1. TITLE PAGE

CLINICAL STUDY REPORT

A Randomized, Double-Blind, Multi-Center Study to Evaluate the Efficacy and Safety of Ethyl Lauroyl Arginate Hydrochloride (LAEH) Formulation Versus a Matching Placebo Formulation Administered as a Nasal Spray to Reduce Viral Load From Nasal Area of Subjects with Coronavirus Disease 2019 (COVID-19)

Investigational Product	:	Covixyl-V (Ethyl lauroyl arginate hydrochloride, 0.1% concentration)
Indication	:	Coronavirus Disease 2019
Study Design	:	Double-Blind, Placebo Controlled, Multi-Center, Randomized Study
Name of the Sponsor	:	Salvacion USA Inc., 210 Sylvan Avenue Suite 24 Englewood Cliffs, NJ, 07632, USA
Protocol Identification Number	:	SLV-CV19-SPRAY
Protocol Version:		Version 1.1 (Amendment 1), dated 29 Sep 2021
Development Phase of the Study	:	Pivotal Study
Study Initiation Date	:	29 May 2021
Study Completion Date	:	04 Oct 2021
Principal Investigator	:	(1) Dr. Altagracia Adalgiza Victoria, MD; 2300 W 84 St Suite 303, Hialeah, FL 33016 USA (2) Dr. Jorge P. Amaya, MD; 8485 Bird Road, Suite 303, Miami FL 33155
Name of the Sponsor Signatory	:	Dr. Abdul Gaffar, PhD
Date of the report	:	06 Jan 2022

This study was conducted in compliance with the protocol, Good Clinical Practice and all other applicable regulatory requirements including the archiving of essential documents.

Confidential Information

2. SYNOPSIS

Name of Sponsor: Salvacion USA Inc.	
Name of the Medical Device: Covixyl-V nasal spray	
Name of the Active Ingredient: Ethyl lauroyl arginate hydrochloride (0.1% concentration)	
Title of Study: A randomized, double-blind, multi-center study to evaluate the efficacy and safety of ethyl lauroyl arginate hydrochloride (LAEH) formulation versus a matching placebo formulation administered as a nasal spray to reduce viral load from nasal area of subjects with coronavirus disease 2019 (COVID-19).	
Investigators: (1) Dr. Altagracia Adalgiza Victoria, MD; 2300 W 84 St Suite 303, Hialeah, FL 33016 USA (2) Dr. Jorge P. Amaya, MD; 8485 Bird Road, Suite 303, Miami FL 33155	
Study centers: 2	
Study period: 8 weeks **Date of first enrolment:** 02 Aug 2021 **Date of last completion:** 04 Oct 2021	**Phase of Development:** Pivotal Study
Objectives: Primary: To evaluate efficacy of LAEH nasal spray on SAR-COVID-2 viral load in nasal areas. Secondary:	

1. To evaluate the efficacy of LAEH on the viral load in terms of proportion of COVID-19 infection-free subjects between the two arms. 2. To evaluate the safety of LAEH versus a matching placebo administered as a nasal spray.
Methodology: This was a multi-center, randomized, double-blind, placebo-controlled clinical study carried out to evaluate and compare the safety and efficacy of LAEH nasal spray (0.1% concentration) against a matching placebo nasal spray, administered to reduce viral load from the nasal area of subjects with Coronavirus Disease 2019 (COVID-19). Subjects were enrolled after obtaining written informed consent and were screened for eligibility for the study based on inclusion and exclusion criteria. For confirmation of COVID-19, subjects underwent Reverse transcription polymerase chain reaction (RT-PCR) test. Only those subjects who had laboratory-confirmed diagnosis of COVID-19 at the time of screening (Day -3 to 0) using RT-PCR method and who met all eligibility criteria were enrolled. Along with viral load values from RT-PCR test, cycle threshold (CT) value was also included in the laboratory reports. Thirty (30) subjects with COVID-19 were randomized into this study with Covixyl-V LAEH nasal spray and placebo nasal spray. Subjects were randomized in a 1:1 proportion to receive either LAEH formulation or matching placebo twice daily. Subjects were instructed to use the assigned treatment as nasal spray (2 to 3 puffs in each nostril at a time) twice a day from Day 1 to Day 5 and only once in the morning on Day 6. Subjects were instructed to refrain from eating, drinking, or using any nasal gavage at least 30 minutes prior to use of nasal spray. Subjects were also informed that the daily second treatment should be taken approximately 6 hours after the first treatment. The site personnel explained the effective use of the nasal spray in a step-by-step manner and documented the same training in the source documents. The subjects were instructed to record his/her initials and date and time he/she administered the assigned treatment on a daily basis in the subject diary. On Day 6/end of study (EOS), all the subjects took the first treatment (11^{th} dose) at home around 8:00 am and then visited their respective site as instructed. Then the site performed the viral load enumeration

using RT PCR test (including CT value) within 3 and 6 hours post last dose (at end of 11th treatment).

Group A assessed 15 subjects with COVID-19 who received Covixyl-V LAEH nasal spray for 6 days.

Group B assessed 15 subjects with COVID-19 who received placebo nasal spray for 6 days.

The site called each subject daily and collected information on Adverse Events (AEs) (if any), concomitant medications, and treatment compliance and completion of subject diary. Adverse Events (AEs) were collected after signing of informed consent through the end of the study.

The frequency of assessment was at screening/baseline and on Day 6.

RT-PCR testing was performed for confirmation of positive COVID-19 test, and enumerating viral load (including CT value). Vital signs such as blood pressure (BP), heart rate (HR), respiratory rate (RR), Oxygen saturation (SpO2), body temperature were noted and nasal and physical examination was performed.

Safety and tolerability of Covixyl-V LAEH nasal spray were assessed by evaluating AEs, serious adverse events (SAEs), vital signs, treatment discontinuation due to AEs, and nasal and physical examinations.

Number of Subjects (Planned and Analyzed):

Total 30 subjects were enrolled in the study as planned. Total 30 subjects were analyzed in the study at 2 sites across United States (US).

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria

A subject was included in the study when he/she met below inclusion criteria:

1. Ability to provide written informed consent or, by his or her legal/authorized representatives when the subject is not capable of giving consent, prior to initiation of any study procedures
2. Male or female of ≥18 years and ≤65 years of age (inclusive) at time of enrollment

3. Subjects with laboratory-confirmed diagnosis of COVID-19 at the time of screening (Day -3 to 0) using RT PCR method.
4. Subject with mild COVID-19 symptoms (e.g., fever, cough, sore throat, headache, muscle pain, nasal congestion, rhinorrhea, loss of smell and taste) but who did not have shortness of breath or dyspnea
5. Subjects who did not require hospitalization
6. Subjects with SpO2 levels ≥ 95%
7. Viral load by RT-PCR between 3.3×10^6 copies/mL to 6.6×10^6 copies/mL
8. Female subject who was not of childbearing potential, defined as postmenopausal for at least 1 year or surgically sterile
9. Female subject of childbearing potential who had negative urine pregnancy test.

Exclusion Criteria

Subjects were not included in the study when he/she met any of the below exclusion criteria

1. Allergy to LAEH or any of the excipients of the formulation
2. History of allergies or flu within 30 days prior to the day of enrollment
3. Sensitivity to nostril skin or irritation or bleeding history within 30 days prior to the day of enrollment
4. Females who were breast-feeding, lactating, pregnant or intending to become pregnant
5. COVID-19 subjects with moderate, severe or critical illness or requiring intensive care or mechanical ventilation
6. History of severe respiratory disease and requirement for long-term oxygen therapy
7. Had received antibiotic/s, antiviral drug, and hormonal drugs within 30 days prior to the day of enrollment
8. Any condition or disease detected during the medical interview/physical examination that would render the subject unsuitable for the study, place the subject at undue risk or interfere with the ability of the subject to complete the study in the opinion of the Investigator
9. Had received or had a plan to receive a SARS-CoV-2 vaccine during the study period
10. Participated in any interventional drug or medical device trials within 30 days prior to the day of enrollment.

Test Product, Dose and Mode of Administration, Batch Number:

Covixyl-V (Nasal Spray) - Ethyl lauroyl arginate hydrochloride (0.1% concentration) formulation administered through nasal spray (2 to 3 puffs in each nostril at a time) twice a day for 6 days (On Day 6, only morning treatment was administered).

Other information: Store at room temperature. Keep away from direct sunlight and heat source.

Batch Number: CVF11R and CVG05R

Reference Therapy, Dose and Mode of Administration, Batch Number:

Vehicle (matching placebo) formulation administered through nasal spray (2 to 3 puffs in each nostril at a time) twice a day for 6 days (On Day 6, only morning treatment was administered).

Other information: Store at room temperature. Keep away from direct sunlight and heat source.

Batch Number: CVG05F

Duration of Treatment:

The duration of the use of study product was 6 days. Subjects were instructed to administer treatment using nasal spray with the assigned formulation (LAEH or matching placebo) twice a day for 6 days (On Day 6, only morning treatment was administered).

Criteria for Evaluation:

Primary Efficacy Endpoint:

- Comparison of change in viral load from baseline between the two treatment arms

Secondary Efficacy Endpoint:

- Proportion of COVID-19 infection-free subjects between the two treatment arms

Safety Endpoint (Secondary):

- The safety of LAEH formulation was compared to Vehicle (matching placebo) with analysis of safety variables including safety assessments (vital signs) and AEs.

Statistical Methods:

Statistical Analysis

Demographics, disposition, and baseline characteristics of subjects were tabulated by treatment assignment. Summary of all the demographic and baseline characteristics was presented for all the subjects in safety population. Descriptive statistics (n, mean, standard deviation [SD], median, minimum, and maximum) was provided for all the continuous variables. Frequency count (n) and percentage (%) of patients was provided for the categorical variables. Statistical tests were performed at 5% level of significance.

Analysis Data Sets:

The statistical analysis was performed using mITT (Modified Intent-to-treat), PP (Per protocol) and safety analysis population.

Modified Intent-to-Treat Analysis Population (mITT): All subjects who were randomized, took at least one dose of study product, and had at least one post baseline evaluation.

Per Protocol population (PP): The PP population included all mITT subjects who remained in the study and had no major protocol violations and received at least 80% of the doses.

Safety Population: All randomized subjects who took at least one dose of study product.

- Safety analysis was performed on safety population.
- Efficacy analysis was performed on mITT and PP populations.
- The results in the PP population were considered definitive with those in the mITT population considered supportive.

Analysis of Efficacy Endpoint

Primary Efficacy Endpoint Analysis

The primary endpoint for this study was the comparison of change in viral load in RT-PCR Test from baseline at Day 6 between the two treatment arms.

Mean viral load and change from baseline in viral load at Day 6 within 3 hours post last dose and Day 6 within 6 hours post last dose was summarized descriptively by treatment group for mITT and PP population.

Analysis of covariance (ANCOVA) was employed to find the statistically significant difference between the treatment groups with baseline viral load as covariate.

Secondary Efficacy Endpoint Analysis

Proportion of COVID-19 infection-free subjects between the two treatment arms.

Proportion of infection-free subjects was presented with frequency count and percentage for each treatment group for mITT and PP population.

Chi square test for independence was used to find the statistical significance between the treatment arms.

Analysis of Safety Endpoints

All safety endpoints were summarized and compared using descriptive statistics between two treatment arms.

- Adverse Events

Summary of AEs, including the number and percentage of patients with any AEs, TEAEs, SAEs, study product-related AEs, study product-related SAEs, discontinuations, and incidence. AE was presented by SOC and PT. Each adverse event was evaluated for the date of start and end, severity, relationship to the study product, action is taken and outcome.

- Change in Vital Signs

Vital signs and change in vital signs were summarized descriptively by treatment arm for safety population.

- Change in Nasal Examination from Baseline

Change in nasal examination was summarized descriptively by treatment arm for safety population.

