Clinical Trial Details (PDF Generation Date :- Sun, 26 Mar 2023 13:58:19 GMT)

CTRI Number	CTRI/2020/08/027162 [Registered on: 14/08/2020] - **Trial Registered Prospectively**
Last Modified On	04/10/2021
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug
Study Design	Randomized, Parallel Group Trial
Public Title of Study	A clinical study to understand the effect of Inosine Pranobex in Covid-19 patients when used along with the standard of Care in Covid patients.
Scientific Title of Study	An Open-Label, Prospective, Randomized, Comparative, Parallel Group, Multi-Center, Proof of Concept Study to Assess the Efficacy and Safety of Inosine Pranobex Added to Current Standard of Care (CSC) in COVID-19 Patients.

Secondary IDs if Any

Secondary ID	Identifier
TML/IAD/2020/01 Version 1.1 24 Jul 2020	Protocol Number

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

Details of Principal Investigator	
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Details Contact Person (Scientific Query)

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Source of Monetary or Material Support

Source of Monetary or Material Support
> Themis Medicare, 11/12, Udyog Nagar, S. V. Road, Goregaon (W), Mumbai – 400104, Maharashtra, India

Primary Sponsor

Primary Sponsor Details	
Name	Themis Medicare
Address	11/12, Udyog Nagar, S. V. Road, Goregaon (W), Mumbai – 400104, Maharashtra, India
Type of Sponsor	Pharmaceutical industry-Indian

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Ranganath T Ganga	All India Institute of Medical Science	Room No.1, Department of Pulmonary Medicine, All India Institute of Medical Science, Great Eastern Road, Tetibandha, Raipur Raipur CHHATTISGARH	8004220308 ranganathtg@gmail.com
Dr Jayanthi C R	Bangalore Medical College and Research Institute	Room No. 1, Director Cabin, Bangalore Medical College and Research Institute, Fort KR Road, Bangalore Bangalore KARNATAKA	9480832400 bmccrj@gmail.com
Dr Padmaja Saraf	District Hospital, Chikalthana	Room No.1, Department of Medicine, District Hospital Chikalthana, Aurangabad, Near Airport, Jalna Road, Aurangabad Aurangabad MAHARASHTRA	9422216825 drpadmajasaraf@gmail.com
Dr Mohammad Siddiqui	Heritage Institute of Medical Sciences	Room No 1, Doctors Cabin, Heritage Institute of Medical Sciences, NH-2, GT Road Bypass, Varanasi Varanasi UTTAR PRADESH	9889352598 drshafaatimam@gmail.com
Dr Mohd Saif Khan	Rajendra Institutes of Medical Science	Room No.1, RIMS CIR, Indraprasth Colony, Bariatu, Ranchi Jharkhand 834009 Ranchi JHARKHAND	8870561682 drsaif2k2@gmail.com
Dr Dnyaneshwar Halnor	Vijay Vallabh Hospital and Medical Research	Room No. 423, Tirupati Nagar, Phase 1, Bolinj,	7507779219

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Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Ethics Committee of Bangalore Medical College & Research Institute, Bangalore	Approved	27/08/2020	No
Ethics Committee of Ishwar Institute of Health Care, Aurangabad	Approved	14/08/2020	No
Ethics Committee, Rajendra Institute of Medical Sciences (RIMS)	Approved	09/09/2020	No
Heritage Institute of Medical Sciences Ethics Committee, Varanasi	Approved	31/08/2020	No
Vijay Vallabh Hospital and Medical Research Centre, Palghar	Approved	12/08/2020	No

Regulatory Clearance Status from DCGI

Status	Date
Approved/Obtained	28/07/2020

Health Condition / Problems Studied

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

Intervention / Comparator Agent

Type	Name	Details
Intervention	Tab. Inosine Pranobex 500 mg in addition with Standard of Care	[Synonyms of API: Inosine Acedoben Dimepranol (INN), Methisoprinol, Isoprinosine] Dose: 500 mg Route: Oral Frequency: 2 Tabltes Four Times in a day.
Comparator Agent	Standard of Care	Standard of Care as per Investigator discretion

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	65.00 Year(s)
Gender	Both
Details	1.Written signed and dated informed consent (patient or LAR). 2.Either gender, in the age group between 18 to 65 years 3.Patients of laboratory confirmed COVID-19 [nasopharyngeal (preferred) or oropharyngeal swab RT-PCR positive] presenting with WHO listed symptoms of COVID-19 c/o fever, headache, myalgia, cough, throat pain or shortness of breath 4.A score of between 3 to 5 on the WHO Modified Ordinal Scale for Clinical Improvement (refer protocol appendix 23.1) 5.SpO2 ?90% for adults and respiratory rate ? 30/minute 6.Patients who provide a agree to abide by the study requirements

Exclusion Criteria

Exclusion Criteria	
Details	1.Known hypersensitivity to any of the ingredients of the study drug

	2.Pregnant and lactating women 3.Children 65 years 4.SpO2 30/minute 5.History of gout or hyperuricemia (serum uric acid level >6mg/dl), urolithiasis, nephrolithiasis or any degree of renal dysfunction 6.Patients with history of diagnosed primary congenital immunodeficiency, or acquired immunodeficiency like HIV, OR any Genetic or developmental anomaly like Cerebral Palsy, coeliac disease, lactose intolerant, cancer in nor remission stage. 7.Patient who are undergoing treatment with xanthine oxidase inhibitors, uricosuric agents, diuretics, immunosuppressive agents or zidovudine. 8.Patients with severe cardiac, hepatic, gastrointestinal, renal, pulmonary and skin diseases. 9.Patients simultaneously participating in another clinical study. 10.Medical or psychological conditions deemed by the investigators to interfere with successful participation in the study 11.A subject who is judged by the investigator as inappropriate to participate in the study for any reason other than those mentioned above

Method of Generating Random Sequence	Computer generated randomization
Method of Concealment	An Open list of random numbers
Blinding/Masking	Open Label

Primary Outcome

Outcome	Timepoints
Percentage of patients with 2 points improvement or becoming asymptomatic (Grade 2 or less) on the modified WHO ordinal scale for clinical improvement between two groups at day 14	at Day 14

Secondary Outcome

Outcome	Timepoints
Percentage of patients with 2 points improvement or becoming asymptomatic (Grade 2 or less) on the modified ordinal scale for clinical improvement for two groups at Day 7 and Day 21	Day 7 and Day 21
Percentage of patients with Grade 1 on WHO modified ordinal scale confirmed (negative swab status) at Day 7, Day 14 and Day 21 for two treatment arms	Day 7, 14 and 21
Percentage of patients with Grade 2 on WHO modified ordinal scale at Day 7, Day 14 and Day 21 for two treatment arms	Day 7, 14 and 21
Time to two-point improvement or becoming asymptomatic (Grade 2 or less) on the modified WHO ordinal scale for patients in the two treatment arms	NIL
Time to resolution of all clinical symptoms of COVID-19 viral infection (Grade 2 on WHO modified ordinal scale) for two treatment arms	NIL
Time to RT-PCR swab negative COVID-19 viral infection (Grade 1 on WHO modified ordinal scale) for two treatment arms	NIL
Mortality rate at Day 21	Day 21
Severity of Dyspnea at Day 7, Day 14 and Day 21	Day 7, 14 and 21

Time to discharge from hospital/duration of hospitalization for inpatients for two groups	NIL
Rate of patients requiring oxygen/ventilation, and/or duration of oxygen use/duration of requiring ventilation for two groups at Day 7 and Day 14	Day 7 and 14
Change in blood levels of NK cell, IL-6 and IL-10 between both treatment groups at Day 7, Day 14 and Day 21 visit.	Day 7, 14 and 21

Target Sample Size	**Total Sample Size=**60 **Sample Size from India=**60 **Final Enrollment numbers achieved (Total)=**83 **Final Enrollment numbers achieved (India)=**83
Phase of Trial	Phase 2
Date of First Enrollment (India)	20/08/2020
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**0 **Months=**2 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Completed
Publication Details	NIL
Brief Summary	This is an open-label, prospective, comparative, multicentre proof of concept study. This multicentre study is to assess the effect of Tab. Inosine Pranobex as an add-on therapy to the standard of care for of patients in patients with confirmed acute COVID-19infection achieving clinical response, when compared to patients only on standard of care. Patients suggestive of RT-PCR [nasopharyngeal (preferred) and oropharyngeal swab positive] acute COVID-19 infection will be enrolled into this study with a score between 3 to 5 on the Modified Ordinal Scale for Clinical Improvement (refer protocol appendix 23.1). Both inpatient and outpatients will be enrolled into this study. The Modified WHO Ordinal Scale for Clinical Improvement, physical and systemic examination will be performed on a daily basis for inpatients and at the scheduled protocol visits for outpatients. The enrolled patients will receive Tab. Inosine Pranobex treatment for a period of 14 days. Patients will be assessed on day 7 (±1 day) and day 14 (±1 day). A follow-up safety assessment will be done on day 21 (±1 day). Croissance Clinical Research is providing the Data management Support to the clinical study. **<u>Summary of Results</u>** **Primary Endpoint:** Clinical Response (CR) at Day 14 was observed in 90% patients in IAD+CSC treatment arm vs. 85.37% patients in CSC treatment arm in the ITT population. The difference between the two treatments arms was not statistically significant (p-value: 0.526). **Secondary Endpoints:**

CR at Day 7 and Day 21 in the IAD+CSC treatment arm and the CSC treatment arm was 57.50% vs. 43.90% (p-value: 0.221) and 90.00% vs. 87.80% (p-value: 0.753). The cumulative number of patients who achieved CR at day 10 in the IAD+CSC treatment group was 83% as compared 61% in CSC group (61%).

Clinical Cure (CC) at Day 7, 14 and 21 in IAD+CSC treatment arm vs. CSC treatment arm in the ITT population was 57.50% vs. 43.90% (p-value: 0.221), 90.00% vs. 85.37% (p-value: 0.526) and 90.00% vs. 87.80% (p-value: 0.753), respectively. The cumulative number of patients who achieved CC at day 10 was 63% in the IAD+CSC group, as compared to 54% the CSC group.

Virological Cure at Day 7, 14 and 21 in IAD+CSC treatment arm vs. CSC treatment arm in the ITT population was 37.50% vs. 34.15% (p-value: 0.753), 75.00% vs. 73.17% (p-value: 0.851) and 82.50% vs. 80.49% (p-value: 0.816), respectively.

For the remaining secondary endpoints, there was no statistically significant difference between the two treatment groups for the ITT population.

Sub-group analysis of patients showed that Inosine Pranobex, when added to standard of care containing Azithromycin and Hydroxychloroquine with or without Ivermectin, produced significantly higher clinical response (CR) at Day-14 than only standard of care (100.00% vs 69.23%; p=0.03).

Overall, there was a trend of (numerically) higher CR, CC and VC on at Day 7, 14 and 21 in the IAD+CSC group compared to the CSC group; however, statistical significance could not be reached. This may be because of small sample size of the study variability in the current standard of care (CSC) among the different sites.

There was no SAE and the drug was well tolerated.