A GUIDE TO PARTICIPATING IN CLINICAL TRIALS FOR PATIENTS WITH MASLD/MASH

PURPOSE OF THIS GUIDE

This is intended to be a brief guide for people at risk for or diagnosed with metabolic dysfunction-associated steatotic liver disease (MASLD) or metabolic dysfunction-associated steatohepatitis (MASH) to understand and assess clinical research opportunities.

QUESTIONS ANSWERED IN THIS GUIDE

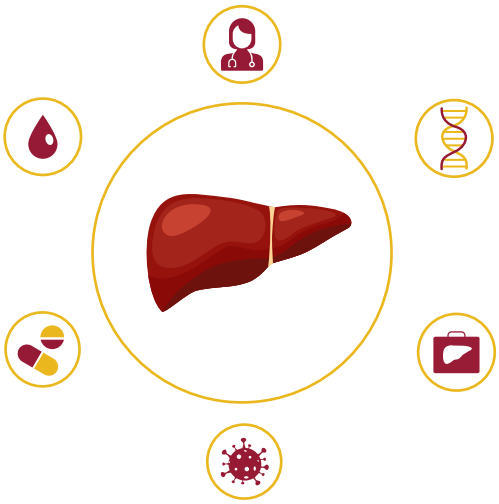
1. ***What is MASLD/MASH?***
2. ***What are clinical trials?***
3. ***How can my participation in a clinical trial advance healthcare for MASLD/MASH?***
4. ***What should I consider when looking for a MASH/MASLD trial?***
5. ***What are my rights as a participant in a clinical trial?***
6. ***Where can I learn more?***

WHAT IS MASLD/MASH?

MASLD stands for metabolic dysfunction-associated steatotic liver disease is a condition caused by a buildup of fat in the liver.

MASH or metabolic dysfunction-associated steatohepatitis is the more severe form of MASLD which includes an accumulation of fat in the liver, inflammation and a type of injury called ballooning, with or without scarring (fibrosis). **MASH can lead to cirrhosis, cancer, or the need for transplant.**

Current estimates show that as many as one in three people already have MASLD or MASH, yet these conditions are underrecognized, underdiagnosed, and undertreated. People who have type 2 diabetes, obesity, and/or over 50 are more likely to have MASLD or MASH but this condition can affect anyone, even those of normal weight or children.



WHAT ARE CLINICAL TRIALS?

Clinical trials are a type of research study used by scientists, healthcare providers, and government entities to advance the knowledge and understanding of a certain disease, virus, medication, or treatment.

There are two main types of clinical trials: interventional studies and observational studies.

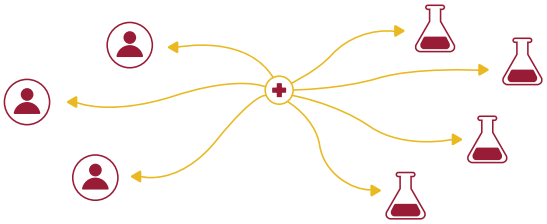
Interventional Study:

The goal of an interventional study is to understand the effects of a certain medication, device, diagnostic tool, or other intervention on a patient. In this study the participant is actively given the intervention as part of the study. Often the intervention is in development, which means it is not accessible to the general public.

Observation Study:

In an observation study researchers observe the effects of different factors such as genetics, age, and environment factors on a disease over time. In this type of study no treatments, medications, or other interventions are given to the participant. There are two main types of observational studies:

- Longitudinal Study: A longitudinal study gathers information and data on an individual over time. By collecting this information over months, years, or even decades, researchers can gain insights on how different exposures such as diet, smoking history, or environmental factors influence disease progression and outcomes.
- Natural History Study: During a natural history study, researchers collect information about a person's genetics and family history to better understand how MASLD/MASH can develop or respond to different treatments.



HOW DOES A CLINICAL TRIAL WORK?

Clinical trials follow a rigorous process. Before researchers can begin a clinical trial and test a drug in people, they must assess whether the drug could cause serious harm. To accomplish this, they conduct either ***in vitro*** (outside of an organism) or ***in vivo*** (within an entire organism) preclinical research. Preclinical studies are usually not large in size.

Once a clinical trial begins, it may normally take several years to be completed. Biomedical clinical trials have four phases: I, II, III, and IV. In Phase II, the goal is to determine the appropriate dose and treatment regimen. Sometimes, Phase II trials are further divided into Phase 2A and 2B. Phase 2A focuses specifically on the dosing requirements, while Phase 2B tests the efficacy of the drug in terms of how successful it is in treating or preventing the disease.

In Phase III, participants are randomly placed into treatment groups, also called trial arms. At this point in research development, a MASH patient will most likely be asked to participate in a clinical trial currently in stage 2B or III. A control group would receive the standard-of-care treatment or a ***placebo;*** the other group(s) would receive the new treatment. Trials can also have more than two groups, with each group receiving different dosages of the new drug.

