Identifying Barriers and Practical Solutions to Conducting Site-Based Research in North America

Exploring Acute Heart Failure Trials As a Case Study

Andrew P. Ambrosy, MD[a,*], Robert J. Mentz, MD[a,b], Arun Krishnamoorthy, MD[a,b], Stephen J. Greene, MD[a], Harry W. Severance, MD[c]

KEYWORDS

• Acute heart failure • Clinical trials • Site-based research

KEY POINTS

- There are more than 1 million hospitalizations for acute heart failure annually in the United States accounting for most of the $40 billion spent directly on HF-related care.
- Although the treatment and prognosis of ambulatory HF patients has improved dramatically because of drug- and device-based therapies, there have been few advancements in the management of AHF and postdischarge readmissions and mortality remain unacceptably high.
- One of the emerging trends in global clinical trials has been the gradual shift of enrollment from predominantly North America and Western Europe to Eastern Europe, South America, and Asia-Pacific where the regulatory burden and cost of conducting research may be less prohibitive.
- The crisis in site-based research in North America is exacerbated by poor visibility of cardiovascular disease and clinical trials, an inability to identify highly performing centers in terms of volume and quality, time-consuming study protocols not reflective of the realities of patient care, inadequate infrastructure for recruitment and study conduct, underdeveloped relationships between the research team and emergency providers and hospital-based physicians, misaligned incentives between principle investigators and the parent clinical facilities, and limited training and support for study coordinators.

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[a] Division of Cardiology, Duke University School of Medicine, 2301 Erwin Road Drive, Durham, NC 27710, USA;
[b] Division of Cardiology, Duke Clinical Research Institute, 2301 Erwin Road Drive, Durham, NC 27710, USA;
[c] Erlanger Institute for Clinical Research, 973 E. 3rd St. Ste B1203, Chattanooga, TN 37403, USA
* Corresponding author. Division of Cardiology, Duke University Medical Center, 2301 Erwin Road Drive, Durham, NC 27710.
E-mail address: andrew.ambrosy@dm.duke.edu

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INTRODUCTION

There are approximately 6 million patients with heart failure (HF) in the United States with the prevalence projected to exceed 8 million by the year 2030.[1,2] In addition, there are more than 1 million hospital admissions annually in the United States accounting for most of the approximately $40 billion in direct costs for HF-related care each year. Following an index hospitalization for HF, the risk of readmission and death, respectively, may be 30% and 15% within 60 to 90 days.[3] Although the treatment of ambulatory HF has been revolutionized by drug- and device-based therapies over the past few decades, inpatient management has remained virtually unchanged over a similar time frame and nearly every clinical trial conducted to date has been neutral in terms of efficacy and/or safety.

The reasons for the lack of success with prior clinical trial programs is likely multifactorial and may be caused by issues related to the study drug and the target patient population (Fig. 1).[4] However, more recently, problems with study execution and enrollment at the level of the trial site and geographic region have received increasing attention. One of the emerging trends in global clinical trials has been the gradual shift of enrollment from predominantly North America and Western Europe to Eastern Europe, South America, and Asia-Pacific where the regulatory burden and cost of conducting research may be less prohibitive (Table 1). However, major regional differences in patient characteristics, background therapy, and event rates (ie, rehospitalizations and mortality) may limit the generalizability of research conducted exclusively outside of North America to the US patient population.[5–7] This article uses acute HF (AHF) as a paradigm and identifies barriers and practical solutions to successfully conducting site-based research (SBR) in North America (Table 2).

BARRIER: POOR VISIBILITY OF CARDIOVASCULAR DISEASE AND CLINICAL TRIALS WITHIN THE INSTITUTION AND THE BROADER COMMUNITY

Cardiovascular disease (CVD) is the number one cause of morbidity and mortality worldwide killing more patients than all cancers combined.[1] In addition, in the developing world the burden of CVD continues to grow because of increased life expectancy as a result of improved sanitation, socioeconomic advancement, and the decline in deaths caused by communicable diseases. Similarly, because of aging of the population and the success of medical therapy, the number of patients worldwide with HF is growing at a truly exponential rate with estimates of the global prevalence approaching 40 million.[8] However, compared with the pandemic proportions of HF-related morbidity and mortality, there is disproportionately low visibility among medical professionals and the general public. In contrast to many common cancers, there are few major not-for-profit organizations, outside of medical professional groups, or philanthropic fundraising efforts targeting CVD in general and HF in specific. Moreover, as compared with HF, patients

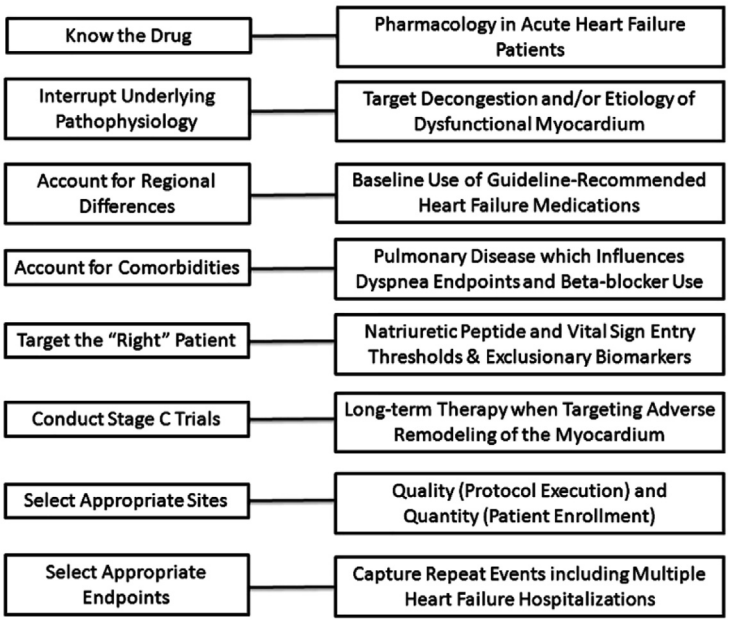

Fig. 1. Considerations for the successful design and conduct of acute heart failure trials. (*Adapted from* Mentz RJ. Learning from recent trials and shaping the future of acute heart failure trials. Am Heart J 2013;166(4):632; with permission.)