SYNOPSIS

<table>
<tr><td colspan="2">Name of Sponsor/Company:
NPO Petrovax Pharm, LLC
1 Sosnovaya St., Pokrov village, Podolsk,
Moscow region, Russian Federation, 142143
Tel.: +7 (495) 730-75-45</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier

Volume:

Page:</td><td rowspan="3">(For National Authority Use only)</td></tr>
<tr><td colspan="2">Name of Finished Product:
Polyoxidonium®, lyophilizate solution for injections 6 mg (NPO Petrovax Pharm LLC, Russia)</td></tr>
<tr><td colspan="2">Name of Active Ingredient:
Azoximer bromide</td></tr>
<tr><td colspan="4">Title of Study:
A multi-centre, adaptive, randomized, double-blind, placebo-controlled comparative clinical trial of the safety and efficacy of 12 mg Polyoxidonium®, lyophilizate solution for injections (NPO Petrovax Pharm LLC, Russia), in patients with coronavirus disease (COVID-19)</td></tr>
<tr><td colspan="4">Investigators:
Study center 02 – Kolobukhina Lyudmila Vasilievna
Study center 04 – Gordeev Ivan Gennadevich
Study center 06 – Tikhomolova Elena Gennadevna
Study center 07 – Sitnikov Ivan Germanovich
Study center 08 – Grebenyuk Anastasia Anatolevna
Study center 09 – Kulabukhov Vladimir Vitalievich
Study center 10 – Zyryanov Sergey Kensarinovich
Study center 12 – Avdeev Sergey Nikolaevich
Study center 13 – Lioznov Dmitry Anatolevich
Study center 14 – Vinnikova Maria Alekseevna
Study center 15 – Agafina Alina Sergeevna
Study center 17 – Filimonov Victor Borisovich
Study center 18 – Kirichenko Natalya Vyacheslavovna
Study center 19 – Zhdanov Konstantin Valerievich
Study center 31 – Dr. Lubica Piesecka
Study center 32 – Dr. Maria Solavova</td></tr>
<tr><td colspan="4">Study centre(s):

Study centers in Russia (only centers with recruited patients listed):

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Gordeev Ivan Gennadevich</td></tr>
</table>

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Publication (reference):
not applicable

Studied period (years): date of first enrolment: first patient randomization on 20 Apr 2020 date of last completed: last visit of the last patient on 05 Mar 2021	**Phase of development:** IIb/IIIa

Objectives:

1. To evaluate clinical efficacy of Polyoxidonium® compared to placebo in hospitalized adult patients with COVID-19,
2. To evaluate safety of Polyoxidonium® compared to placebo in hospitalized adult patients with COVID-19.

Additional objective of the Phase IIb part of the study (prior to the interim analysis): to define the timing of the primary efficacy endpoint for subsequent assessment of efficacy of Polyoxidonium® in adult patients hospitalized with COVID-19.

Methodology:

A multi-centre, adaptive, randomized, double-blind, placebo-controlled comparative clinical study of safety and efficacy (Phase IIb/IIIa). This study follows the WHO Master Protocol and has adaptive design. The first part of the study (100 patients) was a Phase IIb trial, followed by a blinded interim analysis with a possibility to reselect the primary endpoint. The second part of the study was a Phase IIIa trial. Data from patients enrolled in the first part of the study was included in the second part of the study.

The study included hospitalized patients with COVID-19, it was conducted in the clinical centres during hospitalization and subsequent outpatient visits.

Patients was recruited in two subgroups based on severity of COVID-19 at screening:

- severe disease: requiring mechanical ventilation or oxygen, SpO2 ≤ 94% or tachypnoea (respiratory rate ≥ 24 breaths/min);

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• mild-moderate disease: SpO2 > 94% and respiratory rate < 24 breaths/min without supplemental oxygen).