Summary - Conclusions:

Efficacy Results

Although the reduction in the viral load in the Covixyl-V group was observed only within 3 hours post last dose but not within 6 hours post last dose when compared to the placebo group, the results of the study favor Covixyl-V group since there were only 2 subjects having positive COVID-19 infection on EOS visit when compared to that of the placebo group (7 subjects). This indicates that viral load by itself is not an indicating parameter without clinical outcome i.e., positive/negative RT-PCR test results. The mean fold change difference in RT-PCR CT value on Day 6 within 6 hours post last dose was not statistically significant between the two groups. Nonetheless, there was a significant improvement in the RT-PCR CT value of subjects on Day 6 within 6 hours post last dose from baseline in both the individual groups. All subjects in both

groups, Covixyl-V and the placebo at the start of the study were COVID-19 infection positive. **At the end of the treatment, the Covixyl-V group had over 4 times more infection-free subjects than the placebo group based on the calculation of negative/positive ratio.**

Safety Results

A total of 30 randomized subjects were exposed to either Covixyl-V or placebo. One (3.3%) subject reported an AE which was of mild severity and was possibly related to the study product. The event was resolved at the time of final reporting. No action was taken with the study product. No SAEs and no deaths were reported in the study. None of the subjects in Covixyl-V group and Placebo group had abnormal vital signs throughout the study. On completion of study treatment, the Covixyl-V group had higher number of subjects 12 (80.0%) with normal ENT condition than the Placebo group 9 (60.0%). Higher number of subjects were free from nasal inflammation-redness on Day 6 in the Covixyl-V group when compared to placebo group. There was no improvement in nasal inflammation-redness in placebo group on Day 6 from baseline. **The Covixyl-V group showed 2 times greater improvement in nasal discharge free subjects on Day 6 from baseline (Day 1) when compared to placebo group. Overall, the Covixyl-V LAEH Nasal spray was found to be safe for use in nasal cavity.**

Conclusion:

- **The Covixyl-V LAEH Nasal Spray is safe for use in subjects with COVID-19 infection and 4 times more infection-free subjects were observed in the Covixyl-V group at the end of the treatment vs the placebo.**
- **Covixyl-V nasal spray reduces the viral load by improving CT value to better extent in 6 days.**
- **Covixyl-V nasal spray is safe and well tolerated in subjects with COVID-19.**

Date of Report

06 Jan 2022

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LIST OF IN-TEXT FIGURES

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4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	**Definition**
ADL	Activities of Daily Living
AE	Adverse Event
ANCOVA	Analysis of Covariance
CFB	Change from baseline
CFR	Code of Federal Regulations
COVID-19	Coronavirus Disease-19
CRO	Contract Research Organization
CT	Cycle Threshold
CTCAE	Common Terminology Criteria for Adverse Events
eCRF	Electronic Case Record Form
ENT	Ear, Nose and Throat
EOS	End of Study
EU	European Union
GCP	Good Clinical Practice
GRAS	Generally Recognized as Safe
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IEC	Institutional Ethics Committee
IRB	Institutional Review Board
LAE	Lauric Arginate
LAEH	Ethyl lauroyl arginate hydrochloride
LAR	Legally acceptable representative

Abbreviation	**Definition**
LAS	N^{α}-lauroyl-L arginine
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
NOAEL	No-observed-adverse-effect-level
OTC	Over the counter
PP	Per Protocol
PT	Preferred term
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SOC	System organ class
SOPs	Standard Operating Procedures
SpO2	Oxygen Saturation

5. ETHICS

5.1 Institutional Ethics Committee (IEC)

The Investigator submitted the protocol, the ICF, and any other relevant supporting information (e.g., all advertising materials or materials given to the patient during the study) to the appropriate IRB/IEC for review and approval before study initiation. Amendments to the protocol and ICF were also approved by the IRB/IEC before the implementation of changes in this study. The Investigator was responsible for providing the IRB/IEC with any required information before or during the study, such as SAE expedited reports or study progress reports.
The IRB/IEC complied with current US regulations (§ 21 CFR 56 and 812) as well as country-specific national regulations and/or local laws.

The following documents were provided to the sponsor or its authorized representative before entering patients in this study: (1) a copy of the IRB/IEC letter that grants formal approval; and (2) a copy of the IRB/IEC-approved ICF.

5.2 Ethical Conduct of the Study

The study was conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and in compliance with the ethical principles that have their origin in the Declaration of Helsinki, ICH guidelines consolidated Guideline E6 for GCP and applicable regulatory requirement(s):

- Food and Drug Administration Regulations (21 CFR Parts 11, 50, 54, 56, 312, and 812).
- The Health Insurance Portability and Accountability Act as appropriate.

5.3 Written Informed consent

The ICF and process of obtaining and documenting informed consent were compliant with the US regulations (§ 21 CFR Part 50) as well as country specific national regulations and/or local laws. A sample ICF containing the required elements of informed consent was provided by the CRO/Sponsor. Sample form(s) were provided as required by IRB and EC guidelines. Any changes made to these samples were reviewed by the CRO/Sponsor prior to submission to the IRB. After review by the CRO/Sponsor, the informed consent form was submitted to and approved by the IRB or relevant ECs. The informed consent was submitted to the IRB/ECs of the participating countries in the country local language(s).

It was the responsibility of the Investigator to inform each subject of the purpose of this clinical study, including possible risks and benefits, and to document the informed consent process.

Prior to undergoing any study-related procedures, each subject read, signed, and dated the IRB/EC-approved version of the ICF. The original informed consent form was retained by the study site, and copies were given to the subject.

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

The study was administered and monitored by a CRO (Global Clinical Trials Inc). The Medical Monitor was available to provide appropriate medical expertise on study-related medical questions. Global Clinical Trials Inc was responsible for the timely reporting of the SAEs.

6.1 Investigative Site(s)

Site	Principle Investigator Name	Site Name and Address
1	Dr. Altagracia Adalgiza Victoria, MD	2300 W 84 St Suite 303, Hialeah, FL 33016 USA
2	Dr. Jorge P. Amaya, MD	8485 Bird Road, Suite 303, Miami FL 33155

6.2 Study Dates

Study initiation date	29 May 2021
First subject first visit date	02 Aug 2021
Last subject last visit date	04 Oct 2021
Database lock date	17 Nov 2021
Final clinical study report date	06 Jan 2022

6.3 Sponsor information

Salvacion USA Inc., 210 Sylvan Avenue Suite 24, Englewood Cliffs, NJ, 07632, USA.

6.4 Coordinating Investigator and Medical Monitor

1) Dr. Samer Hilan, MD [+359 899 930 381, S.Hilan@gctrials.com],
   Global Clinical Trials, LLC, 104 b. Ivan Geshovblvd., apt. 2, 1612 Sofia, Bulgaria
2) Dr. Abdul Gaffar, PhD [609.647.1088, agaffar@verizon.com]

6.5 Contract Research Organization

Global Clinical Trials, LLC, 256 Bunn Drive, Suite 6, Princeton, NJ 08540.

6.6 Study Statistician

Statiza Statistical Services, 209, South Bopal Trade Centre (SBTC), Near Aryan Gloria, Gala Gymkhana Road, South Bopal, Ahmedabad-380058, Gujarat, India.

6.7 Clinical Supply Management

Salvacion USA Inc., 210 Sylvan Avenue Suite 24, Englewood Cliffs, NJ, 07632, USA.

6.8 Central Laboratory

Not Applicable.

6.9 Clinical Study Report Writing

Innvocept Global Solutions Private Limited (IGSPL), B-7/1 Kothari Compound-27 Acres, Nr Tiku-ji-ni wadi Resort Chitalsar, Manapada, Thane (W) Mumbai-400 607, Maharashtra, India.

7. INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated coronavirus disease (COVID-19) broke out in December 2019 and has quickly become a global pandemic with serious health and social consequences (Koopmans M, 2020). As of 27 Dec, 2021, more than 279 million confirmed cases have been reported around the world and about close to one-fifth are from the U.S. Globally, more than 5,399,977 people have died due to COVID-19 and 816,609 in the U.S. alone (Johns Hopkins, 2021).

The virus can infect respiratory systems through entry via nasal passages. While vaccines have been developed, means are required to arrest or reduce nasal transmission of the virus. Effective antiviral therapies, especially in the early stage of infection, are vitally important to halt viral proliferation long enough for the immune system to respond to the virus and limit cellular damage inflicted by viral invasion as well as to minimize genetic mutations caused by the high replication frequency of the virus, which might lead to therapeutic resistance.

N^{α}-Lauroyl-L-arginine ethyl ester monohydrochloride, hereinafter LAE (Lauric Arginate for labelling purposes under FDA approval), is a derivative of lauric acid, L-arginine and ethanol. The main characteristics of this molecule are a wide range of antimicrobial properties derived from its surfactant chemical structure that additionally yields certain tensioactive properties. The antimicrobial properties of LAE are due to its action on the cytoplasmic membranes of the microorganisms in such a manner that their metabolic processes are altered and their normal cycle is inhibited but without cellular lysis.

LAE shows chemical stability at pH range between 3 and 7 and maintains its antimicrobial activity in this interval; this offers a significant advantage compared to other products currently available in the market. LAE is hydrolyzed in the human body by chemical and metabolic pathways breaking the molecule into natural compounds common in human diet. This feature gives LAE a remarkable degree of safety. This non-toxicity is demonstrated by numerous toxicological studies carried out over the past years. On 01 Sep 2005, FDA issued the No Objection Letter regarding that LAE is Generally Recognized as Safe (GRAS) for use as antimicrobial in several food categories at levels up to 200 ppm. In addition, the USDA approved its use in meat and poultry products.

In the human intestine and in the plasma, LAE is rapidly metabolized to N^{α}-lauroyl-L arginine (LAS) which is subsequently metabolized to arginine and finally to endogenous compounds. LAE

does not produce mutagenic or clastogenic effects and concerning to the LAE effect onto the reproductive and developmental effects, the NOAEL (no-observed-adverse-effect-level) was fixed at 15000 ppm for the reproductive performance and development of F1 and F2 (LMA-041, 2003 and LMA-042, 2004).

The lethal dose in both oral and dermal acute toxicity experiments is greater than 2000 mg/kg bw, the highest dose tested. Subchronic toxicity studies established a NOAEL of 15000 ppm (1143 and 1286 mg/kg bw/day for males and females, respectively) (LMA-031, 2000). The NOAEL fixed for chronic studies was 6000 ppm (307 and 393 mg/kg bw/day for males and females, respectively) (LMA-050). LAE and its hydrolysis products have been sufficiently characterized to assure that human consumption of LAE used as a preservative in foods and human exposure to LAE used as a preservative in cosmetics are safe.

In conclusion, the toxicological profile of lauric arginate looks favorable for its use as a preservative with no risk to consumer health.

Human metabolic studies of LAE were undertaken after the toxicity studies confirmed that the product is safe. The first human experiment was an in vitro study that was helpful to obtain information about the metabolism of LAE after ingestion including the potential points of degradation (intestines, liver and plasma) and it's pharmacokinetic (LMA, 2003). Under all three of the in vitro conditions tested, LAE was rapidly degraded to LAS and subsequently to arginine.

In a second human study, LAE was administered to six volunteers divided into two dose groups. All of the subjects were given clinical examination and samples of blood were extracted for analysis. The clinical examination consisted of identifying any possible adverse physiological effect of LAE after its administration in a single oral dose. The blood work was focused on determining the pharmacokinetic of LAE through determination of the concentrations of LAE and its by-products. Two volunteers received an oral dose of 2.5 mg/kg bw (LMA-047, 2004). Four volunteers received an oral dose of 1.5 mg LAE/kg bw (LMA-049, 2004). Results from the study has shown that LAE was metabolized so quickly that it could not be detected in the blood samples, even those taken immediately following administration. In addition, there were no clinically significant abnormalities in any of the laboratory data for either of the two oral doses. Finally, LAE has no immunological action in either inducing or suppressing normal immunological functions of the body. LAE's mode of action is local and not systemic.

Ethyl Lauroyl Arginate Hydrochloride (LAEH) is monohydrochloride salt of LAE, and hereinafter referred as LAEH formulation.

