



**Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
Office of Biostatistics and Pharmacovigilance (OBPV)**

REAL WORLD EVIDENCE BLA MEMORANDUM

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To: Santosh Nanda, DVM, PhD
Chair of the Review Committee
Office of Vaccines Research and Review

Through: Richard Forshee, PhD
Deputy Director, OBPV
CBER, FDA

Subject: Review of Clinical Overview, Epidemiology Study
Report for EPI-RSV-022 OA BOD

Sponsor: GlaxoSmithKline Biologicals SA (GSK)

Product: AREXVY; Respiratory Syncytial Virus Vaccine
Recombinant, Adjuvanted

Application Type/Number: BLA STN 125775/0

Proposed Indication: For the prevention of lower respiratory tract disease
(LRTD) caused by respiratory syncytial virus RSV-A
and RSV-B subtypes in adults 60 years of age and
older

Submission Date: September 2, 2022

1 OBJECTIVE

The purpose of this review is to assess the adequacy of the real world evidence for Biologics License Application (BLA) 125775/0 for GlaxoSmithKline Biologicals SA (GSK)'s Respiratory Syncytial Virus (RSV) Vaccine Recombinant, Adjuvanted AREXVY for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus RSV-A and RSV-B subtypes in adults 60 years of age and older.

Materials Reviewed

- Clinical Overview (STN 125775/0; received September 2, 2022)
- Epidemiology Study Report for EPI-RSV-022 OA BOD (STN 125775/0; received September 2, 2022)

2 PRODUCT INFORMATION

2.1 Product Description

The GSK's RSV Vaccine Recombinant, Adjuvanted AREXVY contains lyophilized RSVPreF3 antigen component to be reconstituted with the accompanying vial of AS01E adjuvant suspension component. The product is a suspension for intramuscular injection.

The product is administered as a single dose (0.5 mL) by intramuscular injection.

2.2 Proposed Indication

The proposed indication for GSK's RSV Vaccine Recombinant, Adjuvanted AREXVY in the United States is for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus RSV-A and RSV-B subtypes in adults 60 years of age and older.

3 REAL WORLD STUDIES

According to the Clinical Overview (STN 125775/0; received September 2, 2022): "Since RSVPreF3 OA vaccine is not yet authorized in any country, no post-marketing safety data are currently available."

Reviewer comment: No postmarketing safety data are currently available. From the premarket clinical safety database, there are safety signals for Guillain-Barré Syndrome (GBS) and acute disseminated encephalomyelitis (ADEM), and a safety concern for atrial fibrillation. Should the product be approved, postmarketing safety studies will be conducted to assess GBS and ADEM, and to further investigate atrial fibrillation, following vaccination with AREXVY.

Module 5.3.5.4 "Other study Reports" contains the EPI-RSV-022 OA BOD Report.

Reviewer comment: This epidemiological study EPI-RSV-022 OA BOD is a multi-country, multicenter, prospective, descriptive cohort study.

The primary objective of this study is to estimate the incidence rate of confirmed RSV associated acute respiratory infection (cRSV-ARI) in community dwelling (CD) subjects aged 50 years and older during 2 consecutive RSV seasons in the United States and Europe. The secondary objectives included long-term care facility (LTCF) residents aged 65 years and older and other endpoints.

The objectives were analyzed by season: Season 1, October 2019 to March 2020, and Season 2, October 2020 to June 2021. The COVID-19 pandemic could have potential short-term and long-term impact on RSV circulation and people's health-seeking behavior.

The study has several strengths: 1) Minimal outcome misclassification: The occurrence of cRSV-ARI was reliably captured using reverse transcription polymerase chain reaction (RT-PCR). 2) Less impacted by health-seeking behavior: The surveillance plan for ARI included visits prior to RSV season and surveillance contacts were performed every 2 weeks during the RSV season and monthly during the RSV interseason (April to September) to check for ARI signs and/or symptoms.

The COVID-19 pandemic and the non-pharmaceutical interventions used to reduce the spread of SARS-CoV-2 dramatically decreased RSV circulation in Season 2. There were no cRSV-ARI cases reported in the CD setting and one reported cRSV-ARI case in the LTCF setting.

The study report used only RSV Season 1 data to draw conclusions. For Season 1, the incidence and attack rates of cRSV-ARIs (RT-PCR) in CD and LTCF setting were above the study assumption of 1% and in line with the RSV attack rate reported in the GSK meta-analysis. Neither hospitalizations nor deaths were reported among the cRSV-ARIs in both settings.

Due to the impact of COVID-19 pandemic, the incidence rate of cRSV-ARIs for future RSV seasons may be different from the observed incidence rate in pre-COVID RSV Season 1 in this study.

4 OBPV REAL WORLD EVIDENCE RECOMMENDATIONS

Should the product be approved, postmarketing safety studies will be conducted to assess GBS and ADEM, and to further investigate atrial fibrillation, following vaccination with AREXVY. Please see OBPV/DPV pharmacovigilance plan memorandum for recommendations on safety-related postmarketing requirement (PMR) and postmarketing commitment (PMC) studies.