Background: Programmed death-1 (PD-1) immune checkpoint inhibitors are novel immuno-oncology agents. Unlike chemotherapy or targeted agents, which inhibit tumor cell proliferation or induce tumor cell death, immune checkpoint inhibitors are designed to stimulate a patient’s own immune system to eliminate tumors. As a result of their mechanism of action, PD-1 pathway inhibitors are associated with adverse events (AEs) with immunologic etiologies, termed immune-mediated AEs (imAEs). These include skin and gastrointestinal AEs, and endocrine, hepatic, renal, and respiratory AEs, including pneumonitis. Most imAEs can be effectively managed with treatment interruption/discontinuation and/or steroids or other immunosuppressive agents. A specialist consult may be required in some cases, and endocrine imAEs may require permanent hormone replacement therapy.

Objectives: This article provides an overview of PD-1 inhibitors, including the potential mechanism of action, key clinical trial data, and strategies for managing patients who may receive PD-1 inhibitors for the treatment of non-small cell lung cancer.

Methods: Information in the article comes from PubMed literature searches and the author’s experience with these agents in clinical trials.

Findings: Oncology clinicians must thoroughly assess baseline functioning and symptoms and be vigilant for imAEs, which require prompt diagnosis and management. A good understanding of the clinical profile of PD-1 pathway inhibitors is instrumental in helping clinicians manage patients receiving these new therapies.

Colleen Lewis, MSN, ANP-BC, AOCNP®, is a nurse practitioner for the Phase I Clinical Trial Program at the Emory University Winship Cancer Institute in Atlanta, GA. The author takes full responsibility for the content of the article. Writing and editorial support was provided by Britt Anderson, PhD, and Lisa Sullivan, MA, CMPP, at StemScientific, an Ashfield company, through support from Bristol-Myers Squibb. Lewis received personal fees from Array BioPharma, outside of the submitted work. The content of this article has been reviewed by independent peer reviewers to ensure that it is balanced, objective, and free from commercial bias. No financial relationships relevant to the content of this article have been disclosed by the independent peer reviewers or editorial staff. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society. Lewis can be reached at colleen.lewis@emoryhealthcare.org, with copy to editor at CJONEditor@ons.org. (Submitted April 2015. Revision submitted August 2015. Accepted for publication August 23, 2015.)

Key words: immune checkpoint blockade; PD-1; immuno-oncology; nivolumab; pembrolizumab

Digital Object Identifier: 10.1188/16.CJON.319-326

The immune system has the ability to recognize and eliminate tumors, as evidenced by greater cancer incidence in patients with reduced immune function (Grulich, van Leeuwen, Falster, & Vajdic, 2007). Tumors can evade an effective anti-tumor immune response by creating an immunosuppressive microenvironment (Jadus et al., 2012). One key mechanism that tumors use to evade immune responses occurs via effects on immune checkpoint pathways (Nirschl & Drake, 2013). Programmed death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) are immune checkpoint receptors expressed by activated T cells. When PD-1 or CTLA-4 binds one of its ligands, T-cell proliferation and activation is prevented, suppressing T-cell function. Human tumors can express the
ligands for PD-1, programmed death-ligand 1 (PD-L1), or programmed death-ligand 2 (PD-L2) as a mechanism to avoid antitumor T-cell immune responses (Rozali, Hato, Robinson, Lake, & Lesterhuis, 2012; Tauer et al., 2014; Zou & Chen, 2008). PD-L1 expression is associated with worse outcomes in some tumor types, including lung cancer (Azuma et al., 2014; Zhang et al., 2014; Zou & Chen, 2008). Ipilimumab (Yervoy®), which targets CTLA-4, was the first U.S. Food and Drug Administration (FDA)-approved immuno-oncology agent. Numerous agents designed to block PD-1-pathway-mediated inhibition have been approved or are in late-stage clinical development (Nirschl & Drake, 2013; Shih, Arkenau, & Infante, 2014). This review primarily will focus on non-small cell lung cancer (NSCLC) because PD-1 pathway inhibition in melanoma and renal cell carcinoma has been covered in detail elsewhere (Kannan, Madden, & Andrews, 2014; Tripathi, Drake, & Harshman, 2014).

