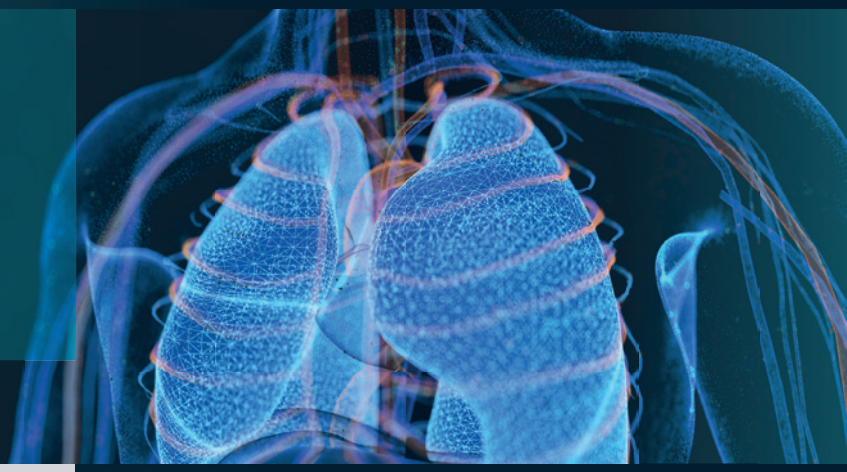
Case study

SIMBEC-ORION

Operational excellence drives healthy volunteer to patient cohort results in 24 months for rare respiratory disease.

Clinical pharmacology case study



A randomised, double blind, multi centre, placebo controlled dose escalation study in healthy subjects investigating the safety, tolerability and pharmacokinetic properties of the study drug, followed by an expansion cohort treating subjects with idiopathic pulmonary fibrosis (IPF).

Background

The biotech sponsor needed to demonstrate the safety and tolerability of the lead molecule in healthy volunteers, as well as direct target engagement and biomarker effects for IPF patients in a short space of time.

Objectives

- SAD study to evaluate the safety and tolerability in healthy male subjects
- To evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of the study drug when administered as a single dose to healthy male subjects
- To evaluate the safety and tolerability of multiple doses of the study drug in male and female patients of non childbearing potential with IPF
- To evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of the study drug when administered in multiple doses to male and female patients of non childbearing potential with IPF

Challenging patient population for Phase I clinical studies

Designed and conducted Umbrella study design– healthy volunteers to rare patient cohort

Site and patient identification ran in parallel to the healthy volunteer study ensuring rapid patient enrolment

Centralised set up and management of all cohorts ensured agile data management and resolution

Patient training to ensure consistent inhaler dosing

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Challenges

IPF is a unmet medical need with an incidence of around 13 to 20 per 100,000 people worldwide. The strict study inclusion and exclusion criteria meant that patient recruitment would be challenging.

Many IPF patients were not able to be enrolled, due to the severity of their condition. Patients not only had to meet study criteria but also had to produce a suitable FEV value to be considered for study inclusion.

Patients were admitted to the hospital sites on D1, D7 and D14, to be given the study drug for home dosing, prior to PK sampling at the hospital. Training on inhaler use to ensure optimal results was also critical to success.

Objectives

- Pre identification of additional sites for set up and study inclusion
- Site inclusion was dependent patient enrolment at other sites
- Site identification and identification of IPF patients ran in parallel to the healthy volunteer study to facilitate rapid patient enrolment
- Challenging patient recruitment was centralised by a Simbec-Orion project manager – crucial to motivate sites and communication
- The PM was located on site with data management, this enables flexibility and rapid decision communication
- This enabled tasks to be split, operated in parallel and reviewed continuously to avoid delay. In turn, the monitor worked with site staff to pre-empt potential discrepancies and have them resolved immediately, rather than waiting for specific timepoints
- Teamwork mitigated the risk of slow recruitment and Simbec-Orion was able to speed up the delivery of data management activities to compensate time
- The efficient, centralised set-up of the Simbec-Orion project and management teams stripped out much of the delay associated with the increased, complexity,and disparate geography of teams, hierarchies, and processes at larger CROs
- Training was conducted by the CRA on the use of the inhaler for patient dosing which ensured consistent dosing and use of the inhaler between both healthy volunteer and patient study populations

Outcomes

Simbec-Orion was able to identify the risk of slow recruitment early and then work to mitigate these risks, resulting in delivery of the final CSR ahead of time.

The sponsor has been able to report positive results on the safety and tolerability in IPF patients.

The sponsor is now in a position to source investment to develop the compound further, or to licence the compound.

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