

Clinical Trial Protocol

Iranian Registry of Clinical Trials

30 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 Anjidanani

Name of organization / entity

Orchid Pharmed

Country

Iran (Islamic Republic of)

Phone

+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 Hypersensitivity 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

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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**

Hypoglycemia

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

Musculoskeletal 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
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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 Pharmed 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

Other areas of specialty/work

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Person responsible for updating data

Contact

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Orchid Pharmed Co.

Full name of responsible person

Nasim Anjidani

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Pharm.D./Clinical trial Department Manager

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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