on vaccination and health care-seeking behaviors.
2. Based on January 2022 RZV uptake report among PsO population, with one year membership prior to index vaccination date (date of the first dose for ≥1-dose cohort or date of the second dose for 2-dose cohort).
3. The number of individuals who received ≥1 dose of RZV
4. Average follow-up time by year was calculated by (follow-up end date – average index date in that year) / 365.25. For example, if index vaccination date for the 2-dose cohort (date of the second dose) is June 2018, the average follow-up for the index vaccination date in 2018 would be 6.3 years (December 31, 2024 - [June 1, 2018 + December 31, 2018] / 2) / 365.25 = 6.3 years).

7.5.1. Sample size and power estimation for VE analyses

The sample size calculation for the primary VE objective was conducted using a two-sided log rank test with α=0.05, to achieve 80% statistical power. The calculation assumed a range of HZ incidence rates in the RZV unvaccinated group (10, 12, 15, 18 per 1,000 person-years) (Yun, 2016), a detectable HR of 0.1 to 0.4 (VE of 60% to 90%), a 1:3 ratio of RZV vaccinated to RZV unvaccinated, and a censoring rate of 7% per year in the RZV vaccinated group (due to termination of membership, death, or receipt of additional dose of RZV) and 25% or 30% per year in the RZV unvaccinated group (due to termination of membership, death, or receipt of RZV). The estimated range for HR of 0.1-0.4 is based on RZV's high vaccine efficacy demonstrated in previous studies. In the ZOE-50 phase 3 clinical trial, overall vaccine efficacy of 2 doses was 97.2% (95% CI: 93.7, 99.0) in adults ≥50 years of age (Lal, 2015). In a post-hoc analysis of clinical trial data from ZOE-50 and ZOE-70, individuals with pre-existing immune-mediated diseases (including PsO) had an overall vaccine efficacy of 90.5% (95% CI: 73.5, 97.5), although individuals on immunosuppressive treatment were excluded from the study (Dagnew, 2021). A more recent study using Medicare data reported a VE of 2 doses of 68% (95% CI: 62.3, 72.8) among individuals aged ≥65 years with an autoimmune disease, which included individuals with PsO and PsA (Izurieta, 2021).

The calculation was performed using SAS software package (version 9.3) PROC POWER procedure.

Table 5 VE sample size required for individuals aged ≥50 years to achieve 80% power (α=0.05) with varying detectable HR or VE

Average length of follow-up (years)	Incidence rate in RZV unvaccinated group* (cases/1000 person-years)	HR	VE (%)	Sample size of RZV vaccinated group[1] with censoring rate of 25% per year in RZV unvaccinated group	Sample size of RZV vaccinated group[1] with censoring rate of 30% per year in RZV unvaccinated group
4.1	10	0.1	90	289	294
		0.2	80	384	392
		0.3	70	526	539
		0.4	60	748	770
	12	0.1	90	241	245
		0.2	80	320	327
		0.3	70	438	449
		0.4	60	624	642
	15	0.1	90	193	196
		0.2	80	256	262
		0.3	70	351	360
		0.4	60	500	515
	18	0.1	90	161	163
		0.2	80	214	218
		0.3	70	293	300
		0.4	60	417	430

HR = hazard ratio; VE = vaccine effectiveness; RZV = recombinant zoster vaccine
1. Estimated required sample size can be compared with **Table 4**, demonstrating that the study is adequately powered to evaluate the primary VE objective.
*(Yun, 2016)

In a cohort study with a 1:3 matching ratio and an average follow-up of 4.1 years, the number of vaccinated subjects needed to detect a VE of 60%, 70%, 80%, and 90% with 80% power (α = 0.05) is 624, 438, 320, and 241 respectively, assuming the incidence of HZ in the unvaccinated population is 12/1,000 person-years and assuming the censoring rate per year in the RZV unvaccinated group is 25% (**Table 5**).

The expected number of individuals who will receive 2 doses of RZV (≥4 weeks apart) during the accrual period is 2,402 for the PsO cohort (**Table 4**). This substantially exceeds the required numbers illustrated in **Table 5**, demonstrating that the study is sufficiently powered to assess the primary VE objective.

The power for analyses of secondary or exploratory VE objectives could vary and may not reach 80% depending on available sample size.

7.5.2. Sample size and power estimation for safety analyses

The power calculation for the SCCS design is based on the signed root likelihood ratio method (Musonda, 2006). The number of flares required in the risk period and comparison period to achieve 80% power is shown in **Table 6** for different values of detectable incidence rate ratio (IRR), with the specifications below:

- K = ratio of length of comparison period and length of risk period

- Vaccination (first dose)[*] = Day 0
- Risk period = +1 to +30 days
- Comparison periods = -90 to -61 days, +31 to +60 days
- Washout period = -60 to -1 days

[*]The current sample size calculations are based on the first RZV dose only. The design can be extended to include second RZV dose exposure. The total length of the risk periods and comparison periods will depend on the timing of receipt of the second dose.

Table 6 Sample size required for individuals aged ≥18 years to achieve 80% power (α=0.05) with varying detectable IRR (chart-confirmed flare)

K	IRR	Number of events in the risk period[1]	Number of events in the comparison period[2]
2	1.2	386	643
2	1.5	87	115
2	1.8	45	49
2	2	34	34
2	2.5	21	17
2	3	16	10

IRR = incidence rate ratio
1. Number of events in the risk period = Total number of events / [IRR x (length of comparison period/length of risk period) +1]
2. Number of events in the comparison period = Total number of events - Number of events in the risk period

Our SCCS design requires ≥49 flare events in the comparison period to achieve 80% power of detecting an increased rate of flare of IRR=1.8, with α=0.05. The expected detectable IRR is described below in **Table 7**.

Table 7 Estimated flares among PsO cohort aged ≥50 years who received ≥1 dose of RZV

Cohort	Sample size of cohort[1]	Flare rate in comparison period (per 60 days)[2]	Number of flares in comparison period (60 days)	Minimally detectable IRR[3]
PsO	3,060	0.8%	25	2.5
PsO	3,060	1.7%	52	1.8
PsO	3,060	2.5%	77	1.8
PsO	3,060	3.3%	101	1.8
PsO	3,060	4.2%	129	1.5

PsO = psoriasis; IRR = incidence rate ratio
1. From **Table 4**, estimated total sample size for ≥1-dose PsO cohort
2. Given the estimate of 5%, 10%, 15%, 20%, and 25% flare rate in one year, i.e. 0.8%, 1.7%, 2.5%, 3.3%, and 4.2% in 60 days of follow up, respectively. (Gregoire, 2021; Hsu, 2017; Leung, 2022)
3. Comparing with **Table 6**, the number of flares in the comparison period

With 3,060 individuals with PsO expected to receive ≥1 dose of RZV during the accrual period (**Table 7**), a total of 52 flares is expected to occur in the 60-day comparison period, with an estimated flare rate of 10% in one year (1.67% in 60 days). This would allow us to detect an IRR of 1.8 (incidence rate of flares in the risk period / incidence rate of flares in the comparison period) with 80% power (α=0.05).

The power for analyses of secondary or exploratory safety objectives could vary and may not reach 80% depending on available sample size.

Estimated flares among the PsA cohort aged ≥50 years who received ≥1 dose of RZV are described in **Appendix 3**.

7.6. Data Management

Data management activities will be performed by KPSC. The KPSC EHR will be the data source for extracting data on exposures, outcomes, and covariates. KPSC will develop the study datasets, maintain documentation, and perform data quality checks.

KPSC programmers will extract data per protocol and reference documentation for KPSC EHR databases. They will conduct data quality checks, which include data integrity control, double programming, and program review. Data integrity control will include checks such as sample size, duplications, formatting, etc. Double programming (i.e., programming independently conducted by 2 programmers) will be performed on the cohort extraction as well as on the outcome variables. The results of the original and validation programming will be compared, discrepancies will be investigated, and discrepancies will be resolved. Program review (i.e., a second person reviews the code of the lead programmer) will be performed on covariate extraction and statistical analyses. All decisions made during data extraction and data quality checks will be documented in a programming decision log.

7.7. Data Analysis

7.7.1. Descriptive analyses

VE objectives

See secondary VE objective 4 (**Section 7.7.4**).

Safety objectives

Baseline demographic and clinical characteristics of individuals with PsO or PsA, such as those listed above, who meet the inclusion criteria will be described. Categorical variables will be presented as absolute numbers and percentages for each cohort. Continuous variables such as age in years will be presented as the mean with standard deviation and/or median with interquartile ranges.

7.7.2. Matching

Matching for VE objectives

For primary VE objective 1, secondary VE objectives 1, 2, and 4, and exploratory VE objective 1, eligible individuals who receive 2 doses of RZV ≥4 weeks apart through the end of the accrual period will be matched with unvaccinated individuals who have not received any doses of RZV as of the index date in a ratio of 1 to up to 3.

For secondary VE objective 3, individuals who receive one dose of RZV, but do not receive a second dose within 6 months after the first dose during the accrual period, will be matched with unvaccinated individuals who have not received any doses of RZV of the index date at a ratio of 1 to up to 3. Individuals who receive a second dose of RZV will be censored upon receipt of the second RZV dose.

Matching is performed separately for the cohort receiving two doses of RZV and the cohort receiving one dose of RZV.

Matching will be performed on the following variables:

- Condition (PsO or PsA)
- Age (by decade, if sample size allows) at index date
- Sex
- Race/ethnicity, if sample size allows
- Medication category at index date (**Appendix 1**).

Matching for the PsO group and the PsA group will be conducted separately. Individuals with both PsO and PsA will be included in the matching for both the PsO group and the PsA group, and will be prioritized to match to individuals with both conditions.

Unvaccinated and vaccinated individuals will be matched on exact combination of matching variables. For example, a black female aged 55 with PsO who is on a topical corticosteroid (medication category 1) who received RZV on 01/01/2022 will be matched to a black female who is in the same age category (in her 50's) who is on a medication in medication category 1, who had not received RZV as of 01/01/2022. In situations where the number of eligible individuals is limited, categories of matching variables may be consolidated and the matching ratio may be reduced.

Unvaccinated individuals who are matched to RZV vaccinated individuals can contribute person-time to a vaccinated cohort if they receive RZV; their unvaccinated person-time is censored upon receipt of the first dose of RZV.

Matching for safety objectives

Not applicable

7.7.3. Primary analyses

Primary VE objective 1

The number of incident HZ cases and the number of person-years of follow-up will be assessed for 2-dose RZV vaccinated individuals and unvaccinated matched individuals in the PsO cohort. The incidence of HZ will be calculated by dividing the number of incident HZ cases by the total number of person-years. Individuals will be followed from the 31st day after the index date (the date of the second dose for the 2-dose cohort) until the end of study follow-up, occurrence of outcome of interest, or occurrence of a censoring event (death, termination of KPSC membership, or receipt of a dose of RZV), whichever comes first.

In addition to matching on key confounders (**Section 7.7.2**), descriptive analysis will assess the balance between vaccinated and unvaccinated groups on other potential confounders (secondary VE objective 4). Unadjusted and adjusted HRs and corresponding 95% CIs comparing HZ incidence rates in the 2-dose RZV individuals and the matched unvaccinated individuals will be estimated by Cox proportional hazards regression models without and with adjustment for potential confounders described above. Unadjusted VE and adjusted VE (%) will be calculated as (1 – HR) × 100 when HR≤1, or – [(HR – 1)/HR] × 100 when HR>1.

Analyses for primary VE objective 1 will also be stratified separately by time between first and second dose of RZV (≤6 months, >6 months), by age (18-49 years, ≥50 years), and by medication category at baseline. Analysis will be conducted separately in each stratum rather than modelling the stratification/interaction term directly in the Cox model.

Primary safety objective 1

Rates of PsO flare for risk periods and comparison periods will be calculated by dividing the number of flares by person-time. IRR with corresponding 95% CIs, comparing the rate of flares in the risk and comparison periods (overall, and by first and second dose), will be estimated using conditional Poisson regression. Analyses for secondary VE objective 1 will also be conducted stratified separately by age (18-49 years, ≥50 years) and by medication category at baseline.

7.7.4. Secondary analyses

Secondary VE objective 1

The number of incident HZ cases and the number of person-years of follow-up will be assessed for 2-dose RZV vaccinated individuals and unvaccinated matched individuals with PsO or PsA. Unadjusted and adjusted HR and VE (%) will be calculated as described under **Section 7.7.3** (primary VE objective 1).

Secondary VE objective 2

In secondary VE objective 2, analyses similar to primary VE objective 1 will be conducted for the PsA cohort. Analyses for secondary VE objective 2 will also be

conducted stratified separately by time between first and second dose of RZV (≤6 months, >6 months), by age (18-49 years, ≥50 years), and by medication category at baseline (**Appendix 1**).

Secondary VE objective 3

Analyses for secondary VE objective 3 will be conducted among the matched cohorts of individuals with PsO or, separately, with PsA receive 1 dose of RZV and do not receive a second dose within 6 months after the first dose. Individuals will be followed from the 31st day after the index date until occurrence of HZ, termination of membership, receipt of a dose of RZV for unvaccinated individuals, receipt of a second dose of RZV >6 months after the first dose among vaccinated individuals, or end of study period, whichever comes first. Analyses for secondary VE objective 3 will employ similar methods as for the primary VE analyses.

Secondary VE objective 4

For both PsA and PsO cohorts, baseline demographic and clinical characteristics of individuals in vaccinated and unvaccinated groups, such as those listed above in **Section 7.3.5**, will be described and compared. Categorical variables will be presented as absolute numbers and percentages for each group, and will be compared between the groups using Pearson χ^2 test or Fisher's exact test, as appropriate. Continuous variables such as age in years will be presented as the mean with standard deviation and/or median with interquartile ranges, and will be compared between the groups using the two-sample t-test or Wilcoxon rank-sum test, as appropriate. Absolute standardized differences will be calculated to assess the balance of the distribution of the covariates between the groups.

Secondary safety objective 1

Analyses for secondary safety objective 1 in adults aged ≥18 years with PsO or PsA will be consistent with the analyses described for primary safety objective 1.

Secondary safety objective 2

Analyses for secondary safety objective 2 in adults aged ≥18 years with PsA will be consistent with the analyses described for primary safety objective 1, and will also be stratified separately by age (18-49 years, ≥50 years) and by medication category at baseline (**Appendix 1**). Descriptive analyses will be performed for the 18-49-year age group, if the sample size in the subgroup is too small to produce meaningful results.

7.7.5. Exploratory analyses

CCI

[redacted]

CCI

[redacted]

7.7.6. Additional analyses

Sensitivity analysis will be performed to assess VE against HZ for individuals with PsO, but without PsA. For this group, we will use similar methods described for the primary VE analyses.

For individuals who received a RZV dose between March 2020 and December 2020 who are not accrued (see Study Period in **Section 7.2.3**), we will describe their demographic and clinical baseline characteristics and incidence of HZ.

7.8. Quality Control and Quality Assurance

Data quality details are provided above (**Section 7.6**).

7.9. Strengths and Limitations of the Research Methods

7.9.1. Strengths

KPSC's large, stable, diverse population

The high retention rate and stability of KPSC membership provide an opportunity to follow individuals over time and conduct long-term effectiveness studies. The large, diverse, and stable population makes rapid accrual of a large, representative sample size possible to evaluate long-term implications of vaccination.

KPSC's large, robust, comprehensive EHR system

Kaiser Permanente Health Connect, KPSC's comprehensive EHR system integrates all aspects of care from all settings, including pharmacy and lab services, as well as appointments, registration, and claims/billing. Care received outside the KPSC system is captured through claims submitted for reimbursement, which are integrated into the EHR databases. Up-to-date details of patient care are available and accessible to researchers near real-time.

Chart reviews for outcome ascertainment

Chart reviews will be performed to ascertain the occurrence of PsO and PsA flare, the primary outcome for safety analyses. Given its complexity and potential for misclassification, standard definitions developed for flare in consultation with rheumatology and dermatology experts will be used identify medically attended flares during chart review.

Chart reviews will be performed to identify and confirm PHN cases, rather than identifying them by diagnosis codes only. Given the expected low positive predictive value and negative predictive value of diagnosis codes for PHN, all HZ cases with

encounters during the ≥3 to 6-month period after HZ diagnosis will be reviewed to ascertain the occurrence of PHN.

SCCS design for safety objectives

For the safety objectives, SCCS analysis will be conducted among individuals with PsO or PsA who receive ≥1 dose of RZV. The SCCS design is a case-only method, in which each case serves as their own control. A major advantage of this design is that the potential confounding by characteristics that vary between individuals and may have an impact on disease outcomes, such as comorbidities, and genetic/socioeconomic factors is removed. (Farrington, 1995; Wilson, 2011) Additionally, with comparison periods within close proximity to the risk period (before and after the risk period), the design also controls for time-varying covariates such as age and seasonality.

7.9.2. Limitations

Confounding by indication

Confounding by indication is a potential limitation. For the VE objectives, this will be addressed by matching on condition (PsO/PsA), age, sex, race/ethnicity (if sample size allows), and medication category, which may have an impact on the development of the outcome and likelihood of RZV vaccination. For the safety objectives, the SCCS design will minimize confounding by implicitly controlling for time-fixed confounders.

Misclassification

Missclassification of individuals with PsO and PsA is possible. However, these definitions for PsO and PsA were selected based on prior knowledge, current literature (Lee, 2021), and KPSC chart review indicating a high positive predictive value.

Misclassification of exposure and outcome is possible. However, given the accuracy of KPSC's vaccine data including dates of administration, misclassification of RZV vaccination status is unlikely. The VE outcome of incident HZ is expected to be accurately captured using an algorithm based on a combination of an ICD-10 code and prescription for an antiviral. This algorithm has been used in previous studies and was found to have high accuracy in identifying incident HZ (Capistran, 2021; Langan, 2013; Tseng, 2020; Zhang, 2012). For the safety outcomes, given the complexity and significant potential for misclassification of disease flare, medical record review using standardized criteria will be performed to ascertain this outcome. Since this study uses EHR data, the effectiveness and safety outcomes being captured are those for which medical attention is sought; mild outcomes may be missed.

