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Drs. Dai and Fan reply

To the Editor:

We thank Wang et al[1] for their interest and suggestions on our study on melanoma differentiation–associated gene 5-related interstitial lung disease (MDA5-ILD), which highlighted that tofacitinib (TOF) use might have a potential effect on improving the outcomes of MDA5-ILD.[2] We completely agree with their valuable suggestions. Indeed, the treatment of MDA5-ILD has always been a huge challenge. Excellent response to tofacitinib had been reported in an open-label clinical study enrolling patients with early diagnosis of MDA5-ILD for less than 3 months, and with predicted forced vital capacity of at least 50%.[3] We performed a limited retrospective study to assess the effect and adverse events of tofacitinib on survival in patients with MDA5-ILD.

First, the composition of patients with different anti-MDA5 antibody titers in the 2 treatment groups could not be matched; that was a limitation of our study due to its retrospective nature. However, our study showed that the 1-year mortality rate in the TOF group was significantly lower than that in the tacrolimus (TAC) group. After further adjustment for confounding factors (including the anti-MDA5 antibody titers), the Cox proportional hazards model showed TOF exposure was associated with a lower risk of 1-year mortality. Due to the even smaller sample size stratified by different anti-MDA5 antibody titers, we did not perform additional subgroup analysis (weak-positive in the TOF vs TAC groups: 16 vs 9; moderate-positive: 6 vs 9; strong-positive: 4 vs 17). Future prospective studies comprising multiple centers with large samples are needed to clarify the effect of TOF on subgroups with different antibody titers.

Indeed, several studies had shown that anti-MDA5 antibody titers were associated with disease activity[4,5]; on the other hand, reported factors that were associated with the disease severity included ferritin levels, Krebs von den Lungen 6 levels, coexistence with anti-Ro52 antibody, and increased serum levels of surfactant protein D in high-resolution computed tomography (HRCT).[6-9] In our study, no significant differences were found regarding baseline clinical characteristics (including ferritin levels, C-reactive protein levels, erythrocyte sedimentation rate levels, partial pressure of oxygen in the arterial blood/fraction of inspired oxygen values, presence of anti-Ro52 antibody, and HRCT patterns) between the 2 treatment groups.

Second, we used the Cox proportional hazards model in survival analysis to adjust for confounding factors, then further verified that TOF use may be beneficial for 1-year survival in patients with MDA5-ILD. Further, the Cox proportional hazards model was also carried out to assess the risk factors predicting the mortality in the 2 treatment groups. However, due to the small sample size and considerable covariates of our study, we only performed univariate analysis.

Third, as suggested by Wang et al,[1] we reviewed and collected comorbidities including hypertension, diabetes, cardiovascular diseases (including coronary heart disease, angina, atrial fibrillation, valvular heart disease, and cardiac dysfunction), and cancers. No significant differences were found in the comorbidities between the 2 groups.

Last, some patients were unable to perform pulmonary function tests (PFTs) due to the severity of the disease. There were 4 patients in the TOF group who re-performed PFTs compared to 3 patients in the TAC group. Chest HRCT was re-performed in 13 patients in the TOF group, with an interval of 113.3 (SD 5.3) days, and in 10 patients in TAC group, with an interval of 257.0 (SD 93.8) days. There were 12 survivors in the TAC group, of which 10 patients had reperformed chest CT tests with an interval of 257.0 (SD 93.8) days. Future well-designed multicenter randomized controlled trials are needed to assess the long-term efficacy of TOF in MDA5-ILD.

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