101034339 – PROMISE

Preparing for RSV Immunisation and Surveillance in Europe

WP3 –Clinical validation studies

D3.7 Report on status of posting results

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Document history

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V1.0	05/10/2023	Final Version

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Definitions

- **Participants** of the PROMISE Consortium are referred to herein according to the following acronyms:
  1. **UEDIN**. The University of Edinburgh (United Kingdom)
  2. **UMCU**. Universitair Medisch Centrum Utrecht (Netherlands)
  3. **UA**. Universiteit Antwerpen (Belgium)
  4. **Imperial**. Imperial College of Science, Technology and Medicine (United Kingdom)
  5. **UOXF**. The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom)
  6. **THL**. Terveyden Ja Hyvinvoinnin Laitos (Finland)
  7. **RIVM**. Rijksinstituut voor Volksgezondheid en Milieu (Netherlands)
  8. **NIVEL**. Stichting Nedelands Instituut voor Onderzoek van de Gezondheidzorg (Netherlands)
  9. **TUCH**. Varsinais-Suomen Sairaanhoitopiirin Kuntayhtymä (Finland)
  10. **TEAMIT**. TEAM IT Research, S.L. (Spain)
  11. **ReSViNET**. Stichting Resvinet (Netherlands)
  12. **SSI**. Statens Serum Institut (Denmark)
  13. **SERGAS**. Servizo Galego de Saúde (Spain)
  14. **PENTA**. Fondazione PENTA - For the treatment and care of children with HIV and related diseases - ONLUS (Italy)
  15. **FISABIO**. Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (Spain)
  16. **MLU**. Martin-Luther-Universitaet Halle-Wittenberg (Germany)
  17. **SP**. Sanofi Pasteur, S.A. (France)
  18. **GSK**. GlaxoSmithKline Biologicals, S.A. (Belgium)
  19. **JANSSEN**. Janssen Pharmaceutica, N.V. (Belgium)
  20. **Novavax**. Novavax, Inc. (United States)
  21. **Pfizer**. Pfizer Limited (United Kingdom)
  22. **AZ**. AstraZeneca AB (Sweden)

- **Grant Agreement**. (including its annexes and any amendments) The agreement signed between the beneficiaries of the action and the IMI2 JU for the undertaking of the PROMISE project (Grant Agreement No. 101034339).
- **Project**. The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan**. Schedule of tasks, deliverables, efforts, dates, and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium**. The PROMISE Consortium, comprising the above-mentioned participants.
- **Consortium Agreement**. The agreement concluded amongst PROMISE participants for the implementation of the Grant Agreement. The agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Abbreviations

Acronym / Abbreviation	Meaning
UMC Utrecht	University Medical Center Utrecht
WP	Work Package
IRB	Institutional Review Board

Publishable summary

PROMISE Work Package (WP) 3 (clinical validation studies) includes 2 clinical studies which aim to generate data in children. Data collection and analysis of results of both studies are currently ongoing.

Study 1 is the PROMISE follow-up study consisting of extended follow-up of eligible infants of the RESCEU infant cohort study and the RESCEU infant case-control study with the aim to evaluate the incidence of asthma/wheeze at the age of 6 years in relation to RSV infection of different severity levels. The RESCEU infant cohort study was a multicentre, prospective, observational birth cohort study which recruited over 9000 healthy infants in the Netherlands, England, Scotland, Finland and Spain between 2017 and 2020. The study is registered with ClinicalTrials.gov, NCT03627572. The RESCEU case-control study was conducted in the Netherlands, England and Spain and aimed to recruit infants <12 months old with RSV infection and controls, who are otherwise healthy infants <12 months old without RSV infection.

Study 2 is the PROMISE case-control biomarker validation study and is conducted at UMC Utrecht. This study aims to validate the biomarkers found in the RESCEU infant studies and to validate a new severity score developed by WP1.

For both studies follow-up and data generation is still ongoing and will continue until (or beyond) the PROMISE project end date (i.e., 30 April 2024). Results/(meta)data of these studies will be made accessible according to the FAIR (Findable, Accessible, Interoperable and Reusable) principles, either as an addition to the RESCEU Elixir LU platform/repository which is used for the RESCEU clinical studies or on another reliable repository. This will be done together with or following publication of the manuscripts describing the main results of both PROMISE clinical studies in 2024-2025.

1. Introduction

WP3 includes 2 clinical studies which will generate data and results. Data collection and analysis of results of both studies are currently ongoing.

