Checkpoint Inhibitors

Common immune-related adverse events and their management

RuthAnn Gordon, MSN, FNP-BC, OCN®; Mary Kate Kasler, MSN, NP, ACNP-BC; Kristen Stasi, BSN, RN; Yelena Shames, MSN, NP; Mimma Errante, MSN, NP; Kathryn Ciccolini, BSN, RN, OCN®; Anna Skripnik Lucas, MSN, RN, DNP; Pam Raasch, BSN, RN; and Erica Fischer-Cartlidge, MSN, CNS, CBCN, AOCNS®

BACKGROUND: Immunotherapy, specifically the use of checkpoint inhibitors, offers patients with cancer an alternative to chemotherapy, targeting different pathways to destroy cancer cells. The side effects of immunotherapies, as well as their impact on normal tissue, need to be assessed and managed based on their mechanisms of action.

OBJECTIVES: This article presents an overview of immune-related adverse events (AEs).

METHODS: Common immune-related toxicities, as well as rare and refractory toxicities, are reviewed.

FINDINGS: Immunotherapy treatment is an option for many patients with cancer, and nurses must understand the distinct side effect profile of these agents. Prompt identification and expert management are the cornerstones of success when dealing with immune-related AEs, and oncology nurses play a key role in improving patient care.

ADVANCES IN CANCER THERAPY INCLUDE THE USE OF IMMUNOTHERAPY, specifically checkpoint inhibitors (CIs). This approach offers patients with cancer an alternative to traditional chemotherapy. The arsenal of CIs has increased and includes drugs in three different classes: anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), anti-programmed cell death protein 1 (PD-1), and anti-programmed death ligand 1 (PD-L1) (see Figure 1). Because chemotherapy and immunotherapy target different pathways to destroy cancer cells, their side effects and impact on normal tissue need to be assessed and managed based on their mechanisms of action.

Common Immune-Related Toxicities

For patients receiving immunotherapy, these side effects are termed immune-related adverse events (AEs). Successful management of immune-related AEs requires standardized grading, such as with use of the Common Terminology Criteria for AEs (see Table 1). In addition, management almost always requires some level of immunosuppression, such as with corticosteroids. Nurses are in an ideal position to identify and manage these toxicities and educate patients about potential immune-related AEs. Education should focus on early detection and reporting to ensure successful outcome following an immune-related AE.

Colitis and Diarrhea

PRESENTATION AND ASSESSMENT

Immunotherapy-induced colitis is one of the most frequent immune-related AEs related to CIs and occurs from autoimmune-related inflammation of normal intestinal tissue (Spain, Diem, & Larkin, 2016). It often presents with frequent, watery bowel movements (BMs). Occasionally, patients may also experience abdominal cramping, or blood or mucus in the stool (Linardou & Gogas, 2016). In other situations, patients may have an incidental finding on routine radiology testing consistent with colitis prior to symptoms developing. Immune-related gastrointestinal inflammation most often occurs in the descending colon (Kaehler et al., 2010), and microscopic analyses show a mixture of inflammatory cell infiltration, including neutrophils and lymphocytes.

KEYWORDS

cancer immunotherapy; immune-related adverse events; checkpoint inhibitors

DIGITAL OBJECT IDENTIFIER

10.1188/17.CJON.S2.45-52
Characteristics and management of immune-related dermatologic adverse events in patients treated with checkpoint inhibitors (CI) are well documented. These AEs often present early in a patient’s treatment with CIs (Fecher et al., 2013). These AEs may include pruritus, rash, dermatitis, erythema, photosensitivity reaction, toxic epidermal necrolysis, urticaria, and vitiligo (Eigentler et al., 2016). Pruritus is commonly associated with the classic maculopapular rash in immunotherapy but may also present without a rash (Naidoo et al., 2015; Silbaud et al., 2016).

CI-related rashes vary, with faint erythematous maculopapular rashes involving the trunk and extremities being the most prevalent (Postow & Wolchok, 2016). These rashes appear within the first few weeks of treatment (Spain et al., 2016) in about 50% of patients receiving ipilimumab and 30%–40% of patients receiving pembrolizumab or nivolumab (Postow & Wolchok, 2016). Median time to presentation of pruritus in patients on ipilimumab occurs about 8–12 weeks after onset of treatment with a CI (Friedman, Proverbs-Singh, & Postow, 2016).

