A prospective randomized controlled trial comparing Sovodak (Sofosbuvir plus Daclatasvir) in participants with moderate to severe Coronavirus disease (COVID-19) compared to standard of care treatment

Protocol summary

Study aim
To evaluate whether Sovodak (Sofosbuvir plus Daclatasvir) increases significant clinical improvement as compared to standard of care in hospitalized patients with moderate to severe COVID-19.

Design
This is a parallel 2-arm randomized, controlled, double-blind, multi center study. 70 patients are enrolled and followed for 14 days.

Settings and conduct
The study will be conducted in Shariati hospital (Tehran), Baharloo (Tehran), Sina (Tehran), Sayyad Shirazi (Gorgan) by investigators of digestive disease research institute (TUMS). Radiologists, physicians who assess outcomes and the statistician analyzing the data will be blinded but the patients and physicians who treat patients will know the assigned treatment group.

Participants/inclusion and exclusion criteria
All moderate to severe COVID-19 infected patients admitted to Shariati hospital (Tehran), Baharloo (Tehran), Sina (Tehran), Sayyad Shirazi (Gorgan) Inclusion criteria: age ≥ 18y; hospitalized patients with: Fever (Oral temperature ≥ 37.8 °C) and at least one of Respiratory rate >24/min / O2Sat<94% or the Pa02/Fi02 ratio <300mgHg; PCR confirmed; diagnostic chest CT scan. Exclusion criteria: known allergic reaction to intervention drug, pregnant or breastfeeding, any prior experimental treatment for COVID-19, heart rate<60/min, taking Amiodarone, evidence of multiorgan failure, requiring mechanical ventilation at screening, eGFR< 50 mL/min

Intervention groups
70 eligible patients with moderate to severe COVID-19 in a 1:1 ratio: • Standard of care treatment • Sovodak tablet (Sofosbuvir 400mg/Daclatasvir 60mg) + Standard of care treatment

Main outcome variables
Clinical recovery (composite) within 14 days from initiation of study treatment until normalization of fever (≤37.2 °C oral), respiratory rate (≤24/minute on room air), and oxygen saturation (≥94% on room air), sustained for at least 24 hours.

General information

Reason for update
The trial was completed.

Acronym
IRCT registration information
IRCT registration number: IRCT20200128046294N2
Registration date: 2020-03-14, 1398/12/24
Registration timing: prospective

Last update: 2020-06-01, 1399/03/12
Update count: 4

Registration date
2020-03-14, 1398/12/24

Registrant information
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Anahita Sadeghi
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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2020-03-26, 1399/01/07

Expected recruitment end date
2020-06-20, 1399/03/31
Actual recruitment start date
2020-03-26, 1399/01/07

Actual recruitment end date
2020-04-26, 1399/02/07

Trial completion date
2020-05-18, 1399/02/29

Scientific title
A prospective randomized controlled trial comparing Sovodak (Sofosbuvir plus Daclatasvir) in participants with moderate to severe Coronavirus disease (COVID-19) compared to standard of care treatment

Public title
Study to Evaluate the Safety and Efficacy of Sofosbuvir/Daclatasvir in Participants with Moderate to Severe Coronavirus Disease (COVID-19)

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Both genders Age ≥18 years at time of signing Informed Consent Form Willing and able to provide written informed consent prior to performing study to any assigned treatment arm Must agree not to enroll in another study of an investigational agent prior to completion of study Will be admitted to Shariati hospital (Tehran), Baharloo (Tehran), Sina (Tehran), Sayyad Shirazi (Gorgan) and not transferred to another hospital Laboratory (RT-PCR) confirmed infection with 2019-nCoV Lung involvement confirmed with chest CT scan Hospitalized patients with: Fever (Oral temperature ≥37.8 ℃) and at least one of Respiratory rate >24/min / O2Sat<94% or the Pa02/Fi02 ratio <300mgHg ≤8 days since illness onset