Prior to any study procedures the patient signed, if possible, the Patient Information Sheet with Informed Consent Form. In Russian centers patients in an unconscious state were allowed to be enrolled in the study, including those subjected to the drug-induced hibernation. In absence of the possibility of making a decision by the patient due to his/her critical condition, the decision to include the patient in this study was made by a Concilium consisting of 3 doctors. As soon as the patient was able to read and understand the information in the Patient Information Sheet with the Informed Consent Form for health reasons, he/she was asked, if he/she voluntarily wished to continue participation in the study, if so, then to sign and date the Patient Information Sheet and the Informed Consent Form.

The study included the following periods:

- Screening (days -1 to 1) - preliminary examination.
- Treatment period (17 days in total, days 1 to 17) - administration of Polyoxidonium®/placebo, assessment of clinical status, recording of AEs.
- Follow-up period (days 18 to 29±3).

Eligible patients were randomized after the screening to one of two groups in 1:1 ratio to receive either the Polyoxidonium® or Placebo.

Following assessments were performed within study visits:

Screening (Study Days -1 to 1):

- Signing of informed consent by the patient (if there was no possibility of signing an informed consent by the patient due to his/her critical condition, the decision to include the patient in this study was made by a Concilium consisting of 3 doctors who signed a special Informed Consent Form. As soon as, in the opinion of the study doctor, the patient had the ability to understand the information and make decisions, the patient's personal consent to continue participation in the study and to comply with all procedures and restrictions provided for in this Protocol was obtained, for this purpose a standard Informed Consent Form was signed).
- Confirmation of positive test for SARS-CoV-2[1].
- Collection of patient history, demographics, and anthropometric data.
- Collection of information about previous/concurrent treatments.

[1] It was permitted to use test results that were obtained from the laboratory sample collected from patient within 14 days before randomization.

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- Physical examination.
- Consultation on contraception methods for the study period.
- Evaluation of chest X-ray (frontal view and lateral view) or Computer Tomography (CT) scans[2].
- Laboratory tests[3]: haematology, blood chemistry, pregnancy test (in WOCBP).
- Blood samples collection for HIV, syphilis, hepatitis B and hepatitis C tests[4].
- Oxygen saturation (SpO_2).
- Evaluation of the eligibility.
- Recording of AEs (related to the study procedures and serious adverse events).

Treatment period (Study days 1 to 17):

Day 1 – randomization and initiation of the treatment:

- Randomization.
- Administration of Polyoxidonium®/placebo.
- Evaluation of measures of clinical support.
- Assessment of clinical status according to the 7-point ordinal scale and to the National Early Warning Score (NEWS) scale.
- Oropharyngeal/nasal (OP/N) sample (conducted in accordance with the center's routine practice).
- Haematology and blood chemistry (only if these tests were not performed earlier from the blood sample collected within 48 hours before the randomization).
- Physical examination.

[2] Recent chest X-ray/CT scans could be used, if the scans were obtained after the symptomatic COVID-19 was diagnosed.

[3] If the patient had results of haematology and blood chemistry laboratory tests that were performed from the blood samples collected within 48 before he signed the Informed Consent, these results could be used to assess the clinical status and eligibility. These data could be used only if they were complete and include all parameters specified in the Protocol. Repeated laboratory tests on Screening were not required in this case.

[4] It was allowed to use test results for HIV, syphilis, hepatitis B and hepatitis C if they were received from the blood sample, obtained within 14 days before the informed consent.

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- Collection of the efficacy data (oxygenation, mechanical ventilation, prolongation of hospitalization).
- Recording of AEs.

Days 2 to 17 - interventional phase:

- Administration of IP/placebo: IV on days 2 and 3; IM on days 5, 7, 9, 11, 13, 15, 17[5].
- Measurement of most efficacy outcomes (every day):
  - collection of the efficacy data*: oxygenation, mechanical ventilation, prolongation of hospitalization;
  - evaluation of the measures of clinical support: every day during hospitalization up to and including Day 17. Not measured after discharge;
  - clinical status according to the 7-point ordinal scale*;
  - clinical status according to the NEWS scale;
- OP/N sample: conducted in accordance with the center's routine practice.
- Haematology and blood chemistry: days 3, 8 ± 1, 17 ± 1.
- Physical examination: days 3 and 17.
- Recording of AEs*: as they occur up to and including day 17.
- Recording of concurrent treatments*: every day.

