Observational Cohort Study Evaluating Real-World ABRYSVO Vaccine Effectiveness and Impact Against Medically-Attended RSV-related and All-Cause Outcomes Among Infants Born to Individuals Vaccinated During Pregnancy

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Study Planned

Administrative details

EU PAS number

EUPAS1000000295

Study ID

1000000295

DARWIN EU® study

No

Study countries

United States

Study description

This study will be conducted in collaboration with an integrated delivery health care organization in the United States using electronic medical record (EMR) data, collected during routine standard of care clinical encounters. This study will use a retrospective cohort design to study the vaccine effectiveness (VE) and impact of ABRYSVO vaccination during pregnancy in a real-world population over multiple RSV seasons.

Study status

Planned

Research institutions and networks

Institutions

Kaiser Permanente Northern California (KPNC)

Networks

Kaiser Permanente Northern California

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Nicola Klein

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 18/06/2024

Actual: 13/11/2024

Study start date

Planned: 01/09/2025

Date of final study report

Planned: 31/03/2028

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer INC

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Other study registration identification numbers and links

C3671048

Methodological aspects

Study type

Study type list

Study topic, other:

Vaccine effectiveness

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This study will use a retrospective cohort design to assess ABRYSVO VE and impact in a large, diverse, real-world setting. This NI study will be conducted within an integrated delivery health care organization using EMR data, collected during routine standard of care clinical encounters.

Main study objective:

The overall aim of this study is to evaluate the effectiveness and impact of maternal ABRYSVO vaccination during pregnancy for the prevention of medically-attended (MA) respiratory syncytial virus (RSV)-associated and all-cause infant outcomes in a large, diverse, real-world population.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

The overall aim of this study is to evaluate the effectiveness and impact of maternal ABRYSVO vaccination during pregnancy for the prevention of medically-attended respiratory syncytial virus associated and all-cause infant outcomes in a large, diverse, real-world population. Primary objective is to estimate vaccine effectiveness of ABRYSVO vaccination during pregnancy against polymerase chain reaction-confirmed RSV lower respiratory tract disease among infants from birth through 6 months of age. Key secondary objective will estimate VE of ABRYSVO vaccination during pregnancy against PCR-confirmed RSV LRTD hospitalization among infants from birth through 6 months of age. Additional secondary objectives for infants from birth through 6

months of age include estimating VE of ABRYSVO vaccination during pregnancy against: PCR-confirmed RSV, PCR-confirmed RSV hospitalization, all-cause LRTD, all-cause LRTD hospitalization, acute otitis media, and new antibiotic prescriptions. Additional secondary objectives for infants from birth through 12 months of age include estimating VE over the entire interval and interval-specific VE against: PCR-confirmed RSV, PCR-confirmed RSV hospitalization, PCR-confirmed RSV LRTD, and PCR-confirmed RSV LRTD hospitalization. Exploratory objectives for infants from birth through 6 months of age include estimating VE against PCR-confirmed RSV LRTD and PCR-confirmed RSV LRTD hospitalization, stratified by: time from vaccination to birth, gestational age at vaccination, infant high-risk status for severe RSV, with/without co-administration with other vaccines. Exploratory objectives for infants from birth through 24 months of age (0 to ≤720 days) include 1)describing the timing, severity, and sequelae of the first PCR-confirmed RSV illness among infants up to 24 months of age, by maternal ABRYSVO status; 2)estimating VE against all-cause LRTD; 3)estimating VE against all-cause LRTD hospitalization; and 4)estimating VE against acute otitis media.

Study drug and medical condition

Name of medicine

ABRYSVO

Population studied

Short description of the study population

The study population will comprise eligible maternal-infant pairs over a 2-year study period, identified from EMR records in the existing databases, which accrue in real-time as pregnancies/births occur. All pregnancies that reach 32

weeks of gestation during the 2-year study period, from September 22, 2023 (start of ABRYSVO vaccination season 1 as of the date of the ACIP recommendation) to January 31, 2025 (estimated end of ABRYSVO vaccination season 2) will be eligible for inclusion, along with all live born infants from the eligible pregnancies.

