Effect of 4 weeks of oral D. piger on safety, pharmacokinetics and ethanol metabolism in overweight individuals (2023)

Published: 14-02-2024
Last updated: 19-07-2024

To assses safety, gut engraftment and effects on sugar- and alcohol metabolism of d. piger in individuals with increased waist circumference.

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON56584

Source
ToetsingOnline

Brief title
PIGER

Condition

- Hepatic and hepatobiliary disorders

Synonym
Metabolic dysfunction associated steatotic liver disease (MASLD), NAFLD

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: VICI Grant 25159

Intervention

Keyword: Ethanol, MASLD, Microbiome, Piger

Outcome measures

Primary outcome

The principal outcome will be patient safety and tolerability (biochemical parameters of kidney and liver function and complete blood count, adverse events as compared to placebo) and engraftment of D. piger in the gut as compared to placebo.

Secondary outcome

Response to fructose challenge test during fomepizol infusion (including fructose metabolites in blood, feces, urine and breath)

Transcriptomics in duodenal biopsies

Microbiome compostion (fecal shotgun metagenomics)

Fructose metabolites in 24 feces and 24h urine

Quality of Life questionnaires

Alcohol production per gram feces using bioreactor analyses

Glycemic control using continuous glucose monitoring

Liver fat, assessed using MRI liver and Fibroscan (V2 and V5)

Study description

Background summary

Fructose is a sugar that is much sweeter than glucose, and has multiple applications in the food industry. Research shows that fructose is associated with obesity, diabetes and cardiovascular disease. An overload of fructose may be handled in the colon, where it is metabolized to alcohol by gut bacteria,

putatively contributing to fatty liver disease. Some bacteria degrade alcohol in the colon, thereby protecting the body from deleterious effects. One of these bacteria is d. piger. Our research group found that d. piger degrades alcohol to acetate, that can be used by other bacteria to produce beneficial metabolites. The current study aims to investigate whether d piger in humans is safe and can lower the alcohol concentration in the blood after an oral fructose challenge. In addition, the effects of d. piger on sugar- and fat metabolism are established. If safe and effective, d piger can be a new therapy or prevention measure for diseases such as fatty liver disease.

Study objective

To assses safety, gut engraftment and effects on sugar- and alcohol metabolism of d. piger in individuals with increased waist circumference.

Study design

A phase I/II, placebo controlled, double blinded safety trial in 2x 10 participants.

Intervention

Participants will be given placebo or 10^9 colony forming units (CFU)/ml of oral D. piger once daily for 4 weeks (n=10 per arm, total of 20 participants).

Study burden and risks

The overall risk of the study is estimated to be moderate, mainly due to the risk of gastroduodenoscopy of bleeding or gastric perforation.
As D. piger is a gut commensal, few side effects are expected. In an earlier trial on D. piger in a dose and duration exceeding ours, no side effects were observed. Fomipezol can cause headache and somnolence in a minority of cases.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Increased waist circumference (>102 cm men, 88>cm women)
- Insulin resistance (HOMA-IR >2,5)
- 18-70 years

Exclusion criteria

- Use of systemic medication (except for paracetamol), including proton pump inhibitors, antibiotics and pro-/prebiotics in the past three months or during the study period.
- A history of a cardiovascular event
- A history of cholecystectomy
- Overt untreated gastrointestinal disease or abnormal bowel habits
- Liver enzymes>2.5*fold higher than the upper limit of normal range
- Smoking
- Alcohol abuse

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2023
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO Date:	14-02-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85441.018.23