Follow-up Visit (study day 18):

- Assessment of clinical status according to the 7-point ordinal scale (measured a day in retrospect so the Day 17 value was obtained on Day 18).

Follow-up Day 18 visit could be done by telephone.

Follow-up/Early Termination (study day 29±3):

- Evaluation of the measures of clinical support: only if the patient remained hospitalized at the follow-up visit.

[5] If the patient is discharged before Day 17 administration of IP/placebo could be carried out during outpatient clinic visits or home visits. During an outpatient clinic visit and a home visit administration of IP/placebo could only be performed by the investigator or by the investigator study team member. It was not allowed for the patient to administer the IP/placebo himself.

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- Assessment of clinical status according to the 7-point ordinal scale*.
- Assessment of clinical status according to the NEWS scale.
- Haematology.
- Blood chemistry.
- Pregnancy test (in patients with childbearing potential).
- Collection of the efficacy data (oxygenation, mechanical ventilation, prolongation of hospitalization) *.
- Collection of information about concurrent treatments*.
- Physical examination.
- Recording of AEs*.

Follow-up/Early Termination visit Day 29±3 could be done as an outpatient clinic visit, at the patient's home, or by telephone.

Additional visits could be performed at the investigator's discretion. The study doctor defined the scope of assessments and procedures for the additional visits individually, based on the patient's needs.

Number of patients (planned and analyzed):
Planned sample size: for randomization 394 patients.
Screened: 399 patients.
Randomized: 394 patients.
Completed the study: 371 patients.

Diagnosis and main criteria for inclusion:
1. Hospitalized (at the time of recruitment) male and female patients from 18 to 85 years of age.
2. Signed and dated written Informed Consent for participation in the study. If it was impossible for the patient to make a decision due to a critical condition, the decision on inclusion was made by the Concilium consisting of 3 doctors.
3. The patient could understand all protocol requirements, perform the study procedures, and agree to all limitations specified in the protocol. If, due to the critical condition of the patient, the decision on his participation in a clinical trial was made by a Concilium of 3 doctors, then when the patient became able to understand the information and make decisions (according to the study

* If the visit occurred by telephone contact, then only these procedures took place.

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doctor), the patient's personal consent to continue participating in the study and comply with all procedures and restrictions provided for by the Protocol was obtained.

4. Confirmed diagnosis of coronavirus disease (COVID-19): information about laboratory-confirmed SARS-CoV-2 infection as determined by PCR, or other commercial or public health assay in any specimen that was collected from patient within 14 days prior to randomization.
5. Illness (coronavirus disease COVID-19) of any duration, and at least one of the following:
   - Radiographic/tomographic chest infiltrates by imaging (chest x-ray, CT scan, etc.), OR
   - Evidence of rales/crackles on clinical exam AND SpO2 ≤ 94% on room air, OR
   - Indications for mechanical ventilation and/or supplemental oxygen.
6. Agreed to use adequate contraception methods (the methods with at least 90% efficacy include combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable), intrauterine device (IUD), intrauterine hormone-releasing system (IUS), condom with intravaginal spermicide, cervical caps with spermicide, diaphragms with spermicide, bilateral tubal occlusion, vasectomized partner) or complete sexual abstinence for the study period and within 30 days after completion of the study (applicable for male patients and women of childbearing potential).

Test product, dose and mode of administration, batch number:
Polyoxidonium®, lyophilizate solution for injections, 6 mg (NPO Petrovax Pharm LLC, Russia) in dose of 12 mg once daily intravenously (IV) for 3 days, then every other day intramuscularly (IM) on days 5–17 (the total treatment course was 10 injections).
Batch number: series number 060220

Duration of treatment:
17 days

Reference therapy, dose and mode of administration, batch number:
Placebo, lyophilizate solution for injections, once daily IV for 3 days, then every other day IM on days 5–17 (the total treatment course was 10 injections).
Batch number: series number 0120320

Criteria for evaluation:
Efficacy:
<u>Primary efficacy outcome:</u>
In line with the WHO Master Protocol, the initial primary endpoint was the clinical status of the patient at Day 15 based on a 7-point ordinal scale:

1. Not hospitalized, no limitations on activities
2. Not hospitalized, limitation on activities
3. Hospitalized, not requiring supplemental oxygen
4. Hospitalized, requiring supplemental oxygen

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5. Hospitalized, on non-invasive ventilation or high flow oxygen devices
6. Hospitalized, on invasive mechanical ventilation or Extracorporeal membrane oxygenation (ECMO)
7. Death.

After reviewing the blinded efficacy data of the first 100 patients the Data Safety Monitoring Board (DSMB) recommended to continue the study without modification the primary endpoint.

<u>Secondary efficacy outcomes:</u>

- The following measures were calculated using clinical status measured on the 7-point ordinal scale:
  - Clinical status on days 3, 5, 8, 11, and 29.
  - Time to improvement by one category of the ordinal scale from admission (measured daily).
  - Change in clinical status from baseline to days 3, 5, 8, 11, 15, and 29.

- National Early Warning Score (NEWS):
  - The time to discharge or to a NEWS of ≤ 2 and maintained for 24 hours, whichever occurs first (measured daily).
  - Change in NEWS from baseline to days 3, 5, 8, 11, 15, and 29.

- Oxygenation:
  - Oxygenation free days in the first 28 days from baseline (to day 29).
  - Incidence and duration of new oxygen use during the study (measured on Day 29).

- Mechanical Ventilation:
  - Ventilator free days in the first 28 days from baseline (to day 29).
  - Incidence and duration of new mechanical ventilation use during the trial (measured on Day 29).

- Hospitalization:
  - Duration of hospitalization from baseline (days; measured on Day 29).

- Mortality:
  - 28-day mortality (measured on Day 29).

Safety:

Safety was evaluated throughout the study (from signing the ICF to the follow-up/Early Termination visit) based on the following:

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- Cumulative rate of SAEs during the study.
- Cumulative rate of adverse reactions (AR) registered during the study and related to the IP administration.
- Discontinuation of treatment (for any reason).
- Results of haematology and blood chemistry laboratory tests compared to baseline.

The safety of the IP was evaluated based on statistical analysis of the specified parameters.

Statistical methods:

Statistical analysis was performed with the use of programming language R (version 3.6.0 or higher), statistical software SAS (version 9.4 or higher) or other special software that ensures adequate quality of the results.

Baseline values were defined as the last observed value before the first dose of study medication.

No missing data were substituted.

The significance level for the study was 0.05 (5%).

The following populations were used for analysis:

1. All enrolled patients (intent-to-treat, ITT): Patients that were enrolled in the study and randomized, according to the treatment assignments.
2. Safety population: Patients who received at least one infusion, according to the treatment assignments.
3. Per-protocol (PP) Set: ITT Patients who have no significant protocol deviations from the Protocol and who have not received other antiviral or immunomodulating drugs due to the worsening of the clinical condition.

Demographic and baseline data

For categorical (qualitative) data the incidences were compared between the groups using the Pearson $\chi 2$-test or Fisher's exact test.

For interval (quantitative) data the outcomes were compared between treatment groups using the non-parametric Mann-Whitney U-test for two independent samples with a distribution different from the normal one or using the parametric Student t-test for two independent samples, if the data in each group had normal distribution. Shapiro-Wilk test is used to test normality of the distribution.

Efficacy Analysis

ITT was the main population for efficacy analysis.

The primary efficacy outcome was:

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- Clinical status of the patient (according to 7-point ordinal scale) on day 15.

The null hypothesis being tested was whether the odds of improvement on the ordinal scale is the same for the placebo and investigational product (i.e., whether the common odds ratio for the treatment is 1).

The proportional odds model with factors “treatment”, “severity” and “baseline score” was used for analysis.

