The form is worded in the masculine form for convenience only and is intended for men and women alike.

You are being asked to voluntary join a clinical trial. A clinical trial is an innovative process that is either unknown or not standard or has not yet been approved for routine treatment in Israel and therefore there is uncertainty about its safety or efficacy. This form explains the experiment you were invited to join. Please read the information carefully and discuss it with anyone you like: friends, family members and doctors or healthcare professionals who are not directly involved in the clinical trial. More information about the trial as well as answers to any questions can be obtained from the clinical trial physician or his representatives.

Before you agree to join this clinical trial, it is very important to be informed about the existing risks and benefits in order to make an informed decision. This process is called “informed consent”.

Your participation in this trial is voluntary and you have the right to choose to not participate in it and to not sign the consent form. You are free to withdraw from the trial at any time without providing a reason. Your decision to refuse to sign or to withdraw from the trial will have no negative effect on your present and future medical care, and you will receive an explanation about the treatment options available to you.

If you are willing to participate in the trial, you will be asked to sign this form. You will receive a signed copy for safekeeping and the original will be kept at the medical institution.

|  |  |
| --- | --- |
| First Name: | Last Name: |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | |  |  |  |  |  |  |  |  |  |   I.D. No.: | |
| Address: | |

1. **Information about the trial**
   1. The trial title: A Phase 2B, Double-blind , Placebo-Controlled Study to Evaluate the Effect of CimetrA in Patients Diagnosed With COVID-19
   2. The investigator **Dr. XXXXXX** was authorized by the institutional Helsinki Committee and the director of the medical institution **XXXX Medical Center** to conduct this trial in accordance with the Public Health Regulations (Clinical Trials), 1980.
   3. The purpose of the trial: **This study is designed to evaluate the efficacy, pharmacokinetic indices, and safety of CimetrA in patients diagnosed with COVID-19.**
   4. The trial treatment:

**CoV virus** is a virus that belongs to the corona virus family. Which causes upper respiratory and gastrointestinal infections in mammals and birds. In humans, it mainly causes a cold, but complications can also occur, such as pneumonia and severe acute respiratory syndrome (SARS). Corona virus with severe acute respiratory syndrome (SARS-CoV) caused a global threat with high mortality in 2003, and again in 2019 and 2020.

The prominent features include a high rate of person-to-person transmission, a significant risk of developing fatal respiratory syndrome and possible failure of additional organs. Risk factors leading to a life-threatening clinical course have also been identified, including advanced age and a variety of comorbidities, such as cardiovascular disease, diabetes, hypertension and cancer.

However, people who have none of the known risk factors are not immune to the severe manifestation of the disease, and once infected, they have a certain risk of mortality, which has been calculated in Italy to be about 2%.

These factors lead to severe manifestations of COVID-19, particularly severe acute respiratory syndrome (SARS), as well as a functional deterioration of organs and additional physiological systems, **hence the importance of offering a new drug that can help COVID patients, the relieve symptoms and delay the exacerbation** **of their disease/condition.**

**Disease Characteristics:**

The disease is characterized by several critical elements that may be life-threatening if not treated in time.

1. There is a connection between a high accumulation of the virus in the human body and deterioration and exacerbation of the COVID-19 disease. The presence of the virus in the body and its spread in the body causes an exacerbation in the patient's condition. Therefore, any intervention to eliminate or delay the process of spread and proliferation of the virus in the human body, known as antiviral therapy, will be considered desirable.
2. After the patient contracted the Corona virus, at some stage, a condition called a “cytokine storm” develops – this phenomenon is associated with acute damage to the respiratory tract and the lungs, mainly causing acute respiratory distress syndrome (ARDS) . The data on COVID-19 from the many clinical reports published so far support that immune system dysfunction causes clinical exacerbation and exacerbation of the COVID-19 disease in the patient's body.
3. The presence of the virus in the patient's body causes the production of free radicals (active substances that have the ability to bind to proteins, tissues and DNA. When free radicals bind to these molecules, they can cause damage), this condition causes severe damage to the lungs, and at the same time, deterioration in COVID-19 patients’ health condition.