Exclusion criteria:
Known allergic reaction to Sofosbuvir or Daclatasvir Pregnant or breastfeeding, or positive pregnancy test Receipt of any experimental treatment for COVID-19 prior to the time of the screening evaluation Heart rate < 60min Taking Amiodarone Evidence of multiorgan failure Requiring mechanical ventilation at screening eGFR< 50 mL/min

Age
From 18 years old

Gender
Both

Phase
3

Groups that have been masked
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: 70
Actual sample size reached: 70

Randomization (investigator's opinion)
Randomized

Randomization description
Patients will be randomized in a 1:1 ratio into one of the treatment groups and standard of care group using computer generated randomization plan. The date and time of randomization will be recorded. Allocation concealment will be done with the sealed envelope method.

Blinding (investigator's opinion)
Single blinded

Blinding description
The treatment assignment will remain unknown until the patient is randomized. Physicians who treat patients and the patients will not be blinded. Radiologists, physicians who assess outcomes and the statistician analyzing the data all will be blinded.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids
empty

Ethics committees

1

Ethics committee
Name of ethics committee
Institutional Research Ethics Committee, Vice-Chancellor in Research Affairs- Tehran University of M

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Central Building of Tehran University of Medical Sciences: No. 226, Qods St., Keshavarz Blvd., Tehran, Iran

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Approval date
2020-03-11, 1398/12/21

Ethics committee reference number
IR.TUMS.VCR.REC.1398.1035

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
Clinical recovery (composite) within 14 days from
initiation of study treatment until normalization of fever (≤37.2 °C oral), respiratory rate (≤24/minute on room air), and oxygen saturation (≥94% on room air), sustained for at least 24 hours.

**Timepoint**
daily up to 14 days after starting the trial

**Method of measurement**
Clinical examination

**Secondary outcomes**

1
**Description**
Requirement for mechanical ventilation

**Timepoint**
daily up to day 14

**Method of measurement**
Clinical evaluation

2
**Description**
Radiological changes

**Timepoint**
day 14 or sooner at the discretion of the physician

**Method of measurement**
Chest CT scan

3
**Description**
Serious adverse events

**Timepoint**
Any time during study up to day 14

**Method of measurement**
Clinical evaluation

4
**Description**
All-cause mortality

**Timepoint**
Any time during study up to day 14

**Method of measurement**
Clinical evaluation

**Intervention groups**

1
**Description**
Control group: Standard of care treatment according to the national guidelines for the treatment of COVID-19

**Category**
Treatment - Drugs

2
**Description**
Intervention group: Sovodak, Company: Rojan, Daily single oral tablet containing 400mg of Sofosbuvir and 60mg of Daclatasvir plus Standard of care treatment

**Category**
Treatment - Drugs

**Recruitment centers**

1
**Recruitment center**
Name of recruitment center
Shariati Hospital

Full name of responsible person
Dr Anahita Sadeghi

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2
**Recruitment center**
Name of recruitment center
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Full name of responsible person
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3
**Recruitment center**
Name of recruitment center
Baharloo hospital

Full name of responsible person
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Province
Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Digestive Disease Research Institute
Full name of responsible person
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Grant name
Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Digestive Disease Research Institute
Proportion provided by this source
50
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

2

Sponsor
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Web page address
https://sovodak.com/

Grant name
Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Fannavaran Rojan Mohaghegh Daru
Proportion provided by this source
50
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
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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
Yes - There is a plan to make this available

Statistical Analysis Plan
Yes - There is a plan to make this available

Informed Consent Form
Yes - There is 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
Not applicable

Data Dictionary
Not applicable

Title and more details about the data/document
The study protocol, statistical analytic plan informed consent forms will be shared as supplementary material at the time of publication of results.

When the data will become available and for how long
At the time of publication

To whom data/document is available
Will be publicly available as a supplement accompanying the published article.

Under which criteria data/document could be used
To interpret the findings of published study, and to use as a reference for future research

From where data/document is obtainable
On the website of journal that will publish the research

What processes are involved for a request to access data/document
They will be publicly available.

Comments