Age groups

Neonate

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Estimated number of subjects

39456

Study design details

Setting

The study setting will be KPNC, which is an integrated delivery healthcare organization in Northern California with over 4.5 million members and approximately 40,000 births each year. KPNC members receive almost all their health care within KPNC clinics, hospitals, pharmacies, and laboratories. Information from encounters within these clinical settings are captured in EMRs which can be linked at an individual level across KPNC settings using a unique medical record number (MRN). The KPNC pregnancy database will be used to identify the maternal-infant study population. This database links records of newborn infants with their mother, enabling integration of maternal data from across pregnancy and delivery encounters, along with infant birth information and longitudinal follow-up for infants who remain enrolled with KPNC. Infant

healthcare encounters after the birth and throughout the follow-up period will be identified in the EMR. As routinely-recommended vaccinations are provided free of charge to KPNC members and can be electronically linked with the pregnancy database and other EMR data, the receipt and gestational timing of ABRYSVO vaccination during pregnancy can be determined.

Outcomes

Medically-Attended Endpoints

Primary: PCR-confirmed RSV LRTD occurring ≤180 days after birth (first episode).

Key Secondary: PCR-confirmed RSV LRTD hospitalization occurring ≤180 days after birth (first episode).

Secondary:

Follow-up from birth through 6 months of age: PCR-confirmed RSV occurring ≤180 days after birth (first episode), PCR-confirmed RSV hospitalization occurring ≤180 days after birth (first episode), LRTD (any cause) occurring ≤180 days after birth (first episode during the RSV season), LRTD hospitalization (any cause) occurring ≤180 days after birth (first episode during the RSV season), Acute otitis media occurring ≤180 days after birth (first episode during the RSV season), New antibiotic prescriptions occurring ≤180 days after birth (first prescription during the RSV season).

Follow-up from birth through 12 months of age:PCR-confirmed RSV occurring ≤360 days

after birth (first episode), PCR-confirmed RSV hospitalization occurring ≤360 days after birth (first episode), PCR-confirmed RSV LRTD occurring ≤360 days after birth (first episode), PCR-confirmed RSV LRTD hospitalization occurring ≤360 days after birth (first episode).

Exploratory:

Follow-up from birth through 6 months of age: PCR-confirmed RSV LRTD

occurring ≤180 days after birth (first episode), stratified by: time from vaccination to birth, gestational age at vaccination, infant high risk status for severe RSV, with/without co-administration with other vaccines
PCR-confirmed RSV LRTD hospitalization occurring ≤180 days after birth (first episode), stratified by: time from vaccination to birth, gestational age at vaccination, infant high-risk status for severe RSV, with/without coadministration with other vaccines.
Follow-up from birth through 24 months of age: Among PCR-confirmed RSV-positive cases through 24 months of age, describe timing, severity, sequelae, LRTD/LRTD hospitalization/acute otitis media (any cause) occurring ≤720 days after birth (total number of episodes)

Data analysis plan

RSV-specific infant analyses
RSV-specific from birth through 6 months of age:
Outcomes among infants born to ABRYSVO-vaccinated and ABRYSVO-unvaccinated mothers will be compared using multivariable Cox proportional hazards regression models, generating aHR and 95% CI. IPTW derived from propensity scores may be considered, instead of conventional multivariable adjustment, to account for confounding bias. Calendar date will be used as the underlying time scale in the Cox models and VE will be calculated as (1 - aHR) and expressed as a percentage.
RSV-specific from birth through 12 months of age:
This analyses will stratify the Cox model by infant age; the exact width of discrete time intervals will be determined based on outcome incidence and ABRYSVO uptake.
RSV-specific from birth through 24 months of age:
Timing, severity, and sequelae will be described according to maternal ABRYSVO status. Among infants born to individuals who received ABRYSVO vaccine during pregnancy, we will describe the gestational age at ABRYSVO

vaccination and the time interval from vaccination to birth.

Non-specific all-cause analyses

To be assessed for two overlapping follow-up periods: from birth through 6 months of age and from birth through 24 months of age.

All-cause analyses from birth through 6 months of age:

Multivariable Cox proportional hazards regression models will be used to estimate VE. VE will be calculated as (1 - aHR) and expressed as a percentage.

All-cause analyses from birth through 24 months of age:

Will the total number of episodes of each outcome during follow-up. Poisson regression to generate aIRR for comparison. VE will be calculated as (1 - aIRR) and expressed as a percentage.

Data management

Data sources

Data sources (types)

Electronic healthcare records (EHR)

Laboratory tests and analyses

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

No