CLINICAL STUDY PROTOCOL

PROTOCOL TITLE

A DOUBLE BLIND, RANDOMIZED, PLACEBO CONTROLLED STUDY TO EVALUATE EFFICACY AND SAFETY OF "VIRACIDE" IN THE MANAGEMENT OF CORONA VIRUS DISEASE 2019 (COVID-19)

Protocol Number: NS-VC-CT01-20
Clinicaltrial.gov ID: NCT04596085

STUDY SYNOPSIS

Title	A double blind, randomized, placebo controlled study to evaluate efficacy and safety of "ViraCide" in the management of corona virus disease 2019 (COVID-19).
Study Description	This is a double blind randomized placebo controlled study will be conducted on 124 subjects, 50 years and older with mild or asymptomatic COVID-19. If symptomatic, symptoms are mild (cough, weakness, sore throat, low grade fever 38.50C, respiratory rate should not be more than 22 / min, resting SpO2 >95%, normal highly sensitive C-reactive protein (HS-CRP) (<10mg/L). There are no signs of dehydration, sepsis or shortness of breath. The study will be conducted at two centers. There will be a screening visit at Day -4 followed by three visits at the center at Days 1, 7 and 15 and a follow-up visit on Day 28. All participants will be randomized to receive either ViraCide (investigational product) or matching placebo. All subjects will receive SOC therapy. Note: If subject is discharged before Day 15 PI's discretion as per patients health condition, then assessments scheduled for Day 15 will be carried out on the discharge day (as far as possible and those not performed will be noted on appropriate CRF page) and Day 15 visit will be done telephonically.
Investigational Product/Study drug	ViraCide softgels given per orally
Comparison product	Matching placebo of ViraCide softgels given per orally
Study Design	Double blind, randomized, placebo controlled study. Subjects will be randomized to the experimental and control groups in a 1: 1 ratio. In each group 62 subjects will be recruited, a total of 124 subjects. Subjects of the experimental arm will receive treatment with Study Drug, ViraCide and SOC. The control group will receive matching placebo and SOC. The study consists of the stages of screening, therapy, observation. There will be no switching of subjects between the arms. Participants will receive Study drug or matching placebo for 14 days during the study.
Sample Size	124, including 10% dropouts
Study Population	• 50 years or older • Positive RT- PCR forSars-Co-V2. • Either asymptomatic or have mild symptoms. Onset of symptoms within no more than 4days • With chronic stable medical conditions: Diabetes Mellitus, or Hypertension, or chronic heart disease.
Study Duration	Total study duration approximately 35 days Screening: 04 days Treatment duration: 14 days Follow-up: 14 days from end of treatment

Number of Sites	02 (two)
Treatment Duration	14 days
Treatment Arms	Two treatment arms • Arm A: ViraCide softgels: 3 soft gels, two times every day after breakfast and dinner for 14 days+ SOC Therapy • Arm B: Placebo softgels: 3 soft gels, two times everyday after breakfast and dinner for 14 days + SOC Therapy
Purpose of the study	To study the effectiveness and safety of the Study Drug, ViraCide
	softgels by oral administration compared with placebo softgels in 50 years or older subjects with asymptomatic or mildly symptomatic coronovirus infection (COVID-19) and stable comorbidities.
Objectives	Primary Objectives 1. To evaluate the efficacy of "ViraCide" in the management of mild COVID-19 disease Secondary Objectives 1. To evaluate the safety of "ViraCide" in the management of mild COVID-19 disease
Primary Endpoints	1. TTCI using NEWS Score [Time Frame: First treatment date up to discharge day (PI's discretion as per patients health condition)] The median time in days from the start of treatment with the study drug / placebo to the persistent achievement of all of the following criteria: • Stopping a fever (which is defined as a decrease in axillary temperature below 37 ° C without the use of anti pyretic drugs); • Respiratory rate <22 /min; • Oxygen saturation (SPO2) > 95% when breathing in atmospheric air. Measured using pulse oximetry • Systolic blood pressure ≤200mmHg • Pulse rate 51-90beats/minute • Is conscious and alert [Note: Persistent achievement means the preservation of each of the criteria for at least 7days.] 2. TTIC using 7-point ordinal scale 3. Rate of progression to severe/critical COVID-19 disease based on NEWS score [Time frame: First treatment date up to 15days] 4. Rate of progression to severe/critical COVID-19 disease based on 7-point ordinal scale [Time frame: First treatment date up to 28days] 5. Time to COVID-19 nucleic acid testing negativity in oropharyngeal/nasal swab) [Time Frame: First treatment date up to 28days]

