Hospital-Acquired Pneumonia/ Ventilator-Associated Pneumonia (HAP/VAP) Case Study

IMPROVING STUDY START UP AND RECRUITMENT FOR A DRUG-DEVICE CLINICAL TRIAL

Ventilated patients in a hospital setting are at risk of developing pneumonia, which is often treated with an IV-delivered antibiotic. In collaboration with an agile biotech company, a large pharmaceutical company was running a program to investigate the clinical efficacy and safety of a drug-device combination for intubated, mechanically ventilated patients by delivering a localized, lower dosage of an antibiotic within the lungs as compared to systemically-administered antibiotics.

Due to the sponsor's shifting alliance agreements, Covance was selected to assume its in-progress, Phase III clinical trial. This case study explores the challenges faced in study start up, recruitment and data management.

The Challenges: Recruiting a global population in a complex infectious disease study

ICU studies are inherently difficult due to the complexities of patients' conditions while in the hospital, the need to obtain consent for temporarily incapacitated patients and the massive amount of associated data that is generated in the medical records.

When Covance received this study, there had already been three amendments to the protocol and the trial was behind schedule for startup and recruitment. With over 250 sites encompassing 25 different countries and their respective regulatory requirements involved, Covance needed to quickly make major progress to get the study back on track.

Key Actions

- Developed hands-on solutions to address lagging recruitment
- Worked directly with sites to understand the barriers to recruitment and share success stories among investigators
- Built a robust communications effort to meet the recruitment goals, achieve database lock and submit the clinical study report (CSR) on time

Initial enrollment criteria were very strict, allowing only a 24-hour window to complete patient screening and start the study regimen. While standard of care assessments were allowed, it was still challenging to enroll patients.

The final challenge involved managing the data cleaning process with the sponsor to support the Data Monitoring Committee (DMC), as many data points were collected and had to be correctly mapped within the Electronic Data Capture (EDC) system.

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The Actions: Setting up sites for success

Covance first worked with the sponsor to amend the protocol and allow for a 48-hour window instead of the initial restrictive 24-hour window to increase the potential for successful enrollment. With the goal of recruiting 725 patients, the team applied lessons learned from historical studies and analyzed how successful sites were recruiting their patients as compared to the lower-enrolling sites. They noted that some sites' recruitment protocols were more geared toward non-ICU studies. As there was no "one size fits all" formula, the team applied a multi-faceted approach to cover all regions and countries to best position the study for success.

Covance CRAs partnered with these sites, providing assistance through motivational visits and discussions with ICU staff. Key success messages were then shared amongst the entire team.

As sites improved their recruitment rates, investigators were sent personal, handwritten thank you notes to recognize their contribution to the research. Covance also incorporated their success stories into the investigator meetings, inviting higher enrolling PIs from the region to share their lessons learned so that other sites could gain insights on how to improve their results.

As the enrollment rapidly progressed, the Covance team tackled a backlog of data entry to support DMC cuts as well as achieve an on-time database lock. Covance CRAs proactively partnered with their sites to establish plans to efficiently enter data prior to the next monitoring visit so Source Data Verification (SDV) could be completed. In turn, the project management team reviewed metrics on a weekly basis and communicated their findings to the CRAs.

The Results: Meeting and beating expectations by 3 weeks

With the coordinated efforts to boost recruitment, the team reached the goal of recruiting 725 patients *three weeks ahead of deadline* and met all site requirements, despite the difficult environment. They also managed the influx of patient data and worked together to reach database lock and deliver the clinical study report on time. From the start up group to the ethics committee, the Covance teams formed cross-functional partnerships to increase communication, identify potential areas of risk and develop mitigation strategies to prevent issues from occurring or solve challenges in real time.

The Lessons Learned: Leveraging established relationships and experience

From this study, Covance has fostered its strong relationships with experienced investigators as well as a robust list of sites that have proven success in enrolling ventilated patients in these complex studies. Along with an understanding of antibiotic resistance rates and an experienced, global, medical monitoring team that can quickly address issues, Covance knows how to ensure a sponsor is fully supported from study start up to the submission of the final clinical study report.

Learn more about our drug development solutions at **www.covance.com**

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