Reply to Chang and Huang

TO THE EDITOR—We appreciated Chang’s and Huang’s comments on our published article entitled “Whole-blood 3-gene signature as a decision aid for rifapentine-based TB preventive therapy” [1] and sharing their experience as well as careful consideration on the predictive power of current 3-gene model on termination of weekly rifapentine plus isoniazid for 12 doses (3HP) treatment due to systemic drug reactions (SDRs).

We, however, want to emphasize the importance of the negative-predictive value (NPV) of the 3-gene model during clinical practice and implementation of a latent tuberculosis infection (LTBI) program. First, do no harm, especially in the setting when the goal of intervention is to prevent, rather than to cure, a disease, which is likely to occur in only 5–10% of the target population [2]. Furthermore, while conducting contact investigation, the occurrence of any adverse reaction in 1 contact might have a butterfly effect, adversely affecting the decision of whether to adhere to the public health policy in others. Among the 125 cases who were predicted to be safe during 3HP treatment in the training and testing cohorts, only one (0.8%) 52-year-old man developed SDR (NPV for SDR development: 99.2%) after taking 3 doses of 3HP. He presented with fever up to 38.4°C, general malaise, headache, muscle ache, epigastralgia, nausea, and conjunctivitis, yet he completed weekly rifapentine plus isoniazid (3HR) and 4R (4 months of daily rifampin) [3]. These regimes are also effective, safe, and convenient [4, 5].

In addition, another short-term rifapentine-based TB-preventive regimen, the 1-month once-daily rifapentine-and-isoniazid regime (1HP), has demonstrated an excellent completion rate up to 90% and also has comparable efficacy and toxicity as 9H in people with human immunodeficiency virus (HIV) [6]. However, the safety of 1HP has never been comprehensively evaluated in non-HIV population. We are currently conducting a randomized controlled trial in a non-HIV population (ClinicalTrials.gov: NCT04094012) to provide a head-to-head comparison between 1HP and 3HP in terms of the completion rate and safety, especially the risk of SDRs. We think this study will provide valuable information to guide individualized TB-preventive therapy. We look forward to sharing the study results in the near future.

Notes

Financial support. The work was supported by grants from Ministry of Science and Technology (MOST109-2314-B-037-085-MY3) and the NYCU-KMU Joint Research Project (NYCU-KMU-111-1003). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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.

References

1. Huang HL, Lee JY, Lo YS, et al. Whole-blood 3-gene signature as a decision aid for rifapentine-based tuberculosis preventive therapy. Clin Infect Dis 2022; 75:743–52.
2. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. World Health Organization, 2018. Report No: 9241550236. Available at: https://apps.who.int/iris/handle/10665/260233/9789241550239-eng.pdf. Accessed 30 June 2022.
3. World Health Organization. WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment. World Health Organization, 2020. Available at: https://apps.who.int/iris/handle/10665/331170. Accessed 30 June 2022.
4. Menzies D, Adjobimey M, Ruslami R, et al. Four months of rifampin or nine months of isoniazid for latent tuberculosis in adults. N Engl J Med 2018; 379: 440–53.
5. Ena J, Valls V. Short-course therapy with rifampin plus isoniazid, compared with standard therapy with isoniazid, for latent tuberculosis infection: a meta-analysis. Clin Infect Dis 2005; 40:670–6.
6. Swindells S, Ramchandani R, Gupta A, et al. One month of rifapentine plus isoniazid to prevent HIV-related tuberculosis. N Engl J Med 2019; 380: 1001–11.

Correspondence: J-Y. Wang, Department of Internal Medicine, National Taiwan University Hospital, #7, Chung-Shan South Rd, Zhongzheng District, Taipei 100225, Taiwan (jywang@ntu.edu.tw).

Clinical Infectious Diseases® 2022;75(10):1867
© The Author(s) 2022. Published by Oxford University Press on behalf of Infectious Diseases Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerives licence (https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

https://doi.org/10.1093/cid/ciac574