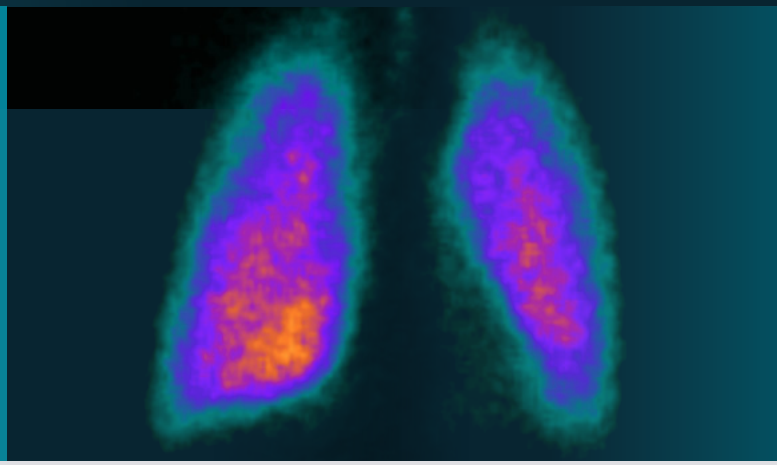
Case study

SIMBEC-ORION

Gamma scintigraphy demonstrates effective lung deposition of a novel triple combination pressurised metered dose inhaler (pMDI) in COPD patient population.



A Phase I, Single-Dose, Gamma Scintigraphy Study to Assess the Pulmonary Deposition of Technetium-99m Radiolabelled Budesonide, Glycopyrronium and Formoterol Fumarate MDI Following a Maximal Breath-Hold of up to 10 seconds in Patients with Moderate to Severe/Very Severe Chronic Obstructive Pulmonary Disease (COPD).

Background

A large pharmaceutical Sponsor needed to demonstrate that its novel triple combination pMDI formulation could effectively deliver drugs to the lungs of patients with moderate and severe/very severe COPD as defined by the European Respiratory Society.

Objectives

- To assess the pulmonary deposition of radiolabelled BGF MDI in patients with moderate to severe/very severe Chronic Obstructive Pulmonary Disease (COPD) following a maximal breath-hold of up to 10 seconds (s).
- To assess the regional airway deposition patterns of radiolabelled BGF MDI in the lungs in patients with moderate to severe/very severe COPD following a maximal breath-hold of up to 10 s.
- To assess the deposited dose of radiolabelled BGF MDI in the oropharyngeal and stomach regions in patients with moderate to severe/very severe COPD following a maximal breath-hold of up to 10 s.
- To assess the deposited dose of radiolabelled BGF MDI detected on the actuator and exhalation filter in patients with moderate to severe/very severe COPD following a maximal breath-hold of up to 10 s.

Recruitment of patients in compliance with inclusion / exclusion criteria.

Validation of a robust radiolabelling method for the pMDI ensuring that product characteristics e.g. aerosol properties were maintained and that the radiolabel was an accurate surrogate for the drugs.

Ensure accurate and reproducible radiolabelling of the pMDI product on multiple dosing days

Co-ordinating personnel from core functions e.g. Cardiff Scintigraphics, Investigational Medicinal Product Management, Quality Assurance Pharmacist, QP, Medical, Quality Assurance, to achieve radiolabelled product release, dose administration and imaging on each dosing day.

information@simbecorion.com | www.simbecorion.com

Challenges

- Timely recruitment of target patient population.
- Developing a robust radiolabelling method and appropriate release testing to ensure high quality and reproducible radiolabelling. All processes had to be conducted on the dosing day due to the short half-life of Techentium-99m radiolabel i.e. approx. 6h. All batches had to comply with release specifications.

Solutions

It was realised that multiple sources of identifying potential patients would be necessary.

- Moderate cohort participants were identified through the Simbec-Orion volunteer database and by partnering with a data mining technology service.
- For the severe/very severe cohort, engagement with secondary care respiratory specialists was required, as patients who met the criteria for this cohort would likely be treated in a hospital setting.
- Early engagement with a Key Opinion Leader enabled identification of respiratory clinics and potential PIs in the region.
- After full feasibility, two NHS sites were selected to recruit and screen patients for the study.
- A flexible approach to participation was required, as dosing could only be performed in the gamma scintigraphy suite of the Simbec-Orion Clinical Pharmacology Unit, to ensure images were captured immediately after dosing.
- Effective and robust radiolabelling method was developed and validated.
- Detailed batch records ensured reproducible product manufacture.
- Release test procedures were optimised to facilitate rapid analysis and data reporting.

Outcomes

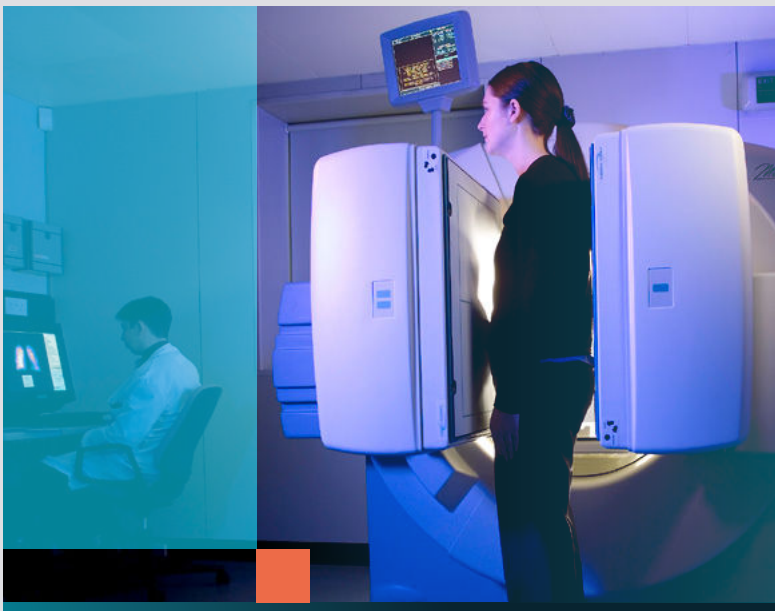
Effective patient recruitment strategy meant the study was conducted within appropriate timelines.

Achieved 100% successful batch production under extremely exacting time restrictions and all patients successfully dosed.

Sponsor provided with scintigraphic images that allowed greater understanding of product performance in a key patient group.

Key learnings

- Effective planning and communication between core business functions ensured complex batch manufacturing was routinely performed and patients were successfully dosed achieving the Sponsor's timelines.



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