

Immune Checkpoint Inhibitor Therapy

Key principles when educating patients

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BACKGROUND: Immune checkpoint inhibitor (ICI) therapy is a fast-developing field within the spectrum of cancer care. ICIs are associated with distinctive immune-related adverse events (irAEs), reflecting their unique mechanisms of action.

OBJECTIVES: Effective management of irAEs requires early recognition and prompt reporting of their signs and symptoms; appropriate patient education is critical to maximizing this opportunity.

METHODS: A comprehensive literature search was conducted in the public domain concerning awareness, assessment, and management of irAEs associated with ICIs.

FINDINGS: Educational resources should provide timely, consistent, and personalized information, using a variety of teaching strategies that consider individual patient needs. Patient education should be developed with interprofessional team input and regularly reviewed in response to emerging guidance. Key messages include timing of therapeutic response and corresponding irAEs, early identification of irAEs, and the unique ability of ICIs to influence immune responses after treatment discontinuation.

KEYWORDS

immune checkpoint inhibitors; side effects; immunotherapy; patient education

DIGITAL OBJECT IDENTIFIER

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IMMUNE CHECKPOINT INHIBITORS (ICIs), A CLASS OF IMMUNOTHERAPY that works by restoring immune system function, have been increasingly used in clinical practice (Haanen, Thienen, & Blank, 2015; Kottschade et al., 2016; Postow, Callahan, & Wolchok, 2015). The U.S. Food and Drug Administration (FDA) approved ipilimumab to treat metastatic melanoma in 2011 and, since then, several ICIs have been approved to treat a range of cancers, including melanoma, Merkel cell carcinoma, Hodgkin lymphoma, and non-small cell and small cell lung, kidney, head and neck, colorectal, liver, bladder, cervical, and microsatellite instability high or mismatch repair deficient cancers (marking the first approval based on a biomarker rather than tumor type) (AstraZeneca, 2018; Bristol-Myers Squibb, 2018a, 2018b; FDA, 2018; Genentech, 2018; Merck & Co., 2018; Pfizer, Inc., 2017).

The aim of ICI therapy is to enhance the body's anti-tumor immunity by disrupting the pathways that tumors use to evade the immune system (Beatty & Gladney, 2015; Kannan, Madden, & Andrews, 2014). In normal tissue, immune checkpoint pathways, including cytotoxic T-lymphocyte antigen 4 (CTLA-4) and programmed cell death protein 1 (PD-1), downregulate T-cell activity to prevent autoimmunity (de Mello, Veloso, Esrom Catarina, Nadine, & Antoniou, 2016; Haanen et al., 2015). Some tumors aberrantly upregulate these pathways to avoid immune surveillance (Dougan & Dranoff, 2009; Kannan et al., 2014). Blocking tumor inhibitory pathways with ICIs can induce an anti-tumor immune response (de Mello et al., 2016) (see Figure 1).

Because immune checkpoints help to balance the immune system, ICIs are associated with immune-related adverse events (irAEs), reflecting their immune-based mechanisms (Haanen et al., 2015; Weber, Postow, Lao, & Schadendorf, 2016). irAEs are commonly dermatologic, gastrointestinal, hepatic, endocrine, or respiratory, but can affect other organ systems (Haanen et al., 2017; Weber et al., 2016). Most are mild to moderate in severity, although serious and occasionally life-threatening irAEs have been reported (Kwon et al., 2014; Puzanov et al., 2017). Although serious irAEs may result in treatment discontinuation, with prompt recognition and management, most resolve and patients can continue ICI treatment (Brahmer et al., 2018; Haanen et al., 2017; Puzanov et al., 2017; Weber et al., 2016). Patient education is critical to maximize early recognition and reporting of irAEs (Fradkin, 2017).

Although multiple patient ICI education resources are available, little has been published regarding best practices for informing patients and caregivers about ICIs. In 2017, the Cancer Support Community conducted a needs assessment of 95 patients receiving ICIs and 45 of their caregivers (Aspiras, Power, & Gonzalo, 2018). Most patients (55%) and caregivers (85%) identified “understanding how to cope with ICI symptoms and side effects” as important, while many patients (50%) and caregivers (73%) reported difficulty obtaining this information (Aspiras et al., 2018).