Secondary Endpoints	1. Incidence of ICU admissions [Time Frame: 28days] 2. Subject survival rate [Time Frame: 28days] 3. Incidence of mechanical ventilation due to COVID-19 infection [Time Frame: First treatment date up to 28days] 4. Change in clinical or laboratory assessment of comorbid condition [Time Frame: First treatment date up to 28days] 5. Percent of participants with worsening comorbid condition [Time Frame: First treatment date up to 28days] 6. Proportion of subjects in the treatment arm who had AE, SAE 7. Proportion of subjects in the placebo arm who had AE, SAE
Subject Selection Criteria	Inclusion criteria 1. 50 years or older
	2. Both male and female subjects will be included 3. Positive oropharyngeal/nasal swab RT-PCR for Sars-Co- V2. Diagnosed not more than 2 days ago(diagnosis ≤2days). 4. Either asymptomatic or have mild symptoms. Onset of symptoms within no more than 4 days If symptomatic, symptoms are mild (cough, weakness, sore throat, low grade fever 38.50C, respiratory rate should not be more than 22 / min, resting SpO2 >95%, normal highly sensitive C-reactive protein (HS-CRP) (<10mg/L). There are no signs of dehydration, sepsis or shortness of breath. 5. Chronic stable medical conditions: diabetes mellitus, or hypertension, or chronic heart disease. Under treatment and controlled by medication 6. Signed informed consent/or consent given through text message, WhatsApp ore-mail. 7. Ability to understand the requirements of the Research Protocol and follow the research procedures. 8. Subject should be willing to be managed in isolation wards 9. Negative pregnancy test (for female participants) 10. Adequate contraception for study duration Exclusion criteria 1. Less than 50years 2. With severe COVID-19 symptoms requiring immediate hospitalization 3. Investigator considers the subject unsuitable for ViraCide 4. History of symptoms of more than 4days 5. COVID-19 diagnosed >2 days ago using oropharyngeal/nasal swab RT-PCR forSars-Co-V2 6. History of cardiopulmonary resuscitation

	7. Subjects having history of organ failure or conditions requiring ICU monitoring and treatment, such as severe liver disease, severe renal dysfunction, upper gastrointestinal hemorrhage, disseminated intravascular coagulation or any other condition that in the PI‟s opinion makes the subject unfit to participate 8. Respiratory failure, ARDS or need of mechanical ventilation 9. History of acute exacerbation of comorbidity like heart failure, diabetic ketoacidosis, myocardial infection, major cardiac rhythm disorder or any other condition that in the PI‟s opinion makes the subject unfit to participate 10. History of or current hepatic failure or severely compromised liver function, or renal failure or having chronic kidney disease or acute renal failure 11. History of or currently receiving treatment for an endocrine disorder like hypothyroidism, hyperthyroidism that is likely to affect the basal heart rate. 12. History of or currently under treatment for asthma [exception: patients with history of asthma, not on medications/inhalers/nebulizers for at least 6 months
	before study start), COPD, bronchiectasis, asbestosis and other such chronic lung conditions that can compromise SpO2 and RR. 13. HIV, HBsAg, HCV positive 14. Any condition causing immunodeficiency 15. Systemic connective tissue disease or any autoimmune disease that is likely to affect HS-CRP levels 16. History of epilepsy/epileptic fit/convulsions in last 6 months or currently on treatment for it 17. History of or currently having malignancy and being treated for it. (exception: histologically confirmed and cured carcinoma in situ) 18. Hypersensitivity reaction to Study drug/placebo 19. Any psychiatric issue for which the subject is currently undergoing treatment 20. Any history of drug/alcohol dependence within 30 days of screening or current drug/alcohol dependence 21. Inability to understand the requirements of the Research Protocol and follow the research procedures. 22. Pregnant or lactating; 23. Not willing to use adequate contraception during study duration 24. Participation in any other clinical study less than 3months before the start of the study.
Stopping the Study Drug	1. Completing 14 days of treatment 2. Progression to severe COVID-19: ViraCide will be stopped if subjects progresses to severe COVID-19 and require ICU admission, mechanical ventilation and any such situation where according to the PI the subject

