Advancing Heart Failure Research Through Innovative Clinical Trial Design

Cardiovascular disease remains public enemy number one in healthcare. Taking the top spot on the mortality scale, diseases of the heart are predicted to affect nearly 10 million people over the age of 18 by 2020 – a 25 per cent increase in just a decade.[1]

Heart failure is one of the more serious cardiovascular conditions, amassing a 23 per cent readmission rate and resulting in death within five years across 50 per cent of cases.[2] It includes a complex set of diseases that typically are treated in the US by cardiology subspecialists. From a research perspective, heart failure should be ripe for progress. However, statistics and treatments have remained relatively static for decades.

Many factors contribute to limited advances in heart failure discovery and treatment. The fact that several drugs for heart failure have shown detrimental effects on long-term outcomes, despite showing beneficial effects on shorter-term surrogate markers, has led regulatory bodies and clinical practice guidelines to seek mortality/morbidity data for approving/recommending therapeutic interventions for heart failure. However, it is now recognized that preventing heart failure hospitalization and improving functional capacity are important benefits to be considered if a mortality excess is ruled out.

Yet the value proposition for heart failure research is not lost on the industry. In sync with current initiatives to lower healthcare costs and improve clinical outcomes, better therapies are needed to move the needle on unacceptable heart failure statistics. It's a priority that sits at the heart of the research community's mission to improve the quality of life for healthcare's most important asset: patients.

Heart Failure Clinical Trial Challenges: A Deeper Look

Heart failure clinical trials are inherently complex due to the variability in patients' conditions and the intricacies of a disease with numerous causes. A patient's clinical course is often marked by repeated hospitalisations, rapid disease progression, and death. Consequently, clinical trials must account for multiple risks; there are numerous pitfalls for sponsors that lack heart failure study experience.

Depending on the aim of a heart failure trial, patient recruitment and retention becomes increasingly challenging. Clinical trials designed to test efficacy in stopping disease progression may encompass patient samples that represent more stable conditions. However, clinical trials often must involve acute, decompensated patients if the study goal is to reduce patients' need for emergency care.

Within these situations, investigators must identify patients most likely to have an acute event. Partnering with heart failure specialists whose historical data indicates a strong heart failure population can produce some enrolment wins in a more controlled clinic environment. The reality, however, is

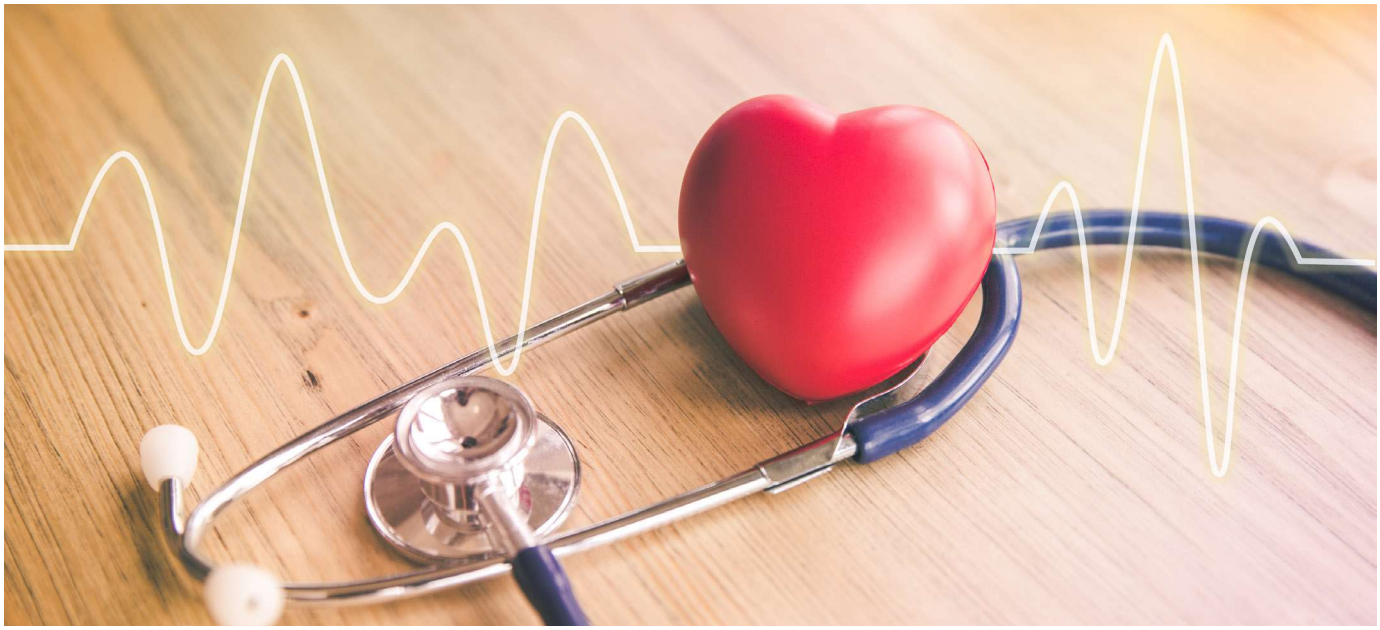
that enrolment must often occur when patients present in an emergency setting.

