KURZPROTOKOLL
CALVID-1

Öffentlicher Titel	Phase II Studie zu Immunmodulator IMU-838 plus SOC bei COVID-19
Wissenschaftl. Titel	A Prospective, Multi-Center, Randomized, Placebo-Controlled, Double-Blinded Study to Evaluate the Efficacy, Safety and Tolerability of IMU-838 as Addition to Investigator's Choice of Standard of Care Therapy, in Patients with Coronavirus Disease 19
Kurztitel	CALVID-1
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase II
Erkrankung	Infektionen: Virusinfektionen: SARS-Cov-2
Einschlusskriterien	- Male or female patients at least 18 years old (may be extended to include also children 12 years or older after the 1st interim analysis) - Admitted to the hospital or other medical in-patient treatment facility for treatment of COVID-19 The hospitalization needs to be for medical reasons (treatment of COVID-19 disease) and cannot be for social reasons or due to housing insecurity. For US sites only: If the investigator would commonly hospitalize the patient but for healthcare resource reasons decides to treat the patient in a specially designed out-patient setting, then such patients are also allowed to enter the trial (please note that in this case the patient would be counted as clinical status category 3). The investigator then must assure that the patient has at least a twice daily assessment by qualified trial personnel and all laboratory assessments can be adequately performed as per protocol. The Sponsor reserves the right to discontinue this option via administrative letter if such assurances cannot be met by any site - SARS-CoV-2 infection confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) test in a nasopharyngeal, oropharyngeal or respiratory sample at <= 4 days before randomization - Moderate COVID-19 disease defined as fulfilling clinical status category 3 or 4 on the WHO 9-point ordinal scale [21]: a) Category 3: Hospitalized (see note above for US only), virus-positive, no oxygen therapy with the following conditions: b) The hospitalization needs to be for medical reasons (treatment of COVID-19 disease) and cannot be for social reasons or due to housing insecurity c) Category 4: Hospitalized, virus-positive, oxygen by mask or nasal prongs (excluding high-flow oxygen therapy) with the following conditions: d) Peripheral capillary oxyhemoglobin saturation (SpO2) >92% at maximum of 6 liters oxygen flow per minute e) Stable respiratory rate <= 30 breaths/min at maximum of 6 liters oxygen flow per minute - Presence of at least 1 symptom characteristic for COVID-19 disease i.e., fever, cough or respiratory distress - Willingness and ability to comply with the protocol - Written informed consent given prior to any trial-related procedure

- For women of childbearing potential: Application of a highly effective method of birth control (failure rate less than 1% per year when used consistently and correctly) together with a barrier method between trial consent and 30 days after the last intake of the IMP. Highly effective forms of birth control are those with a failure rate less than 1% per year and include: a) oral, intravaginal, or transdermal combined (estrogen and progestogen containing) hormonal contraceptives associated with inhibition of ovulation b) oral, injectable, or implantable progestogen-only hormonal contraceptives associated with inhibition of ovulation c) intrauterine device or intrauterine hormone-releasing system d) bilateral tubal occlusion e) vasectomized partner (i.e., the patient's male partner underwent effective surgical sterilization before the female patient entered the clinical trial and is the sole sexual partner of the female patient during the clinical trial) f) sexual abstinence (acceptable only if it is the patient's usual form of birth control/lifestyle choice; periodic abstinence [e.g., calendar, ovulation, symptothermal, postovulation methods] and withdrawal are no acceptable methods of contraception) Barrier methods of contraception include: a) Condom b) Occlusive cap (diaphragm or cervical/vault caps) with spermicidal gel/film/cream/suppository
- Male patients must agree not to father a child or to donate sperm starting at Screening, throughout the clinical trial and for 30 days after the last intake of the IMP. Male patients must also a) abstain from sexual intercourse with a female partner (acceptable only if it is the patient's usual form of birth control/lifestyle choice), or b) use adequate barrier contraception during treatment with the IMP and until at least 30 days after the last intake of the IMP, and c) if they have a female partner of childbearing potential, the partner should use a highly effective contraceptive method as outlined in inclusion criterion 8 d) if they have a pregnant partner, they must use condoms while taking the IMP to avoid exposure of the fetus to the IMP

