



# Real-World Experiences in Immunotherapy Delivery

In 2016 and 2017, the American Society of Clinical Oncology (ASCO) named cancer immunotherapy the “advance of the year” in its Annual Cancer Progress Report.<sup>1,2</sup> As of May 2017, the U.S. Food and Drug Administration (FDA) has approved immune checkpoint inhibitors for the treatment of many different types of malignancies including skin cancers, lung cancer, head and neck cancer, bladder cancer, kidney cancer, and lymphoma. The next evolution of immunotherapy, which ASCO has referred to as Immunotherapy 2.0, focuses on personalizing the use of these agents so that the right patients receive therapies that are most likely to work best in them. Immunotherapy 2.0 also addresses issues around treatment resistance mechanisms and better ways to reduce the toxicities associated with immunotherapy.

While excitement around cancer immunotherapy continues to grow, cancer programs need guidance around practical implications surrounding the real-world delivery of immunotherapy. The ACCC education project, “Real-World Experiences in Immunotherapy Delivery,” addresses some of the practical issues that cancer programs must navigate to provide immunotherapy safely and effectively in their own communities.



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For this project, ACCC conducted interviews with cancer clinicians at two ACCC member programs who provided input about their real-world experiences using immunotherapy to treat cancer patients:

- Sandra & Malcolm Berman Cancer Institute at Greater Baltimore Medical Center, Towson, Md.
- The Center for Cancer Prevention and Treatment at St. Joseph Hospital of Orange County, Orange, Calif.

### Strategy 1. Identifying Local Experts & Resources

As cancer programs consider how they will be providing immunotherapy for various types of cancers, assessing the levels of experience across members of the cancer care team is an important first step. While some clinicians may have many years of experience using immunotherapies for clinical research, others may have very limited experience and may have difficulty identifying and managing immune-related adverse events (irAEs). Cancer clinicians at The Center for Cancer Prevention and Treatment and the Sandra & Malcolm Berman Cancer Institute noted that the oncologists and nurses who had experience using immunotherapies in clinical trials became recognized as “local experts” and as resources for other oncology providers who were starting to use immunotherapies in their practice. Since some of these local experts may have treated patients using higher doses of immunotherapy agents for clinical trial protocols, they may also have more experience managing more severe forms of irAEs.

Local experts may also provide formal education to other oncologists and nurses in the region. A recent survey of oncologists found that nearly 75 percent report being only somewhat confident or not confident in their abilities to work interprofessionally and manage patients receiving immunotherapy.<sup>3</sup> Since some oncologists are not able to attend annual national educational conferences, there are missed opportunities to inform and educate these providers about the optimal use of immunotherapies in real-world settings. Using grand rounds, tumor boards, and case conferences, the local immunotherapy experts at both The Center for Cancer Prevention and Treatment and the Sandra & Malcolm Berman

Cancer Institute have been educating their colleagues about the use of these newer agents by sharing case presentations and reviewing the science of immunotherapy.

### Practical Suggestions for Improvement

- Identify local oncologists and nurses with extensive experience using immunotherapy so that they can be a resource for other clinicians in your region. Some may be willing to provide formal education to other providers in established settings, such as tumor boards or grand rounds.
- Increase awareness about ongoing clinical research opportunities around the use of immunotherapy. Some large studies such as ALCHEMIST (The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials) now include an immunotherapy treatment arm.

### Strategy 2. Coordinating the Management of Immune-Related Adverse Events

Given that immune-related adverse events may be difficult to identify and manage, cancer programs need to educate and engage emergency medicine, urgent care, primary care, and radiology clinicians about the unique differences between irAEs and toxicities that may occur from standard chemotherapy or the use of molecularly targeted agents. Some of the main irAEs associated with checkpoint inhibitors include:<sup>4</sup>

- Diarrhea
- Colitis
- Hepatitis
- Skin problems
- Hypophysitis (inflammation of the pituitary gland)
- Pneumonitis
- Thyroid dysfunction.

Early recognition and proper treatment remain essential in patients receiving treatment with immunotherapy agents.<sup>5</sup>

Emergency medicine clinicians may not recognize that certain symptoms are irAEs, so patients may not receive the required



therapies in a timely fashion. For example, cancer patients treated with certain immunotherapies may develop gastrointestinal symptoms that require urgent treatment with high doses of corticosteroids. If the emergency room clinicians do not identify the problem and coordinate care with medical oncology, then the patient may leave the ER hydrated, but inadequately managed. The use of high doses of corticosteroids remains a critical component of the treatment algorithm when cancer patients treated with immunotherapy present with emergent symptoms.<sup>6</sup>

In another example, a patient may undergo a radiologic study and the radiologist may not recognize that the unusual findings are due to an irAE or may be due to a phenomenon known as pseudoprogression. Radiologists may need to learn how to distinguish hypophysitis from other brain abnormalities on MRI scans.