HOW CAN CLINICAL TRIALS ADVANCE HEALTHCARE FOR MASLD/MASH?

Current MASH/MASLD clinical trials are trying to answer a wide variety of questions such as:

1. **Can a particular medication reduce the scarring associated with MASH?**
2. **Can a particular medication or combination of medications reduce the inflammation associated with MASH?**
3. **Are there certain genes or other drivers that predispose someone to progress to MASH faster than other people?**
4. **Is there a specific diet that helps people with MASH?**
5. **Is there a type, duration, or intensity of exercise that most helps people with MASH?**

1 in 3 people already have MASLD/MASH

By participating in a MASLD/MASH clinical trial you can help answer those questions by providing essential data that shapes the understanding of the disease and leads to advancements in medications and therapies. As a result, researchers and healthcare providers can better address and treat MASLD or MASH in future patients.

Moreover, studies need volunteers with diverse characteristics and backgrounds to ensure that researchers understand the risks and outcomes for the different groups affected by a particular disease.

Demographics that can affect risk, benefit, and outcomes for treatment include: race, ethnicity, age, gender, and concurrent diseases.

Thanks to previous clinical trials we have access to life saving treatments like insulin, antibiotics, and chemotherapy. Recently, from the results of MASLD and MASH focused clinical trials, the FDA was able to approve medications such as resmetirom and semaglutide for the general public use in the United States and Europe.

WHAT SHOULD I CONSIDER WHEN LOOKING FOR A MASH/MASLD STUDY?

When looking for a MASH or MASLD study one should understand the study's purpose, potential risks and benefits, eligibility criteria, and the time commitment involved.

You should ask the research team any questions you have about participating in the trial, such as:

1. *How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?*
2. *What tests and procedures would I undergo?*
3. *How long will the study last?*
4. *If I benefit from the intervention, can I continue receiving it after the trial ends?*
5. *Who will oversee my medical care during the trial?*
6. *Where do I have to go to participate in this trial?*
7. *Is there travel involved?*

View additional possible questions to ask, as shared by the National Institutes of Health in the U.S., at https://clinicaltrials.gov/ct2/about-studies/learn.

ADDITIONAL SPECIFIC CONSIDERATIONS FOR PARTICIPATING IN A CLINICAL TRIAL

Pregnancy:

The guidelines for studies of certain treatments may prohibit participants from conceiving during the trial and for a period of time following the study due to safety concerns for the baby. If you are interested in conceiving, speak with your provider about how long you would need to wait to conceive as well as for advice on contraception.

Vacations:

Studies may prohibit travel abroad if participants must be monitored regularly. Speak with your provider first about any travel plans before enrolling in a study.

Speak with your health care provider about your treatment and interest in clinical trials

WILL I BE ACCEPTED INTO THE TRIAL AUTOMATICALLY?

Acceptance and enrollment into a study are not automatic. Studies have both inclusion criteria as well as exclusion criteria. Furthermore, not every person who meets the criteria will be accepted into a trial.

- ***How can I tell if a specific MASH trial is right for me?***
- ***What should I consider when looking for a MASH trial?***
- ***What can I expect when participating in a MASH clinical trial***

Consult with your physician on whether a clinical trial would be appropriate for you and if they would suggest clinical trials available in your area. The location of the study could be a hospital, university, physician's office, community clinic, or another location, depending on the organization conducting the study. The length of a trial may also range from six months to five years or longer.

In addition, take time to carefully assess whether you can complete the activities involved in a particular MASH drug or device trial. Potential activities may include fasting, lifestyle modifications (e.g. nutrition, exercise), completing blood work (e.g. ALT, AST levels), undergoing imaging tests (e.g. ultrasound, MRI), and even having one or more biopsies, a procedure in which a sample of tissue is taken from the body for further examination.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN A CLINICAL TRIAL?

Right to Informed Consent

Before any trial participants must be provided with an informed consent form. Through the process of informed consent, researchers communicate to potential and enrolled participants about the risks and potential benefits of participating in a clinical study, allowing possible participants and those already enrolled to make informed decisions.

The process may involve multiple aspects, such as recruitment materials, instructions given verbally, question-and-answers sessions, and additional opportunities to ask questions. In general, volunteers must sign an informed consent document before enrolling in a study, though they may still leave the study at any time if they choose to.

Right to Confidentiality

Throughout the trial the only people who will have access to your personal medical data are the doctors, researchers, and specific authorized personnel managing the trial. However this information is never attached to any identifying information such as your name. You are entitled to keep all of your medical information private and confidential. Because of strict regulations like HIPAA privacy rules, your identity will never be attached to any published results.

Right to Quit or Leave a Clinical Trial

Participation in a clinical trial is a voluntary process. The voluntary nature of participation in clinical research requires that the investigators inform each participant, prior to start, that they have the right to exit the study at any given time, without any given reason. When withdrawing from a study, be sure to let the research team know.