**Programmed Death-1 Pathway Immune Checkpoint Inhibitors**

PD-1 pathway immune checkpoint inhibitor monoclonal antibodies are designed to prevent suppression of T-cell activity to restore antitumor immune responses (see Figure 1). Approved inhibitors targeting the PD-1 receptor are the monoclonal antibodies nivolumab (Opdivo®) and pembrolizumab (Keytruda®). Nivolumab and pembrolizumab are approved by the FDA for the treatment of metastatic NSCLC with progression on or after platinum-based chemotherapy and for the treatment of unresectable or metastatic melanoma (Bristol-Myers Squibb, 2016; Merck, 2015b). Nivolumab also is approved for patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy (Bristol-Myers Squibb, 2016). Inhibitors targeting the PD-L1 ligand are in development (Shih et al., 2014); none are approved for cancer treatment.

**Clinical Activity**

PD-1 pathway inhibitors offer promise to patients with limited treatment options. Some patients who have failed two or more prior therapies have had responses with PD-1 pathway inhibitors (Rizvi, Mazières, et al., 2015). In contrast to chemotherapy and targeted agents, responses to PD-1 pathway inhibitors can last two or more years (Gettinger et al., 2015). Superior survival with PD-1 inhibitors versus standard of care chemotherapy has been documented in advanced NSCLC (Borghaei et al. 2016; Brahmer et al., 2015). The antitumor activity of nivolumab and pembrolizumab observed in key NSCLC trials is summarized in Table 1.

Combinations of immune checkpoint inhibitors are being tested, with phase II and III trial data from patients with melanoma recently being published (Larkin et al., 2015; Postow et al., 2015). In the phase III trial, progression-free survival with nivolumab plus ipilimumab was significantly longer than with ipilimumab monotherapy; progression-free survival also was longer with nivolumab alone than with ipilimumab alone. However, improved efficacy with the combination was associated with greater toxicity. Preliminary data in patients with advanced NSCLC suggest that combining nivolumab and ipilimumab also is feasible in this population, producing durable responses in some patients (Antonia et al., 2014). Trials combining PD-1 pathway inhibitors with chemotherapy and targeted agents in multiple tumor types also are underway (www.clinicaltrials.gov).

Because immune checkpoint inhibitors stimulate immune responses, they may be associated with novel response patterns. Although most responses are seen at the first scan (typically at 8–12 weeks), delayed responses, occurring more than three months after starting treatment, also have been reported (Garon et al., 2014; Gettinger et al., 2015; Herbst et al., 2014). The time to first response with pembrolizumab in patients with NSCLC ranged from 6–31 weeks, and 50% of responding patients with NSCLC receiving nivolumab did so by the first assessment (eight weeks) (Garon et al., 2014; Gettinger et al., 2015).

The majority of responding patients in clinical trials (about 90%–95%) have conventional responses, according to Response Evaluation Criteria In Solid Tumors (RECIST) (Eisenhauer et al., 2009); however, a subset may have unconventional responses, including pseudoprogression (initial evidence of tumor progression followed by clinical benefit) (Gettinger et al., 2015; Herbst et al., 2014; Topalian et al., 2012). The increase in tumor burden after starting therapy can result from true tumor progression.
TABLE 1. Efficacy and Safety of Programmed Death-1 Immune Checkpoint Inhibitors Nivolumab and Pembrolizumab in Key NSCLC Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Cancer Type and Trial Phase</th>
<th>Agents</th>
<th>Objective Response Rate</th>
<th>Response Duration</th>
<th>Stable Disease</th>
<th>Survival</th>
<th>Treatment-Related Grade 3–4 AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borghesi et al., 2015</td>
<td>Previously treated non-squamous NSCLC; phase III trial</td>
<td>Nivolumab 3 mg/kg (n = 292) versus docetaxel 75 mg/m² BSA (n = 290)</td>
<td>Nivolumab: 19%, docetaxel: 12%</td>
<td>Nivolumab: median = 17.2 months (range = 1.8–22.6); docetaxel: median = 5.6 months (range = 1.2–15.2)</td>
<td>Nivolumab: 25%, docetaxel: 42%</td>
<td>OS (95% CI [9.7, 15]): nivolumab: median = 12.2 months; OS (95% CI [8.1, 10.7]): docetaxel: median = 9.4 months</td>
<td>Nivolumab: 10%, docetaxel: 54%</td>
</tr>
<tr>
<td>Brahmer et al., 2015</td>
<td>Previously treated squamous NSCLC; phase III trial</td>
<td>Nivolumab 3 mg/kg (n = 135) versus docetaxel 75 mg/m² BSA (n = 137)</td>
<td>Nivolumab: 20%, docetaxel: 9%</td>
<td>Nivolumab: NR (2.9–20.5 months); docetaxel: median = 8.4 months (range = 1.4–15.2)</td>
<td>Nivolumab: 29%, docetaxel: 34%</td>
<td>OS (95% CI [7.3, 13.3]): nivolumab: median = 9.2 months; OS (95% CI [5.1, 7.3]): docetaxel: median = 6 months</td>
<td>Nivolumab: 7%, docetaxel: 55%</td>
</tr>
<tr>
<td>Garon et al., 2015</td>
<td>Advanced NSCLC; phase I trial</td>
<td>Pembrolizumab (various doses)</td>
<td>Median = 12.5 months (range = 1–23.3)</td>
<td>22%</td>
<td>PFS (95% CI [2.9, 4.1]): median = 3.7 months; OS (95% CI [9.3, 14.7]): median = 12 months</td>
<td>9%</td>
<td></td>
</tr>
</tbody>
</table>

