PO 040

# MONITORING 1,5-ANHYDROGLUCITOL IN A NEONATAL CASE OF GSD1B: THE ROLE OF VAMS TECHNOLOGY.

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## Background

In glycogen storage disease type 1b (GSD1b), neutropenia and neutrophil dysfunction are caused by the accumulation of 1,5-anhydroglucitol-6-phosphate (1,5-AG6P) in granulocytes. Recently, empagliflozin, a SGLT2 inhibitor, has been shown to reduce tubular reabsorption of its precursor, 1,5-anhydroglucitol (1,5-AG), and restore neutrophil counts and functions. Recently, DBS was proposed as a useful technology for monitoring the treatment. We have evaluated a new method for home monitoring 1,5-AG by using the volumetric absorptive microsampling (VAMS).

## Methods

VAMS (Mitra® from Neoteryx,10 ul of blood) were collected from 3 GSD1b patients (age 0.5 months-23 years old) treated by empagliflozin. One of them was diagnosed at 10 days of life. Treatment with empagliflozin was started, and 1,5 AG was monitored using VAMS. The 1,5-AG was extracted from the matrix with methanolic solution (90%) containing internal standard 13C6-1,5 AG (IS). The quantification of 1,5-AG was performed by LC-MSMS analysis using a Acquity I-class coupled with a Xevo TQS micro operated in negative ESI mode. Multiple reaction monitoring (MRM) analysis was applied to detect ion transitions at m/z 162.7 > 100.8 and 168.7 > 104.8 for 1,5-AG and IS, respectively. Plasma and VAMS samples were taken in parallel from all patients.

**Fig 1. VAMS Sampler.**

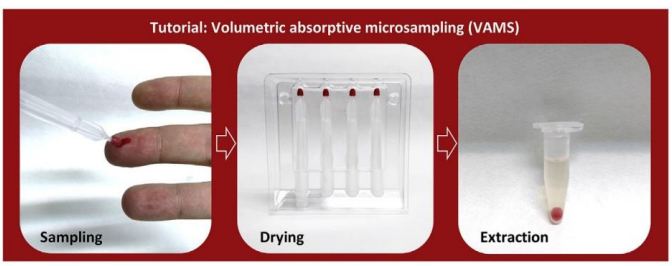


**Fig 2. Capillary blood VAMS sampling: 1- sampled by touching the blood surface with the device; 2-multiple VAMS blood samples enclosed in the clamshell; 3-sampled VAMS tip detached from the handle, in a microtube containing extraction solvent.**

## Results

1,5-AG and IS retention time are at 3.83 min. Linearity for VAMS was R2=0.997, with 8 points (4 -800 µmol/L). Intraday and interday precision showed a CV of 6.7% and 7.8% respectively. LOQ was 4 µmol/L. In patients' samples, the correlation between plasma and VAMS was linear ($R^2$=0.9994). In neonatal patient, VAMS 1,5AG decreased from 40 µM to 11 µM on day 6 and to 5.29 at the last follow up. In figure 6 results from the 3 patients.

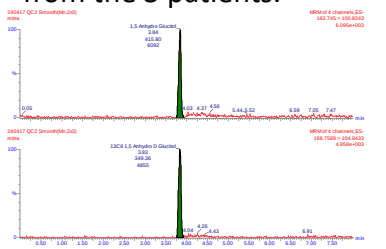

**Fig 3: Extracted ion chromatograms of 1,5-AG and 1,5-AG-U[13C6] internal standard in VAMS.**

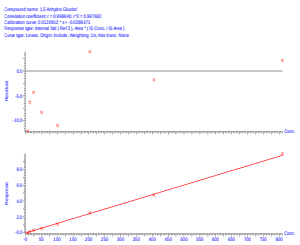

**Fig 4: Linearity of 1,5-AG.**

| | DBS | MITRA reparto |
|---|---|---|
| Goodness of Fit | | |
| $r^2$ | 0.9982 | 0.9994 |

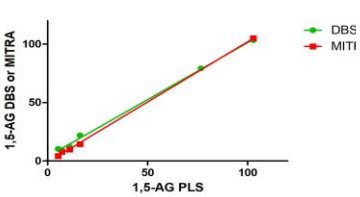


**Fig 5: Correlation between plasma and VAMS (MITRA). The correlation with DBS has also been evaluated**

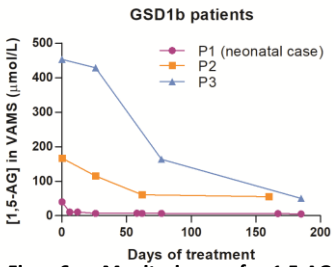


**Fig 6: Monitoring of 1,5-AG concentration in VAMS following empaglifozin treatment in 3 patients.**

## Conclusions

Our study showed that VAMS technology is suitable for detecting 1,5-AG in patients with GSD1b.
Because VAMS microsampling needs small amounts of blood allows home monitoring patients at any age. It is important because of the individual variability of response to the treatment and the need to adjust the dose during treatment, especially in pediatric populations.

**The authors declare that they have no conflict of interest.**

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