Preparing for RSV Immunisation and Surveillance in Europe: Biomarker Infant study

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To validate biomarkers that are associated with severe RSV infection and respiratory sequelae.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON52142

Source
ToetsingOnline

Brief title
PROMISE study

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
Respiratory Syncytial Virus, RSV, RS-virus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Innovative Medicine Initiative (IMI): EU/Horizon2020 en EFPIA (European Federation of Pharmaceutical Industries and

Associations)

Intervention

Keyword: Biomarkers, Disease severity, Infant, Respiratory Syncytial Virus (RSV)

Outcome measures

Primary outcome

Validation of biomarkers that are associated with severe RSV infection and respiratory sequelae.

Secondary outcome

1. Dynamics of biomarkers in the upper and lower airways of children with RSV infection and compare these with blood and with children without airway infection

2. Validation of currently used case definitions and severity measures for RSV infection in infants

3. Risk factors for severe RSV disease

4. Long-term sequelae of RSV infection in the first year of life

Study description

Background summary

Human respiratory syncytial virus (RSV) causes severe disease in the very young, elderly and in high risk groups. Worldwide in 2015 there were an estimated 34 million cases of acute lower respiratory tract infection (ALRI), 3.4 million ALRI hospitalisations and 55,000 to 199,000 deaths associated with RSV in children <5 years old. The majority of children admitted to the hospital with RSV are previously healthy. Although a younger age is a risk factor for severe disease in children without comorbidities, this cannot totally explain the difference in severity between young children of the same age. There is an unmet need to identify the correlates of severe RSV disease for clinical management, classification of disease severity in clinical trials and

identification of biomarkers for severe disease, which are currently lacking.

The RESCEU (Respiratory Syncytial virus Consortium in Europe) consortium, an IMI funded effort which brought together clinicians, epidemiologists, basic scientists, health economists, statisticians, public health professionals and industry from across Europe to answer key research questions relating RSV, conducted a biomarker discovery study in healthy young infants with RSV infection in 2 prospective studies, the RESCEU infant cohort study and the RESCEU infant case-control study. First, possible biomarkers were identified by means of a systematic literature review. Biomarkers discovered in RESCEU include, but are not limited to: an array of RSV antibodies, including preF, postF and neutralizing antibodies; gene expression profiles in infant whole blood at birth (susceptibility) as well as during disease (severity, prognosis). Results are currently being analysed and will be prepared for publication in the coming months.

A critical step in biomarker development is external clinical validation as biomarkers are often identified in data-driven exploratory studies which increase the chance of false positive associations. Therefore, they need to be externally validated to minimise this risk and become acceptable for clinical implementation. This is also part of the regulatory requirements before introduction in routine care. In PROMISE we will establish a clinical study large enough to externally validate the biomarkers identified from RESCEU as well as those that are still being analysed. Gene expression profiles related to neutrophil degranulation as well as innate immunity and antiviral responses will be of specific interest for validation. The most promising candidates will be selected for verification, based on their biological relevance, statistical significance, and potential contribution to a clinical question (if the potential contribution is very small, candidates that did show statistically significance may not be developed further).

Study objective

To validate biomarkers that are associated with severe RSV infection and respiratory sequelae.

Study design

Prospective, observational case-control study. This case-control study will validate discovered biomarkers related to RSV infection susceptibility and disease severity in the RESCEU case-control study and birth cohort study. For this a validation cohort of previously healthy infants with different severities of RSV infection and healthy infants will be compared.

Study burden and risks

Blood, respiratory, buccal, urine and stool samples will be collected at the moment of medical attendance for RSV infection and 6-8 weeks after infection.Controls will have only one timepoint (baseline) at which samples are collected. In ventilated infants with RSV also broncheo-alveolar/tracheal aspirates will be collected. In the ventilated control group only blood, respiratory samples and broncheo-alveolar/tracheal aspirates will be collected. A questionnaire will be completed by the parents at baseline followed by a diary for two weeks (14 consecutive days) for RSV positive children. A yearly questionnaire up to the age of 3 years old will be completed by the parents. None of the study procedures is associated with any risk for serious complications. However, there is a minimal risk of minor complications due to study procedures (for example a nose bleed after a nose swab or bruise after blood sampling). Bronchoalveolar/tracheal aspirate will be collected during routine care of ventilated children, during which the ventilation tube is regularly suctioned. The collection of urine and feces is without any risks.

This study is group related and can only be done in this patient group because severe RSV disease is mainly seen in infants and very rare in older children and adults.

Benefits of participating in the study: There are no particular benefits to participating in this study, apart from knowing knowledge obtained from it may benefit other patients in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

• Parents/carer of infant are willing and able to give informed consent for participation in the study.
• Less than 12 months of age at enrolment.
• Hospitalized with (suspected) RSV infection for <96 hours at enrolment or within 96hrs of onset of illness (for those not admitted).*

* Not applicable for control infants

Exclusion criteria

• History of concurrent clinically significant medical illness (not directly attributable to RSV infection) including but not limited to, cardiovascular, respiratory, renal, gastrointestinal, haematology, neurology, endocrinology, immunology, musculoskeletal, oncological or congenital disorders, as judged by the investigator.
Specifically excluded examples include, but are not limited to:
- Known congenital or acquired immunosuppression
- Bronchopulmonary dysplasia/chronic lung disease of infancy
- Congenital heart disease*
- Down*s syndrome
• Prematurity, as defined as gestational age <37 weeks at birth
• History of receipt of medication to treat RSV infection (e.g. ribavirin)
• Prior exposure to an RSV investigational vaccine or medication.
• History of receipt of immunoglobulin or monoclonal antibodies (including palivizumab).
• Use of steroids or montelukast within 7 days of enrolment in the study.
• Participation in another clinical study for an investigational drug within 12 weeks before entry into this study
• Parents not able to understand and communicate in the local language or English.

* not applicable for ventilated children without airway inflammation

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-11-2021
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	16-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-11-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-12-2022
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78337.041.21