Response by Butt et al to Letter Regarding Article, "Efficacy and Safety of Dapagliflozin According to Frailty in Patients With Heart Failure: A Prespecified Analysis of the DELIVER Trial"

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In Response:

Drs Wong and Demers are of course correct that there is an association between frailty and age, but it is also well recognized that frailty can develop at any age. The frailty-associated gradient in age in any specific population likely reflects many different factors, including the disease in question, sex distribution, and the extent of comorbidity. Among patients with heart failure, all of these vary by ejection fraction phenotype. Many of these factors also vary by geographic region, and clinical trials may include patients from up to 50 countries. How frailty is assessed may also be relevant.

Although it is interesting that the age gradient appeared greater in patients with reduced ejection fraction compared with preserved ejection fraction, in the trial publication mentioned by the authors[1] (and in a second article[1]), this was not the case in another heart failure with reduced ejection fraction trial.[2] In 2 recent studies of "real-world" as opposed to trial patients, the age gradient related to frailty was small and similar to that observed in our analysis of the DELIVER trial.[3,4]

We do not agree that trials include few elderly patients. The proportion of patients ≥80 years of age in PARAGON-HF was 22.4%, and in DELIVER, it was 21.4%. The median age among patients from North America in each of these trials was 75 years, not so different from similar patients in the Get With the Guidelines-Heart Failure Registry (median age, 76 years).[5]

We see no reason not to apply the findings of trials to older patients because the benefits of treatment are generally consistent across the range of age in both heart failure with reduced ejection fraction and heart failure with midrange ejection fraction/heart failure with preserved ejection fraction. Indeed, what the studies of frailty and older age emphasize is the large absolute benefits of treatment in these vulnerable patients who are often needlessly denied therapy.

Article Information

Disclosures J.H.B. reports advisory board honoraria from Bayer, consultant fees from Novartis, and travel grants from AstraZeneca. S.D.S. has received research grants from Actelion, Alnylam, Amgen, AstraZeneca, Bellerophon, Bayer, Bristol Myers Squibb, Celladon, Cytokinetics, Eidos, Gilead, GlaxoSmithKline, Ionis, Lilly, Mesoblast, MyoKardia, National Institutes of Health/National Heart, Lung, and Blood Institute, Neurotronik, Novartis, NovoNordisk, Respicardia, Sanofi Pasteur, Theracos, US2.AI; and has consulted for Abbott, Action, Akros, Alnylam, Amgen, Arena, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cardior, Cardurion, Corvia, Cytokinetics, Daiichi-Sankyo, GlaxoSmithKline, Lilly, Merck, Myokardia, Novartis, Roche, Theracos, Quantum Genomics, Cardurion, Janssen, Cardiac Dimensions, Tenaya, Sanofi-Pasteur, Dinaqor, Tremeau, CellProThera, Moderna, American Regent, and Sarepta. J.J.V.M. reports payments through Glasgow University for work on clinical trials, consulting, and other activities from Alnylam, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Cardurion, Cytokinetics, Dal-Cor, GSK, Ionis, KBP Biosciences, Novartis, Pfizer, and Theracos, as well as personal lecture fees from the Corpus, Abbott, Hikma, Sun Pharmaceuticals, Medscape/Heart.Org, Radcliffe Cardiology, Servier Director, and Global Clinical Trial Partners.

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