ISRCTN21085622 https://doi.org/10.1186/ISRCTN21085622

Assessing the safety and effectiveness of sofosbuvir plus daclatasvir or ravidasvir in Egyptian adults with COVID-19

Submission date
18/03/2021

Recruitment status
No longer recruiting

Registration date
23/03/2021

Overall study status
Completed

Last Edited
09/12/2021

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.

In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.

Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.

The aim of this study is to evaluate the safety and efficacy of Sofosbuvir plus Daclatasvir (SOF+DCV) or Sofosbuvir plus Ravidasvir (SOF+RVD) in COVID-19.

Who can participate?
Patients with laboratory-confirmed Symptomatic COVID-19

What does the study involve?
Participants will be randomly allocated to receive:
Group 1: the standard of care therapy (as per the Egyptian MOH protocol) together with a daily dose of [SOF+RVD] for 10 days.
Group2: the standard of care therapy (as the Egyptian MOH protocol) together with a daily dose

of [SOF+DCV] for 10 days.
Group 3: the standard of care therapy (as the Egyptian MOH protocol) without any of the experimental drugs or other direct-acting antiviral therapies.
Participants will be closely monitored in hospital for 10 days, and there is a follow up visit at home 7 days later.

What are the possible benefits and risks of participating?
It is possible that no direct health benefits may result during or following the completion of this study. However, the overall conclusion drawn from the results of this study might lead to better care and future treatment for subjects who will suffer from such a condition. Side effects may be caused by Sofosbuvir

Where is the study run from?
National Liver Institute, Menufia, Egypt

When is the study starting and how long is it expected to run for?
March 2020 to March 2021

Who is funding the study?
European Egyptian Pharmaceutical Industries (Egypt)

Who is the main contact?
Mostafa Salah, mostafa.salah@tcdmena.com

Contact information

Type(s)
Scientific

Contact name
Mr Mostafa Salah

Contact details
Third Floor
112B Ammar Ibn Yasser Street
Heliopolis
Cairo
Egypt
-
+20 (0)1062256804
mostafa.salah@tcdmena.com

Type(s)
Public

Contact name
Mr Mostafa Salah

Contact details
Third Floor
112B Ammar Ibn Yasser Street

Heliopolis
Cairo
Egypt
-
+20 (0)1062256804
mostafa.salah@tcdmena.com

Additional identifiers

Protocol serial number
PHA-SDR-002

Study information

Scientific Title
Randomized, open-label, prospective study to evaluate the safety and efficacy of sofosbuvir plus daclatasvir or ravidasvir in Egyptian adults with COVID-19

Acronym
SAVE

Study objectives
Sofosbuvir plus daclatasvir or sofosbuvir plus ravidasvir effectively treat COVID-19 infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 20/04/2020, Menoufia University National Liver Institute IRB (Shebin Elkom, Menoufia, Egypt, NLI IRB 00003413; +20 (0)482222740; gamalelsaidmousa@gmail.com), ref: NLI IRB 00003413
2. Approved 05/08/2020, Research Ethics Committee, Egyptian Ministry of Health (Saad Zaglool Street, Kasr Elainy, Cairo, Egypt; +202 27946369; mohp.rec@gmail.com), ref: IRB 0000687

Study design
Multicenter randomized open-label prospective interventional controlled parallel-group study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Upon entry into the study (screening visit), each patient will be allocated to a Subject Identifier (Subject ID) number. This will be a 6 digit number where the first 3 digits identify the study center and the last 3 digits, which increase incrementally, will identify each subject at a given

study center. The subject ID will be retained throughout the study and will be used to uniquely identify each patient.

For patients eligible to receive study treatment, a randomization number will be allocated at the time of randomization. This randomization number will be used to identify and dispense the drug kits allocated to each subject.
Note that the subject identifier number (Subject ID) which uniquely identifies the subject is different to the randomization number (uniquely identifies a drug kit).

Patients will be randomized within each site to three groups:
Group 1 (Experimental 1, n=40): Patients will continue the standard of care therapy (as per the Egyptian Ministry of Health [MOH] protocol) together with a daily oral dose of one gratisovir (sofosbuvir) 400 mg tablet combined with one ravidasvir 200 mg tablet orally [SOF+RVD] for 10 days, OR
Group 2 (Experimental 2, n=40): Patients will continue the standard of care therapy (as per the Egyptian MOH protocol) together with a daily oral dose of one gratisovir (sofosbuvir) 400 mg tablet combined with one daktavera (daclatasvir) 60 mg tablet [SOF+DCV] for 10 days, OR
Group 3 (Control, n=40): Patients will continue the standard of care therapy (as per the Egyptian MOH protocol) without any of the experimental drugs or other direct-acting antiviral therapy.

