



AIG - ASSOCIAZIONE ITALIANA GLICOGENOSI

XXIII CONVEGNO NAZIONALE AIG

**Endogenous Glucose Production in Subjects with Glycogen Storage Disease Type Ia estimated by a single oral dose of stable isotopes (ENGLUPRO GSDIa):  
*an investigator-initiated human pilot study***  
(NL73191.042.20; NCT04311307)

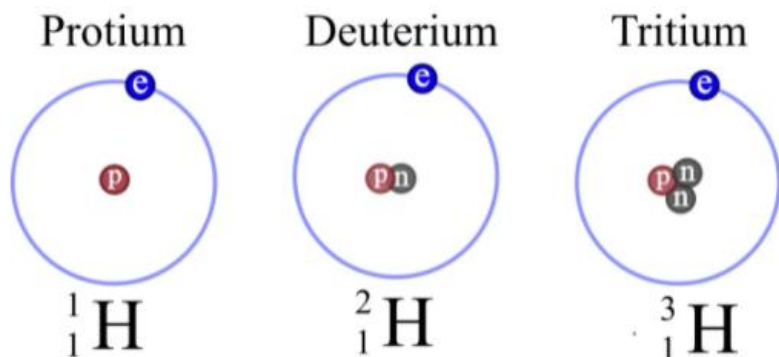
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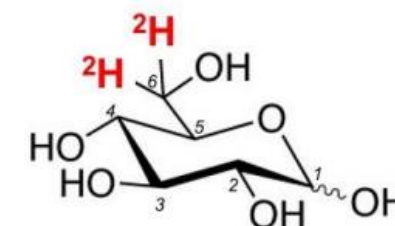
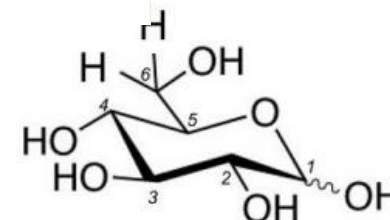
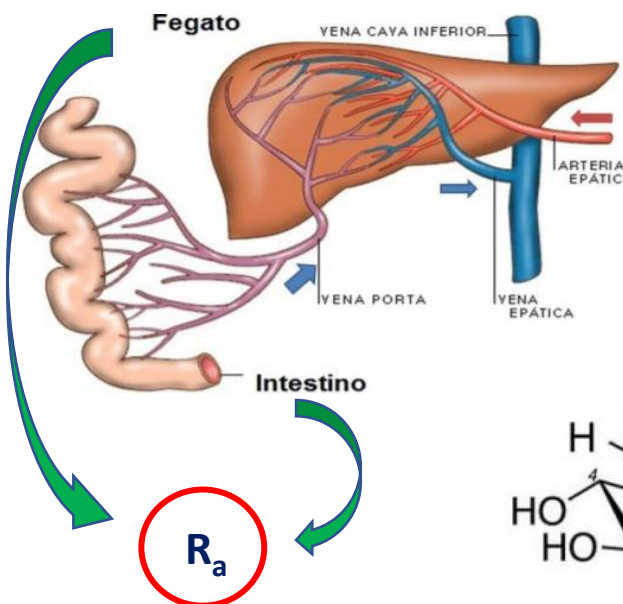
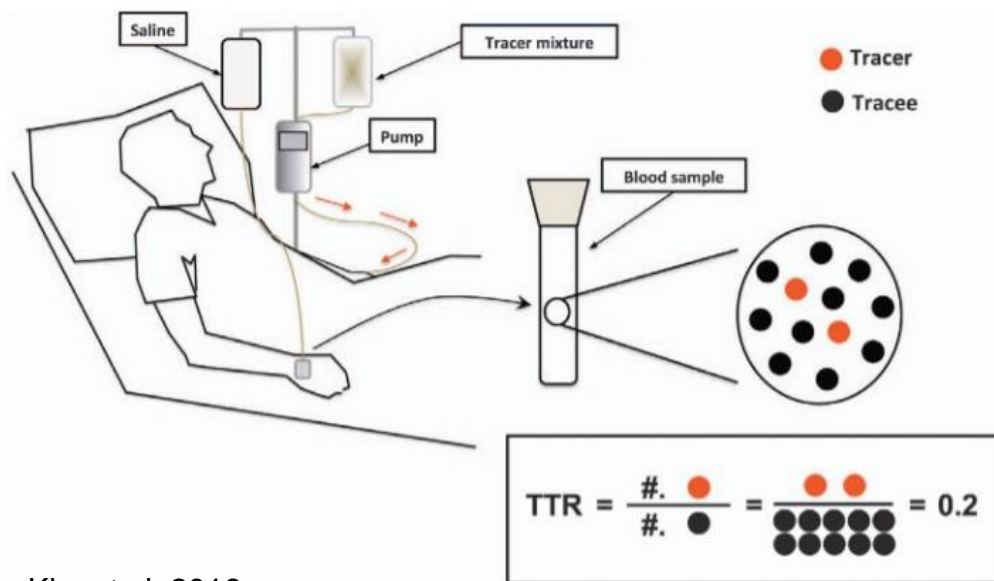
*10 October 2021*

