ALMAC

Partnering to Advance Human Health

Case study

Expert project management and an effective comparator sourcing strategy streamlines sponsor's complex global trial

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The evolution of drug development has produced a record number of drug approvals in 2018, with 59 novel treatments reaching patients in the United States alone.

The focus on developing new treatments, expediting study timelines, managing regulatory requirements and optimising trial costs has prompted a surge in globalised clinical trials. This trend that has the potential to deliver significant benefits to patients, sponsors and society yet requires significant expertise to successfully mitigate the inherent operational risks global studies entail.

One sponsor required both operational expertise and robust project management capabilities to help them manage a global study involving sensitised IMP (Investigational Medicinal Product) and difficult-to-procure comparator products. However, several factors threatened the sponsor's overarching objective of leading the fight against one of the most significant threats to humanity – antibiotic resistance.

The challenges

Complexity and inflexible timeline increases pressure and risk

In the face of increasing antibiotic resistance, which is projected to kill more people than cancer and diabetes combined by 2050[ii], this biotechnology company was determined to successfully develop new antibiotics that overcome the challenges of drug resistant bacteria.

The sponsor needed to operate a randomized, double blind, double dummy, multi-center, prospective study to assess the safety and efficacy of the sponsor's IP against the current market-leading drug. This trial would involve approximately 400 patients across 75 centers worldwide. The trial was anticipated to last 24 months, with ridged deadlines in place due to overarching commercial goals.

The sponsor needed to create a streamlined, efficient and effective clinical supply chain, incorporating clinical labelling of highly sensitised IMP, storage, global distribution, QP Release Certification, comparator sourcing and return and destruction handling strategy for expired or unused product.

The complexity of the trial threatened the sponsor's ability to meet its objective and deliver a much-needed drug to market.

Some of the sponsors most critical complexities were broken down into a number of core areas including communication, timeframes, comparator sourcing, sensitised drug product and intricate kit design.

Where timeframes were concerned, the sponsor had set the first patient dosing date prior to the trial being scoped. This date was unable to be pushed back, due to stringent corporate goals the sponsor had committed to.

Comparator sourcing was also proving difficult, due to a global shortage with the comparator required for the trial. Procuring small quantities from multiple sources was possible but because these were received sporadically throughout the duration of the trial, there were additional, scheduling, labelling and QP activities required that, if not appropriately coordinated, could cause significant disruption and delays

Another challenge threatening the success of the trial was the sensitised nature of one of the comparator antibiotic products, which required labelling in a dedicated building, thus adding to the scheduling complexities

A complicated kit design added even more challenges. Not only were there multiple components within each kit that needed to be labeled, the stability data for the IMP needed to remain under frozen temperature conditions throughout the labelling process. This meant utilising dry ice during labelling to maintain the necessary conditions. Due to the double dummy trial design, the kits needed to be successfully blinded at site by an unblinded pharmacist and this required sourcing and shipping blinded materials to be utilised at clinical site.

Finally to accommodate the aggressive timelines and due to sourcing restrictions with the comparators, labelling and secondary packaging activity would need to take place in both the US and EU.

The Almac solution

Complete clinical supply management

The sponsor understood how critical it was to meticulously manage clinical supply for the study. The risk of not doing so could see the study fail to meet vital timelines, which would lead to negative patient impact, wasted product and the additional cost associated with reworking materials. Without appropriate intervention and expertise, the sponsor's goal of successfully developing new antibiotics that overcome the challenges of drug resistant bacteria would be compromised.

To avoid this fate, the sponsor turned to Almac Clinical Services to devise a holistic strategy including:

- labelling,
- comparator sourcing,
- storage & distribution,
- QP
- returns & destruction.

Understanding the pressure the sponsor was under to deliver against its key commercial milestones and expedite the process of delivering its drug to market safely and compliantly, Almac went over and above from the outset.

To improve efficiency Almac appointed additional project contacts to facilitate continous communication, ensuring the focus was always where it needed to be and issues were proactively identified and addressed immediately.

To mitigate risk Almac needed to address timeframes. The first patient dosing date had been set by the sponsor before the trial had been thoroughly scoped. During the study start-up phase, it became clear that this demand verged upon unobtainable, yet the sponsor was unable to realign its timeline due to enormous commercial pressure. To save time, Almac's dedicated team expedited several processes, such as documentation generation, labelling activity and QA batch document review. To further hasten the timelines, clinical supplies for initial startup countries were labelled with single panel labels which were quicker to produce in the first instance whilst the team worked on generating the booklet labels required for the rest of world supplies. This enabled Almac to successfully meet the seemingly impossible deadlines.

To address the comparator supply shortage, Almac harnessed its global contacts to source enough comparator product to fulfil the need. This required daily communication with suppliers to ensure that as soon as comparator product was released Almac was in position to procure the product. Although acquiring small quantities when available meant Almac received product intermittently throughout the duration of the trial, they were able to effectively manage the associated multiple labelling and QP release activities and coordinate supply.

Coordinating storage of a sensitised drug product was another aspect Almac needed to manage for the sponsor. Whereas the IMP needed to be stored within frozen temperatures -15C to -25C, the comparators, as well as the ancillaries, needed ambient temperature conditions. From receipt of IMP and comparators, to dispatch, the Almac in-house building management system was used to monitor the storage conditions in each temperature controlled areas.

Utilising its global footprint, Almac was able to optimise distribution by shipping directly to most sites in the EU from its facility in Craigavon, Northern Ireland, and directly to sites in the US from its facility in Durham, North Carolina. The sponsor maintained responsibility for managing shipments to some parts of Eastern Europe. Shipments of the temperature sensitive clinical supplies were successfully dispatched to sites and depots in Almac Phase Change Shippers (Pods) with iTag temperature monitors used to track transit temperatures.

Finally, Almac designed a strategy to effectively manage the returns and destruction handling for the trials. Full accountability of clinical material utilised throughout the trial was documented.

The results

Study delivered on time and on budget

Despite the notable complexity, and working with an ambitious and inflexible timeline, Almac was able to harness its expertise in project management and comparator sourcing, combined with its ability to streamline and expedite core processes, to deliver multiple shipments to sites and depots on time and within specified conditions.

By partnering with Almac, the sponsor was able to not only satisfy its pressing commercial pressures but, most importantly, take a giant leap forward for human health, by establishing a new treatment for drug resistant bacteria; giving thousands of patients around the world new hope.

References

[i]The Changing Landscape of Research and Development, IQVIA Institute for Human Data Science, April 2019
[ii]The Review on Antimicrobial Resistance (May 2016)

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