Assessment, Development, and Evaluation methodology, which they used to develop these guidelines. The section on management of high-risk comorbidities includes strong recommendations for managing hepatitis B virus (HBV) and HCV infection and endorses the use of immunosuppressive therapy when prophylactic antiviral therapy is administered. Although we wholeheartedly agree with those recommendations, we were disappointed that no changes from the 2008 ACR recommendations (2) were put forth regarding screening for HBV (and accordingly HCV). We suggest that because the standards of screening and preventing HBV reactivation have changed dramatically, the ACR guidelines are accordingly overdue for changes.

The 2008 ACR guidelines (2) suggested screening for HBV when administering methotrexate and leflunomide and in patients at high risk of acquiring HBV infection (e.g., engaging in parenteral drug use or high-risk sexual activity). In 2010, we proposed that it was time to change these guidelines to include a more liberal policy that, at the minimum, would include screening prior to initiation of biologic therapy (3). Since that time, a Boxed Warning regarding HBV reactivation has been added to the prescribing information for the biologic agent rituximab (4). Screening for HBV infection prior to initiating treatment with rituximab is now mandatory, which serves as evidence of the veracity of screening before beginning treatment with a biologic agent. It also should be noted that the ACR guidelines have been out of step with the 2008 Centers for Disease Control and Prevention Guidelines (5), which recommended screening of all patients scheduled to receive immunosuppressive medications.

Finally, we draw attention to a key meeting in early 2014 that was sponsored by the American Association for the Study of Liver Diseases (AASLD) with support from the American Academy of Dermatology, the American Society of Clinical Oncology, and the ACR at which one of the authors (LHC) presented the concerns of the rheumatology community. An article synthesizing the recommendations from this workshop, enhanced by a systematic review of the literature and crafted by an expert panel of world-renowned hepatologists, was published online in January 2015 and in print in February 2015 (6). In this article, the authors again assert that there is "good evidence to support routine screening of all patients prior to undergoing chemotherapy or immunosuppressive therapy." Gone are caveats regarding high-risk behavior, the geographic origin of patients (e.g., areas with a high prevalence of infection), and the precise immunosuppressive agent. The authors simply state that when immunosuppressive therapy is being contemplated, screening should be performed. In an elegant editorial published in 2012, Lok and colleagues summarized the challenges posed and solutions needed in the title, "Reactivation of hepatitis B during immunosuppressive therapy: potentially fatal yet preventable" (7). The opinion piece was a call to arms to increase screening and prevention, and we strongly believe it is time for the ACR to align itself with these changes.

Although we understand the rigor of the process that has gone into developing the ACR guidelines, we must also question whether such a process is adequate to keep pace with important treatment issues especially in terms of safety, where the publishing of even a few instances of a rare complication (e.g., progressive multifocal leukoencephalopathy) can generate letters from regulatory agencies to health care providers. Perhaps we should take note of other organizations similarly generating guidelines in fast-changing fields. We would like to draw attention in particular to the HCV treatment guidelines published by the AASLD and the Infectious Disease Society of America (8). These organizations now use a web-based process for the rapid formulation and dissemination of evidence-based, expert-developed recommendations and in fact explicitly state that "static versions" (i.e., printouts, slides, etc.) may be outdated and urge practitioners to review the evidence provided on the web site. Guidelines are being increasingly scrutinized and need to be assessed for their efficacy and cost effectiveness (9). It has been suggested that increased efficiency in guideline utilization (e.g., HBV/HCV screening) may be enhanced by attempts to construct common themes across guidelines. This could be achieved if all organizations involved in the treatment of patients with immunosuppression or receiving immunosuppressive therapy could actually agree on and disseminate a cohesive front.

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Recommendations in the American College of Rheumatology guideline for the treatment of rheumatoid arthritis related to the use of biologic agents in patients with a history of cancer need reconsideration: comment on the article by Singh et al

To the Editor:

There are important problems in the American College of Rheumatology (ACR) 2015 guideline for the treatment of

rheumatoid arthritis (RA) (1) related to the use of biologic agents to treat patients with a history of neoplasm. According to the ACR guideline, a patient with a lymphoproliferative disorder should be treated with traditional disease-modifying antirheumatic drugs, with or without the addition of abatacept or tocilizumab. Information from one of the references (2) cited in the article, suggesting that a higher cumulative methotrexate dose was associated with more lymphoproliferative disease in patients with RA, was taken out of context. The guideline also recommends that the presence of a previously treated solid cancer should not affect the decision to initiate treatment with a biologic agent. Both of the related references (3,4) refer to observational studies in relatively few patients (<200). In those articles, the authors had duly advised caution when interpreting their data, but this is not adequately reflected in the guideline. In the study by Raaschou et al (4) the anti–tumor necrosis factor (anti-TNF) treatments were started a median of 9 years after diagnosis of the initial cancer. At the least, a time frame after which patients with previous cancer could be started on treatment with a biologic agent could have been included in the new guideline.

Based on observational studies comparing the observed cancer incidence in an RA cohort with that reported in a national cancer registry, it has also been stated that treatment with a biologic agent does not appreciably increase the incidence of neoplasms among RA patients (5,6). However, as we recently pointed out, there has been a common methodologic error in such comparisons (7). There are 3 important considerations. First, one-sixth of cancer patients have a second or a higher-order primary cancer (8). Second, national cancer registries such as SEER (Surveillance, Epidemiology, and End Results) do not differentiate between a first primary cancer and second or higher-order primary cancer in their cancer incidence rates in the general population (9). Finally, the majority of RA patients, especially those who have been treated with an anti-TNF agent, do not have a history of cancer (3). These observations add up to the fact that there is a definite "depletion of susceptible bias" (10) when one compares the cancer incidence in a cohort of patients treated with anti-TNF agents with that in the general population, due to the fact that the second or higher-order cancers are almost always represented only in the denominator of a standardized incidence ratio.

Thus, we believe that the new ACR guideline for treating RA is too liberal in its interpretation of solid cancer harm as related particularly to anti-TNF agents. This needs immediate reconsideration.

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Reply

To the Editor:

In his letter, Dr. Conn raises concerns regarding the positioning of low-dose oral glucocorticoids in the treatment of patients with RA. It is worth noting that this is the first time that ACR RA guidelines, which have in the past focused on the use of traditional and biologic DMARDs, have included glucocorticoids. The decision to include glucocorticoids in the treatment of both early and established RA was prompted by important feedback previously received from Dr. Conn, members of the ACR, and the international arthritis community (1,2), as well as the accumulating evidence supporting the benefits of short-term, low-dose glucocorticoid therapy concurrent with the use of DMARDs in patients with RA.

Dr. Conn infers that Figure 2 in the 2015 ACR guideline article showing early RA management mandates a rigid sequence of therapeutic options for early RA, including the use of glucocorticoids; however, it is the intent of this guideline to suggest the addition of glucocorticoid treatment at any time after the initial use of a DMARD if disease activity remains moderate or high (see Figure 3 in the article). For established RA, the recommendations for the use of glucocorticoids are similar. Figure 5 in the 2015 ACR guideline shows the recommended flow of treatment in patients with established RA, suggesting that glucocorticoids are a good therapeutic option at any point after initial DMARD monotherapy fails to adequately lower disease activity below the moderate level. Glucocorti-