Clinical Trial Protocol
Iranian Registry of Clinical Trials

20 Oct 2020

The evaluation of safety and efficacy of Pembrolizumab (CinnaGen Co, Iran) in patients with COVID-19

Protocol summary

Study aim
The evaluation of safety and efficacy of Pembrolizumab (CinnaGen Co, Iran) in patients with COVID-19

Design
This is a phase II, open-label, and single-arm study with the sample size of 62 patients.

Settings and conduct
This phase-II, single-arm, open-label, two-centered (Iran) clinical trial will be conducted in patients with COVID-19 with a follow-up duration of at least 7 days. Pembrolizumab will be administered to the eligible patients on day 1, duration of treatment of standard of care is due to physician. The outcomes will be investigated within at least 7 days.

Participants/Inclusion and exclusion criteria
Inclusion:patients aged 18 – 75 years while signing ICF, Patient with confirmed diagnosis of 2019-ncov infection, Clinical manifestation of:1- SpO2≤ 93% while resting and 2- Bilateral pulmonary involvement in radiographic results and 3- IL-6 < 7 pg/mL and 4- CRP < 50 mg/L and 5- Lymphocyte count > 800 cells/µL and 6- Ferritin < 300 µg/L, Adequate organ and marrow function Exclusion: Critical patients, hepatitis B or C, HIV or active tuberculosis, Patient with COPD and ILD, The underlying disease is very serious and the expected survival time is less than 6 months, Active hepatic disease and hepatic failure, Active or history of autoimmune disease, Patients with myocarditis, History of transplantation, Received radiotherapy and chemotherapy for malignant tumor within 6 months, Has received or will receive a live vaccine within 30 days prior to the first administration, Hypersensitivity, 90 days of retinal detachment or eye surgery, Participated in other clinical intervention trials within the last 3 months, Pregnancy and breastfeeding

Intervention groups
Intravenous pembrolizumab 200 mg in combination with standard of care

Main outcome variables
Incidence of death during the study

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20150303021315N19**
Registration date: **2020-05-27, 1399/03/07**
Registration timing: **prospective**

Last update: **2020-05-27, 1399/03/07**
Update count: **0**

Registration date
2020-05-27, 1399/03/07

Registrant information

Name
Nassim Anjidani

Name of organization / entity
Orchid Pharmed

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Iran (Islamic Republic of)

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+98 21 4347 3000

Email address
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Recruitment status
recruiting

Funding source

Expected recruitment start date
2020-06-06, 1399/03/17

Expected recruitment end date
2020-11-05, 1399/08/15

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
The evaluation of safety and efficacy of Pembrolizumab (CinnaGen Co, Iran) in patients with COVID-19

Public title
Pembrolizumab (CinnaGen Co, Iran) in COVID-19
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Male or female patients aged 18 – 75 years while signing ICF Able and willing to sign the informed consent Patient with confirmed diagnosis of 2019-ncov infection based on RT-PCR and/or radiographic results Clinical manifestation of:1- SpO2≤ 93% while resting and 2- Bilateral pulmonary involvement in radiographic results and 3- IL-6 < 7 pg/mL and 4- CRP < 50 mg/L and 5- Lymphocyte count > 800 cells/µL and 6- Ferritin < 300 µg/L Adequate organ and marrow function
Exclusion criteria:
Critical patients defined as: 1- respiratory failure which requiring mechanical ventilation or 2- Shock or 3- combined with other organ failure, need to be admitted to ICU Patients with hepatitis B or C, HIV or active tuberculosis Patient with COPD or end-stage lung disease requires home oxygen therapy Patients with interstitial lung disease (ILD) The underlying disease is very serious and the expected survival time is less than 6 months (such as advanced malignant tumor) Active hepatic disease and hepatic failure Active or history of autoimmune disease Patients with myocarditis History of organ, bone marrow or hematopoietic Stem Cell transplantation Received radiotherapy and chemotherapy for malignant tumor within 6 months Has received or will receive a live vaccine within 30 days prior to the first administration of study medication. Seasonal flu vaccines that do not contain a live virus are permitted Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-CTLA-4 antibody Is receiving systemic steroid therapy < 3 days prior to the first dose of trial treatment or receiving any other form of immunosuppressive medication Major surgery within 3 weeks before randomization Hypersensivity to pembrolizumab, standard of care or any components of the formulation 90 days of retinal detachment or eye surgery Permanent blindness in one eye, history of iritis, endophthalmitis, scleral inflammation or retinitis Participated in other clinical intervention trials within the last 3 months Pregnancy and breastfeeding The competent physician considered it inappropriate to participate in the study
Age
From **18 years** old to **70 years** old
Gender
Both

Phase
2
Groups that have been masked
No information
Sample size
Target sample size: **62**
Randomization (investigator's opinion)
N/A
Randomization description
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Single
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
National Research Institute of Tuberculosis and Lung Diseases Masih Daneshvari
Street address
Masih Daneshvari Hospital, Darabad Avenue, Shahid Bahonar roundabout, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1956944413
Approval date
2020-05-21, 1399/03/01
Ethics committee reference number
IR.SBMU.NRITLD.REC.1399.117

Health conditions studied

1

Description of health condition studied
COVID-19
ICD-10 code
U07.1
ICD-10 code description
COVID-19

Primary outcomes

1

Description
Incidence of death during the study
Timepoint
at least 7 days
Method of measurement
Recording the incidence of death

Secondary outcomes

1

Description
Days of hospitalization
Timepoint
Daily
Method of measurement
Counting the days of hospitalization

2

Description
Changing patient’s condition to critical (Critical patients defined as:1- respiratory failure which requiring mechanical ventilation or 2- Shock or 3- combined with other organ failure, need to be admitted to ICU)
Timepoint
Daily
Method of measurement
Examination and diagnosis by competent physician

3

Description
Percentage of patients with negative RT-PCR for nCoV-2019
Timepoint
Screening day, day 7 or discharge day
Method of measurement
Diagnostic kit

4

Description
Changes in percentage of SpO2 during study
Timepoint
Several times in a day
Method of measurement
Oxygen saturation test

5

Description
The lesions of the pulmonary segment numbers involved in pulmonary graphy
Timepoint
Screening day, day 7 or discharge day
Method of measurement
CT-scan or chest x-ray

6

Description
Changes in lymphocyte count
Timepoint
Daily
Method of measurement
Laboratory Test

7

Description
Changes in neutrophil count
Timepoint
Daily
Method of measurement
Laboratory Test

8

Description
Changes in CRP level
Timepoint
Daily
Method of measurement
Laboratory Test

9

Description
Peripheral edema
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

10

Description
Cardiac arrhythmia
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

11

Description
Fatigue
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

12

Description
Pain
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

13

Description
Headache
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

14

Description
Pruritus
Timepoint
In each visit by physician

Method of measurement
Clinical Evaluation

15

Description
Skin rash
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

16

Description
Vitiligo
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

17

Description
Hyperglycemia
Timepoint
Daily
Method of measurement
Laboratory test

18

Description
Hyperalbuminemia
Timepoint
every other day
Method of measurement
Laboratory test

19

Description
Hypocalcemia
Timepoint
every other day
Method of measurement
Laboratory test

20

Description
Hyponatremia
Timepoint
every other day
Method of measurement
Laboratory test

21

Description
Hypophosphatemia
Timepoint
every other day
Method of measurement
Laboratory test

22

Description
Hypocalcemia
Timepoint
every other day
Method of measurement
Laboratory test

23

Description
Hypokalemia
Timepoint
every other day
Method of measurement
Laboratory test

24

Description
Hypogycemia
Timepoint
Daily
Method of measurement
Laboratory test

25

Description
Hypercalcemia
Timepoint
every other day
Method of measurement
Laboratory test

26

Description
Hyperkalemia
Timepoint
every other day
Method of measurement
Laboratory test

27

Description
Hypothyroidism
Timepoint
Screening day, day 7 or discharge day
Method of measurement
Laboratory test

28

Description
Diarrhea
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

29

Description
Decreased appetite
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

30

Description
Constipation
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

31

Description
Abdominal pain
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

32

Description
Nausea
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

33

Description
Vomiting
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

34

Description
Urinary tract infection
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

35

Description
Hematuria
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

36

Description
Anemia
Timepoint
Daily
Method of measurement
Laboratory test

37

Description
Leukopenia
Timepoint
Daily
Method of measurement
Laboratory test

38

Description
Thrombocytopenia
Timepoint
Daily
Method of measurement
Laboratory test

39

Description
Hemorrhage
Timepoint
In each visit by physician
Method of measurement
Clinical evaluation

40

Description
Increased INR
Timepoint
every other day
Method of measurement
Laboratory test

41

Description
Prolonged partial thromboplastin time
Timepoint
every other day
Method of measurement
Laboratory test

42

Description
Increased serum alkaline phosphatase
Timepoint
every other day
Method of measurement
Laboratory test

43

Description
Increased serum alanine aminotransferase
Timepoint
every other day
Method of measurement
Laboratory test

44

Description
Increased serum aspartate aminotransferase
Timepoint
every other day
Method of measurement
Laboratory test

45

Description
Infection
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

46

Description
Masculoskeletal pain
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

47

Description
Back pain
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

48

Description
Asthenia
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

49

Description
Increased serum creatinine
Timepoint
every other day
Method of measurement
Laboratory test

50

Description
Upper respiratory tract infection
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

51

Description
Cough
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

52

Description
Dyspnea
Timepoint
In each visit by physician
Method of measurement
Clinical Evaluation

Intervention groups

1

Description
200 mg intravenous pembrolizumab (produced by CinnaGen company) single dose on day 1, in combination with standard of care during treatment
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Massih Daneshvari Hospital
Full name of responsible person
Payam Tabarsi
Street address
Darabad, Shahid Bahonar Ave,Tehran
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2

Recruitment center

Name of recruitment center
Namazi Hospital

Full name of responsible person
Alireza Rezvani

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Zand Street, Namaz Square, Shiraz, Fars, Iran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
CinnaGen Company

Full name of responsible person
Nasim Anjidani

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CinnaGen research and production Company. Simin Dasht Industrial Park, Karaj, Alborz, Iran

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Alborz

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6670337 263 98

Phone
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Email
cinnagen@cinnagen.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
CinnaGen Company

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Orchid Phramed Co.

Full name of responsible person
Nasim Anjidani

Position
Pharmacist (PharmD), Medical Manager

Latest degree
Medical doctor

Other areas of specialty/work
Medical Pharmacy

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Person responsible for scientific inquiries

Contact

Name of organization / entity
Shahid Beheshti University of Medical Sciences

Full name of responsible person
Payam Tabarsi

Position
Associate professor

Latest degree
Medical doctor

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Infectious diseases

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Person responsible for updating data

Contact

Name of organization / entity
Orchid Pharmed Co.

Full name of responsible person
Nasim Anjidani

Position

Pharm.D./Clinical trial Department Manager

Latest degree

Medical doctor

Other areas of specialty/work

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available