Missing data

Inherent in the observational study design is potential missing patient data during follow-up. However, patients within KPSC are incentivized to use care inside the health care system, thus it is expected that the majority of care, including dermatology and rheumatology visits, will occur within the KPSC network. There will also be comprehensive longitudinal capture of a patient's baseline disease activity, medication

regimens, and flares so long as they remain KPSC members. Details on KPSC's membership retention are provided in **Section 7.2.2**. Missingness in demographic data (e.g., race/ethnicity) will be reported.

Generalizability

A potential limitation is generalizability as this study will be conducted at a single health care organization. However, the KPSC population exhibits significant racial/ethnic diversity, and the age distribution of patients with PsO or PsA in the KPSC system is expected to reflect the national distribution. In addition, although the practices of care for patients with PsO or PsA (e.g., treatment regimens) are expected to be largely standardized across U.S. health care systems, the results of this study may not be generalizable to care settings with different care practices.

Impact of COVID-19 pandemic

The COVID-19 pandemic significantly affected vaccine uptake in the general population and study population specifically. The pandemic also indirectly impacted behaviors and policies such as health care delivery, insurance eligibility, and health care-seeking behaviors, and ascertainment of and control for these known and unknown variables may not be fully possible. Thus, subjects will not be accrued in the study from March through December 2020. KPSC will continue to monitor RZV uptake in these patient populations in the KPSC system on a regular basis during study conduct.

Ascertainment bias

During chart reviews for outcome identification, ascertainment bias is possible because vaccination status is available in medical records. However, vaccination status is typically documented in a section designated for immunizations, separate from encounter charts that are reviewed by chart abstractors to determine outcome status. Chart abstractors are also trained not to look at immunization records.

7.9.3. Study closure/uninterpretability of results

Not applicable

7.10. Other Aspects

Not applicable

8. PROTECTION OF HUMAN SUBJECTS

8.1. Ethical Approval and Subject Consent

This study will be conducted in accordance with the protocol and:

- Ethical principles derived from Declaration of Helsinki and Council for International Organisations of Medical Sciences International Ethical Guidelines
- Food and Drug Administration Code of Federal Regulations Title 21 (21 CFR)
- Guidelines for Good Pharmacoepidemiology Practices
- International Epidemiological Association Guidance on Good Epidemiological Practices
- All other applicable regulations and local laws

The protocol, protocol amendments, and other relevant documents must be submitted to an Institutional Review Board (IRB) by the investigator for review and approval. These documents will be signed and dated by the investigator before the study is initiated. A waiver of informed consent from the IRB will be obtained as this observational research involves no more than minimal risk to the subjects.

Any amendments to the protocol will require IRB approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will provide written summaries of the status of the study to the IRB in accordance with the requirements, policies, and procedures established by the IRB. The investigator will provide oversight of the conduct of the study at the site and adherence to all applicable regulations and local laws.

8.2. Subject Confidentiality

The protocol will be reviewed and approved by the KPSC IRB. All study staff with access to protected health information are trained in procedures to protect the confidentiality of subject data.

The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule governs the use and disclosure of protected health information from covered entities. Throughout the course of this study, no personally identifiable information will be disclosed, however it will be accessed through the EHR. This information will only be accessed by those authorized to do so and will not be shared with GSK or anyone outside of the KPSC study team. As this data-only study presents no more than minimal risk to individuals and the research could not be practically done if required to obtain written authorization for usage, KPSC will obtain a waiver for written HIPAA authorization for research involving use of the EHR.

9. LEGAL BASIS FOR PROCESSING INDIVIDUAL HUMAN DATA

The authors confirm that study data is Individual Human Data not owned by GSK, but that the proposed use of the Individual Human Data aligns with the 'purpose of use' outlined in the source contract and/or the terms and conditions of use of the data source and will comply with any specified prohibitions of use.

Data will be analysed and reported in aggregate; individual human data will not be shared or reported outside of KPSC.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

10.1. Collection of adverse events/reactions (Solicited Events)

The purpose of the study is to monitor exposure to Shingrix and to evaluate flare. For Shingrix, pre-defined safety events of interest flare, will be systematically recorded in aggregate. These will be summarised in interim, if applicable, and final study reports. This study is based on secondary use of existing health data and as such Individual Case Safety Reporting (ICSRs) to regulatory agencies is not required.

10.2. Reporting of Adverse Events/Reactions (Spontaneous Events)

This study is based on data previously collected for other purposes e.g., routine healthcare encounters. As such, there is no requirement for the collection and reporting of Individual Case Safety Reports (ICSRs). Although the study is based on human review of unstructured data, the nature of the secondary data protocol driven data collection and analysis does not allow for reporting of serious and non-serious AEs, pregnancy exposures, or incidents related to any GSK/ViiV product during the conduct of this research. In addition, the minimum criteria of identifiable patient, reporter, exposure and event, needed to report individual case safety reports may not be present in the information reviewed within the context of the study. The data also may lack an identifiable patient and reporter and may be insufficient to establish attribution between a potential safety event and an individual patient using a GSK/ViiV product.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

The key design elements of this protocol and summaries of results will be posted on the GSK Clinical Study register in compliance with the applicable regulations/GSK policy according to the timelines described below. Key design elements of this protocol will also be posted on the European Union Post Authorization Study (EUPAS) register in compliance with applicable regulations.

Protocol summaries will be registered prior to analysis start. The protocol summary along with redacted protocol will be published on EUPAS register prior to commencement of the study.

Results summaries along with redacted protocol and Statistical Analysis Plan will be posted within 12 months of analysis completion date on GSK study register. Redacted clinical study report will be posted on EUPAS register within 12 months of analysis completion date.

Where required by regulation, summaries will also be posted on applicable national or regional clinical trial registers.

Study results may be presented at local, national, or international professional conferences and will be submitted as manuscripts for peer-reviewed publication.

12. REFERENCES

Anderson, T. C., Masters, N. B., Guo, A., Shepersky, L., Leidner, A. J., Lee, G. M., . . . Dooling, K. L. (2022). Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged >/=19 Years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. *MMWR Morb Mortal Wkly Rep, 71*(3), 80-84. doi:10.15585/mmwr.mm7103a2

Baker, M. A., Lieu, T. A., Li, L., Hua, W., Qiang, Y., Kawai, A. T., . . . Nguyen, M. D. (2015). A vaccine study design selection framework for the postlicensure rapid immunization safety monitoring program. *Am J Epidemiol, 181*(8), 608-618. doi:10.1093/aje/kwu322

Baumrin, E., Van Voorhees, A., Garg, A., Feldman, S. R., & Merola, J. F. (2019). A systematic review of herpes zoster incidence and consensus recommendations on vaccination in adult patients on systemic therapy for psoriasis or psoriatic arthritis: From the Medical Board of the National Psoriasis Foundation. *J Am Acad Dermatol, 81*(1), 102-110. doi:10.1016/j.jaad.2019.03.017

Capistran, E., Morin, V., Marcoux, D., Trudel, E., Gagne, M., Proulx, S., . . . Carignan, A. (2021). Validation of algorithms using International Classification of Diseases for the identification of herpes zoster episodes requiring hospitalization in Quebec, Canada. *Vaccine, 39*(41), 6074-6080. doi:10.1016/j.vaccine.2021.08.100

Centers for Disease Control and Prevention, Immunization Information Systems (IIS). 2023. Retrieved from https://www2a.cdc.gov/vaccines/iis/iisstandards/vaccines.asp?rpt=cvx

Chen, S. Y., Suaya, J. A., Li, Q., Galindo, C. M., Misurski, D., Burstin, S., & Levin, M. J. (2014). Incidence of herpes zoster in patients with altered immune function. *Infection, 42*(2), 325-334. doi:10.1007/s15010-013-0550-8

Chiu, H. Y., Hung, Y. T., Huang, S. W., & Huang, Y. H. (2022). Comparative risk of herpes zoster in patients with psoriatic disease on systemic treatments: a systematic review and network meta-analysis. *Ther Adv Chronic Dis, 13*, 20406223221091188. doi:10.1177/20406223221091188

Chovatiya, R., & Silverberg, J. I. (2021). Association of herpes zoster and chronic inflammatory skin disease in US inpatients. *J Am Acad Dermatol, 85*(6), 1437-1445. doi:10.1016/j.jaad.2019.12.073

Dagnew, A. F., Rausch, D., Herve, C., Zahaf, T., Levin, M. J., Schuind, A., & group, Z. O. E. s. (2021). Efficacy and serious adverse events profile of the adjuvanted recombinant zoster vaccine in adults with pre-existing potential immune-mediated diseases: a pooled post hoc analysis on two parallel randomized trials. *Rheumatology (Oxford), 60*(3), 1226-1233. doi:10.1093/rheumatology/keaa424

Didierlaurent, A. M., Laupeze, B., Di Pasquale, A., Hergli, N., Collignon, C., & Garcon, N. (2017). Adjuvant system AS01: helping to overcome the challenges of modern vaccines. *Expert Rev Vaccines, 16*(1), 55-63. doi:10.1080/14760584.2016.1213632

Dooling, K. L., Guo, A., Patel, M., Lee, G. M., Moore, K., Belongia, E. A., & Harpaz, R. (2018). Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. *MMWR Morb Mortal Wkly Rep, 67*(3), 103-108. doi:10.15585/mmwr.mm6703a5

Dworkin, R. H., Johnson, R. W., Breuer, J., Gnann, J. W., Levin, M. J., Backonja, M., . . . Whitley, R. J. (2007). Recommendations for the management of herpes zoster. *Clin Infect Dis, 44 Suppl 1*, S1-26. doi:10.1086/510206

Farrington, P., Pugh, S., Colville, A., Flower, A., Nash, J., Morgan-Capner, P., . . . Miller, E. (1995). A new method for active surveillance of adverse events from diphtheria/tetanus/pertussis and measles/mumps/rubella vaccines. *Lancet, 345*(8949), 567-569. doi:10.1016/s0140-6736(95)90471-9

GlaxoSmithKline Biologicals, (2021). SHINGRIX (Zoster Vaccine Recombinant, Adjuvanted), suspension forintramuscular injection. Retrieved from https://www.fda.gov/media/108597/download

Gnann, J. W., Jr., & Whitley, R. J. (2002). Clinical practice. Herpes zoster. *N Engl J Med, 347*(5), 340-346. doi:10.1056/NEJMcp013211

Gregoire, A. R. F., DeRuyter, B. K., & Stratman, E. J. (2021). Psoriasis Flares Following Systemic Glucocorticoid Exposure in Patients With a History of Psoriasis. *JAMA Dermatol, 157*(2), 198-201. doi:10.1001/jamadermatol.2020.4219

Gunes, A. T., Fetil, E., Akarsu, S., Ozbagcivan, O., & Babayeva, L. (2015). Possible Triggering Effect of Influenza Vaccination on Psoriasis. *J Immunol Res, 2015*, 258430. doi:10.1155/2015/258430

Gupta, S., Arasaratnam, R. J., Solow, E. B., & Bajaj, P. (2022). A Medical Records Review Study Assessing Safety of Zoster Vaccine Recombinant, Adjuvanted in Patients With Rheumatic Disease. *J Clin Rheumatol, 28*(2), e528-e531. doi:10.1097/RHU.0000000000001790

Harpaz, R., Ortega-Sanchez, I. R., Seward, J. F., Advisory Committee on Immunization Practices Centers for Disease, C., & Prevention. (2008). Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep, 57*(RR-5), 1-30; quiz CE32-34. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/18528318

Hechter, R. C., Qian, L., Tartof, S. Y., Sy, L. S., Klein, N. P., Weintraub, E., . . . Jacobsen, S. J. (2019). Vaccine safety in HIV-infected adults within the Vaccine Safety Datalink Project. *Vaccine, 37*(25), 3296-3302. doi:10.1016/j.vaccine.2019.04.080

Hsu, M.-A. (2017). Frequency, Prevalence, and Burden of Flares on Patients with Moderate to Severe Psoriasis: A Retrospective Cross-Sectional Analysis. *JOURNAL OF PSORIASIS AND PSORIATIC ARTHRITIS, 2*.

Icen, M., Crowson, C. S., McEvoy, M. T., Gabriel, S. E., & Maradit Kremers, H. (2008). Potential misclassification of patients with psoriasis in electronic databases. *J Am Acad Dermatol, 59*(6), 981-985. doi:10.1016/j.jaad.2008.08.034

Insinga, R. P., Itzler, R. F., Pellissier, J. M., Saddier, P., & Nikas, A. A. (2005). The incidence of herpes zoster in a United States administrative database. *J Gen Intern Med, 20*(8), 748-753. doi:10.1111/j.1525-1497.2005.0150.

Izurieta, H. S., Wu, X., Forshee, R., Lu, Y., Sung, H. M., Agger, P. E., . . . Dooling, K. (2021). Recombinant Zoster Vaccine (Shingrix): Real-World Effectiveness in the First 2 Years Post-Licensure. *Clin Infect Dis, 73*(6), 941-948. doi:10.1093/cid/ciab125

Kawai, K., & Yawn, B. P. (2017). Risk Factors for Herpes Zoster: A Systematic Review and Meta-analysis. *Mayo Clin Proc, 92*(12), 1806-1821. doi:10.1016/j.mayocp.2017.10.009

Koebnick, C., Langer-Gould, A. M., Gould, M. K., Chao, C. R., Iyer, R. L., Smith, N., . . . Jacobsen, S. J. (2012). Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J, 16*(3), 37-41. doi:10.7812/TPP/12-031

Lal, H., Cunningham, A. L., Godeaux, O., Chlibek, R., Diez-Domingo, J., Hwang, S. J., . . . Group, Z. O. E. S. (2015). Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *N Engl J Med, 372*(22), 2087-2096. doi:10.1056/NEJMoa1501184

Langan, S. M., Smeeth, L., Margolis, D. J., & Thomas, S. L. (2013). Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study. *PLoS Med, 10*(4), e1001420. doi:10.1371/journal.pmed.1001420

Lee, H., He, M., Cho, S. K., Bessette, L., Tong, A. Y., Merola, J. F., . . . Kim, S. C. (2021). Validation of claims-based algorithms to identify patients with psoriasis. *Pharmacoepidemiol Drug Saf, 30*(7), 868-874. doi:10.1002/pds.5229

Leung, J., Anderson, T. C., Dooling, K., Xie, F., & Curtis, J. R. (2022). Recombinant Zoster Vaccine Uptake and Risk of Flares Among Older Adults With Immune-Mediated Inflammatory Diseases in the US. *Arthritis Rheumatol, 74*(11), 1833-1841. doi:10.1002/art.42261

Mullooly, J. P., Riedlinger, K., Chun, C., Weinmann, S., & Houston, H. (2005). Incidence of herpes zoster, 1997-2002. *Epidemiol Infect, 133*(2), 245-253. doi:10.1017/s095026880400281x

Musonda, P., Farrington, C. P., & Whitaker, H. J. (2006). Sample sizes for self-controlled case series studies. *Stat Med, 25*(15), 2618-2631. doi:10.1002/sim.2477

Orbai, A. M., Tillett, W., Grieb, S., Peterson, S., Holdsworth, E. A., Booth, N., . . . Gossec, L. (2023). Impact of Physician-Defined Flares on Quality of Life and Work Impairment: An International Survey of 2238 Patients With Psoriatic Arthritis. *J Rheumatol, 50*(1), 76-83. doi:10.3899/jrheum.211302

Robinson, J., Borgo, Lina., Fennell, Kevin., and Funahashi, Tadashi T. . (2020). The Covid-19 Pandemic Accelerates the Transition to Virtual Care. *NEJM Catalyst*. Retrieved from https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0399#f3

Sbidian, E., Eftekahri, P., Viguier, M., Laroche, L., Chosidow, O., Gosselin, P., . . . Bachelez, H. (2014). National survey of psoriasis flares after 2009 monovalent H1N1/seasonal vaccines. *Dermatology, 229*(2), 130-135. doi:10.1159/000362808

Simpson, S. E. (2013). A positive event dependence model for self-controlled case series with applications in postmarketing surveillance. *Biometrics, 69*(1), 128-136. doi:10.1111/j.1541-0420.2012.01795.x

Spinelli, F. R., Favalli, E. G., Garufi, C., Cornalba, M., Colafrancesco, S., Conti, F., & Caporali, R. (2022). Low frequency of disease flare in patients with rheumatic musculoskeletal diseases who received SARS-CoV-2 mRNA vaccine. *Arthritis Res Ther, 24*(1), 21. doi:10.1186/s13075-021-02674-w

Stevens, E., Weinblatt, M. E., Massarotti, E., Griffin, F., Emani, S., & Desai, S. (2020). Safety of the Zoster Vaccine Recombinant Adjuvanted in Rheumatoid Arthritis and Other Systemic Rheumatic Disease Patients: A Single Center's Experience With 400 Patients. *ACR Open Rheumatol, 2*(6), 357-361. doi:10.1002/acr2.11150

Thomas, S. L., & Hall, A. J. (2004). What does epidemiology tell us about risk factors for herpes zoster? *Lancet Infect Dis, 4*(1), 26-33. doi:10.1016/s1473-3099(03)00857-0

Tseng, H. F., Sy, L. S., Ackerson, B. K., Hechter, R. C., Tartof, S. Y., Haag, M., . . . Jacobsen, S. J. (2017). Safety of Quadrivalent Meningococcal Conjugate Vaccine in 11- to 21-Year-Olds. *Pediatrics, 139*(1). doi:10.1542/peds.2016-2084

Tseng, H. F., Bruxvoort, K., Ackerson, B., Luo, Y., Tanenbaum, H., Tian, Y., . . . Sy, L. S. (2020). The Epidemiology of Herpes Zoster in Immunocompetent, Unvaccinated Adults >/=50 Years Old: Incidence, Complications, Hospitalization, Mortality, and Recurrence. *J Infect Dis, 222*(5), 798-806. doi:10.1093/infdis/jiz652

