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START (Siddha Treatment Accelerating Recovery from SARS-CoV-2 Test) trial of Siddha treatment for patients with novel coronavirus infectious disease (COVID-19)

Submission date
17/04/2020

Recruitment status
No longer recruiting

Registration date
24/04/2020

Overall study status
Completed

Last Edited
19/03/2021

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

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 as of April 2020, neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. On 11 March 2020, WHO declared Novel Coronavirus Disease (COVID-19) outbreak as a pandemic and reiterated the call for countries to take immediate actions and scale up response to treat, detect and reduce transmission to save people's lives. As of 7 April 2020 (9:00 AM), according to the Ministry of Health & Family Welfare (MoHFW) of India, a total of 4421 COVID-19 cases, (including 66 foreign nationals) have been reported in 31 states/union territories. These include 325 who have been cured/discharged, 1 who has migrated and 114 deaths. Hospital isolation and home quarantine of all cases is ongoing at the time of writing.

Emerging claims regarding the efficacy of several alternative measures currently have no supporting scientific evidence. While traditional medicine like Siddha or Ayurvedha is a treasure of India with an ample of classical literary evidence, the safety and effectiveness of these medicines are still under debate among both adherents and skeptics. Though many of the remedies have been in use for hundreds of years, critics argue the claims of therapeutic efficacy of traditional medicine. In this aspect through this research study, we have hypothesized a scientific basis for Siddha herbal regimen Kabasura kudineer and Siddha herbomineral regimen Brammanandha Bairavam to have possible clinical efficacy for the prevention and management of COVID-19 Stage-1 infection thereby enabling the disease management and to aid in inhibiting the progression of COVID-19 to stage 2 and stage-3.

This trial will aim to test whether outcomes in symptomatic patients testing positive for SARS-Cov-2 are better with Siddha treatment in addition to standard care compared to standard care alone.

Who can participate?
Patients aged between 18 and 75 years who have laboratory-confirmed mild or moderate COVID-19

What does the study involve?
The study involves some screening assessment before receiving either Siddha treatment in addition to standard care or standard care alone over a treatment period of 14 days. Participants will attend five study assessments at 0 (baseline assessment), 2, 8, 15 and 29 days to assess their response to treatment.

What are the possible benefits and risks of participating?
An anticipated benefit is that the study drug regimen could be used as a mainstream model treatment for the COVID-19 Stage-1 and will be recommended to the WHO for its global benefits.

Brammanandha bairavam may cause mild gastritis and swelling in tongue occasionally.

Kabasura kudineer may cause moderate respiratory allergy, skin rashes may arise due to the presence of Mulli, Akragaram and Siru Kanjori. A test dose of 5 ml may be given prior to use.

Where is the study run from?
Rajiv Gandhi Government General Hospital (India)

When is the study starting and how long is it expected to run for?
From April 2020 to June 2020

Who is funding the study?
Eminentlabs GmbH (Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NV-05-943-2020

Study information

Scientific Title
The efficacy and safety of Siddha Treatment in Symptomatic Participants with novel coronavirus infectious disease (COVID-19): A Multicenter, Randomized, Open-Label, Active-controlled Randomised Clinical Trial

Acronym
START

Study objectives
Siddha treatment regimen + Standard of care treatment group has at least 30% proportion difference in achieving primary endpoint favoring the "Siddha treatment regimen + Standard of care" compared to "Standard of care".
H0: P1 - P0 <= 30%
H1: P1 - P0 > 30%

where P1 = Proportion of patients achieved primary endpoint in Siddha treatment regimen + Standard of care group
P0 = Proportion of patients achieved primary endpoint in Standard of care group

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/04/2020, Department of Health and Family Welfare of State of Tamil Nadu (Chennai 600009 India; +91 25671875, PABX-5671; hfsec@tn.gov.in)

Primary study design
Interventional

Study design
A Multicenter, Randomized, Open-Label, Active-controlled Randomised Clinical Trial