Currently, there is no specific registered treatment with proven efficacy for the treatment of serious COVID\_19 disease; in addition, many preventative vaccines are still under study, and 8 vaccines have been recently approved by the FDA, but there is still a great need to find an effective antiviral drug that can treat the CoV virus that can help to treat patients who contract the disease, particularly since many countries have not been vaccinated yet and are at risk of contracting the disease.

**Hence the research initiative, MGC-PHARMA offers the experimental treatment CimetrA**

**CimetrA formulation and its active ingredients:**

## The study drug is called **CimetrA** and is currently manufactured and marketed as a natural preparation that is composed of natural active components: Curcumin, vitamin C and Boswellia, the study drug is administered in the form of a spray, by spraying into the mouth.

**The study drug is composed of**

### Curcumin

A natural substance found in nature, which has beneficial effects on human health. Curcumin has anti-inflammatory, immunomodulatory (immune system stabilization), antioxidant and antimicrobial activity, which is clinically significant. Positive effects of curcumin have also been observed in situations of acute lung injury, reduced activity of inflammatory cytokines, decreased filtration and concomitant pulmonary edema, and concomitant improvement in patient survival.

### Boswellia

Also known as frankincense, it provides an advantage in the treatment of endothelial (tissues that make up the heart cells) injury, as well as other blood clotting, which appear in the advanced stages of the disease in COVID-19. The active component in Boswellia has an antioxidant, anti-inflammatory effect, which therefore supports the proposal to include it in a compound formulation intended for use in the treatment of the COVID-19 virus.

# A clinical trial with an old ArtemiC formulation

A randomized, controlled Phase 2 clinical trial was conducted with the participation of 50 moderate-severity COVID-19 patients in Israel (40 patients were recruited) and in India (10 patients) to measure the safety and efficacy of ArtemiC.

The patients were randomized in a 2:1 ratio to receive ArtemiC: Placebo, respectively.

The study product demonstrated a complete safety profile. During the trial, serious adverse events were observed, but they were not found to be related to the study product. At the same time, several laboratory studies were performed on a new formulation called CimetrA, which showed better efficacy and results, **and therefore it was decided to continue testing it in Phase 2B in the present study, with some changes to the drug formulation**

The purpose of the study is to evaluate the efficacy, pharmacokinetic indices, and safety of CimetrA in patients diagnosed with COVID-19.

* 1. The trial methods:

# This study will involve a total of 240 patients, who are hospitalized due to the corona virus.

This is an international multicenter study, up to 240 patients in total from Israel, Brazil, the United States and Africa, will participate in this study. In Israel, 80 patients will be recruited, who are hospitalized at the Scottish Medical Center EMMS in Nazareth, and at Rambam Medical Center in Haifa.

The study will be conducted during your hospitalization due to COVID-19 infection.

The study preparation, or placebo, will be taken on the first and second days of the study only (Day 1 and Day 2).

The study will continue for 4 weeks until the end of the study on Day 28, the study period. Follow-up will continue in accordance with the protocol until day 28, regardless of where you are.

In the event of your discharge from hospital during the study period (prior to Day 28), follow-up will continue in accordance with the protocol (partial form), visits will be performed by telephone only, but if you are still hospitalized, visits will be performed by the study staff at the Corona department in which you will be hospitalized.

All patients are required to attend a “Day 28” visit – which will take place at the study clinic. If you recover (a negative result), you will be asked to attend only a final visit (day 28) at the study clinic, but if you are still isolated at that time, Visit 28 will be performed by telephone.