To address these and other educational needs, a comprehensive literature search of irAE management practices and patient irAE education resources was performed, and included publications from PubMed, congress abstracts, professional and patient advocacy groups, practice guidelines, and ICI prescribing information. This review summarizes patient education regarding chemotherapy, shares information about best practices, and identifies barriers to patient education about ICIs, as well as provides information about patient education methods and support tools. To provide appropriate and effective education to patients and caregivers, nurses must become knowledgeable about immunotherapy and irAEs (Aim With Immunotherapy Foundation, 2019; Dine, Gordon, Shames, Kasler, & Barton-Burke, 2017; Kannan et al., 2014; Kottschade et al., 2016).

Patient Education

Experience based on chemotherapy education shows that education is essential for patients with cancer to understand how to

“Patient education is most effective when provided before treatment initiation.”

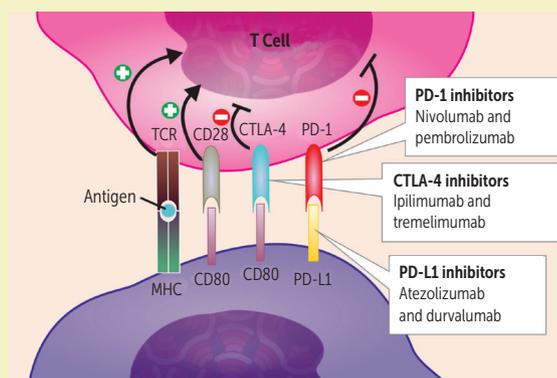
best care for themselves by managing treatment side effects and contacting healthcare providers (HCPs) for assistance (Valenti, 2014). Effective patient education during the initial diagnosis and treatment can improve anxiety and self-care decisions, decrease side effects, and enhance quality of life (Shahsavari, Matory, Zare, Taleghani, & Kaji, 2015; Tian, Lia, & Cheng, 2015).

Patient education is most effective when provided before treatment initiation, in a quiet environment that supports learning, and by oncology team members in the primary oncology setting (Garcia, 2014). Treatment side effects, management strategies, and infusion center orientation are consistently shown as the most important topics to help reduce patient anxiety (Garcia, 2014). Education structure is an important consideration to maximize information retention. However, a review of teaching methods (e.g., audio or video recording, in-person class, one-on-one discussion, telephone calls) reported no single method to be significantly more effective than any other in delivering information to patients because knowledge retention is largely based on individual learning preferences (Valenti, 2014).

Patient use of different teaching resources is associated with different factors, including sociodemographics (e.g., age, gender, education), psychosocial characteristics (e.g., stress level, coping strategies), unfulfilled information needs, and perceived credibility of information sources (Mekuria, Erku, & Belachew, 2016). For example, education through audio or video recordings may benefit patients with literacy issues (Valenti, 2014). Before planning educational activities, oncology nurses can conduct a learning needs assessment with individual patients to determine factors such as health literacy level, reading skills, personal preferences for learning, cultural or religious aspects, pain level, and amount of anxiety (Canadian Partnership Against Cancer, 2018; Goldsmith & Terui, 2018; Marcus, 2014). Although no single needs assessment is recommended, examples of wider needs assessment tools incorporating educational elements were developed and reviewed (Australian Cancer Survivorship Centre, 2016). Involving patients in resource selection can help ensure that patients’ needs and preferences are addressed, improving acceptance and effectiveness (Jewitt et al., 2016).

Although initial education is essential, it is important to continually reinforce teaching, particularly when irAE occurrence

FIGURE 1.
MECHANISMS OF ACTION OF IMMUNE CHECKPOINT INHIBITORS



CD—cluster of differentiation; CTLA-4—cytotoxic T-lymphocyte antigen 4; FDA—U.S. Food and Drug Administration; MHC—major histocompatibility complex; PD-1—programmed cell death protein 1; PD-L1—programmed cell death ligand 1; TCR—T-cell receptor

Note. Since original publication of this figure, the PD-L1 inhibitor avelumab has been approved by the FDA. Tremelimumab is not approved by the FDA at the time of this writing.