* Ongoing response
AE—adverse event; BSA—body surface area; CI—confidence interval; NR—not reached; NSCLC—non-small cell lung cancer; OS—overall survival; PFS—progression-free survival

Management of Immune-Mediated Adverse Events With Programmed Death-1 Pathway Immune Checkpoint Inhibitors

Because immune checkpoint inhibitors act by stimulating immune responses, they may be associated with AEs with immune etiologies. These immune-mediated AEs (imAEs) can occur at any time during treatment or even after treatment cessation. The most commonly reported imAEs in patients with NSCLC include rash/pruritus, diarrhea, and endocrinopathies. Pneumonitis caused the death of three patients with NSCLC in the phase I nivolumab trial (Gettinger et al., 2015). Across trials, rates of pneumonitis were 7% or less (all grades), 3% or less of events classified as grade 3 or greater. Infusion-related AEs with PD-1 inhibitors were uncommon in initial trials with patients with NSCLC (3%–4% for all grades, 1% or less for grades 3–4) (Garon et al., 2015; Gettinger et al., 2015).

Safety Profile

PD-1 immune checkpoint inhibitors have a more favorable toxicity profile than conventional chemotherapy and targeted agents. Commonly reported adverse events (AEs) in NSCLC trials of PD-1 immune checkpoint inhibitors are shown in Table 3. The incidence of treatment-related AEs grade 3 and greater in key NSCLC trials of PD-1 immune checkpoint inhibitors ranged from 7%–10%, which was lower than what was reported in many trials of chemotherapy or targeted agents.

PD-1 inhibitors are generally well tolerated, but imAEs can occur and should be managed appropriately. Most imAEs are managed with treatment delay or discontinuation of treatment and the addition of steroids (Topalian et al., 2012) (see Table 4). For mild imAEs, lower doses of steroids (e.g., methylprednisolone [Medrol®] 0.5–1 mg per kg per day) should be considered. However, high-dose steroids (1–2 mg per kg per day) may be needed for more severe imAEs and a prolonged steroid taper may be required for complete resolution. Consulting a specialist

or, possibly, from an influx of tumor-infiltrating immune cells mounting an antitumor immune response. In melanoma studies, patients with unconventional responses had overall survival similar to that of patients with conventional responses (Hodi et al., 2016). Therefore, continued treatment may be considered in the context of initial evidence of progression with other clinical parameters showing benefit.

Once achieved, most responses are durable. In patients with NSCLC, the median duration of response with nivolumab and pembrolizumab was more than one year (Garon et al., 2015; Gettinger et al., 2015) (see Table 2). Trials of these and other PD-1 pathway inhibitors with shorter follow-up have reported ongoing responses, some lasting more than one year in various tumor types, including NSCLC (Herbst et al., 2014; Brahmer et al., 2015). Responses also can persist in patients who have discontinued therapy for reasons other than progression, indicating an ongoing antitumor immune response (Gettinger et al., 2015; Herbst et al., 2014).
with expertise in the organ system affected is recommended in the case of moderate to severe AEs.