Incidences, percentages, odds ratios for comparison between placebo and investigational product and 95% confidence intervals for the odds ratios are calculated during the study to verify the hypothesis for the primary efficacy outcome for clinical status evaluated with the 7-point ordinal scale on day 15 for each clinical status category.

ITT set with LOCF imputations for death as patient’s clinical status (according to 7-point ordinal scale) was used. Additionally, the sensitivity analysis was conducted with LOCF data imputation for all patients and in the Per-Protocol Set.

Secondary Efficacy Endpoints

The time to event data were processed via survival analysis with the use of Kaplan-Meier curves and 95% confidence intervals. The Cox regression with age and severity of disease as covariates were used for group comparison.

The following standard parametric tests were planned for comparison of quantitative data with normal distribution: Student t-test for dependent/independent samples, analysis of variance (ANOVA) for repeated measurements.

The following standard non-parametric tests were planned for comparison of quantitative data with distribution other than normal: Mann-Whitney U-test (performed with Benjamini-Yekutieli correction for OS and NEWS), Wilcoxon T-test, Friedman test. Shapiro-Wilk test was used to test normality of the distribution.

The incidences of new oxygen and new ventilation needs were compared between the treatment groups with Fischer’s exact test.

ITT set with LOCF imputation for deaths as clinical status of the patient (according to 7-point ordinal scale) on days 3, 5, 8, 11, 15 and 29 and changes from baseline was used.

Safety Evaluation

Safety analysis was performed in the safety population. Safety data were analyzed using the methods chosen for efficacy analysis.

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Incidences of adverse events/serious adverse events were calculated. Incidences of adverse events were presented as numbers of patients with AE in total and in each treatment group. The incidences were compared between the treatment groups with Pearson's χ2-test or Fischer's exact test. Also, numbers of AEs per each severity category and per causal relationship with the study drugs are presented.

All reported terms were coded according to the current version of MedDRA dictionary and summarized by preferred terms and system organ classes.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

After reviewing the blinded efficacy data of the first 100 patients the Data Safety Monitoring Board (DSMB) recommended to continue the study without modification the primary endpoint.

Primary efficacy endpoint:

- *Clinical status of the patient (according to 7-point ordinal scale) on day 15 was as follows:*

The odds ratio of improvement on the ordinal scale for Polyoxidonium® vs Placebo for primary analysis was 1.14 with 95% CI 0.76 – 1.70 (no statistically significant difference between arms). The sensitivity analysis and age and severity subgroup analysis showed similar results:

- in the sensitivity analysis for ITT set the odds ratio was 1.13 (95% CI 0.76 - 1.68, no statistically significant difference between arms),
- in the sensitivity analysis for PP set the odds ratio was 1.08 (95% CI, 0.69 - 1.69, no statistically significant difference between groups),
- the odds ratio of clinical improvement in mild-moderate patients was 1.17 (95% CI 0.67 - 2.06, no statistically significant difference between arms),
- the odds ratio of clinical improvement in severe patients was 1.13 (95% CI 0.63 - 2.04, no statistically significant difference between arms),
- the odds ratio of clinical improvement in patients below 65 years was 0.99 (95% CI 0.62 - 1.56, no statistically significant difference between groups),
- the odds ratio of clinical improvement in patients ≥ 65 years was 1.38 (95% CI 0.56 - 3.42, no statistically significant difference between groups).

Secondary efficacy endpoints:

- *Time to improvement by one category from admission on the ordinal scale*:

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Median time to improvement by one category from admission on the ordinal scale was 13.0 days in both treatment arms, no statistically significant difference between arms (p=0.9935 for Cox regression).

Age and severity subgroup analysis showed similar results:

- in the mild-moderate subgroup of patients no statistically significant difference between arms was observed (p=0.7279, Cox regression analysis was),
- in the subgroup of severe patients, no statistically significant difference between groups was observed (p=0.8246, Cox regression analysis was),
- in patients below 65 years there was no statistically significant difference between arms (p=0.6790, Cox regression analysis),
- in patients ≥ 65 years there was no statistically significant difference between arms (p=0.2606, Cox regression analysis was).

