A Post-Authorization Safety Study of Atrial Fibrillation Following Respiratory Syncytial Virus Vaccine (ABRYSVOTM) Among Older Adults in the Veterans Affairs Health System (C3671037)

First published: 16/08/2024

Last updated: 02/09/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000290

Study ID

1000000290

DARWIN EU® study

No

Study countries

United States

Study description

This study will answer the research question: what are the incidence rates of atrial fibrillation and supraventricular arrhythmia, overall and in sub-cohorts of interest, among individuals vaccinated with ABRYSVO within the US Veterans Health Administration (VHA) system as compared to expected rates of those events?

Study status

Ongoing

Research institutions and networks

Institutions

Pfizer

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Institution

Analysis Group

Contact details

Study institution contact

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Primary lead investigator

Joanne (Juan) Wu

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 02/06/2023

Actual: 02/06/2023

Study start date

Planned: 01/09/2024

Actual: 12/02/2025

Data analysis start date

Planned: 01/03/2027

Date of interim report, if expected

Planned: 30/06/2026

Date of final study report

Planned: 29/02/2028

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

C3671037_RSV VACCINE FINAL UPDATED PROTOCOL VERSION 1.0_29NOV2023.pdf (610.4 KB)

C3671037_PROTOCOL- ADULT AFIB_V2.0_04DEC2024.pdf (866.44 KB)
C3671037_PROTOCOL RSV VACCINE VERSION 3.0_14FEB2025.pdf (808.23 KB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This non-interventional PASS will assess the incidence and risk of atrial fibrillation and supraventricular arrhythmia following ABRYSVO among adults 60 years of age and older in the VHA system from earliest date of vaccine availability to 31 May 2026.

Main study objective:

The primary objective of the study is to estimate the incidence of atrial fibrillation following administration of ABRYSVO among adults 60 years of age and older in the US Veterans Health Administration (VHA) system.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

ABRYSVO

Anatomical Therapeutic Chemical (ATC) code

(J07BX05) respiratory syncytial virus vaccines

respiratory syncytial virus vaccines

Population studied

Short description of the study population

The study population will consist of individuals with a record of at least one dose of ABRYSVO who are at least 60 years of age on the date of vaccination (i.e., index date).

Individuals who receive a respiratory syncytial virus (RSV) vaccine from a manufacturer other than Pfizer will be excluded from the study.

Contemporary vaccinated controls will be included if they have no record of RSV vaccine and have a record for another vaccine (e.g., influenza vaccine, COVID-19 vaccine, and other pre-specified vaccines such as shingles, hepatitis B) within 30 days of a corresponding ABRYSVO vaccinee's vaccination date; the control's index date will be the date of the control's non-RSV vaccine and they will be required to be at least 60 years of age on the index date.

Contemporary unvaccinated controls will be included if they have no record of any vaccine on the index date but had at least one vaccination record in the year prior to the index date; they will be assigned an index date matched to a corresponding ABRYSVO vaccinee's vaccination date and will be required to be at least 60 years of age on the matched index date.

All individuals must be enrolled in (i.e., not disenrolled from) VHA benefits during the 2 years prior to the index date (i.e., baseline period).

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)

Study design details

Setting

The study population will consist of individuals with a record of at least one dose of ABRYSVO who are at least 60 years of age on the date of vaccination (i.e., index date).

Individuals who receive an RSV vaccine from a manufacturer other than Pfizer will be excluded from the study.

The VHA is the largest integrated health care system in the US, providing both inpatient and outpatient clinical care to over 9 million Veterans enrolled at more than 170 medical centers and 1,113 community-based outpatient clinics.

Comparators

Contemporary vaccinated controls will be included if they have no record of RSV vaccine and have a record for another vaccine (e.g., influenza vaccine, COVID-19 vaccine, and other pre-specified vaccines such as shingles, hepatitis B) within 30 days of a corresponding ABRYSVO vaccinee’s vaccination date; the control’s index date will be the date of the control’s non-RSV vaccine and they will be required to be at least 60 years of age on the index date.

Contemporary unvaccinated controls will be included if they have no record of any vaccine on the index date but had at least one vaccination record in the year prior to the index date; they will be assigned an index date matched to a

corresponding ABRYSVO vaccinee’s vaccination date and will be required to be at least 60 years of age on the matched index date.
All individuals must be enrolled in (i.e., not disenrolled from) VHA benefits during the 2 years prior to the index date (i.e., baseline period).

Outcomes

The study’s primary outcome, new onset atrial fibrillation, will be identified by a diagnosis code for atrial fibrillation in any setting during the 0-3 day risk interval for the primary analysis (or 0-1 day or 0-30 day risk interval for secondary analysis), or day 4-10 post vaccination control interval, followed by a confirmatory diagnosis within 30 days after the initial diagnosis and no diagnosis for atrial fibrillation or other supraventricular arrhythmias in the 2 years prior to the index date (i.e., “clean window,” to rule out pre-existing events).
The secondary outcome of the study will be new onset supraventricular arrhythmia, including atrial fibrillation, and will be identified in the same manner as the primary outcome.

Data analysis plan

Baseline demographics and clinical characteristics for individuals administered ABRYSVO and contemporary vaccinated or unvaccinated controls will be summarized using descriptive statistics.
Descriptive statistics will also be used to summarize vaccination patterns for ABRYSVO.
Incidence rates per 1,000 patient years (and corresponding 95% confidence intervals (CIs)) will be calculated for the primary and secondary outcomes and will be compared to rates observed in the control groups.
Diagnostic validation of identified atrial fibrillation cases among individuals administered ABRYSVO will be conducted in a randomly selected representative sample of up to 100 cases per interim/final report, as available and feasible.

Positive predictive value (PPV) will be calculated as the proportion of atrial fibrillation cases deemed as true cases via adjudication among the total number of adjudicated cases. If the lower bound of the 95% CI of the PPV is less than 70% at the interim analysis, the algorithm used to identify incident atrial fibrillation using codified data may be updated in subsequent analyses and atrial fibrillation cases identified with the new algorithm will be re-adjudicated. If the lower bound of the 95% CI for PPV is equal to or greater than 70% in the interim report, chart adjudication may be waived for the final report.
If an increased risk of atrial fibrillation following ABRYSVO vaccination is observed from the analyses described above, a risk factor analysis will be conducted via logistic regression among individuals vaccinated with ABRYSVO, adjusting for baseline characteristics and co-administration of vaccines selected a priori.
Analyses may also be conducted in the subgroups of interest described above, depending on feasibility, sample size, and data availability.
Various sensitivity analyses may be conducted, including analysis of negative control outcomes.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

US Veterans Health Administration (VHA) system

Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown