Case Study:
Handok Inc. & OCT Clinical

How to Recruit 236 Patients for a Ph3 Osteoarthritis Study Despite Hurdles Caused by the Pandemic

OCT Clinical, a leading Eastern European contract research organization, successfully completed the recruitment of 236 subjects in a Phase III osteoarthritis study for the Korean pharmaceutical manufacturer, Handok Inc., despite hurdles caused by the COVID-19 pandemic.

Study details

An open, comparative, randomized clinical trial with the goal to study the efficacy and safety of an adhesive plaster for knee osteoarthritis. Handok Inc.'s treatment was tested with the application schedule of every 12 hours against a comparator plaster applied every 24 hours. Within the project, OCT Clinical was responsible for medical writing, regulatory support, project management, medical monitoring, data management, biostatistics, logistics and pharmacovigilance.

HANDOK is a leading innovation-driven pharmaceutical/healthcare company in Korea, develops, manufactures and distributes healthcare solutions to improve the health and quality of human life.

Challenges & Solutions

The project was conducted during the first COVID-19 outbreak. This development had a significant influence on the initially planned study timelines which, obviously, did not consider such contingencies. **Site closures, all-around lockdowns, travel limitations**, and site personnel or trial participants becoming infected with COVID-19 posed a serious threat to **start-up timelines, recruitment rates and data cleaning processes**. As a result, the OCT Clinical team faced multiple challenges affecting every part of the study and had to come up with a swift and effective set of actions to ensure continuity of the trial.

Risk-management approach

The OCT strategy has always involved a **risk-management approach**. For example, when it comes to site selection, the number of sites submitted and selected should exceed the number of sites to be initiated by 10-15%. Such an approach fully justified itself during this study. For this trial, 9 active sites had initially been planned to open for patient recruitment. However, as a risk-mitigation measure, 3 additional back-up sites were initiated, making it 12 sites in total. When the pandemic hit, it turned out that several sites were closed because they were only treating COVID-19-infected patients, and this is when the added back-up sites saved the situation. As a result of this strategy, due to a risk-based approach, the CRO managed to initiate 8 sites – almost as many as initially planned.

Optimal research site mix

It is also important to find the **optimal proportion of state medical institutions and private clinics** within the overall site mix. In this study specifically it proved a sound strategy since private clinics remained almost unaffected by COVID-19 restrictions.

2

Remote Monitoring

In the course of the study, there was a one-month delay in site initiation. During this period, OCT Clinical's team analyzed the situation, **assessed new potential risks**, and waited for travel restrictions and hospital visiting restrictions to be lifted. First, the reasonsfor cancelled on-site monitoring visits were documented and made available for review by the sponsor and during inspections. Next, as soon as it became obvious that the situation would not be resolved in the near future, the CRO developed **a new Monitoring Plan** enabling **remote initiation and monitoring** through video and audio calls. Having this diverse approach from the start allowed OCT Clinical team to meet all timelines.

3

On-site re-verification

The necessity to reverify on-site visits were stipulated in the Monitoring Plan. All sites planned for opening had the possibility to conduct patient visits on-site, although not all the sites accepted CRAs for initiation and monitoring. The overall delay in the beginning of actual recruitment period was 2 months. However, due to **effective site management**, t was possible to catch up with the initial plan and finish the enrolment of 236 subjects by the end of July 2020, in other words, managing to stay within initially stipulated timelines.

As mentioned above, despite regular remote SDV and database reviews according to Monitoring Plan ICFs, critical study data, IMP accountability and study logs needed on-site re-verification. As a result, the CRAs had **very tight schedules for on-site visits** to complete this task as soon as travel restrictions were lifted. Three CRAs were assigned to meet the initial deadline for DBL. **The monitoring schedule was adjusted** accordingly, and **additional days on-site were added** to avoid lost time for frequent travel. The database was cleaned and put on hold, while the IMP was reconciled according to the initial plan.

4

> “Managing clinical trials is a multifaceted job even under ‘normal’ conditions. Obviously, a pandemic situation adds some extra work and complexity. Many procedures have been subjected to rigorous testing both by OCT Clinical team and sites. A thorough analysis of the situation and the introduction of necessary adjustments required considerable effort from all parties involved in runninga clinical trial. However, with a risk-based approach, proactive measures, and focusing on critical safety, it is feasible to keep the situation under control and to maintain engagement, participation and data integrity in clinical research. Our team was delighted to be able to give a great performance for Handok Inc.,”
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> **Irina Petrova, Director of Clinical Operations.**

> “We are very pleased with the OCT Clinical team for meeting our recruitment goal under such difficult conditions,” said **BokJin Hyun, Head of Clinical Research, Handok Inc.** “The achievement is quite impressive, considering the challenging circumstances imposed by the global pandemic.”

Major drivers for success

1. Implementation of and adherence to effective risk-management strategy before start of the study

2. Flexibility and quick adjustment to the current conditions (amendment of monitoring strategy)

3. Effective site-management allowing rapid enrolment despite the pandemic

4. Sound team management, which enabled quick and effective resolution of back-logs with on-site data verification

Outcomes

The disruptive effect of the COVID-19 pandemic has shifted how clinical trials are conducted, pushing towards digitalization and alternative methods. Nevertheless, the OCT Clinical CRO successfully achieved the enrollment of 236 subjects in a osteoarthritis study at 8 sites in just 4 months. The database lock was completed within a month after LPLV, considering that on-site visits to the majority of the sites became possible only 1 or 2 months (depending on the site) before LPLV. The OCT Clinical team also managed to wisely deal with budget matters, for instance, allocating unused travel budgets to cover additional monitoring and remote monitoring hours, and those put in by data managers for query resolution. Apart from the immediate contribution to the overall research, the study has extended the knowledge of the efficacy and safety of an adhesive plaster for knee osteoarthritis.