ImmunONCOVID-20 - A prospective, controlled, randomized, multicenter study of the efficacy of an autophagy inhibitor (GNS561), an anti-NKG2A (monalizumab) and an anti-C5aR (avdoralimab) compared to the standard of care in patients with advanced or metastatic cancer and SARS-CoV-2 (COVID-19) infection.

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General

Identification

Detailed name	A prospective, controlled, randomized, multicenter study of the efficacy of an autophagy inhibitor (GNS561), an anti-NKG2A (monalizumab) and an anti-C5aR (avdoralimab) compared to the standard of care in patients with advanced or metastatic cancer and SARS-CoV-2 (COVID-19) infection.
Sign or acronym	ImmunONCOVID-20
CNIL registration number, number and date of CPP agreement, AFSSAPS (French Health Products Safety Agency) authorisation	EudraCT : 2020-001373-70 - Sponsor ID: ET20-076

General Aspects

Medical area	Cancer research
Study in connection with Covid-19	Yes
Pathology (details)	Any type of primary tumors
Health determinants	Medicine

Scientific investigator(s) (Contact)

Name of the director	AVRILLON
Surname	Virginie
Organization	Centre Léon Bérard

Collaborations

Participation in projects, networks and consortia	Yes
Details	Banque Publique d'Investissement
Others	Innate Pharma - Assistance Publique des Hôpitaux de Marseille

Funding

Funding status	Public
Details	Banque Publique d'Investissement

Governance of the database

Sponsor(s) or organisation(s) responsible	Centre Léon Bérard
Organisation status	Private
Presence of scientific or steering committees	Yes

Additional contact

Main features

Type of database

Type of database	Others
Specify	Clinical database
Database recruitment is carried out by an intermediary	A selection of health institutions and services
Database recruitment is is made on the basis of:	Another treatment or procedure
Database recruitment is carried out as part of an interventional study	Yes
Details	Performed at individual level
Additional information regarding sample selection.	This is a muticenter clinical program including a staging phase and 2 different therapeutic cohorts according to the patient's level of symtoms. Patients with mild symtoms of COVID-19 will be included in cohort 1; patients with moderate or severe symtoms will be included in cohort 2.

	A total of 219 patients will be included in the IMMUNONCOVID-20 program. In cohort 1 randomization will be stratified on patient age (<70 vs. ?70 years old) and in cohort 2 on the basis of respiratory support methods at the time of enrollment: hospitalization associated or not with oxygen support with nasal duct or mask (<5 on the WHO-ISARIC seven-category ordinal scale) versus non-invasive mechanical ventilation or high flow oxygen therapy or invasive mechanical ventilation (?5 on the WHO-ISARIC seven-category ordinal scale). In the experimental arms of cohort 1, patients will be treated either with oral GNS561 during 10 consecutive days, or with a single intravenous administration of monalizumab. In the experimental arm of cohort 2, patients will be treated with intravenous administration of avdoralimab during 14 days. In patients from cohort 1, the anticancer treatment may be continued (as per investigator's decision). In patients from cohort 2, anticancer treatment must be temporarily interrupted before randomization and at least up to 28 days after the date of randomization. In both cohorts, patients will be followed-up continuously until the hospitalization discharge and then weekly for a minimum period of 28 days after the randomization. After this 28-day follow-up visit, respiratory symptoms and treatment-emergent averse events will be collected weekly in the clinical database for 1 additional month and then at 3 months and 6 months after the date of randomization. In each cohort, the data cut-off will be 2 months after the last randomization. All efficacy analyses will be performed on the intent-to-treat populations. The end of the study will be defined as the 6-month follow-up visit of the last patient randomized. Vital status will be updated once for all patients at the end of the study. The steering committee will be composed of the coordinating and associated investigators, representatives of the coordinating center (medical monitor, statistician, and project manager) and principal investigators of the participating sites.
Database objective	
Main objective	The main objective is to compare versus standard of care short-term mortality rates in advanced or metastatic cancer patients who are positive for COVID-19 treated with an autophagy inhibitor

	(GNS561), an anti-NKG2A (monalizumab) or an anti-C5aR (avdoralimab). The primary endpoint will be the 28-day survival rate, defined by the proportion of patients still alive 28 days after randomization. The 28-day survival rate will be described in each arm of each cohort.
Inclusion criteria	Inclusion criteria I1. Age 18 or older at the time of enrolment for women and age 60 or older at the time of enrolment for men. I2. Histologically or cytologically confirmed diagnosis of advanced or metastatic hematological or solid tumor (hematological or solid tumor, any type and any localization). I3. Documented diagnosis of COVID-19 (diagnostic test performed in a certified laboratory) without indication of transfer in a rescucitation unit. . Nota Bene : A maximum time of 7 days may have elapsed between the date of first symptoms and the date of consent for patient cohort 1 (mild). In cohort 2 (severe), up to 10 days may have elapsed since the first symptoms. I4. Cohort 2: patients with pneumonia confirmed by chest imaging, and an oxygen saturation (Sao2) of 94% or less while they are breathing ambient air or a ratio of the partial pressure of oxygen (Pao2) to the fraction of inspired oxygen (Fio2) (Pao2:Fio2) at or below 300 mg Hg. I5. Multidisciplinary approach that patient is not eligible for a transfer to Resuscitation Unit (either due to underlying medical condition ? including cancer ? or due to lack of available bed). Note: Item cancelled (addendum 2 ? October 2020) I6. Life-expectancy longer than 3 months. I7. Adequate bone marrow and end-organ function defined by the following laboratory results: ? Bone marrow: - Hemoglobin ? 9.0 g/dL, - Absolute Neutrophils Count (ANC) ? 1.0 Gi/L, - Platelets ? 100 Gi/L; ? Hepatic function: - Total serum bilirubin ? 1.5 x ULN (except patients with Gilbert's syndrome who must have total serum bilirubin ? 3.0 x ULN), - AST and ALT ? 5 ULN ? Renal function: - Serum creatinine ? 2.0 x ULN or Cr. Cl. ? 30ml/min/1.73m² (MDRD or CKD-EPI formula); I8. Willingness and ability to comply with the study requirements; I9. Signed and dated informed consent indicating