The most experience in managing imAEs with PD-1 inhibitors comes from nivolumab trials. Management algorithms have been published for nivolumab and pembrolizumab, and online resources are available for nivolumab and pembrolizumab (Bristol-Myers Squibb, 2015; Merck, 2015a; Robert et al., 2014). In a nivolumab trial in squamous NSCLC, eight of nine nonendocrine imAEs completely resolved using these management strategies; however, most patients with endocrinopathies required permanent hormone replacement (Bristol-Myers Squibb, 2015b). In trials of patients with previously treated melanoma receiving pembrolizumab or nivolumab, the investigators reported that most imAEs resolved with appropriate management (Bristol-Myers Squibb, 2015; Merck, 2015a; Robert et al., 2014). In a nivolumab trial in squamous NSCLC, eight of nine nonendocrine imAEs completely resolved using these management strategies; however, most patients with endocrinopathies required permanent hormone replacement (Bristol-Myers Squibb, 2015b).

Endocrinopathies typically are managed using hormone replacement; however, some cases may be irreversible and require permanent hormone replacement (Fecher, Agarwala, Hodi, & Weber, 2013; Rubin, 2012; Topalian et al., 2012). Patients should have their thyroid-stimulating hormone levels checked prior to treatment and periodically during treatment to assess for any emerging changes. Changes in thyroid-stimulating hormone can occur in the absence of symptoms and may require appropriate treatment to ensure normalization. No dose adjustments of nivolumab are recommended in the event of hypothyroidism or hyperthyroidism (Bristol-Myers Squibb, 2015, 2016).

Rash and/or pruritus can occur with PD-1 inhibitors. If patients report new-onset mild itching or rash, a thorough evaluation of possible causes should occur because causes for a rash may be unrelated to treatment, such as new medications, new skin products, or exposure to irritants. If the symptoms are mild, treatment can continue; the use of mild moisturizers and, if needed, over-the-counter hydrocortisone cream, can be encouraged. If symptoms worsen or become bothersome, treatment should be delayed and skin biopsy considered. If severe rash occurs, oral steroids are indicated.

If patients report new gastrointestinal complaints, such as diarrhea or abdominal pain, all possible causes should be considered. Once infection is ruled out, steroids may need to be started while the workup is ongoing if an imAE is suspected. Treatment should be delayed until resolution of symptoms. Having a point of contact within a gastrointestinal team or hospital who can ensure timely ordering of flexible sigmoidoscopy for patients with suspected colitis is helpful. Infliximab (Remicade®) may be used to treat colitis not responding to steroids. Any worsening in respiratory symptoms must be evaluated promptly to rule out pneumonitis and to treat it if present. Patients with any evidence of pneumonitis on imaging should have treatment held and steroids started. If symptoms do not improve with starting doses of steroids, the pulmonary team should be consulted and steroid doses increased. On improvement of symptoms, steroids should be tapered over a longer period of time, ranging from weeks to months, depending on severity of the pneumonitis. In mild cases, treatment may be restarted at the same dose on resolution of symptoms; however, in more severe cases, immunotherapy should be discontinued. Asymptomatic pneumonitis (radiographic changes only) also can occur and may be identified on restaging scans. These patients will require more frequent imaging, and other possible causes for the radiographic findings should be investigated.

Amylase and lipase elevations can occur, and, if patients are asymptomatic without any signs of underlying issues, such as

### TABLE 2. Comparison of Chemotherapy, Targeted Therapy, and Immune Checkpoint Therapy for the Treatment of Previously Treated Advanced NSCLC

<table>
<thead>
<tr>
<th>Examples of Agents</th>
<th>Mechanism of Action</th>
<th>Response Rates</th>
<th>Median Response Duration</th>
<th>Median OS</th>
<th>One-Year Survival Rate</th>
<th>Patients With Treatment-Related AEs Grade 3 and Greater</th>
<th>AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib, erlotinib, ceritinib, crizotinib</td>
<td>Interferes with mutated growth and survival, signaling pathways in the tumor</td>
<td>8%–9%; 58%–65%*</td>
<td>4–8 months</td>
<td>7–20 months</td>
<td>31%–73%</td>
<td>33%–79%</td>
<td>Diarrhea, rash/ acne, nausea, and elevated liver enzymes</td>
</tr>
<tr>
<td>Nivolumab, pembrolizumab</td>
<td>Restores anti-tumor immune responses</td>
<td>19%–20%</td>
<td>12.5 months (not reached)</td>
<td>9–12 months</td>
<td>42%–51%</td>
<td>7%–10%</td>
<td>Fatigue, rash, and immune-related AEs</td>
</tr>
<tr>
<td>Pemetrexed, docetaxel</td>
<td>Induces death of dividing cells</td>
<td>9%–12%</td>
<td>3–8 months</td>
<td>6–9 months</td>
<td>24%–39%</td>
<td>About 55%; 5% pemetrexed (neutropenia)</td>
<td>Neutropenia, thrombocytopenia, anemia, nausea, and vomiting</td>
</tr>
</tbody>
</table>