Whitaker, H. J., Farrington, C. P., Spiessens, B., & Musonda, P. (2006). Tutorial in biostatistics: the self-controlled case series method. *Stat Med, 25*(10), 1768-1797. doi:10.1002/sim.2302

Wilson, K., Hawken, S., Kwong, J. C., Deeks, S., Crowcroft, N. S., Van Walraven, C., . . . Manuel, D. (2011). Adverse events following 12 and 18 month vaccinations: a population-based, self-controlled case series analysis. *PLoS One, 6*(12), e27897. doi:10.1371/journal.pone.0027897

Winthrop, K. L. (2017). The emerging safety profile of JAK inhibitors in rheumatic disease. *Nat Rev Rheumatol, 13*(5), 320. doi:10.1038/nrrheum.2017.51

Winthrop, K. L., Curtis, J. R., Lindsey, S., Tanaka, Y., Yamaoka, K., Valdez, H., . . . Bananis, E. (2017). Herpes Zoster and Tofacitinib: Clinical Outcomes and the Risk of Concomitant Therapy. *Arthritis Rheumatol, 69*(10), 1960-1968. doi:10.1002/art.40189

Winthrop, K. L., Tanaka, Y., Lee, E. B., Wollenhaupt, J., Al Enizi, A., Azevedo, V. F., & Curtis, J. R. (2022). Prevention and management of herpes zoster in patients with rheumatoid arthritis and psoriatic arthritis: a clinical review. *Clin Exp Rheumatol, 40*(1), 162-172. doi:10.55563/clinexprheumatol/cpu6r9

Xu, S., Glenn, S., Sy, L., Qian, L., Hong, V., Ryan, D. S., & Jacobsen, S. (2021). Impact of the COVID-19 Pandemic on Health Care Utilization in a Large Integrated Health Care System: Retrospective Cohort Study. *J Med Internet Res, 23*(4), e26558. doi:10.2196/26558

Yawn, B. P., Saddier, P., Wollan, P. C., St Sauver, J. L., Kurland, M. J., & Sy, L. S. (2007). A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clin Proc, 82*(11), 1341-1349. doi:10.4065/82.11.1341

Yun, H., Yang, S., Chen, L., Xie, F., Winthrop, K., Baddley, J. W., . . . Curtis, J. R. (2016). Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases: Implications for Vaccination. *Arthritis Rheumatol, 68*(9), 2328-2337. doi:10.1002/art.39670

Zhang, J., Xie, F., Delzell, E., Chen, L., Winthrop, K. L., Lewis, J. D., . . . Curtis, J. R. (2012). Association between vaccination for herpes zoster and risk of herpes zoster infection among older patients with selected immune-mediated diseases. *JAMA, 308*(1), 43-49. doi:10.1001/jama.2012.7304

Zisman, D., Bitterman, H., Shalom, G., Feldhamer, I., Comanesther, D., Batat, E., . . . Cohen, A. D. (2016). Psoriatic arthritis treatment and the risk of herpes zoster. *Ann Rheum Dis, 75*(1), 131-135. doi:10.1136/annrheumdis-2013-205148

Zou, A., Chen, Y., Shi, N., & Ye, Y. (2021). Risk of herpes zoster associated with biological therapies for psoriasis and psoriatic arthritis: A systematic review and meta-analysis. *Medicine (Baltimore), 100*(40), e27368. doi:10.1097/MD.00000000000273

13. APPENDICES

Appendix 1 Medication categories for PsO and PsA

Medication categories will be used as an indicator for disease severity and risk for HZ to match vaccinated and unvaccinated individuals. Vaccinated and unvaccinated individuals will be matched on age, sex, race/ethnicity (if sample size allows), condition (PsO and PsA), and medication category at the beginning of follow-up (index date). CCI [redacted]

The medication categories were developed based on consultation with KPSC and external experts (rheumatologists and dermatologists) to ensure matching based on differences in disease severity and risk of HZ.

Medication categories may be consolidated to ensure at least 1:1 matching. Medication category will be determined by the highest category of medication prescribed during the search periods specified below:

- Biologic disease-modifying anti-rheumatic drugs (DMARDs), intralesional/Intramuscular corticosteroids, psoralen and ultraviolet A (PUVA), photodynamic therapy (PDT), narrowband ultraviolet B (NB-UVB) (with or without tar), UV phototherapy (with or without tar), and excimer laser: 3 months before index date[1]
- Targeted synthetic DMARDs (JAK inhibitors): 3 months before index date to 1 month after index date[2]
- Nonsteroidal anti-inflammatory drugs (NSAIDs), topical medications, steroids, and conventional synthetic DMARDs: Medication prescribed/refilled within 6 months prior to index date AND medication duration covers the index date[3]

[1] Some biologics are given as far apart as approximately every 8 weeks, thus the search period for biologics is 3 months before the index date.

[2] The search period for JAK inhibitors (a type of biologic) is extended to 1 month after the index date; because JAK inhibitors are associated with a significantly increased risk of HZ, providers may administer RZV prior to initiating treatment with a JAK inhibitor.

[3] While medications are typically dispensed as a ≤90-day supply, some medications are occasionally dispensed as a ≥100-day supply. To ensure identification of prescriptions covering the index date, medications prescribed/refilled within 6 months prior to the index date will be searched to identify those medications with a duration covering the index date.

Individuals who meet the criteria for both PsO and PsA will be included in both the PsO and PsA cohorts. The most advanced medication category used for treatment of either

condition will be used for both cohorts. For example, if an individual identified as having both PsO and PsA is using a Category 2 medication for PsO (e.g., UV phototherapy) and a Category 4 medication for PsA (e.g., Orencia), then Category 4 will be used for both PsO and PsA analyses.

Medication category for PsO

Category 1 (least severe)	Topical medications (topical corticosteroids, calcineurin inhibitors, vitamin D analogues, tazarotene, salicylic acid, anthralin [dithranol], coal tar/liquor carbonis detergens [LCD], roflumilast [Zoryve], tapinarof [Vtama]), or no treatment from Category 2 to Category 5
Category 2	Psoralen and ultraviolet A (PUVA), photodynamic therapy (PDT), narrowband ultraviolet B (NB-UVB) (with or without tar), UV phototherapy (with or without tar), and excimer laser.
Category 3	**Conventional synthetic DMARDs:** Traditional DMARD: methotrexate (MTX) (Trexall, Xatmep, Otrexup, Rheumatrex, Rasuvo), cyclosporine, acitretin, apremilast (Otezla), azathioprine (Imuran, Azasan), hydroxyurea, mycophenolate mofetil (MMF), tacrolimus, leflunomide (Arava), thioguanine (6-TG, Tabloid, Lanvis) **Intralesional/IM corticosteroids:** triamcinolone (Kenalog, Aristocort-Forte, Aristospan, Cinacort Span, Triamcort, Triam-Forte)
Category 4	**Biologic DMARDs[1]:** TNF-α inhibitors: etanercept (Enbrel), infliximab and biosimilars (Avsola, Inflectra, Remicade, Renflexis), adalimumab and biosimilars (Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Humira, Hyrimoz, Idacio, Yusimry), certolizumab pegol (Cimzia), golimumab (Simponi, Simponi Aria) IL-12/IL-23 inhibitors: ustekinumab (Stelara) IL-17 inhibitors: secukinumab (Cosentyx), ixekizumab (Taltz), brodalumab (Siliq), bimekizumab (Bimzelx) IL-23 inhibitors: guselkumab (Tremfya), tildrakizumab-asmn (Ilumya), risankizumab-rzaa (Skyrizi)
Category 5 (most severe)	**Targeted synthetic DMARDs:** JAK inhibitors: tofacitinib (Xeljanz, Xeljanz XR), upadacitinib (Rinvoq), deucravacitinib (Sotyktu)

1. Biologics are administered as either SC or IV. Both SC or IV forms are available for golimumab (SC [Simponi] or IV [Simponi Aria]) and ustekinumab (Stelara). Infliximab and biosimilars are administered as IV only. All others are administered as SC.

IM = intramuscular; IV = intravenous; PO = oral; SC = subcutaneous

Medication category for PsA

Category 1 (least severe)	Non-pharmacologic therapies, or no treatment from Category 2 to Category 5
Category 2	**Nonsteroidal anti-inflammatory drugs (NSAIDs):** ibuprofen (Motrin, Advil), naproxen (Aleve, Anaprox, Mediproxen), indomethacin (Indocin, Tivorbex), meloxicam (Vivlodex, Mobic, Comfort Pac Meloxicam), celecoxib (Celebrex), nabumetone (Relafen), etodolac (Lodine), diclofenac (Xrylix, Voltaren, Solaraze, Flector, Zorvolex, Zipsor, Cambia), sulindac (Clinoril), salsalate (Disalcid), ketorolac (Toradol, Acular) **Low dose steroids (PO):** methylprednisolone (Medrol), prednisolone, prednisone (<20 mg prednisone or equivalent)
Category 3	**Conventional synthetic DMARDs:** Oral small molecules (OSMs): MTX (Trexall, Xatmep, Otrexup, Rheumatrex, Rasuvo), sulfasalazine (Azulfidine), leflunomide (Arava), apremilast (Otezla) **High-dose systemic steroids:** hydrocortisone (IM/IV), methylprednisolone (Medrol [IM/IV], Solu-Medrol [IM/IV], Depo-Medrol [IM/IV]), prednisolone (IM/IV), triamcinolone (Kenalog, Aristocort-Forte, Aristospan, Cinacort Span, Triamcort, Triam-Forte) [IM/IV]), prednisone (PO) (≥20 mg prednisone or equivalent)
Category 4[1]	**Biologic DMARDs**[2]**:** TNF-α inhibitors: etanercept (Enbrel), infliximab and biosimilars (Avsola, Inflectra, Remicade, Renflexis), adalimumab and biosimilars (Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Humira, Hyrimoz, Idacio, Yusimry), certolizumab pegol (Cimzia), golimumab (Simponi, Simponi Aria) IL-12/IL-23 inhibitors: ustekinumab (Stelara) IL-17 inhibitors: secukinumab (Cosentyx), ixekizumab (Taltz) CTLA4-immunoglobulin: abatacept (Orencia) IL-23 inhibitors: guselkumab (Tremfya), risankizumab-rzaa (Skyrizi) and biosimilars (risankizumab-AbbVie, risankizumab-rzza)
Category 5[1]	**Targeted synthetic DMARDs:** JAK inhibitors: tofacitinib (Xeljanz, Xeljanz XR), upadacitinib (Rinvoq) and biosimilars (upadacitinib-AbbVie)

1. For safety objectives, Categories 4 and 5 will be combined into Category 4, indicating most severe disease, as use of JAK inhibitors (Category 5) is not indicative of more severe disease than use of Category 4 medications. For VE objectives, Categories 1 – 5 will be used as listed, as the risk of HZ is greater in those treated with JAK inhibitors compared to the risk in those treated with medications in Category 4.
2. Biologics are administered either as SC or IV. Both SC or IV forms are available for abatacept (Orencia), ustekinumab (Stelara) and golimumab (SC [Simponi] or IV [Simponi Aria]). Infliximab and biosimilars are administered as IV only. All others are administered as SC.

IM = intramuscular; IV = intravenous; PO = oral; SC = subcutaneous

Appendix 2 Definition of Clinically Relevant Flare for PsO and PsA

The definitions below will be used for chart reviews to identify medically attended PsO/PsA flares for the safety objectives (assess the rate of PsO/PsA flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods).

Flare will be defined as clinically relevant new-onset flare or new-onset disease worsening of PsO (primary safety objective 1, secondary safety objectives 2 & 3, exploratory safety objective 1) or PsA (secondary safety objective 1 & 4, exploratory safety objective 2). These definitions were selected in consultation with rheumatology and dermatology experts, recognizing that new-onset disease worsening can be difficult to differentiate from flare. Trained research associates and PsO/PsA specialists will review all potential flare events to identify a new onset or worsening of flare as meeting the criteria listed below:

1. Contact with health care provider via documented email, phone call, telehealth visit, in-person office visit, Emergency Department visit, urgent care visit, or inpatient visit

AND

2. New or worsening signs and/or symptoms suggestive of a flare (≥1 of the signs or symptoms for each condition [i.e., for PsO, A and/or C; for PsA, B and/or C]):

A. For PsO only:

1. Pain in the location of prior invovement, severe itching/sensation, patches/plaques, inflamed/red skin, soreness, skin flaking/thickening/scarring, nail involvement, skin lesions.
2. Shift to a higher Body Surface Area involvement category (mild <3%, moderate 3-10%, severe >10%)

B. For PsA only:

1. Peripheral arthritis (joint pain, swelling, tenderness or stiffness), joint damage (actively inflamed joints, joint deformities, restricted motion, ankylosis, or unstable joints), axial disease, extra-articular manifestations (enthesitis, dactylitis, tendonitis, nail disease, uveitis, iritis, or inflammatory bowel disease [Crohn's disease or ulcerative colitis]).
2. Shift to a higher visual analog score category (mild 1-3, moderate 4-6, severe 7-10)

C. For both Pso and PsA: Provider mention of flare, worsening of disease, aggravation, recurrence, relapse, deterioration, complaints, exacerbation, acute onset, sudden onset/change, change from baseline/previously controlled, or disease progression

AND

1. Change in medication for flare[1]:

   Medication regimen change/escalation algorithm for flare (applies to both PsO and PsA unless otherwise indicated)

   a. Intra-articular corticosteroid joint injection(s) (PsA only), or
   b. Initiation of systemic (oral, intramuscular, or intravenous) corticosteroid (e.g., prednisone) (PsA only), or
   c. Increase in dose of baseline systemic corticosteroid (e.g., prednisone 5 mg daily to prednisone 40 mg daily with taper) (PsA only), or
   d. Initiation of intralesional or intramuscular corticosteroid (e.g., triamcinolone) (PsO only), or
   e. Switch in MTX from oral route to subcutaneous, or
   f. Increase in dose and/or frequency of administration of any medication in current baseline regimen, or
   g. Addition of another medication to current medication regimen (e.g., adding a DMARD to current regimen of ibuprofen, adding golimumab to current regimen of MTX), or
   h. Switch of a current medication to another medication, in the same or different category (e.g., MTX + TNF-α inhibitor to MTX + tofacitinib; MTX + TNF- α inhibitor to MTX + a different TNF-α inhibitor)

[1] Exclude medication changes for any reasons other than for flare, such as acute kidney injury or other adverse effects from prior medication.

Chart review will be performed among individuals eligible for the safety analysis. Trained research associates will review medical records from health care encounters during risk windows, comparison windows, and the 30 days after a risk or comparison window (while masked to the precise window) for evidence of clinically relevant flare. They will identify new or worsening signs and/or symptoms suggestive of a flare and capture the date of onset of new or worsening signs and/or symptoms. They will determine whether a change in medication was made for flare by a provider. Cases with unclear sign and/or symptoms, date of onset, or change in medication for flare will be reviewed by a PsO or PsA specialist.

Appendix 3 Study Size for PsA cohort

Appendix Table 3.1. Sample size and average follow-up time per person (individuals with PsA aged ≥50 years)

	Average follow-up time by 12/2024 (years)	**2-dose PsA cohort**	**≥1-dose PsA cohort[3]**
2018	6.3	22	64
2019	5.5	107	160
2020/1-2020/2[1]	4.9	27	33
2021	3.5	153	166
2022 (estimated)	2.5	153	166
Average follow up time (weighted)	4.1	N/A	N/A
Total sample size[2]	N/A	462	589

N/A = not applicable; PsA = psoriatic arthritis
1. Vaccine accrual period in 2020 shortened due to impact of COVID-19 on vaccination and health care-seeking behaviors.
2. Based on Jan 2022 RZV uptake report among PsA population, with one year membership prior to index vaccination date (date of the first dose for ≥1-dose cohort or date of the second dose for 2-dose cohort).
3. The number of individuals who received at least 1 dose of RZV

Appendix Table 3.1 describes estimated RZV uptake in the PsA population as of January 2022. Based on updated estimates of uptake (as of end of 2022), we expect the sample size of eligible individuals with PsA for safety analyses to be approximately 1,150. The sample size for the vaccine effectiveness analysis will remain at 462 since this sample size is powered (α=0.05, to achieve 80% statistical power) to detect a VE of 70% if the incidence rate of HZ in the unvaccinated group is 15 per 1000 (**Table 5**).

Appendix Table 3.2. Estimated flares among PsA cohort aged ≥50 years who received ≥1 dose of RZV

Cohort	**Sample size of cohort[1]**	**Flare rate in comparison period** (per 60 days)[2]	**Number of flares in comparison period** (60 days)	**Minimally detectable IRR[3]**
PsA	1,150	1.7%	20	2.5
PsA	1,150	2.5%	29	2.5
PsA	1,150	3.3%	38	2
PsA	1,150	4.2%	49	1.8

PsA = psoriatic arthritis; IRR = incidence rate ratio
1. Estimated total sample size for ≥1-dose PsA cohort
2. Given the estimate of 10%, 15%, 20%, and 25% flare rate in one year, i.e. 1.7%, 2.5%, 3.3%, and 4.2% in 60 days of follow up, respectively. (Hsu, 2017; Leung, 2022; Orbai, 2023).
3. Comparing with **Table 6**, the number of flares in the comparison period

With approximately 1,150 individuals with PsA expected to receive ≥1 dose of RZV during the accrual period, an estimated total of 20 flares is expected to occur in the 60-day comparison period, with an estimated flare rate of 10% in one year (1.67% in 60

days). This would allow us to detect an IRR of 2.5 (incidence rate of flares in the risk period / incidence rate of flares in the comparison period) with 80% power (α=0.05).

ANNEX 1 LIST OF STAND-ALONE DOCUMENTS

None

ANNEX 2 TABLES

None

Tables are included in the Statistical Analysis Plan.

ANNEX 3 FIGURES

None

Figures are included in the Statistical Analysis Plan.

