Clinical Infectious Diseases
CORRESPONDENCE

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 3HP treatment without interruption (NPV for SDR-related treatment incompletion: 100%). Furthermore, among the 125 cases, a total of 4 cases terminated 3HP treatment because of flu-like symptoms rather than SDRs, such as flush, dizziness, general malaise, and nausea/vomiting (NPV for treatment incompletion due to flu-like symptoms: 96.8%). This 3-gene model can therefore facilitate safely implementing a 3HP regimen for LTBI intervention.

For those who are predicted to have SDRs, they may receive rifamycin-containing tuberculosis (TB)-preventive regimens other than 3HP, such as 3HR (3 months of daily Isoniazid and Rifampin) and 4R (4 months of daily rifampin) [3]. These regimens 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

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