*In patients with tumors containing relevant mutation

AE—adverse event; NSCLC—non-small cell lung cancer; OS—overall survival

Note. Targeted agents typically are studied in and indicated for patients with tumors containing a relevant mutation.

Note. Based on information from Brahmer et al., 2015; Garon et al., 2015; Hanna et al., 2004; Katakami et al., 2013; Shaw et al., 2013, 2014; Shepherd et al., 2005.
pancreatitis, treatment can continue. Liver enzyme elevations can occur and, if mild, treatment can continue in many cases. If elevations become more severe, treatment should be delayed and steroids started. If liver enzyme elevations occur and respond well to steroids, treatment can be restarted at the original dose in many cases.

**Implications for Nursing**

Key strategies for managing patients receiving immune checkpoint inhibitors include education of the healthcare team, patients, and family caregivers about immune checkpoint inhibitors and their clinical profiles. Nurses play a critical role in educating patients and families prior to treatment initiation, as well as reassessing patient symptoms prior to every infusion. During treatment, using a questionnaire or list of standard questions for patients on these agents may be helpful for nurses to identify possible imAEs (Ledezma & Heng, 2013). Consistent assessment questions at every treatment can aid in identification of changes that may develop over time. Patients may not be aware that symptoms are treatment-related and may fail to report symptoms unless specifically asked. Patients need to know that side effects typically can be managed very effectively, particularly when they are mild and identified early. Clinicians should conduct a thorough baseline symptom burden assessment to better identify changes that may develop during treatment. For example, establishing the baseline severity of any respiratory symptoms in the NSCLC population is particularly helpful to allow identification of changes during treatment. Patients and caregivers also can be told about possible changes to look for in a pretreatment discussion. The patient should be assessed more frequently if possible drug-related symptom changes occur to determine the cause and initiate appropriate interventions. Because imAEs can occur at any time during treatment and even after completing treatment, a detailed review of patients’ symptoms must be maintained and patients should be questioned directly to identify possible AEs.

**Patient Education Resources**

The Cancer Research Institute is a nonprofit, global organization dedicated exclusively to using the immune system to conquer cancer and has developed an extensive website to inform and educate patients about cancer immunotherapy (www.theanswertocancer.org). The Society for Immunotherapy of Cancer is also a nonprofit, global society for professionals working in the field of cancer immunology and immunotherapy. Its website has a downloadable patient guide, as well as a video (www.sitcancer.org/resources/patient-information).

Additional patient education resources include immunotherapy information from the American Cancer Society (http://bit.ly/1DMzTDC), as well as patient and caregiver guides to immuno-oncology produced by Bristol-Myers Squibb (http://bit.ly/IWeESW1).

**Conclusion**

PD-1 immune checkpoint inhibitors have entered the clinic as novel therapies for the treatment of squamous NSCLC after other treatments have failed. Responses with PD-1 pathway inhibitors may be rapid or delayed but typically are durable. Prompt recognition and management of imAEs are essential, and most imAEs can be managed using steroids. A good understanding of the clinical profile of PD-1 pathway inhibitors and education of the patient and family caregivers about the clinical

