

Transcript Details

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How Do We Identify Patients With Chronic HFrEF Experiencing Worsening Heart Failure Events?

Announcer: This is ReachMD. Welcome to Spotlight on Worsening Heart Failure Events. This program, titled “How Do We Identify Patients With Chronic HFrEF Experiencing Worsening Heart Failure Events?,” is brought to you by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., and is intended for health care professionals in the United States. Here is your host, Dr. Javed Butler.

KOL Moderator (Dr. Javed Butler): Welcome to the first episode of this three-part series, Spotlight on Worsening Heart Failure Events. I am Dr. Javed Butler from University of Mississippi, and I am joined today by Dr. Robert Mentz from Duke University and Dr. Bill Colucci from Boston University. We are here to discuss worsening heart failure events in patients with chronic heart failure with reduced ejection fraction, or HFrEF—what these events are, how to identify them, and why this topic should be of concern. Rob, Bill, it's great to have you here.

Before we get started, I'd like to mention that this podcast is part of a series focusing on patients with HFrEF experiencing worsening heart failure events. A worsening heart failure event is characterized by an episode of worsening signs and symptoms, despite a period of stabilization on recommended therapy.^{1,2}

So, Rob, I'd like to start by asking you about the current landscape of heart failure. Can you tell me about the prevalence of this disease?

Dr. Robert Mentz: Thanks, Javed. Sure. Heart failure is a prevalent condition that carries immense health burden in the United States.³ In fact, according to data published by the National Health and Nutrition Examination Survey, the one from 2013 to 2016, an estimated 6.2 million American adults over the age of 20 had heart failure.⁴ So, the total number of American adults living with heart failure is actually projected to increase 46 percent, from approximately 5.8 million in 2012 to approximately 8.5 million in 2030.^{4,5} Heart failure is a serious condition that is associated with a heightened risk of both hospitalization and death,¹ and many patients continue to experience worsening heart failure events that may lead to these outcomes.¹

And as you mentioned in the opening of the podcast, worsening heart failure events are characterized by escalating signs and symptoms requiring medical evaluation and treatment intensification.^{1,2} Many patients with HFrEF are at risk for progression, so close monitoring is crucial to ensure the timely identification of patients who may be at risk of experiencing worsening heart failure events.^{1,2}

KOL Moderator (Dr. Javed Butler): Thanks, Rob. Bill, can you please elaborate on Rob's comment about the signs and symptoms that are common in patients with chronic heart failure with reduced ejection fraction experiencing worsening heart failure events?

Dr. Wilson Colucci: Certainly, Javed. The trajectory of these patients is characterized by episodes of worsening signs and symptoms of heart failure, such as breathlessness, fatigue, and swollen ankles and legs, that may require the patient to seek medical attention, either in an outpatient or in-patient setting.^{2,6} It is increasingly understood that these worsening heart failure events are not isolated symptom exacerbations but may actually be signals of deterioration of the underlying condition and may suggest an unfavorable prognosis.^{2,7}

Dr. Robert Mentz: Yes, certainly. Let us look at the results from an observational cohort analysis of patients with newly diagnosed HFrEF identified from the PINNACLE data registry that looked between January of 2011 and December of 2014 that, as a matter of fact, you, Javed, conducted. So, in this study, 1,851 patients out of approximately 11,000 patients, which is around 17%, experienced a worsening heart failure event within 1.5 years on average of their initial diagnosis. While worsening heart failure events occurred in a greater proportion of patients who had a higher NYHA class and a lower ejection fraction, patients with less severe disease also

experienced these events. So, these data suggest that all patients with HFrEF may be at risk of progressing.¹

KOL Moderator (Dr. Javed Butler): You're absolutely right, Rob. Thank you. Bill, are there any other patient characteristics that we should note from the PINNACLE study?

Dr. Wilson Colucci: Well, you will see similarities and differences between subcohorts in any study. In the PINNACLE study, the mean systolic and diastolic blood pressures, heart rate, and serum creatinine in the overall population were not much different than in patients in either subcohort. While all patients with HFrEF may be at risk of progressing, a greater proportion of those who experienced worsening heart failure events in this study were African American, were over the age of 80, and had a higher NYHA class and a lower ejection fraction.¹

KOL Moderator (Dr. Javed Butler): Yes, that is what we found. Another identifier for risk of worsening heart failure events is the cardiac biomarker, NT-proBNP.⁸ Let's shift our focus to the PROTECT study that looked into this. The PROTECT study was a prospective, randomized, single-center trial of 151 patients with NYHA functional class II to IV and an ejection fraction of 40 percent or less. This study found that over 80 percent of patients experiencing worsening heart failure events had NT-proBNP levels of more than 1,000 pg/mL, and 70 percent had levels greater than 2,000 pg/mL.⁶ Rob, can you explain briefly to our listeners why this is important?

Dr. Robert Mentz: Sure. High levels of NT-proBNP are observed in pathologic hypertrophy and heart failure. In fact, increased NT-proBNP secretion from the stressed heart is a widely used biomarker in this disease.⁸ The PROTECT study was not the only study to show the association between elevated NT-proBNP levels and increased risk of poor outcomes.⁶ Another study that looked into this biomarker is the GUIDE-IT study. The GUIDE-IT study was a randomized, multicenter clinical trial that ran from January of 2013 to July of 2016, and it enrolled patients with HFrEF with a history of a prior heart failure event, whose NT-proBNP levels were >2000 pg/mL or a BNP level >400 pg/mL, that was within the past 30 days. So one analysis of this study, which included over 600 patients with known NT-proBNP levels after 90 days post-randomization, showed that lowering NT-proBNP levels to less than or equal to 1,000 pg/mL was associated with a lower risk of hospitalizations, cardiovascular death, and all-cause mortality.⁹

Dr. Wilson Colucci: Indeed. Given the high risk associated with worsening heart failure events, the timely identification of patients at risk and the close monitoring of patients with known risk can play a crucial role in effectively managing the challenging course of this disease.^{1,2,6}

Moderator KOL (Dr. Javed Butler): Well, we're going to have to leave it here for now. Thank you, Rob and Bill, for this very informative and important discussion. To quickly summarize: today, we discussed the landscape of heart failure and how to identify patients with chronic HFrEF experiencing worsening heart failure events. Be sure to tune in into our two subsequent podcasts in the Spotlight on Worsening Heart Failure Events series. There, we take a closer look at the risks and pathways associated with worsening heart failure events in HFrEF. Thank you for tuning in.

Announcer: This program was brought to you by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. If you missed any part of this discussion or to find others in this series, visit ReachMD.com/HFEvents. This is ReachMD. Be part of the knowledge.

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