Case study

SIMBEC-ORION

How a FiH trial in healthy volunteers successfully moved into a clinical development trial including patients with rare disease under one single protocol in a matter of months.

Primary Hyperoxaluria

Placebo Controlled Single Blind Single Centre Phase I and Normal, Healthy Volunteers and Open Label Multicentre Study in Patients with Primary Hyperoxaluria to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single Ascending Doses of IMP Solution for Injection.

Background

Primary Hyperoxaluria (PH) is an ultra-rare autosomal recessive disease characterised by excessive production of oxalate in the liver. Oxalate is a highly insoluble metabolic end-product that is eliminated mainly by the kidney. Patients with PH are predisposed to the development of multiple and recurrent urinary tract (urolithiasis) and kidney (nephrolithiasis) stones. At present, no therapies are approved by regulatory authorities for the treatment of patients with PH. Incidence of PH is around 0.05 in 10,000 in the European Union.

A North American biotech sponsor required a Phase I study in Healthy Volunteers and primary hyperoxaluria patients for their novel IMP which was an Antisense RNAi Oligonucleotide being developed as a treatment for PH.

Objectives

- To characterise the pharmacokinetics (PK) of single doses of the lead molecule in Healthy Volunteers (HV) and patients with PH.
- To evaluate the pharmacodynamic (PD) effects of single doses of the lead molecule in HV and patients with PH on biochemical markers including, but not limited to, changes in plasma oxalate and glycolate, and urine oxalate, and glycolate concentrations.

Early determination of proof of concept and an understanding of PK in a more heterogeneous patient population.

Dedicated lab Project Manager (PM) to co-ordinate safety, PK and PD samples coming from five different referral labs.

Single protocol but two parallel submissions to ethics committee (HV and patients).

Principle Investigator for HV study was also national co-ordinating investigator for both parts of study and attended Scientific Review Committee meetings for part B patient studies.

Two PMs worked collaboratively to find efficiencies and ensure knowledge transfer across both parts of the study.

information@simbecorion.com | www.simbecorion.com

Challenges

The relatively high concentration of drug solution meant it was challenging to accurately measure the correct (undiluted) volume at the lowest doses (0.3 mg/Kg), so dilution was necessary.

It was identified early on that the laboratory analysis could be a potential project risk due to complexity of the study and high demand on resource. This was addressed by having dedicated lab PM and practice runs for sample handling.

Solutions

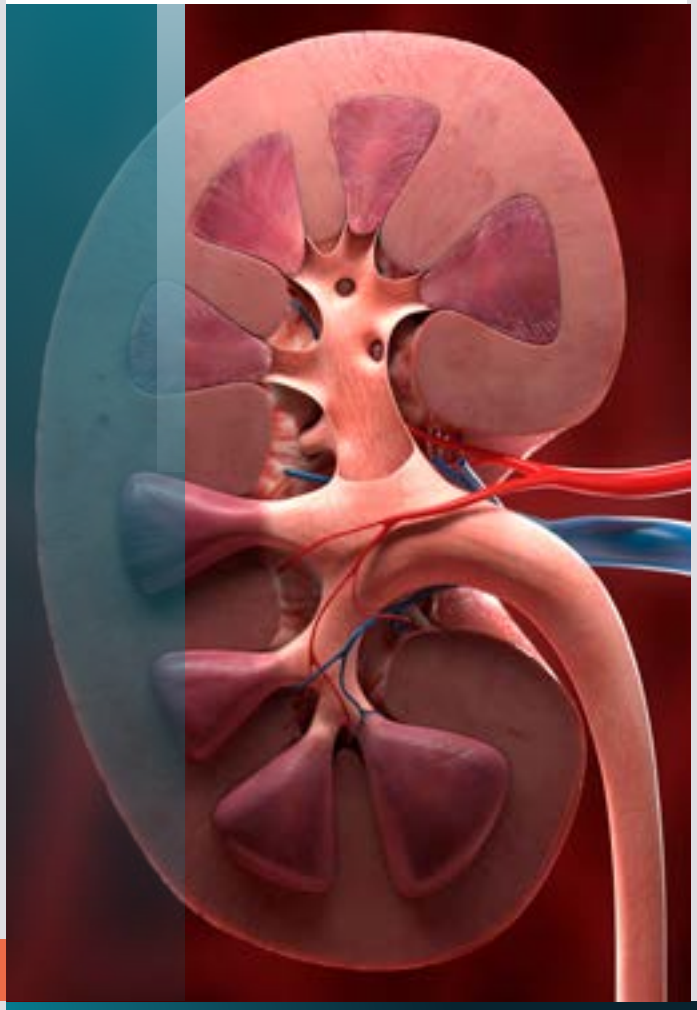
- Two subject groups allow for the generation of controlled safety data and a detailed PK analysis in healthy volunteers.
- Early determination of proof of concept and an understanding of PK in a more heterogeneous patient population, including paediatric patients.
- Dedicated lab PM to co-ordinate safety, PK and PD samples coming from five different referral labs and communicate practicalities to the sites.
- Single protocol but two parallel submissions to ethics committee allowed HV study to commence while HRA reviewed the patient study.
- PI for HV study was also national co-ordinating investigator for both parts of study.
- Two PMs worked collaboratively to find efficiencies and ensure knowledge transfer across both parts of the study.
- Regular governance meetings with the client further ensured clear communication.

Outcome

Simbec-Orion's proactive, risk-mitigating plan ensured that the learnings from the HV study were taken forward into the patient arm of the program.

A total of 41 patients were enrolled for this second phase, which was conducted at 6 sites, across 5 countries (UK, Europe & USA).

The asset is now in pre-registration having been acquired by a global pharmaceutical organisation.



SIMBEC-ORION

information@simbecorion.com | www.simbecorion.com