

were similar for zanubrutinib. The correspondents also ask about the possible effect of the interim analysis reported at the European Hematology Association in June 2021. Rates of discontinuation across the groups remained stable throughout the trial, and only five patients who stopped ibrutinib for any reason received acalabrutinib. In addition, patients who discontinued or changed therapy without progression remained in the analysis of progression-free survival.

The correspondents note, and we acknowledge, a small imbalance between the groups in the number of previous therapies that the patients had received at baseline, with a greater frequency of more than two previous therapies in the ibrutinib group (20.9% in the ibrutinib group vs. 15.0% in the zanubrutinib group). In an ad hoc analysis among the patients in the two groups who had received more than two previous lines of therapy, zanubrutinib was associated with longer progression-free survival than ibrutinib, with a hazard ratio for progression or death of 0.49 (95% confidence interval, 0.51 to 0.95). This result is consistent with the results of the primary analysis and the preplanned analysis involving patients who had received more than three previous lines of therapy. Finally, our results are consistent with those of multiple real-world trials<sup>2</sup> and compassionate-use studies<sup>3</sup> that reflect the use of ibrutinib in actual clinical practice. Because the ALPINE trial was con-

ducted during the early period of the coronavirus disease 2019 (Covid-19) pandemic with limited or no access to vaccination or effective treatment, the number of deaths from Covid-19 in the two trial groups should be noted, a factor that potentially reduced overall survival below what would normally have been expected.

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Since publication of their article, Dr. Shadman reports receiving consulting fees from Janssen. No further potential conflict of interest relevant to this letter was reported.

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## Cystatin C–Based Equation to Estimate GFR without Race and Sex

**TO THE EDITOR:** In our view, the inferences by Pottel et al. (Jan. 26 issue)<sup>1</sup> are muddled. The National Kidney Foundation–American Society of Nephrology (NKF-ASN) Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease<sup>2</sup> asserted that race is a social, not a biologic, construct and successfully removed it from kidney-function estimation. The unifying approach of the Task Force was built on the principles of assay availability, ease of implementation, and the diversity of the population in the

United States in their development of the equation, assessment of its performance, and focus on patient centeredness, including transparency. The European Kidney Function Consortium (EKFC) creatinine-based equation (eGFR<sub>cr</sub>) and cystatin C–based equation (eGFR<sub>cr-cys</sub>) for the estimation of glomerular filtration rate (GFR) opaquely incorporate race in the rescaling factor (Q value). The NKF-ASN Task Force believed that the infeasibility of implementation of the EKFC equation rescaling factors and that the cost and

limited availability of cystatin assays would impede timely adoption in the United States, as recent studies suggest.<sup>2,3</sup> The populations in the study by Pottel et al. are not representative of the United States, despite including U.S. participants. The NKF-ASN Task Force supported the use of the eGFR<sub>cr</sub>-cys equation, when data on cystatin C levels are available, for greater accuracy — but without any underlying adjustment for race. EKFC equations may be appropriate for use in some countries but are suboptimal for use in the United States.

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**THE AUTHORS REPLY:** The NKF-ASN Task Force recommended the use of the creatinine-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation refit without the race variable in all laboratories in the United States.<sup>1</sup> Although this had the important benefit of eliminating race-based reporting of estimated GFR, there was a cost. The CKD-EPI equation, by de-

sign, underestimates GFR in self-identified Black patients and overestimates GFR in self-identified non-Black patients.<sup>2</sup> It is problematic in medicine for a main test of organ function to be intentionally inaccurate. Why not instead have a more accurate estimated GFR that is reported in a race-free manner? In our opinion, the Q value accomplishes this by rescaling everyone's serum creatinine level such that the rescaled value would be 1.0 if they were healthy for their age, sex, or self-reported race. This approach can be automated in electronic medical records without race-based reporting; it also decreases the effect of non-GFR factors (correlated with demographic variables) on serum creatinine level, regardless of whether these are due to genetics or environment. Underdiagnosis of chronic kidney disease in Black persons in the United States is an important problem, but let's find a path forward with respect to serum creatinine levels that does not promote inaccurate testing.

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Since publication of their article, the authors report no further potential conflict of interest.

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## Transient Global Amnesia

**TO THE EDITOR:** Ropper (Feb. 16 issue)<sup>1</sup> presents a concise review on the subject of transient global amnesia. As emergency physicians who see patients with transient global amnesia early in the course of the episode, we would recommend

against performing diffusion-weighted magnetic resonance imaging (MRI) soon after symptom onset. Diffusion-weighted MRI is not part of the diagnostic clinical criteria proposed by Caplan<sup>2</sup> and Hodges and Warlow,<sup>3</sup> and it rarely changes