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
Name
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 °C) 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 < 60/min 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

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

City  
Tehran

Province  
Tehran

Postal code  
1416753955

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

2. **Description**
   - Radiological changes

3. **Description**
   - Serious adverse events

4. **Description**
   - All-cause mortality

**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
   - **Street address**
     - Shariati Hospital, North Kargar Street, Tehran
   - **City**
     - Tehran
   - **Province**
     - Tehran
   - **Postal code**
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   - **Phone**
     - +98 21 8241 5000
   - **Fax**
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   - **Email**
     - a-sadeghi@tums.ac.ir
   - **Web page address**

2. **Recruitment center**
   - **Name of recruitment center**
     - Sina Hospital
   - **Full name of responsible person**
     - Mahnaz Montazeri
   - **Street address**
     - Sina Hospital, Hassan Abad Square, Imam Khomeini Ave, Tehran, Iran
   - **City**
     - Tehran
   - **Province**
     - Tehran
   - **Postal code**
     - 1136746911
   - **Phone**
     - +98 21 6634 8500
   - **Email**
     - mahnazmontazeri@yahoo.com

3. **Recruitment center**
   - **Name of recruitment center**
     - Baharloo hospital
   - **Full name of responsible person**
     - Hadiseh Hosemi Roudsari
   - **Street address**
     - Baharloo Hospital - Behdari.street - Railway.square
   - **City**
     - Tehran
   - **Province**
     - Tehran
4

Recruitment center
    Name of recruitment center
    Sayad Shirazi Hospital
    Full name of responsible person
    Alireza Norouzi
    Street address
    Shahid Sayyad Shirazi Boulevard
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    Province
    Golestan
    Postal code
    4917867439
    Phone
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    norouzi54@gmail.com

Sponsors / Funding sources

1

Sponsor
    Name of organization / entity
    Digestive Disease Research Institute
    Full name of responsible person
    Dr Anahita Sadeghi
    Street address
    Digestive Disease Research Institute, Shariati Hospital, Kargar Street, Tehran
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    Province
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    Postal code
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    Phone
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    Fax
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    Email
    info@ddri.ir
    Web page address
    https://ddri.ir/

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
    Name of organization / entity
    Fannavaran Rojan Mohaghegh Daru
    Full name of responsible person
    Fannavaran Rojan Mohaghegh Daru
    Street address
    Number 10, block 8, Hamedan Street, North Kargar Street, Tehran
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    Province
    Tehran
    Postal code
    1418693918
    Phone
    +98 21 6658 2689
    Fax
    +98 21 6658 2689
    Email
    info@rojanpharma.com
    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
    Tehran University of Medical Sciences
    Full name of responsible person
    Dr Hossein Poustchi
Position
Associate Professor

Latest degree
Specialist

Other areas of specialty/work
Epidemiology

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Person responsible for scientific inquiries

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Tehran University of Medical Sciences

Full name of responsible person
Shirin Afhami

Position
Associate Professor

Latest degree
Specialist

Other areas of specialty/work
Infectious diseases

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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 publically 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 publically available.

Comments