ANNEX 4 DATA COLLECTION TOOLS

None

Not applicable

ANNEX 5 LIST OF INVESTIGATORS

None

Not a multiple site study, not applicable

ANNEX 6 ENCEPP CHECKLIST

Section 1: Milestones	Yes	No	N/A	Section Number
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☒	☐	☐	2, 4, 7.2.3.
1.1.2 End of data collection[2]	☒	☐	☐	2, 4, 7.2.3.
1.1.3 Progress report(s)	☐	☐	☒	
1.1.4 Interim report(s)	☐	☐	☒	
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	Page 2
1.1.6 Final report of study results.	☒	☐	☐	2, 4

Comments:

1.1.1 and 1.1.2: This is an observational retrospective study and existing data sources will be used. 1.1.3: No formal progress reports will be written for this study. 1.1.4: No interim reports will be written for this study.

Section 2: Research question	Yes	No	N/A	Section Number
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	5
2.1.2 The objective(s) of the study?	☒	☐	☐	6
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	5, 7.2.4
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no a priori hypothesis?	☐	☐	☒	

Comments:

2.1.4 and 2.1.5: Sponsor and study site have decided to remove the hypothesis section from the protocol template (not applicable for this study design).

[1] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.

[2] Date from which the analytical dataset is completely available.

Section 3: Study design	Yes	No	N/A	Section Number
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	7.1
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	7.4
3.3 Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☒	☐	☐	7.7
3.4 Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☒	☐	☐	7.7
3.5 Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	10

Comments:

Section 4: Source and study populations	Yes	No	N/A	Section Number
4.1 Is the source population described?	☒	☐	☐	7.2.2
4.2 Is the planned study population defined in terms of:				
4.2.1 Study time period	☒	☐	☐	7.2.3
4.2.2 Age and sex	☒	☐	☐	7.2.2
4.2.3 Country of origin	☒	☐	☐	7.2.2
4.2.4 Disease/indication	☒	☐	☐	7.2.2
4.2.5 Duration of follow-up	☒	☐	☐	7.2.3
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	7.2.4

Comments:

Section 5: Exposure definition and measurement	Yes	No	N/A	Section Number
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☒	☐	☐	7.3.1, 7.3.2, 7.3.3
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☒	☐	☐	7.4, 7.9
5.3 Is exposure categorised according to time windows?	☒	☐	☐	7.3.2, 7.3.3
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	☒	☐	☐	7.3.2, 7.3.3

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.6 Is (are) (an) appropriate comparator(s) identified?	☒	☐	☐	7.3.2, 7.3.3, 7.7.2

Comments:

5.5: Biological mechanism of action is not applicable.

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	7.3.4
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	7.3.4
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☒	☐	☐	7.4, 7.9
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☐	☒	

Comments:

6.4: Health Technology Assessment is not applicable.

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☒	☐	☐	7.3.5, 7.9
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☒	☐	☐	7.9
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☒	☐	☐	7.9.2

Comments:

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☒	☐	☐	7.3.5

Comments:

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	7.4
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☒	☐	☐	7.4
9.1.3 Covariates and other characteristics?	☒	☐	☐	7.4
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	7.3.1, 7.3.2, 7.3.3
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☒	☐	☐	7.3.4
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☒	☐	☐	7.3.5
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☒	☐	☐	7.3.1
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☒	☐	☐	7.3.4
9.3.3 Covariates and other characteristics?	☒	☐	☐	7.3.5
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☒	☐	☐	7.4

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	7.7
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	7.5
10.3 Are descriptive analyses included?	☒	☐	☐	7.7
10.4 Are stratified analyses included?	☒	☐	☐	7.7
10.5 Does the plan describe methods for analytic control of confounding?	☒	☐	☐	7.7

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☐	☒	☐	
10.8 Are relevant sensitivity analyses described?	☒	☐	☐	7.7.6

Comments:

10.6: Outcome misclassification will be accounted for in non-analytic ways; it will be controlled by chart confirmation of PHN and flare outcomes as well as an algorithm for HZ detailed in Section 7.3.4 and 7.9.

10.7: Methods for handling missing data will be addressed in the Statistical Analysis Plan.

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☐	☒	☐	
11.2 Are methods of quality assurance described?	☒	☐	☐	7.6
11.3 Is there a system in place for independent review of study results?	☐	☐	☒	

Comments:

11.1 Data storage will be addressed in the Data Management Plan.

11.3: There is no independent data monitoring committee for this observational study.

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	7.9
12.1.2 Information bias?	☒	☐	☐	7.9.2
12.1.3 Residual/unmeasured confounding?	☒	☐	☐	7.3.5, 7.9
(e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).				
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	7.5

Comments:

Section 13: Ethical/data protection issues		**Yes**	**No**	**N/A**	**Section Number**
13.1	Have requirements of Ethics Committee/ Institutional Review Board been described?	☒	☐	☐	8
13.2	Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3	Have data protection requirements been described?	☒	☐	☐	8, 9

Comments:

13.2: The study has not yet been submitted to the Institutional Review Board for review.

Section 14: Amendments and deviations		**Yes**	**No**	**N/A**	**Section Number**
14.1	Does the protocol include a section to document amendments and deviations?	☒	☐	☐	3

Comments:

Section 15: Plans for communication of study results		**Yes**	**No**	**N/A**	**Section Number**
15.1	Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	11
15.2	Are plans described for disseminating study results externally, including publication?	☒	☐	☐	11

Comments:

***Note*: The Sponsor confirms his/her agreement with the completed ENCePP checklist by signing the Protocol Sponsor Signatory Approval page.**

Signature Page for 216976 TMF-16226474 v1.0

Reason for signing: Approved	Name: PPD Role: A Date of signature: 16-Jun-2023 13:14:38 GMT+0000

Reason for signing: Approved	Name: PPD Role: A Date of signature: 23-Jun-2023 10:08:30 GMT+0000

Signature Page for TMF-16226474 v1.0

EPI-ZOSTER-045 VE US, Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis

Version: 2.0

Statistical Analysis Plan

Project Name	EPI-ZOSTER-045 VE US, Non-interventional (observational) post-licensure study to assess the effectiveness and safety of recombinant zoster vaccine in adults aged ≥18 years with psoriasis or psoriatic arthritis
GSK e-Track study number and Abbreviated Title	216976 (EPI-ZOSTER-045 VE US)
Study Delivery Lead (SDL)	PPD
Research Organization	Kaiser Permanente Southern California Department of Research and Evaluation 100 S. Los Robles Ave., Pasadena, CA 91101, US Principal Investigator: Hung-Fu Tseng Co-investigators: Brad Ackerson, Jennifer Ku Lina Sy, Lei Qian, Emily Rayens, Maheen Humayun
Sponsor Organization	GlaxoSmithKline Biologicals S.A. 14200 Shady Grove Road, Rockville, MD, 20850 USA Sponsor representative: PPD Viral Vaccines Epidemiology Head
Prepared by	PPD Research Scientist Biostatistician Kaiser Permanente Southern California

Approvals

Approvers, Organization & Role Signature	Approval Status		Date
PPD KPSC Research and Evaluation Research Scientist Biostatistician			27-Aug-2025
PPD GSK PPD, Real World Analytics			27-Aug-2025
PPD GSK PPD, Epidemiology			27-Aug-2025

VERSION HISTORY

SAP Version	Approval Date	Protocol Version [Date] on which SAP is Based	Change	Rationale
SAP 1.0	09 Nov 2023	Protocol [23 June 2023]	Not Applicable	Original version
SAP 2.0	27 Aug 2025	Protocol [23 June 2023]	Updated Figure 1; Added "up to" in section 3.1.2.1 and 3.1.2.2; added history of HZ in section 3.1.3.3; updated figure 2 and associated text in section 3.2.3.1; added text in sections 4 and 4.1.4; d added VE stratified by in section 4.1.2	Fixed a typo in Figure 1; clarified VE exposed-control matching ratio in section 3.1.2.1 and 3.1.2.2; added history of HZ regardless of association with exposure and race/ethnicity if it cannot be matched in section 3.1.3.3; clarified SCCS windows in section 3.2.3.1 for safety analysis; clarified that descriptive analysis will be provided if sample sizes are small to conduct VE analyses in sections 4 and 4.1.4; added VE stratified by decade in 50+ in section 4.1.2 to align with table shells

ABBREVIATIONS

ASD	Absolute Standardized Difference
CI	Confidence Interval
CIR	Case Identification and Review
COVID-19	Coronavirus Disease 2019
DMP	Data Management Plan
ED	Emergency Department
EHR	Electronic Health Record
FDA	Food and Drug Administration
GSK	GlaxoSmithKline Biologicals SA
HR	Hazard Ratio
HZ	Herpes Zoster
IRR	Incidence rate ratio
KPSC	Kaiser Permanente Southern California
NDI	National Death Index
CCI	[redacted]
PsA	Psoriatic Arthritis
PsO	Psoriasis
QC	Quality Control
RZV	Recombinant Zoster Vaccine
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SAS	Statistical Analysis System
SCCS	Self Controlled Case Series
SCRI	Self Controlled Risk Interval
SOP	Standard Operating Procedures
Tdap	Tetanus, Diphtheria and Pertussis Vaccine
US	United States
VE	Vaccine Effectiveness
ZVL	Zoster Vaccine Live

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1 INTRODUCTION

Individuals with autoimmune disease are at higher risk of herpes zoster (HZ) compared to immunocompetent individuals. In July 2021, the Food and Drug Administration (FDA) expanded the indication for use of recombinant zoster vaccine (RZV) to include immunodeficient or immunosuppressed adults. In October 2021, the Advisory Committee on Immunization Practices (ACIP) recommended 2 doses of RZV for the prevention of herpes zoster and related complications in immunodeficient or immunosuppressed adults [Anderson, 2022]. RZV may provide a substantial benefit in preventing HZ in these populations, although more data are needed on vaccine effectiveness (VE) and safety. Through partnership between Kaiser Permanente Southern California (KPSC) and the sponsor, GlaxoSmithKline Biological SA (GSK), we will conduct an observational cohort study to assess the VE and safety of RZV in individuals aged ≥18 years with psoriasis (PsO) and psoriatic arthritis (PsA) using real-world electronic health records (EHR) data.

This Statistical Analysis Plan (SAP) provides a detailed description of the data considerations, statistical methods, data analysis and results presentation as previously proposed in the protocol and Data Management Plan (DMP), where applicable. The SAP also describes quality assurance procedures.

2 STUDY OBJECTIVES

2.1 VE

We will assess the VE among individuals with PsO or PsA who received RZV compared to individuals who did not receive RZV, addressing the objectives below.

2.1.1 Primary VE objective

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥ 18 years of age with PsO.

2.1.2 Secondary VE objectives

1. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥ 18 years of age with PsO or PsA.
2. To estimate the VE of 2 doses of RZV in preventing HZ in Southern California adults ≥ 18 years of age with PsA.
3. To estimate the VE of 1 dose of RZV in preventing HZ in Southern California adults with PsO or PsA, separately.
4. To describe baseline characteristics of individuals vaccinated with 2 doses of RZV compared to their unvaccinated matches in Southern California adults ≥18 years of age with PsO or PsA, separately.

CCI

CCI

[redacted]

2.2 Safety

We will assess the risk of flares among individuals with PsO or PsA who received at least one dose of RZV, addressing the objectives below.

2.2.1 Primary safety objective

1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsO.

2.2.2 Secondary safety objectives

1. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsO or PsA.

2. To assess the rate of flares within 30 days following RZV vaccination as compared to the rate in self-controlled comparison periods, in Southern California adults ≥18 years of age with PsA.

3 STUDY DESIGN

3.1 VE

3.1.1 Overview of VE study design

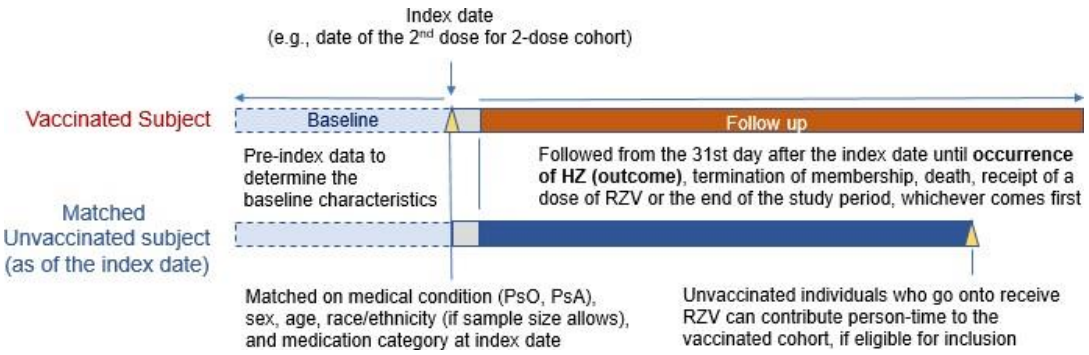
We will use an observational, matched cohort study design to assess RZV effectiveness against HZ (Figure 1). The analysis will be conducted among individuals with PsO or with PsA aged ≥18 years who are members of KPSC. RZV unvaccinated individuals will be up to 3:1 matched without replacement to RZV vaccinated individuals by age, sex, PsO or PsA condition, medication category, and race/ethnicity (if sample size allows) for comparisons of incidence of HZ between the two groups.

Approximately 2,402 eligible individuals with PsO who receive 2 doses of RZV (≥4 weeks apart) during the accrual period will be included in the analysis of the primary VE objective. The vaccine accrual period will be from 04/01/2018 to 12/31/2023 with follow-up through 12/31/2024 for HZ, and CCI [redacted] (180 days after the end of follow-up for incident HZ). The vaccine accrual period may end earlier once the target sample size is met, particularly for adults ≥50 years, and possibly for adults 18-49 years, if the uptake in this age group increases substantially upon implementation of alerts in the KPSC EHR. We will construct 2-dose RZV cohorts and 1-dose RZV cohorts, separately by PsO and PsA conditions to address different study objectives.

Individuals will be followed from the 31st day after the index date (the date of the second dose for the 2-dose cohort and the date of the first dose for the 1-dose cohort) until the end of study follow-up, occurrence of outcome of interest, or occurrence of a censoring event (death, termination of KPSC membership, or receipt of a dose of zoster vaccine), whichever comes first.

Due to the coronavirus disease 2019 (COVID-19) pandemic, vaccinated individuals with an index date from March 1, 2020 through December 31, 2020 will not be included in the study. Their demographic and clinical baseline characteristics and incidence of HZ information will be kept for descriptive purposes only.

Figure 1 Study design for vaccine effectiveness



3.1.2 VE study population

Individuals will be eligible for the VE study cohort if the following inclusion and exclusion criteria are met. Two RZV cohorts will be constructed to address different study objectives. Each cohort including index date and follow-up period will be defined in Section 3.1.2.1 and Section 3.1.2.2.

Inclusion criteria:

- Age 18 years or older at the index date (Day 0)
- At least 1 year (365 days) continuous KPSC membership prior to index date and until 31 days after index date, allowing for a 31-day gap in membership
- Has PsO or PsA (defined in the DMP) in the year prior to and including index date (Day -365 to Day 0, inclusive)

Exclusion criteria:

- HZ diagnosed in the 6 months prior (-183 days to -1 day, inclusive) to index date
- HZ diagnosed on or within 30 days (0 to 30 days, inclusive) after the index date
- Receipt of zoster vaccine within 30 days after index date (0 to 30 days, inclusive)
- Death during 30 days after index date (0 to 30 days, inclusive)

3.1.2.1 Two-dose RZV cohort

The 2-dose RZV cohort will include eligible individuals who receive 2 doses of RZV separated by at least 4 weeks by the end of the accrual period. The index date is the vaccination date of the second RZV dose.

RZV unvaccinated individuals who meet the inclusion/exclusion criteria and are unvaccinated on the index date will be randomly selected with no replacement and up to 3:1 matched to the 2-dose RZV vaccinated individuals by age group (18-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, and 80+ years), sex, condition (PsO, PsA) and medication category at index date. Further matching will be done on race/ethnicity (White, Black, Hispanic, Asian, and Other) if 95% of exposed individuals can be fully matched to 3 unexposed individuals. The index date for the 2-dose RZV unvaccinated match will be the same as his/her matched 2-dose RZV vaccinated counterpart. In situations where the number of eligible individuals is limited, categories of matching variables may be consolidated, and the matching ratio may be reduced.

Matching for the PsO group and the PsA group will be conducted separately. Individuals with both PsO and PsA will be included in the matching for both the PsO group and the PsA group, separately, and will be prioritized to match to individuals with both conditions. Individuals with PsO or PsA only will be matched to those with PsO or PsA only. For individuals with both PsO and PsA, their most advanced medication category used for treatment of either condition will be used for matching in both cohorts. For the objective to estimate the VE of RZV among individuals with PsO or PsA, vaccinated individuals with PsO only and their matches will be added to the PsA cohort. Flow charts with

inclusion/exclusion criteria applied for the 2-dose RZV cohort with PsO and the 2-dose RZV cohort with PsA will be provided. See Appendix A: Figure 1 and Figure 2.

Individuals will be followed from the 31st day after the index date until the end of study follow-up, occurrence of a censoring event (i.e., death, termination of KPSC membership, receipt of a dose of zoster vaccine among the RZV unvaccinated individuals), or occurrence of event of interest (for event-specific analyses), whichever comes first. Due to the nature of this real-world observational study, it is possible for a vaccinated individual to receive an additional dose of zoster vaccine during follow-up. Follow-up will end upon receipt of the additional dose of zoster vaccine if this is the case.

3.1.2.2 One-dose RZV cohort

The 1-dose RZV cohort will include eligible individuals who receive 1 dose of RZV but do not receive a 2nd dose within 6 months after the 1st dose during the vaccine accrual period. Such individuals may go on to receive a second RZV dose more than 6 months after the first RZV dose or no subsequent RZV doses by the end of the accrual period. The index date is the vaccination date of the first dose of RZV.