COVID-19 infections are worldwide. While effective treatments are being developed, the current emphasis is on prevention utilizing facial masks, applying hand sanitizers and social distancing. Masks alone cannot protect against transmission of infections through aerosol and droplets. Therefore, effective antiseptics that can be used in nasopharynx or oral routes is needed to reduce and prevent transmission. Salvacion USA Inc., announced that Covixyl-V, antiseptic, demonstrated virucidal activity against SAR-CoV-2, the virus that causes COVID -19. It is a proprietary combination of two FDA approved ingredients developed to inactivate SAR-CoV-2 for nasal and oral administration. The proprietary combination proved to be effective in inactivating the viruses up to 100%. The combination is effective at low concentrations, applicable for nasal sprays and/ or oral rinse to inactivate the virus.

A study conducted by Shrivastava and et al., showed natural course of symptoms of the viral COVID-19 infection. Viral load increased from Day 1 to Day 7, however after Day 7, it started to decrease (Shrivastava R, 2021). Also, COVID-19 infected patients normally show respiratory symptoms during first 4-6 days due to viral growth, inflammation and nasal mucosal damage and start stabilizing after 6 days (Singhal T, 2020). Additionally, in vivo study conducted in Syrian Hamsters at BIOQUAL, Inc., showed similar pattern to human COVID-19 virus progression. Therefore, our five days planned treatment period should be within disease progression pattern (Study No.: SALV-20-1A and SALV-20-02, 2021).

The aim of this study was to evaluate the efficacy of nasal spray containing LAEH formulation versus a matching placebo formulation administered as a nasal spray to reduce SAR CoV-2 viral levels in nasal area of COVID-19 positive patients.

8. STUDY OBJECTIVES

Primary:

To evaluate efficacy of LAEH nasal spray on SAR-COVID-2 viral load in nasal areas.

Secondary:

1. To evaluate the efficacy of LAEH on the viral load in terms of proportion of COVID-19 infection-free subjects between the two arms.

2. To evaluate the safety of LAEH versus a matching placebo administered as a nasal spray.

9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan:

This was a multi-center, randomized, placebo-controlled, double-blind clinical study carried out to evaluate and compare the safety and efficacy of LAEH nasal spray (0.1% concentration) against a matching placebo nasal spray, administered to reduce viral load from the nasal area of subjects with COVID-19. Pretreatment and post treatment viral load enumeration (including CT values) using RT-PCR was performed to assess the effect (LAEH formulations or matching placebo) after 6 days of nasal spray administration.

A total of thirty (30) subjects with COVID-19 were randomized into this study with Covixyl-V LAEH nasal spray and placebo nasal spray. Subjects were randomized in a 1:1 proportion to receive either LAEH formulation or matching placebo twice daily.

Group A assessed 15 subjects with COVID-19 who received Covixyl-V LAEH nasal spray for 6 days.

Group B assessed 15 subjects with COVID-19 who received placebo nasal spray for 6 days.

The frequency of assessment was at screening/baseline and on Day 6.

9.2 Discussion of Study Design, Including the Choice of Control Groups

This was a multi-center, randomized (1:1), placebo-controlled, double-blind clinical study carried out to evaluate and compare the safety and efficacy of LAEH nasal spray against a matching placebo nasal spray, administered to reduce viral load from the nasal area of subjects with COVID-19.

This pivotal clinical study was designed to be conducted in United States (US) at 2 clinical research centers during year 2021.

Subjects were enrolled after obtaining written informed consent and were screened for eligibility for the study based on inclusion and exclusion criteria. For confirmation of COVID-19, subjects underwent RT-PCR test. Prior to nasal swabbing at screening, subjects were instructed to refrain from eating, drinking, or using any nasal gavage or nasal spray at least 30 minutes. A nasal mid-turbinate specimen for COVID-19 testing was collected initially from all enrolled subjects as per the protocol of Center for Disease Control and Prevention (CDC 2020) for enumerating viral load

using RT-PCR. Only those subjects who had laboratory-confirmed diagnosis of COVID-19 at the time of screening (Day -3 to 0) using RT-PCR method and who met all eligibility criteria were enrolled. Along with viral load value from RT-PCR, CT value was also included in the laboratory reports. Subjects were randomized in a 1:1 proportion to receive either LAEH formulation or matching placebo twice daily.

Subjects were instructed to use the assigned treatment as nasal spray (2 to 3 puffs in each nostril at a time) twice a day from Day 1 to Day 5 and only once in the morning on Day 6. Subjects were instructed to refrain from eating, drinking, or using any nasal gavage at least 30 minutes prior to use of nasal spray. Subjects were also informed that the daily second treatment should be taken approximately 6 hours after the first treatment. The site personnel explained the effective use of the nasal spray in a step-by-step manner and documented the same training in the source documents.

Investigators informed all the subjects to follow below instructions prior to each use of nasal spray:

- Washing of hands thoroughly with soap and water
- Blowing of nose to clear nostrils before using nasal spray (if needed)
- While keeping the bottle upright, shaking and then removing cap to spray into the air until a mist to comes out
- Keeping head upright
- Careful placement of the spray nozzle inside the nostril and not too deep in the nose
- Spraying 2-3 puffs into one nostril and repeating the same into the other nostril
- Putting protective cap back after use
- Avoiding blowing of nose shortly after taking a dose of the medication
- Avoiding contact with the eyes
- Stopping the usage of spray if experienced any allergic reaction, swelling or irritation and then calling the investigator
- Keeping away the nasal spray from direct sunlight and heat source
- Storage at room temperature

The subjects were instructed to record his/her initials and date and time he/she administered the assigned treatment on a daily basis in the subject diary. On Day 6/EOS, all the subjects took the first treatment (11^{th} dose) at home around 8:00 am and then visited their respective site as instructed. Then the site performed the viral load enumeration using RT PCR (including CT value) within 3 and 6 hours post last dose (at end of 11^{th} treatment).

Basic demographic data including medical history (including ENT history), and details on any concomitant medications was recorded. The RT-PCR testing was performed for confirmation of positive COVID-19 test, and enumerating viral load (including CT value). Vital signs such as BP, HR, RR, SpO2, body temperature were noted and nasal and physical examination was performed.

Subjects fulfilling inclusion and exclusion criteria received respective doses of Covixyl-V LAEH nasal spray (test) or placebo nasal spray. The site called each subject daily and collected information on AEs (if any), concomitant medications, and treatment compliance and completion of subject diary. Adverse events (AEs) were collected after signing of informed consent through end of study.

Safety and tolerability of Covixyl-V LAEH nasal spray were assessed by evaluating AEs, SAEs, vital signs, treatment discontinuation due to AEs, nasal and physical examinations.

Subjects were randomized to one of the two groups according to the randomization scheme on Day 1/Baseline in the ratio of 1:1.

Group A: Total 15 subjects received Covixyl-V nasal spray (2 to 3 puffs in each nostril at a time) twice a day from Day 1 to Day 5 and only once in the morning on Day 6/EOS.

Group B: Total 15 subjects received Placebo nasal spray (2 to 3 puffs in each nostril at a time) twice a day from Day 1 to Day 5 and only once in the morning on Day 6/EOS.

9.3 Selection of Study Population

9.3.1 Inclusion Criteria

A subject was included in the study when he/she met below inclusion criteria:

1. Ability to provide written informed consent or, by his or her legal/authorized representatives when the subject is not capable of giving consent, prior to initiation of any study procedures

2. Male or female of ≥18 years and ≤65 years of age (inclusive) at time of enrollment
3. Subjects with laboratory-confirmed diagnosis of COVID-19 at the time of screening (Day -3 to 0) using RT-PCR method.
4. Subject with mild COVID-19 symptoms (e.g., fever, cough, sore throat, headache, muscle pain, nasal congestion, rhinorrhea, loss of smell and taste) but who did not have shortness of breath or dyspnea
5. Subjects who did not require hospitalization
6. Subjects with SpO2 levels ≥ 95%
7. Viral load by RT-PCR between 3.3×10^6 copies/mL to 6.6×10^6 copies/mL
8. Female subject who was not of childbearing potential, defined as postmenopausal for at least 1 year or surgically sterile
9. Female subject of childbearing potential who had negative urine pregnancy test.

9.3.2 Exclusion Criteria

Subjects were not included in the study when he/she met any of the below exclusion criteria:

1. Allergy to LAEH or any of the excipients of the formulation
2. History of allergies or flu within 30 days prior to the day of enrollment
3. Sensitivity to nostril skin or irritation or bleeding history within 30 days prior to the day of enrollment
4. Females who were breast-feeding, lactating, pregnant or intending to become pregnant
5. COVID-19 subjects with moderate, severe or critical illness or requiring intensive care or mechanical ventilation
6. History of severe respiratory disease and requirement for long-term oxygen therapy
7. Had received antibiotic/s, antiviral drug, and hormonal drugs within 30 days prior to the day of enrollment
8. Any condition or disease detected during the medical interview/physical examination that would render the subject unsuitable for the study, place the subject at undue risk or interfere with the ability of the subject to complete the study in the opinion of the Investigator
9. Had received or had a plan to receive a SARS-CoV-2 vaccine during the study period

10. Participated in any interventional drug or medical device trials within 30 days prior to the day of enrollment.

9.3.3 Removal of Subjects from Therapy or Assessment (Withdrawal Criteria)

The criteria for considering withdrawal from the study (Study discontinuation prior to Day 6) were as follows:

- Withdrawal of subject's consent to continue with study visits.
- If the site and/or the overall study was terminated for any reason.
- The Investigator considers it is in the best interest for the subject to leave the study.

If a subject withdraws from the study, the reason for the withdrawal was recorded in the eCRF.

9.4 Treatment

9.4.1 Treatment Administered

Covixyl-V Nasal spray

Covixyl-V nasal spray (2 to 3 puffs in each nostril at a time) was self-administered twice a day from Day 1 to Day 5 and only once in the morning on Day 6/EOS.

Placebo

Placebo nasal spray (2 to 3 puffs in each nostril at a time) was self-administered twice a day from Day 1 to Day 5 and only once in the morning on Day 6/EOS.

9.4.2 Identity of Investigational Medical Device

Covixyl -V LAEH

Investigational Medical Device	Formulation	Strength	Batch number
Covixyl-V LAEH	Nasal spray	Ethyl lauroyl arginate hydrochloride 0.1 Wt% concentration Gl) 1, I I ca S P La C C S A	

Placebo

Placebo	Formulation	Strength	Batch number
Placebo	Nasal spray	C X 1, 2 I P ca So I	

Placebo	Formulation	Strength	Batch number

9.4.3 Method of Assigning Subjects to Treatment Groups

After obtaining written informed consent, subjects received a subject identifier number. Subject was screened according to the inclusion and exclusion criteria. Subjects who complied with all criteria were enrolled into the study.

Randomization of the subjects to one of the two treatment groups was performed based on the pre-defined blinded randomization list provided to each site. The study was conducted with two groups as Covixyl-V LAEH (Group A) and placebo (Group B). Each group had 15 evaluable subjects. The study was of double-blinded nature hence neither the investigator or study staff were aware of Covixyl-V LAEH/placebo assignment to the subject. Whenever it was necessary to unblind a subject's treatment assignment in case of emergency, the Investigator was supposed to obtain the treatment arm for a given randomized subject from the unblinded study manager.

9.4.4 Selection of Doses in the Study

LAEH has been extensively studied for toxicity, metabolism, and effectiveness studies in vitro and in vivo. Its antimicrobial effects are well documented and regulatory approvals have been granted by both the EU and the US FDA for the use of this chemical as a safe and effective ingredient for use in preserving a variety of food and consumer products. The extensive metabolism data in humans indicated LAEH breaks down in body to two ingredients; arginine and lauric acids. The toxicological and metabolic studies demonstrated that LAEH has no metabolic, pharmacologic, or immunologic action against human body. It is listed as GRAS ingredient by FDA and safe to use in food and other over the counter products in the EU, UK, and Germany.

On 01 Sep 2005, FDA issued the Non-Objection Letter regarding that lauric arginate is GRAS for use as an antimicrobial in the above food categories at levels up to 200 ppm of ethyl Nα-lauroyl-L-arginate hydrochloride. The clinical spectrum of SARS-CoV-2 infection ranges from asymptomatic infection to critical illness. Among patients who are symptomatic, the median

incubation period is approximately 4 to 5 days, and 97.5% have symptoms within 11.5 days after infection. A major challenge to containing the spread of SARS-CoV-2 is that asymptomatic and presymptomatic people are infectious. Patients may be infectious 1 to 3 days before symptom onset, and up to 40 to 50% of cases may be attributable to transmission from asymptomatic or presymptomatic people. Just before and soon after symptom onset, patients have high nasopharyngeal viral levels, which then fall over a period of 1 to 2 weeks (Gandhi RT, 2020).

Considering early stage of viral infection, 5 days treatment of LAEH formulation would benefit the subjects to reduce the transmission from mild to moderate stage of the COVID-19 at initial stage of the infection.

Hence, each subject administered Covixyl-V nasal spray or placebo nasal spray, twice daily (2 to 3 puffs in each nostril at a time) from Day 1 to Day 5 and only once in the morning on Day 6/EOS.

9.4.5 Selection and Timing of Dose for Each Subject

Subjects were provided sufficient study product/placebo at the time of visit, provided instructions about the effective use of the nasal spray in a step-by-step manner on study product/placebo administration at home and were requested to comply with the instruction given by the Investigator or the designated study team. Subjects were also informed that the daily second treatment should be taken approximately 6 hours after the first treatment. Nasal spray (2 to 3 puffs in each nostril at a time) was administered twice daily from Day 1 to Day 5 and only once in the morning on Day 6/EOS. Subject were encouraged to record their dosing on a daily basis, starting from the Day 1 till completion of study period on Day 6 in a subject diary.

9.4.6 Blinding

The study was conducted in double-blinded manner. Hence, neither the Investigator, study staff and nor the subjects were aware of which formulation (LAEH or placebo) the subjects received. Whenever it was necessary to unblind a subject's treatment assignment in case of emergency, the Investigator was supposed to obtain the treatment arm for a given randomized subject from the unblinded study manager.

9.4.7 Prior and Concomitant Therapy

All the treatments which were prescribed to subject including over the counter (OTC) medications, vitamins, herbal and other medications include but not limited to antibiotics, antiviral drug,

hormonal drugs, antipyretic and analgesic drugs for all indications [ENT and other] taken 28 days prior to the Screening/Baseline visit and/or throughout the course of the study apart from study treatments were recorded in concomitant medication form in the source document and eCRF. Information regarding the dates of first and last dose, route of administration (e.g., nasal, oral, topical, inhaled), and the reason for which the concomitant medication was taken was also recorded in the eCRF.

9.4.7.1 Permitted Medications and Treatments

Any therapy which was considered to be necessary for the subject's welfare and would not interfere with the evaluation of the study product was given at the discretion of the Investigator. If there was any question as to whether the medication may interfere, the Investigator was supposed to contact the Medical Monitor or Sponsor. Whenever possible, medications were administered in dosages that remained constant throughout the study duration.

9.4.7.2 Prohibited Medications

Medications that were prohibited by the protocol, include but not limited to antibiotics, antiviral drug, and hormonal drugs for all indications [ENT and other]. The Medical Monitor was supposed to be notified before prohibited medication or therapy was administered unless the safety of the subject required immediate action. The decision to administer a prohibited medication or therapy was supposed to be taken by keeping the safety of the subject as the primary consideration. The Medical Monitor was supposed to be contacted to determine the permissibility of a specific medication or therapy and whether or not the subject should continue with the use of nasal spray device.

9.4.8 Treatment Compliance

The study product/placebo was self-administered by the subject at home in accordance with the protocol specified instructions and training provided. Subject adherence/compliance to treatment was monitored by reviewing the Subject Diary entries as outlined in the Schedule of Procedures. Subjects were counseled regarding proper treatment adherence/compliance and re-trained if needed in the proper use of the nasal spray device at the specified visits by phone calls.

9.5 Efficacy and Safety Endpoints

9.5.1 Efficacy and Safety Measurements Assessed

9.5.1.1 Study Procedures

Before performing any study procedures, the Investigator or designee explained the nature of the study to the potentially interested subjects in detail and if he/she voluntarily agreed to participate in the study, they were given an opportunity to ask any questions before signing. Once all queries were resolved and once subjects voluntarily agreed to participate in the study and they signed an ICF. After meeting the eligibility criteria, subjects were enrolled into the study and were assigned a unique identification number to maintain confidentiality; their study records were not be identified by names. The study was conducted in accordance with the protocol. The details of study assessments per visit is explained in the schedule of assessment Table 1. The Investigator also signed the ICF and provided a copy to the participating subjects.

Table 1: Schedule of Assessments

Assessment	**Screening / Baseline**	**Treatment Period**					
Day	**-3 to 0**	**D1/P1**	**D2/P2**	**D3/P3**	**D4/P4**	**D5/P5**	**D6/EOS Visit**
Informed consent	X						
Demographics	X						
Medical history (including ENT history)	X						
Urine pregnancy test[a]	X						
Height and weight	X						
Vital signs (HR, RR, BP, temperature, SpO2) and nasal examination	X						X
Inclusion/exclusion criteria assessment	X						
RT-PCR test results for viral loads[b]	X						X[c]
Randomization[d]	X						
Study product and material distribution[e]	X						
Treatment through nasal spray[f]		X	X	X	X	X	X[g]
Concomitant medication review	X	<<< ongoing >>>					
Adverse event record[h]	X	<<< ongoing >>>					
Subject diary record[i]		X	X	X	X	X	X
Treatment and subject diary compliance[j]		X	X	X	X	X	X

BP=Blood Pressure; D=Day; ENT= Ear, Nose, Throat; EOS=End of Study; HR=Heart Rate; P= Phone Call; RR= Respiratory Rate; RT-PCR= Reverse Transcription Polymerase Chain Reaction; SpO2= Oxygen Saturation.

[a] Female participant of childbearing potential only

[b] Subjects were asked to refrain from eating, drinking, or using any nasal gavage at least 30 minutes prior to use of nasal spray. Nasal swabs were collected initially for enumerating viral load using RT-PCR (including CT value) at baseline (Day -3 to 0) by swabbing for 30 seconds from each nostril.

[c] After 6 days (at the end of 11 treatments, i.e. post morning treatment on Day 6), subjects visited the site and nasal swab was taken within 3 and 6 hours post 11th treatment for viral load enumeration using RT-PCR (including CT value).

[d] Based on RT-PCR test report, and other eligibility criteria; subjects were randomized in a 1:1 fashion to either receive twice daily LAEH formulation or matching placebo through nasal spray twice a day for 5 days and only once in the morning on Day 6.
[e] Materials (Subject Diary and Treatment Instructions) were provided to subjects.
[f] Subjects were administered assigned treatment (LAEH or matching placebo) through nasal spray twice a day from Day 1 to Day 5 and only once in the morning on Day 6 (11 treatments). Subjects were asked to refrain from eating, drinking, or using any nasal gavage at least 30 minutes prior to treatment. Nasal swabs were collected for enumerating viral load using RT-PCR at baseline by swabbing for 30 seconds from each nostril. Site was responsible to provide the training to the subject and document the training in the source documents.
[g] On Day 6/EOS, the subject took the first treatment (administered through nasal spray by themselves at home around 8:00 am) and recorded the same in the subject diary and then visited to the site.
[h] The site called the subject daily and collected AE information (adverse event [AE]; Serious Adverse Event [SAE])
[i] Subjects recorded in the subject diary his/her initials and date and time he/she administered the assigned treatment on a daily basis. The site called and confirmed the compliance for treatment administration and completion of subject diary with the subject daily.
[j] The site called the subject daily and checked for treatment compliance and completion of subject diary.

9.5.1.2 Adverse Events

Adverse Events:

An AE is defined as any untoward medical occurrence associated with the use of a medicinal product in humans, whether or not considered to have a causal relationship to this treatment. An AE can, therefore, be any unfavorable and unintended sign (that could include a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Events meeting the definition of an AE included:

- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition
- New conditions detected or diagnosed after study product administration that occur during the reporting periods, even though it may have been present prior to the start of the study
- Signs, symptoms, or the clinical sequelae of a suspected interaction (e.g. drug-drug interaction)

Events that did not meet the definition of an AE included:

- Medical or surgical procedure (e.g., endoscopy, appendectomy); the condition that led to the procedure was reported as an AE if it meets the criteria of an AE
- Situations where an untoward medical occurrence did not occur (e.g., social and/or convenience admission to a hospital)
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

If there was evidence of an AE through report or observation, the Investigator or designee evaluated this further and recorded the following information:

- Time of onset and resolution
- Severity
- Seriousness
- Causality/relation to study product

- Action taken regarding study product
- Action taken regarding AE
- Outcome

Serious Adverse Events

If an event met any of the following criteria, it was considered an SAE:

- Death
- Life threatening (in the opinion of the Investigator, the subject is at immediate risk of death from the event [substantial risk of dying at the time of the adverse event])
- In-patient hospitalization into intensive care or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- Congenital anomaly or birth defect
- Important medical event that may jeopardize the participant or may require medical intervention to prevent one of the outcomes listed above.

9.5.1.3 Recording of Adverse Events

Subjective or objective symptoms spontaneously reported by the participant and/or in response to an open question from the study personnel or revealed by observation were recorded in accordance with the Investigator's normal clinical practice and on the AE page of the eCRF during the study at the investigational site. Information about AEs and SAEs was collected from the time of consent until the end of the study. The AE term was reported in standard medical terminology when possible. For each AE, the Investigator evaluated and reported the onset (date and time), resolution (date and time), intensity, causality, action taken, serious outcome (if applicable), and whether or not it caused the participant to discontinue the study.

9.5.1.4 Severity

The Investigator assigned a severity rating to each AE. The severity of AE was assessed as per the "Common Terminology Criteria for Adverse Events" (CTCAE) version 4.03, 2010.

- Grade 1 - Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

- Grade 2 - Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)*.
- Grade 3 - Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**.
- Grade 4 - Life-threatening consequences; urgent intervention indicated.
- Grade 5 - Death related to AE.

*Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

**Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

9.5.1.5 Study product-Event Relationship/Causality

The Investigator assessed the relationship between study product and the occurrence of each AE. The Investigator's assessment of the relationship of each AE to study product was recorded in the source documents and the eCRF. Alternative causes, such as medical history, concomitant therapy, other risk factors, and the temporal relationship of the event to the study product were considered and investigated, if appropriate.

The following definitions were used as a general guideline to help assign grade of attribution:

Not related: The event is clearly related to other factors such as the participant's environment or clinical state, therapeutic interventions or concomitant drugs administered to the participant. This is especially so when an event occurs prior to the commencement of treatment with the study product.

Possible: The event follows a reasonable temporal sequence from the time of study product administration or follows a known response to the study product but could have been produced by other factors such as the participant's clinical state, other therapeutic interventions, or concomitant drugs administered to the participant.

Probable: The event follows a reasonable temporal sequence from the time of study product administration and follows a known response to the study product and cannot be reasonably

explained by other factors such as the participant's clinical state, other therapeutic interventions, or concomitant drugs administered to the participant.

Definite: The event follows a reasonable temporal sequence from the time of study product administration or control abates upon discontinuation or cannot be explained by known characteristics of the participant's clinical state.

9.5.1.6 Action Taken with Study Product

In case, the Investigator needed to alter the administration of the study product from the procedure described in the protocol due to the well-being and safety of the participant then the action taken was recorded as one of the following options:

- Study Product Interrupted
- Study Product Withdrawn
- Not Applicable
- Other

9.5.1.7 Event Outcome

Outcome of an AE was recorded as follows:

- Recovered/Resolved
- Recovering/Resolving
- Recovered/Resolved with Sequelae
- Not Recovered/Not Resolving
- Fatal
- Unknown

9.5.2 Appropriateness of Measurement

At screening prior to nasal swabbing for RT-PCR, all the subjects were asked to refrain from eating, drinking, or using any nasal gavage or nasal spray at least 30 minutes. A nasal mid-turbinate specimen for COVID-19 testing was collected initially from all enrolled subjects as per the protocol of Center for Disease Control and Prevention (CDC 2020) for enumerating viral load using RT-PCR test. Subjects were screened to determine whether an individual satisfied all

eligibility criteria. Only those subjects who had laboratory-confirmed diagnosis of COVID-19 at the time of screening (Day -3 to 0) using RT-PCR method and who met all eligibility criteria were enrolled.

Efficacy measures were established measures of the symptoms known to be reliable and valid. All outcome measures were conducted at screening/baseline, and on Day 6.
The measures of safety used in this study were routine clinical procedures. Vital parameters (BP, HR, RR, SpO2 and body temperature) were measured at screening/baseline and EOS (Day 6). Safety measures were conducted by the investigators from signing of informed consent till end the study for an individual subject. Safety measure included AEs, SAEs, nasal and physical examination as well as vital parameters.

The efficacy and safety assessments performed in this study are widely used and generally recognized as reliable, accurate, and relevant.

9.5.3 Study Endpoints

9.5.3.1 Primary Efficacy Endpoint

- Comparison of change in viral load from baseline between the two treatment arms

9.5.3.2 Secondary Efficacy Endpoints

- Proportion of COVID-19 infection-free subjects between the two treatment arms

9.5.3.3 Safety Endpoint (Secondary):

The safety of LAEH formulation was compared to Vehicle (matching placebo) with analysis of safety variables including safety assessments (vital signs) and AEs.

9.6 Data Quality Assurance

The Sponsor utilized standard operating procedures (SOPs) designed to ensure that research procedures and documentation were consistently conducted/prepared to the highest quality standards. These SOPs were required to be in compliance with FDA regulations and the ICH GCP guidance. The study was monitored to verify that the rights and well-being of human subjects are being protected, the reported data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved protocol, the ethical principles that have their origin in the Declaration of Helsinki, ICH guidelines, on GCP (ICH E6), and Food and Drug

Administration Regulations (21 CFR Parts 11, 50, 54, 56, 312, 812).

To ensure compliance with GCP and all applicable regulatory requirements, the Sponsor or its agent were supposed to conduct a quality assurance audit at any time during or after completion of a study. The Investigator was supposed to receive adequate notice if he/she was selected for an audit. The audit could include, but is not limited to: a review of all ICFs, medical records, and regulatory documentation; an assessment of study conduct and protocol compliance; and a review of the study product receipt, storage, and administration. At the conclusion of an audit, the auditor would conduct a brief meeting with the Investigator to review the findings of the audit.

9.7 Statistical Methods Planned and Determination of Sample Size

9.7.1 Statistical and Analytical Plans

9.7.1.1 Statistical Methods:

Demographics, disposition, and baseline characteristics of subjects were tabulated by treatment assignment. Summary of all the demographic and baseline characteristics was presented for all the subjects in safety population. Descriptive statistics (n, mean, standard deviation [SD], median, minimum, and maximum) was provided for all the continuous variables. Frequency count (n) and percentage (%) of patients was provided for the categorical variables. Statistical tests were performed at 5% level of significance.

All statistical analyses were performed using SAS® Version 9.4 [SAS Institute Inc., USA].

9.7.1.2 Statistical Analysis

The statistical analysis was performed using mITT (Modified Intent-to-treat), PP (Per protocol) and safety analysis population

9.7.1.2.1 Analysis Data Sets

Modified Intent-to-Treat Analysis Population (mITT): All subjects who were randomized, took at least one dose of study product, and had at least one post baseline evaluation.

Per Protocol population (PP): The PP population included all mITT subjects who remained in the study and had no major protocol violations and received at least 80% of the doses.

Safety Population (SP): All randomized subjects who took at least one dose of study product.

- Safety analysis was performed on safety population.

- Efficacy analysis was performed on mITT and PP populations.
- The results in the PP population were considered definitive with those in the mITT population considered supportive

9.7.1.3 Analysis of Primary Efficacy Endpoint

The primary endpoint for this study was the comparison of change in viral load in RT-PCR Test from baseline at Day 6 between the two treatment arms. Mean viral load and change from baseline in viral load at Day 6 within 3 hours post last dose and Day 6 within 6 hours post last dose was summarized descriptively by treatment group for mITT and PP population. Analysis of covariance (ANCOVA) was employed to find the statistically significant difference between the treatment groups with baseline viral load as covariate.

9.7.1.4 Analysis of Secondary Efficacy Endpoints

Proportion of COVID-19 infection-free subjects between the two treatment arms.

Proportion of infection-free subjects was presented with frequency count and percentage for each treatment group for mITT and PP population. Chi square test for independence was used to find the statistical significance between the treatment arms.

9.7.1.5 Analysis of Safety Endpoints

All safety endpoints were summarized and compared using descriptive statistics between two treatment arms.

- Adverse Events

Summary of AEs, including the number and percentage of patients with any AEs, TEAEs, SAEs, study product-related AEs, study product-related SAEs, discontinuations, and incidence. AE was presented by SOC and PT. Each adverse event was evaluated for the date of start and end, severity, relationship to the study product, action is taken and outcome.

- Change in Vital Signs

Vital signs and change in vital signs were summarized descriptively by treatment arm for safety population.

- Change in Nasal Examination from Baseline

Change in nasal examination was summarized descriptively by treatment arm for safety population.

9.7.2 Determination of Sample Size

No formal sample size calculation was performed. A total of 30 patients were enrolled and considered as sufficient sample size to compare the estimates of tests treatment with reference treatment. Sample size determination was based on Singapore human clinical trial (Seneviratne CJ, 2021), which evaluated the effectiveness of mouth rinses on viral load in saliva. The data observed to obtain 2 log difference in initial and post treatment PCR viral load. Based on the standard deviation of the study of mean difference at 95% and standard deviation of mean ranging from 0.2-0.4, the sample size was estimated as follows for 2 log difference in viral PCR counts:

N= z^2xp(1-p)/sd

Thus, N=1.96x0,5/0.2=5

In this study, 15 subjects were enrolled per treatment to see 2 log difference. Therefore, it should be sufficient to detect differences in nasal viral load.

9.8 Changes in the Conduct of the Study or Planned Analyses

9.8.1 Protocol Changes

The original protocol Version 1.0 dated 27 May 2021 was amended to include administrative changes. Final version of the Protocol: Version 1.1 dated 29 Sep 2021.

9.8.2 Statistical Changes

There were no statistical changes in the planned analysis.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

In the study, 33 subjects were screened and 3 of them failed in screening tests. Total 30 subjects were enrolled in the study. Out of these 30 enrolled subjects, 15 subjects were randomized to Covixyl-V group and 15 subjects were randomized to placebo group.

All the enrolled subjects from both the groups (Covixyl-V and placebo) completed the study.

A summary of subject disposition in Covixyl-V and placebo groups is presented in Table 2.

Table 2: Summary of Subject Disposition – All Subjects

	Covixyl-V (N =15) n (%)	**Placebo (N =15) n (%)**	**Total (N=30) n (%)**
Number of subjects screened [1]			33
Number of screen failures [2]			3
Number of randomized subjects.	15	15	30
Number of subjects in Safety population	15(100)	15(100)	30(100)
Number of subjects in mITT population	15(100)	15(100)	30(100)
Number of subjects in PP population	15(100)	15(100)	30(100)
Number of subjects who completed the study	15(100)	15(100)	30(100)
Number of subjects withdrawal/ discontinuations	0	0	3(10.0)
Reasons for subject withdrawal/discontinuation			
Lost to follow- up	0	0	0
Subject withdrew consent	0	0	0
Subject withdrawn by Principal Investigator	0	0	0
NAE / SAE	0	0	0
Pregnancy	0	0	0
Other, Specify	0	0	0

	Covixyl-V (N =15) n (%)	**Placebo (N =15) n (%)**	**Total (N=30) n (%)**
Death	0	0	0

Source: Table 14.1.1.1

Abbreviations: N = number of subjects in the specified treatment group; n = number of subjects in specified category.
Note 1: Percentages are based on number of subjects in the specified treatment in Safety population.
Note 2: [1] Subjects who provided informed consent
Note 3: [2] Counts taken from eligibility conducted on screening visit
Note 4: [3]Screen failure percentage calculated from number of screened subjects
Reference Listing 16.2.1.2

10.2 Protocol Deviations

Total 17 (56.7%) subjects had at least 1 protocol deviation [9 (60%) in Covixyl-V group and 8 (53.3%) in Placebo group. For some of the subjects, the RT-PCR test on EOS visit was conducted only within 3 hrs post last dose and for the others, it was conducted only within 6 hrs post last dose. This was the most common reason for the protocol deviations in both the groups. However, all protocol deviations were found to be minor.

A summary of Protocol Deviations in Covixyl-V and placebo groups is presented in Table 3.

Table 3: Summary of Protocol Deviations /Violations – Safety Population

Protocol Deviation Type	**Covixyl-V (N=15) n (%)**	**Placebo (N=15) n (%)**	**Total (N =30) n (%)**
Subjects having at least one protocol deviation/violation [1]	9(60.0)	8(53.3)	17(56.7)
Subjects with at least one major protocol deviation	0	0	0

Source: Table 14.1.1.2

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category.
Note1: Percentages are based on the number of subjects in the specified treatment group
Note2: [1] = Percentages for the subjects with at least one protocol deviation is based on the number of subjects in respective treatment group in safety population.
Reference Listing 16.2.1.5

11. EFFICACY EVALUATION

11.1 Data sets Analyzed

In the study, efficacy analyses were performed on mITT and PP population set. All 30 randomized subjects, were analyzed under mITT and PP population set in both the groups.

A summary of distribution of subjects in mITT and PP population sets in Covixyl-V and placebo groups is presented in Table 4.

Table 4: Summary of Analysis Populations by Overall – Safety Population

	Covixyl-V (N =15) n (%)	**Placebo (N =15) n (%)**	**Total (N=30) n (%)**
Number of subjects in mITT population	15(100)	15(100)	30(100)
Number of subjects in PP population	15(100)	15(100)	30(100)

Source: Table 14.1.1.1

Abbreviations: N = number of subjects in the specified treatment group; n = number of subjects in specified category.
Note 1: Percentages are based on number of subjects in the specified treatment group.
Reference Listing 16.2.1.2

11.2 Demographic and other Baseline characteristics

11.2.1 Study Demographics

All demographic characteristics like race, ethnicity and other baselines characteristics like mean body weight and height were well balanced between Covixyl-V and placebo groups.

However, there were more males than females in the placebo group. The mean age of subjects in the Covixyl-V group was a bit higher than the subjects in placebo group.

A summary of subject demographics and other baseline characteristics in Covixyl-V and placebo groups is presented in Table 5.

Table 5: Demographic Characteristics and Anthropometry Results – Safety Population

Characteristic (Unit)	**Statistics**	**Covixyl-V (N=15)**	**Placebo (N=15)**	**Total (N =30)**
Gender				
Male	n (%)	7 (46.7)	9 (60.0)	16 (53.3)
Female	n (%)	8 (53.3)	6 (40.0)	14 (46.7)

Characteristic (Unit)	Statistics	Covixyl-V (N=15)	Placebo (N=15)	Total (N =30)
Age (Years)	N	15	15	30
	Mean (SD)	43.6 (13.14)	37.6 (13.62)	40.6 (13.50)
	Median	48.0	34.0	44.0
	Min, Max	21, 63	19, 60	19, 63
Weight (kg)	N	15	15	30
	Mean (SD)	73.0 (13.26)	75.5 (17.25)	74.3 (15.17)
	Median	71.0	71.0	71.0
	Min, Max	56, 100	53, 115	53, 115
Height (cms)	N	15	15	30
	Mean (SD)	166.2 (8.78)	167.2 (7.78)	166.7 (8.17)
	Median	166.0	167.0	166.5
	Min, Max	152, 183	150, 178	150, 183
Ethnicity				
Hispanic or Latino	n (%)	15 (100)	15 (100)	30 (100)
Not Hispanic or Latino	n (%)	0	0	0
Race				
American Indian or Alaska Native	n (%)	0	0	0
Asian	n (%)	0	0	0
Black or African American	n (%)	0	0	0
Native Hawaiian or Other Pacific Islander	n (%)	0	0	0
White	n (%)	15 (100)	15 (100)	30 (100)
Not Reported	n (%)	0	0	0
Other, Specify	n (%)	0	0	0

Source: Table 14.1.2.1

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category
Note 1: Percentages are based on the number of subjects in the specified treatment group.
Reference Listing 16.2.2.1

11.2.2 Medical History

Most of the subjects in the study did not have history of any disease or any ongoing medical condition. All the randomized 30 subjects in both the groups had ongoing medical condition of COVID-19 infection per the inclusion criteria of the study. There were 3 subjects in Covixyl-V group with 6 medical history/current medical conditions and 2 subjects in Placebo group with 3 medical history/current medical conditions (Listing 16.2.2.2).

A summary of medical history/current medical conditions in Covixyl-V and placebo groups is presented in Table 6.

Table 6: Medical History – Safety Population

System Organ Class Preferred Term	Statistics	Covixyl-V (N =15) n (%)	Placebo (N =15) n (%)	Total (N=30) n (%)
Subjects having at least one medical history	n (%)	15(100)	15(100)	30(100)
Infections and infestations	n (%)	15(100)	15(100)	30(100)
COVID-19	n (%)	15(100)	15(100)	30(100)
Reproductive system and breast disorders	n (%)	2(13.3)	1(6.7)	3(10.0)
Menopausal symptoms	n (%)	2(13.3)	1(6.7)	3(10.0)
Respiratory, thoracic and mediastinal disorders	n (%)	0	1(6.7)	1(3.3)
Asthma	n (%)	0	1(6.7)	1(3.3)
Surgical and medical procedures	n (%)	3(20.0)	0	3(10.0)
Abdominoplasty	n (%)	1(6.7)	0	1(3.3)
Cholecystectomy	n (%)	1(6.7)	0	1(3.3)
Female sterilisation	n (%)	1(6.7)	0	1(3.3)
Vascular disorders	n (%)	1(6.7)	1(6.7)	2(6.7)
Hypertension	n (%)	1(6.7)	1(6.7)	2(6.7)

Source: Table 14.1.2.2
Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category
Note 1: System organ class and preferred terms are coded using the standards of MedDRA.
Note 2: Percentages are based on number of subjects in specified treatment group in Safety population.
Reference Listing 16.2.2.2

11.2.3 Prior or Concomitant Medications

Details of concomitant medications taken by subjects in both groups is presented in Table 14.1.2.3.

11.3 Measurement of Treatment Compliance

Treatment compliance was achieved by all subjects in both the groups (Listing 16.2.1.2).

11.4 Efficacy Results and Tabulations of Individual Subject Data

11.4.1 Analysis of Efficacy (Primary and Secondary Endpoints)

11.4.1.1 Primary Efficacy Endpoint

11.4.1.1.1 Comparison of change in viral load from baseline between the two treatment arms

The viral load values on Day 6 within 6 hrs post last dose were available only for COVID-19 infection positive subjects. After 6 days' use of nasal spray, the number of COVID-19 infection positive subjects was lower (2) in Covixyl-V group than the number of COVID-19 infection positive subjects in the placebo group (7).

The mean (SD) change in viral load from baseline on Day 6 within 3 hrs post last dose between Covixyl-V group and placebo group was found to be -1.51(0.917) × 10^6copies/mL and -1.16(0.685) × 10^6copies/mL, respectively. The mean difference of change in viral load between two groups was not statistically significant (p=0.4253).

The mean (SD) change in viral load from baseline on Day 6 within 6 hrs post last dose between Covixyl-V group and placebo group was found to be -0.60(0.141) × 10^6 copies/mL and -1.76(0.562) × 10^6 copies/mL, respectively. The mean difference of change in viral load between two groups was statistically significant (p=0.0282).

A summary of change in viral load from RTPCR test in Covixyl-V and placebo groups is presented in Table 7: Change in Viral Load from RTPCR Test – PP Population

Table 7: Change in Viral Load from RTPCR Test – PP Population

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	p value
Viral Load (x 10^6 copies/mL)	Day 1	n	15	15	0.4941[#]
		Mean (SD)	5.07(0.811)	4.89(0.595)	

	Visit	**Statistics**	**Covixyl-V (N=15)**	**Placebo (N=15)**	**p value**
		Median	5.10	4.90	
		Min, Max	3.7, 6.0	3.8, 6.0	
Viral Load (x 10^6 copies/mL)	Day 1[$]	n	7	7	0.4826#
		Mean (SD)	5.13(0.898)	4.84(0.532)	
		Median	5.70	5.10	
		Min, Max	3.9, 6.0	4.0, 5.4	
Viral Load (x 10^6 copies/mL)	Day 6 (within 3 hr)	n	7	7	0.6893[#]
		Mean (SD)	3.61(0.393)	3.69(0.241)	
		Median	3.50	3.60	
		Min, Max	3.2, 4.4	3.4, 4.0	
Viral Load (x 10^6 copies/mL)	CFB at Day 6 (within 3hr)	n	7	7	0.4253#
		Mean (SD)	-1.51(0.917)	-1.16(0.685)	
		Median	-1.40	-1.40	
		Min, Max	-2.4, -0.1	-1.8, -0.1	
		P-value	0.0001*	0.0000*	
Viral Load (x 10^6 copies/mL)	Day 6 (within 6 hr)	n	2	7	0.2236[#]
		Mean (SD)	3.80(0.566)	3.39(0.348)	
		Median	3.80	3.30	

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	p value
		Min, Max	3.4, 4.2	3.1, 4.1	
Viral Load (x 106 copies/mL)	CFB at Day 6 (within 6hr)	n	2	7	0.0282#
		Mean (SD)	-0.60(0.141)	-1.76(0.562)	
		Median	-0.60	-2.00	
		Min, Max	-0.7, -0.5	-2.1, -0.5	
		P-value	0.0760*	0.0000*	

Source: Table 14.2.1.1

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category; CFB = Change From Baseline.
Note 1: *P-value for CFB to Day 6 is calculated using paired t test.
Note 2: #p- value is calculated using two sample independent t-test
Note 3: $Baseline values with subjects who have positive values at Day 6.
Reference Listing 16.2.3.2

Fold change in RT-PCR CT value:

The mean (SD) for fold change in RT-PCR CT value on Day 6 within 6 hours post last dose in Covixyl-V group was 1.2(0.12) and 1.1(0.05) in placebo group. The mean (SD) fold change difference in RT-PCR CT value on Day 6 within 6 hours post last dose was not statistically significant between the two groups (p=0.4282). The mean (SD) fold change in RT-PCR CT value from baseline to Day 6 within 6 hours post last dose showed high statistical significance (p=0.0000) in both the individual groups.

A summary of change in RT-PCR CT Value in Covixyl-V and placebo groups is presented in Table 8: Fold Change in RT-PCR CT Value.

Table 8: Fold Change in RT-PCR CT Value

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	p value
CT Value	Day 1	n	15	15	0.6278#
		Mean (SD)	24.2(1.52)	24.5(1.46)	
		Median	24.00	25.00	
		Min, Max	21, 27	22, 27	
CT Value	Day 6 (within 3 hr)	n	12	9	0.2548#
		Mean (SD)	27.3(0.87)	26.8(0.97)	

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	p value
		Median	27.00	27.00	
		Min, Max	25, 28	25, 28	
CT Value	Fold Change at Day 6 (within 3 hr)	n	12	9	0.6066#
		Mean (SD)	1.1(0.09)	1.1(0.08)	
		Median	1.12	1.08	
		Min, Max	1.00, 1.29	1.04, 1.23	
		P-value	0.0000*	0.0000*	
CT Value	Day 6 (within 6 hr)	n	8	12	0.1009#
		Mean (SD)	28.0(0.76)	27.3(1.06)	
		Median	28.00	27.00	
		Min, Max	27, 29	25, 29	
CT Value	Fold Change at Day 6 (within 6 hr)	n	8	12	0.4282#
		Mean (SD)	1.2(0.12)	1.1(0.05)	
		Median	1.14	1.12	
		Min, Max	1.00, 1.33	1.07, 1.23	
		P-value	0.0000*	0.0000*	

Source: Table 14.3.6.2
Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category; CFB = Change From Baseline.
Note 1: Fold change in CT value will be estimated on the transformed data by calculating the ratio between Ct values at each time point 3hr and 6 hr versus the Ct value at baseline (at 0 min) for each patient i.e (Cttimepoint/Ctbaseline)
Note 2: #p value is calculated using two sample Independent t-test.
Note 3: *P-value for CFB to Day 6 is calculated using paired t test.
Reference Listing 16.2.3.2

11.4.1.2 Secondary Efficacy Endpoints

11.4.1.2.1 Proportion of COVID-19 infection-free subjects between the two treatment arms

All subjects in both groups, Covixyl-V and the placebo at the start of the study were COVID-19 infection positive. After 6 days (within 3 hours) use of nasal spray, the number of infection-free subjects was 6 (40%) in Covixyl-V group and the number of infection-free subjects in the placebo group was 3 (20%). These differences were not statistically significant (p=0.3189). The negative/positive ratio in Covixyl-V and the placebo group was found to be 0.85 and 0.42, respectively.

After 6 days (within 6 hours) use of nasal spray, the number of infection-free subjects was higher (7 [46.67%]) in Covixyl-V group than the number of infection-free subjects in the placebo group (6 [40%]). These differences were statistically significant at significance level $\alpha = 0.10$ (p=0.088) as calculated by using independent Chi-square test. Additionally, the negative/positive ratio in Covixyl-V group was 4 times higher (3.5) than the placebo group (0.85).

A summary of infection-free subjects between Covixyl-V and placebo groups in PP population is presented in Table 9: Summary of infection-free subjects – PP Population

Table 9: Summary of infection-free subjects – PP Population

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	P-value
COVID-19 infection-free subjects	Day 1				
	Negative	n(%)	0	0	
	Positive	n(%)	15 (100)	15 (100)	
		95% CI	NA		
COVID-19 infection-free subjects	Day 6 (within 3hrs)				0.3189*
	Negative	n(%)	6 (40.00)	3 (20.00)	
	Positive	n(%)	7 (46.67)	7 (46.67)	
	Missing	n(%)	2 (13.33)	5 (33.33)	
		95% CI	-5.96, 19.29	0	

	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)	P-value
		Ratio (Negative/Positive)	0.8571	0.4286	
COVID-19 infection-free subjects	Day 6 (within 6hrs)				0.0883*
	Negative	n(%)	7 (46.67)	6 (40.00)	
	Positive	n(%)	2 (13.33)	7 (46.67)	
	Missing	n (%)	6 (40.00)	2 (13.33)	
		95% CI	-5.96, 19.29	0	
		Ratio (Negative/Positive)	3.5000	0.8571	

Source: Table 14.2.2.1

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category; NA = Not Applicable.
Note 1: *p value for comparison between treatment group is calculated using Chi-square test.
Note 2: 95% confidence interval is calculated for the subject's percentage whose RT-PCR test is negative (i.e COVID-19 infection-free subjects) in Covixyl-V treatment group.
Reference Listing 16.2.3.2

11.4.2 Statistical/Analytical issues

11.4.2.1 Adjustments for Covariates

No adjustment of covariates was performed in this study.

11.4.2.2 Handling of Dropouts or Missing Data

Missing data was not replaced.

11.4.2.3 Interim Analysis and Data Monitoring

No interim analysis was performed for this study.

11.4.2.4 Multicenter Studies

The study was conducted at 2 clinical sites across United States and the analysis was performed on the data available from whole population.

11.4.2.5 Multiple Comparison/Multiplicity

No statistical adjustment was made for multiple comparisons/multiplicity.

11.4.2.6 Use of an "Efficacy Subset" of Subject

Not applicable

11.4.2.7 Active-Control Studies Intended to Show Equivalence

This section is not applicable as the current study was placebo control study.

11.4.2.8 Examination of Subgroups

No subgroups were defined in this study.

11.4.3 Tabulation of Individual Response Data

Tabulation if individual patient response data is presented Listing 16.2.

