

Response to: 'Can we prescribe TMP/SMX prophylaxis without any concerns equally for all patients with rheumatic disease?' by Suyama and Okada

We deeply appreciate the comments by Suyama and Okada on our recent report regarding efficacy and safety of primary prophylaxis for pneumocystis pneumonia (PCP) using trimethoprim-sulfamethoxazole (TMP-SMX) in patients with rheumatic disease receiving prolonged, high-dose glucocorticoid treatment.^{1 2} They pointed out the possibility that patients with systemic lupus erythematosus (SLE) could have higher risk for adverse events related to TMP-SMX. They also indicated that discontinuation due to adverse events can be lowered by a graded administration strategy. In our cohort, the incidence rate of overall adverse drug reactions (ADR) was numerically higher in patients with SLE as compared with those with other rheumatic diseases, which is in line with the comment by Suyama and Okada (27.8 vs 16.6 per 100 person-years; incidence rate ratio 1.63, 95% CI 0.84 to 3.14). However, all ADRs in our SLE subgroup were mild to moderate in severity, and did not require urgent intervention or immediate discontinuation of TMP-SMX prophylaxis. Various clinical factors such as patient's ethnicity, concomitant medications or underlying rheumatic diseases can affect the frequency and seriousness of adverse events. However, we would like to remind that the previous studies reporting high adverse event rate of sulfa-antibiotics, which Suyama and Okada cited, were case-control studies and that most of the information was obtained by survey.³⁻⁵ In addition, there were no data on the severity of the adverse events. Considering high mortality and morbidity of PCP in rheumatic diseases, the risk benefit of TMP-SMX prophylaxis should be estimated by the incidence of adverse events and by their severity.

There remain many issues that need to be addressed before making a universal recommendation for primary PCP prophylaxis in patients with rheumatic diseases receiving high-dose glucocorticoids. An evidence-based, protocolised approach may be the first step. Establishment of the risk-benefit ratio of PCP prophylaxis for specific rheumatic diseases could then be a

logical next step, as Suyama and Okada suggested, and we thank them for their important comment.

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