Study type(s)
Treatment

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

Interventions

The study consists of the following periods/assessments for participants in both the intervention and control arms.
1. Screening period: -3 to -1 days. This will involve taking informed consent, assessing eligibility and comorbidity (e.g. Hypertension, Diabetes, Cardiovascular disease, etc.) through taking a medical and surgical history, smoking history, previous medication history, demographic history, physical examination, serology, 12-lead ECG, and vital signs.
2. Treatment period: 0 to 14 days
3. Follow-up period: 0 to 28 days. Patients will attend five study assessments at 0 (baseline assessment), 2, 8, 15 and 29 days. If nasal swabs taken at 15 days are negative participants will be invited to return 24 h later on day 16 for a second swab.
4. Safety Follow-up assessment: 28 days after the last dose of the Siddha treatment was received in the event of early termination

The patients selected for participation will be assigned randomly to one of the two treatment groups, Siddha treatment regimen + Standard of Care, or Standard of Care only, in 1:1 ratio balancing the stratification factor of co-morbidity status.

The stratified permuted block randomization design will be used to randomize the patients in 1: 1 ratio among the two treatment groups.

Siddha treatment regimen + Standard of care will involve Siddha treatment with Kabasura kudineer and Brammanandha bairavam where indicated in addition to standard care as per local /government guidance. Kabasura kudineer will be given in the dose of 60 ml, twice a day for 7 days taken 90 minutes before food. Brammanandha bairavam will be given in the dose of 100 mg, three times a day for 7 days, taken immediately after food with honey or ginger juice.

Kabasurakudineer has been Standardized as per PLIM guidelines (Anitajohn, 2015) tested for its Antipyretic, Anti-inflammatory and Anti-bacterial properties. It has been helpful in the management of Swine flu. The drug is found to be safe in its acute toxicity (Saravanan, 2018) and our unpublished data reveals its efficacy in inhibiting Neuraminidase the glycoprotein in H1N1.

Bramanandha bairavam happened to be the repeatedly used during Chickungunya epidemic by the Siddha practitioners. Studies have proven the efficacy of this treatment against the Chickungunya virus. Another study proved that Bramanandha bairavam was effective in blocking Chikungunya virus from entering susceptible cells in the concentrations range of 0.0625 and 0.5 mg/ml.

Standard of care will involve standard care as per local/government guidance.

A Rescue treatment option is foreseen for patients on Siddha treatment+Standard of Care arm as well as the Standard of Care arm if the disease progresses.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
1. Kabasura kudineer, The Siddha Formulary of India 2. Brammanandha bairavam, Siddha vaithya thirattu

Primary outcome(s)
Proportion of patients confirmed as negative for COVID-19 in 2 consecutive throat/nasal swabs (taken 24 hours apart) at 15 and 16 days

Key secondary outcome(s)
1. Time taken from patients to become asymptomatic from symptomatic assessed using nasal swabs at 0, 2, 8, 15 and 28 days
2. Viral load change from baseline at Day 15 assessed from blood and swab samples at 0 and 15 days
3. Mortality rate assessed using patient notes at 28 days
4. Length of hospitalization using patient notes at 28 days. Hospitalization is defined as admission where patients require parenteral/Intravenous (IV) medications or IV fluids, oxygen or ventilatory support in hospital. Isolation or quarantine inside the hospital premises alone will not be considered as hospitalization.
5. Time to achieve National Early Warning Score (NEWS) (1) equal to zero using patient notes at 28 days. NEWS equal to zero is defined as clinical recovery and respiration 12-20 breaths/minute, oxygen saturation percent greater than 96, (without breathing aid), systolic blood pressure 111-180 mmHg, pulse 51-90 beats/minute, alert consciousness and 95.1-99.0 degree Fahrenheit body temperature.
6. Lymphocyte count, lymphocyte percentage assessed at 0, 2, 8 and 15 days
7. White blood cell count assessed at 0, 2, 8 and 15 days
8. C-reactive protein assessed at 0, 2, 8 and 15 days
9. Chest X-ray features assessed at 0, 2, 8 and 15 days
10. Proportion of patients requiring rescue medication assessed using patient notes at 28 days
11. The proportion of patients at each level of outcome severity measured from participant reporting using severity rating on a 7-point ordinal scale at 28 days. The options in this scale include 1= Not hospitalized, no limitations on activities; 2= Not hospitalized, limitation on activities; 3= Hospitalized, not requiring supplemental oxygen; 4= Hospitalized, requiring supplemental oxygen; 5= Hospitalized, on non-invasive ventilation or high flow oxygen devices; 6= Hospitalized, on invasive mechanical ventilation or ECMO; 7= Death.