11.4.4 Drug Dose, Drug Concentration, and Relationships to Response

Not applicable

11.4.5 Drug-Drug and Drug-Disease Interactions

Not applicable

11.4.6 By-Subject Displays

Individual patient data are presented in Listing16.2.

11.4.7 Efficacy Conclusions

Although the reduction in the viral load in the Covixyl-V group was observed only within 3 hours post last dose but not within 6 hours post last dose when compared to the placebo group, the results of the study favor Covixyl-V group since there were only 2 subjects having positive COVID-19 infection on EOS visit when compared to that of the placebo group (7 subjects). This indicates that viral load by itself is not an indicating parameter without clinical outcome i.e., positive/negative RT-PCR test results. The mean fold change difference in RT-PCR CT value on Day 6 within 6 hours post last dose was not statistically significant between the two groups. Nonetheless, there was a significant improvement in the RT-PCR CT value of subjects on Day 6 within 6 hours post last dose from baseline in both the individual groups. All subjects in both groups, Covixyl-V and the placebo at the start of the study were COVID-19 infection positive. **At the end of the treatment, the Covixyl-V group had over 4 times more infection-free subjects than the placebo group based on the calculation of negative/positive ratio.**

12. SAFETY EVALUATION

12.1 Extent of Exposure

All subjects who were randomized and took at least one dose of study product and had at least one safety follow-up been included in safety analyses. A total of 30 randomized subjects were exposed to either Covixyl-V or placebo, provided post-baseline safety data and were included in the safety population.

12.2 Adverse Events

12.2.1 Brief Summary of Adverse Events

As the investigators and subjects were blinded during the study, any medical conditions or any medical condition deteriorating from baseline were recorded as an AE. Only 1 (3.3%) subject reported one adverse event. This AE was of mild severity and was possibly related to the study product which was resolved. No action was taken with the study product. No serious AEs and no deaths were reported in the study (Listing 16.2.5.1).

Summary of subjects with overall AEs is presented in Table 10.

Table 10: Summary of Subjects with Overall Adverse Events – Safety Population

	Covixyl-V (N=15) n (%)	Placebo (N=15) n (%)	Total (N=30) n (%)
Subjects with Adverse Events	1 (6.7)	0	1 (3.3)
Subjects with Study Product Related AEs	1 (6.7)	0	1 (3.3)
Subjects with Serious AEs	0	0	0
Subjects with Study Product Related Serious AEs	0	0	0
Seriousness Criteria			
Hospitalization	0	0	0
Life-threatening	0	0	0
Significant Disability	0	0	0
Congenital Anomaly or Birth Defect	0	0	0
Death	0	0	0
Other Medically Important Event	0	0	0
Subjects with overall AEs by Severity			

	Covixyl-V (N=15) n (%)	**Placebo (N=15) n (%)**	**Total (N=30) n (%)**
Mild	1 (6.7)	0	1 (3.3)
Moderate	0	0	0
Severe	0	0	0
Relationship to the Study Treatment			
Unrelated	0	0	0
Possible related	1 (6.7)	0	1 (3.3)
Definitely related	0	0	0
Action taken with Study Treatment			
Dose Delayed	0	0	0
Study Product Withdrawn Temporarily	0	0	0
Study Product Withdrawn Permanently	0	0	0
Unknown	0	0	0
Not applicable	1 (6.7)	0	1 (3.3)
Outcome of the AEs			
Recovered/ resolved	1 (6.7)	0	1 (3.3)
Recovered/Resolved with sequelae	0	0	0
Recovering/Resolving	0	0	0
Not Recovered/Not resolving	0	0	0
Fatal	0	0	0
Unknown	0	0	0
Action Taken for AE			
None	1 (6.7)	0	1 (3.3)
Medication	0	0	0
Non drug treatment	0	0	0
Patient withdrawn	0	0	0
Other (Specify)	0	0	0
Surgery/Procedure	0	0	0

Source: Table 14.3.1.1

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category.
Note 1: Percentages are based on number of subjects in respective treatment in Safety population.
Reference Listing 16.2.5.1

12.2.2 Display of Adverse Events

An overview of subjects experiencing AEs is presented in Table 14.3.1.1. A summary of AEs by SOC and PT is presented in Table 14.3.1.2. Summary of subjects with SAE by SOC and PT is presented in Table 14.3.1.3 (No SAE was reported in the study). Summary of subjects with study product related AEs by SOC and PT is presented in Table 14.3.1.4. Summary of subjects with AEs leading to death by SOC and PT is presented in Table 14.3.1.5 (No death was reported in the study). Summary of subjects with AEs leading to permanent discontinuation of study product by SOC and PT is presented in Table 14.3.1.6. A summary of subjects with AE and severity by SOC and PT is presented in Table 14.3.2.1

12.2.3 Analysis of Adverse Events

12.2.3.1 Summary of AEs

Out of 30 randomized subjects, only 1 subject reported a 1 AE i.e., Nasal pruritus (3.3%).

Summary of subjects with AE is presented in Table 11.

Table 11: Summary of Subjects with Adverse Events- Safety Population

System Organ Class Preferred Term	Covixyl-V (N=15) n (%)	Placebo (N=15) n (%)	Total (N=30) n (%)
Subjects having at least one AE	1 (6.7)	0	1 (3.3)
Respiratory, thoracic and mediastinal disorders	1 (6.7)	0	1 (3.3)
Nasal pruritus	1 (6.7)	0	1 (3.3)

Source: Table 14.3.1.2

Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category.
Note 1: System organ class and preferred terms are coded using the standards of MedDRA 24.0
Note 2: Percentages are based on number of subjects in respective treatment groups in Safety population.
Reference Listing 16.2.5.1

12.2.3.2 AE and Severity

No severe AE was reported by any subject in the study. The only reported AE (Nasal pruritus) was of mild intensity.

Summary of subjects with AE and severity is presented in Table 12.

Table 12: Summary of Subjects with AE and Severity

System Organ Class Preferred Term	Covixyl-V (N=15) n (%)	Placebo (N=15) n (%)	Total (N=30) n (%)
Subjects having at least one AE	1 (6.7)	0	1 (3.3)
Mild	1 (6.7)	0	1 (3.3)
Moderate	0	0	0
Severe	0	0	0
Respiratory, thoracic and mediastinal disorders	1 (6.7)	0	1 (3.3)
Mild	1 (6.7)	0	1 (3.3)
Moderate	0	0	0
Severe	0	0	0
Nasal pruritus	1 (6.7)	0	1 (3.3)
Mild	1 (6.7)	0	1 (3.3)
Moderate	0	0	0
Severe	0	0	0

Source: Table 14.3.2.1
Abbreviations: N = number of subjects in specified treatment group; n = number of subjects in specified category.
Note 1: System organ class and preferred terms are coded using the standards of MedDRA version 24.0
Note 2: Percentages are based on number of subjects in respective treatment in Safety population.
Reference Listing 16.2.5.1

12.2.4 Listing of Adverse Events by subjects

Individual subject AE data is presented in Listing 16.2.5.1.

12.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

There were no deaths and no serious adverse events reported in this study (Table 14.3.1.3).

12.3.1 Deaths Listing of Deaths, Other Serious Adverse Events, and Other Significant

12.3.1.1 Death

There were no deaths reported in this study (Table 14.3.1.5).

12.3.1.2 Other Serious Adverse Events

There were no other serious adverse events reported in this study (Table 14.3.1.3).

12.3.1.3 Other Significant Adverse Events

There were no other significant adverse events reported in this study (Table 14.3.1.3).

12.3.2 Narratives of Deaths, Other Serious Adverse Events, and Certain Other

There were no deaths and serious adverse events reported in this study, hence this section is not applicable.

12.3.3 Analysis and Discussion of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

There were no deaths and serious adverse events reported in this study (Table 14.3.1.5).

12.4 Clinical Laboratory Evaluation

12.4.1 Listing of Individual Laboratory Measurements by Subject (Appendix 16.2.8) and Each Abnormal Laboratory Value

There were no clinical laboratory evaluations performed in this study.

12.4.2 Evaluation of Each Laboratory Parameter

12.4.2.1 Laboratory Values Over Time

There were no clinical laboratory evaluations performed in this study.

12.4.2.2 Individual Subject Changes

There were no clinical laboratory evaluations performed in this study.

12.4.2.3 Individual Clinically Significant Abnormalities

There were no clinical laboratory evaluations performed in this study.

12.5 Vital signs, Physical findings, and other Observations related to Safety

12.5.1 Vital Signs

None of the subject in Covixyl-V group and Placebo group had abnormal systolic/diastolic BP results at baseline and on EOS/Day 6 Visit. Mean BP (systolic/diastolic) results were similar in both groups at baseline and on EOS/Day 6 Visit.

None of the subject in Covixyl-V group and Placebo group had abnormal RR at baseline and on EOS/Day 6 Visit. Mean RR results were similar in both groups at baseline and on EOS/Day 6 Visit.

None of the subject in Covixyl-V group and Placebo group had abnormal HR at baseline and on EOS/Day 6 Visit. Mean HR results were similar in both groups at baseline and on EOS/Day 6 Visit.

None of the subject in Covixyl-V group and Placebo group had abnormal body temperature (°C) at baseline and on EOS/Day 6 Visit. Mean body temperature (°C) results were similar in both groups at baseline and on EOS/Day 6 Visit.

None of the subject in Covixyl-V group and Placebo group had abnormal oxygen saturation SpO2 (%) at baseline and on EOS/Day 6 Visit. Mean oxygen saturation SpO2 (%) results were similar in both groups at baseline and on EOS/Day 6 Visit.

The details of results of vital signs by visit in safety population are presented in Table 13.

Table 13: A Summary of Results – Safety Population

Vital Signs Test Name (Unit)	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
Systolic Blood Pressure/(mmHg)	Day 1	n	15	15
		Mean (SD)	117.0(6.39)	115.7(4.82)
		Median	114.0	116.0
		Min, Max	110, 131	109, 126
	Day 6	n	15	15
		Mean (SD)	115.8(4.66)	117.8(4.48)
		Median	117.0	117.0
		Min, Max	108, 122	108, 125
	CFB at Day 6	n	15	15
		Mean (SD)	-1.2(4.49)	2.1(3.11)
		Median	-2.0	3.0
		Min, Max	-10, 8	-4, 7
Diastolic Blood Pressure/(mmHg)	Day 1	n	15	15
		Mean (SD)	78.1(5.91)	75.9(6.01)

Vital Signs Test Name (Unit)	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
		Median	78.0	76.0
		Min, Max	68, 87	67, 86
	Day 6	n	15	15
		Mean (SD)	77.0(5.04)	75.4(3.94)
		Median	78.0	75.0
		Min, Max	67, 84	66, 82
	CFB at Day 6	n	15	15
		Mean (SD)	-1.1(4.10)	-0.5(5.00)
		Median	-2.0	-3.0
		Min, Max	-8, 6	-7, 7
Heart rate (beats / min)	Day 1	n	15	15
		Mean (SD)	87.5(8.57)	86.7(10.81)
		Median	88.0	88.0
		Min, Max	68, 98	66, 102
	Day 6	n	15	15
		Mean (SD)	80.5(5.91)	82.4(7.53)
		Median	82.0	82.0
		Min, Max	66, 86	64, 92
	CFB at Day 6	n	15	15
		Mean (SD)	-7.0(5.33)	-4.3(6.25)
		Median	-6.0	-6.0
		Min, Max	-20, 0	-14, 6
Respiratory Rate (breaths/min)	Day 1	n	15	15
		Mean (SD)	19.1(1.25)	18.5(0.99)
		Median	19.0	18.0
		Min, Max	18, 22	17, 20
	Day 6	n	15	15
		Mean (SD)	18.9(1.13)	18.9(1.28)
		Median	18.0	20.0
		Min, Max	17, 20	16, 20

Vital Signs Test Name (Unit)	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
	CFB at Day 6	n	15	15
		Mean (SD)	-0.3(1.49)	0.5(0.99)
		Median	0.0	0.0
		Min, Max	-4, 2	-1, 2
Temperature (°C)	Day 1	n	15	15
		Mean (SD)	37.5(0.53)	37.5(0.62)
		Median	37.6	37.8
		Min, Max	37, 39	37, 38
	Day 6	n	15	15
		Mean (SD)	37.1(0.28)	37.2(0.37)
		Median	37.2	37.1
		Min, Max	37, 38	37, 38
	CFB at Day 6	n	15	15
		Mean (SD)	-0.4(0.40)	-0.3(0.60)
		Median	-0.3	-0.3
		Min, Max	-1, 0	-2, 1
Oxygen Saturation (Pulse Oximetry) SpO2 (%)	Day 1	n	15	15
		Mean (SD)	97.1(0.64)	97.2(0.68)
		Median	97.0	97.0
		Min, Max	96, 98	96, 98
	Day 6	n	15	15
		Mean (SD)	98.0(0.38)	98.1(0.59)
		Median	98.0	98.0
		Min, Max	97, 99	97, 99
	CFB at Day 6	n	15	15
		Mean (SD)	0.9(0.74)	0.9(0.74)
		Median	1.0	1.0

Vital Signs Test Name (Unit)	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
		Min, Max	-1, 2	0, 2

Source: Table 14.3.3.1

Abbreviations: N = number of subjects in specified treatment; n = number of subjects in specified category; CFB=Change from baseline

Reference Listing 16.2.4.1

12.5.2 Physical Examination

Most of the subject from Covixyl-V group and Placebo group had normal physical examination results at baseline and on EOS/Day 6 Visit.