	cannot continue ViraCide. However, subject will be followed-up to capture data on ICU admission, incidence and mortality 3. Progression of comorbid condition requiring admission to ICU or inability of the subject to take anything orally. However, subject will be followed-up to capture data on ICU admission, incidence and mortality 4. Subject's participation to the study is terminated 5. Study is terminated
Termination of Subject's Participation in the Study	Any participant can be removed from the study: 1. By his/her own free will to not continue in the study. Subject withdrawal of informed consent. 2. Loss of contact with the subject during the study. 3. Does not comply with dosing schedule (75%-125% non-compliance) 4. The development of AE / SAE requiring the withdrawal of the study drug. However all AE / SAE will be followed-up till the study duration 5. Pregnancy confirmed anytime during the study duration 6. Another reason, which, according to the PI, requires the termination of the subject's participation in the study.
Study Termination	The study can be terminated if 1. There is a major deviation in Protocol 2. Another reason, which, according to the PI, requires study termination
Visits of Assessment	Screening and 3 visits and one telephonic follow-up Screening Inclusion/Exclusion Criteria, Subject Inform Consent, Demography, Medical History, Physical Examination, Vital Signs, HIV; HBsAg; HCV; Hs-CRP; Pulse oximetry; NEWS scoring; 7- point ordinal scoring; Medication list review (medications being taken for comorbid conditions), Lab assessment; Urine analysis Note: Patients who do not meet the study inclusion exclusion criteria during screening should not be randomized into the study. Day 1 Randomization, Vital Signs, Pulse oximetry, AE/SAE, Concomitant Medication, ViraCide/ Placebo treatment start, NEWS scoring; 7-point ordinal scoring Day 7 Physical Examination, Vital Signs, AE/SAE, Concomitant Medication, ViraCide/ Placebo Compliance check, Pulse oximetry; NEWS scoring; 7-point ordinal scoring. (Note: If the subject is discharged on this day as per PI's discretion and patient's health condition then assessment scheduled for day 15 will be carried out on discharge day). Day 15 Physical Examination, Vital Signs, AE/SAE, Concomitant Medication, ViraCide/ Placebo treatment end, RT-PCR for

	Sars- Co-V2, Hs-CRP, Safety Lab Tests, Pulse oximetry; NEWS scoring; 7-point ordinal scoring, ViraCide/ Placebo Compliance check, Lab assessment including urine analysis Day 28 Phone call follow up for time : • until negative RT-PCR for Sars-Co- V2, COVID-19 related mortality, • development of any COVID-19 symptom, • development of any worsening of comorbid condition; • Development of new AE/SAE; Resolution status of previous AE/SAEs Note: If subject is discharged before Day 15on PI's discretion as per patients health condition, then assessments scheduled for Day 15 will be carried out on the discharge day (as far as possible and those not performed will be noted on appropriate CRF page) and Day 15 visit will be done telephonically.
Laboratory Investigations	Screening: Recording RT-PCR- Sars-Co-V2 result; Urine pregnancy test; HIV; HBsAg; HCV;Hs-CRP; Hematology* + Biochemistry +Urine analysis*; ECG Day 1: No labs Day 7: No labs Day 15: Oropharyngeal/nasal swab for PCR- Sars-Co-V2; Hematology* + Biochemistry + Urine analysis*; ECG; Serological biomarker: Hs-CRP
	Note: *Hematology: Complete blood count (CBC); erythrocyte sedimentation rate (ESR) *Biochemistry: • Random Blood Sugar, • Serum Creatinine • SGOT,SGPT • Alkaline Phosphatase • Bilirubin-Total/Direct/Indirect • Total Proteins/Albumin/Globulin/A:Gratio • Low density lipoprotein (LDL) Cholesterol(Direct) • LDH • Total Cholesterol • Triglycerides • High Sensitive C-reactive protein(HS-CRP) • BUN (Blood Urea Nitrogen) /Urea • Serum Calcium • Serum Sodium • Serum Potassium • Uric Acid *X-ray PA view is an optional test at screening. It may be done

	at any other time during the study if deemed necessary by the Investigator *Urine pregnancy test (for females only) at screening Note: If subject is discharged before Day 15 PI's discretion as per patients health condition, then assessments scheduled for Day 15 will be carried out on the discharge day (as far as possible and those not performed will be noted on appropriate CRF page) and Day 15 visit will be done telephonically.
Standard of Care Therapy	SOC therapy for coronavirus infection (COVID-19,SARS-CoV- 2) has not been developed yet. Treatment will be given as per the discretion of the PI or as per the guidelines issued by the GOI. GOI guidelines can be accessed here: https://www.mohfw.gov.in/
Concomitant Medications Allowed by the Protocol	1. Medications for Diabetes Mellitus 2. Medications for hypertension 3. Statins 4. Blood thinners like aspirin at PI discretion 5. Any medication deemed necessary by the PI to manage the AE/SAE 6. Any other medication deemed necessary by the PI to manage a comorbid condition that is not likely to affect the treatment Protocol
Prohibited Concomitant Medications	Any other herbal medicine or dietary supplement
Statistical Analysis	Sample size of total 112(56 cases in each arm) completed cases needed to assess the study objective at 80% power and 5% level of significance. Considering 10 % dropout total 124 (62 cases in each arm) cases will be enrolled in this study.