Trial Description

Title

Clinical, molecular and functional biomarkers for PROgnosis, pathomechanisms and treatment strategies of COVID-19 (PROVID) - (PROVID-PROGRESS)

Trial Acronym

PROVID-PROGRESS

URL of the trial

https://www.gesundheitsforschung-bmbf.de/de/provid-klinische-molekulare-und-funktionelle-biomarker-fur-prognose-pathomechanismen-und-11690.php

Brief Summary in Lay Language

The pandemic triggered by the new virus SARS-CoV-2 presents the German and international health systems with previously unknown challenges. There are currently no effective specific therapies for the treatment of the lung disease COVID-19 caused by this virus. The effects of infection with SARS-CoV-2 range from symptomless to typical upper respiratory tract infections, which may result in pneumonia, which in turn may result in failure of the lungs and other organs, associated with high mortality.
The aim of the joint project PROVID is to contribute to better outcome prediction for COVID-19 patients, to better clinical management, and to the development of new therapies. To this end, we will collect detailed data of on the course of COVID-19 patients and deeply characterize them at the molecular level. We also aim to identify compounds with the potential to improve outcome.
Patient recruitment for the PROVID study is supported by three well-established clinical research platforms: CAPNETZ (competence network CAP, since 2002, world's largest database and biobank for CAP), PROGRESS (Pneumonia Research Network on Genetic Resistance and Susceptibility for the Evolution of Severe Sepsis, since 2007) and CAPSyS (Systems Medicine of Community-Acquired Pneumonia, since 2014). Through these platforms, patients will be recruited into three separate patient cohorts (PROVID-CAPNETZ, PROVID-PROGRESS, PROVID-CAPSyS). Data and biomaterials will be jointly analyzed to reach the envisaged aims.

Brief Summary in Scientific Language

Infections with the novel Severe Acute Respiratory Syndrome - Coronavirus-2 (SARS-CoV-2) manifest with a broad spectrum of clinical presentations ranging from asymptomatic infections, upper respiratory tract infections with mild symptoms, and uncomplicated pneumonia to severe pneumonia with lung failure and high mortality. With more close to 40 million documented infections and more than one million deaths (as of October 19, 2020, Johns Hopkins CSSE), there still is a great need to improve the development of therapies and the clinical treatment of COVID-19. We would like to contribute to respective international efforts. Based on current data, COVID-19 associated lower respiratory tract infections and lung damage are not directly comparable to any known types of pneumonia, including

viral infections such as influenza or MERS-CoV. Therefore, specific instructions, such as guidelines defined for other forms of pneumonia (CAP), likely have to be adapted for COVID-19.
With COVID-19, severe lung damage can be associated with relative well-being. In the course of disease (several days), sudden lung failure may occur. While the lung initially shows a relatively high compliance after intubation, lung function deteriorates rapidly to severe ARDS in most patients. After intubation, patients require mechanical ventilation over a relatively long period of time (17 days on average).
To improve the clinical management of COVID-19 and its complications, there is an urgent need for clinical (e.g., scores) and molecular (e.g., biomarkers) predictors of COVID-19 progression and for new therapeutic targets. Advanced age and comorbidities have been identified as risk factors for fatal disease progression. A recent multivariate analysis confirmed that higher age, a higher Sequential Organ Failure Assessment (SOFA) score and a D-dimer concentration > 1 µg/l at hospitalization are associated with higher mortality. However, a severe course of COVID-19 is not excluded in younger and seemingly healthy patients. The course of COVID-19 currently remains unpredictable. Since SARS-CoV-2 is a new virus, host- and virus-dependent mechanisms associated with the clinical appearance of COVID-19 are not yet well understood. Therefore, PROVID aims to identify clinical and molecular predictors of COVID-19 progression and therapeutic targets to improve the clinical management of COVID-19 patients. Specific objectives are:
1) Analysis of established clinical pneumonia and sepsis scores and biomarkers/molecular signatures to predict COVID-19 disease progression,
2) Identification of host factors (RNA, proteins, antibodies) determining the severity and/or course of COVID-19,
3) Analysis of barrier-destabilizing plasma mediators in COVID-19 and evaluation of barrier-stabilizing candidate substances,
4) Comparison of COVID-19 phenotypes, from uncomplicated pneumonia to ARDS, at the clinical and molecular level with CAP caused by other pathogens to improve clinical management, and
5) Analysis of variations of the SARS-CoV-2 genome and their association with specific clinical courses of COVID-19.