Note. Republished with permission of *OncoTargets and Therapy*, from Potential role of immunotherapy in advanced non-small-cell lung cancer; de Mello, R.A., Veloso, A.F., Catarina P.E., Nadine, S., and Antoniou, G., volume 10, 2016: 21–30.

results in treatment plan changes. The teach-back method, which allows patients to repeat what they learned to the HCP, enabling the HCP to determine which information was confusing or not understood, is useful for assessing patient comprehension and understanding (Portz & Johnston, 2014). Patients should understand the goals and importance of activities they take part in, and they should be encouraged to ask their oncology team any questions they have before and after teaching and throughout the treatment process (Valenti, 2014). Patients value the expertise of oncology nurses and group support from others receiving treatment (Fee-Schroeder et al., 2013).

Best-Practice Sharing in Patient Education

The experiences of teaching about the early stages of ICI development, such as ipilimumab in advanced melanoma, suggest that early recognition of symptoms and frequent monitoring are central to irAE management; patients and caregivers should be educated about signs and symptoms to monitor and report (Fecher, Agarwala, Hodi, & Weber, 2013). Patients may not accurately report side effects for fear of being taken off treatment; therefore, patients should be encouraged to “call early and call often” to discuss any changes in health status with their cancer team (Fecher et al., 2013). Patients should be taught that irAEs can often be managed effectively without permanent treatment discontinuation, particularly when identified early (Bayer et al., 2017; Brahmer et al., 2018).

ICI-related toxicity patterns based on tumor type are not well established, and evidence for which patients are at elevated risk remains unclear (Brahmer et al., 2018). Patients with preexisting autoimmune conditions may be at risk of underlying disease recurrence and require close monitoring; therefore, effective ICI education for patients with preexisting autoimmune disease or prior organ transplantation requires a thoughtful discussion of potential risks and benefits (Brahmer et al., 2018).

Barriers to Patient Education

As ICIs continue to evolve with increasing availability and new combinations, nurses can provide patients and caregivers with timely ICI education, including mechanisms of action and clinical profiles of irAEs (Brahmer et al., 2018). However, in this fast-developing field, information can become antiquated quickly. For example, the nature and range of irAEs are becoming more clearly defined with increasing patient exposure to ICIs, and new rare side effects, such as meningoradiculitis, polyradiculitis, cardiac arrhythmia, asystolia, aphasia, paresis, and Parkinson syndrome, have been reported (Puzanov et al., 2017; Zimmer et al., 2016). Cancer centers can obtain new data relating to safety and side effect management of ICI treatment, as well as regularly review and update ICI patient education materials and activities, to ensure that clinical staff are equipped to deliver ICI treatment.

Organizing high-quality patient education initiatives takes time and commitment by nurses, doctors, pharmacists, psychologists, and administrative staff (Cipolat Mis et al., 2015; Fradkin, 2017). Education covering irAE management is complex, requiring message consistency and an interprofessional approach involving oncologists and internal medicine specialists (e.g., endocrinologists, gastroenterologists, pulmonologists) (Abdel-Wahab, Alshawa, & Suarez-Almazor, 2017; Fay, Moreira, Nunes Filho, Albuquerque, & Barrios, 2016). Oncology nurses have frequent contact with patients and other staff members and play a critical role in ensuring that education initiatives are patient-centered and collaborative (Fay et al., 2016; Garcia, 2014).

Patient Education for Immune Checkpoint Inhibitors

Guidelines on the management of ICI-associated irAEs were published by the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) (Brahmer et al., 2018), the Society for Immunotherapy of Cancer (SITC) (Puzanov et al., 2017), and the European Society for Medical Oncology (ESMO) (Haanen et al., 2017). Guidelines recommend providing ICI-specific information to patients and caregivers before initiating therapy (Brahmer et al., 2018; Haanen et al., 2017; Puzanov et al., 2017). ASCO–NCCN guidelines also recommend continued patient and caregiver education throughout treatment and survivorship (Brahmer et al., 2018).

ICIs are associated with a spectrum of AEs that differ from other systemic therapies. Patients should be informed that ICIs work differently than chemotherapy or targeted therapies that patients may have received previously, producing unique therapeutic responses and corresponding irAEs (Brahmer et al., 2018). In particular, irAEs can have delayed onset and prolonged duration compared with chemotherapy-related AEs (Puzanov et al., 2017).