This is a double-blind, placebo (dummy) controlled study, as is common in clinical trials in humans subjects. This means that there are **three** possible arms:The study drug CimetrA will be administered as follows:

**Arm 1** (the group that will receive treatment with CimetrA-1): Receiving the study product CimetrA-1 at a maximal daily dose, which contains a combination of 28 mg of curcumin - curcuma longa extract, 60 mg of frankincense - Boswellia serrata resin extract in the form of a spray, divided into 4 separate doses, administered as a supplement to the routine treatment. Two morning doses and two evening doses given over 48 hours.

Each dose contains 1 ml of (curcumin 7 mg, boswellia 15 mg)

**Arm 2** (the group that will receive treatment with CimetrA-2): Receipt of the study product CimetrA-2 at a maximal daily dose, which contains a combination of 19.6 mg of curcumin - curcuma longa extract, 42 mg of frankincense - Boswellia serrata resin extract in the form of a spray, divided into 4 separate doses, given as a supplement to the routine treatment, including two morning doses and two evening doses administered over 48 hours.

Each dose contains 1 ml of (curcumin 4.9 mg, boswellia 10.5 mg)

**Arm 3** (control group): Receiving a placebo (dummy) which is composed of the same solvent but without any active components, administered as an supplement to the routine treatment in the form of a spray, divided into 4 separate doses, two morning doses and two evening doses administered over 48 hours.

The patient will be randomly assigned to one of the 3 study arms in a 1:1:1 ratio, to receive the study preparation CimetrA (Arm 1 (CimetrA-1) or Arm 2 (CimetrA-2)) in addition to the routine treatment for COVID\_19 or to receive placebo (Arm 3) in addition to the routine treatment for COVID\_19.

The study preparation, or the placebo, will be taken on the first and second days of the study only (Day 1 and Day 2). The drug will be administered twice a day, in the morning and in the evening (every 12 hours). (CimetrA-1) is administered at a volume of 1 ml, equal to 5 bottle sprays, and the maximum dosage is 2 doses per day, i.e., 2 ml per day.

(CimetrA-2) is administered at a volume of 0.7 ml, equal to 5 bottle sprays, and the maximum dosage is 2 doses per day, i.e., 1.4 ml per day.

Each patient will receive a total of 10 bottle sprays per day, **a total of 20 bottle sprays, within 48 hours**.

**The study treatments will be administered as a supplement to the regular standard treatment of the disease,** so that you will receive the study drug in addition to the concomitant/routine treatment you are taking, or you will receive a placebo in addition to the concomitant/routine treatment you are taking

The routine treatment includes:

Supportive care - symptomatic

Analgesics

Anticoagulant treatment

Steroids

REMDESIVIR - Compassionate treatment

Antibiotic treatment as needed

Inhalations as needed

oxygen

The treatments offered above are given in accordance with the Ministry of Health and WHO guidelines, as recommended for the treatment of COVID 19 patients.

The treatment will be given to you according to the discretion of physician team and according to your health and clinical condition, therefore the treatment you receive does not have to be the same as that of other patients participating in the study at your site or at one of the medical centers participating in the study.

**Study visits**

**Day 1**

The investigator will explain to you the objective and details of the study in detail, answer all your questions, **and hand you this informed consent form to read and sign. An assessment of the inclusion and exclusion criteria will be performed in order to determine your suitability for the requirements of the study**.

**During the visit, the following assessments will be performed-**

Review of medical history and demographic information, concomitant drugs, physical examination, vital signs test, ECG, blood test, hematology and biochemistry, completion of VAS scale (pain level index), completion of COVID\_19 quality of life questionnaire, Covid\_19 virus detection test (an exemption will be accepted provided that there are previous valid results up to 5 days before recruitment), **pharmacokinetics - PK test (central laboratory, will not be performed for patients recruited in Israel, only relevant for Brazil and Africa)**

Blood test for inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ) (local laboratory)

D-Dimer test (local), urine test to rule out pregnancy (for women of childbearing potential)

Completion of the World Health Organization (WHO) Ordinal Scale for Clinical Improvement and completion of the change in the COVID-19-related symptoms questionnaire

Randomization into one of the 3 study arms in a 1:1:1 ratio, to receive the study preparation CimetrA (Arm 1 or 2) in addition to the routine treatment for COVID\_19 or to receive placebo (Arm 3) in addition to the routine treatment for COVID\_19.