The team at St. Joseph Hospital of Orange County The Center for Cancer Prevention and Treatment is planning a formal education project for their emergency medicine clinicians. Their nurses are also involved with the International Association for the Study of Lung Cancer (IASLC) nursing committee and have been corresponding with nurses around the world about the optimal management of irAEs in the real-world setting. The team is currently planning to deliver a series of educational in-service programs for teams of emergency medicine providers and nurses who work at their hospital. Some of the irAE topics to be covered are pneumonitis, colitis, rashes, and other common reactions. The educational curriculum will be based on resources like the Oncology Nursing Society “Putting Evidence into Practice: Immunotherapy-Induced Diarrhea.”<sup>7</sup>

In addition to educating emergency department clinicians, St. Joseph Hospital of Orange County The Center for Cancer Prevention and Treatment is evaluating other ways to educate and inform patients and family members about the differences in immunotherapy toxicities. One consideration is to provide patients with some form of identification, such as a laminated medical identification card that informs emergency medicine clinicians that the patient is on an immunotherapy agent for cancer. This type of card can help empower patients and family members to advocate for emergency care that is always coordinated with oncology providers. In addition to providing the card, clinicians are spending extra time to educate patients about immunotherapy using resources, including:

- ASCO Answers: Understanding Immunotherapy<sup>8</sup>
- The American Cancer Society’s, *What is Cancer Immunotherapy?*<sup>9</sup>
- The American Lung Association’s, *What You Need to Know About Lung Cancer Immunotherapy*,<sup>10</sup>
- The Lung Cancer Alliance’s, *Immunotherapy for Lung Cancer: A Guide for the Patient*<sup>11</sup>

- The Cancer Research Institute’s videos, *Immunotherapy & Chemotherapy: What’s the Difference?* that explain to patients the concept of how immunotherapy will work to combat their cancer.<sup>12</sup>



### Practical Suggestions for Improvement

- Develop a coordinated outreach, communication, and education plan to inform emergency medicine, urgent care, and radiology clinicians in your region about the identification and coordinated management of irAEs.
- Engage team members in ongoing discussion and dialogue by presenting unusual findings during case conferences and inviting other specialists, such as dermatologists, radiologists, gastroenterologists, and pathologists, to learn about the unique aspects of irAEs.
- Since the concept of immunotherapy can be confusing for patients, leverage existing patient education resources that are clear, concise, and produced at the appropriate health literacy level.
- Engage and empower patients to have a more active role in their care if they develop signs of irAEs. If they need to go to an emergency room, have a caregiver or family member notify the medical oncology office.



### Strategy 3. Ensuring Adequate Patient Access & Communication

In the state of Maryland, the All-Payer Model has led hospitals to be more vigilant when tracking and managing drug inventory based on patient treatment schedules.<sup>13</sup> The Sandra & Malcolm Berman Cancer Institute at Greater Baltimore Medical Center has a dedicated oncology pharmacist who performs these tasks and helps to monitor drug acquisition costs, prior authorizations, medication billing, and reimbursements to the hospital. Oncology pharmacists can also play a key role in detecting signs and symptoms of irAEs and resources like the NCCN Immunotherapy Teaching/Monitoring Tool ([nccn.org/immunotherapy-tool/pdf/NCCN\\_Immunotherapy\\_Teaching\\_Monitoring\\_Tool](http://nccn.org/immunotherapy-tool/pdf/NCCN_Immunotherapy_Teaching_Monitoring_Tool)) can be incorporated into treatment plans to ensure that the right questions are being asked to assess for potential toxicities.

Both the Sandra & Malcolm Berman Cancer Institute and The Center for Cancer Prevention and Treatment have strong teams of financial advocates who use copay and patient assistance programs to reduce the risk of financial toxicity in patients treated with immunotherapies. The Affordable Care Act has led to more patients entering the cancer care system with health insurance. When immunotherapy agents are used on-label, patients do not seem to have difficulty getting coverage from their health insurance plans. However, researchers have noted that when these agents



are not used for their specific indications, the costs of these therapies to patients and health systems can be significant.<sup>14</sup>

The Center for Cancer Prevention and Treatment sees many cancer patients who are highly educated and knowledgeable about the latest medical advances and research developments. As a result, the cancer program often gets direct inquiries from patients and family members about the possibility of receiving immunotherapy for their cancer. Clinicians need to know how to manage demands and expectations from patients by properly discussing the appropriate use of immunotherapy, as well as offering opportunities for clinical trial enrollment if patients are eligible. At The Center for Cancer Prevention and Treatment, an integrated approach to improve access to immunotherapy has impacted the clinical workflow in several ways:

- Physicians spend more time in team-based discussions to plan and coordinate care with other medical specialists and nurses. These discussions may also include brief educational opportunities and patient case studies.
- Oncology nurses, infusion nurses, and nurse navigators coordinate their approach to educating patients and documenting and communicating patient-reported symptoms. This care coordination allows the team to collect information from patients when they come for follow-up appointments, when they come for their treatments, or when they call with questions.



### Practical Suggestions for Improvement

- Work with oncology pharmacists to manage and track drug orders and inventory based on treatment schedules. Identify potential bottlenecks in the process that may lead to drug delivery delays so that treatment schedules are not affected.
- Leverage copay and patient assistance programs for all patients, including those who appear to have adequate health insurance coverage.

### Going Forward

Advances in immunotherapy will lead to more cancer programs offering these treatments to patients. While these therapies are exciting developments for oncologists, patients receiving them may require carefully coordinated monitoring and treatment by non-cancer clinicians in the surrounding community. Patients treated in real-world settings are often more complex than those represented in clinical trials and multiple specialists working in different health systems may get involved with the identification and management of pseudoprogression and irAEs.

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