This hepatitis is often identified through routine surveillance of laboratory work or clinical symptoms. In the absence of symptoms, monitoring laboratory work prior to every dose is essential (Weber et al., 2016). Alternative etiologies (e.g., use of other hepatotoxic agents, viral syndrome) must also be eliminated. Computed tomography should be used to rule out disease progression (Weber et al., 2016).

**MANAGEMENT**

For patients experiencing grade 1 AEs, surveillance by obtaining serial laboratory work two or three times per week to follow the trajectory of elevation is recommended (Fecher, Agarwala, Hodi, & Weber, 2013). If a patient develops grade 2 or 3 elevations, immunotherapy will be held, and corticosteroids are recommended, followed by close surveillance. Corticosteroids are tapered very slowly for four to six weeks, and if symptoms recur during the taper, doses are adjusted to achieve optimal symptom control.

**Dermatologic Toxicities**

**PRESENTATION AND ASSESSMENT**

Dermatologic immune-related AEs often present early in a patient’s treatment with CIs (Fecher et al., 2013). These AEs may include pruritus, rash, dermatitis, erythema, photosensitivity reaction, toxic epidermal necrolysis, urticaria, and vitiligo (Eigentler et al., 2016). Pruritus is commonly associated with the classic maculopapular rash in immunotherapy but may also present without a rash (Naidoo et al., 2015; Silbaud et al., 2016).

CI-related rashes vary, with faint erythematous maculopapular rashes involving the trunk and extremities being the most prevalent (Postow & Wolchok, 2016). These rashes appear within the first few weeks of treatment (Spain et al., 2016) in about 50% of patients receiving ipilimumab and 30%–40% of patients receiving pembrolizumab or nivolumab (Postow & Wolchok, 2016). Median time to presentation of pruritus in patients on ipilimumab occurs at about week 3, just before the second dose (Villadolid & Amin, 2015). Pruritus presentation can be limited to an isolated area or generalized in patients with systemic disease (Krajnik & Zylicz, 2001).

Patients initiating treatment with a CI should have a complete physical examination of the skin and mucosa at baseline and then throughout therapy at each cycle. In addition, patients should be
assessed for previous drug reactions, allergies, and medications (Solensky et al., 2010). Assessment of pruritus should be geared toward evidence of excoriations, swelling, crusting, the presence of nodules on the extremities, thickening of the skin, or symptoms of infection (Fischer, Rosen, Ensslin, Wu, & Lacouture, 2013; Rosen et al., 2013; Santoni et al., 2015). Patients with an uncertain diagnosis or intractable symptoms should be referred to a dermatologist for specialty examination and skin biopsies for histologic examination and further serum assessment (Michot et al., 2016; Spain et al., 2016). Patients should also be carefully assessed for symptoms consistent with Stevens-Johnson syndrome or toxic epidermal necrolysis because these are dermatologic emergencies (Naidoo et al., 2015). These symptoms include diffuse erythematous macules and target lesions, full-thickness epidermal necrosis, and involvement of more than 30% of body surface area and mucocutaneous involvement (Croom & Dela Rosa, 2015).

**MANAGEMENT**

For grade 1 or 2 pruritus, an oral antipruritic is introduced, and dosing can range from one to two times a day, as needed for relief (Postow & Wolchok, 2016). A grade 1 or 2 maculopapular rash is primarily treated with topical steroids and oral antihistamines. If symptoms are controlled and activities of daily living are not negatively affected, treatment can continue. For grade 3 pruritus and maculopapular rash, a systemic corticosteroid is recommended, and treatment should be held until symptoms are adequately controlled (Postow & Wolchok, 2016). However, in the event that the rash does not respond to oral steroids, hospitalization and steroids administered via IV may be required. In cases where Stevens-Johnson syndrome or toxic epidermal necrolysis is suspected, immediate hospitalization is required, and immunotherapy should be discontinued (Fecher et al., 2013).

