Trial Description

Title

PROVID-CAPSyS - Systems Medicine of COVID-19, extension Study on PROVID-PROGRESS

Trial Acronym

PROVID-CAPSyS

URL of the trial

https://www.capsys.imise.uni-leipzig.de/index.jsp
https://www.gesundheitsforschung-bmbf.de/de/provid-klinische-molekulare-und-funktionelle-biomarker-fur-prognose-pathomechanismen-und-11690.php

Brief Summary in Lay Language

In the PROVID-CAPSyS study, which is part of the collaborative project CAPSyS (Systems Medicine of Community-Acquired Pneumonia), the course of disease of hospitalized patients infected with the SARS-CoV-2 virus is observed when these patients already require ventilation, i.e. when they have a severe course of COVID-19 disease. The clinical data thus obtained and the molecular parameters measured from biomaterials collected from these patients complement the data obtained in the PROVID-PROGRESS and PROVID-CAPNETZ studies from patients with mostly milder courses of COVID-19 disease. This allows to gain a comprehensive systems medicine understanding of the course of COVID-19 disease and thus to support the development of new prevention and therapy approaches. Our systems medicine approach rests on three pillars:
1) Establishment of the PROVID-CAPSyS cohort of ventilator-dependent patients with severe disease courses, complementing the PROVID-CAPNETZ and PROVID-PROGRESS cohorts with patients primarily in normal wards, to contribute to a comprehensive characterization of different severe disease courses.
2) Conduct targeted interventional animal experiments analogous to our work in pneumococcal pneumonia to establish a detailed data base for mechanistic models; and
3) biomathematical modeling of the disease starting from epidemiological models to describe the disease course of hospitalized patients to models of endothelial barrier failure, corresponding systemic effects and potential novel therapeutic approaches.

Brief Summary in Scientific Language

To improve clinical management of COVID-19 and its complications, there is an urgent need for clinical (e.g. scoring systems) and molecular (e.g. biomarkers) predictors of COVID-19 progression as well as better understanding of disease mechanisms leading to new therapeutic targets. Host- and virus-dependent mechanisms associated with the clinical appearance of COVID-19 are not yet well understood. In the PROVID-CAPSyS study, which is part of the collaborative project CAPSyS (Systems Medicine of Community-Acquired Pneumonia), the course of disease of hospitalized patients infected with the SARS-CoV-2 virus is

observed in a severe phase, i. e. when these patients already require ventilation. Clinical data thus obtained and the molecular parameters (transcriptome, proteome, cytokines, clinical biomarkers) measured from biomaterials collected from these patients complement the data obtained in the PROVID-PROGRESS and PROVID-CAPNETZ studies from patients with mostly milder courses of COVID-19. Systematic biostatistical analysis and mathematical modelling will allow to gain a comprehensive systems medicine understanding of the course of COVID-19 and thus to support the development of new prevention and therapy approaches. Our systems medicine approach rests on three pillars:
1) Establishment of the PROVID-CAPSyS cohort of ventilator-dependent patients with severe disease courses, complementing the PROVID-CAPNETZ and PROVID-PROGRESS cohorts with patients primarily in normal wards, to contribute to a comprehensive characterization of different severe disease courses.
2) Conduct targeted interventional animal experiments analogous to our work in pneumococcal pneumonia to establish a detailed data base for mechanistic models; and
3) biomathematical modeling of the disease starting from epidemiological models to describe the disease course of hospitalized patients to models of endothelial barrier failure, corresponding systemic effects and potential novel therapeutic approaches.

Do you plan to share individual participant data with other researchers?

Yes

Description IPD sharing plan

De-identified individual-level participant data along with the study protocol will be made available for qualified research on respiratory tract infections and immunology as defined by informed consent given by patients. Researchers may send a short research proposal for approval by the PROVID Board via progress-study-group@imise.uni-leipzig.de. A data access and use agreement needs to be signed. Provided data may be used only for approved purposes and for the duration agreed upon in the data access and use agreement. Data use applications will be accepted by the CAPSyS board after the study has finished and data quality has been assured.

Organizational Data

- DRKS-ID: **DRKS00023389**
- Date of Registration in DRKS: **2021/01/29**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2020-911-f-S , Ethik-Kommission der Ärztekammer Westfalen-Lippe und der med. Fakultät der Westfälischen Wilhelms-Universität Münster**

Secondary IDs

- Other Secondary-ID: **DRKS00023277 (DRKS)**

Health condition or Problem studied

- ICD10: **U07.1 - Emergency use of U07.1**
- ICD10: **J12 - Viral pneumonia, not elsewhere classified**
- ICD10: **J13 - Pneumonia due to Streptococcus pneumoniae**
- ICD10: **J14 - Pneumonia due to Haemophilus influenzae**
- ICD10: **J15 - Bacterial pneumonia, not elsewhere classified**
- ICD10: **J16 - Pneumonia due to other infectious organisms, not elsewhere classified**
- ICD10: **J17 - Pneumonia in diseases classified elsewhere**
- ICD10: **J18 - Pneumonia, organism unspecified**
- MedDRA: **10084268**
- MedDRA: **10084272**

