

Project title:**VLCKD (VERY LOW-CALORIE KETOGENIC DIET) IN PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVER STEATOSIS: THE KETOMI PROJECT****Acronym/working title:****KETOMI****Principal Investigator**

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Registration number of the Ethical approval

Comitato Etico Interaziendale di Novara N° CE296/2021

Project summary

Study design: a pilot randomized controlled study. A sample of 40 patients with obesity, T2D, and NAFLD will be recruited (20:20) and a random number generator will be used to randomize patients to VLCKD (intervention group) or Mediterranean diet (control group). The study will be developed in 5 work packages (WPs) and will last 12 ± 2 weeks, with regular follow-up visits (T0 - T15 days - T30 days - T60 days – Tend). First aim: to study the effect of VLCKD in patients with T2D and NAFLD on glucose control, and liver disease. Second aim: to decipher the interplay among VLCKD, microbiota changes in composition and function, and potential tissue mediators as EVs.

VLCKD is known for the treatment of obesity. The studies of the last decade hypothesized and, in part, demonstrated the therapeutic potential of KDs in many pathological conditions, including DM2, NAFLD, neurological diseases, tumors and cardiovascular diseases. This project aims to study the effects on VLCKD on pathological manifestation of western diet-induced metabolic alterations, mainly T2D and NAFLD, focusing on its effects on human microbiota. The project, in fact, investigates several unexplored aspects of T2D and NAFLD that are potentially able to reveal new pathogenetic mechanisms involved in the development of the disease, by using omics techniques and new players as EVs. The WP1 will provide data on the systemic effects of VLCKD in humans with T2D and NAFLD with respect to classical medical nutritional therapy with a Mediterranean style diet. Specifically, data arising from WP1 allow to find out if VLCKD can modulate the inflammatory and hormonal response, improving metabolic outcomes in patients affected by T2D and NAFLD, and adding clinical data to the existent body of evidence. The WPs 2-5 will explore the modification of microbiota, metabolites and EVs induced by VLCKD and the relationship between metabolic, inflammatory, and clinical parameters. In fact, the gut microbiota is considered to make an important impact on obesity/insulin resistance/NAFLD development as it plays a crucial role in the host immune system, modulation of inflammatory processes, extraction of energy from the host diet, and alterations of human gene expression. However, the interplay among microbiota-linked mechanisms and signature of efficacy are lacking. With these WPs we expect to decipher some of the less unexplored involved mechanisms.

Duration of StudyTotal duration of the study: 12 ± 2 weeks

Study start: 07/01/2022

Study end: 30/06/2023

Total number of participants involved:

40



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Samples collected:

- ✓ Buffy coat
- ✓ Plasma EDTA
- ✓ Plasma sodium-citrate
- ✓ Plasma lithium-heparin
- ✓ Serum
- ✓ Urine
- ✓ Feces