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Letter

The Use of Tofacitinib Has a Potential Effect on Improving the Outcomes of Melanoma Differentiation–Associated Gene 5–Related Interstitial Lung Disease

To the Editor:

We read with great interest the recent retrospective analysis by Fan and colleagues on the outcomes of tofacitinib (TOF) or tacrolimus (TAC) in combination with glucocorticoids for melanoma differentiation–associated gene 5 (MDA5)-related interstitial lung disease (MDA5-ILD), published in *The Journal of Rheumatology*.[1] The authors mainly investigated whether TOF exposure was associated with reduced mortality at 6 months and 1 year, and also compared the incidence of adverse events and discontinuation rates in the TOF and TAC groups for the treatment of MDA5-ILD. Fan et al ultimately concluded that the use of TOF has a potential effect on improving the outcomes of MDA5-ILD. We support and appreciate the authors' work and agree with the conclusion, but we have some concerns regarding certain details in the article.

First, several studies have shown that anti-MDA5 antibody titers are associated with disease activity (ie, higher antibody titers are more active) and can indicate disease severity and predict adverse outcomes.[2-4] In the study by Fan et al, the composition of anti-MDA5 antibody titers was different between the 2 groups of patients prior to treatment initiation, with 16 (61.5%) in the TOF group having weak-positive antibody titers compared to 9 (25.7%) in the TAC group.[1] Theoretically, this implies that relatively few patients in the TOF group were in an active state of the disease compared to those in the TAC group. Since its interference with the study results could not be excluded, additional subgroup analysis regarding the different antibody titers between the 2 groups of patients was necessary to explain the effect of the different antibody titers on the overall study.

Second, the authors compare the differences between survivor and nonsurvivor indicators in their article and use univariate analysis to account for predictors of mortality. In fact, in this situation, the results of univariate analysis are often inaccurate, and many variables can confound the findings. Although the authors added that multivariate analysis could not be achieved for both groups due to the large number of covariates and the small sample size, we suggest that some of the covariates, such as blood cell count variables, could be excluded so that other covariates can be included for analysis and compensate for the small sample size to achieve multivariate analysis and obtain satisfactory results.

Third, from the data in the article,[1] the mean age in the TAC group was 55.94 (SD 1.72) years compared with 55.42 (SD 2.20) years in the TOF group. Although there was no statistically significant difference in the age of the patients in the 2 groups, the age was generally older. The impact on survival due to increasing age and the consequent complications such as diabetes, hypertension, and cardiovascular disease cannot be ignored. However, the information about the abovementioned complications is not stated in the text and it is not known whether they differed between the 2 groups. In addition, the authors mention at the end of the article that only a few patients had re-performed lung function tests. However, the main observation in this study was MDA5-ILD, and it was strongly associated with mortality events. Therefore, re-performed pulmonary function tests or even computed tomography (CT) lung examinations are important and necessary. It is not clear how many patients in both groups had re-performed lung CT tests and the imaging data on their pre- and posttreatment comparisons, which are actually more convincing for the efficacy of drug therapy.

Finally, we would like to thank Fan and colleagues again for their contributions[1] to the body of work on this disease and we look forward to hearing from them.

Gang Wang[1], MD
Ning Zhuo[2], MD
Jie Li[3], MD
Zhenhua Wen[1], MD
[1]Department of Rheumatology and Immunology, Zhuzhou Hospital Affiliated to Xiangya Medical College, Central South University, Zhuzhou;
[2]Department of Nephrology, The Second Xiangya Hospital of Central South University, Changsha;
[3]Department of Nephrology, Zhuzhou Hospital Affiliated to Xiangya Medical College, Central South University, Zhuzhou, Hunan, China.

The authors declare no conflicts of interest relevant to this article.

Address correspondence to Dr. Z. Wen, Department of Rheumatology and Immunology, Zhuzhou Hospital Affiliated to Xiangya Medical College, Central South University, Zhuzhou, Hunan, China.
Email: zhenhuawen2021@126.com.

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