Patients may present with irAEs late in ICI treatment or even months after treatment discontinuation (Haanen et al., 2017; Puzanov et al., 2017). At any point, effective management depends on early recognition of irAEs and prompt intervention (Puzanov et al., 2017). Therefore, patients are encouraged to report changes to their providers (Brahmer et al., 2018).

Educating Patients and Caregivers

The following section provides key messages to be communicated to patients and caregivers regarding what to expect from ICI treatment, with supporting information to provide additional context for HCPs.

BACKGROUND AND MECHANISM OF ACTION: ICIs work with the immune system to fight cancer. This can result in unique response patterns and side effects that differ from the cancer treatments patients may have previously received (such as chemotherapy). Tumors can avoid immune system detection through upregulating pathways that limit immune responses

TABLE 1.
COMMON SIGNS AND SYMPTOMS OF IRAEs AND MANAGEMENT CONSIDERATIONS

| AUDIENCE | COMMON SIGNS AND SYMPTOMS | MANAGEMENT GUIDANCE* |
|-----------------------------------|---|---|
| Skin (dermatologic) | | |
| Patients | <ul style="list-style-type: none"> ■ Rashes, redness, itching, or skin changes ■ Pain, swelling, or soreness ■ Peeling skin, blisters, or sores | <ul style="list-style-type: none"> ■ Avoid scratching or using soap and hot water on sensitive skin. ■ Applying a cool cloth or cooling cream to your skin may help provide relief. ■ Your HCP may conduct tests to determine the cause of your rash and may recommend a steroid or numbing medicine, an antihistamine, medicated creams, or antibiotics. ■ Seek treatment immediately, regardless of time of day, if you experience severe inflammation or swelling, intense itching, or a widespread or quickly worsening rash. |
| HCPs | <ul style="list-style-type: none"> ■ Erythematous and/or maculopapular rash ■ Dry skin, pruritus, or vitiligo ■ Blisters, ulceration, bullae, or necrotic or hemorrhagic lesions | <ul style="list-style-type: none"> ■ Evaluate patients for signs and symptoms of pruritus, vitiligo, or maculopapular rash. ■ Consider dermatology referral and skin biopsy. ■ Topical moisturizers may help relieve mild symptoms. ■ Topical or systemic corticosteroids and/or antihistamines may be required for moderate to severe symptoms; withhold ICI therapy in patients with severe symptoms and initiate prednisone (or methylprednisolone equivalent) until symptoms abate. ■ Permanently discontinue ICI therapy in those with Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full-thickness dermal ulceration or necrotic, bullous, or hemorrhagic manifestations. |
| Abdomen (gastrointestinal) | | |
| Patients | <ul style="list-style-type: none"> ■ Diarrhea, stomach pain, or cramps ■ Nausea, vomiting, or loss of appetite ■ Fever or fatigue | <ul style="list-style-type: none"> ■ Call your healthcare team if you experience an increase or changes in your bowel movements, particularly if your stools are mushy or watery. ■ Drink plenty of water to prevent dehydration and avoid rich or spicy foods. ■ Call your healthcare team if you experience symptoms that interfere with your daily activities, such as severe abdominal cramping, or that cause you to fear leaving your home. ■ Seek treatment immediately, regardless of time of day, if you experience severe abdominal pain, particularly if you also have a fever. |
| HCPs | <ul style="list-style-type: none"> ■ Diarrhea, constipation, increase in stool count, or blood or mucus in stool with or without fever ■ Abdominal cramping or pain, nausea, or vomiting ■ Peritoneal signs consistent with bowel perforation, ileus | <ul style="list-style-type: none"> ■ Assess patients for changes in bowel habits. ■ Dietary modifications and loperamide may help relieve mild symptoms. ■ In patients with moderate to severe symptoms, initiate prednisone (or methylprednisolone equivalent) and conduct differential diagnosis. ■ Withhold ICI therapy until improvement to mild symptoms or complete resolution; for severe reactions, discontinue ICI therapy. |
| Lung (respiratory) | | |
| Patients | <ul style="list-style-type: none"> ■ Cough, shortness of breath, or chest pain | <ul style="list-style-type: none"> ■ Call your healthcare team if you develop a new cough, or if your existing cough worsens. ■ Avoid environments that can irritate your lungs or make it hard to breathe. ■ Adhere to any preexisting asthma or allergy treatment plans during your cancer therapy. ■ Seek treatment immediately, regardless of time of day, if you experience chest pain or trouble breathing, particularly if symptoms come on suddenly. |
| HCPs | <ul style="list-style-type: none"> ■ Dyspnea, cough, or chest pain ■ Difficulty breathing or acute respiratory distress syndrome | <ul style="list-style-type: none"> ■ Monitor baseline and ongoing oxygen saturation levels at rest and during ambulation. ■ Conduct chest imaging and consider pulmonary and infectious disease consultations. ■ Withhold ICI therapy; if chest imaging abnormalities resolve, consider resuming therapy with close follow-up monitoring. ■ In patients with moderate to severe symptoms, initiate prednisone (or methylprednisolone equivalent) until symptoms improve. ■ Consult a pulmonologist. ■ Hospitalize patients with severe symptoms and permanently discontinue ICI therapy. |