- *Clinical status of the patient (according to 7-point ordinal scale):*

No statistically significant difference between treatment arms was found for Days 3, 5, 8, 11 and 29. Subgroup analysis showed no difference between treatment arms either (p>0.05 for all comparisons, Mann-Whitney U-test with Benjamini-Yekutieli correction).

- *Change in the ordinal scale from baseline:*

No statistically significant difference between treatment arms was found for Days 3, 5, 8, 11, 15 and 29 (p>0.05 for all comparisons, Fisher's exact test for categorical analysis and Mann-Whitney U-test with Benjamini-Yekutieli correction for continuous analysis). Subgroup analysis showed no difference between treatment arms either (p>0.05 for all comparisons, Mann-Whitney U-test with Benjamini-Yekutieli correction).

- *The time to discharge or to a NEWS of ≤ 2 and maintained for 24 hours, whichever occurs first:*

The median time to discharge or to a NEWS of ≤ 2 was 8.0 days for Placebo and 7.0 days for Polyoxidonium®, however no statistically significant difference between treatment arms was revealed (p=0.4603, Cox regression).

- *Change in NEWS from baseline to day 3, 5, 8, 11, 15, 29:*

No statistically significant difference between treatment arms was found for Days 3, 5, 8, 11, 15 and 29. Similar results were obtained within age and subgroup analysis (p>0.05 for all comparisons, Mann-Whitney U-test with Benjamini-Yekutieli correction).

- *Oxygenation-free days in the first 28 days (to day 29):*

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The mean number of oxygenation free days for Placebo was 24.24±5.19 days and 24.17±6.01 days for Polyoxidonium®, no statistically significant difference between treatment arms was found (p=0.7614, Mann-Whiney test).

- *Incidence and duration of new oxygen use during the study:*

– The number of patients with new oxygen use incidence was 19 (9.5%) for Placebo and 16 (8.2%) for Polyoxidonium®, however no statistically significant difference between treatment arms was found (p=0.7242, Fisher's test),

– The mean number of new oxygen use days for Placebo was 3.22±2.24 days and 2.47±2.37 days for Polyoxidonium®, no statistically significant difference between treatment arms was found (p=0.2473, Mann-Whitney test).

- *Ventilator free days in the first 28 days (to day 29):*

The mean number of ventilator free days for Placebo was 28.79±1.16 days and 28.93±0.57 days for Polyoxidonium®, no statistically significant difference between treatment arms was found (p=0.1664, Mann-Whiney test).

- *Incidence and duration of new mechanical ventilation use during the trial:*

– The number of patients with new mechanical ventilation use was 5 (2.5%) for Placebo and 1 (0.5%) for Polyoxidonium®, no statistically significant difference between treatment arms was found for both parameters (p=0.2153, Fisher's test),

– The mean number of days of new mechanical ventilation use was 3.60±2.70 for Placebo and 5.0 for Polyoxidonium®, no statistically significant difference between treatment groups was found for both parameters, p=0.5582, Mann-Whitney test).

- *Duration of hospitalization (days):*

Duration of hospitalization was 17.57±5.78 and 17.98±6.49 days for Placebo and Polyoxidonium® respectively with no statistically significant difference between treatment arms (p=0.9653, Mann-Whitney test).

- *28-day mortality:*

Ten deaths (5%) occurred in Placebo group, six deaths (3.1%) occurred in Polyoxidonium® group, mortality rates were 5.03% (95% CI 2.44–9.05%) and 3.08% (95% CI 1.14 – 6.58 %) respectively. No statistically significant difference was observed for mortality rate between Placebo group and Polyoxidonium® group.

SAFETY RESULTS:

<u>Adverse events (AEs)</u>

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There were 127 AEs recorded in 71 patients in the Placebo group and 123 AEs were recorded in 66 patients in Polyoxidonium® group. No statistically significant difference in the number of AEs was found between treatment arms (p=0.7028, Pearson $\chi 2$ -test). In the Placebo group 3 patients had 3 AEs, related to the study drug, in the Polyoxidonium® group 2 patients had 2 AEs, related to the study drug.

In the Placebo group 80 mild AEs were recorded in 54 patients, 25 moderate AEs were recorded in 14 patients, 11 severe AEs were in 6 patients and 11 life-threatening AEs were in 10 patients.

In the Polyoxidonium® group 85 mild AEs were recorded in 52 patients, 27 moderate AEs were in 17 patients, 3 severe AEs were in 3 patients and 8 life-threatening AEs were in 6 patients.

In the Placebo group 12 patients had 13 SAEs, 8 patients had 10 SAEs in Polyoxidonium® group.

There were 10 deaths in Placebo group and 6 deaths – in the Polyoxidonium® group.

Results of laboratory tests (blood biochemistry and haematology)

Among clinically significant abnormalities the most frequent were changes in the level of ALT and AST in both groups:

- AST: Placebo –8 patients (4%) on Days 3 and 8; Polyoxidonium® – 5 patients (2.6%) on Day 3 and 4 (2.1%) patients on Day 8),
- ALT: Placebo – 10 patients (5.1%) on Day 3 and 18 (9.1%) patients on Day 8; Polyoxidonium® – 11 patients (5.7%) on Day 3 and 14 (7.2%) patients on Day 8).

By the end of the Study no clinically significant changes in ALT and AST values were observed.

More rarely clinically significant abnormal values were found for glucose, creatinine, C-reactive protein, erythrocyte sedimentation rate, hemoglobin, erythrocytes, platelets, leukocytes, neutrophils segmented (%), neutrophils segmented, neutrophils band form (%), neutrophils band form and lymphocytes (%). By the end of study, of all these values there remained only 1 clinically significant change in the levels of creatinine, C-reactive protein, ESR, platelets, leukocytes, neutrophils, lymphocytes (%) in the Polyoxidonium group (1 case (0.5%) per each value). For all other parameters with clinically significant changes reported during the Study no clinically significant changes were observed by the end of the Study.

Among physical examination parameters 2 clinically significant changes were found: results of lung auscultation on Day 1 – 1 patient (1.0%) in Placebo group and on Day 29 – 1 (1.0%) patient in Polyoxidonium® group.

Among vital signs following clinically significant abnormalities were recorded:

- Blood Pressure: on Days 17 and 29 – 1 (0,5%) patient in Polyoxidonium® group;

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- Heart rate: on Days 17 and 29 – 1 (0,5%) patient in Placebo group;
- Oxygen saturation: at screening – 2 (2.0%) patients in the Placebo group.

CONCLUSION:

This study demonstrates no superiority of Polyoxidonium® over Placebo in hospitalized patients with COVID-19, evidenced by absence of statistically significant difference in the following treatment outcomes between Polyoxidonium® and placebo:

- patients' clinical status on Day 15 assessed with 7-point ordinal scale (primary outcome);
- patient's clinical status and changes in patient's clinical status assessed with 7-point ordinal scale on days 3, 5, 8, 11, and 29;
- time to improvement by one category of the ordinal scale from admission;
- time to discharge or to a NEWS of ≤ 2 and maintained for 24 hours, whichever occurs first;
- change in NEWS from baseline to days 3, 5, 8, 11, 15, and 29;
- oxygenation-free days, incidence and duration of new oxygen use during the study;
- ventilator free days, incidence and duration of new mechanical ventilation use during the trial;
- duration of hospitalization;
- 28-day mortality.

Polyoxidonium® has an acceptable safety and tolerability profile in hospitalized patients with COVID-19, evidenced by:

- absence of statistically significant difference between Polyoxidonium® and placebo arms in the number of adverse events.
- low level of Polyoxidonium-related AEs: 2 mild AEs in 2 patients - hot flashes on the face, allergic reaction (urticaria).

Date of the report: 06 Jul 2021