Ausschlusskriterien

- Involvement in the trial is not in the patient's best interest according to the investigator's decision, including the presence of any condition that would, in the assessment of the investigator, not allow the protocol to be followed safely Note: The investigator should particularly consider exclusion of patients at increased risk for serious or fatal AEs in case of worsening of the pulmonary perfusion. This includes, but is not limited to, pre-existing pulmonary hypertension, severe chronic respiratory disease, severely increased risk for thromboembolic complications and moderate to severe left ventricular ejection fraction (LVEF) dysfunction. In addition, other known risk factors of highest risk of mortality in COVID-19 patients should be considered
- Presence of respiratory failure, shock, and/or combined failure of other organs that requires ICU monitoring in the near foreseeable future
- Critical patients whose expected survival time <48-72 hours
- Presence of the following laboratory values at screening: a) White blood cell count (WBC) <1.0 x 109/L b) Platelet count <100,000/mm^3 (<100 x 109/L) c) Total bilirubin>2 x ULN d) Alanine aminotransferase (ALT) or gamma glutamyl transferase (GGT) >5 x ULN
- Participation in any other interventional clinical trial
- Hospitalization primarily for other reasons than COVID-19 (including primarily for concomitant conditions during ongoing SARS-CoV-2 infection)
- Anticipated transport to a different hospital or institution, in particular when such transport is anticipated for pending ECMO or RRT treatment
- Clinical suspicion of a bacterial superinfection at Screening IMP-related exclusion criteria
- Patients who cannot take drugs orally
- Allergic or hypersensitive to the IMP or any of the ingredients

	- Use of the following concomitant medications is prohibited from Screening to end of treatment with IMP in this trial (up to Day 14) if not indicated otherwise in this protocol: a) Concurrent use of any mycophenolate mofetil or of methotrexate exceeding 17.5 mg weekly b) Any medication known to significantly increase urinary elimination of uric acid, in particular lesinurad (Zurampic™) as well as uricosuric drugs such as probenecid c) Current treatments for any malignancy, in particular irinotecan, paclitaxel, tretinoin, bosutinib, sorafenib, enasidenib, erlotinib, regorafenib, pazopanib and nilotinib d) Any drug significantly restricting water diuresis, in particular vasopressin and vasopressin analogs e) Use of rosuvastatin at daily doses higher than 10 mg f) Arbidol and Colchicine g) Any use of other DHODH inhibitors, including teriflunomide (Aubagio™) or leflunomide (Arava™) h) Chloroquine and Hydroxychloroquine during the entire trial unless taken for indicated use before entering the trial - Use of any investigational product within 8 weeks or 5x the respective half-life before the date of informed consent, whichever is longer, and throughout the duration of the trial General exclusion criteria - Patients who have a "do not intubate" or "do not resuscitate" order (unless the patient waives in writing this order and will allow intubation for the duration of the trial period) - Patients with end-stage liver disease (Child Pugh C score) - History or presence of serious or acute heart disease such as uncontrolled cardiac dysrhythmia or arrhythmia, uncontrolled angina pectoris, cardiomyopathy, or uncontrolled congestive heart failure (New York Heart Association [NYHA] class 3 or 4) Note: NYHA class 3: Cardiac disease resulting in marked limitation of physical activity. Patients are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain. NYHA class 4: Cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased - Legal incapacity, limited legal capacity, or any other condition that makes the patient unable to provide consent for the trial - Pregnant or breastfeeding - An employee of an investigator or Sponsor or an immediate relative of an investigator or Sponsor - Patients institutionalized due to judicial order
Alter	18 Jahre und älter
Prüfzentren	**Innere Medizin 2** (Geschlossen) Infektiologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Franziska Ebeling
Sponsor	Immunic AG
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT04379271 (primäres Register) EudraCT 2020-001264-28