CTRI Number	CTRI/2020/06/025664 [Registered on: 05/06/2020] - **Trial Registered Prospectively**
Last Modified On	19/05/2021
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug
Study Design	Randomized, Parallel Group, Active Controlled Trial
Public Title of Study	Phase II study to evaluate the Safety and Efficacy of 2-Deoxy-D-Glucose in COVID -19 patients
Scientific Title of Study	A Randomized, Open Label, 2-Treatment Groups Clinical Trial Evaluating the Safety and Efficacy of 2-Deoxy-D-Glucose as an adjunctive therapy to standard of care, in comparison to standard of care alone, in the Acute Treatment of moderate to severe COVID -19 patients

Secondary IDs if Any

Secondary ID	Identifier
CVD-19-CD-002, Version 5.0, 22 July 2020	Protocol Number

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	
Designation	
Affiliation	
Address	
Phone	
Fax	
Email	

Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	D Mallikarjuna Rao
Designation	Senior Director
Affiliation	Dr. Reddys Laboratories Limited
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Details Contact Person (Public Query)

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Name	D Mallikarjuna Rao
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Affiliation	Dr. Reddys Laboratories Limited
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Source of Monetary or Material Support

Source of Monetary or Material Support
> Dr. Reddy's Laboratories Limited 8-2-337, Road No. 3 Banjara Hills, Hyderabad 500043

Primary Sponsor

Primary Sponsor Details	
Name	Dr Reddys Laboratories Limited
Address	8-2-337, Road No.3, Banjara Hills, Hyderabad-500 034, Telangana, India
Type of Sponsor	Pharmaceutical industry-Global

Details of Secondary Sponsor

Name	Address
Institute of Nuclear Medicine and Allied Sciences	DRDO, Ministry of Defence, Brig. S K Mazumdar Marg, Timarpur, Delhi-110054

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Akshay Budhraja	Aakash Healthcare Super Speciality Hospital	Department of Respiratory and Sleep Medicine, Hospital Plot Rd Number 201, Sector-3 Dwarka New Delhi DELHI	9893322007 drakshay.budhraja@aakashhealthcare.com
Dr G Balachandra	BGS Global Institute of Medical Sciences	Professor and HOD, General Medicine, #67, BGS Health and Education City, Uttarhalli Road, Kengeri, Bengaluru – 560060 Bangalore KARNATAKA	9845111559 9845111559 drgbalachandra@gmail.com
Dr Vinoth Kumar Athinarayanan	Chengalpet Government Medical College & Hospital	Senior Resident, Department of Chest and TB GST Road, Chengalpattu, Kancheepuram, Tamilnadu-603001 Kancheepuram TAMIL NADU	04427431225 mbbs.vinoth@gmail.com
Dr Apurva Agarwal	Ganesh Shankar Vidyarthi Memorial Medical College	Department of Anesthesiology Professor and Head Swaroop Nagar, Kanpur Kanpur Nagar UTTAR PRADESH	05122535483 dr.apurva.agarwal@gmail.com
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		MAHARASHTRA	
Dr Viny Kantroo	Indraprastha Apollo Hospitals	Consultant, Department of Respiratory Medicine, Sarita Vihar, NEW DELHI 110076 East DELHI	9811120777 vinykantroo@gmail.com
Dr Ajay Jhaveri	Kasturba Hospital of Infectious Diseases	Consultant Physician and Gastroenterologist, Sane Guruji Marg, Arya Nagar, Chinchpokli Mumbai MAHARASHTRA	022-23027700 022-23027700 drajayjhaveri@gmail.com
Dr Y G Sundara Raju	King George Hospital	Department of General Medicine, Rajendra Prasad Ward, KGH Down Rd, Opp KGH OP Gate, Maharani Peta Visakhapatnam ANDHRA PRADESH	9573606609 drysundararajuresearch@gmail.com
Dr Sudhir Kumar Verma	King George Medical University (Erstwhile Chhatrapati Shahuji Maharaj Medical University)	Associate Professor, Department of Medicine, Shah Mina Rd, Chowk Lucknow UTTAR PRADESH	05222258880 sudhirkgmu@gmail.com
Dr Jigar Modia	Medistar Hospital	GIDC Vadsar Road, Flyover, adjoining Vadsar, Vadodara, Gujarat 390010 Vadodara GUJARAT	99913041639 drjigarmodianm@gmail.com
Dr Kapil Zirpe	Ruby Hall Clinic	Head, Dept of Neuro Critical Care 40, Sasoon Rd, Sangamvadi Pune MAHARASHTRA	02026124529 kapilzirpe@gmail.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Aakash Healthcare Institutional Ethics Committee	Approved	14/08/2020	No
Anand Institutional Ethics Committee	Approved	12/08/2020	No
Ethics Committee GSVM Medical College	Approved	03/06/2020	No
IEC King George hospital	Approved	16/08/2020	No
IEC, Jaslok Hospital and Research Centre	Approved	19/06/2020	No
Institutional Ethics Committee (IEC-GMCA)	Approved	05/08/2020	No
Institutional Ethics Committee, BGS Global Institute of Medical	Approved	11/08/2020	No

Sciences			
Institutional Ethics Committee, Govt. Medical College, Nagpur	Approved	05/08/2020	No
Institutional Ethics Committee-Chengalpattu Medical College	Approved	10/08/2020	No
Institutional Ethics Committee-Clinical Studies, Indraprastha Apollo Hospital, New Delhi	Approved	11/08/2020	No
King Georges Medical University Institutional Ethics Committee	Approved	17/06/2020	No
Poona Medical Research Foundation Institutional Ethics Committee	Approved	31/07/2020	No

Regulatory Clearance Status from DCGI

Status	Date
Approved/Obtained	20/07/2020

Health Condition / Problems Studied

Health Type	Condition
Patients	Coronavirus as the cause of diseases classified elsewhere

Intervention / Comparator Agent

Type	Name	Details
Intervention	2-Deoxy-D-Glucose Oral Powder	45 mg/kg Morning + 18 mg/kg Evening as long as SoC is being administered, but no longer than discharge or Day 28 (whichever is earlier)
Comparator Agent	Standard of Care	Upto Day 28 discharge but no more than Day 28

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	65.00 Year(s)
Gender	Both
Details	1. Male, female and transgender patients aged ? 18 years and ? 65 years 2. Patients testing positive for SARS-CoV-2 by rRT-PCR on a nasopharyngeal or oropharyngeal swab Note: A re-treated/ relapsed patient may be enrolled if he/she meets all of the following criteria: a. Documented re-conversion on nasopharyngeal or oropharyngeal swab from negative to positive for SARS-CoV-2 OR nasopharyngeal or oropharyngeal swab continues to be positive for SARS-CoV-2 after previous treatment AND b. Clinical symptoms associated with COVID-19 (fever, cough, difficulty in breathing, fatigue, body ache, headache, diarrhea, nasal congestion) have either re-appeared after previous treatment OR continued to be present without improvement OR are aggravated AND c. Patient meet the below-mentioned criterion (# 3) for ‘moderate’ or ‘severe’ COVID-19 disease severity 3. Patients clinically assigned as ‘moderate’ (Pneumonia with no signs of severe disease, respiratory rate 15 to 30/minute, SpO2 90%-94%) or ‘severe’ (Severe Pneumonia with respiratory rate ?30/minute and/or SpO2 < 90% in room air) but not critically ill (acute respiratory

	distress syndrome [ARDS], multi organ failure or septic shock) Note: The severity is as defined by the Guidance document on appropriate management of suspect/confirmed cases of COVID-19 published by the Ministry of Health & Family Welfare on 07 Apr 2020. 4. Females should have a negative serum pregnancy test at baseline; female patients of child bearing potential should either be abstinent or comply with one or more contraception methods (with low user dependency and failure rate of <1%) for the entire duration of the treatment period and until 90 days after receiving the last dose of study treatment 5. Able and willing to provide informed consent 6. Able to understand the trial requirements and comply with trial medications and assessments in the opinion of the Investigator 7. Agrees not to participate in other clinical studies within 30 days after the last administration of the study treatment

Exclusion Criteria

Method of Generating Random Sequence Computer generated randomization

Method of Concealment Pharmacy-controlled Randomization

Blinding/Masking Open Label

Primary Outcome

Outcome	Timepoints
Time to ‘Clinical improvement	Day 3,7,10,14 and 28 (until patient reaches score of 4 or lower on 10 point ordinal scale for clinical status or discharge, whichever is earlier).

Secondary Outcome

Outcome	Timepoints
Change from baseline in mean viral load (determined by rRT-PCR on nasopharyngeal/oropharyngeal swab)	Days 3, 7, 10, 14 and 28
Percentage of patients showing negative conversion (of detectable SARS-CoV-2 viral RNA) on nasopharyngeal/oropharyngeal swab	Day 10 and Day 28
Mean/Median time (no. of days) to negative conversion (of detectable SARS-CoV-2 viral RNA) on nasopharyngeal swab from day of first treatment intake	Day 1 to Day 28
Percentage of patients who achieve the endpoint of Clinical improvement	Day 14 and by Day 28
Mean/median time (no. of days) from start of study treatment to discharge from the ‘isolation ward’ of the COVID management facility.	Day 1 to Day 28
Mean/ median time (no. of days) from start of study treatment to clinical status score improvement by 1 and by 2 (from baseline) on the 10-point ordinal scale used in the SOLIDARITY trial by WHO	Day 1 to Day 28
Mean change from baseline in patient’s clinical status on a 10-point ordinal scale (SOLIDARITY trial)	Days 3, 7, 14, 21 and 28 (or discharge, if discharge happens before)
Mean change from baseline in NEWS-2 score	Days 3, 7, 14, 21 and 28 (or discharge, if discharge happens before)
Percentage of patients requiring, until Day 28 of treatment: a. Management in intensive care unit (ICU) b. Oxygen supplementation c. Invasive mechanical ventilation	Day 28
Mean/median time (no. of days) to a. Management in intensive care unit	Day 28