RZV unvaccinated individuals who meet the inclusion/exclusion criteria and are unvaccinated on the index date will be randomly selected with no replacement and up to 3:1 matched to the 1-dose RZV vaccinated individuals using the same matching algorithm described in Section 3.1.2.1. An unvaccinated individual is allowed to be matched to both a vaccinated individual in the 2-dose RZV cohort and a vaccinated individual in the 1-dose RZV cohort. The index date for the 1-dose RZV unvaccinated match will be the same as his/her matched 1-dose RZV vaccinated counterpart. Flow charts with inclusion/exclusion criteria applied for the 1-dose RZV cohort with PsO and the 1-dose RZV cohort with PsA will be provided. See Appendix A: Figure 3 and Figure 4.

Individuals will be followed from the 31st day after the index date until the end of study follow-up, occurrence of a censoring event (i.e., death, termination of KPSC membership, receipt of a dose of zoster vaccine among the RZV unvaccinated individuals, receipt of an additional dose of zoster vaccine among the RZV vaccinated individuals), or occurrence of event of interest (for event-specific analyses), whichever comes first. Unvaccinated individuals will stop contributing person-time upon their matched vaccinated individuals' receipt of the second RZV dose.

3.1.3 Exposures, outcomes, and covariates

3.1.3.1 Exposures

RZV vaccination will be received as part of routine clinical care. We will identify RZV exposure (CVX=187) from the EHR, which is available and accessible in real-time, providing the ability to view vaccine details and collect patient immunization history at the point of care. We are able to determine the dose sequence based on the vaccination dates.

- The exposure for primary VE objective 1, secondary VE objectives 1, 2, and 4, and CCI is receipt of 2 doses of RZV, with the second dose received ≥4 weeks (28 days) after the first dose
- The exposure for secondary VE objective 3 is receipt of 1 dose of RZV

The exposure for primary VE objective 1 and secondary VE objective 2 will also be considered by timing of the second dose of RZV received 4 weeks to 6 months (28 to 183 days, inclusive) or >6 months (183 days) after the first dose.

3.1.3.2 Outcomes

The outcomes for specific VE objectives are listed below in. Table 1. The algorithms for identification of outcomes are described in the DMP and the Case Identification and Review (CIR) Plan. HZ, CCI CG will be identified by automated EHR search algorithms. CCI CCI

Table 1 List of outcomes of interest for VE analyses

Outcome	Objectives	Cohorts	Chart Review
HZ	Primary VE objective 1 Secondary VE objectives 1, 2, 3	2-dose RZV cohort with PsO 2-dose RZV cohort with PsA 1-dose RZV cohort with PsO 1-dose RZV cohort with PsA 2-dose RZV cohort with PsO or PsA	No chart review
CCI			

All outcomes are dichotomous. Analyses of outcomes will be based on automated cases or chart confirmed cases if chart review is required.

3.1.3.3 Covariates

Covariates (Table 2) to be collected and explored include demographic variables, health care utilization, comorbidities, immunocompromised status, and other relevant baseline characteristics. The algorithms for identification of medication category, comorbidities, and immunocompromised status are described in the DMP. All covariates will be treated as categorical in the multivariable analyses to avoid bias due to outliers and non-linear effects.

Table 2 List of covariates for VE analyses

Demographics (matching variables)
Age at index date, years (18-29/30-39/40-49/50-59/60-69/70-79/80+)
Sex (Female/Male)
Race/Ethnicity (White/Black/Hispanic/Asian/Other)
Conditions and severity (matching variables)
Condition (PsO, PsA, PsO+PsA)
Medication category (Category 1/2/3/4/5)
Health care utilization
Number of outpatient/virtual visits (0-4/5-10/11+)
Number of Emergency Department (ED) visits (0/1/2+)
Number of hospitalizations (0/1/2+)
Comorbidities
Kidney disease (Yes/No)
Heart disease (Yes/No)
Lung disease (Yes/No)
Liver disease (Yes/No)
Diabetes (Yes/No)
Other autoimmune diseases (Yes/No)
SARS-CoV-2 infection/COVID-19 diagnosis (Yes/No)
Immunocompromised
Immunocompromised status (Yes/No)
Vaccine
History of zoster vaccine live (ZVL) or varicella vaccination (No/Yes; Yes: ≤5 years, >5 years)
Concomitant vaccinations (Yes/No)
Other covariates
History of HZ (Yes/No)
Length of continuous membership prior to index date, years (≤5/6-10/11+)
Time between first and second RZV doses (4 weeks -6 months/>6 months)

The "Other" category of the race/ethnicity variable includes race/ethnicity other than White, Black, Hispanic, and Asian; multiple race; and unknown race/ethnicity. White/Black/Asian means non-Hispanic White, non-Hispanic Black, and non-Hispanic Asian, respectively.

Medication category will be assessed at the index date, as a surrogate of severity of PsO or PsA condition.

Health care utilization will be defined as number of outpatient/virtual, ED, and inpatient visits in the one year (-1 to -356 days, inclusive) prior to the index date.

Baseline comorbidities will be defined in the one year prior to the index date.

Immunocompromised status will be assessed at the index date.

ZVL and varicella vaccination history will be ascertained using all available records of vaccination prior to the index date.

Concomitant vaccinations will be defined as receipt of vaccines such as influenza vaccine, pneumococcal vaccine, Tdap vaccine, or COVID-19 vaccine at the time (same date) of either the first or the second dose of RZV. Concomitant vaccinations only apply to vaccinated individuals.

History of HZ will be ascertained using all available diagnosis records prior to the index date. Since individuals with HZ 6 months prior to index date will be excluded, the actual lookback window for a history of HZ events is any time on or prior to -184 days from the index date.

Since history of ZVL/varicella vaccination and HZ will be ascertained using all available records prior to the index date, and since eligible individuals are required to only have one year of KPSC membership prior to the index date, we will also capture length of continuous membership prior to the index date as a covariate.

Time between first and second doses only applies to the 2-dose RZV cohort vaccinated individuals.

The covariates included in adjusted analyses will be determined by scientific relevance, association with exposure, and data availability. Specifically, we will select covariates by following these steps:

1. The distribution of covariates will be reviewed. Some categories of a categorical variable with small sample sizes will likely be redefined or combined into one category.
2. The association of baseline covariates with exposure will be assessed. We will use standardized difference to assess the balance of covariates between exposed and unexposed cohorts. Unlike p-values, for which magnitude is highly related to sample size, standardized difference is a unified approach to quantifying the magnitude of difference between groups regardless of sample size, where an absolute value less than 0.1 is considered a negligible difference [Austin, 2011]. We will use a SAS macro %stddiff developed by Yang and Dalton [Yang, 2012] to calculate the standardized differences for continuous and categorical variables. A categorical variable with multiple categories will be assessed and selected as one variable. Potential confounders will be determined by absolute standardized difference (ASD) >0.1.
3. All potential confounders (identified from step 2) will be included in the analyses. Step 1 and 2 will be repeated for each 2-dose RZV cohort with PsO and PsA and for each 1-dose RZV cohort with PsO and PsA. Immunocompromised status and history of HZ, which is considered an important risk factor, will be kept in the adjusted model

regardless of its association with exposure. If matching on race/ethnicity cannot be performed, it will be included in the adjusted model.

3.1.4 Sample size and power estimation

We computed the sample size needed to assess RZV effectiveness against HZ for the primary VE objectives. The calculation was conducted using a two-sided log rank test with alpha=0.05, to achieve 80% statistical power, assuming a range of HZ incidence rates in the RZV unvaccinated group (10, 12, 15, 18 per 1000 person-years) [Yun, 2016], a detectable hazard ratio (HR) of 0.1 to 0.4 (VE of 60% to 90%)[Dagnew, 2021; Izurieta, 2021], a 1:3 ratio of RZV vaccinated to RZV unvaccinated, and a censoring rate of 7% per year in the RZV vaccinated group (due to termination of membership, death, or receipt of an additional dose of zoster vaccine) and 25% or 30% per year in the RZV unvaccinated group (due to termination of membership, death, or receipt of zoster vaccine). The calculation was performed using SAS software package (version 9.3) PROC POWER procedure.

Table 3 below presents the sample size required to detect various HRs given different senarios of HZ incidence rates and censoring rates. It shows that in a cohort study with a 1:3 matching ratio and an average 4.1 years of follow-up, the number of vaccinated subjects needed to detect a VE of 60%, 70%, 80%, and 90% with 80% power and a type 1 error rate of 5% is 624, 438, 320, and 241, respectively, assuming the incidence of HZ in the unvaccinated population is 12/1000 person-years and the censoring rate per year in the RZV unvaccinated group is 25%.

We expect to include 2,402 individuals with PsO who will receive 2 doses of RZV (≥4 weeks apart) during the accrual period for the analysis of primary objective, substantially exceeding the required numbers illustrated in Table 3. This demonstrates that the study is sufficiently powered to assess the primary VE objectives.

The power for analyses of secondary or CCI [redacted] VE objectives could vary and may not reach 80% depending on available sample size.

Table 3 VE sample size required to achieve 80% power, given alpha=0.05, and different detectable HR (or VE)

Average length of follow-up (years)	Incidence rate in RZV unvaccinated group[1] (cases/1000 person-years)	HR[2]	VE (%)	Sample size of RZV vaccinated group with censoring rate of 25% per year in RZV unvaccinated group	Sample size of RZV vaccinated group with censoring rate of 30% per year in RZV unvaccinated group
	10	0.1	90	289	294
		0.2	80	384	392
		0.3	70	526	539
		0.4	60	748	770
	12	0.1	90	241	245
		0.2	80	320	327
		0.3	70	438	449
		0.4	60	624	642

Average length of follow-up (years)	Incidence rate in RZV unvaccinated group[1] (cases/1000 person-years)	HR[2]	VE (%)	Sample size of RZV vaccinated group with censoring rate of 25% per year in RZV unvaccinated group	Sample size of RZV vaccinated group with censoring rate of 30% per year in RZV unvaccinated group
4.1	15	0.1	90	193	196
		0.2	80	256	262
		0.3	70	351	360
		0.4	60	500	515
	18	0.1	90	161	163
		0.2	80	214	218
		0.3	70	293	300
		0.4	60	417	430

HR = Hazard ratio; VE = Vaccine effectiveness; RZV = Recombinant zoster vaccine; % = Percentage
1. Yun, 2016
2. Dagnew, 2021; Izurieta, 2021

3.2 Safety

3.2.1 Overview of safety study design

We will conduct a self-controlled case series (SCCS) analysis to assess the risk of flares following RZV vaccination. The SCCS method was developed to investigate associations between acute outcomes and transient exposures; it is self-controlled, so all fixed (or near time-fixed) confounders are automatically controlled for [Farrington, 1995; Whitaker, 2006].

The study will be conducted among individuals aged ≥18 years with PsO or PsA who are members of KPSC and receive at least one dose of RZV. The observation time will be partitioned into a 30-day risk window right after each RZV dose, a 30-day pre-vaccination comparison window, and a 30-day post-vaccination comparison window. There will be a washout period right before the date of vaccination. Flares from the washout window will not be counted. An individual could have multiple risk windows and comparison windows. Multiple flares per individual are allowed. The incidence of flare in the risk window will be compared with that in the comparison window.

Approximately 3,060 eligible individuals with PsO who receive their first dose of RZV during the accrual period will be included in the analysis of primary safety objective. The vaccine accrual period will be from 04/01/2018 to 12/31/2023. The vaccine accrual period may end earlier once the target sample size is met, particularly for adults ≥50 years, and possibly for adults 18-49 years, if the uptake in this age group increases substantially upon implementation of alerts in the KPSC EHR. Due to the COVID-19 pandemic, vaccinated individuals with an index date (the date of the first dose) from March 1, 2020 through December 31, 2020 will not be included in the study.

3.2.2 Safety study population

Individuals who received at least 1 dose of RZV will be eligible for the safety cohort if the following inclusion and exclusion criteria are met. The index date is the vaccination date of the first RZV dose.

Inclusion criteria:

- Receipt of the first RZV dose during the accrual period
- Age ≥18 years at the index date (Day 0)
- 1-year continuous KPSC membership prior to and including index date (Day -365 to Day 0, inclusive), allowing for a 31-day gap in membership
- PsO or PsA (defined in the DMP) in the year prior to and including index date (Day -365 to Day 0, inclusive)

Exclusion criteria:

- Receipt of a second RZV dose less than 4 weeks after the first RZV dose (date of second dose < date of first dose + 28 days)

Flow charts with inclusion/exclusion criteria applied for RZV recipients with PsO and RZV recipients with PsA will be provided (see Appendix B: Figure 1 and Figure 2). Individuals with both PsO and PsA will be included in both the PsO group and the PsA group.

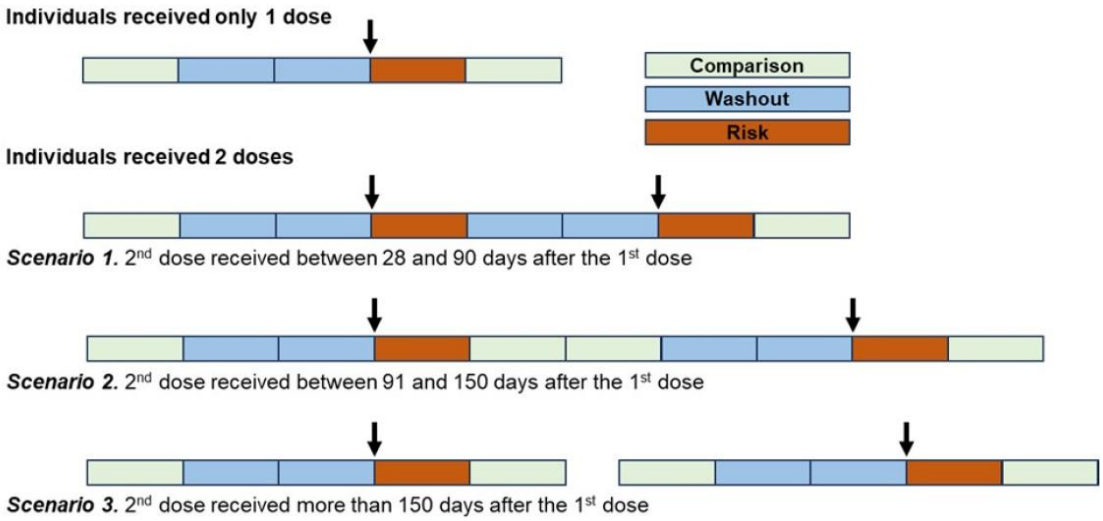
3.2.3 Exposures, outcomes, and other variables

3.2.3.1 Exposures

In the SCCS design, the observation time of a vaccinated individual is partitioned into risk (exposed) windows and comparison (unexposed) windows. The risk window is defined as the 30-day period right after each RZV dose. The comparison window is defined as two 30-day periods, one 90 to 61 days before the vaccination and one right after the risk window. We also build a washout window which is defined as the 60-day period prior to each RZV dose. Outcomes from the washout window will not be counted.

Figure 2 illustrates the risk windows, comparison windows, and washout windows under different scenarios. For example, for patients receiving only 1 dose of RZV, the date of vaccination with the first dose of RZV will be defined as Day 0, the risk window will be defined as +1 to +30 days, and comparison windows will be defined as -90 to -61 days and +31 to +60 days. For individuals receiving a second dose of RZV within 300 days of the first RZV dose, additional risk and comparison windows depend on the time interval between the two doses (Scenarios 1-3). The details of the algorithm are described in the DMP. Scenerios 1-3 in Figure 2 represent the maximum time period between the first and second dose.

Figure 2 SCCS design overview for safety analysis



The risk and comparison windows will be censored at death, termination of KPSC membership (allowing for a 31-day gap in membership), or a third dose of RZV vaccination, whichever comes first.

3.2.3.2 Outcomes

The outcomes for specific safety objectives are listed below in Table 4. The algorithms for identification of PsO flare and PsA flare are described in the DMP and the CIR Plan. Flare will be identified by targeted chart review. Flares will be counted in the window (risk or comparison) in which flare onset occurs. Outcomes in each window are counts. Multiple flares per individual is possible.

Table 4 List of outcomes of interest for safety analyses

Outcome	Objectives	Cohort	Chart Review
PsO flare	Primary safety objective 1	RZV vaccinated cohort with PsO	Chart review
PsO or PsA flare	Secondary safety objective 1	RZV vaccinated cohort with PsO or PsA	Chart review
PsA flare	Secondary safety objective 2	RZV vaccinated cohort with PsA	Chart review

3.2.3.3 Other variables

Other variables (Table 5) to be collected include demographic variables, conditions, medication category, and concomitant vaccinations for descriptive purposes. The algorithms for identification of medication category are described in the DMP. No covariates are planned for adjusted analysis except calendar month, as the SCCS design

inherently controls for fixed individual-level confounders. With comparison periods before and after the risk period, the design also controls for time-varying covariates such as age and seasonality.

Table 5 List of variables for safety analyses

Demographics
Age at index date, years (18-49/50-59/60-69/70-79/80+)
Sex (Female/Male)
Race/Ethnicity (White/Black/Hispanic/Asian/Other)
Conditions and severity
Condition (PsO, PsA, PsO+PsA)
Medication category (Category 1/2/3/4/5)
Vaccine
Number of RZV doses (one dose/two doses)
Concomitant vaccinations (Yes/No)
Month of the index dose (January, February…)

3.2.4 Sample size and power estimation

The sample size calculation for the SCCS design is based on the signed root likelihood ratio method [Musonda, 2006]. Given a 30-day risk window and a total 60-day (pre + post) comparison window, the ratio (k) of the length of comparison window vs. length of risk window is 2. The number of flares that need to be observed in the risk window and comparison window to achieve 80% power is shown in Table 6 for different values of detectable incidence rate ratio (IRR). Our SCCS design requires at least 115 events in the comparison window to achieve 80% power of detecting an increased risk of flare of IRR=1.5 with a type 1 error rate of 5%.

The calculations are based on the first RZV dose only which gives the most conservative power estimation. The design can be extended to include second RZV dose exposure. The total length of the risk windows and comparison windows will depend on the timing of receipt of the second dose.

