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


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

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

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

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).