---

**FIGURE 1.**

U.S. FOOD AND DRUG ADMINISTRATION–APPROVED CHECKPOINT INHIBITORS AND PREVALENCE OF COMMON TOXICITIES

| ATEZOLIZUMAB (TECENTRIQ®) | Hepatitis: 1.8%  
| Anti-programmed death ligand 1 (PD-L1) inhibitor; used in bladder cancer | Pneumonitis: 3.1%  
| ■ Colitis/diarrhea: 19.7% |  
| ■ Dermatitis: 15%-15% |  
| ■ Endocrinopathies  
| □ Hyperthyroidism: 1% |  
| □ Hypophysitis: Less than 1% |  
| □ Hypothyroidism: 3.9% |  
| ■ Hepatitis: 1.6%-2.5% |  
| ■ Pneumonitis: 2.6% |  
| IPILIMUMAB (YERVOY®) |  
| Anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) inhibitor; used in melanoma |  
| ■ Colitis/diarrhea: 5%-16% |  
| ■ Dermatitis: 2%-21% |  
| ■ Endocrinopathies: 1.8%-20% |  
| ■ Hepatitis: 2%-11% |  
| ■ Pneumonitis: Less than 1% |  
| NIVOLUMAB (IN COMBINATION WITH IPILUMINAB) | NIVOLUMAB (IN COMBINATION WITH IPILUMINAB)  
| Anti-programmed cell death protein (PD-1) inhibitor given with a CTLA-4 inhibitor for melanoma |  
| ■ Colitis/diarrhea: 26% |  
| ■ Dermatitis: 22.6% |  
| ■ Endocrinopathies  
| □ Hyperthyroidism: 8% |  
| □ Hypophysitis: 9% |  
| □ Hypothyroidism: 22% |  
| ■ Hepatitis: 13% |  
| ■ Pneumonitis: 6% |  
| PEMBROLIZUMAB (KEYTRUDA®) | PEMBROLIZUMAB (KEYTRUDA®)  
| Anti-programmed cell death protein 1 (PD-1) inhibitor; used in melanoma, small cell lung cancer, and head and neck cancers; used off label in small cell lung cancer |  
| ■ Colitis/diarrhea: As much as 2% |  
| ■ Dermatitis: 12%-18% |  
| ■ Endocrinopathies  
| □ Hyperthyroidism: 1.8%-3.3% |  
| □ Hypophysitis: Less than 1% |  
| □ Hypothyroidism: 6.9%-14.6% |  
| ■ Hepatitis: 1% |  
| ■ Pneumonitis: 2%-3.5% |  

**Note.** Based on information from American Cancer Society, 2016; Bristol-Myers Squibb Company, 2015, 2017; Genentech, Inc., 2016; Merck Sharp & Dohme Corp., 2016.
Pneumonitis is an immune-mediated inflammation of the lung lining that can occur at any time during or after treatment. Although not as frequently occurring as colitis, it is still a prevalent immune-related AE; incidence almost doubles with combination immunotherapy regimens (Friedman et al., 2016). Patients with cancer can have a diminished lung reserve and respiratory complications that elevate risk for this toxicity; therefore, patient education on potential symptoms of pneumonitis and continual respiratory status assessment is imperative (Linardou & Gogas, 2016).

The diagnosis of pneumonitis is based on clinical presentation and radiographic findings. Any new symptoms of cough, dyspnea, decreased breath sounds, or decreased oxygen saturation during treatment require further evaluation to determine infection or pneumonitis (Linardou & Gogas, 2016). Prior to initiation of treatment, baseline oxygen saturation should be obtained to provide an accurate assessment of change. The severity of symptoms may vary among patients and may mimic other common respiratory illnesses. Chest imaging is recommended to rule out infectious causes and to look for radiographic findings consistent with pneumonitis. Figure 2 lists radiologic presentations of immune-related toxicities. Pulmonary function tests and arterial blood gases are recommended for patients presenting with hypoxia. Most patients treated for pneumonitis require symptom management in an emergency department or hospitalization.

### MANAGEMENT

For patients with grade 1 pneumonitis, clinicians should consider holding treatment and monitor symptoms. Reimaging is recommended every two to four weeks until resolution (Weber et al., 2016). On resolution of radiographic findings, treatment may resume with close surveillance for symptom recurrence. Higher-grade pneumonitis requires that treatment be held and that corticosteroids be administered orally or via IV at 1–2 mg/kg, with consideration of hospitalization and imaging every one to three days (Weber et al., 2016).

Continued immunosuppression should be based on objective findings, such as imaging and oxygen saturation, as well as subjective findings, such as dyspnea and cough. If both show improvement, steroids can be tapered during four to six weeks.

