MEDICAL RESEARCH AGENCY

MEDICAL UNIVERSITY OF GDAŃSK

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# Evaluation of the metoprolol treatment efficacy

## in preventing cardiomyopathy

## IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

**The project aim:**

evaluation of the efficacy of the early metoprolol treatment (a beta-blocker drug class) in DMD patients.

**The research carried out from 2020 to 2026**

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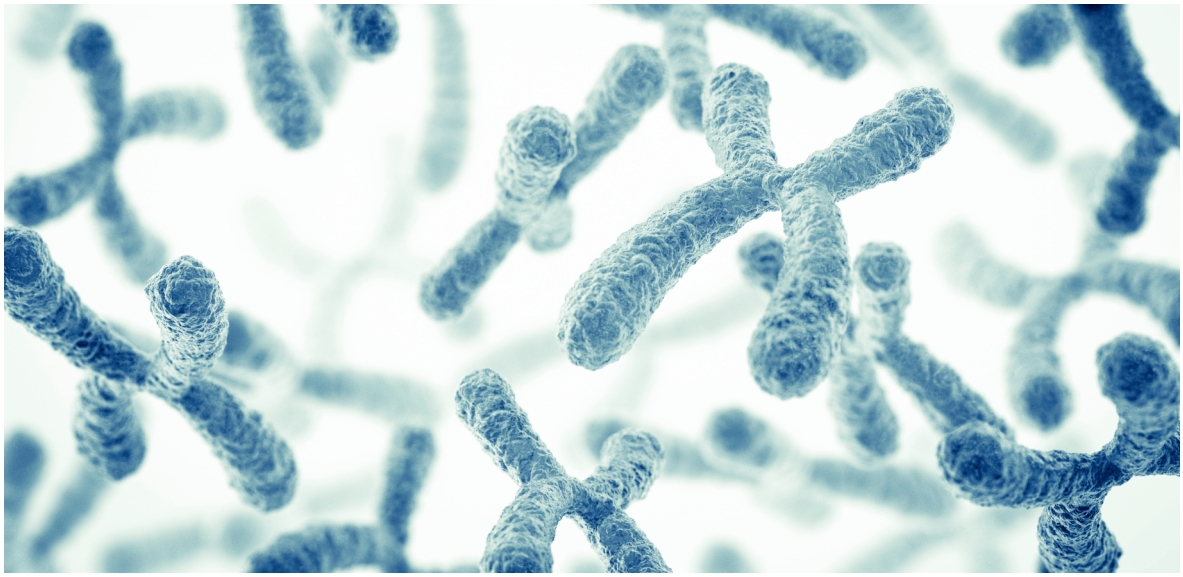
**Safety and Efficacy of Metoprolol as supplementary treatment in the Prevention of Cardiomyopathy in Patients with Duchenne Muscular Dystrophy**

Metoprolol Safety and Efficacy in the Prevention of Cardiomyopathy in Patients with Duchenne Muscular Dystrophy (DMD)

**Duchenne muscular dystrophy (DMD)** is inherited in an X-linked recessive pattern and is characterized by the progressive degeneration of not only skeletal and respiratory muscles but also the heart muscle. Due to the specificity of the way the heart muscle is affected in DMD, the cardiological care of DMD patients plays a key role in their prognosis improvement and it consists of the regular evaluation that comprises an interview, a medical examination and additional exams such as a resting ECG, a 24h Holter monitoring and echocardiography.

As cardiovascular magnetic resonance imaging (CMR) allows a comprehensive assessment of fibroblastic foci (LGE) with unequalled levels of reproducibility and it is independent of the acoustic window, the exam is becoming increasingly important. Such complex care, in line with the most recent medical knowledge, has been provided to over 100 patients with DMD at the University Clinical Centre in Gdańsk for years. According to Birnkrant and all, the part of the aforementioned exams should be conducted every year.



## Project stages:

Below, we present the planned stages of the project along with the corresponding interventions allowing for monitoring the patient's health, side effects of drugs, and positive effects of therapy. The planned intervention comprises the inclusion of one drug (metoprolol) administered in one daily dose adjusted to the patient's weight. It should be taken into account that the dose will be regularly verified with respect to the patient's body weight, and if necessary, it will be modified to match the current measurements.

1. Eligibility criteria for patients to be included in the study.

2. Randomization procedure.

3. Initiation of the drug or placebo therapy.

4. Periodic analysis.

5. Project completion.

The patient's health status will be monitored and reported both during follow-up visits at the University Clinical Centre in Gdańsk and at home, according to the project protocol. The guardians of the project participants will be provided with drug education, monitoring at the patient's home, telemetry reporting, and information how to act in case side effects occur.