# Stable isotopes



- # of protons: same
- # of electrons: same
- # of neutrons: different
- Mass: different
- **Non radioactive**
- Do not decay into other elements

Stable	Abundance
${}^1\text{H}$	99.98%
${}^2\text{H}$	0.02%
${}^{12}\text{C}$	98.9%
${}^{13}\text{C}$	1.1%
${}^{14}\text{N}$	99.6%
${}^{15}\text{N}$	0.4%
${}^{16}\text{O}$	99.76%
${}^{17}\text{O}$	0.04%
${}^{18}\text{O}$	0.20%

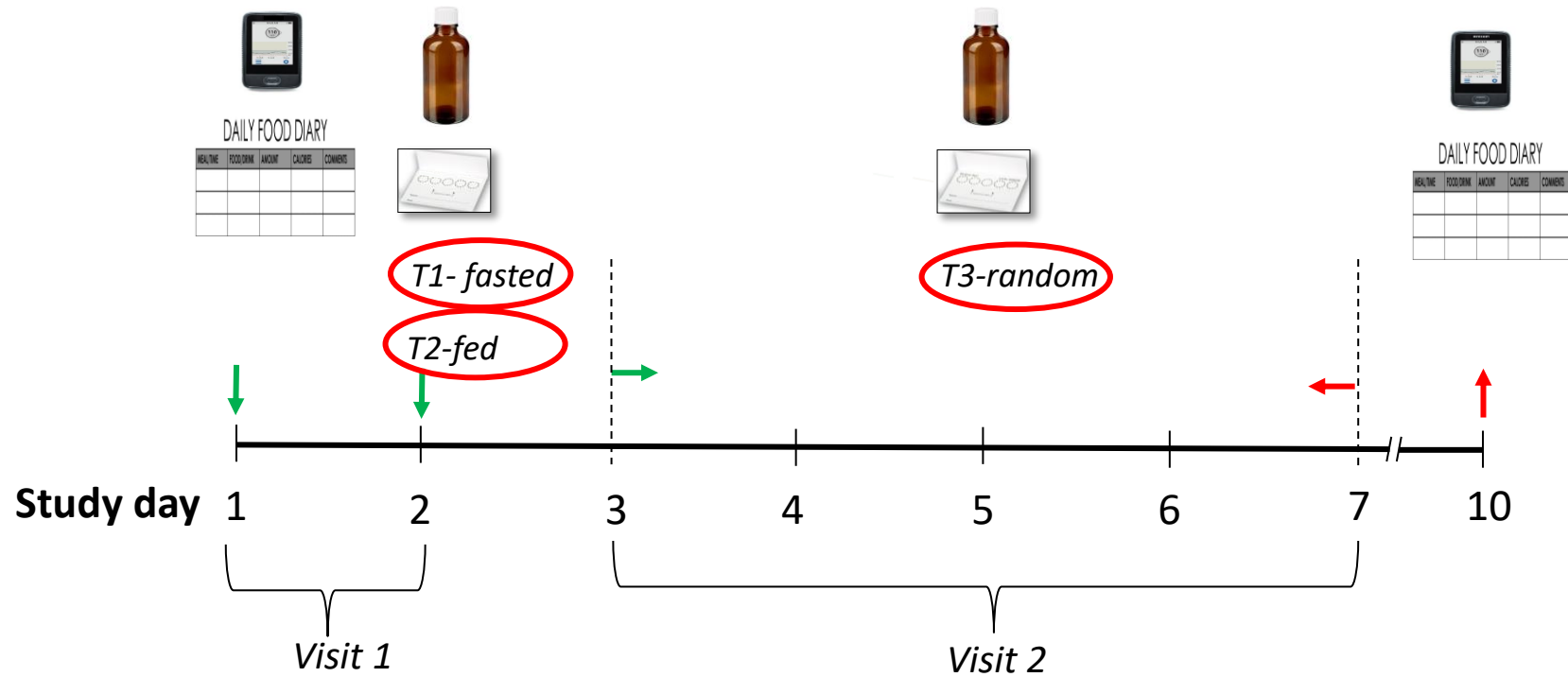


**To define a simple and minimally invasive method to assess EGP in GSDIa patients**

## **Objectives**

- To test the feasibility of EGP quantification in adult GSDIa subjects by stable isotopes after a single oral D-[6,6-<sup>2</sup>H<sub>2</sub>] glucose dose
- To compare EGP assessed by a single oral D-[6,6-<sup>2</sup>H<sub>2</sub>] glucose dose:
  - in GSDIa patients vs matched healthy subjects
  - within GSDIa patients (severe vs attenuated)
  - in the fasted state vs fed state
  - in the controlled (hospital) setting vs home setting