Table 6 Safety sample size required to achieve 80% power, given alpha=0.05, k=2 and different detectable IRR (chart-confirmed flare)

k	IRR	Number of events in the risk period[1]	Number of events in the comparison period[2]
2	1.2	386	643
2	1.5	87	115
2	1.8	45	49
2	2	34	34
2	2.5	21	17
2	3	16	10

IRR = incidence rate ratio
1. Number of events in the risk period = Total number of events / [1/IRR x (length of comparison period/length of risk period) +1]
2. Number of events in the comparison period = Total number of events - Number of events in the risk period

We expect to include 3,060 individuals with PsO who receive at least one dose of RZV during the accrual period for the analysis of the primary objective. With 3,060 individuals with PsO, there will be 52 flares in the 60-day comparison period, assuming the flare rate of 10% in one year (1.67% in 60 days). This would allow us to detect an an IRR of 1.8 (incidence rate of flares in the risk period / incidence rate of flares in the comparison period) with 80% power and 5% type 1 error rate (Table7).

Table 7 Estimated flares and detectable RR for safety among PsO patients who receive at least one dose of RZV

Cohort	Sample size of cohort	Flare rate in comparison period[1] (per 60 days)	Number of flares in comparison period (60 days)	Minimally detectable IRR[2]
PsO	3,060	0.8%	25	2.5
PsO	3,060	1.7%	52	1.8
PsO	3,060	2.5%	77	1.8
PsO	3,060	3.3%	101	1.8
PsO	3,060	4.2%	129	1.5

PsO = psoriasis; IRR = incidence rate ratio
1. Given the estimate of 5%, 10%, 15%, 20%, and 25% flare rate in one year, i.e. 0.8%, 1.7%, 2.5%, 3.3%, and 4.2% in 60 days of follow up, respectively. (Gregoire, 2021; Hsu, 2017; Leung, 2022)

The power for analyses of secondary or CCI [redacted] safety objectives could vary and may not reach 80% depending on available sample size.

4 ANALYSES OF OBJECTIVES

Only descriptive analyses will be performed if the sample size is too small to produce meaningful results for any study objective.

4.1 VE

All analyses will be performed by statisticians at KPSC using the SAS statistical software package (version 9.4 or later).

4.1.1 Description of VE study population

Baseline characteristics of the 2-dose RZV cohort with PsO will be described and compared between the vaccinated and unvaccinated groups. See Appendix A: Table Shell 1 for details. Bivariate analyses will be conducted for all covariates listed in Section 3.1.3.3. Continuous covariates such as age in years will be summarized by mean, standard deviation, median, quartiles, and range, and compared using t-test or Wilcoxon rank-sum test, as appropriate; categorical covariates will be summarized by frequency and percentage and compared using chi-square test or Fisher's exact test, as appropriate. Absolute standardized difference will be calculated to assess the balance of covariates. Potential confounders will be determined based on bivariate analyses (based on ASD>0.1) and scientific relevance (see Section 3.1.3.3.)

Similar descriptive analyses will be conducted for the 2-dose RZV cohort with PsA. See Appendix A: Table Shell 2 for details.

Similar descriptive analyses will be conducted for the 1-dose RZV cohort with PsO and with PsA. See Appendix A: Table Shells 3 and 4 for details.

4.1.2 Analyses of primary VE objective

Analyses will be conducted to address primary VE objective 1 described in Section 2.1.1.

The analysis will be conducted among the 2-dose RZV cohort with PsO who receive the 2nd dose at least 4 weeks after the first dose. The incidence of HZ for the 2-dose (≥4 weeks) RZV cohort and matched unvaccinated cohort will be calculated by dividing the number of incident HZ cases by the total number of person-years. The 95% confidence interval (CI) will be calculated using SAS Proc GENMOD assuming the incident HZ cases follow a Poisson distribution. The person-years for an individual in the 2-dose RZV cohort will be the time from the 31st day after the index date to the date of event of interest, death, disenrollment, end of follow-up, or receipt of a dose of RZV, whichever comes first. The date of the incident HZ case is the diagnosis date of the first eligible HZ diagnosis after the index date.

The cumulative incidence of HZ will be estimated by the Kaplan–Meier method using SAS Proc LIFETEST. Vaccinated and the unvaccinated cumulative incidence estimates will be plotted and the difference between two curves will be tested by the log-rank test. See

Appendix A, Figure 5. We will visually evaluate the proportional hazards assumption, looking for parallel cumulative incidence curves without any crossover or use an appropriate test (e.g., testing interactions of the exposure and survival time, a lack of interaction defined as P>0.05 to support the assumption) if cumulative incidence curves cross.

Unadjusted and adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) comparing HZ incidence rates in the 2-dose RZV vaccinated cohort and the matched unvaccinated cohort will be estimated by Cox stratified proportional hazards regression models without and with adjustment for potential confounders. The estimates can be obtained from the SAS Proc PHREG with stratification on the matched sets (`STRATA match_id`) [Cummings, 2004]. Death will be considered a competing risk. We will use cause-specific hazards models [Prentice, 1978; So, 2014] in which the competing events are treated as censored observations. Unadjusted VE and adjusted VE (%) will be calculated as (1 –HR) × 100 when the HR is less than or equal to 1, and ([1/HR] – 1) × 100 when the hazard ratio is greater than 1. The results will be summarized in Appendix A: Table Shell 5.

Analyses for primary VE objective 1 will also be stratified separately by time between first and second dose of RZV (4 weeks to 6 months, >6 months), by age (18-49 years, ≥50 years, 50-59 years, 60-69 years, and 70+ years), and by medication category at baseline. Analysis will be conducted separately in each stratum rather than modelling the stratification/interaction term directly in the Cox model. For each stratum, we will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, and unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the overall analysis. Matched sets will be maintained in the analysis of each stratum. Strata (e.g., medication categories) with small sample sizes may be combined into one stratum to produce meaningful estimates. The results will be summarized in Appendix A: Table Shell 5.

The incidence of HZ by follow-up year after vaccination (index date) will be calculated by dividing the number of incident HZ cases occurring within that year by the number of person-years of follow-up for individuals in that year. VE (%) by follow-up year after vaccination will be estimated as (1 – HR) × 100 or ([1/HR] – 1) × 100, using data from the vaccinated and unvaccinated cohorts at risk for HZ at the start of each year following vaccination. Specifically, time-varying Cox regression models which model the risk of HZ by time interval of year will be used to estimate the unadjusted HRs and adjusted HRs and 95% CIs for each follow-up year. The results will be summarized in Appendix A: Table Shell 5. The VEs and 95% CIs by follow-up year will also be plotted as Appendix A: Figure 7.

4.1.3 Analyses of secondary VE objectives

Analyses will be conducted to address the secondary VE objectives described in Section 2.1.2.

4.1.3.1 Secondary VE objective 1

The analysis will be conducted among the 2-dose (≥4 weeks) RZV cohort with PsO or PsA. To combine PsO and PsA cohorts, we will add vaccinated individuals with PsO only and their matches to the PsA cohort. We will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, and unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the analysis of primary VE objective 1. The results will be summarized in Appendix A: Table Shell 7.

4.1.3.2 Secondary VE objective 2

The analysis will be conducted among the 2-dose (≥4 weeks) RZV cohort with PsA, overall and stratified by time between first and second dose of RZV (4 weeks to 6 months, >6 months), by age (18-49 years, ≥50 years), and by medication category at baseline. For analysis overall and for each stratum, we will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, and unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the analysis of primary VE objective 1. Matched sets will be maintained in the analysis of each stratum. Strata (e.g., medication categories) with small sample sizes may be combined into one stratum to produce meaningful estimates. Descriptive analyses only will be performed for the 18-49-year age group, if the sample size in the subgroup is too small to produce meaningful results. The results will be summarized in Appendix A: Table Shell 6.

The cumulative incidence of HZ will be estimated by the Kaplan–Meier method using SAS Proc LIFETEST. Vaccinated and the unvaccinated cumulative incidence estimates will be plotted and the difference between two curves will be tested by the log-rank test. See Appendix A, Figure 6.

4.1.3.3 Secondary VE objective 3

The analysis will be conducted among the 1-dose RZV cohort with PsO or PsA, separately. For the 1-dose PsO cohort, we will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, unadjusted and adjusted VEs and 95% CIs for preventing HZ, HZ incidence by follow-up year, and HRs and VEs and 95% CIs by follow-up year using methods similar to the analysis of primary VE objective 1. See Appendix A: Table Shell 8 for details. For the 1-dose PsA cohort, we will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the analysis of primary VE objective 1. See Appendix A: Table Shell 9 for details.

4.1.3.4 Secondary VE objective 4

The analysis will be conducted among the 2-dose (≥4 weeks) RZV cohort with PsO or PsA, separately. See Section 4.1.1 description of VE study population.

CCI [redacted]

CCI [redacted]

CCI

[redacted]

4.1.5 Additional analysis

Sensitivity analysis will be conducted among the 2-dose RZV cohort with PsO, but without PsA. We will calculate HZ incidence, unadjusted and adjusted HRs and 95% CIs, unadjusted and adjusted VEs and 95% CIs for preventing HZ using methods similar to the analysis of primary VE objective 1. See Appendix A: Table Shell 7 for details.

For 2-dose vaccinated individuals with an index date (the date of 2nd dose) between March 2020 and December 2020 who are not accrued for the analysis of primary VE objective 1, we will describe their demographic and clinical baseline characteristics and incidence of HZ. See Appendix A: Table Shell 14 for details.

4.2 Safety

All analyses will be performed by statisticians at KPSC using the SAS statistical software package (version 9.4 or later).

4.2.1 Description of safety study population

Baseline characteristics of RZV recipients with PsO will be described. See Appendix B: Table Shell 1 for details. Analyses will be conducted for all variables listed in. Section 3.2.3.3 Continuous variables will be summarized by mean, standard deviation, median, quartiles, and range; categorical covariates will be summarized by frequency and percentage.

Similar descriptive analyses will be conducted for RZV recipients with PsA. See Appendix B: Table Shell 2 for details.

4.2.2 Analyses of primary safety objectives

Analyses will be conducted to address the primary safety objective 1 described in Section 2.2.1.

4.2.2.1 Primary safety objective 1

Analysis will be conducted among RZV recipients with PsO. We will report number of flares occurring during pre-specified risk and comparison windows. Incidence of flare will be calculated by dividing the number of flares by person-time. To describe the secular pattern, incidence of flare by day from Day -90 to Day 60 of Dose 1 and Dose 2 will be plotted. See Appendix B: Figures 3 and 4 for details. Incidence rate ratio (IRR) and 95% CI will be estimated by comparing the incidence in the risk windows vs. the incidence in the comparison windows using conditional Poisson regression, accounting for person-time in each window. The first RZV dose and second RZV dose will be treated as repeat exposures with one risk level (assuming same risk for each exposure in the analyses) [Whitaker, 2006]. To estimate the risk of flare by first dose and second dose, we will assign two risk levels to risk windows after first dose and second dose (code risk window after first dose=1, risk window after second dose =2, and all comparison windows=0 as a categorical exposure variable). The conditional Poisson regression will be conducted using SAS macro poisreg.sas, which can be downloaded from SCCS method website (`%poisreg(data=InputData,y=flare,covar=int risk month, offset=person_year, elim=studyid)`). Only individuals with a flare occurring in a risk window or comparison window will be included. We will create a time-varying covariate month, specifically further partitioning the risk window and comparison window of each person by calendar month. Month will be included in the regression model to test and adjust for possible seasonality. Months may be combined into seasons to avoid model convergence issues. No other covariates will be adjusted for in the analysis. The results will be summarized in Appendix B: Table Shell 3.

Analyses for primary safety objective 1 will also be stratified separately by age (18-49 years, ≥50 years) and by medication category at baseline. Analysis will be conducted

separately in each stratum rather than modelling the stratification/interaction term directly in the conditional Poisson regression model. For each stratum, we will calculate flare incidence, IRR and 95% CIs using methods similar to the analysis of primary safety objective 1. If we observe zero cases in the risk window or comparison window, IRR will not be estimated. The results will be summarized in Appendix B: Table Shell 3.

4.2.3 Analyses of secondary safety objectives

Analyses will be conducted to address the secondary safety objectives described in Section 2.2.2.

4.2.3.1 Secondary safety objective 1

The analysis will be conducted among RZV recipients with PsO or PsA. We will calculate flare incidence, IRR and 95% CIs overall and by first and second dose using methods similar to the analysis of primary safety objective 1. For individuals with both PsO and PsA, either PsO flare or PsA flare will be counted as flare. See Appendix B: Table Shell 4 for details.

4.2.3.2 Secondary safety objective 2

The analysis will be conducted among RZV recipients with PsA. We will calculate flare incidence, IRR and 95% CIs overall and by first and second dose using methods similar to the analysis of primary safety objective 1. Incidence of flare by day from Day -90 to Day 60 of Dose 1 and Dose 2 will be plotted. The results will be summarized in Appendix B: Table Shell 5, Figure 5 and Figure 6. Analyses will also be stratified by age (18-49 years, ≥50 years) and by medication category at baseline. Analysis will be conducted separately in each stratum. If we observe zero cases in the risk window or comparison window, IRR will not be estimated. Descriptive analyses will be performed for the 18-49-year age group, if the sample size in the subgroup is too small to produce meaningful results. See Appendix B: Table Shell 5 for details.

4.2.4 Signal investigation

If a primary analysis detects an elevated risk, i.e., the lower limit of IRR > 1, further exploration of the data will be completed to investigate alternative potential sources for the RZV-flare association. Risk of flare by age, interval between doses, overlap of risk and comparison windows with the COVID-19 pandemic period from March 1, 2020 through December 31, 2020, concomitant vaccination, and other vaccinations within 30 days prior to risk window and during the risk and comparison windows may be explored.

The KPSC team will work together with GSK team to conduct signal investigation, with consideration of timelines and data/resource availability.

5 STATISTICAL CONSIDERATIONS AND LIMITATIONS

5.1 Statistical considerations

5.1.1 SCCS method

The SCCS method was developed to investigate associations between acute outcomes and transient exposures. It has been widely used in vaccine safety studies [Farrington, 1995; Weldeselassie, 2011; Tseng, 2017; Hechter, 2019]. By design, each individual serves as their own comparator. All time-fixed (or near time-fixed) confounding factors, known and unknown, are controlled for implicitly. Additionally, with comparison periods within close proximity to the risk period (before and after the risk period), the design also controls for time-varying covariates such as age and seasonality. Further adjustment for residual seasonal confounding can be considered in the analysis model. These features of the SCCS method make it advantageous to use this method for the safety objectives rather than using a cohort design.

The SCCS design assumes that flare events: (1) are independent and do not influence the probability of subsequent flares; (2) do not influence the probability of RZV exposure; and (3) do not cause censoring or affect the observation period. Although some individual patients may be predisposed to frequent flares, the SCCS design allows individuals to have different risk levels of flares, that is, allowing events at different time points to be conditionally independent given the individual. We also have chart review procedures in place, such as review of complex cases by specialists, to distinguish whether a flare is a new event or a continuation of a previous flare. Regarding flares influencing the probability of RZV exposure, it is possible that individuals are less likely to be vaccinated during a flare, and the incidence of flare may be lower just before vaccination (i.e., healthy vaccinee effect) (Baker, 2015). Therefore, we will exclude a 60-day time period immediately prior to vaccination from the analysis (i.e., washout period) to correct for the effect of event-dependent exposures (Whitaker, 2006). Lastly, individuals can continue to be followed after having a flare and flare is unlikely to lead to death (censoring event). Our study meets these assumptions.

The SCCS likelihood is equivalent to a product multinomial likelihood, which can be fitted directly using software for conditional Poisson models with offsets. Overdispersion in the counts data is typically generated by a random frailty (individual level incidence), i.e., events occur at different rates for different individuals. The conditional Poisson model allows for overdispersion as the individual level incidence cancels out of the likelihood upon conditioning (Armstrong, 2014).

Unlike the traditional SCCS design in which the risk window and comparison window extend over a pre-specified calendar period, we define two comparison periods within close proximity to the vaccination date and risk period to minimize bias due to time-varying covariate effects. Our approach bears certain similarities to the self-controlled risk interval (SCRI) approach (Baker, 2015; Li, 2016); however, our approach

accommodates multiple exposures and is more flexible for censoring events. Notably, the SCRI approach is often regarded as a special case of the SCCS design.

5.1.2 Multiplicity considerations

Multiplicity refers to the potential inflation of the type I error rate as a result of multiple testing, in this study, specifically due to multiple subgroup comparisons, and multiple analyses of the same outcome at different times. Adjustment for multiple comparisons would reduce the false positives due to multiple comparisons, while possibly increasing the false negatives (e.g., missing the opportunity to detect potential safety findings) due to inadequate power, especially in analyses conducted in early years and in some subgroups with small sample size. Therefore, we will focus the inference of VE and safety of RZV on the full analysis of primary objectives. No formal adjustment for multiple comparisons is planned.

5.1.3 Handling of missing data

No imputation is planned for missing data in covariates. Unknown race/ethnicity is grouped into the "Other" category by convention, which can be matched between exposed and unexposed cohorts. If race/ethnicity is included in the adjusted model, "Other" will be a category for the covariate along with the other categories. History of ZVL/varicella vaccination and HZ will be ascertained using all available EHR records prior to the index date. If a member joined KPSC more recently, we may underestimate his/her ZVL/varicella vaccination and HZ history status. We will include a variable "length of continuous membership prior to index date" as a surrogate for completeness of historical medical information. Length of membership will be included in the adjusted model if it is determined to be a potential confounder. We do not expect missing values in other covariates and outcomes.

5.1.4 Loss to follow-up

For a long-term matched cohort study, loss to follow-up could break the matched sets and possibly cause imbalance on matching variables. We will use stratified proportional hazards models to analyze matched survival data. The HR will be estimated within matched sets where the values of matching variables are the same. Shinozaki at el. showed that the approach unbiasedly estimated a common HR under the proportional hazards within matched sets, which is less sensitive to censoring patterns (Shinozaki, 2017). For SCCS analysis, we assume that loss to follow-up is not associated with occurrence of the flare. The flare is unlikely to increase short-term mortality.

