Case Study

Respiratory Programme
Rapid Start-Up & Complex Vendor Management

Description

A respiratory programme consisting of three studies (phase II, multicentre, randomised, double-blind, placebo and active controlled dose-ranging 6-arm parallel group) to identify the optimal dose of the trial drug with respect to lung function and other clinical efficacy and safety outcomes in adult subjects with either asthma or COPD.

Study 1: A 14 week study evaluating safety and efficacy of four doses of Investigational Product (IP) compared to placebo in asthmatic subjects.

Study 2: An eight week study evaluating safety and efficacy of three doses of alternate IP compared to placebo in asthmatic subjects.

Study 3: A six week study evaluating safety and efficacy of four doses of IP compared to placebo in COPD subjects.

Primary Endpoints: Study 1: To evaluate the efficacy of the IP's pMDI by comparison with placebo in terms of acute bronchodilator effect (change from baseline in FEV_1 AUC_0-12h normalized by time at Day 14).

Study 2: To evaluate the efficacy of the IP's pMDI by comparison with placebo in terms of change from base line in pre-dose morning FEV_1 at week eight.

Study 3: To evaluate the efficacy of the IP's pMDI by comparison with placebo in terms of change from base line in FEV_1 AUC_0-12h normalized by time at week six.

Services: Full service (including vendor management - central lab, ECG, centralised spirometry, clinical trial supply management, equipment distribution – AM3, Holter Monitor).

Study Phase: II

Indication: Study 1: Patients > 18 < 75 years old with asthma

Study 2: Patients > 18 < 75 years old with asthma

Study 3: Patients > 40 years old with COPD

Clinical Sites
Total sites = 268 across all studies (10, 144 and 114 respectively) but a total of 216 unique sites as several sites participated in two of the three studies (19% overlap)

Patients
Study 1: 154 Screened, 67 randomised
Study 2: 1940 Screened, 615 randomised
Study 3: 1855 Screened, 735 randomised

Regions
United States

Introduction

These studies were managed by CROMSOURCE on behalf of a mid-sized European pharmaceutical company with a strong US presence. The trials involved rapid site selection and qualification in order to achieve the client's goals for the first patients enrolled. CROMSOURCE conducted a feasibility on 500 sites and qualified 216 unique sites that were utilised for the study.

Primary endpoints were changed in spirometry at specific timepoints in each study. The spirometry equipment and results were managed by a third party vendor but training and adherence to proper technique was managed by CROMSOURCE.

Study drug management (packaging, labelling, storage, distribution and central randomisation) was supported by specialised vendors as shipments contained subject training kits as well as the investigational product and strict adherence to temperature management was required.

The Challenges

The first challenge was to achieve first patient enrolled within four months of contract signature with the client.

The second challenge was managing multiple vendors that provided very different services across all the three studies of the programme and ensuring that results were reported appropriately and timely.

Operational Plan

Rapid Start Up

CROMSOURCE created a feasibility survey that would collect relevant information for all three studies in order to determine the best suited sites as well as sites that could possibly participate in two of the three studies. A full Feasibility Plus™ analysis was conducted on a rolling basis as the data was submitted and follow up questions were posed of sites via teleconference to ensure the best sites were visited for Pre-Study Qualification visits.

A face to face training was scheduled with the US CRAs and the operational leaders prior to the conduct of any study visits. Training included protocol overview, study drug management, monitoring manual, communication and training from third party vendors on each of the required assessments that utilised vendor equipment.

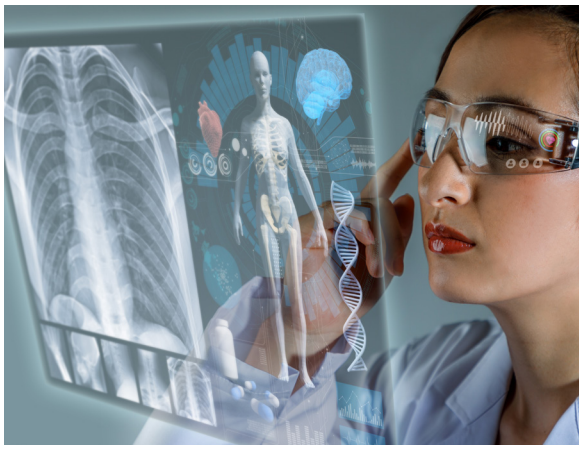
Pre-Study Visits (PSVs) were scheduled as data was received and greater than 200 PSVs were conducted in the first month following the study contract execution in order to determine eligible sites and how many studies to engage each site on. CROMSOURCE combined visits (for those sites participating in two studies) and looped visits to ensure the most efficient and cost effective plan.