### TABLE 1.

**CTCAE GRADING CRITERIA FOR COMMON IMMUNOTHERAPY TOXICITIES**

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>GRADE 1</th>
<th>GRADE 2</th>
<th>GRADE 3</th>
<th>GRADE 4</th>
<th>GRADE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase increased</td>
<td>As much as three times the ULN</td>
<td>3–5 times the ULN</td>
<td>5–20 times the ULN</td>
<td>More than 20 times the ULN</td>
<td>–</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>As much as three times the ULN</td>
<td>3–5 times the ULN</td>
<td>5–20 times the ULN</td>
<td>More than 20 times the ULN</td>
<td>–</td>
</tr>
<tr>
<td>Colitis</td>
<td>Asymptomatic; clinical or diagnostic observation only</td>
<td>Abdominal pain; mucus or blood in stool</td>
<td>Severe abdominal pain; change in bowel habits</td>
<td>Life-threatening consequences</td>
<td>Death</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Increase of less than four stools a day over baseline</td>
<td>Increase of 4–6 stools a day over baseline</td>
<td>Increase of seven or more stools a day over baseline; incontinence</td>
<td>Life-threatening consequences; hospitalization indicated</td>
<td>Death</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>Asymptomatic; clinical or diagnostic observation only</td>
<td>Symptomatic; limiting instrumental ADL</td>
<td>Severe symptoms; limiting self-care ADL; oxygen indicated</td>
<td>Life-threatening respiratory compromise</td>
<td>Death</td>
</tr>
<tr>
<td>Pruritis</td>
<td>Mild or localized</td>
<td>Intense or widespread; intermittent; skin changes from scratching; limiting instrumental ADL</td>
<td>Intense or widespread; constant; limiting self-care ADL or sleep</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Rash (maculopapular)</td>
<td>Covering less than 10% of body with or without symptoms</td>
<td>Covering 10%–30% of body with or without symptoms</td>
<td>Covering more than 30% of body with or without symptoms</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

ADL—activities of daily living; CTCAE—Common Terminology Criteria for Adverse Events; ULN—upper limit of normal

with frequent observations and assessments. Delayed treatment of pneumonitis can lead to chronic, irreversible lung tissue damage and necessitate treatment discontinuation; prompt symptom recognition and early management has been associated with improved prognosis and reduced morbidity and mortality.

**Endocrinopathies**

**PRESENTATION AND ASSESSMENT**

Immune-related AEs of the endocrine system may include hypophysitis (inflammation of the pituitary gland), thyroiditis, hypothyroidism, adrenal insufficiency, and diabetes, with hypophysitis and thyroid dysfunction being the most common. Patients treated with CTLA-4 inhibitors most commonly experience hypophysitis, whereas those on PD-L1 inhibitors equally present with hypophysitis and thyroid dysfunctions (Snyder, 2015).

Hypophysitis of the anterior pituitary bulb is most common and causes abnormal production of the adrenocorticotropic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), free thyroxine or triiodothyronine, and gonadotropins (Fecher et al., 2013). In rare instances, the posterior lobe of the pituitary gland is involved, with subsequent development of hyponatremia secondary to syndrome of inappropriate antidiuretic hormone secretion or diabetes insipidus (Joshi, Whitelaw, Palomar, Wu, & Carroll, 2016). A diagnosis of hypophysitis is based on clinical presentation, laboratory evaluation, and dedicated pituitary magnetic resonance imaging. Clinical manifestations include headaches, dizziness, diplopia, peripheral vision loss, extreme fatigue, irritability, cold intolerance, nausea, or vomiting (Fecher et al., 2013). Laboratory work may reveal hyponatremia, abnormal thyroid function, and low cortisol, ACTH, luteinizing hormone, follicle-stimulating hormone, prolactin, or testosterone.

In some cases, hypophysitis is associated with adrenal insufficiency or adrenal crisis, which is potentially life threatening, requiring immediate medical attention. In addition to those symptoms, patients with adrenal insufficiency may present with hypotension, lethargy, electrolyte imbalance, and dehydration. Lifelong hormone replacement may be necessary.

Immune-mediated thyroid dysfunction can present as primary or secondary hypothyroidism, destructive thyroiditis, or hyperthyroidism (Postow & Wolchok, 2016). The incidence of thyroid disorders is similar for CTLA-4 blockage and anti–PD-1 monotherapy, but increases significantly with combination therapy (Joshi et al., 2016). Symptoms of thyroid dysfunction may include extreme fatigue, unusual headaches, changes in weight, irritability, insomnia, hair loss, cold or heat intolerance, and constipation (Eigentler et al., 2016).