Safety endpoints:
1. Number of patients with treatment-emergent Adverse Events (AE) identified through patient notes at 28 days. These will be defined as any AE occurring or worsening following treatment, and will be summarized by body system and preferred term.
2. Mean changes of parameters at [each assessment during 28 days of the treatment/follow-up period, compared to baseline] for:
2.1. Vital signs: body temperature, heart rate, respiratory rate systolic/diastolic blood pressure and oxygen saturation.
2.2. Safety laboratory tests: hematology, serum chemistry, urinalysis.
2.3. 12-lead ECG: heart rate, QTc interval, ST segment and T wave changes.

Completion date
26/06/2020

Eligibility

Key inclusion criteria
1. Aged between 18 and 75 years
2. Laboratory-confirmed COVID-19
3. Presence of any 2 symptoms of COVID-19: fever, cough, sore throat, myalgia, fatigue,

headache or dyspnea
4. Not currently hospitalized or under immediate consideration for hospitalization. Hospitalization is defined as admission where patients require parenteral/Intravenous (IV) medications or IV fluids, oxygen or ventilatory support in hospital. Isolation or quarantine inside the hospital premises alone will not be considered as hospitalization.
5. Meets clinical features of the following grades of severity:
5.1. Suspected/confirmed cases in COVID Care Centres, clinically assigned as mild and very mild, presenting with fever and/or upper respiratory tract illness
5.2. Suspected/confirmed cases in Dedicated COVID Health Centres, clinically assigned as moderate, presenting with pneumonia with no signs of severe disease (Respiratory Rate 15 to 30 breaths/minute, SpO2 90%-94%)
6. Willing to practice contraception during the entire study treatment period and for 3 months after the last treatment of IMP is administered, using either double barrier contraception or sexual abstinence (when this is in line with the preferred and usual lifestyle of the participant)
7. Patients or their legal representatives have personally signed and dated signed the informed consent form (ICF) before completing any study-related procedure, which means before any assessment or evaluation that would not have formed a part of his normal medical care
8. Willing to adhere and comply with the protocol-related procedures
9. Willing to take Siddha drug regimen for COVID-19 infection
10. Willing to not participate in other clinical studies within 30 days after the last administration from the first administration of the study drug

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Viral pneumonia with cause other than SARS-CoV-2
2. Severe or critical COVID-19 infection
3. Taken antibiotics/antivirals in the past 1 week
4. History of Asthma, COPD or any other chronic lung disease
5. Active malignancy
6. Received organ transplantation in the past 6 months or planning surgery
7. Unable to take food or drugs orally
8. Malabsorption or GI abnormalities which may affect drug absorption
9. Severe underlying diseases affecting survival, including but not limited to: blood diseases, dyscrasia, active bleeding, severe malnutrition, etc.
10. Subjects who are pregnant or lactating, have a pregnancy plan (including plans for sperm donation or egg donation), or who may fail to take effective contraceptive measures within the next 6 months

11. Allergic constitution, or known allergy to investigational products
12. Testing positive for HIV, Hepatitis B and Hepatitis C at screening
13. Patients whose ALT/AST levels are 5 times higher than the normal upper limit and total bilirubin is 3 times higher than the upper limit of normal.
14. Requiring Extracorporeal Life Support Program (ECLS), i.e. Extracorporeal Membrane Oxygenation (ECMO), Extracorporeal carbon dioxide removal (ECCO2R) or Registered Respiratory Therapist (RRT)
15. Life expectancy < 48 h

Date of first enrolment
30/04/2020

Date of final enrolment
20/05/2020

Locations

Countries of recruitment
India

Study participating centre
Rajiv Gandhi Government General Hospital
Poonamallee High Rd
Park Town
Tamil Nadu
Chennai
India
600003

Sponsor information

Organisation
Eminentlabs GmbH

Funder(s)

Funder type
Industry

Funder Name
Eminentlabs GmbH

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publically available repository

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes