LETTERS TO THE EDITOR

Readers are encouraged to write letters to the editor concerning articles that have been published in Clinical Gastroenterology and Hepatology. Short, general comments are also considered, but use of the Letters to the Editor section for publication of original data in preliminary form is not encouraged. Letters should be typewritten and submitted electronically to http://www.editorialmanager.com/cgh.

Should Nivolumab-Induced Colitis Be Treated by Infliximab?

Dear Editor:

We read with interest the case described by Yanai et al[1] in which these investigators described a patient who developed ulcerative colitis under uveal melanoma-indicated nivolumab therapy. Nivolumab is an immunologic check-point inhibitor that combats oncologic disease by removing regulatory control on the T-cell compartment and thus up-regulating cytotoxic T-cell–mediated antitumor immunity. The resulting up-regulation of T-cell immunity, however, can be accompanied by autoimmunity, and colitis is especially a side effect of immune check-point inhibition.[2] In the described case the colitis was managed successfully by infliximab therapy.

Anti–tumor necrosis factor (TNF)-α medication in general and infliximab in particular has revolutionized the treatment of inflammatory bowel disease. Intriguingly, however, infliximab does not counteract colitis through neutralization of soluble TNF-α, as also evident from the failure of the anti-TNF-α medication etanercept to control colitis.[3] In contrast, infliximab binds directly to membrane-bound TNF-α on lymphocytes and causes T-cell apoptosis.[4] Indeed, the clinical efficacy of infliximab shows a strict correlation with T-lymphocyte apoptosis in patients in vivo.[5] Therefore, infliximab should be expected to counteract the clinical effect of nivolumab in oncologic disease by impairing T-cell–mediated immunity. Hence, infliximab thus is not a rational choice for counteracting nivolumab-induced colitis.

There are other options to manage nivolumab-associated colitis available that do not interfere with nivolumab-mediated anticancer immunity (eg, vedolizumab). However, we also would like to point to the study by Kubo et al[6] that documented the efficacy of mesalazine in controlling nivolumab-associated colitis. Mesalazine is safe, inexpensive, and is not expected to counteract nivolumab-induced anticancer immunity. If the observations of Kubo et al[6] are confirmed, mesalazine would constitute a superior alternative to infliximab.

MENG LI
QIUWEI PAN, PhD
MAIKEL P. PEPPELENBOSCH, MD
Department of Gastroenterology and Hepatology
Erasmus MC
Erasmus University of Rotterdam
Rotterdam, The Netherlands

References

1. Yanai S, et al. Clin Gastroenterol Hepatol 2017;15:e80–e81.
2. Postow MA. Am Soc Clin Oncol Educ Book 2015;35:76–83.
3. Sandborn WJ, et al. Gastroenterology 2001;121:1088–1094.
4. Van den Brande JM, et al. Gastroenterology 2003;124:1774–1785.
5. Van den Brande JM, et al. Gut 2007;56:509–517.
6. Kubo K, et al. Clin Gastroenterol Hepatol 2017. Epub ahead of print.

Conflicts of interest
The authors disclose no conflicts.

Most current article

http://dx.doi.org/10.1016/j.cgh.2017.05.012

Reply. We read with interest the comments by Li et al.[1] Our reported case developed corticosteroid-resistant, severely active, nivolumab-induced colitis.[2] Our initial treatment with intravenous corticosteroids (1000 mg methylprednisolone) for 3 days followed by oral prednisolone (90 mg/d) for 2 weeks was ineffective. We therefore started intravenous administration of infliximab, which resulted in resolution of both the patient's symptoms and colonoscopic findings.[2] Pagès et al[3] and Marthey et al[4] also reported that infliximab was effective for corticosteroid-resistant immune checkpoint inhibitor–induced severe colitis. We believe that treatment with mesalazine would not be effective in such patients.

By contrast, the case of nivolumab-associated colitis reported by Kubo et al[5] seemed less severe. The colonoscopic images showed mild to moderate active colitis, and the histologic picture of a biopsy specimen showed only mild inflammation without any crypt abscesses.[5] We agree that mesalazine should be tried in cases of mild or moderately active nivolumab-induced colitis.

We believe that the treatment strategy for immune checkpoint inhibitor (including nivolumab)–induced colitis should be determined by the clinical, endoscopic, and histopathologic severity of the colitis.

SHUNICHI YANAI, MD
SHOTARO NAKAMURA, MD
TAKAYUKI MATSUMOTO, MD
Division of Gastroenterology
Department of Internal Medicine
School of Medicine, Iwate Medical University
Morioka, Japan