Administration of the study drug/placebo (twice a day, morning and evening):

In each administration of the study drug / placebo, the doctor will perform 5 sprays into your mouth and 2 administrations will be performed per day, i.e., you will receive a total of 10 sprays of the study product / placebo per day.

**Day 2**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test for hematology and biochemistry, completion of VAS scale (pain level index) blood test for inflammatory markers (IL-6, IL-1β, IL -12, TNF α, IFN-γ) (local laboratory), D-Dimer test (local) Administration of the study drug / placebo (twice a day, morning and evening)

In each administration of the study drug / placebo, the doctor will perform 5 sprays into your mouth and 2 administrations will be performed per day, i.e., you will receive a total of 10 sprays of the study product / placebo per day.

**Days 3-6**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test, hematology and biochemistry-\*\* to be performed according to the schedule of the medical center (routine), blood test for inflammatory markers (IL-6, IL -1β, IL-12, TNF α, IFN-γ) (local laboratory - mandatory), completion of VAS scale (pain level index)

**Follow-up - Day 7**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test for hematology and biochemistry (local, mandatory even if there are available results from the previous day, see details below under “Study Assessment Details”), completion of VAS scale (pain level index), completion of a COVID\_19 quality of life questionnaire, blood test for inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ) (local laboratory), D-Dimer test (local), completion of the World Health Organization (WHO) Ordinal Scale for Clinical Improvement and completion of the change in the COVID-19-related symptoms questionnaire

**Days 8-13**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test, hematology and biochemistry (to be performed according to the schedule of the medical center -routine), completion of VAS scale (pain level index)-mandatory.

**Follow-up - Day 14**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test for hematology and biochemistry (local, mandatory even if there are available results from the previous day, see details below under “Study Assessment Details”), completion of VAS scale (pain level index), completion of a COVID\_19 quality of life questionnaire, blood test for inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ) (local laboratory), D-Dimer test (local), Covid\_19 detection test (mandatory), completion of the World Health Organization (WHO) Ordinal Scale for Clinical Improvement and completion of the change in the COVID-19-related symptoms questionnaire

**Follow-up - Day 21 (telephone visit)**

**During the visit/conversation, the following assessments will be performed-** review of concomitant drugs, side effect evaluation , completion of the VAS scale (pain level index), completion of a quality of life questionnaire, COVID\_19, completion of the World Health Organization (WHO) Ordinal Scale for Clinical Improvement and completion of the change in the COVID-19-related symptoms questionnaire.

**Follow-up - Day 28 (Clinic visit - end of study visit)**

**During the visit, the following assessments will be performed-** Review of concomitant drugs, side effect evaluation, physical examination, vital signs test, blood test for hematology and biochemistry (local, mandatory), blood test for inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ) (local laboratory), D-Dimer test (local), D-Dimer test (local), completion of VAS scale (pain level index),Covid\_19 detection test, urine test to rule out pregnancy (for women of childbearing potential), ECG, completion of a COVID\_19 quality of life questionnaire, completion of the World Health Organization (WHO) Ordinal Scale for Clinical Improvement and completion of the change in the COVID-19-related symptoms questionnaire after their recovery from COVID-19.

Details of the Study Evaluations

**Medical History**: Your demographic information will be documented, including your age and gender, as well as your medical history and drug history, including a history of clinically significant abnormalities in all body systems and comorbidities.

**Vital signs measurement**: Blood pressure, pulse, temperature, body weight and height, room air saturation/oxygen supply, respiration rate.