5.1.5 Impact of COVID-19

On March 4, 2020, the Governor of California declared a State of Emergency following the first official COVID-19 death in the state. On March 13, 2020, the US declared a national emergency, and on March 19, 2020, a stay-at-home order was enacted in California to slow the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As a consequence, vaccination, utilization, and enrollment of KPSC members could be affected

by the COVID-19 pandemic. We observed a significant drop in adult vaccinations during the early pandemic period. We will exclude individuals who were vaccinated with index RZV dates during March 2020 to December 2020 to prevent potential selection bias. We observed a significant drop in the number of outpatient visits and an increase in the number of telephone and video encounters after March 2020. Therefore, we included virtual encounters in the HZ case identification algorithm, as described in the DMP. The impact of utilization pattern changes are expected to be similar for the RZV vaccinated and RZV unvaccinated groups. HZ outcomes will continue to be assessed during this period. By the end of 2021, we have not observed a decrease in KPSC member enrollment.

5.2 Limitations

5.2.1 Confounding by indication

Confounding by indication is a potential limitation. For the VE analyses, we will match vaccinated and unvaccinated individuals on the most important risk factors, i.e., condition (PsO, PsA), age, sex, race/ethnicity (if sample size allows), and medication category. We will adjust for differences in demographic characteristics, health care utilization, and comorbidities, but differences in other unmeasured factors could result in residual confounding. By design, we will follow matched individuals over the same calendar time (index date) to minimize bias due to secular confounding. We will allow RZV unvaccinated individuals to become vaccinated at any time during follow-up to reduce confounding by indication. For the safety analyses, the SCCS design mitigates bias through implicit control for time-fixed confounders. While the short risk window minimizes changes in confounders during follow-up, our design of using pre- and post- vaccination comparison windows can also inherently control for potential time-varying confounders.

5.2.2 Misclassification

Misclassification of individuals with PsO and PsA is possible. However, these definitions for PsO and PsA were selected based on prior knowledge/literature and KPSC chart review indicating a high positive predictive value.

Misclassification of exposure is possible. The EHR included vaccines administered within KPSC as well as vaccines from the California Immunization Registry (manually reconciled by providers), Care Everywhere (Epic EHR feature which allows health care systems to exchange medical information), claims (e.g., pharmacies), and member self-report with documentation. Although misclassification of RZV vaccination status is less likely, this could lead to a potential under-estimation of VE.

Misclassification of outcome is possible. Despite high validity of diagnostic algorithms, misclassification of HZ status could occur inherently in EHR studies using automated data, but this would only be a concern if misclassification was differential between exposure groups. It is unknown if HZ vaccination leads to modified or atypical HZ presentations that are more likely to be underdiagnosed or misdiagnosed. If these cases are never diagnosed or are diagnosed as other conditions, they will not be identified through ICD-10 codes for

HZ. This could lead to a potential over-estimation of VE. It is also possible that there is differential misclassification of HZ due to differential health care seeking behaviors, but to address this, prior health care utilization is included as a covariate.

Given the complexity and potential for misclassification of the safety outcome of disease flare, medical record review using standardized criteria will be performed to ascertain this outcome. In general, there can be a delay between symptom onset and a medical encounter for flare. To avoid missing flare events due to delayed care-seeking, medical records within 30 days after each risk or comparison window will also be reviewed.

5.2.3 Delay of death data

Member death status will be identified by death records from KPSC hospitals and EDs, membership termination information, and outside claims. Deaths outside of KPSC will also be captured from the National Death Index (NDI). There is usually a 1- to 2-year delay in receiving and processing the NDI files, so these resources will be utilized only if available. Since the study will only include active members during the follow-up period, the proportion of additional deaths identified from the NDI files beyond those identified through KPSC sources is expected to be small (< 5%).

6 QUALITY CONTROL

KPSC will follow the Department of Research and Evaluation's Analytical Research Project Standard Operating Procedures (SOP), including data extraction, data analysis, communication, and documentation. SAS programs used for the analysis will be reviewed by second statistician. Statistical analysis (results tables) will be discussed in the multisite meetings with GSK prior to study report finalization. KPSC will provide a quality control (QC) checklist of statistical analysis validation signed and dated by statisticians for analyses. A template of the QC checklist is included in Appendix C.

6.1 Quality control steps

During the analysis, when analytic data are created and analyzed, the following quality control steps will be performed by the study statisticians as appropriate:

1. Read study protocol, DMP, CIR Plan, and SAP. Communicate with the principal investigator, senior statistician, and study team with any questions regarding study design and analysis plan. Document any decisions related to statistical analysis.

2. Check data quality (sample size, duplicates, range of values, number of missings, proper data type and format, inconsistency, etc.). Any aberrant data that have been missed by data cleaning and discovered by the statistician will be described in the results table.

3. Develop SAS programs for analysis. Programs will include a program header and section headers. The program header contains information on the purpose of the program, a list of prerequisite programs if applicable, a list of input datasets with full path, a list of output datasets, and a history log if applicable. Revision of the program will be noted in the history log to capture the change made, the change date, identification of the individual making the change, and type of change (e.g., modification, addition, removal). Each program might have several sections executing various analytic steps. Programs will be annotated with comments that describe the intent or purpose.

4. Perform statistical analysis. Use appropriate procedures and tests. SAS logs and outputs will be reviewed for any warnings, error messages, and model convergence issues. Organize the output into results tables. When possible, automate the generation of results tables to minimize the need to copy/paste. Proofread the results tables to prevent any copy/paste and editing errors. SAS logs and outputs will be saved.

5. Use established SAS macros. Use established SAS macros for analyses, including but not limited to the macro for creating baseline covariate tables and the macro for calculating standardized difference.

6.2 Program review

All SAS analysis programs, logs, and outputs will be reviewed by a second statistician. The second statistician will review the program logic against the analysis requirements.

Comments from the second statistician will be documented and followed up until resolved.

6.3 Quality control findings

A record of quality problems and resolutions will be kept in the form of an Excel spreadsheet or other method appropriate to the circumstances (e.g., commented code, detailed correspondence).

6.4 Analysis deviation

Any analyses differing from the protocol, DMP, and pre-specified analyses in this SAP will be documented. The rationale for the change in approach will be provided.

7 STUDY REPORTS

7.1 Monthly vaccine uptake report

The monthly vaccine uptake report is described in the DMP. The report will be generated monthly during the accrual period.

7.2 Analysis report

The effectiveness and safety of RZV in individuals ages ≥18 years with PsO or PsA at KPSC will be examined. The vaccine accrual period for the analysis will occur from April 1, 2018 to December 31, 2023. The cohorts for VE analysis will be followed through December 31, 2024 for HZ and CCI [redacted]. All objectives will be included in the analysis results tables and report. The report will be available to GSK at the end of the study (June 2026).

8 LIST OF REPORT TABLES

Appendix A	Description
Table 1	Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsO
Table 2	Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsA
Table 3	Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsO
Table 4	Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsA
Table 5	Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsO
Table 6	Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsA
Table 7	Incidence rate, hazard ratio, and VE of 2 dose of RZV in preventing HZ among individuals with PsO or PsA, or PsO only
Table 8	Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsO
Table 9	Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsA
CCI [redacted]	
Table 14	Baseline characteristics and HZ incidence of 2-dose RZV vaccinated individuals with PsO, index date between March 2020 and December 2020 (not accrued)
Figure 1	Flow chart for 2-dose RZV cohort with PsO
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Appendix B	**Description**
Table 1	Baseline characteristics of RZV recipients with PsO
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Table 3	Incidence and incidence rate ratio of PsO flare after RZV among individuals with PsO

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Figure 1	Flow chart for RZV recipients with PsO
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Figure 3	Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsO
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Figure 5	Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsA
Figure 6	Incidence of flare by day during the risk and comparison windows of second dose among RZV recipients with PsA

9 REFERENCES

Anderson TC MN, Guo A, et al. 2022. Use of recombinant zoster vaccine in immunocompromised adults aged ≥ 19 years: Recommendations of the Advisory Committee on Immunization Practices—United States, *MMWR Morb Mortal Wkly Rep*. 2022;71:80-84.

Armstrong BG, Gasparrini A, Tobias A. Conditional Poisson models: a flexible alternative to conditional logistic case cross-over analysis. BMC Med Res Methodol. 2014 Nov 24;14:122.

Austin PC**.** An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res*. 2011;46(3):399-424.

Baker MA, Lieu TA, Li L, Hua W, Qiang Y, Kawai AT, Fireman BH, Martin DB, Nguyen MD. A vaccine study design selection framework for the postlicensure rapid immunization safety monitoring program. Am J Epidemiol. 2015 Apr 15;181(8):608-18.

Cummings, P. and McKnight, B. (2004). Analysis of Matched Cohort Data. The Stata Journal 4, 274-81.

Dagnew AF, Rausch D, Hervé C, Zahaf T, Levin MJ, Schuind A; ZOE-50/70 study group. Efficacy and serious adverse events profile of the adjuvanted recombinant zoster vaccine in adults with pre-existing potential immune-mediated diseases: a pooled post hoc analysis on two parallel randomized trials. Rheumatology (Oxford). 2021 Mar 2;60(3):1226-1233.

Farrington P, Pugh S, Colville A, Flower A, Nash J, Morgan-Capner P, Rush M, Miller E. A new method for active surveillance of adverse events from diphtheria/tetanus/pertussis and measles/mumps/rubella vaccines. *Lancet* 1995. 345(8949):567-569.

Gregoire ARF, DeRuyter BK, Stratman EJ. Psoriasis Flares Following Systemic Glucocorticoid Exposure in Patients With a History of Psoriasis. JAMA Dermatol. 2021 Feb 1;157(2):198-201.

Hechter RC, Qian L, Tartof SY, Sy LS, Klein NP, Weintraub E, Mercado C, Naleway A, McLean HQ, Jacobsen SJ. Vaccine safety in HIV-infected adults within the Vaccine Safety Datalink Project. *Vaccine*. 2019 May 31;37(25):3296-3302.

Hsu M-A, Lucas J, Wood R, Cappelleri JC, Piercy J. Frequency, Prevalence, and Burden of Flares on Patients with Moderate to Severe Psoriasis: A Retrospective Cross-Sectional Analysis. Journal of Psoriasis and Psoriatic Arthritis. 2017;2(3):64-70.

Izurieta HS, Wu X, Forshee R, Lu Y, Sung HM, Agger PE, Chillarige Y, Link-Gelles R, Lufkin B, Wernecke M, MaCurdy TE, Kelman J, Dooling K. Recombinant Zoster Vaccine (Shingrix): Real-World Effectiveness in the First 2 Years Post-Licensure. Clin Infect Dis. 2021 Sep 15;73(6):941-948.

Leung J, Anderson TC, Dooling K, Xie F, Curtis JR. Recombinant Zoster Vaccine Uptake and Risk of Flares Among Older Adults With Immune-Mediated Inflammatory Diseases in the US. Arthritis Rheumatol. 2022 Nov;74(11):1833-1841.

Li R, Stewart B, Weintraub E. Evaluating efficiency and statistical power of self-controlled case series and self-controlled risk interval designs in vaccine safety. J Biopharm Stat. 2016;26(4):686-93. doi: 10.1080/10543406.2015.1052819.

Musonda P, Farrington CP, Whitaker HJ. Sample sizes for self-controlled case series studies. *Stat Med*. 2006.25(15):2618-2631.

Prentice RL, Kalbfleisch JD, Peterson Jr. AV, Flournoy N, Farewell VT, Breslow NE: The analysis of failure times in the presence of competing risks. *Biometrics* 34: 541–554, 1978

Shinozaki T, Mansournia MA, Matsuyama Y. On hazard ratio estimators by proportional hazards models in matched-pair cohort studies. *Emerg Themes Epidemiol*. 2017;14:6.

So Y, Lin G, Johnson G: Using the PHREG procedure to analyze competing-risks data. Presented at the SAS Global Forum, Washington, DC, March 23–26, 2014.

Tseng HF, Sy LS, Ackerson BK, Hechter RC, Tartof SY, Haag M, Slezak JM, Luo Y, Fischetti CA, Takhar HS, Miao Y, Cunnington M, Solano Z, Jacobsen SJ. Safety of Quadrivalent Meningococcal Conjugate Vaccine in 11- to 21-Year-Olds. *Pediatrics*. 2017 Jan;139(1):e20162084.

Weldeselassie YG, Whitaker HJ, Farrington CP. Use of the self-controlled case-series method in vaccine safety studies: review and recommendations for best practice. *Epidemiol Infect*. 2011 Dec;139(12):1805-17.

Whitaker HJ, Farrington CP, Spiessens B, Musonda P. Tutorial in biostatistics: the self-controlled case series method. *Stat Med* 2006;25(10):1768–97.

Yang D, Dalton JE. A unified approach to measuring the effect size between two groups using SAS. SAS Global Forum, Statistics and Data Analysis. 2012;Paper 335-2012.

Yun, H., Yang, S., Chen, L., Xie, F., Winthrop, K., Baddley, J. W., . . . Curtis, J. R. (2016). Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases: Implications for Vaccination. Arthritis Rheumatol, 68(9), 2328-2337.

10 APPENDICES

Appendix A: Table shells for VE analyses

Appendix B: Table shells for safety analyses

Appendix C: Quality control checklist

Appendix A: Table shells for VE analyses

Table 1. Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsO

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
Age at index date, years					
mean (sd)					
median					
Q1, Q3					
range					
Age at index date, years, n (%)				N/A[c]	N/A
18-29					
30-39					
40-49					
50-59					
60-69					
70-79					
≥80					
Sex, n (%)				N/A	N/A
Female					
Male					
Race/Ethnicity, n (%)				N/A	N/A
White					
Black					
Hispanic					
Asian					
Other					
Medication category, n (%)				N/A	N/A
Category 1					
Category 2					
Category 3					
Category 4					
Category 5					
PsO, n (%)					
PsO only					
PsO+PsA					
Number of outpatient visits[a], n (%)					
0-4					
5-10					
≥11					

	Vaccinated	Unvaccinated	Total	p value	Absolute
	N =	N =	N =	-	Standardized Difference
Number of ED visits[a], n (%)					
0					
1					
≥2					
Number of hospitalization[a], n (%)					
0					
1					
≥2					
Baseline Comorbidities[a], n (%)					
Kidney disease					
Heart disease					
Lung disease					
Liver disease					
Diabetes					
Other autoimmune diseases					
SARS-CoV-2 infection/COVID-19 diagnosis					
Immunocompromised status at index date, n (%)					
Yes					
No					
History of ZVL/varicella vaccination[b], n (%)					
No					
Yes, ≤ 5 years					
Yes, > 5 years					
History of HZ[b], n (%)					
Yes					
No					
Length of continuous membership[b], years, n (%)					
≤5					
6-10					
≥11					
Concomitant vaccination[d], n (%)				N/A	N/A
Yes		N/A	N/A		
No		N/A	N/A		

	Vaccinated	Unvaccinated	Total	p value	Absolute
	N =	N =	N =	-	Standardized Difference
Time between first and second doses, n (%)				N/A	N/A
4 weeks - 6 months		N/A	N/A		
>6 months		N/A	N/A		

[a] Defined in the one year prior to index date

[b] Defined based on all available medical records prior to index date

[c] N/A= not applicable

[d] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%); XX% concomitant with 1st dose and XX% concomitant with 2nd dose.

Table 2. Baseline characteristics of 2-dose RZV vaccinated and unvaccinated cohort with PsA

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
Age at index date, years					
mean (sd)					
median					
Q1, Q3					
range					
Age at index date, years, n (%)				N/A[c]	N/A
18-29					
30-39					
40-49					
50-59					
60-69					
70-79					
≥80					
Sex, n (%)				N/A	N/A
Female					
Male					
Race/Ethnicity, n (%)				N/A	N/A
White					
Black					
Hispanic					
Asian					
Other					
Medication category, n (%)				N/A	N/A
Category 1					
Category 2					
Category 3					
Category 4					
Category 5					
PsA, n (%)					
PsA only					
PsA+PsO					
Number of outpatient visits[a], n (%)					
0-4					
5-10					
≥11					
Number of ED visits[a], n (%)					

	Vaccinated	Unvaccinated	Total	p value	Absolute
	N =	N =	N =	-	Standardized Difference
0					
1					
≥2					
Number of hospitalization[a], n (%)					
0					
1					
≥2					
Baseline Comorbidities[a], n (%)					
Kidney disease					
Heart disease					
Lung disease					
Liver disease					
Diabetes					
Other autoimmune diseases					
SARS-CoV-2 infection/COVID-19 diagnosis					
Immunocompromised status at index date, n (%)					
Yes					
No					
History of ZVL/varicella vaccination[b], n (%)					
No					
Yes, ≤ 5 years					
Yes, > 5 years					
History of HZ[b], n (%)					
Yes					
No					
Length of continuous membership[b], years, n (%)					
≤5					
6-10					
≥11					
Concomitant vaccination[d], n (%)				N/A	N/A
Yes		N/A	N/A		
No		N/A	N/A		
Time between first and second doses, n (%)				N/A	N/A
4 weeks - 6 months		N/A	N/A		
>6 months		N/A	N/A		

[a] Defined in the one year prior to index date

	Vaccinated	Unvaccinated	Total	p value	Absolute
	N =	N =	N =	-	Standardized Difference

[b] Defined based on all available medical records prior to index date

[c] N/A= not applicable

[d] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%); XX% concomitant with 1st dose and XX% concomitant with 2nd dose.

