Studies have also shown that T cell–dependent and T cell–independent vaccine responses are unaffected by tofacitinib (3,4). In one study, patients with rheumatoid arthritis receiving treatment with tofacitinib 10 mg twice a day (with or without methotrexate) were randomized to continue or to stop tofacitinib treatment 1 week prior and 1 week following immunization with the pneumococcal polyvalent-23 vaccine (PPV23) or the trivalent influenza vaccine (3). Antibody titers measured 35 days postimmunization were satisfactory in both the continue and hold groups for the PPV23 (75.0% and 84.6%, respectively [T cell–independent response]) and the influenza vaccine (66.3% and 63.7%, respectively [T cell–dependent response]) (3). In another study, patients with psoriasis receiving treatment with tofacitinib 10 mg twice a day demonstrated a robust vaccine response to T cell–dependent tetanus toxoid (88%) and T cell–dependent 13-valent conjugate pneumococcal vaccines (80%) (4).

As with any clinical decision, risk–benefit analysis for each patient includes consideration of the potential for disease flares. In the aforementioned study, tofacitinib treatment interruption led to a steady increase in disease activity scores compared with continuous treatment (Figure 1) (5). Therefore, in addition to the ACR guidelines, we encourage clinicians to consider the above data during shared decision-making with patients when advising on medication management in the context of COVID vaccination.

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Reply

To the Editor:

We appreciate the comment by Dr. Mortezavi and colleagues describing COVID-19 vaccine response and the frequency of disease worsening in patients receiving tofacitinib. The ACR COVID-19 Vaccine Clinical Guidance Task Force was aware of the 2 studies cited and appreciate their summary of the results. We would point out that in the rheumatoid arthritis study by Winthrop et al (1), patients receiving tofacitinib in Study A had a lower likelihood of a satisfactory response to pneumococcal vaccination (45.1%) compared to placebo-treated patients (68.4%), a difference of 23.3% (95% confidence interval [95% CI] −36.6, −9.6). The differences were numerically even larger for patients receiving concomitant tofacitinib and methotrexate (31.6% of patients with a satisfactory response, difference of −30.2% [95% CI] −47.3, −11.4) compared to methotrexate monotherapy. Our challenge was in considering the appropriateness of extrapolating results from vaccine studies of influenza, pneumococcal, and tetanus toxoid vaccines to make inferences regarding the anticipated response to vaccination against SARS–CoV-2, a novel antigen to which most individuals have not previously been exposed.

The Task Force recognized that infection rates, and perhaps response to vaccinations against those infections, might be heterogeneous according to pathogen. For example, JAK inhibitors approximately double the incidence of herpes zoster compared to biologics such as tumor necrosis factor inhibitors, yet they do not meaningfully increase rates of other infections (e.g., pneumonia) (1–3). We noted that in the Oral Strategy study, adalimumab-treated patients receiving vaccination with the live herpes zoster vaccine had lower incidence rates of herpes zoster (0.0 per 100 patient-years) compared to nonvaccinated patients (incidence rate 2.1 per 100 patient-years) (4). In contrast, and recognizing that numbers were small, tofacitinib-treated patients had similar rates of herpes zoster regardless of vaccination (incidence rate 3.0 per 100 patient-years in vaccinated versus 2.2 per 100 patient-years in nonvaccinated patients).

We also appreciate the data provided by Dr. Mortezavi and colleagues regarding the rate of disease worsening in patients whose treatment with tofacitinib was briefly interrupted. At ~2 weeks, the mean worsening in the 4-variable DAS28 of 0.7 units was of smaller magnitude than typically considered the minimum clinically important difference (MCID) for the DAS28 (i.e., >1.2

units) (5). The MCID for defining disease worsening using the Clinical Disease Activity Index (CDAI) in patients who had moderate disease activity at the start of treatment is undefined, although a 1-unit change in each of the 4 CDAI components (tender joint count, swollen joint count, patient global assessment, and physician global assessment) is often considered to be the measurement error for each of these (6). Taken together, the mean amount of disease worsening associated with brief interruptions in therapy seems small and likely not of clinical importance for most patients, especially in light of the guidance recommending that JAK inhibitors be withheld for 1 week at the time of each vaccine administration, rather than for 2 consecutive weeks.

Ultimately, we await prospective data regarding the influence of JAK inhibitors and other immunomodulatory therapies used at the time of COVID-19 vaccination on immunogenicity and correlates of serologic protection. Since the ACR COVID-19 Vaccine Guidance is a living document, our plan is to rapidly update it and incorporate new evidence as it accumulates.

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Are there thresholds of conflict of interest with gifts from industry? Comment on the article by Wayant et al

To the Editor:

I would like to thank Dr. Wayant and colleagues for their analysis of financial conflicts of interest among physician-authors of American College of Rheumatology clinical practice guidelines (1). Given the known challenges with the Open Payments Database, as was described in their evaluation, I am curious if the data show a natural demarcation between small gifts and significantly larger gifts. While there are not defined levels of conflict of interest, I would like to know if the data suggested that there may be a threshold for authors with small gifts (for example, <$200 for smaller gifts and ≥$500 for larger gifts). The data may better define thresholds of conflict of interest. A gift with an estimated value of <$200 on a $200,000 physician salary would likely carry less influence than a $10,000 gift. A scatterplot with linear or logged y-axis for gift amount may be instructive. I would be grateful if Dr. Wayant and colleagues could provide this analysis to supplement their article.

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