- To compare EGP data with continuous glucose monitoring (CGM) data

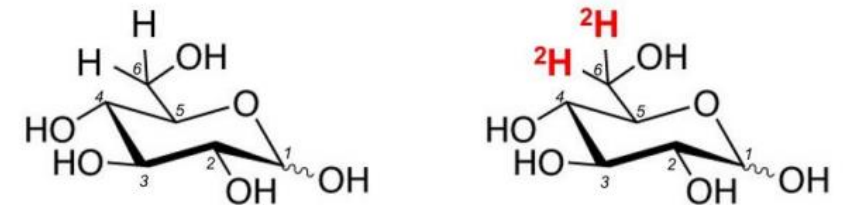
# Study design



## Study time-points

Baseline	+50
+10	+60
+20	+75
+30	+90
+40	+120

- DBS collection
- Capillary glucose
- CGM value



1 study vial= 1.25 grams D-[6,6-<sup>2</sup>H<sub>2</sub>] glucose powder

# Study population

**10 GSDIa patients** (4 severe, 6 attenuated)

**10 healthy volunteers (HV)**

## **INCLUSION CRITERIA**

- G6PC mutation analysis available
- Age > 16 years
- Stable medical condition before the start of the test procedures

## **EXCLUSION CRITERIA**

- Age < 16 years
- Recent hospitalization due to hypoglycemia
- Metabolic instability
- Intercurrent illness
- Pregnancy

## **EXCLUSION CRITERIA**

- Diagnosis/history suggestive of diabetes
- First grade family member with fasting intolerance
- Symptoms/signs suggestive of fasting intolerance
- Recent hospitalization due to hypoglycemia
- Intercurrent illness
- Pregnancy