Obtaining TSH, free triiodothyronine, and free thyroxine levels at baseline and prior to each immunotherapy cycle is recommended (Eigentler et al., 2016). High TSH with low triiodothyronine and thyroxine is usually indicative of hypothyroidism, whereas low TSH and elevated triiodothyronine and thyroxine indicate hyperthyroidism. In some cases, primary hypothyroidism is usually preceded by transient hyperthyroidism.

**MANAGEMENT**

Patients with hypophysitis and adrenal insufficiency are typically referred to an endocrinologist for management guidance. Treatment for hypophysitis includes an initial dose of corticosteroids to decrease acute symptoms of inflammation, followed by lifetime replacement with hydrocortisone (Bertrand, Kostine, Barnetche, Truchetet, & Schaeeverbeke, 2015). Adrenal insufficiency or crisis is a potentially life-threatening condition requiring immediate medical attention, including high-dose steroids and hospitalization (Postow & Wolchok, 2016). Immune-mediated hyperthyroidism rarely requires medical management. However, severe symptoms may be treated with beta blockers or corticosteroids. Hypothyroidism will require lifelong replacement of levothyroxine (Synthroid®), with initial recommended dosing for healthy adults being 1.6 mcg/kg per day and later adjustment based on repeat laboratory assessments.

**Less Common Toxicities**

The incidence of immune-mediated ophthalmic AEs resulting from CIs is less than 1% (Antoun, Titah, & Cochereau, 2016). This includes ocular or orbital inflammation and retinal and choroidal diseases. Clinical manifestations of uveitis may include symptoms like eye pain, redness, photophobia, excessive tearing, floaters, and decreased visual acuity (Antoun et al., 2016). Patients presenting with uveitis symptoms require a thorough evaluation by an ophthalmologist regardless of grade. In many cases,
ophthalmologic evaluation reveals macular edema and papillitis, requiring hold of CIs and the use of steroid eye drops for four to six weeks. Patients should continue close follow-up with an ophthalmologist (Robinson et al., 2004).

Another underreported toxicity is joint inflammation, which presents as joint pain, tenderness, and swelling. Unlike other toxicities, symptoms usually occur later in the treatment course but rarely require treatment disruption or discontinuation. If clinically appropriate, patients may find relief with nonsteroidal anti-inflammatory drugs. A rheumatology consult and systemic corticosteroids are recommended for persistent pain (Spain et al., 2016).

Refractory Toxicities
Refractory immune-related AEs are those toxicities not responsive to maximal steroid support and/or to tapering of steroids with successful resolution to at least grade 1 toxicity. Workup should include bronchoscopy and tissue biopsy for refractory pneumonitis, liver biopsy to confirm T-cell infiltration for hepatitis, or endoscopy/colonoscopy for diarrhea remaining at grade 3 or 4 or persisting for seven or more days despite steroids (Eigentler et al., 2016). Once other etiologies are ruled out, additional immunosuppression, including treatment with tumor necrosis factor blockade agents, such as infliximab (Remicade®), is recommended. Patients will require an escalation in care and may need inpatient admission for observation, management, and supportive care (Eigentler et al., 2016).

Patients with prolonged high frequency colitis are at risk for colonic perforation. If no improvement is noted within 48 hours of maximal steroid support, the addition of infliximab at 5 mg/kg is recommended. Forty-eight hours following infliximab infusion, patients should begin to taper steroids for four to six weeks if symptoms do not recur. Similarly, infliximab should be considered for those with refractory pneumonitis that is proved to be noninfectious. Patients should titrate off oxygen supplementation as tolerated and begin a six-week taper of steroids (Eigentler et al., 2016).

Although many patients with refractory immune-related hepatitis often continue to remain asymptomatic, these patients are at risk for liver impairment. Patients who do not achieve therapeutic benefit on maximal glucocorticoid support (2 mg/kg) within 48 hours should start mycophenolate mofetil (CellCept®) at 1,000 mg twice daily as the additional line of immunosuppression (Villadolid & Amin, 2015). Infliximab should be avoided in immune-related hepatitis because it is contraindicated in patients with alteration in liver function (Postow & Wolchok, 2016). A discharge plan can be pursued for hospitalized patients when a downward trend in liver function tests has been achieved and the patient does not demonstrate signs of hepatoencephalopathy. The discharge plan should include twice-weekly laboratory work to determine the taper of the steroid and mycophenolate mofetil; the taper is generally continued for at least six weeks. Patients who are managed in the ambulatory setting require frequent surveillance with the aforementioned laboratory evaluation and steroid taper (Weber et al., 2016).