b. Oxygen supplementation c. Invasive mechanical ventilation	
Mean/ median time (no. of days) the patient is: a. Managed in intensive care unit b. On Oxygen supplementation c. On Invasive mechanical ventilation	Day 28
Mean/ Median Time to achieve symptom improvement of at least 30% in the COVID-19 symptoms sum score from baseline	Day 14
Percentage of patients dying due to COVID-19 complication	Day 1 to Day 28
Number (and percentage) of patients reporting treatment emergent adverse events (TEAEs) (by MedDRA system organ class and preferred term)	Days 3, 7, 10, 14 and 28
Changes of parameters at each assessment during the study/follow-up period, compared to baseline for: o Vital signs: body temperature, heart rate, respiratory rate, systolic/diastolic blood pressure and oxygen saturation. o Clinical laboratory assessments: hematology, serum chemistry, urinalysis. o 12-lead ECG: Changes in heart rate, PR, QRS, QT and QTcB intervals.	Days 3, 7, 10, 14 and 28

Target Sample Size **Total Sample Size=**40
Sample Size from India=40
Final Enrollment numbers achieved (Total)=110
Final Enrollment numbers achieved (India)=110

Phase of Trial Phase 2

Date of First Enrollment (India) 15/06/2020

Date of First Enrollment (Global) No Date Specified

Estimated Duration of Trial **Years=**0
Months=3
Days=0

Recruitment Status of Trial (Global) Not Applicable

Recruitment Status of Trial (India) Completed

Publication Details NIL

Brief Summary

COVID-19 is currently a major global public health crisis and in the absence of an effective vaccine and ‘herd’ immunity, there are no known interventions for effectively dealing with this pandemic (other than broad public-health measures like physical distancing and containment). At an individual COVID-19 patient level, there is a lack of proven specific treatment options that improve symptoms, influence disease severity progression and clinical outcomes or aid the treating physician in better patient management. Different medicines and medicinal systems are being explored to find remedial measures for this new infection. Antiviral drugs, and other antimicrobial agents are being evaluated and being utilized off-label in treating patients, largely those with more severe COVID-19. However, no breakthrough has been achieved to date either in curtailing the pandemic or improving patient outcomes.

2-deoxy-D-glucose (2-DG), an inhibitor of glucose transport and glycolysis, is known to inhibit the growth of neoplastic cells in vitro and in vivo. While 2-DG is not an approved drug, it has been studied in 218 clinical trials for the treatment of various cancers globally. 2-DG has not been evaluated in the acute treatment of moderate to severe COVID-19. However, based on mechanistic and in-vitro-evidence (see below) as well efficacy seen in the interventional clinical studies in malignancies and genital herpes, the Sponsors believe that 2-DG could be developed for the specific treatment of patients with COVID-19 disease in conjunction with other anti-viral therapies.

2-DG was chosen based on its in vitro inhibition potential (EC50 = 1.0 mM, EC90 = 3.7 mM; supernatant) towards SARS-CoV-2 from the studies conducted by Institute of Nuclear Medicine & Allied Sciences (INMAS), Delhi of the Defence Research and Development Organization (DRDO) at Centre for Cellular and Molecular Biology, Hyderabad. The Sponsor of this study, INMAS, DRDO, Ministry of Defence, Govt of India, was responsible for genesis of this hypothesis and testing of efficacy of 2-DG against SARS-CoV2. These effective concentrations are within the range that can be achieved in human plasma upon oral dosing of 63 mg/kg/day.

Moreover, Positron Emission Tomography (PET) with the radiotracer, 18FDG (Fludeoxyglucose, an analog of 2-DG) has shown accumulation of the radiolabel in the inflamed lungs of COVID-19 patients, due to high metabolic activity induced by the coronavirus infection. Dr Reddy’s believes that this phenomenon could potentially result in a preferential and disproportionately high accumulation of 2-DG in inflamed lung tissue of COVID-19 patients thereby leading to starvation in the lung cells, which in turn would lead to inhibition of viral replication.