Table 3. Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsO

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
Age at index date, years					
mean (sd)					
median					
Q1, Q3					
range					
Age at index date, years, n (%)				N/A[c]	N/A
18-29					
30-39					
40-49					
50-59					
60-69					
70-79					
≥80					
Sex, n (%)				N/A	N/A
Female					
Male					
Race/Ethnicity, n (%)				N/A	N/A
White					
Black					
Hispanic					
Asian					
Other					
Medication category, n (%)				N/A	N/A
Category 1					
Category 2					
Category 3					
Category 4					
Category 5					
PsO, n (%)					
PsO only					
PsO+PsA					
Number of outpatient visits[a], n (%)					
0-4					
5-10					
≥11					
Number of ED visits[a], n (%)					
0					
1					

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
≥2					
Number of hospitalization[a], n (%)					
0					
1					
≥2					
Baseline Comorbidities[a], n (%)					
Kidney disease					
Heart disease					
Lung disease					
Liver disease					
Diabetes					
Other autoimmune diseases					
SARS-CoV-2 infection/COVID-19 diagnosis					
Immunocompromised status at index date, n (%)					
Yes					
No					
History of ZVL/varicella vaccination[b], n (%)					
No					
Yes, ≤ 5 years					
Yes, > 5 years					
History of HZ[b], n (%)					
Yes					
No					
Length of continuous membership[b], years, n (%)					
≤5					
6-10					
≥11					
Concomitant vaccination[d], n (%)				N/A	N/A
Yes		N/A	N/A		
No		N/A	N/A		

[a] Defined in the one year prior to index date

[b] Defined based on all available medical records prior to index date

[c] N/A= not applicable

[d] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%)

Table 4. Baseline characteristics of 1-dose RZV vaccinated and unvaccinated cohort with PsA

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
Age at index date, years					
mean (sd)					
median					
Q1, Q3					
range					
Age at index date, years, n (%)				N/A[c]	N/A
18-29					
30-39					
40-49					
50-59					
60-69					
70-79					
≥80					
Sex, n (%)				N/A	N/A
Female					
Male					
Race/Ethnicity, n (%)				N/A	N/A
White					
Black					
Hispanic					
Asian					
Other					
Medication category, n (%)				N/A	N/A
Category 1					
Category 2					
Category 3					
Category 4					
Category 5					
PsA, n (%)					
PsA only					
PsA+PsO					
Number of outpatient visits[a], n (%)					
0-4					
5-10					
≥11					
Number of ED visits[a], n (%)					
0					
1					

	Vaccinated N =	Unvaccinated N =	Total N =	p value -	Absolute Standardized Difference
≥2					
Number of hospitalization[a], n (%)					
0					
1					
≥2					
Baseline Comorbidities[a], n (%)					
Kidney disease					
Heart disease					
Lung disease					
Liver disease					
Diabetes					
Other autoimmune diseases					
SARS-CoV-2 infection/COVID-19 diagnosis					
Immunocompromised status at index date, n (%)					
Yes					
No					
History of ZVL/varicella vaccination[b], n (%)					
No					
Yes, ≤ 5 years					
Yes, > 5 years					
History of HZ[b], n (%)					
Yes					
No					
Length of continuous membership[b], years, n (%)					
≤5					
6-10					
≥11					
Concomitant vaccination[d], n (%)				N/A	N/A
Yes		N/A	N/A		
No		N/A	N/A		

[a] Defined in the one year prior to index date

[b] Defined based on all available medical records prior to index date

[c] N/A= not applicable

[d] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%)

Table 5. Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsO

HZ	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Overall												
Time between first and second doses												
4 weeks to 6 months												
>6 months												
Age at index date, years												
18-49												
≥50												
50-59												
60-69												
≥70												
Medication category												
Category 1												
Category 2												
Category 3												
Category 4												
Category 5												
Year after index date												
0-<1												
1-<2												
2-<3												
3-<4												
…												

HZ	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]

[a] Adjusted for covariates XXX (place holder)

Table 6. Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsA

HZ	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	N	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Overall												
Time between first and second doses												
4 weeks to 6 months												
>6 months												
Age at index date, years												
18-49												
≥50												
Medication category												
Category 1												
Category 2												
Category 3												
Category 4												
Category 5												

[a] Adjusted for covariates XXX (place holder)

Table 7. Incidence rate, hazard ratio, and VE of 2 doses of RZV in preventing HZ among individuals with PsO or PsA, or PsO only

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**Unadjusted**	**Adjusted[a]**	**Unadjusted**	**Adjusted[a]**
Among individuals with PsO or PsA												
Among individuals with PsO only												

[a] Adjusted for covariates XXX (place holder)

Table 8. Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsO

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**Unadjusted**	**Adjusted[a]**	**Unadjusted**	**Adjusted[a]**
Overall												
Year after index date												
0-<1												
1-<2												
2-<3												
3-<4												
…												

[a] Adjusted for covariates XXX (place holder)

Table 9. Incidence rate, hazard ratio, and VE of 1 dose of RZV in preventing HZ among individuals with PsA

	Vaccinated				Unvaccinated				Hazard Ratio (95% CI)		VE (95% CI)	
HZ	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**N**	**Number of cases**	**Number of person-years**	**Incidence per 1000 person-years (95% CI)**	**Unadjusted**	**Adjusted[a]**	**Unadjusted**	**Adjusted[a]**
Overall												

[a] Adjusted for covariates XXX (place holder)

CCI

CCI

CCI

CCI

[redacted]

Figure 5: Cumulative incidence estimates of HZ by RZV vaccination status in 2-dose RZV cohort with PsO

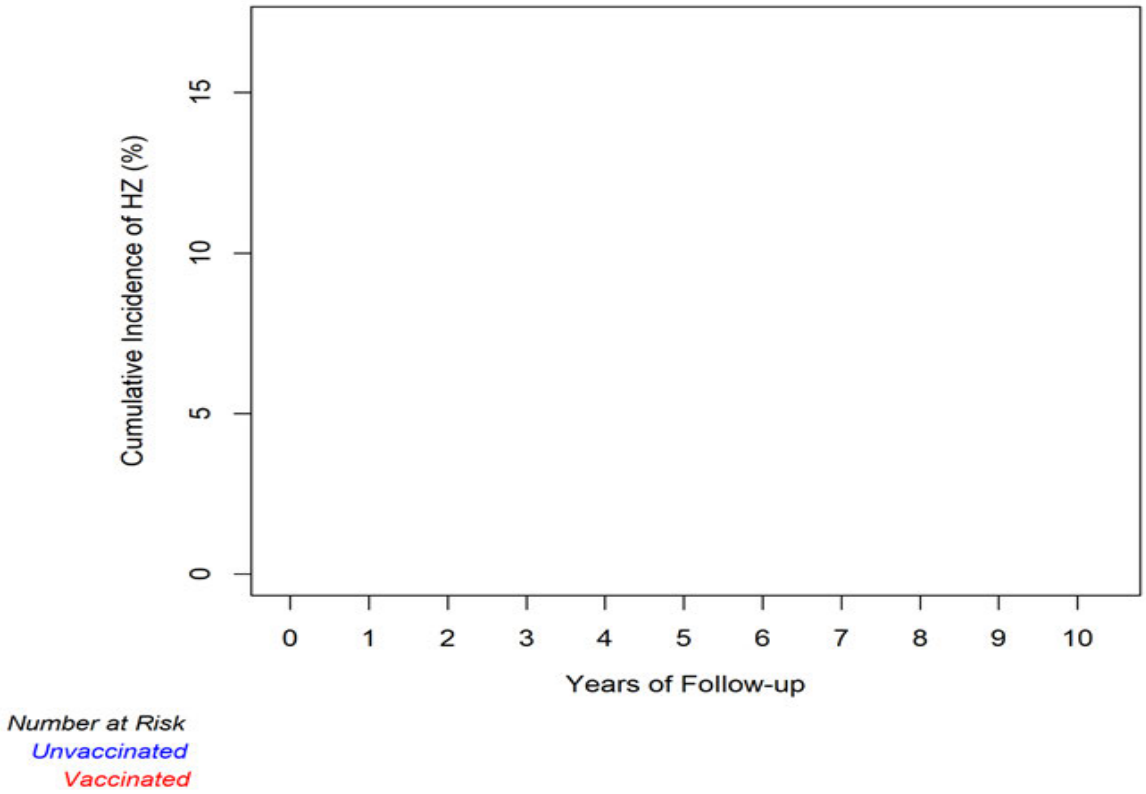

Figure 6: Cumulative incidence estimates of HZ by RZV vaccination status in 2-dose RZV cohort with PsA

Figure 7. Effectiveness of 2 doses of RZV in preventing HZ by year after vaccination among individuals with PsO (example)

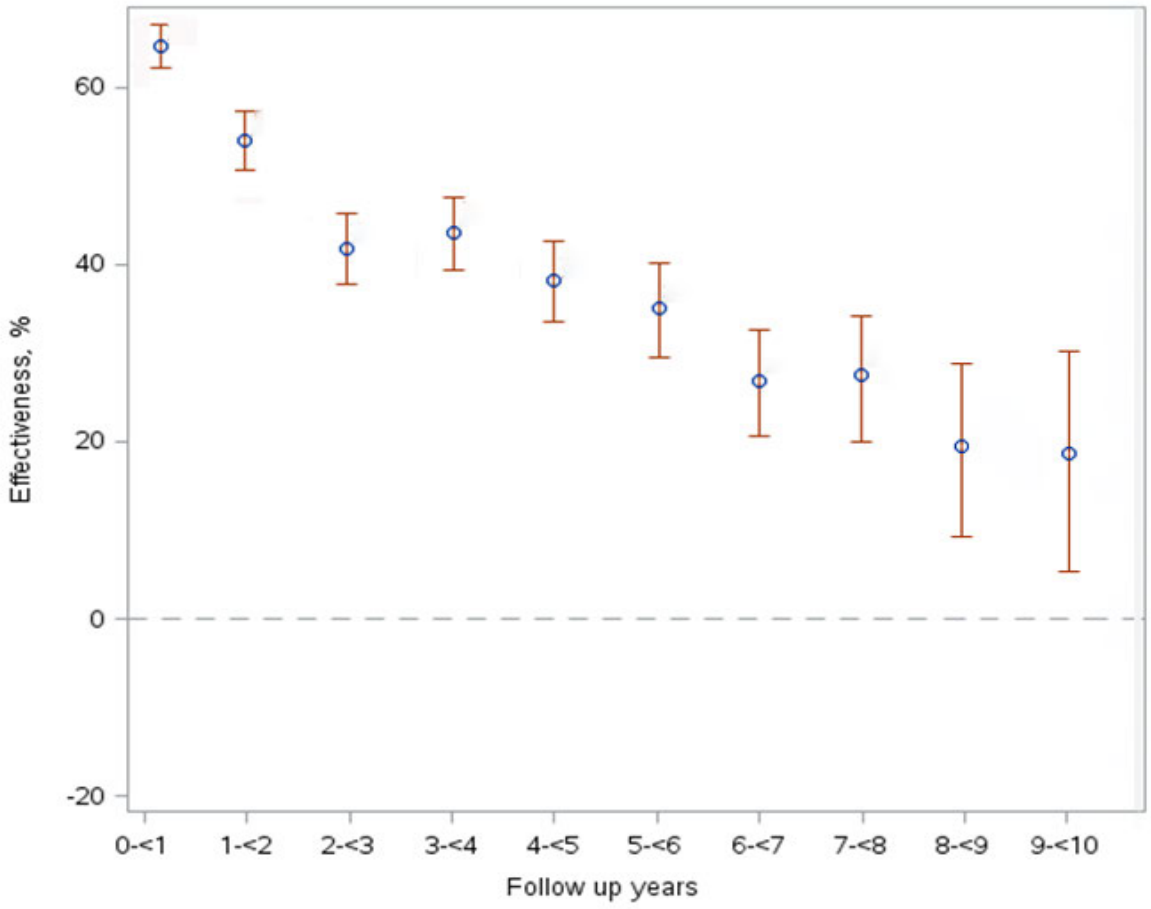

Table 14. Baseline characteristics and HZ incidence of 2-dose RZV vaccinated individuals with PsO, index date between March 2020 and December 2020 (not accrued)

	Not accrued
	N =
Age at index date, years	
mean (sd)	
median	
Q1, Q3	
range	
Age at index date, years, n (%)	
18-49	
50-59	
60-69	
70-79	
≥80	
Sex, n (%)	
Female	
Male	
Race/Ethnicity, n (%)	
White	
Black	
Hispanic	
Asian	
Other	
Medication category, n (%)	
Category 1	
Category 2	
Category 3	
Category 4	
Category 5	
Number of outpatient visits[a], n (%)	
0-4	
5-10	
≥11	
Number of ED visits[a], n (%)	
0	
1	
≥2	
Number of hospitalization[a], n (%)	
0	
1	

	Not accrued N =
≥2	
Baseline Comorbidities[a], n (%)	
Kidney disease	
Heart disease	
Lung disease	
Liver disease	
Diabetes	
Other autoimmune diseases	
SARS-CoV-2 infection/COVID-19 diagnosis	
Immunocompromised status at index date, n (%)	
Yes	
No	
History of ZVL/varicella vaccination[b], n (%)	
No	
Yes, ≤ 5 years	
Yes, > 5 years	
History of HZ[b], n (%)	
Yes	
No	
Length of continuous membership[b], years, n (%)	
≤5	
6-10	
≥11	
Concomitant vaccination[c], n (%)	
Yes	
No	
HZ cases during the follow up	
Number of cases	
Number of person-years	
Incidence per 1000 person-years (95% CI)	

[a] Defined in the one year prior to index date

[b] Defined based on all available medical records prior to index date

[c] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%); XX% concomitant with 1st dose and XX% concomitant with 2nd dose.

Appendix B: Table shells for safety analyses

Table 1. Baseline characteristics of RZV recipients with PsO

	Vaccinated **N =**
Age at index date, years	
mean (sd)	
median	
Q1, Q3	
range	
Age at index date, years, n (%)	
18-49	
50-59	
60-69	
70-79	
≥80	
Sex, n (%)	
Female	
Male	
Race/Ethnicity, n (%)	
White	
Black	
Hispanic	
Asian	
Other	
Medication category, n (%)	
Category 1	
Category 2	
Category 3	
Category 4	
Category 5	
PsO, n (%)	
PsO only	
PsO+PsA	
Number of RZV doses, n (%)	
One dose	
Two doses	
Concomitant vaccination[a], n (%)	
Yes	
No	
Month of the index dose, n (%)	
January	
February	
…	

[a] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%); XX% concomitant with 1st dose and XX% concomitant with 2nd dose.

Table 2. Baseline characteristics of RZV recipients with PsA

	Vaccinated **N =**
Age at index date, years	
mean (sd)	
median	
Q1, Q3	
range	
Age at index date, years, n (%)	
18-49	
50-59	
60-69	
70-79	
≥80	
Sex, n (%)	
Female	
Male	
Race/Ethnicity, n (%)	
White	
Black	
Hispanic	
Asian	
Other	
Medication category, n (%)	
Category 1	
Category 2	
Category 3	
Category 4	
PsA, n (%)	
PsA only	
PsA+PsO	
Number of RZV doses, n (%)	
One dose	
Two doses	
Concomitant vaccination[a], n (%)	
Yes	
No	
Month of the index dose, n (%)	
January	
February	
…	

[a] Among subjects with concomitant vaccines: influenza vaccine (xx%), COVID-19 vaccine (xx%), PCV13/PPSV23 (xx%), Tdap (xx%), and other (xx%); XX% concomitant with 1st dose and XX% concomitant with 2nd dose.

Table 3. Incidence and incidence rate ratio of PsO flare after RZV among individuals with PsO

	Risk Window			Comparison Window			Incidence Rate Ratio (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall							
RZV dose							
First							
Second							
Age at index date, years							
18-49							
≥50							
Medication category, n (%)							
Category 1							
Category 2							
Category 3							
Category 4							
Category 5							

Table 4. Incidence and incidence rate ratio of PsO or PsA flare after RZV among individuals with PsO or PsA

	Risk Window			Comparison Window			Incidence Rate Ratio (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall							
RZV dose							
First							
Second							

Table 5. Incidence and incidence rate ratio of PsA flare after RZV among individuals with PsA

	Risk Window			Comparison Window			Incidence Rate Ratio (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall							
RZV dose							
First							
Second							
Age at index date, years							
18-49							
≥50							
Medication category, n (%)							
Category 1							
Category 2							
Category 3							
Category 4							

	Risk Window			Comparison Window			Incidence Rate Ratio (95% CI)
	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	Number of cases	Number of person-years	Incidence per 1000 person-years (95% CI)	
Overall							
RZV dose							
First							
Second							
Age at index date, years							
18-49							
≥50							
Medication category, n (%)							
Category 1							
Category 2							
Category 3							
Category 4							

Figure 3: Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsO

Figure 4: Incidence of flare by day during the risk and comparison windows of second dose among RZV recipients with PsO

Figure 5: Incidence of flare by day during the risk and comparison windows of first dose among RZV recipients with PsA

Figure 6: Incidence of flare by day during the risk and comparison windows of second dose among RZV recipients with PsA

Appendix C: Quality control checklist

Table 1. Statistical analysis quality control checklist

	Statistician I				Statistician II				
	Action completed	**Date completed**	**Action performed by**	**Signature**	**Type of validation**	**Date completed**	**Action performed by**	**Signature**	**Comments**
Statistical Analysis	Review statistical analysis plan								
	Check data quality before conducting the analysis (sample size, duplicates, range of values, number of missings, proper data type and format, inconsistency, etc.)				N/A				
	Develop SAS analytic programs (Programs should include program header, section headers, and annotation comments. **Check model assumptions and multi-**				Program review				

Table 1. Statistical analysis quality control checklist

	Statistician I				Statistician II				
	Action completed	**Date completed**	**Action performed by**	**Signature**	**Type of validation**	**Date completed**	**Action performed by**	**Signature**	**Comments**
	collinearity. Use appropriate procedures and tests. The programming logic is consistent with the SAP.)								
	Perform statistical analysis (SAS logs and outputs will be reviewed for any warnings, error messages, and model convergence issues. Save SAS logs and outputs.)				N/A				
	Create results tables (Check for consistency and accuracy. Proofread the SAS log, outputs, and results tables to prevent any				Proofreading				

Table 1. Statistical analysis quality control checklist

	Statistician I				Statistician II				
	Action completed	**Date completed**	**Action performed by**	**Signature**	**Type of validation**	**Date completed**	**Action performed by**	**Signature**	**Comments**
	copy/paste and editing errors.)								
	Document analysis decisions and deviations				N/A				
	Keep SAS analytic programs, outputs, and logs of final analyses				N/A				
	Document analysis validation	N/A							