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**TABLE 3. Commonly Reported Treatment-Related Adverse Events in Non-Small Cell Lung Cancer Trials of PD-1 Pathway Inhibitors**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Patients With an Adverse Event (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
</tr>
<tr>
<td><strong>Adverse Events</strong></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>5–9</td>
</tr>
<tr>
<td>Asthenia</td>
<td>5–12</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>9–19</td>
</tr>
<tr>
<td>Fatigue</td>
<td>16–33</td>
</tr>
<tr>
<td>Nausea</td>
<td>6–15</td>
</tr>
<tr>
<td><strong>Immune-Mediated Adverse Events</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7–12</td>
</tr>
<tr>
<td>Endocrinopathies</td>
<td>4–7</td>
</tr>
<tr>
<td>Hepatic</td>
<td>2–5</td>
</tr>
<tr>
<td>Pulmonary, including pneumonitis</td>
<td>7 or less</td>
</tr>
<tr>
<td>Rash or pruritus</td>
<td>6–16</td>
</tr>
<tr>
<td>Renal</td>
<td>3</td>
</tr>
</tbody>
</table>

*PD-1=programmed death-1*

*Note. Data from trials of MPDL3280A, nivolumab (Opdivo®), and pembrolizumab (Keytruda®).*

*Note. Based on information from Brahmer et al., 2015; Garon et al., 2014, 2015; Gettinger et al., 2015; Herbst et al., 2014; Rizvi, Brahmer, et al., 2015.*

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### TABLE 4. Algorithms of General Guidelines for Managing Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Management</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild to Moderate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Delay I-O, symptomatic treatment</td>
<td>If persists longer than five to seven days or recurs, 0.5–1 mg/kg methylprednisolone (Medrol®) per day²</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Delay I-O, monitor every three days</td>
<td>If persists longer than five to seven days or worsens, 0.5–1 mg/kg methylprednisolone per day²</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Delay I-O, symptomatic treatment, consider 0.5–1 mg/kg methylprednisolone per day⁴</td>
<td>–</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Delay I-O, pulmonary and infectious disease consults, daily symptom monitoring, reimage every three days, consider hospitalization, 1 mg/kg methylprednisolone per day⁴</td>
<td>–</td>
</tr>
<tr>
<td>Renal</td>
<td>Delay I-O, monitor every two to three days, 0.5–1 mg/kg methylprednisolone per day⁴, consider renal biopsy</td>
<td>–</td>
</tr>
<tr>
<td>Skin</td>
<td>Continue I-O, symptomatic treatment</td>
<td>If persists longer than one to two weeks or recurs, consider skin biopsy, delay I-O, and consider 0.5–1 mg/kg methylprednisolone per day⁴.</td>
</tr>
<tr>
<td><strong>Moderate to Severe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Discontinue I-O, 1–2 mg/kg methylprednisolone per day⁴, consider lower endoscopy</td>
<td>If persists longer than three to five days or recurs, add infliximab (Remicade®) 5 mg/kg.</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Discontinue I-O, daily monitoring, 1–2 mg/kg methylprednisolone per day⁴, gastroenterology consult</td>
<td>If does not improve in three to five days, worsens, or rebounds, add mycophenolate mofetil (CellCept®) 1 g twice daily, and consider other immunosuppression if no response.</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Discontinue I-O, 1–2 mg/kg methylprednisolone per day⁴, neurology consult</td>
<td>If worsens or atypical presentation, consider IV immunoglobulin or other immunosuppression.</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Discontinue I-O, hospitalize, pulmonary and infectious disease consults, 2–4 mg/kg methylprednisolone per day⁴</td>
<td>If does not improve after 48 hours or worsens, add additional immunosuppression.</td>
</tr>
<tr>
<td>Renal</td>
<td>Discontinue I-O, daily monitoring, 1–2 mg/kg methylprednisolone per day⁴, nephrology consult</td>
<td>–</td>
</tr>
<tr>
<td>Skin</td>
<td>Delay or discontinue I-O, 1–2 mg/kg methylprednisolone per day⁴, dermatology consult</td>
<td>Can resume I-O if resolution to grade 1</td>
</tr>
</tbody>
</table>

²If improves to grade 1, taper steroids for more than one month, consider prophylactic antibiotics for opportunistic infections and resume I-O; if does not improve, treat as severe.

³If improves to grade 1, taper steroids for more than one month and consider prophylactic antibiotics for opportunistic infections.

¹I-O—immuno-oncology agent

Note. Some mild immune-mediated adverse events had no follow-up because they will either resolve or worsen to become moderate to severe; no follow-up for renal immune-mediated adverse events was provided.

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profile are instrumental in helping nurses care for patients who will receive these treatments.

### References


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June 2016 • Volume 20, Number 3 • Clinical Journal of Oncology Nursing