The question then becomes: How does the trial design address the needs of patients and families who present in an emergency room (ER) with an acute episode?

Unlike studies conducted solely in clinical settings, acute heart failure studies require 24/7 coverage and must account for the nuances of busy ER workflows. Trials must work parallel to ER processes and not hinder the course of patient care. For example, study teams must be experts in handling informed consent thoroughly and delicately, giving patients and their families the information and time necessary to make informed decisions, even within the dynamics of an emergency situation. While there is often some tension between adherence to study protocols and supporting the needs of families, these strains are intensified with heart failure recruitment and retention.

Strategies for Better Clinical Trial Design

Recognising the many opportunities offered by successful heart failure trials, health authorities are increasingly open to alternative, innovative clinical trial designs that uphold safety and improve results. Current movements point to greater treatment effect, smaller sample sizes, better characterisation of patient



subgroups targeted for more intensive therapy, and increased information capture to enhance understanding of outcomes.

One way to tighten the belt on mammoth cardiovascular clinical trials is to combine a Phase II and Phase III programme into one fluid, adaptive clinical trial. This way, the study can leverage existing patient enrolment for safety and efficacy data review, as well as re-evaluate the sample size based on the Phase II period treatment effect. This parallel effort reduces timeframes between the Phase II and III trials and health authority discussions. Consequently, this approach can reduce costs, recruitment needs and the overall duration of a trial.

Partnering with a contract research organisation (CRO) experienced with innovative heart failure clinical trials can improve success rates by implementing best practices that include:

- Effective site selection that considers more than just the expertise of the principal investigator and their staff, but also the experience of the ancillary services that will support the protocol schedule of assessments.
- Trial design that includes an operational strategy for 24/7 coverage not only from investigators but also from medical monitors (to answer provider questions) and from ancillary services (such as echocardiogram or cardiac catheterisation services).
- Methods for reducing the burden of a trial on the clinical site. These might include customised training materials and reference tools, such as "pocket protocol" cards to help on-site staff quickly and easily identify study protocols.
- Processes to improve experiences for patients and families. Offering a concierge service that can help with transportation needs, meals, or even arranging for follow-ups from a visiting nurse have proven effective for patient retention.
- Recruitment that considers retention during screening and enrolment. This includes trying to determine upfront whether a patient is likely to be compliant and reliable throughout the course of the trial. Important questions include: Does the patient have a history of medication or therapy non-adherence? Where does a patient live in proximity to the clinical site? Does the patient have reliable transportation?

Great opportunity exists to advance heart failure trials and improve quality outcomes for all stakeholders. Going forward, however, it's important that the industry start setting aside traditional approaches to these complex research undertakings. Researchers must take advantage of innovative and emerging best practices to bring new discovery to market and to give heart failure patients new options for better outcomes.

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