RESEARCH INFORMATION FOR PARTICIPANTS

STUDY TITLE: Improving the diagnosis and treatment of cardiovascular diseases in Kazakhstan through the introduction of metabolic correction with glucagon-like peptide-1 (GLP-1) drugs.

Use of Tirzepatide (Mounjaro) in the treatment of patients with cardiovascular disease (chronic heart failure with preserved function (EF not less than 45%)).

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PROJECT LEADER:

RESEARCHERS:

Principal Investigator:

Monitor:

SOURCE OF FUNDING: Center for Life Sciences, National Laboratory Astana, within the framework of the targeted scientific program of the Ministry of Science and Higher Education of the Republic of Kazakhstan BR24993023 “Improvement of diagnosis and treatment of cardiovascular diseases in Kazakhstan through the introduction of metabolic correction with glucagon-like peptide 1 (GLP-1) drugs.”

Who is eligible to participate in this study?

The research team is looking for patients with cardiovascular disease (CVD) and chronic heart failure (CHF) with preserved function (LVEF ≤ 45%), aged 18 years and older, to help us evaluate the effectiveness of the new drug Tirzepatide (Mounjaro) from the group of glucagon-like peptide-1 receptor agonists in the treatment of patients with CVD.

We plan to recruit approximately 60, but no fewer than 30 patients. This scientific and innovative biomedical study will be conducted at the Heart Center (University Medical Center Corporate Foundation) Astana, and will consist of weekly subcutaneous administration of the study drug Tirzepatide (Mounjaro) 2.5 mg, with a dose increase of 2.5 mg every four weeks up to 10 mg. The total course of treatment is 40 weeks, followed by follow-up for up to 72 weeks. The effectiveness of the treatment and the possible development of side effects of the drug will be evaluated, which will be confirmed by the results of examinations during the treatment.

Brief description of the drug

Tirzepatide is a new drug originally developed for the treatment of type 2 diabetes mellitus. It is a dual-action incretin, i.e., it is simultaneously an agonist of glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptors.

Studies completed to date have demonstrated the high efficacy of tirzepatide in correcting hyperglycemia in patients with type 2 diabetes. Tirzepatide proved to be superior to many drugs, including insulin degludec.

The SURMOUNT-1 randomized, double-blind, placebo-controlled study is investigating the effectiveness of tirzepatide in reducing body weight in patients with obesity/overweight who do not have type 2 diabetes. The primary endpoint in this study is the percentage change in body weight from baseline.

On April 28, the drug manufacturer announced the first results of the study. The use of tirzepatide was accompanied by a 22.5% reduction in body weight from baseline after 72 weeks of treatment. This is indeed a very significant result.

The full results of SURMOUNT-1 are expected to be reported at one of the upcoming cardiology or endocrinology conferences. However, it is already

possible to say with a high degree of certainty that tirzepatide is highly effective in terms of weight loss.

Tirzepatide is likely to become the main competitor to glucagon-like peptide-1 receptor agonists. Currently, drugs in this class are considered to be among the most effective medications for treating obesity.

Obesity is a cause of a number of CVDs. Tirzepatide has proven effective in treating patients with obesity and obstructive sleep apnea syndrome. However, the most interesting group is patients with obesity, which was one of the causes of **chronic heart failure** with preserved LVEF. Treatment options for this group of patients remain limited, so the efficacy and safety of tirzepatide was studied in the **SUMMIT** Phase 3 randomized trial. Preliminary results of the study were presented by the manufacturer (Lilly) in a press release entitled "Lilly's tirzepatide successful in phase 3 study showing benefit in adults with heart failure with preserved ejection fraction and obesity" dated August 1, 2024.

What is the purpose of this study?

The main purpose of this study is to evaluate the effectiveness of Tirzepatide (Mounjaro) in patients with CVD.

What procedures will be performed for research purposes?

Upon admission to the hospital, the research physician will interview you and ask you questions about your contact information, demographic data, general medical history, history of your disease, medications and supplements you are taking, and the therapy you are receiving. During this visit, we will evaluate your eligibility for participation in this clinical study: we will test your blood for standard biochemical parameters such as AST, ALT, blood glucose, etc., and perform an ECG, ultrasound, and echocardiogram of certain organs. As part of this scientific and innovative biomedical study, blood will be collected for molecular genetic testing (DNA testing), lipid profile determination, and stool samples will be collected for intestinal microbiome testing. If you meet the inclusion criteria, you may agree or disagree to participate in our study by signing this informed consent form (ICF).

After signing the IC, you will be assigned to either the study group (the group receiving Tirzepatide (Mounjaro)) or the comparison group (the group receiving standard treatment). You will be given a questionnaire about

your health before and after receiving treatment to determine your quality of life (QoL) and a **self-monitoring diary.**

Your treatment will begin after the initial examination. You will receive a subcutaneous injection of the study drug at a dose of 2.5 mg once a week.

