Anti-Drug-Antibodies (ADAs)

Antibody status has been determined by using Replagal-Antibody-ELISA at the university hospital of Mainz. No formation of ADAs was observed.

Conclusions

DUE TO THE DEFINED AND RELIABLE PRODUCTION OF MOSS-AGAL, THE PRE-CLINICAL AND CLINICAL DATA, WE EXPECT:

- The fast uptake of *moss-aGal* via the mannose receptor into the organ tissue might translate into an improved therapy of kidney symptoms in Fabry patients compared to the drugs on the market.
- *Moss-aGal* will show good and continuous efficacy due to consistent production.
- *Moss-aGal* might be better tolerable with less side effects in Fabry patients due to fast cellular uptake, short exposure to immune system, and batch-to-batch consistency.

REFERENCES

Hennermann JB, Arash-Kaps L, Fekete G, Schaaf A, Busch A, Frischmuth T (2018): Pharmacokinetics, pharmacodynamics, and safety of moss agalactosidase A in patients with Fabry disease. *Mol Genet Metab 123: 61–62*

Shen JS, et al (2016): Mannose receptor-mediated delivery of moss-made α-galactosidase A efficiently corrects enzyme deficiency in Fabry mice. *J Inherit Metab Dis 39: 293–303*

CONTACT
Karin Heidenreich
Director Medical Alliance
Phone + 49 761 470 99 0
bd@greenovation.com
www.greenovation.com

Phase I Clinical Trial **Results**

Pharmacokinetics, Pharmacodynamics, and Safety of *moss-aGal* in Patients with Fabry Disease

m
aGal

Moss-aGal proven effective and safe in phase I clinical trial

The first biopharmaceutical ever produced in moss, Greenovation's *moss-aGal,* was successfully tested in a phase I clinical trial (11/2017). Six female patients suffering from a rare genetic lysosomal storage disorder, Fabry disease, tolerated the treatment very well.

Fabry disease is characterized by deficient activity of alpha-galactosidase that *moss-aGal* aims to replace. A single injection of *moss-aGal* led to significant decrease of Gb3 levels in urine 14 and 28 days post administration, that indicates an efficient targeting of *moss-aGal* to the kidneys of the patients – one of the most affected organs.

Moss-aGal is a recombinant form of human alpha-galactosidase produced in moss *(physcomitrella patens)* using Greenovation's BryoTechnology. Expression in moss creates a protein that is identical to the human protein with customized glycosylation pattern. The production is free of human pathogens and animal compounds.

The plans for a clinical trial II/III are already in progress.

Study setup and population

One dose group with 6 patients: 0.2 mg/kg i. v.; single dose; clinical schedule of 28 days.

PRIMARY ENDPOINTS

- Safety
- Pharmacokinetics

SECONDARY ENDPOINTS

- Efficacy (Gb3/lyso-Gb3 levels in plasma and urine)

ENROLLED PATIENTS

- All females
- Age 38–59 years (mean 50 years)
- All completed

Study closed, last patient out 11/2017

The study was conducted in study centers in Germany and Hungary.

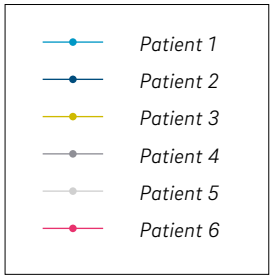
Safety: Moss-aGal is safe and was well tolerated

- No SAEs (serious adverse events)
- 5 AEs (adverse events) in 4 patients
- 1 drug related AE (dysgeusia, reversible)
- No formation of anti-drug antibodies

Pharmacokinetics

Measurement of pharmacokinetics was performed by using validated enzymatic assays (Fig. 1).

Figures 1–3:



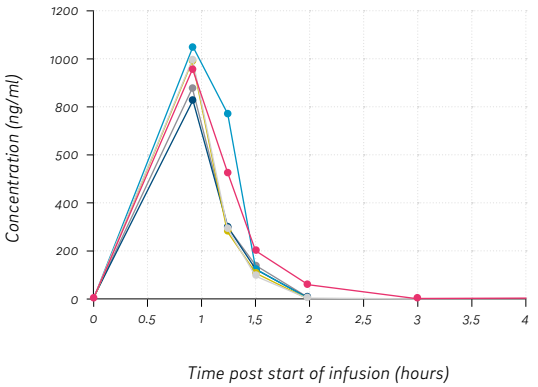


Fig. 1: Serum concentrations of moss-aGal

Gb3 concentrations in plasma and urine

SIGNIFICANT DECREASE OF GB3 CONCENTRATIONS IN URINE WERE MEASURED IN ALL PATIENTS AFTER ONLY ONE DOSE.

Measurements of Gb3 by MS-analysis at screening, baseline, 24 h postdose (plasma only), and day 7, 14, 28 postdose. Gb3-C24-0 isoform was used for quantification (Fig. 2 & 3).

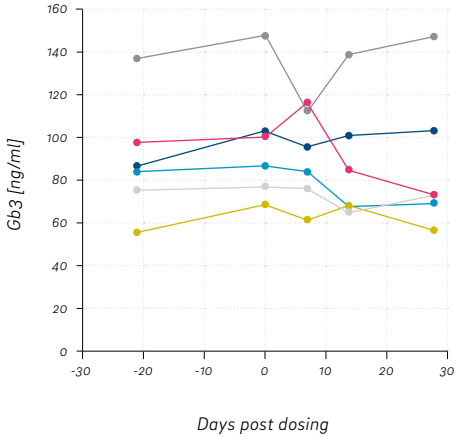


Fig. 2: Gb3 concentrations in plasma

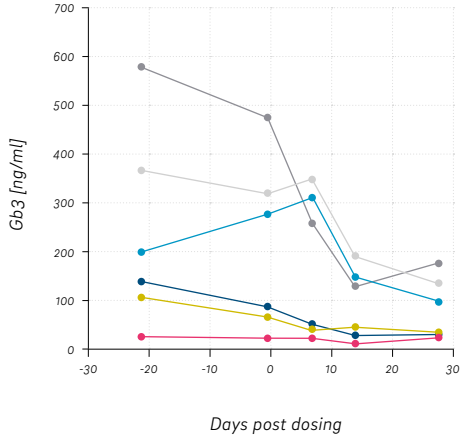


Fig. 3: Gb3 concentrations in urine