Interventions/Observational Groups

- Arm 1: <style fontName='DejaVu Sans' isBold='true'>The PROVID-CAPSyS study will include adult hospitalized patients with SARS-CoV-2 infection / COVID-19 with severe course and ventilation. The PROVID-CAPSyS target of N=60 evaluable patients is in addition to the PROVID-PROGRESS planned case number of N=200 patients.
  The baseline study protocol for the PROVID-CAPSyS study is the PROVID-PROGRESS protocol (DRKS00023277). Enrolment, baseline documentation, documentation on study visit days, COVID-19 specific documentation, and follow-up interviews are also described in the PROVID-PROGRESS protocol, as is the asservation of nasopharyngeal swab blood samples.
  Extensive data on pre-existing conditions will be collected at baseline. On the day of inclusion (day 0) and on study visit days 1-7 and 13 - or at discharge if this occurs before day 6 or day 13 after inclusion - routine laboratory values, score-relevant data, concomitant medication and microbiological findings are documented.
  Upon patient discharge, additional information on the patient's whereabouts is collected. Should the patient die, the date and cause of death are documented.
  On days 28, 180 and 360 after inclusion in the study, a follow-up survey is conducted with special attention to the patient's living conditions and quality of life (EuroQol Health Questionnaire EQ-5D-3L), health-related events such as stroke or myocardial infarction, and vital status. If the patient is not available for the follow-up interviews, the enrolling study center will attempt to determine the current contact data or vital status via relatives, the family physician or, if necessary, via data from the population registration offices or other governmental registers, provided that appropriate consent has been obtained.
  On study visit days 0, 1-4, 6, and 13, 4 blood samples (P100 EDTA plasma, citrate plasma, serum, and PAXgene RNA) will be collected. A DNA sample (EDTA whole blood) will be collected once at any time.
  A nasopharyngeal swab will be obtained on day 0, 3 and 6. Tracheal secretions will be obtained at inclusion and on visit days 3 & 6.
  The PROVID-CAPSyS supplemental protocol comes into effect no earlier than the day ventilation is initiated, assuming appropriate consent. This is then supplemented by the

collection of morning urine on study visit days with blood sampling after study visit day 1 and a bronchoscopy within 6-8 hours of ventilator initiation with asservation of a bronchial aspirate, as far as this is judged feasible by the attending physician, for obtaining a microbiological diagnosis or characterization of the microbiome. In patients who are not (or no longer) ventilated, the collection of sputum may be considered as an alternative. If hemodynamic monitoring using the PiCCO™ system is performed as part of the patient's treatment, the results, especially on extravascular lung water, are documented on days 0-7 (basic documentation, rounds 1-7), as are the current ventilation parameters and central venous oxygen saturation and central venous pressure. Medication administration, especially the need for use of catecholamines, and volume administration are documented daily. Special features such as renal replacement therapy or extrapulmonary oxygenation are also documented in the eCRF.</style>

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Other**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Prognosis**
- Assignment: **Other**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

death

Secondary Outcome

Length of hospitalization
length of ICU treatment
length of mechanical ventilation
organ involvement (complications)
long-term effects
changes in quality of life

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Universitätsklinikum Münster, Münster**
- University Medical Center **Charité - Universitätsmedizin Berlin, Berlin**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2021/03/10**
- Target Sample Size: **60**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Positive detection of SARS-CoV-2-virus, ventilation (invasive, non-invasive, high-flow, ECMO), informed consent

Exclusion criteria

Patient participation in PROVID-CAPNETZ, PROVID-PROGRESS or PROVID-CAPSyS at an earlier time, simultaneous participation in PROVID-CAPNETZ, pregnancy, breast feeding, active tuberculosis

Addresses

■ **Primary Sponsor**

Charité – Universitätsmedizin Berlin, Med. Klinik m. S. Infektiologie und Pneumologie und Arbeitsbereich pulmonale Inflammation
Mr. Prof. Dr. med. Norbert Suttorp
Charitéplatz 1
10117 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **norbert.suttorp at charite.de**
URL: **www.charite.de**

■ **Contact for Scientific Queries**

Universität Leipzig, Institut für Medizinische Informatik, Statistik und Epidemiologie
Mr. Prof. Dr. rer. nat. Markus Scholz
Härtelstr. 16-18
04107 Leipzig
Germany

Telephone: **+49(341)9716100**
Fax: **+49(341)9716109**
E-mail: **markus.scholz at imise.uni-leipzig.de**
URL: **https://www.imise.uni-leipzig.de/homepage**

■ **Contact for Public Queries**

Charité - Universitätsmedizin BerlinMedizinische Klinik mit Schwerpunkt Infektiologie und Pneumologie
Ms. Dr. med. Agata Mikolajewska
Campus Virchow-Klinikum, Augustenburger Platz 1
13353 Berlin
Germany

Telephone: **+49 30 450 653559**
Fax: **+49 30 450 7565935**
E-mail: **agata.mikolajewska at charite.de**
URL: **https://infektiologie-pneumologie.charite.de/**

Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

  BMBF/DLR-Projektträger
  Heinrich-Konen-Str. 1
  53227 Bonn
  Germany

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruting started": **[---]***
- Reason, if Reason for Recruiting Stop "Other": **[---]***
- Study Closing (LPLV): **[---]***
- Number of Participants in Germany after Recruiting complete: **[---]***
- Total Number of Participants (all Sites worldwide) after Recruiting complete: **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*