that the patient has been informed of all the aspects of the trial prior to enrollment (in case of emergency situation, please refer to protocol section 12.1 PATIENT INFORMATION AND INFORMED CONSENT);
I10. Women of childbearing potential (Appendix 1) are required to have a negative serum pregnancy test within 72 hours prior to study treatment start. A positive urine test must be confirmed by a serum pregnancy test;
I11. Women of childbearing potential and male patients must agree to use adequate highly effective contraception (Appendix 1) for the duration of study participation and up to 6 months following completion of therapy;
I12. Patient must be covered by a medical insurance.

Non-inclusion criteria
E1. For cohort 1 only : Patient currently receiving therapy with an anti-NKG2A.
E2. For cohort 2 only: Patient currently receiving therapy with an anti-C5aR.
E3. Contraindication to treatment with monalizumab (cohort 1 only) or avdoralimab (cohort 2 only) as per respective IB, including known hypersensitivity to one of these study drugs or severe hypersensitivity reaction to any monoclonal antibody.
E4. For cohort 1 only : Patient known to have intolerance or hypersensitivity to chloroquine or any quinoline derivates (quinine, chloroquine, tafenoquine, hydroxychloroquine, mefloquine). Patients previously exposed to CQ, HCQ or other quinoline derivates should have interrupted their treatment at least 72h prior to randomization.
E5. Patient has active autoimmune disease that has required systemic treatment in the past 3 months before the date of randomisation or a documented history of clinically severe autoimmune disease, or a syndrome that requires systemic steroids at doses higher than 10 mg/d prednisone equivalents or immunosuppressive agents.
a. Note 1: Patients with vitiligo or resolved childhood asthma/atopy would be an exception to this rule. Patients that require intermittent use of bronchodilators or local steroid injections would not be excluded from the study. Patients with hypothyroidism stable on hormone replacement or Sjögren's syndrome will not be excluded from the study.
b. Note 2: Patients may receive corticosteroids as required for the management of SARS-CoV-2-

related symptoms.
E6. Patient requires the use of one of the following forbidden treatment during the study treatment period, including but not limited to :
? Major surgery.
? Live vaccines. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, chicken pox, yellow fever and BCG. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however intranasal influenza vaccines (e.g. Flu-Mist®) are live attenuated vaccines, and are not allowed.
E7. Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction within 3 months prior to the date of randomisation unstable arrhythmias or unstable angina, Known Left Ventricular Ejection Fraction (LVEF) < 50%.
a. Note: Patients with known coronary artery disease, congestive heart failure not meeting the above criteria must be on a stable medical regimen that is optimized in the opinion of the treating physician and in consultation with a cardiologist if appropriate.
E8. Patient has known active hepatitis B (chronic or acute; defined as having a positive hepatitis B surface antigen [HBsAg] test at screening), known active hepatitis C (Patients positive for hepatitis C virus (HCV) antibody are eligible only if PCR is negative for HCV RNA at screening) or known Human Immunodeficiency Virus (HIV) infection (HIV 1/2 antibodies).
E9. Prior allogeneic bone marrow transplantation or solid organ transplant in the past.
E10. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject's participation for the full duration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating Investigator.
E11. Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
E12. Pregnant or breastfeeding patient, or expecting to conceive children within the projected duration of the trial, starting with the screening visit through 6 months after the last dose of study drugs.

Population type

Age	Adulthood (19 to 24 years) Adulthood (25 to 44 years) Adulthood (45 to 64 years) Elderly (65 to 79 years) Great age (80 years and more)
Population covered	Sick population
Pathology	C00-C97 - Malignant neoplasms
Gender	Male Woman
Geography area	National
Detail of the geography area	France

Data collection

Dates

Date of first collection (YYYY or MM/YYYY)	2020
Date of last collection (YYYY or MM/YYYY)	2021

Size of the database

Size of the database (number of individuals)	< 500 individuals
Details of the number of individuals	219 expected

Data

Database activity	Current data collection
Type of data collected	Clinical data Biological data Cost data
Clinical data (detail)	Direct physical measures Medical registration
Details of collected clinical data	Medical and cancer history, COVID-19 history (diagnosis and symptoms), study treatments exposure, efficacy and safety data
Presence of a biobank	Yes

Contents of biobank	Plasma Blood cells isolated
Health parameters studied	Health event/morbidity Health event/mortality Health care consumption and services Quality of life/health perception
Care consumption (detail)	Hospitalization Medical/paramedical consultation Medicines consumption

Procedures

Data collection method	Electronic Case Report Form
Quality procedure(s) used	Remote and on-site monitoring
Participant monitoring	Yes
Monitoring procedures	Monitoring by contact with the participant (mail, e-mail, telephone etc.) Monitoring by convocation of the participant Monitoring by contact with the referring doctor
Details on monitoring of participants	Daily follow-up dring the hospitalisation period then weekly until 2 months after study treamtents start
Followed pathology	C00-C97 - Malignant neoplasms
Links to administrative sources	No

Promotion and access

Promotion

Access