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Correspondence

Reply: Correspondence Regarding the Article Titled "Low Lymphocyte Proportion in Bronchoalveolar Lavage Fluid as a Risk Factor Associated with the Change from Trimethoprim/sulfamethoxazole Used as First-Line Treatment for *Pneumocystis jirovecii* Pneumonia"

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Conflict of Interest
No conflicts of interest

▸ See the letter "Correspondence Regarding the Article Titled "Low Lymphocyte Proportion in Bronchoalveolar Lavage Fluid as a Risk Factor Associated with the Change from Trimethoprim/sulfamethoxazole Used as First-Line Treatment for Pneumocystis jirovecii Pneumonia"" in volume 50 on page 263.

Dear Editors:

We appreciated the interest and insightful comments regarding the article titled "Low lymphocyte proportion in bronchoalveolar lavage fluid as a risk factor associated with the change from trimethoprim/sulfamethoxazole used as first-line treatment for *Pneumocystis jirovecii* pneumonia" [1]. First, regardless of the reason for the change from trimethoprim/sulfamethoxazole (TMP/SMX), through our study, we wanted to reveal the risk factors associated with the changing of treatment regimens from TMP/SMX for *P. jirovecii* pneumonia (PCP) in a real-world case because patients who are likely to change medications may also consider using alternative regimens, such as clindamycin plus primaquine as first-line treatment [2]. As commented, composite outcomes may not be appropriate to draw relevant conclusions regarding the risk factors of treatment failure; severity, as one of the important prognostic factors [3], should be calibrated. Kim T et al, the correct proportion of patients categorized as having severe PCP according to the need for oxygen was 88.5% (23/26) among patients who failed to respond to TMP/SMX. In subgroup analysis including only patients with severe PCP (30 patients with first-line therapy success *vs.* 23 patients with first-line therapy failure), diabetes mellitus (adjusted odds ratio [OR], 27.24; 95% confidence interval [CI], 2.99–248.55) and bronchoalveolar lavage fluid (BALF) lymphocyte ≤45% (adjusted OR, 22.76; 95% CI, 2.15–240.43) were still significant risk factors. In this subgroup analysis, solid organ transplantation, hematologic malignancy, tacrolimus usage, diabetes mellitus, and BALF lymphocytes ≤45% were used for multivariate analysis. Second, because of the nature of the retrospective study, clinicians may have arbitrarily changed the regimen without

following the criteria for treatment failure. As experience with regard to PCP research has accumulated, judgment regarding treatment failure has been consistently made by the specialists on infectious diseases at Asan Medical Center. A prospective study design is a solution for overcoming this limitation. Third, diffuse ground-glass opacities were observed in all patients. Consolidation and pleural effusion were additional radiologic findings. Fourth, 21 patients with cytomegalovirus (CMV) co-infection were found to have viremia, and 5 of them had positive CMV cultures for BALF. Among the patients with CMV co-infection, only 14 (66.7%) received anti-CMV regimens. We have already published a report suggesting that anti-CMV therapy may not be mandatory for CMV co-infection in patients with PCP [4]. Lastly, the cut-off value of BALF lymphocyte proportion for binary logistic regression analysis was determined using a receiver-operating characteristic curve. The area under the curve for the BALF lymphocyte proportion being a predictor of treatment failure and/or adverse drug reactions (ADRs) was 0.679 (95% CI, 0.566–0.791). Of the 53 patients with BALF lymphocytes ≤45%, treatment failure and/or ADRs were found in only 23 (43.3%) patients. Therefore, it may not be appropriate to predict treatment failure and/or ADRs based only on BALF lymphocyte proportion. The choice of a primary treatment regimen other than TMP/SMX for PCP should be individually determined by considering the host factor and other risk factors. Owing to several limitations, we also recommend caution while applying the study results in real practice. However, we would like to emphasize the need to study the role of BALF lymphocytes in the treatment of PCP.

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