Continued on the next page

TABLE 1. (CONTINUED)

COMMON SIGNS AND SYMPTOMS OF IRAEs AND MANAGEMENT CONSIDERATIONS

| AUDIENCE | COMMON SIGNS AND SYMPTOMS | MANAGEMENT GUIDANCE* |
|---|--|--|
| Liver (hepatic) | | |
| Patients | <ul style="list-style-type: none"> Flu-like symptoms (fever, chills, muscle or joint aches, headaches, drowsiness, fatigue, sweating, nausea, vomiting, or loss of appetite) Abdominal pain, particularly on the upper right side Yellowing skin or eyes, pale stools, or dark urine Bruising or bleeding more easily | <ul style="list-style-type: none"> Drink plenty of water to prevent dehydration and eat a well-balanced diet. Avoid alcohol and more prescription pain medication than recommended. Seek treatment immediately, regardless of time of day, if you experience high fever, drowsiness, or confusion, if your skin has turned yellow, or if you have severe stomach pain or swelling. |
| HCPs | <ul style="list-style-type: none"> Elevated AST, ALT, or total bilirubin Abdominal pain in right upper quadrant Jaundice, fever, nausea or vomiting, or encephalopathy | <ul style="list-style-type: none"> Evaluate liver function before each infusion or more frequently if clinically indicated and monitor patients for any signs of hepatitis. Withhold ICI therapy for patients with moderate AST, ALT, or total bilirubin elevation. In patients with moderate to severe symptoms, initiate prednisone (or methylprednisolone equivalent) until symptoms improve. Consult gastroenterologist or hepatologist. Permanently discontinue ICI therapy in patients with severe AST, ALT, or total bilirubin elevations. |
| Hormonal (endocrine) | | |
| Patients | <ul style="list-style-type: none"> Fatigue (some people get extreme fatigue) Headache, fever, nausea, or vomiting Dizziness, confusion, drowsiness, or fainting Vision changes or loss of sexual function | <ul style="list-style-type: none"> Eat a healthy diet and exercise regularly. Continue taking any thyroid supplements you were prescribed prior to starting therapy. Seek treatment immediately, regardless of time of day, if you experience severe headaches with dizziness, confusion, drowsiness or fainting, vision changes, fever, nausea, or vomiting. |
| HCPs | <ul style="list-style-type: none"> Abnormal electrolytes Abnormal thyroid function tests, cortisol or ACTH levels, or increased fasting plasma glucose Headaches, vision changes or field cuts, or mental status changes Fatigue, nausea or vomiting, weight gain or loss, or dizziness or fainting Abdominal pain, constipation, or unusual bowel habits Dysphonia, excessive thirst or increased urination, impotence, or loss of libido | <ul style="list-style-type: none"> Obtain appropriate blood work. Refer to ASCO–NCCN or SITC guidelines for recommendations. Consult endocrinologist. Consider long-term hormone-replacement therapy, as necessary. Withhold ICI therapy for patients with moderate symptoms until complete resolution or stable on hormone-replacement therapy. In patients with moderate to severe symptoms, initiate prednisone (or methylprednisolone equivalent) until symptoms improve. Permanently discontinue ICI therapy in patients whose symptoms do not resolve with appropriate hormone-replacement therapy. |
| <p>*Steroids should be administered cautiously to patients receiving chimeric antigen receptor T-cell therapy. ACTH—adrenocorticotropic hormone; ALT—alanine aminotransferase; ASCO—American Society of Clinical Oncology; AST—aspartate aminotransferase; HCP—healthcare provider; ICI—immune checkpoint inhibitor; irAE—immune-related adverse event; LFT—liver function test; NCCN—National Comprehensive Cancer Network; SITC—Society for Immunotherapy of Cancer Note. Based on information from Anadkat & Cowen, 2018; Brahmer et al., 2018; Cancer Support Community, 2018; Fecher et al., 2013; Haanen et al., 2017; Kannan et al., 2014; Kottschade et al., 2016; Melanoma Nursing Initiative, 2017; National Cancer Institute, 2018; Puzanov et al., 2017; SITC, 2017; Spain et al., 2016; Weber et al., 2016.</p> | | |