# Methods

## Primary endpoint

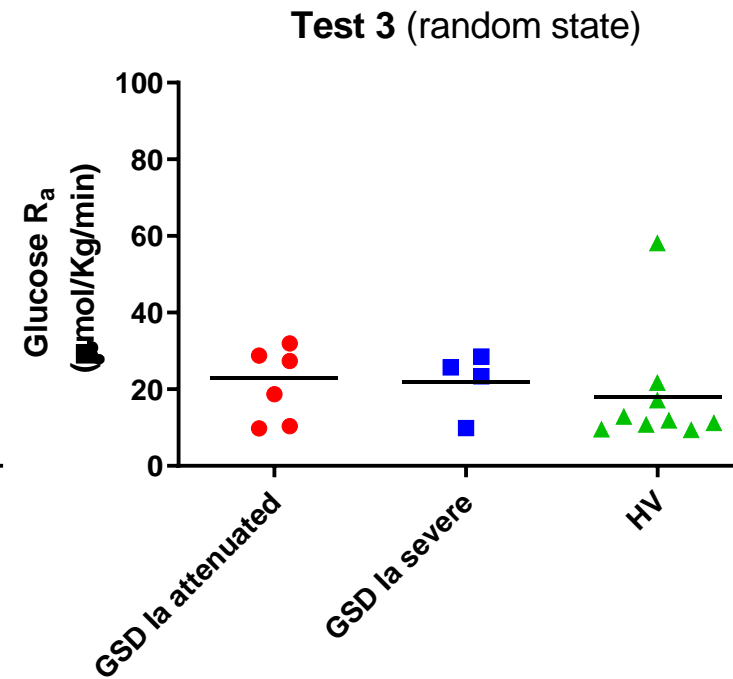
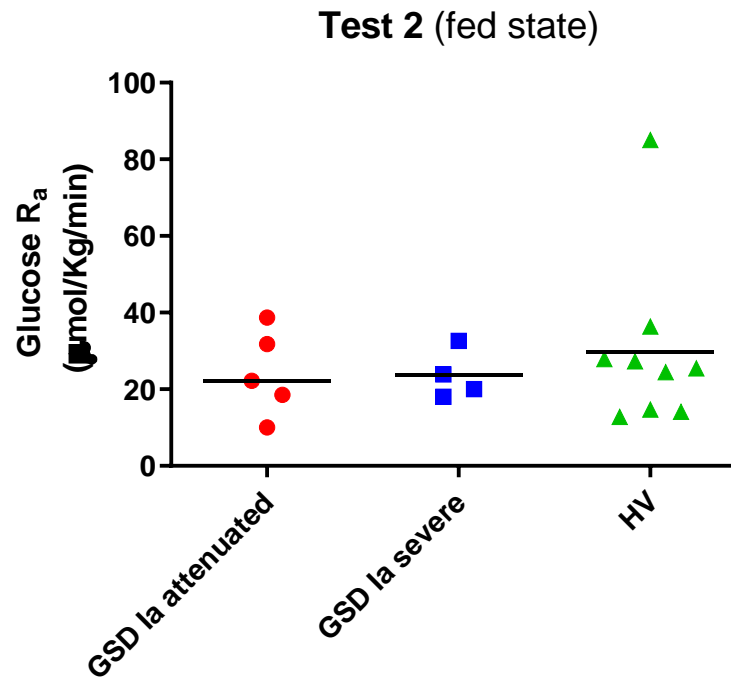
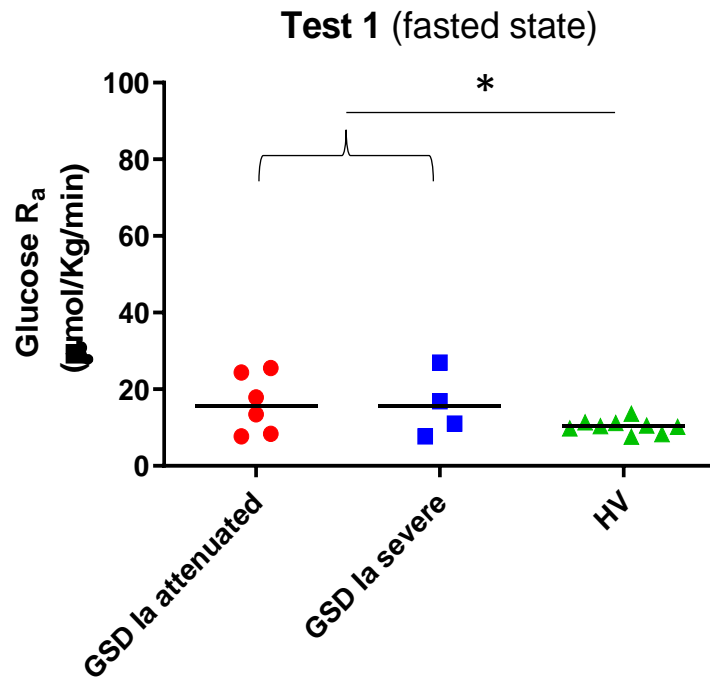
Glucose Rate of appearance ( $R_a$ ) after a single oral D-[6,6- $^2\text{H}_2$ ]glucose dose

## Secondary endpoint

CGM data analysis

Additional parameters: gender, weight, height, medication, genotype, dietary history

# Glucose $R_a$ is higher in GSD Ia patients than HV in the fasted state



\* $p < 0.05$

# Conclusions

- A single oral D-[6,6-<sup>2</sup>H<sub>2</sub>] glucose dose can estimate glucose R<sub>a</sub> in GSD Ia patients and HV
- Large variability was found in glucose R<sub>a</sub> among GSD Ia patients
- Dietary information is crucial to adequately interpret the estimated glucose R<sub>a</sub>
- Potentially, this method can help monitoring GSD Ia patients receiving novel treatments

## Next steps

- Dissect the proportion of single factors contributing to glucose R<sub>a</sub>
- Integration with CGM data