## Project participation inclusion criteria:

1. Parents or legal guardians of project participants must express a written informed consent prior to performing any study related procedures, and if patients are over 13 years old, they also have to do it themselves.

2. Declared readiness to follow all the research procedures and availability for the duration of the project.

3. Boys aged ≥ 8 years and <17 years at the moment of entering the study (from reaching the age of 8 years until the last day before the 17th birthday).

4. An ability to take pills and willingness to follow the intervention schedule in the study.

5. The patient with confirmed DMD.

6.Taking drugs from the ACE inhibitor or ARB group in the minimum required doses for at least 30 days prior to the enrollment in the study.

## Project participation exclusion criteria:

1. A current or previous regular use of any drugs from the beta group blockers.

2. Participating in any other clinical trial of new DMD therapies.

3. Clinically significant bradycardia at rest or by Holter ECG, based on age and sex adjusted normal values, the atrioventricular block higher than the first degree at rest and the Wenckebach second degree AV block at night, breaks longer than 2.5 sec.

4. The presence of a pacemaker or an ICD.

5. Heart failure symptoms.

6. Left ventricular ejection fraction (LVEF) <57% (assessed by echocardiography using Teichholz formula).

7. A failure to obtain the appropriate quality of echocardiography images (necessary for monitoring the primary efficacy endpoint and safety).

8. Known allergic reactions to any of the components of the investigational medicinal product (Investigational Medicinal Product – IMP).

If the patient meets all the inclusion criteria apart from taking ACE inhibitors or ARBs, please, contact our center. On the basis of the telephone conversation, the further strategy will be presented to you.

We encourage you to fill out the project application form even if you have doubts. Our doctors will contact you after the preliminary analysis of the information and present the possibilities of the patient's participation in the project.

## Information on the project

**Project Title:** Metropol Safety and Efficacy as supplementary treatment in the Prevention of Cardiomyopathy in Patients with Duchenne Muscular Dystrophy aged 8-16 years, randomized double blind placebo control studies.

Total duration:
maximum project duration is 60 months

Territorial Scope:
patients from all over Poland

Recipients:
a group of patients (circa 140 persons), aged from 8 to 16 years with genetically confirmed DMD

Location and Implementation:
a centralized health care model (the research will be carried out in the University Clinical Centre in Gdańsk 7 Dębinki Street, 80-952 Gdańsk).

- As part of the project, diagnostic exams will be carried out periodically, aimed at the assessment of the patient's condition and the disease progression. If side effects occur, patients will have additional follow-up visits at the University Clinical Centre in Gdańsk.
- The project will be executed in such a way till the 30th month, which will be calculated from the moment the first patient entered the project. The first efficacy analysis will be performed in the project midway.
- The effect of this assessment may result in covering all the patients participating in the project with metoprolol treatment. Such implementation of the project may have a significant impact on updating subsequent care guidelines for patients with DMD.

## Project participation benefits for the Patient:

- access to the specialist medical care in the experienced DMD patient medical centre

- regular specialist consultations (clinical exams are supervised by the specialists from the Department of Paediatric Cardiology and Congenital Heart Defects at the Medical University of Gdańsk )

- access to specialist medical consultations and exams such as:

• transthoracic echocardiography

• electrocardiography

• 24-hour Holter monitoring (ECG)

• 24-hour ambulatory blood pressure monitoring (ABPM)

• spirometry

• laboratory tests

• cardiovascular magnetic resonance imaging

- patients participating in the project will receive a blood pressure monitor, a peak flow meter and access to the internet platform to monitor the health and well-being of the patient at home

- participation in this project can change the quality of life of the patients suffering from the disease

- financial support to cover part/all of the travel and accommodation costs

- active participating in science and medicine development in Poland.

## Project promoter

The project Evaluation of the metoprolol treatment efficacy in preventing cardiomyopathy in patients with Duchenne Muscular Dystrophy will be carried out by a team of scientists under the supervision of Dr. Habil. Joanna Kwiatkowska, the head of the Department of Paediatric Cardiology and Congenital Heart Defects at the Medical University of Gdańsk.

The Medical University of Gdańsk (MUG) is a modern academic centre recognized both in Poland and round the world. The university is characterized by a high research and development potential, which includes in particular: experienced and reputable research teams, a growing number of prestigious international publications and grants, as well as a wide range and quality of research confirmed by high categorization of units. The MUG is also the only medical university selected to the elite group of 10 best Polish universities in the prestigious competition: Initiative of Excellence – Research University.

The project will be carried out based on the infrastructure of the University Clinical Centre (UCC) - one of the largest and most modern hospitals in Poland. The UCC has the appropriate personnel and technical potential, ensuring access to innovative treatment methods and medical equipment at the highest world level.

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