(Beatty & Gladney, 2015; Kannan et al., 2014). ICIs block these pathways, restoring balance to a patient's immune response by allowing T cells to work against cancer cells (de Mello et al., 2016; Dougan & Dranoff, 2009; Kannan et al., 2014). Currently approved ICIs include antibodies that block specific immune checkpoint molecules, such as CTLA-4, PD-1, and PD-L1 (a ligand of PD-1) (Michot et al., 2016; Spain, Diem, & Larkin, 2016).

EXPECTED RESPONSE TO TREATMENT: ICIs can result in long-term responses and survival, even if the initial response is delayed or if progression is experienced before the response to treatment (Michot et al., 2016). Immune responses to therapy can vary between patients and from typical response patterns seen with chemotherapy or radiotherapy (Fay et al., 2016; Kannan

et al., 2014). This is because immune responses can occur months after treatment, even after an initial increase in tumor size or appearance of new tumors (Wolchok et al., 2009).

MONITORING AND MANAGEMENT OF SIDE EFFECTS: Patients should inform the cancer team immediately if any changes are noticed. Most side effects of ICIs can be managed if treated early, and stopping ICIs is not always necessary. Depending on how serious the side effects are, patients may receive steroids and/or delay further ICIs until they improve. Prompt reporting of potential side effects is key to effective management and completion of ICIs. A thorough baseline symptom assessment before starting ICIs is important to better identify possible treatment-emergent changes (Lewis, 2016). Such discussions also facilitate patient

TABLE 2.
ONLINE PATIENT AND CAREGIVER RESOURCES AND COMPARISON

| RESOURCE | CRI ^a | CSC ^b | CC ^c | SITC ^d | ACS ^e | NCI ^f | MNI ^g | IOE ^h |
|---|------------------|------------------|-----------------|-------------------|------------------|------------------|------------------|------------------|
| Content | | | | | | | | |
| Introduction to ICI | X | X | X | X | X | X | | |
| Guide to different cancer/treatment types | X | X | X | X | X | X | X | X |
| Taking medication | | | | | | X | X | X |
| Side effects | X | X | X | X | | X | X | X |
| Potential benefits | X | | | | | X | | |
| Patient case studies | X | X | X | | | | | |
| Action plan | | | | | | | X | X |
| Areas of research | | | | | X | X | | |
| Clinical trials | X | X | | X | | | | |
| Patient workshops or classes | | | X | X | | | | |
| Counseling services | | | X | | | | | |
| Financial assistance | | | X | | | | | |
| General cancer support | | | | | X | | | |
| FAQs | X | | X | | | | | |
| Timeline of ICI milestones | X | | | | | | | |
| News and events | X | | | | | | | |
| Format | | | | | | | | |
| Website content | X | X | | X | X | X | X | X |
| Video guides | X | X | | X | X | X | | |
| Downloadable guides | X | X | X | X | X | X | X | X |
| Downloadable diary, worksheet, checklist, question sheet, action plan | | | | | X | X | X | X |
| Interactive decision tools | | | | | X | | | |
| Webinars | X | X | | X | | | | |
| Live events | X | | | | | | | |
| Telephone/online workshops | | | X | X | | | | |
| Online search tool (clinical trials/support programs and services) | X | | | | X | X | | |
| Blog/e-news | X | X | X | | | | | |
| Podcasts | | | X | | | | | |
| Radio show | | X | | | | | | |
| <i>Continued on the next page</i> | | | | | | | | |

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TABLE 2. (CONTINUED)