CROMSOURCE conducted 68 SIVs within a month in order to achieve first subject enrolled within the client's required timelines. In total, 327 PSVs and 270 SIVs were conducted across all three studies.

Complex Vendor Management

Multiple vendors were utilised for these studies in order to ensure consistency and protocol adherence throughout the study. As all three studies had primary endpoints related to spirometry, a specialised vendor was utilised to provide equipment to the sites along with training manuals. Sites were responsible for the calibration of their equipment on a routine basis and this was closely monitored by CROMSOURCE as uncalibrated devices could provide false results.

Enrolment criteria for each study was based on a required spirometry range for a minimum of three attempts for each subject but up to eight attempts. Results received through the vendor were also reviewed and validated by CROMSOURCE's trained medical staff to ensure the eligibility criteria was met. This verification required careful coordination and oversight of screening visits and test result reporting in order to provide each site permission to enrol subjects that qualified for the study.



Additionally, a randomisation vendor, drug supply vendor, central ECG readers, Holter monitor vendor and lab vendor were essential to the conduct of this study. CROMSOURCE assigned a dedicated vendor manager and team to set up the vendors specifications and coordinate required supplies and re-supplies to each site as the equipment required site specific programing and was very costly.

Result

Rapid Start Up

Due to the rapid planning and subsequent development of a detailed feasibility questionnaire, CROMSOURCE was able to contact over 500 potential sites quickly utilising our investigator database and other resources through our FERMI system which enabled us to have nearly paperless contact with sites while ensuring confidentiality. Rapid feedback from sites coupled with immediate action in scheduling 327 PSVs allowed CROMSOURCE to identify the best sites suited for participation in all three studies.

The end result was that CROMSOURCE was able to achieve the goal of First Patient In (FPI) for all three studies within the client's timelines despite the delays by the client during contracting process.

Complex Vendor Management

With careful coordination, continual communication and oversight, CROMSOURCE successfully collaborated with each vendor to ensure a smooth process from project specifications to study drug shipment/re-supply to collection of primary endpoints and safety parameters. There were no instances where delays in subject randomisation or subsequent visits were affected due to vendors and as such the study was conducted in accordance to the protocol with a high level of compliance from all vendors involved. Further, there were cost savings recognised with equipment and supplies due to the close management of distribution to the sites by the vendors in collaboration with CROMSOURCE.

With immediate action by CROMSOURCE and close collaboration with vendors, we achieved highly successful recruitment and enrolment and study conduct for all three studies.

RESPIRATORY EXPERTISE

For over 25 years, CROMSOURCE has conducted trials focused on respiratory disease. We are able to advise clients on the design and implementation of the entire respiratory development plan.

CROMSOURCE's respiratory experience includes hundreds of studies in thousands of patients, both in adult and paediatric populations, Phase I through Registry, in a wide range of indications including, but not limited to, asthma, COPD, cystic fibrosis, lower respiratory tract infections, lung cancer, smoking cessation, upper respiratory tract infections, rhino sinusitis, and chronic bronchitis.

About CROMSOURCE

CROMSOURCE is an ISO-certified international provider of outsourced services to the pharmaceutical, biotechnology and medical device industries, specialising in clinical development and staffing solutions. CROMSOURCE was founded in 1997, over 25 years ago. Its successful growth has been built on stability, integrity, and high levels of customer satisfaction, all of which contribute to a high rate of repeat and referral business. We have grown steadily, but responsibly, to become an organisation of over 350 organised and well-trained experts.

CROMSOURCE Quality
ISO 9001:2015 multi-site certified quality management system
ISO 14155:2020 conformity confirmed

European Headquarters
Via Giorgio De Sandre, 3
37135 Verona - Italy
Direct: +39 045 8222811

North American Headquarters
8000 Regency Parkway, Suite 575
Cary, NC 27518 – USA
Direct: +1 919 626 9882

www.cromsource.com