Patients with refractory immune-related AEs maintained on a prolonged course of immunosuppression or those treated with additional lines of immunosuppression, specifically infliximab, are at elevated risk for opportunistic infections (Postow & Wolchok, 2016). Although recommendations exist for patients on prolonged immunosuppression regarding the introduction of prophylactic antimicrobial or antifungal treatments (Ali et al., 2013), limited data are available for patients receiving immunotherapy. However, clinicians may opt to use a pneumocystis pneumonia prophylaxis regimen or antifungal medication to reduce the risk of opportunistic infections for those expected to receive prolonged immunosuppressive therapy. Patients who demonstrate ongoing diarrhea despite multiple lines of immunosuppression should be evaluated for cytomegalovirus (CMV) colitis. CMV colitis is a potential infection that can develop with prolonged immunosuppression (Del Castillo et al., 2016).

Conclusion
Immunotherapy has an expanding portfolio of options for patients, including checkpoint inhibition. This requires nurses to understand the distinct side effect profile of these agents. The cornerstone to successful management includes prompt identification of immune-related AEs, use of management guidelines, and initiation of close surveillance practices. For those requiring a course of steroids, slow taper and careful symptom monitoring during that time frame is necessary to identify rebounding or refractory toxicities. In addition, prolonged surveillance beyond treatment completion can assist with early identification of delayed toxicity.

Nursing best practices for management of this unique population include providing thorough patient education (verbal and written) prior to initiation of therapy and ensuring that patients and caregivers understand when and how to contact the office, during and after hours, if new symptoms arise. Patients should be encouraged to report signs and symptoms of immune-related toxicity. To facilitate early symptom recognition, nurses play an essential role in monitoring patients with surveillance telephone calls and promptly coordinating necessary assessments and referrals in collaboration with the primary oncologist. This ensures timely decision making related to withholding immunotherapy and the initiation of immunosuppressive treatment. Regardless of the

IMPLICATIONS FOR PRACTICE

- Acknowledge that immunotherapy for some types of advanced malignancies offers an alternative to the traditional approach to chemotherapy.
- Realize that patients are at risk for immune-related adverse events (AEs) during and after treatment with immunotherapeutic agents.
- Understand that nurses play a key role in the identification, assessment, and management of these immune-related AEs.
toxicity, the approach to managing refractory immune-related AEs requires ongoing surveillance, early recognition of steroid failure, and consideration of additional immunosuppressive agents. Patients and healthcare providers must know that once toxicity has occurred, the patient remains vulnerable for recurrence at any time, even once CIs are discontinued (Michot et al., 2016).

Treatment with CIs is associated with a multitude of immune-related toxicities. Although symptom location and severity may vary among patients, delayed recognition and management of immune-related AEs may lead to increased morbidity, prolonged hospitalizations, premature termination of treatment, and potentially lethal outcomes. Oncology nurses are instrumental in early symptom recognition, ongoing patient education, and toxicity management.

RuthAnn Gordon, MSN, FNP-BC, OCN®, is a clinical trials nurse coordinator, Mary Kate Kasler, MSN, NP, ACNP-BC, is a clinical research nurse practitioner, Kristen Stasi, BSN, RN, is a research nurse, Yelena Shames, MSN, NP, and Mimma Errante, MSN, NP, are both clinical research nurse practitioners, Kathryn Ciccoli, BSN, RN, OCN®, DNC, and Anna Skripnik Lucas, MSN, RN, DNC, FNP-BC, are both clinical nurses, Pam Raasch, BSN, RN, is a clinical research nurse, and Erica Fischer-Cartilidge, MSN, CNS, CBCN, AOCNS®, is a clinical nurse specialist coordinator, all in the Department of Nursing at Memorial Sloan Kettering Cancer Center in New York, NY. Gordon can be reached at gordonr@mskcc.org, with copy to editor at CJONEditor@ons.org. (Submitted October 2016. Accepted January 11, 2017)

The authors gratefully acknowledge their colleagues who work to care for patients receiving immunotherapy as a treatment option; Marisol Hernandez, MLS, MA, for her expert assistance with literature searches for this article; and their patients for teaching them every day through their courage and spirit.

The authors take full responsibility for this content. The article has been reviewed by independent peer reviewers to ensure that it is objective and free from bias. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Society.

REFERENCES


Naidoo, J., Page, D.B., Li, B.T., Connell, L.C., Schindler, K., Lacouture, M.E.,… Wolchock, J.D.
CHECKPOINT INHIBITORS


