TARGET-EU: Effectiveness of nirsevimab for RSV-lower respiratory tract infection hospitalization in infants ≤12 months of age

First published: 19/05/2026

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Study Planned

Administrative details

EU PAS number

EUPAS1000000993

Study ID

1000000993

DARWIN EU® study

No

Study countries

Italy

Study description

This case study is part of the broader TARGET EU project (EUPAS1000000539), which aims to advance the regulatory use of real-world data through the application of target trial emulation and estimand methodologies.

Background: Nirsevimab, a recombinant monoclonal antibody approved by EMA in September 2022, provides sustained protection throughout the RSV season with a single dose by binding to the RSV F protein and preventing viral entry. While systematic reviews demonstrate nirsevimab effectiveness (OR 0.17,95%CI 0.12–0.23; I2=85.8%, for RSV-related hospitalization), most real-world evidence comes from Spain, France, and the US, with only one small Italian regional study.

Objectives: The primary objective is to assess nirsevimab effectiveness in preventing RSV-LRTI hospitalization within 6 months of administration among infants ≤12months compared to no immunization within the Italian healthcare system.

Methods: We will conduct a cohort study using PEDIANET from October 2024 to March 2025. Exposed infants are those receiving nirsevimab; controls are unexposed infants. Inclusion criteria: age <12months, born at ≥29weeks gestational age. Exclusion criteria: ongoing LRTI infection, maternal RSV vaccination during pregnancy, or palivizumab eligibility. Time zero for exposed infants is the first nirsevimab administration date; controls are matched 1:1 on age group (≤3.0, >3.0–≤6.0, >6.0 months) and calendar week of exposure. Follow-up is six months, ending at outcome occurrence, death, disenrollment, or study end. The primary outcome is RSV-LRTI hospitalization and confounders include age, sex, prior LRTI episodes, healthcare utilization (visits and antibiotic prescriptions), and area deprivation index, all measured before time zero. Inverse probability of treatment weighting using propensity scores estimated via logistic regression will adjust for confounding. Stabilized weights will be

applied in log-binomial regression models to estimate marginal risk ratios.

Study status

Planned

Research institutions and networks

Institutions

Electronic Health Records (EHR) Research Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010

Last updated: 04/11/2026

Institution | Educational Institution | ENCePP partner

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

First published: 01/03/2010

Last updated: 27/05/2026

Institution | Educational Institution | ENCePP partner

Clinical Pharmacology, Vall d'Hebron Institut de Recerca (VHIR)

Spain

First published: 18/05/2021

Last updated: 20/05/2021

Institution | Outdated | Hospital/Clinic/Other health care facility | ENCePP partner

University Medical Center Utrecht (UMCU)

Netherlands

First published: 24/11/2021

Last updated: 22/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

Teamit Institute

Spain

First published: 12/03/2024

Last updated: 12/03/2024

Institution | Other | ENCePP partner

Societa' Servizi Telematici

Networks

Vaccine monitoring Collaboration for Europe (VAC4EU)

- Belgium
- Denmark
- Finland
- France
- Germany
- Italy
- Netherlands
- Norway
- Spain
- United Kingdom

First published: 22/09/2020

Last updated: 22/09/2020

Network | Outdated | ENCePP partner

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

- Netherlands

First published: 01/02/2024

Last updated: 24/09/2025

Network

Pedianet network (So.Se.Te)

Italy

First published: 23/10/2025

Last updated: 08/04/2026

Network

Contact details

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Study timelines

Date when funding contract was signed
Planned: 19/09/2024

Study start date
Planned: 09/03/2026

Date of final study report
Planned: 10/06/2026

Sources of funding

- EMA

Study protocol

Emulation_Protocol_CS8_REV6_clean.pdf (777.25 KB)

Regulatory

Was the study required by a regulatory body?

No

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:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

A cohort design is well suited to emulation of the target trial for interventions such as nirsevimab, where the exposure is fixed at a single point in time (i.e. single administration) rather than repeatedly administered.

Main study objective:

The primary objective is to assess nirsevimab effectiveness in preventing RSV-LRTI hospitalization within six months of administration among infants ≤12 months compared to no immunization. Two estimands are defined: Estimand 1 evaluates effectiveness under a hypothetical scenario where control group participants would never receive nirsevimab, while Estimand 2 applies a treatment policy strategy, evaluating effectiveness regardless of subsequent nirsevimab receipt in controls.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

NIRSEVIMAB

Medical condition to be studied

Hospitalisation

Population studied

Short description of the study population

In this cohort study we will include infants <12 months of age at exposure and born at ≥29 weeks gestational age who are continuously enrolled since birth in the PEDIANET database starting from January 2023. We restricted the population only to those ≤ 12 months of age because this is the target population for immunization programs implemented and we restricted the population only to those born at or after 29 weeks of gestational age because those born before are usually exposed to palivizumab or might have had a previous prophylaxis with palivizumab and then a prophylaxis also with nirsevimab.

Exclusion criteria: ongoing LRTI infection, maternal RSV vaccination during pregnancy, or palivizumab eligibility.