ONLINE PATIENT AND CAREGIVER RESOURCES AND COMPARISON

| RESOURCE | CRI ^a | CSC ^b | CC ^c | SITC ^d | ACS ^e | NCI ^f | MNI ^g | IOEI ^h |
|--|------------------|------------------|-----------------|-------------------|------------------|------------------|------------------|-------------------|
| Format (continued) | | | | | | | | |
| Telephone helpline | | X | X | | | | | |
| Live webchat | | X | X | | | | | |
| Links to additional resources | X | | X | X | X | | X | X |
| ^a www.cancerresearch.org ^b www.cancersupportcommunity.org/immunotherapy-right-you ^c www.cancercares.org/tagged/immunotherapy ^d www.sitcancer.org/connectedold/p/patient ^e www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html ^f www.cancer.gov/about-cancer/treatment/types/immunotherapy ^g https://themelanomanager.org/patient-resources/action-plans ^h https://aimwithimmunotherapy.org/about ACS—American Cancer Society; CC—CancerCare; CRI—Cancer Research Institute; CSC—Cancer Support Community; FAQs—frequently asked questions; ICI—immune checkpoint inhibitor; IOEI—Immuno-Oncology Essentials Initiative; MNI—Melanoma Nursing Initiative; NCI—National Cancer Institute; SITC—Society for Immunotherapy of Cancer | | | | | | | | |

and caregiver education about potential symptoms or symptom changes to look for. Side effects of ICIs often involve inflammation of the skin, stomach, lung, liver, and endocrine system, but can potentially affect any system (Kannan et al., 2014; Kottschade et al., 2016; Michot et al., 2016). Some patients experience fatigue, which may be a standalone symptom or an indication of immune-related endocrinopathies (potentially secondary to hypophysitis) (Puzanov et al., 2017). Table 1 provides information for patients and HCPs on signs and symptoms of common irAEs and appropriate management. Although these side effects are usually mild to moderate and manageable, they can become severe or even life-threatening if not identified and managed quickly (Kannan et al., 2014; Kottschade et al., 2016; Michot et al., 2016). Appropriate management depends on location and severity, often involving temporary treatment to suppress immune system overactivation (Puzanov et al., 2017). Tumor responses have been seen in patients who discontinued therapy because of AEs (Schadendorf et al., 2017).

WHEN TO EXPECT SIDE EFFECTS: Side effects of ICIs can occur at any time, including as early as the day after the first treatment infusion or even after ending treatment. ICIs can influence a patient's immune response even after treatment has ended (Brahmer et al., 2018; Haanen et al., 2017; Puzanov et al., 2017). Most side effects occur within three months of starting ICIs but can also develop as long as a year after ending treatment (Haanen et al., 2017).

WHEN TO CONTACT THE CANCER TEAM AND OTHER HEALTHCARE PROVIDERS: Patients should quickly alert the cancer team and other HCPs if they experience potential side effects of ICIs or if any symptoms change or worsen. Because side effects can occur even after therapy has ended, patients should stay in contact with their cancer team and tell other HCPs (e.g.,

general practitioners, emergency department physicians) that they are receiving or have received ICIs (Kannan et al., 2014). This is important because patients often see multiple HCPs, who should be aware of the potential for irAEs (Brahmer et al., 2018).

Patient Education Methods and Support Tools

ICI-specific patient and caregiver educational materials are in relative infancy, but the importance of providing unique ICI education and support is increasingly recognized. Stakeholders, ranging from the pharmaceutical industry, professional societies, and cancer programs to patient advocacy and support groups, are developing ICI-related patient education and support resources, including print and online materials, events, and workshops (Association of Community Cancer Centers, 2016).

Although HCPs are still the most highly trusted source for information about cancer and cancer treatment, more than half of patients seek additional related information online (George et al., 2018; Shea-Budgell, Kostaras, Myhill, & Hagen, 2014). Online ICI resources for patients are available from various organizations, including general cancer care and patient advocacy and support groups, tumor-specific organizations, hospitals and cancer centers, professional organizations and societies, and pharmaceutical companies (Association of Community Cancer Centers, 2016) (see Table 2). These typically include information on how ICIs work, different cancer and treatment types, treatment-related side effects, clinical trial participation, and practical or emotional support, which can help patients stay up to date on ICI advances. However, lack of Internet access and limitations in computer literacy can be potential barriers to accessing these resources.