HOW CAN I FIND TRIALS FOR MASLD AND MASH TREATMENTS?

Acceptance and enrollment into a study are not automatic. Studies have both inclusion criteria as well as exclusion criteria. Furthermore, not every person who meets the criteria will be accepted into a trial.

European Union

In the European Union (EU), the EU Clinical Trials Register lists protocol and results information on interventional clinical trials conducted in the EU and the European Economic Area (EEA) as well as clinical trials conducted outside the EU and EEA that are linked to European pediatric medicine development.

United States and Worldwide

The U.S. National Library of Medicine hosts a database of privately and publicly funded clinical studies conducted around the world, in all 50 states, and in 219 countries. (Note that being listed does not mean a study has been evaluated by the U.S. Federal Government).

ON THE SITE, VISITORS CAN FILTER THE LIST OF STUDIES BY:

- **Recruiting Status**
  (e.g., "Recruiting", "Enrolling by Invitation", or "Completed")
- **Eligibility Criteria**
  (e.g., Age and Sex)
- **Key Words**
  (e.g., steatotic liver, MASLD, MASH)
- **Study Type**
  (e.g., Interventional [Clinical Trial] or Observational)
- **Study Results**
- **Study Phase**
- **Funder Type**
  (e.g., Industry, Academic research institution, or Individual)
- **Location**
  (e.g., country, state, city)

WORLD HEALTH ORGANIZATION REGISTRY NETWORK

In addition, the World Health Organization (WHO) Registry Network includes registries from around the world that are specific to individual countries, such as the Australian New Zealand Clinical Trials Registry (ANZCTR), Clinical Trials Registry - India (CTRI), and the Clinical Research Information Service (CRiS) in the Republic of Korea.

Visit www.who.int/clinical-trials-registry-platform/ network for a full listing and to learn more

No matter how you learn about a clinical trial, it is imperative that you speak with your health care provider before participating in a study

ARE THERE OTHER WAYS TO SUPPORT RESEARCH OTHER THAN BY PARTICIPATING IN A TRIAL?

There are many opportunities for supporting MASLD/MASH research and clinical trials. Patients are often included in clinical trial design advisory boards, asked to participate in observational trials, and needed for advocacy for better funding for research. Join Global Liver Institute's Advanced Advocacy Academy to learn more and support MASLD/MASH research.

Learn more at *www.globalliver.org/advanced-advocacy-academy.*

GLOSSARY OF CLINICAL TRIAL TERMS

Following are terms you may hear frequently as you navigate the clinical trial experience.

BALLOONING
A type of cell degeneration associated with cell swelling and enlargement.

BIOMARKER
Measurable substance or physiological activity in the body that can be used as a sign of stable condition, an abnormal state, or disease; can be used to determine how well the body responds to new treatments.

BIOPSY
An examination of tissue removed from the body to discover the presence, cause, or extent of a disease.

BLINDING
Concealing how groups are allocated from one or more individuals involved in a clinical research study, most commonly a randomized controlled trial. Randomization minimizes the differences between treatment groups at the start of a trial; blinding helps prevent differential treatment or assessments.

EXCLUSION CRITERIA
Factors that prevent a person from participating.

INFORMED CONSENT
To give permission for something to happen or agree to do something.

IMAGING STUDIES
Non-invasive tests that can produce detailed pictures of the body's organs and structures; include x-rays, computerized tomography (CT) scan, magnetic resonance imaging (MRI), and ultrasound.

INCLUSION CRITERIA
Factors that a participant must meet, such as age or sex.

INSTITUTIONAL REVIEW BOARD (IRB)
A group of people who review, approve, and monitor the clinical study's protocol. Their role is to protect the rights and welfare of people participating in a study (referred to as human research subjects), such as by reviewing the informed consent form. The group typically includes people with varying backgrounds, including a community member, to make sure that research activities conducted by an organization are completely and adequately reviewed. Also called a human subjects protection review board or an ethics committee.

INTERVENTIONAL STUDY
A type of study where researchers test a specific treatment, device, or other intervention on participants to evaluate its effects.

IN VITRO
Outside of an organism.

IN VIVO
Within an entire organism.

OBSERVATION STUDY
A type of study in which the data is collected from observations without manipulating any factors.

PLACEBO
An inactive substance or treatment that looks the same as, and is given in the same way as, an active drug or intervention/treatment being studied.

PRINCIPAL INVESTIGATOR
The person who is responsible for the scientific and technical direction of the entire clinical study.

PROHIBITED DRUGS/MEDICATIONS
Drugs that participants may not take during the clinical trial because they could affect the study.

REGIMEN
A prescribed course of medical treatment, way of life, or diet for the promotion or restoration of health.

SCREENING
Checking for disease when there are no symptoms with the hope of finding disease at early stages.

SPONSOR/STUDY SPONSOR
The organization or person who initiates the study and who has authority and control over the study.

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