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

Yes

Description IPD sharing plan

Psydonomized clinical data and biomaterials that are collected within the framework of the PROVID-PROGRESS cohort are made available to the PROVID consortium for research purposes.
The results of the study are incorporated into joint publications.

Organizational Data

- DRKS-ID: **DRKS00023277**
- Date of Registration in DRKS: **2020/11/09**
- 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.: **465-2009 , Ethikkommission der Medizinischen Hochschule Hannover**

Secondary IDs

- Other Secondary-ID: **DRKS00022871 (Teilstudie)**

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**

Interventions/Observational Groups

- Arm 1: **The PROVID-PROGRESS study is being carried out as a prospective, longitudinal, multicenter observational study (case cohort study) with material reservation for genomic, transcriptomic and proteomic analyzes on adult patients with COVID-19.**

  After study inclusion, comprehensive baseline documentation of anamnestic, clinical and laboratory data is collected on the same day if possible. In addition, all parameters are collected that may be necessary to assess the severity of a COVID-19 disease (e.g. SOFA, PSI, C (U) RB-65, ATS minor criteria). Furthermore, data is collected which, according to the current state of knowledge, may be suitable for an assessment of the prognosis of the COVID-19 disease. In particular, questions are asked about known infection risks (living environment of the patient, lifestyle, previous illnesses, immune competence), the history of symptoms and tests relating to COVID-19, preexisting medication, the familial risk of infection as well as ethnicity.
  On the day of inclusion (day 0) and on study visit days 1-6 and 13 - or for

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.
On discharge of the patient, additional information about his whereabouts is collected. If the patient dies, the date and cause of death are documented.
On days 28, 180 and 360 after inclusion in the study, a follow-up survey takes place with particular attention to the living conditions and quality of life of the patient (EuroQol health questionnaire EQ-5D-3L), to health-related events such as stroke or heart attack and to the vital status. If the patient cannot be reached for the follow-up questionnaires, the including study center will attempt to determine the current contact details or vital status from relatives, the family doctor or, if necessary, from data from the residents' registration offices or other state registers, provided that consent is given.

On study visit days 0, 1-3, 6 and 13, 4 blood samples each (P100 EDTA plasma, citrate plasma, serum and PAXgene RNA) are taken. A DNA sample (EDTA whole blood) is taken once and at any time.
A nasopharynx swab is obtained on days 0, 3 and 6. If possible, sputum is obtained for inclusion and on visit day 6.

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

Severe course of disease (Necessity of treatment on intensive care unit or 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**
- AT **Austria**

Locations of Recruitment

- Medical Center **KWM Missioklinik Würzburg Mitte, Würzburg**
- University Medical Center **Universitätsklinikum Halle, Halle Saale**
- University Medical Center **Universitätsklinikum Leipzig, Leipzig**
- University Medical Center **Kepler Universitätsklinikum Linz (A), Linz (A)**
- Medical Center **Klinikum St. Georg Leipzig, Leipzig**
- University Medical Center **Charité - Universitätsmedizin Berlin, Berlin**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2021/01/20**
- Target Sample Size: **200**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

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, Informed consent signed

Exclusion criteria

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

Addresses

■ **Primary Sponsor**

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■ **Contact for Scientific Queries**

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- **Collaborator, Other Address**

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  Germany

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  Fax: **[---]***
  E-mail: **office at capnetz.de**
  URL: **http://www.capnetz.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.*