The study duration will be as follows:
Pre-treatment: 1 day for screening and baseline data collection.
On treatment: 10 days of daily treatment.
Post-treatment: One follow-up visit after end of treatment within 7 days.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Sofosbuvir, daclatasvir, ravidasvir

Primary outcome(s)
Measured using case report forms unless otherwise indicated
1. Sum of the counted symptoms (fever, headache, generalized aches (myalgia/arthralgia), respiratory distress combined with no evidence of deterioration (ICU admission and mechanical ventilation) at days3, 7 and 10
2. Mean Oxygen saturation from day 1 to day 10 (based on daily recording as per CRF)

Key secondary outcome(s))
1. The percentage of patients with undetectable plasma SARS-CoV-2 RNA for two consecutive nasopharyngeal swabs at day 7 and day 10
2. Percentage of reported AEs/SAEs at any time point from day 1 to day 10, and follow up visit on week 1 measured using patient records
3. The percentage of patients who need ICU admission at any time point from day 1 to day 10, and follow up visit on week 1, measured using patient records

Completion date
10/03/2021

Eligibility

Key inclusion criteria
1. Written informed consent signed and dated by the study subject or their legal representatives
2. Age ≥18 years old
3. Female or male patients with laboratory-confirmed symptomatic COVID-19 (SARS-CoV-2 infection) as determined by polymerase chain reaction (PCR) assay in any specimen collected <72 hours before randomization
4. Patients with any category of the following disease severity:
4.1. Moderate:
4.1.1. Symptoms of moderate illness with COVID-19, which could include any symptom of mild illness or shortness of breath with exertion
4.1.2. Clinical signs suggestive of moderate illness with COVID-19, such as respiratory rate ≥20 breaths per minute, saturation of oxygen (SpO_2) 90% on room air at sea level, heart rate ≥90 beats per minute
4.1.3. No clinical signs indicative of severe or critical illness severity
4.2. Severe (not critical): meeting the following criteria:
4.2.1 Symptoms suggestive of severe systemic illness with COVID-19, which could include any symptom of moderate illness or shortness of breath at rest, or respiratory distress
4.2.2. Clinical signs indicative of severe systemic illness with COVID-19, such as respiratory rate ≥30 per minute, heart rate ≥125 per minute, SpO_2 ≤90% on room air at sea level or PaO_2/FiO_2 <300
4.2.3. No criteria for critical severity
5. Radiographic evidence of pulmonary infiltrate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
120

Key exclusion criteria
1. Critically severe COVID-19 acute respiratory distress syndrome (ARDS) cases requiring invasive mechanical ventilation at screening
2. Patients who have a severe concomitant illness that affects survival, including uncontrolled malignant tumor, blood dyscrasia, active bleeding, or patients with shock/or multiple organ failure at screening
3. Hypersensitivity or contraindication to any of the drugs used in the study

4. Patients with liver disease or cirrhosis (Child-Pugh >9 for ravidasvir and 12 for daclatasvir) or abnormal liver enzyme tests above three times the upper limit values (alanine aminotransferase [ALT] and aspartate aminotransferase [AST])
5. Cardiac ischemia with history of recurrent angina, clinically symptomatic cardiac abnormalities, or requirement for cardiac pacemaker
6. History of any malignancy within the last 5 years
7. History of solid organ or bone marrow transplantation
8. Patients who received treatment with any other investigational drug/device or involved in another clinical trial within 6 months prior to Screening
9. People living with HIV
10. Pregnant or breastfeeding subjects
11. Patients unable to comply with the procedures described in the protocol
12. Mentally or neurologically disabled patients not able to consent to their participation in the study

Date of first enrolment
29/09/2020

Date of final enrolment
29/12/2021

Locations

Countries of recruitment
Egypt

Study participating centre
National Liver Institute
Shebin Elkom
Menoufia
Egypt
32511

Sponsor information

Organisation
European Egyptian Pharmaceutical Industries (EEPI)

Funder(s)

Funder type
Industry

Funder Name
European Egyptian Pharmaceutical Industries (EEPI)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/08/2021	09/12/2021	Yes	No