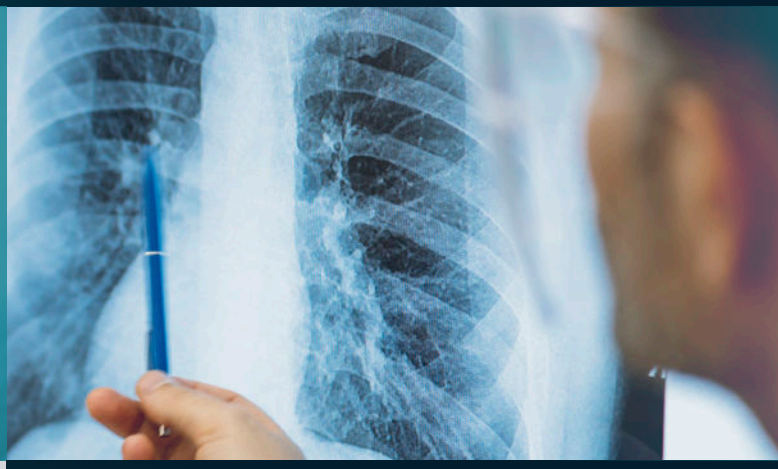
Case study

SIMBEC-ORION

Adaptive trial design, transparent communication and single team approach drive transition from Healthy Volunteers to patient studies for novel small molecule therapy.

Adaptive trial design



A SAD/MAD, Double-Blind, Placebo-Controlled, First-In-Human, Phase 1 Study to Evaluate the Safety, Tolerability and Pharmacokinetcs of an NCE asset followed by an Open-label, multi-cohort Part to Assess the Drug-drug Interaction With Rosuvastatin and Metformin in Healthy Males.

Background

A small biotech client had developed an asset that was a potential treatment for Idiopathic Pulmonary Fibrosis (IPF). Simbec-Orion was able to provide regulatory advice and support for submission to the MHRA, EMA and FDA, along with a study program that accelerated the delivery of their studies, saved cost and facilitated the transition from Healthy Volunteers (HV) to Phase II trials.

Objectives

- To leverage an adaptive SAD/MAD trial design that would both streamline the delivery of the overall programme and maximise data available through the addition of further cohorts to investigate the DDI and Food Effect.
- To use lessons learned in the early phase trials to design the Phase II study.

Adaptive, multi-part study design – allowing changes to be made to the study design in response to emerging data and rapid study delivery

Site and patient identification ran in parallel to the Healthy Volunteer study ensuring accelerated patient enrolment

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

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Challenges

- Idiopathic Pulmonary Fibrosis affects just 200,000 – 300,000 patients globally
- Strict inclusion and exclusion criteria
- Complex samples/sample management
- Multiple vendors for speciality endpoint criteria
- Post-COVID challenges still being experienced at sites
- Multiple changes in scope for Phase II
- To identify and set up a large number of sites who had the capacity and capability to participate in the study

Solutions

- Set up and identification of IPF patients whilst the HV study was in progress.
- Close collaboration between Simbec-Orion PM and study team leads to quickly address challenges– same team leads for the HV and patient studies.
- Use of Simbec-Orion labotatories for sample management and coordination of shipments.
- Widespread feasibility across multiple countries / Using historic data from specialist respiratory vendor to ensure we were targeting the most capable site / Early and regular communication with sites to keep them engaged.

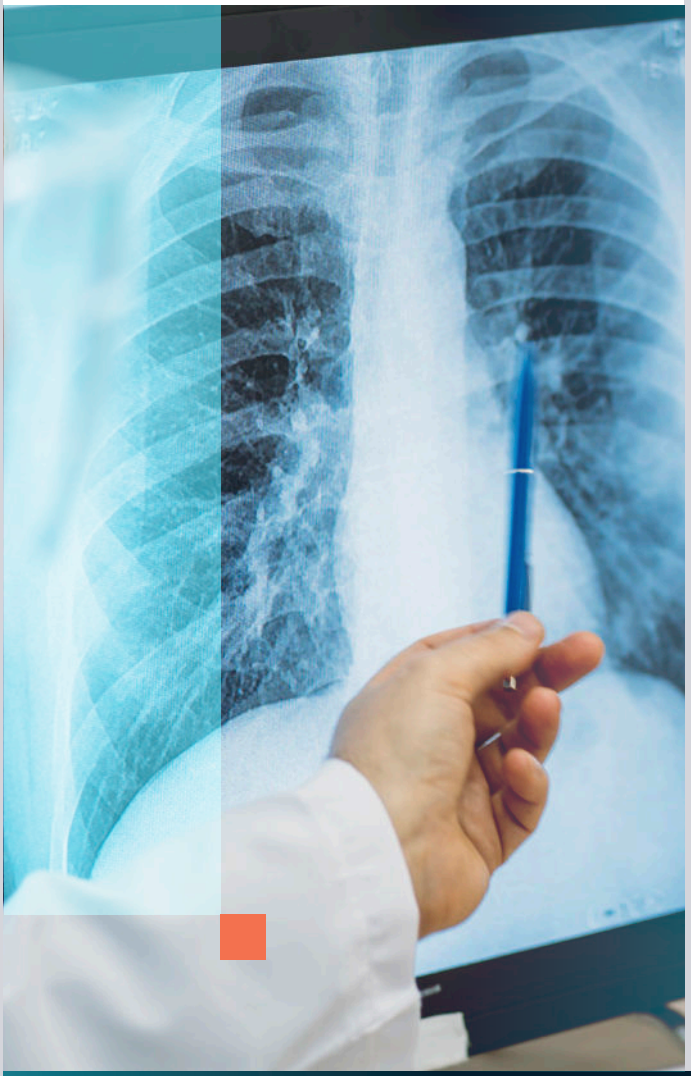
Key learnings

Two SAD cohorts and two MAD cohorts were dosed twice per day rather than once daily as initially planned. We were then able to adapt the safety and pharmacokinetic assessments align with the new dosing schedule without the need for a substantial amendment, saving time and budget for the sponsor.

The emerging blinded data from the SAD/MAD studies was used to inform the starting dose, threshold and frequency for the Phase II study while the Healthy Volunteer study was ongoing.

Outcomes

The multiple adaptive trial design elements allowed sufficient flexibility to be incorporated based on emerging safety and pharmacokinetic data without the need for a substantial amendment.



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