**COVID-19 virus detection test**: A sample will be taken from your nostril and pharyngeal cavity with a swab and transferred to a laboratory in order to test for the presence of the virus. The test result can be positive or negative, and interpreting it indicates whether the virus is still present in your body or not, respectively. Or in the acceptable manner for each country

**Physical examination:** The examination will be performed by a skilled physician and will include diagnosis and documentation of significant abnormalities or concurrent diseases.

**Blood tests (local laboratory): For each test, about 5 ml of blood will be taken (equivalent to one teaspoon)**

* Hematology: Complete blood count (CBC)
* D-dimer test: A blood test intended rule out a thromboembolic disease when its likelihood is low, or to help confirm such a disease when the dimer level is high
* Biochemistry: Sodium (Na), Potassium (K), Chloride (Cl), Creatinine, Glucose, Urea, Albumin, Calcium total, Alkaline Phosphatase (ALP), ALT, AST, Total Bilirubin, Direct Bilirubin, LDH, Total Protein, Uric Acid, CRP, and Lipid Profile (including Total Cholesterol, HDL, LDL, Triglycerides)
* Inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ) The blood will be centrifuged and frozen in accordance with the local laboratory guide and will be analyzed at a later stage.
* PK indices: **These tests will not be performed for patients recruited in Israel, they will be performed for 14 patients who will be recruited in Brazil and Africa only, 11 tests will be performed according to a time table, a total of 55 ml of blood will be taken.**

|  |  |
| --- | --- |
| Visit No. 1 - After the administration of the first dose (5 inhaler sprays) | |
| Time point 0 | Baseline - Prior to the administration of the study drug |
| Time point 1 | 15 minutes after receiving the first dose |
| Time point 2 | 30 minutes after receiving the first dose |
| Time point 3 | 45 minutes after receiving the first dose |
| Time point 4 | An hour after receiving the first dose |
| Time point 5 | 1.5 hours after receiving the first dose |
| Time point 6 | 2 hours after receiving the first dose |
| Time point 7 | 4 hours after receiving the first dose |
| Time point 8 | 6 hours after receiving the first dose |
| Time point 9 | 8 hours after receiving the first dose |
| Time point 10 | 10 hours after receiving the first dose |
| Time point 11 | 12 hours after receiving the first dose |

Urine test: For women of childbearing potential, a test will be performed to rule out pregnancy.

**VAS scale (pain level index)**: To be performed by a member of the study staff.

**COVID\_19 quality of life questionnaire** – A questionnaire on the impact of COVID-19 on the patients’ quality of life will be completed by a member of the study staff based on your answers.

**Assessment of the change in the score of the symptoms related to COVID-19:** The questionnaire will be completed by a member of the study staff based on your answers

**The World Health Organization (WHO) Ordinal Scale for Clinical Improvement:** The questionnaire will be completed by a member of the study staff based on your answers.

**The patients functional scale after his recovery from COVID-19:** The questionnaire will be completed by a member of the study staff based on your answers.

* 1. What is your responsibility as a participant in the trial in meeting the study requirements?

**Your participation in this study is entirely voluntary, and you are free to consent or refuse to participate in it. If you refuse, you will receive the standard of care treatment you would have received in a normal clinical setting.**

Additionally, you are free to wighdraw from the treatment or from the study at any time without having to provide reasons for your withdrawal, and without affecting or compromising future treatments that you receive or their quality, and without affecting your relationship with your doctor. You can be monitored by the same medical staff that treated you before.

**Hereby declare that at the time of signing this document, I do not participate in any other clinical trial involving the use of any other study product, and that I undertake not to participate in any other clinical trial involving the use of a study product during the entire period of this trial.**

If you need any medical treatment during the study (including alternative treatment and food supplements), consult with the principal investigator or the study staff before taking the treatment.

* 1. What are the known risks and/or inconveniences expected as a result of participating in the trial?

**Blood tests:** As part of the study, blood tests will be taken from a peripheral vein in your arm. The blood taking usually has no complications, but you may experience fainting, pain, or bleeding, or a hemorrhage may occur in the blood taking area, which usually passes within a few days. Rarely, there may be a small blood clot or an infection the area the needle puncture. The blood pressure cuff may also cause discomfort or an internal hemorrhage in the upper arm.