Out of 15 subjects in the Covixyl-V group, 8 (53.3%) had abnormal ENT conditions like hyperemic nasal mucosa, clear discharge, and loss of smell and taste on Day 1. Similarly, out of 15 subjects in the Placebo group, 9 (60.0%) had abnormal ENT conditions like hyperemic nasal mucosa, clear discharge, and loss of smell and taste on Day 1. On Day 6, the Covixyl-V group had 12 (80.0%) subjects with normal ENT condition and the Placebo group had 9 (60.0%) subjects with normal ENT condition. Thus, the improvement in ENT conditions was higher in the Covixyl-V group when compared to Placebo group.

The details of physical examination results by visits in safety population are presented in Table 14.

Table 14: Physical Examination – Safety Population

Body System	Visit	Result	Statistics	Covixyl-V (N=15)	Placebo (N=15)
Skin	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
ENT	Day 1	Normal	n(%)	7 (46.7)	6 (40.0)
		Abnormal	n(%)	8 (53.3)	9 (60.0)
	Day 6	Normal	n(%)	12 (80.0)	9 (60.0)
		Abnormal	n(%)	3 (20.0)	6 (40.0)

Body System	Visit	Result	Statistics	Covixyl-V (N=15)	Placebo (N=15)
Head	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
Lung/Chest	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
Heart	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
Abdomen	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
Musculoskeletal	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
Extremities	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
		Abnormal	n(%)	0	0
Lymphatic	Day 1	Normal	n(%)	15 (100)	15 (100)
		Abnormal	n(%)	0	0
	Day 6	Normal	n(%)	15 (100)	15 (100)

Body System	Visit	Result	Statistics	Covixyl-V (N=15)	Placebo (N=15)
		Abnormal	n(%)	0	0
Other	Day 1	Normal	n(%)	0	1 (6.7)
	Day 6	Normal	n(%)	1 (6.7)	1 (6.7)

Source: Table 14.3.4.1

Abbreviations: N = number of subjects in specified treatment; n = number of subjects in specified category
Note 1: Percentages are based on number of subjects in respective group in Safety population.
Reference Listing 16.2.4.2

12.5.3 Nasal Examination

Out of 15 subjects in the Covixyl-V group, 12 (80.0%) subjects were free from nasal inflammation-redness on Day 6. However, nasal inflammation-redness in placebo group remained the same on Day 6, 5(33.3%) without any improvement when compared to Day 1. Overall, higher number of subjects were free from nasal inflammation-redness on Day 6 in the Covixyl-V group when compared to placebo group. On Day 6, both the groups showed almost similar improvement in case of loss of nasal function.

The number of subjects without any nasal discharge on Day 6 were almost similar in both the groups (Covixyl-V group [13(86.7%)], and placebo group [12(80.0%)]); however, Covixyl-V group showed 2 times greater improvement in nasal discharge free subjects on Day 6 from baseline (Day 1) when compared to placebo group. None of the subjects had nasal pain on EOS visit/Day 6 in both the groups.

The details of nasal examination results by visits in safety population are presented in Table 15.

Table 15: Nasal Examination for Signs and Symptoms – Safety Population

Signs and Symptoms	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
Inflammation-redness	Day 1			
	Present	n(%)	8 (53.3)	5 (33.3)
	Absent	n(%)	7 (46.7)	10 (66.7)
	Day 6			
	Present	n(%)	3 (20.0)	5 (33.3)

Signs and Symptoms	Visit	Statistics	Covixyl-V (N=15)	Placebo (N=15)
	Absent	n(%)	12 (80.0)	10 (66.7)
Swelling	Day 1			
	Present	n(%)	2 (13.3)	3 (20.0)
	Absent	n(%)	13 (86.7)	12 (80.0)
	Day 6			
	Present	n(%)	2 (13.3)	2 (13.3)
	Absent	n(%)	13 (86.7)	13 (86.7)
Discharge	Day 1			
	Present	n(%)	6 (40.0)	5 (33.3)
	Absent	n(%)	9 (60.0)	10 (66.7)
	Day 6			
	Present	n(%)	2 (13.3)	3 (20.0)
	Absent	n(%)	13 (86.7)	12 (80.0)
Pain	Day 1			
	Present	n(%)	2 (13.3)	1 (6.7)
	Absent	n(%)	13 (86.7)	14 (93.3)
	Day 6			
	Present	n(%)	0	0
	Absent	n(%)	15 (100)	15 (100)
Loss of function	Day 1			
	Present	n(%)	9 (60.0)	8 (53.3)
	Absent	n(%)	6 (40.0)	7 (46.7)
	Day 6			
	Present	n(%)	7 (46.7)	7 (46.7)
	Absent	n(%)	8 (53.3)	8 (53.3)

Source: Table 14.3.6.1

Note 1: Percentages are based on number of subjects in respective group in Safety population.
Reference Listing 16.2.3.1

12.6 Safety Conclusion

A total of 30 randomized subjects were exposed to either Covixyl-V or placebo. One (3.3%) subject reported an AE which was of mild severity and was possibly related to the study product. The event was resolved at the time of final reporting. No action was taken with the study product. No SAEs and no deaths were reported in the study. None of the subjects in Covixyl-V group and Placebo group had abnormal vital signs throughout the study. On completion of study treatment, the Covixyl-V group had higher number of subjects 12 (80.0%) with normal ENT condition than the Placebo group 9 (60.0%). Higher number of subjects were free from nasal inflammation-redness on Day 6 in the Covixyl-V group when compared to placebo group. There was no improvement in nasal inflammation-redness in placebo group on Day 6 from baseline. **The Covixyl-V group showed 2 times greater improvement in nasal discharge free subjects on Day 6 from baseline (Day 1) when compared to placebo group. Overall, the Covixyl-V LAEH Nasal spray was found to be safe for use in nasal cavity.**

13. DISCUSSION AND OVERALL CONCLUSIONS

COVID-19 infections are worldwide and the virus can infect respiratory systems through entry in nasal area. Nasal pathway can carry a risk of transmission of COVID-19, either by direct person to person or indirect contact with aerosol droplets. Although the vaccines have been developed, we required the means to arrest or reduce nasal transmission of the virus. Effective antiviral therapies, especially in the early stage of infection, are vitally important to halt viral proliferation long enough for the immune system to respond to the virus and limit cellular damage inflicted by viral invasion as well as to minimize genetic mutations caused by the high replication frequency of the virus, which might lead to therapeutic resistance. Keeping all these requirements in mind, the present study was conducted with the Covixyl-V Nasal Spray with the active ingredient of Ethyl lauroyl arginate hydrochloride (LAEH), 0.1% concentration, which is known to have a wide range of antimicrobial properties. Its antimicrobial effects are well documented and regulatory approvals have been granted by both the EU and the US FDA for the use of this chemical as a safe and effective ingredient for use in preserving a variety of food and consumer products. The toxicological and metabolic studies demonstrated that LAEH has no metabolic, pharmacologic, or immunologic action against human body.

Therefore, this present clinical study was designed to assess the efficacy and safety of LAEH formulation versus a matching placebo formulation administered as a Nasal Spray to reduce the viral load from nasal area of subjects with COVID-19.

Considering early stage of viral infection, this clinical study included 6 days treatment of Covixyl-V LAEH Nasal spray in order to reduce the transmission from mild to moderate stage of the COVID-19 at initial stage of the infection. Results showed that the Covixyl-V group had over 4 times more infection-free subjects than the placebo group based on the calculation of negative/positive ratio at the end of the treatment (Day 6). Therefore, it can be concluded that Covixyl-V LAEH Nasal spray was found to be effective in treatment of early stage COVID-19 infection. Similar results were obtained from a double-blind placebo-controlled phase IIb clinical trial which was carried out to evaluate the efficacy of nitric oxide in the treatment of mild, symptomatic COVID-19 infection. The nasal sprays were self-administered 5–6 times daily (two sprays per nostril) for 9 days. The results showed that accelerated SARS-CoV-2 clearance with

nitric oxide nasal spray may reduce symptom duration, decrease infectivity period, reduce hospital admissions, and lower disease severity (Winchester S 2021).

The mean fold change difference in RT-PCR CT value on Day 6 within 6 hours post last dose was not statistically significant between the two groups. However, there was a significant improvement in the RT-PCR CT value of subjects on Day 6 within 6 hours post last dose from baseline in both the individual groups. This finding is supported by a similar randomized, triple-blinded, placebo-control clinical trial comparing low and high concentration povidone-iodine (PVP-I) and saline nasal sprays as treatments to reduce the nasopharyngeal viral load of SARS-CoV-2 in outpatients. Although the saline and PVP-I nasal sprays were not significantly different in altering CT values in COVID-19 positive patients, the CT values were noted to be increased with time in the overall cohort, which indicated a decline in SARS-CoV-2 nasopharyngeal viral load in all groups (Zarabanda D 2021). Similarly, in the present study, a significant improvement in the RT-PCR CT value (CT values were increased) was observed likely indicating decline in nasal viral load and is of prime importance. The reduction in the viral load in the Covixyl-V group was observed within 3 hours post last dose and there were 2 subjects having positive COVID-19 infection at the end of study.

Additional supporting findings include improvement in the ENT condition, nasal inflammation-redness and relief from nasal discharge. After completion of study treatment, **a greater number of subjects had normal ENT condition in Covixyl-V group and higher number of subjects were free from nasal inflammation-redness on Day 6 in the Covixyl-V group. The Covixyl-V group showed 2 times greater improvement in nasal discharge free subjects on Day 6 from baseline (Day 1). In the present study, only one subject reported an AE of mild severity and was resolved. None of the subjects had serious adverse event and no deaths were reported in the study.**

Overall, the Covixyl-V LAEH Nasal spray was found to be safe and can be considered as effective for use in subjects with COVID-19 infection at early stage of infection. However, the sample size was too small and further studies with higher sample size, more stringent study endpoints as well as outcomes are needed to determine the effectiveness of Covixyl-V LAEH Nasal spray in reducing the viral load from nasal area of subjects with COVID-19 infection.

CONCLUSION:

- **The Covixyl-V LAEH Nasal Spray is safe for use in subjects with COVID-19 infection and 4 times more infection-free subjects were observed in the Covixyl-V group at the end of the treatment vs the placebo.**
- **Covixyl-V nasal spray reduces the viral load by improving CT value to better extent in 6 days.**
- **Covixyl-V nasal spray is safe and well tolerated in subjects with COVID-19.**

14. LIST OF TABLES REFERRED BUT NOT INCLUDED IN THE TEXT

Separate attachment

15. REFERENCES

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16. APPENDICES

Separate attachment