You will receive the study drug Tirzepatide (Mounjaro) every week, taking into account the assessment of adverse effects, with a subsequent increase in the dose by 2.5 mg every 4 weeks up to a maximum of 10 mg. The course of treatment in this study will be 40 weeks, followed by follow-up for up to 72 weeks. Physical condition, laboratory, and diagnostic tests will be monitored. Based on the results of the examination, a decision will be made on whether to further increase the dose.

Injections of tirzepatide (Mounjaro) will be administered at the UMC for up to 40 weeks inclusive.

After completing the study, you may continue treatment with this medication on your own after consulting with your doctor.

What are the possible inconveniences and risks of participating in this study?

Risks associated with the study drug: pancreatitis, gastrointestinal reactions: nausea, mild stomach pain, diarrhea, decreased appetite; decreased blood sugar (hypoglycemia); allergic reactions; vision changes; kidney failure.

What are the potential benefits of participating in this study?

After enrolling in this study and receiving the study drug, you may see improvements in your cardiometabolic parameters (decreased glycated hemoglobin (HbA1c) levels, improved lipid profile, decreased blood pressure and systolic pressure, weight loss, etc.) as prevention of complications of cardiovascular diseases such as stroke and myocardial infarction. Treatment with Tirzepatide will be provided to you free of charge. Your health will be monitored throughout the study period. By participating in this study, you can help improve our understanding of the potential benefits, risks, and side effects of treatment with Tirzepatide (Mounjaro).

If I agree to participate in this study, will I be informed of any new risks that may be discovered during the course of the study?

During this study, we may discover any new risks that may be important to you. This includes information that, after review, may change your mind about participating in the study. We will inform you as soon as possible if such risk information becomes available.

What if new information becomes available about the study?

During the course of this study, we may find additional information that may be important to you. This includes information that, after review, may change your mind about participating in the study. We will notify you as soon as possible if such information becomes available.

What will happen to my health information if I decide to leave this study?

If you leave the study, no additional information will be collected. We will keep the information that has already been collected. All information about you will be coded and will not be accessible to third parties. You may request that your stored biomaterial samples be destroyed by writing a request to the principal investigator of the study.

Will I be charged for any new procedures performed as part of this study?

You are not responsible for the cost of procedures performed for the purpose of this study. All laboratory and diagnostic tests and the drug itself will be free of charge as part of the study.

Will I be paid if I participate in this study?

No, unfortunately, you will not be paid for participating in this study.

Who will know about my participation in this study?

Any information collected about you during this study will be kept as confidential as possible. All records related to your participation in this study will be kept in a locked file. Your identity in these records will be indicated by an identification number (ID #) instead of your name, and information linking these identification numbers to your identifying information will be kept separate from the study records. The only people who will have access to these separate records will be the researchers directly involved in this study.

The results of the study will be published, but you will not be identified by name in any publication of the study results.

Can I access my medical records as a result of participating in this study?

You will not receive a copy of any of your results from this study. The research physicians will notify you of the status of your condition regarding your illness.

Is my participation in this study voluntary?

Your participation in this study, including the use and disclosure of your identifying information for the purposes described above, is entirely voluntary. (Please note that if you do not consent to the use and disclosure of your identifying information for the purposes described above, you will not be allowed to participate in the study). Given that the study is being conducted within the framework of the state budget and considering the high cost of the drug, it is desirable to participate in the study until its completion in order to evaluate the effectiveness of the treatment being conducted.

Regardless of whether you consent to participate in this Study, your decision will not affect your current or future relationship with ……. and other clinics.

Who to contact?

You can contact the project manager: ……

• if you have questions about the study or your participation in it,

• if you have a problem related to the study, or

• if you have questions or complaints about the study

INFORMED CONSENT FORM

I, _____, have read the information about the clinical trial “Improving the diagnosis and treatment of cardiovascular diseases in Kazakhstan through the introduction of metabolic correction with glucagon-like peptide-1 (GLP-1) drugs” and I agree to participate in it.
I have had sufficient time to decide whether to participate in the study, trial, or experiment.
I understand that I may withdraw from further participation in the study in the event of force majeure circumstances and that doing so will not affect my subsequent treatment and care by doctors.
I voluntarily agree that my data obtained during the study, trial, or experiment may be used for scientific purposes and published, subject to confidentiality rules.
I have received a copy of the “Patient Information and Informed Consent Form.”

_____
_____

Patient's full name (in block letters) Date and time

_____

Patient's signature

_____
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Full name of guardian, relative (in block letters) Date and time

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Full name of the investigating physician (in block letters) Date and time

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Signature of the investigating physician