**COVID-19 Virus Detection Test:** A sample will be taken from your nostril and pharynx cavity using a swab, there are no risks in taking this sample but you may experience discomfort while performing the test.

**Side effects of the study drug:**

Side effects have been observed in a Phase 2 study, which, although defined as unrelated to the study drug, 9 patients out of 50 who participated in the study (treated with the old formulation, ArtemiC) had the following symptoms: Abdominal pain, chest pain, anemia, coughing, bradycardia (slow heart rate), elevation in BUN (blood urea) values, a decrease in blood potassium values, sepsis infection, elevation in the level of blood leukocytes”. All of the symptoms have been defined as being related to patients’ background diseases or as a result of being COVID-19 patients, and that this is part of the consequences of the disease. But it is still important to indicate them to you.

In addition, there may be risks that are not known/cannot be foreseen.

* 1. What are the expected benefits to you as a participant or to others in your condition, as a result of the trial?

You may or may not benefit as a result of participating in this trial, i.e., during the study, your disease symptoms may improve, worsen or remain unchanged. By agreeing to participate in the trial, you are contributing to our ability to learn whether CimetrA can be used to treat the COVID-19 virus, which may be beneficial in the future for patients with the same medical condition.

* 1. Are there alternative therapies?

Currently, there is no specific treatment for CoV infection and additionally, many preventative vaccines are still under study, and 8 vaccines by Pfizer and Moderna have recently been approved.

But there is still a strong need to find an effective antiviral drug that will treat the CoV virus

* 1. What are the circumstances under which your participation in the clinical trial may be discontinued at the decision of the investigator or the sponsor?

1. If during your study eligibility visit, it is found that you do not meet the required criteria for your inclusion in the study.
2. If the continuation of the study does not appear to be in your medical interest, your participation may be discontinued by the principal investigator or the study director.
3. If you do not want or are unable to meet the requirements and the schedule of treatment, follow-up or safety monitoring as specified in the study protocol.

1.11) Your participation in the research is of your own free will and voluntary, the participation in the study is free of charge.

1. **Information about samples and/~~or genetic tests~~**

**Use of these samples** and~~/or genetic tests~~ **will be for the purposes of this study only.**

~~The genetic part of this study is designed to test whether genetic differences between people affect the efficacy and safety of the study product, its mechanisms of action and the side effects it may cause. Sometimes during the study, information on a very large scale is obtained; however the investigators examine in depth only aspects that are related to the current study, and they will not examine the possible connection to other medical conditions.~~

**2.1)**

**2.1) The samples to be collected during the trial:** Blood and urine

samples and a swab sample.

* 1. **The purpose of taking the samples, the methods and the test to be used in the study:**

**Blood samples:** Will be performed at Visit 1, Visit 2, follow-up visits (3-14), Visit 28.

About 5 ml of blood will be taken for each test (equivalent to one teaspoon).

The blood samples will be analyzed for the following tests:

Hematology: Complete blood count (CBC).

Chemistry: Sodium (Na), Potassium (K), Chloride (Cl), Creatinine, Glucose, Urea, Albumin, Calcium total, Alkaline Phosphatase (ALP), ALT, AST, Total Bilirubin, Direct Bilirubin, LDH, Total Protein, Uric Acid, CRP, and Lipid Profile

Blood test for inflammatory markers (IL-6, IL-1β, IL-12, TNF α, IFN-γ)

D-dimer test

PK test (Central laboratory, relevant for Brazil and Africa only)

**Urine tests:** The test will be performed in order to rule out pregnancy in women of childbearing potential on Visits 1, 28

**COVID-19 virus detection test:** The test is performed by taking a sample from the nostril and the pharynx using a swab, to be performed on Visits 1, 14, 28.