Study 1 PROMISE follow-up study
The PROMISE follow-up study aims to evaluate asthma/wheeze at school age in relation to RSV infection of different severity levels. Parents of children of the RESCEU infant cohort and infant case-control study, who are already participating in the 2- and 3-year follow-up will be asked to continue follow-up until school age (age 6 years) with yearly questionnaires. The RESCEU infant cohort study was a multicenter, prospective, observational birth cohort study which recruited over 9000 healthy infants in the Netherlands, England, Scotland, Finland and Spain between 2017 and 2020. The study is registered with ClinicalTrials.gov, NCT03627572. The RESCEU case-control study was conducted in the Netherlands, England and Spain and aimed to recruit infants <12 months old with RSV infection of different severity and controls, who are otherwise healthy infants <12 months old without RSV infection.

Study 2 PROMISE infant case-control validation study
In this validation study biomarkers identified from the RESCEU infant case-control study will be validated. We will also validate a new severity score which is being developed by WP1. This study maintains a similar design to the RESCEU infant case-control study.

2. Methods

Study 1 PROMISE follow-up study
Parents of children of the RESCEU infant cohort and infant case-control study, who are already participating in the 2- and 3-year follow-up (around 1500 participants) are asked to continue follow-up until school age (age 6 years) with yearly questionnaires. The 4-, 5- and 6-year questionnaires have been built in Castor electronic data capture (EDC), a GCP-compliant electronic EDC system. Baseline data and data about the first 3 years is available through the RESCEU studies, for which a database is available.

Study 2 PROMISE infant case-control validation study
The case-control validation study is being conducted at UMC Utrecht (monocenter) and provides biological samples for the PROMISE biobank (for analysis in WP3 and WP4) with the aim to validate biomarkers of severe disease and of sequelae in infants after RSV infection identified in the RESCEU case-control study. This study is also used to validate a new severity score, which has been developed by WP1. The study design is similar to the RESCEU case-control study allowing comparison of clinical data and results of both studies.

We have collected biological samples and clinical information from 102 previously healthy infants (<1 year of age) sub-divided into the following groups:

- Hospitalized, ventilated infants with RSV infection (N=22)
- Hospitalized, non-ventilated infants with RSV infection (N=24)
- Medically attended, non-hospitalized infants with RSV infection (N=27)
- Healthy infants without respiratory tract infection (N=29)

Clinical data are collected through a GCP-compliant EDC system (Castor EDC).

3. Results

Clinical data collection for both studies is being done in Castor EDC, a GCP-compliant EDC system to guarantee correct, complete and consistent data collection. Web-based case report forms have been developed and implemented on the EDC system.

Clinical and biomarker data from the RESCEU infant cohort and infant case-control studies are in the process of being stored on the Elixir LU platform. Elixir LU provides secure storage of the data on their platform, secure data transfer channels, storage of metadata of the datasets in a Data Registry to further improve findability of the data and basic curation of the Data. In addition they will provide management of the Data Access Committee and allow accepted users to access the Data from the Luxembourg ELIXIR Platform.

For the PROMISE follow-up study the aim is to add the data on the same platform and, if possible, integrate them on an individual level with the RESCEU data in order to have all information in one database. If this is not possible, (meta)data will be made available according to the FAIR principles on a trusted and well-suited repository (e.g. Dataverse). Data collection for the PROMISE follow-up study is still ongoing and is expected to continue until (and possibly beyond) the end date of PROMISE (i.e., 30 April 2024).

For the PROMISE infant case-control validation study we will look at the possibilities to integrate the clinical data with the clinical data from the RESCEU case-control study (the study set-up and questionnaires have been built in a similar way in both studies). Clinical and biomarker data for the RESCEU case-control study are in the process of being stored on the Elixir platform. If integration of clinical data of both studies is not feasible, (meta)data will be made available according to the FAIR principles on a trusted and well-suited repository (e.g. Dataverse). Data collection for the PROMISE case-control study is still ongoing and is expected to continue until (and possibly beyond) the end date of PROMISE (i.e., 30 April 2024).

Results/(Meta)data will be made available together with or following publication of the manuscripts describing the main outcomes of the PROMISE clinical studies in 2024-2025.

4. Conclusion and next steps

Results/(meta)data of both clinical studies of WP3 will be made accessible according to the FAIR principles, either as an addition to the RESCEU Elixir LU platform/repository or on another reliable repository. This will be done together with or following publication of the manuscripts describing the main results of the PROMISE clinical studies in 2024-2025.