treatment research by using a modified intent-to-treat analysis and statistical methods to compare variables between arms. However, we believe that further discussion is needed on the research design.

First, we would suggest extending the follow-up period to evaluate whether the long-term efficacy and safety outcomes of TCZ treatment are beneficial, as the study did not clarify whether the primary endpoint measured two weeks after the last dose of treatment in each study period could fully reflect the persistence of TCZ treatment effect.

Second, although the authors did not explicitly mention other potential confounding factors that could affect the study observations, they may exist and could have an impact on the results. For instance, the study did not account for other potential confounders such as lifestyle factors (eg, diet, exercise), comorbidities (eg, hypertension, diabetes), or medication use (excluding antiretroviral therapy [ART]) [2]. These factors could potentially confound the association between exposure and outcome, and their influence may not have been adequately considered in the statistical analysis. Additionally, although the authors acknowledge that IL-6 is a robust predictor of morbidity and mortality in both aging and people with HIV (PWH), they did not control for age in the study design or analysis (Figure 1 in this original article indicates that the age range of participants was 18–60 years old). We suggest that future studies by the authors should consider controlling for age and other potential confounding factors to better understand the underlying mechanisms of increased age-related comorbidities in people with HIV infection.

Third, the results of this study are helpful for improving the treatment of HIV infection. However, the participants in this study are only divided into Black patients and Nonblack by dichotomy, their ages ranging from 18 to 60. Considering different races and ethnicities may affect the results due to many factors, for example, social determinants, genetic diversity, and historical and structural inequities. Besides, the outcomes may vary with the age of the participants as well. We suggest that the authors do further research using different races or different age brackets as exposure and the effect of TCZ as outcome. By doing so, the results of this research can benefit many more people.

To sum up, this article contributes toward TCZ validation in lowering the morbidity and mortality in ART-treated PWH with double-blind, placebo-controlled crossover trials. If it is possible to extend the observation period, improve the research method, and explore the influence of race and ages in the research, this study will make a significant contribution to the field of AIDS treatments research.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Reply to Chen et al.

To the Editor—We appreciate the opportunity to respond to the comments by Dr. Chen and colleagues related to our manuscript "Interleukin 6 Blockade With Tocilizumab Diminishes Indices of Inflammation That Are Linked to Mortality in Treated Human Immunodeficiency Virus Infection." Understanding the potential mediators of age-related comorbidities in people with human immunodeficiency virus (HIV, PWH) is an important area of clinical research and interventional studies aimed at improving the lifespans and healthspans of this population are needed. We agree with many of the important considerations brought up by Chen et al. This was a small, short-term pilot study examining the safety and tolerability of tocilizumab (TCZ) treatment in PWH, the first study of interluekin-6 (IL-6) receptor blockade in PWH. Increasing the number of participants would give us greater power to detect differences in immune profiles during treatment and placebo and would make our results more generalizable to the global population. Taking greater account of lifestyle factors that may contribute to inflammation and lipid levels will be important in future studies. A longer duration of TCZ treatment may provide insights into the sustainability of the reductions of inflammatory and immune activation markers we identified in our study. Furthermore, a longer treatment period with TCZ may enable future studies to determine the long-term effects of TCZ on lipid levels, on CD4+ T-cell counts, immune cell function, and potentially, on clinical endpoints. Future intervention studies, using TCZ or another immunomodulatory treatment, should try to enroll participants at more advanced age and a greater proportion of women, as these factors also contribute to inflammatory profiles and age-related comorbidities in PWH. Although our enrollment criteria included individuals between 18 and 60 years old, the actual age range of participants was 26–60 years. We did collect information on other medication use among participants and included the

proportion of statin users in Table 1 [1]; again, with a trial that enrolled 34 total individuals, the numbers of participants on certain medications were insufficient for stratification. We also considered several other comorbid conditions in our inclusion and exclusion criteria, including cancer, active infections, and liver disease. Without performing this initial study assessing the safety of TCZ in this population and the immune and metabolic profiling described in our study, we would not have been able to justify a long-term study with a larger enrollment.

Notes

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Decoding the 2023 Duke-ISCVID Criteria

To the Editor—This correspondence is in regard to the recently published article, "The 2023 Duke–International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria" [1]. First, we would like to thank the authors of this manuscript for their efforts in producing a much-needed revised diagnostic criteria for infective endocarditis (IE) and the editor for publishing this manuscript. However, we would like to highlight a point of confusion arising from the new criteria.

In this paper, the authors emphasize that 2 new predisposing conditions (a previous history of IE and presence of an endovascular intracardiac implantable electronic device) for IE were included as part of the minor criteria. This change was outlined in Table 2, subheading IIA (Figure 1), under minor criteria and predisposition. Notably, these 2 new conditions were included in bold type, along with 6 other conditions (prosthetic valve, previous valve repair, congenital heart disease, more than mild regurgitation or stenosis of any etiology, hypertrophic obstructive cardiomyopathy, or injection drug use) that were purported to be listed in prior versions of the Duke criteria published in 1994 and 2000 [3, 4]. However, on close review of these 2 prior papers, no specific predisposing conditions are clearly identified except for intravenous drug use.

In the original 1994 Duke criteria [3], the authors state that, "The risk posed by various cardiac conditions for endocarditis has been ranked previously" and cite a 1990 paper by Dajani et al [2]. Dajani et al does include a table with conditions for which endocarditis prophylaxis is recommended and conditions for which it is not recommended (Figure 1). Notably, previous IE is already included as an indication for antibiotic prophylaxis in this table. The Von Reyn criteria, published in 1981 and the primary diagnostic tool used before the Duke criteria, state that "only definite valvular or congenital heart disease or a cardiac prosthesis are accepted as evidence of predisposing heart disease" [5]. Notably, the vagueness of predisposing conditions in the Duke criteria has been highlighted before by Büchi et al in 2016 [6].

It would therefore appear that the table of predisposing conditions listed in the 2023 Duke– International Society for Cardiovascular Infectious Diseases (Duke-ISCVID) paper is not based on recommendations from either of the previously published Duke criteria studies, or the Von Reyn criteria. This poses challenges to researchers who are attempting to validate these new criteria in comparison to the modified Duke criteria. Should we use all the criteria listed in Table 2 and retroactively apply them to the modified Duke criteria? How were these criteria determined? There are no listed references and they are not consistently reproduced in any of the aforementioned studies.

We would urge the authors to revise the manuscript to highlight these inconsistencies and propose a mechanism for how to validate the 2023 criteria in light of this issue. Otherwise, any future studies attempting to compare the 2023 and 2000 criteria will carry the risk of substantial variability and error [1].

Note

Potential conflicts of interest. D. H. reports passive investments in index funds (retirement/investments). S. E.-D. reports no potential conflicts.

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