* 1. **) To whom the samples will be given, the location and manner of ther retention:** Hematology, biochemistry and inflammatory marker samples will be sent to a local laboratory in a medical center, inflammatory markers will be stored in a freezer and their results will then be analyzed by the external company BIOTEST. PK (pharmacokinetics) will be sent to a central laboratory, **this test will be performed exclusively in Brazil and Africa**.
  2. **) Duration of sample retention, what will be done with the samples and the information when the trial ends or is discontinued:** The samples will be destroyed after the test is performed and their results will be given to the principal investigator and the study staff.
  3. ~~[The samples will be marked with a code and sent to a study laboratory abroad].~~
  4. ~~[The investigators will prepare permanent cell lines from your sample, in order to continue using the samples].~~

~~The investigators are committed to making every effort to maintain the confidentiality of the information arising from your genetic sequence. The results of the genetic test will not be included in the medical record, and in accordance with the Law, only information on the actual conduct of the test without its results will be documented. If information of medical significance to you or to your family members is found in the study, it will be brought to your attention in accordance with the Law and as part of free genetic counseling. After you receive an explanation about the significance of the genetic tests, you have the right not to receive their results.~~

1. **General Information**

**With any problem related to the clinical trial, you may contact the investigator, Dr. Shadi Hamoud, any time of the day, at telephone No.: 0523591876**

* 1. In any case of medical problem, injury or another health incident during the trial period, you must report it immediately in order to receive appropriate medical treatment as well as additional details about your rights in this regard.
  2. The investigator will forward information about your participation in the study ~~(including the very performance of the genetic test)~~ to your attending physician in the community for medical knowledge and follow-up. If previously unknown clinical findings of clinical significance are discovered during the trial, the information ~~(except for the genetic findings)~~ will be provided to the physician in the community. Positive results for diseases that require reporting by Law will be sent to the Ministry of Health (e.g., jaundice, tuberculosis, measles, HIV, etc.).
  3. New information, which may influence your decision to participate or continue in the trial, will be brought to your attention as soon as possible.
  4. As part of the study, you may be asked to answer a questionnaire. You can choose not to answer all or some of the questions in the questionnaire.
  5. The trial sponsor **MGC PHARMA** pays the medical institution the costs involved in conducting the trial. The principal investigator and the sub-investigators have no affiliation with the trial sponsor **MGC PHARMA**.
  6. The trial sponsor will provide the study product free of charge for the entire period of the trial.

* 1. The trial sponsor and the medical institution have ensured an insurance coverage in case of a trial-related injury.
  2. ~~You may continue to receive the study product free of charge even after the clinical trial has ended, for a period of up to three years after the end of the trial. This option to receive the study product (according to a follow-up protocol) will be the decision of the investigator and the medical institution and includes the following terms:~~
* ~~It is clearly known that you have been taking the study product at its determined dosage.~~
* ~~The investigator recommends continuing this treatment.~~
* ~~The study product has not been approved for marketing in the state of Israel for the requested indication and has not yet become a part of the national formulary.~~
  1. There are situations where the sponsor will not supply the product after the end of the trial:
* The study product is medical cannabis
* The development of the product has been discontinued or the clinical trials on the product have not yielded the desired outcomes.
* Supplying the study product for a prolonged period of time is not suitable for your treatment and may harm your health.
  1. The trial's results may be of value and may be used as a part of a patent, or in the development of drugs, medical products, etc. The trial's participants have no rights with relation to patents, medicines, or products that will be developed following the trial they have participated in.
  2. A description of this clinical trial appears in the clinical trials website of the Ministry of Health: MyTrials. The website will not include information that may identify you. You can search this website at any time.

1. **Maintaining the privacy and confidentiality of the information**
   1. Medical and personal data are collected during the trial you were requested to participate in, as part of the trial. This information is saved in the medical records, and it is the responsibility of the team treating you to maintain medical confidentiality. It is your right to receive information from the medical record under the Patient Rights Law. If you know that the information in the medical record is incorrect or incomplete, you must inform the treating team.
   2. The medical record will retain information such as: Medical test results, provision of preparations, instruments or implants, experimental treatments or procedures, etc.
   3. By consenting to participate in the trial you also agree to allow transfer of the medical and personal information collected during the trial to an external organization, who will use it for processing the data. Only coded data will be transferred to the external organization. The information will **not** include: Your name, last name, ID number, residential address or another identifying number given to you by the state authorities.

Overall, coded information is considered identifiable information. The link between the code and your identifying details will be secured by the principal investigator in Israel. In certain instances, unlocking the code by the investigator will be made possible.

* 1. The sponsor will save the coded information and data for the time period determined by law (at least 25 years after the end of the trial).
  2. ~~[You will not be given any specific information collected during the study, such as: Test results for pharmaco-kinetics, biomarkers, etc.].~~
  3. Viewing permissions for verification of the methods of the clinical trial and the data, will only be granted to authorized parties (e.g., authorized sponsor representatives, the Helsinki Committee, the medical institution internal auditor and regulatory authority inspectors). This access to your medical information will be carried out by the investigator, and in accordance with confidentiality rules and regulations.
  4. Your identifying details will not appear in any scientific or other publication.

1. **Withdrawal from the clinical trial**

You have the right to withdraw at any stage of the trial by notifying the principal investigator or her representatives. You are not obliged to give reasons for leaving the trial. If you decide to withdraw from the study, the sample and identifiable data will be destroyed. The investigator may only use samples and/or coded data collected up to the date of withdrawal.

From the moment you notify of your withdrawal from the trial no further information about you will be collected. However, if information of medical significance to you is obtained, you will be contacted. You have the right to refuse to receive the information.

1. **Information about fertility (including spouses), future fertility / pregnancy / fetus or a nursing infant**:]

6.1) [If the toxicological information indicates that the reproductive system is a target organ for toxicity – the investigator will provide an explanation, that is in line with your personal philosophy, about the most efficient and safest way to prevent pregnancy].

* 1. [If women of childbearing age or partners of participants - in case of pregnancy during the clinical trial, the investigator will advise you about possible effects on the fetus and about the fate of the pregnancy].
  2. [In case of pregnancy during the clinical trial, the investigator will ask to collect data on the pregnancy, the birth and/or the newborn- the investigator will ask for the consent of the partner separately].
  3. [If there is information concerning potential harm to fertility in the future - you will receive an explanation concerning the preservation of fertility].

1. **Consent documentation**:

**The participant**: By signing, I declare that I have read the contents of this document, the trial has been explained to me and I agree to participate in it.

Name (first and last): \_\_\_\_\_\_\_\_\_\_Signature:\_\_\_\_\_\_\_\_\_\_Date:\_\_\_\_\_\_\_\_\_\_\_\_

**The explaining investigator**: By my signature, I declare that I provided an oral explanation about this trial to the participant, in accordance with this form. I believe that the participant has understood the explanation, had ample time and opportunity to read this form, and willingly consented to participate in the trial.

Name (first and last) :\_\_\_\_\_\_\_\_\_\_Signature:\_\_\_\_\_\_\_\_\_\_\_Date:\_\_\_\_\_\_\_\_\_\_\_

(including a stamp and a license number)

**Independent witness**\*: I, the undersigned, was present during the explanation about the clinical trial, confirming that the contents of this document were conveyed to the patient orally in my presence, I had the impression that he understood it and heard that the participant expressed his verbal consent to participate in the trial.

Name (first and last name):\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature:\_\_\_\_\_\_\_\_\_\_Date:\_\_\_\_\_\_\_\_\_\_\_\_

\* To be used only in case the participant is unable to read the informed consent form (has impaired vision or is illiterate) or in a situation of medical urgency (as defined by Law). The independent witness must be present during the explanation about the clinical trial.