In this study:

- For the exposed group, “time 0” is defined as the date of first receipt of nirsevimab during the study period. This date represents the earliest point at

which the individual could reasonably be expected to experience any potential effects associated with the intervention. Anchoring “time 0” at the time of administration ensures that follow-up and outcome ascertainment are appropriately aligned with the biologically plausible period of risk or benefit.
- For the comparator group, “time 0” is defined as the date of receipt of nirsevimab for the matched exposed individual. This matching date is selected to mirror the temporal distribution of cohort entry in the exposed group, thereby minimising biases related to calendar time and seasonality (especially relevant in studies involving respiratory pathogens), as well as temporal changes in healthcare delivery or data capture. At time 0, comparator individuals are required to be alive, eligible, and not yet exposed to nirsevimab. Individuals in the comparator group who subsequently will receive nirsevimab during follow-up will be not contribute data to the study after the nirsevimab administration. To emulate a parallel-arm target trial, matching will be performed without replacement at each index date. Individuals can enter the study only once, at their first eligible index date.

Because infants in the unexposed group do not have a treatment administration date, a 1:1 matching procedure will be used to assign a comparable index date (time 0). For each infant receiving nirsevimab, one infant who did not receive nirsevimab will be selected and assigned the same index date, matched on age group at the time of nirsevimab administration (≤3.0 months, >3.0 to ≤6.0 months, and >6.0 months) and calendar week of administration. This matching procedure ensures alignment of follow-up time between exposure groups and accounts for age and calendar time. All subsequent assessments, such as the application of inclusion and exclusion criteria, outcome surveillance, and follow-up duration, are defined relative to this primary temporal anchor.

Age groups

- Neonate

    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)

Study design details

Setting

This study is conducted using routinely collected electronic health records from 2023 to 2025, reflecting the period of nirsevimab use in routine clinical practice. Pedianet is a national population database that contains anonymous patient-level data of paediatric population who received healthcare from family paediatricians (FPs) in Italy who were part of the PEDIANET network. The network links FPs distributed throughout several Italian regions designated by the Italian NHS, including Friuli-Venezia Giulia, Liguria, Lombardia, Piemonte, Veneto, Lazio, Marche, Toscana, Abruzzo, Campania, Sardegna, and Sicilia.

Comparators

Each eligible infants exposed to nirsevimab will be matched with a non-exposed infants (comparator) at time 0. For the comparator group, “time 0” is defined as the date of receipt of nirsevimab for the matched exposed individual. This matching date is selected to mirror the temporal distribution of cohort entry in the exposed group, thereby minimising biases related to calendar time and seasonality (especially relevant in studies involving respiratory pathogens), as well as temporal changes in healthcare delivery or data capture. At time 0, comparator individuals are required to be alive, eligible, and not yet exposed to nirsevimab. Individuals in the comparator group who subsequently will receive nirsevimab during follow-up will be not contribute data to the study after the nirsevimab administration. To emulate a parallel-arm target trial, matching will

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Outcomes

RSV-LRTI hospitalization is the primary outcome of interest. This is a hard outcome that is of great interest to patients, clinicians, and policy decision makers.

Data analysis plan

This study employs the target trial and the estimand frameworks to assess nirsevimab effectiveness in preventing RSV-LRTI hospitalization within six months of administration among infants ≤12 months compared to no immunization. For Estimand 1, the main estimand supporting decision making, we will estimate the relative risk (RR) under a hypothetical scenario in which participants in the control arm would not experience the intercurrent event of receiving nirsevimab. The status of the outcome of interest, RSV-LRTI hospitalisation, of subjects who experience this intercurrent event, will be considered missing. For the primary analysis, the RR will be estimated using an inverse probability of treatment weighted log-binomial regression model

including group assignment as the main predictor and age. Sensitivity analyses will be performed to investigate the robustness of the results to assumptions made in the primary analysis.

For Estimand 2, a log-binomial regression model will be used as well, including all participants' follow-up as randomised, regardless of receiving nirsevimab in the untreated group.

Supplementary analyses including diagnostic and descriptive assessments to support the main analysis will be conducted to contextualise data and results from the primary analysis.

An additional supplementary analysis will be produced whereby individuals in the control arm can contribute data multiple times to the control arm and also to the nirsevimab arm after reception of nirsevimab.

Documents

Study, other information

CS8_Feasibility_Assessment_final.pdf (311.2 KB)

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)

Pedianet

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

ConcepTION CDM

CDM website

https://www.imi-conception.eu/

CDM release frequency

6 months

CDM version

v 2.2

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation details

The feasibility assessment for this case study, detailed in the appendix of the study protocol, was conducted as part of the broader TARGET-EU feasibility assessment (EUPAS1000000791). Data source suitability was evaluated using a structured framework based on the EMA data quality framework, assessing system characteristics, data quality, and fitness for the research question.

Briefly, with an approximate estimated sample size of 7,408 individuals and considering that PEDIANET includes data on 24,572 toddlers aged between 28 days and 23 months, and ~ 30K births every year it offers large, high-quality, population-based electronic health records of the paediatric population in Italy. It provides the required data elements to operationalize the study design, including demographics, diagnoses, prescriptions, immunization registry and hospitalizations.