HCPs should be aware that not all online sources of information are reliable. In addition, availability of multiple patient

resources can lead to contradictory information and be confusing for some patients (Nagler & LoRusso, 2017). A need for consistent patient education was identified through evaluation of existing educational processes at one U.S. cancer center (Hoff & Tonne, 2017). Survey responses from 154 interprofessional team members within inpatient and ambulatory care settings identified five key areas for improvement in consistency: individual learning needs assessment, approach to education delivery, resource standardization and availability, handoff processes between departments and disciplines, and documentation of learner progress. Addressing these inconsistencies reduced patient confusion and increased trust and satisfaction (Hoff & Tonne, 2017). In another U.S. cancer center, implementing a standardized approach to ICI education improved patient outcomes, including decreased serious AEs and emergency department visits, and improved ability to continue treatment related to early symptom recognition (Fradkin et al., 2017). Providing concise, consistent, and relevant patient education is critical for empowering patients and caregivers to manage side effects of ICIs (Fee-Schroeder et al., 2013).

Materials are available to support continuing patient education regarding ICIs, particularly potential side effects. Patient diaries, questionnaires, or standard assessment forms are recommended to help patients identify, keep track of, and report any potential side effects (Brahmer et al., 2018). Patient and caregiver guides are available in various formats, including frequently asked questions for discussion between patients and their cancer team. Wallet cards detailing symptoms to monitor and how to notify the cancer team may be an effective tool for empowering patients to recognize and manage potential irAEs (Brahmer et al., 2018; Fecher et al., 2013). When patients are away from their treating medical center or care teams, patients who carry wallet cards can help to facilitate communication between providers, particularly if emergency situations arise (Fecher et al., 2013; Oncology Nursing Society, 2019). The Oncology Nursing Society has developed an ICI wallet card for use by patients and their HCPs; copies of the card and additional information are available at www.ons.org/toolkits/immunotherapy-patient-wallet-card-1.

Conclusion

ICIs represent a fast-developing cancer treatment option; patients with multiple types of malignancies can now potentially receive ICI therapy. The provision of timely, consistent, relevant, and personalized information for patients and caregivers is, therefore, essential. General learnings from patient education on chemotherapy suggest that educational resources should include a variety of teaching strategies that consider individual patient needs and preferences and are oriented toward patient empowerment. Although pretreatment patient education is essential, continued support and assessment of learning needs should also be made available. ICI-specific patient education should be developed with the input of an interprofessional

IMPLICATIONS FOR PRACTICE

- Understand the mechanisms of action of immune checkpoint inhibitors (ICIs) and the toxicities that may occur with them to provide appropriate education to patients and their caregivers.
- Inform staff about the adverse events that occur with ICIs, which are distinctly different from those resulting from chemotherapy or targeted therapy.
- Educate patients about the symptoms of immune-mediated adverse reactions, which may improve early detection, intervention, and evaluation of care to maximize clinical outcomes and quality of life.

team and regularly reviewed in line with emerging guidelines. Key messages for patients receiving ICIs include expected timing of therapeutic response and corresponding irAEs, importance of early irAE identification for effective management, and the unique ability of ICIs to influence immune response even after discontinuation. Several online resources are available to support patients and caregivers in understanding and managing ICIs. Additional patient supporting materials include symptom diaries or questionnaires and wallet cards to notify HCPs of ICI treatment. Oncology nurses play a vital role in ensuring that patients receive appropriate education related to their ICIs, which can support improved early irAE detection and appropriate intervention.

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QUESTIONS FOR DISCUSSION

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Journal club programs can help to increase your ability to evaluate the literature and translate those research findings to clinical practice, education, administration, and research. Use the following questions to start the discussion at your next journal club meeting.

- How will you prepare to best teach patients and caregivers about immune checkpoint inhibitors (ICIs)?
- When using the teach-back method to reinforce teaching about ICIs, what do you want patients and caregivers to relay back to you about ICI-related inflammation of the skin, stomach, lung, liver, and/or endocrine system?
- When educating your patients and their caregivers about online ICI patient and caregiver resources, what will you emphasize?
- What information do you want your patients to include on their immunotherapy wallet card?

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