worse outcomes than outcomes after colectomy, and the ability to undergo reanastomosis after recovery is a benefit of an intact colon. Although data are lacking on which surgical technique offers the best survival and long-term outcomes, we would argue that this question is secondary to the question of how best to predict which patients will not have a response to antibiotic therapy and would benefit from surgery before becoming critically ill. Recently published results of a study on predicting severe *Clostridium difficile* infection may help to inform this difficult clinical decision.5

Daniel A. Leffler, M.D.
J. Thomas Lamont, M.D.
Beth Israel Deaconess Medical Center
Boston, MA
dleffler@bidmc.harvard.edu

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**Anti–PD-1–Related Pneumonitis during Cancer Immunotherapy**

**TO THE EDITOR:** The use of antibodies against programmed cell death 1 (PD-1), which block inhibitory T-cell checkpoints, is a promising new therapy for advanced cancers.1 Recent trials have shown substantial clinical activity of anti–PD-1 antibodies in advanced cancers and led to the approvals of these agents, including pembrolizumab for melanoma and nivolumab for melanoma and squamous-cell lung cancer.2–4 Pneumonitis related to the use of antibodies against PD-1 is an immune-mediated toxic effect that resulted in three drug-related deaths in a phase 1 trial.1 Clinical identification and management of pneumonitis are contingent on radiographic assessment. We report three cases of pneumonitis associated with the use of anti–PD-1 antibodies in patients with melanoma.

A 70-year-old man (Patient 1) received nivolumab and ipilimumab sequentially. A 38-year-old woman (Patient 2) and a 58-year-old man (Patient 3) were treated with nivolumab alone; Patient 2 had previously received ipilimumab before starting the nivolumab trial. The onset of pneumonitis occurred 7.4 to 24.3 months after the initiation of therapy (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Computed tomographic (CT) imaging of pneumonitis at the time of diagnosis showed a spectrum of findings that are typically seen in interstitial pneumonias.5 These conditions were morphologically classified as acute interstitial pneumonia–acute respiratory distress syndrome (ARDS) in Patients 1 and 2 and as nonspecific interstitial pneumonia in Patient 3 (Table S2 in the Supplementary Appendix).

In Patients 1 and 2 with ARDS-pattern pneumonitis, diffuse ground-glass opacities, reticular opacities, consolidation, and traction bronchiectasis involved all lobes, with decreased lung volumes and effusions (Fig. 1A, 1B, and 1C). In Patient 1, the symptoms rapidly progressed during the 2 weeks before the diagnosis (Fig. 1A and 1B). The two patients were admitted to the intensive care unit and received intravenous antibiotic agents, glucocorticoids, and infliximab. Patient 1 required intubation, and his condition improved over the course of 10 weeks. Patient 2 died 4 weeks after the diagnosis of pneumonitis.

Patient 3 had ground-glass opacities and reticular opacities in the peripheral and lower lungs, indicative of nonspecific interstitial pneumonia (Fig. 1D). He discontinued nivolumab for 8 weeks and received oral glucocorticoids as an outpatient, and the pneumonitis resolved after


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2 weeks. The patient restarted nivolumab and has completed the 2-year treatment period with 12 cycles; he is currently participating in the follow-up period of the trial. He remains progression-free from melanoma, with no recurrent pneumonitis for 39 months.

The clinical oncology community has rapidly expanding access to a variety of immunotherapeutic agents for the treatment of several types of cancers. Thus, knowledge of the spectrum of manifestations of autoimmune pneumonitis may assist other clinicians in managing this rare but potentially serious toxic effect.

Mizuki Nishino, M.D.
Lynette M. Sholl, M.D.
F. Stephen Hodi, M.D.
Dana–Farber/Brigham and Women’s Cancer Center
Boston, MA
mizuki_nishino@dfci.harvard.edu

and Others

Figure 1. CT of the Chest Performed in Three Patients with Pneumonitis Associated with the Use of Anti–Programmed Cell Death 1 Antibodies.

In Patient 1, a 70-year-old man with advanced melanoma who was treated in a trial of nivolumab given sequentially with ipilimumab, chest CT at 22 weeks of therapy revealed consolidation in the bilateral lower lobes with reticular and ground-glass opacities (Panel A, arrows). Two weeks later, the findings significantly progressed (Panel B, asterisks) and involved all lobes, with decreased lung volumes and pleural effusion. In Patient 2, a 38-year-old woman with advanced melanoma who was treated with nivolumab, chest CT at 15 weeks of therapy revealed diffuse ground-glass opacities, reticular opacities, consolidations, traction bronchiectasis, and areas of centrilobular nodularity (Panel C) involving all lobes and more than 50% of all lung zones, with decreased lung volumes. In Patient 3, a 58-year-old man with advanced melanoma who was treated with nivolumab, chest CT at 7 weeks of therapy revealed bilateral ground-glass opacities, reticular opacities, and small areas of consolidation in predominantly lower and peripheral distribution (Panel D, arrows), indicative of a pattern of nonspecific interstitial pneumonia.
TO THE EDITOR: We previously reported 4-month culture conversion rates among patients with chronic extensively drug-resistant tuberculosis (XDR-TB) who received linezolid.\(^1\) By 4 months, 15 of 19 patients (79%) in the immediate-start group and 7 of 20 (35%) in the delayed-start group had conversion to a negative sputum culture (P=0.001). After 6 months of linezolid treatment, 34 of 39 patients (87%) had negative sputum cultures. Here, we report final study outcomes for these patients 1 year after the end of treatment, 36 months after they began the study.

Among 39 patients who were enrolled in this trial, 38 received linezolid. Of these patients, 27 had negative results on sputum culture 1 year after the end of treatment, 3 were lost to follow-up, and 8 withdrew before the end of the study, including the 4 patients in whom linezolid failed, as reported previously. The median duration of tuberculosis treatment was 789 days overall, with 781 days of linezolid. Final regimens included any remaining active second-line drugs (as described in the Supplementary Appendix of our original article, available with the full text of the article at NEJM.org).

Among the 27 patients who completed the study, 4 had a dose reduction from 600 mg to 300 mg of linezolid per day before the second randomization. Among the 13 patients who were assigned to continue receiving the 600-mg dose, 9 had a subsequent reduction in the dose to 300 mg. All the dose reductions were due to tumor remission, and long-term safety in patients with advanced melanoma receiving nivolumab. J Clin Oncol 2014;32:1020-30.


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