Best Practices for Implementing Cancer Immunotherapy in the Community

The Association of Community Cancer Centers (ACCC) recently hosted live continuing medical education (CME)-certified learning workshops at two community cancer programs to review current barriers to immunotherapy implementation in the community setting. During the workshops, an expert faculty panel engaged participants in discussion on the challenges that they may face as they integrate immunotherapy into their clinical practice, as well as practical solutions and strategies they can apply to overcome these barriers. This article summarizes the guidance and information provided by the faculty on the various issues raised during the workshop discussions.

Decision-Making in Therapy Selection

It is not always clear which checkpoint inhibitor, or combination regimen, provides better efficacy than others. In order to establish clarity as a foundation for therapy selection, it is critical for clinicians to review the available clinical data and, where available, comparator data, for the indication of interest. Clinical practice guidelines from the National Comprehensive Cancer Network (NCCN) provide evidence-based, tumor-specific recommendations and guidance for decision-making, and biomarkers for response also provide a valuable tool to guide therapy across malignancies (see Figure 1, right).

Response and Toxicity Monitoring

Monitoring response to therapy and managing immune-related adverse events (irAEs) pose additional challenges in using checkpoint inhibitors. Although most patients show response to treatment at approximately 6 to 10 weeks after therapy initiation, responses can be nuanced. For instance, pseudoprogression can occur (e.g., in about 10 percent of patients with melanoma), in which there is a transient worsening of disease prior to disease stabilization or regression. Clinicians should be familiar with response evaluation criteria monitoring parameters to measure treatment response.[1]

Early recognition of irAEs is essential for effective management; therefore, clinicians need to have a high index of suspicion for irAEs. The type and broad distribution of irAEs differ considerably from toxicities associated with chemotherapy, and immune-related side effects can also occur or recur months after discontinuation of therapy. Routine baseline monitoring prior to initiating therapy is paramount, and should, at minimum, include tests for renal, liver, and thyroid function, repeated at 4- to 6-week intervals. Immune-related adverse event management is based on the grade of severity. The most commonly encountered grade 1-2 irAEs are skin- and gastrointestinal-related, with differences noted across checkpoint inhibitors (e.g., colitis and diarrhea are more commonly associated with CTLA-4 agents). Although relatively uncommon, endocrine toxicities such as hypophysitis, hyper- or hypothyroidism, can be challenging to identify; however, they contribute to greater morbidity. Combination therapies increase the likelihood of patients experiencing irAEs. Fortunately,

most irAEs are manageable when recognized early and addressed immediately, and evidence-based guidelines provide recommendations for monitoring and managing immune-related toxicities.[2]

Enhancing Patient Care Through Multidisciplinary Team Communication

Effective irAE management starts with timely and current education for patients and their caregivers at treatment initiation and throughout treatment into survivorship. Such education should include:

- Information about mechanisms of action
- How checkpoint inhibitors differ from chemotherapy and other cancer therapies
- How to recognize irAEs during therapy as well as when treatment has ended
- The importance of ongoing communication with members of the oncology multidisciplinary team.

In addition, all clinicians involved in the care of patients treated with checkpoint inhibitors, such as providers in radiology, radiation oncology, and emergency medicine need ongoing education on these agents including mechanisms of action, how to recognize irAEs, how immunotherapy differs from chemotherapy, how to contact the treating oncology team, and more. Because irAEs involve many organ systems, specialists outside of the field of oncology need to become members of the multidisciplinary team to provide assessment, share their expertise about which laboratory panels to order in the event of emergent irAEs, and to support system-based irAE management. Establishing a list of "go-to" specialists and organizing multidisciplinary case-based irAE discussions before treatment initiation (e.g., via tumor boards and grand rounds) offer channels for cross-specialty communication, education, and a foundation for multidisciplinary collaboration. Figure 2, page 78, summarizes several tools that support multidisciplinary communication and education.

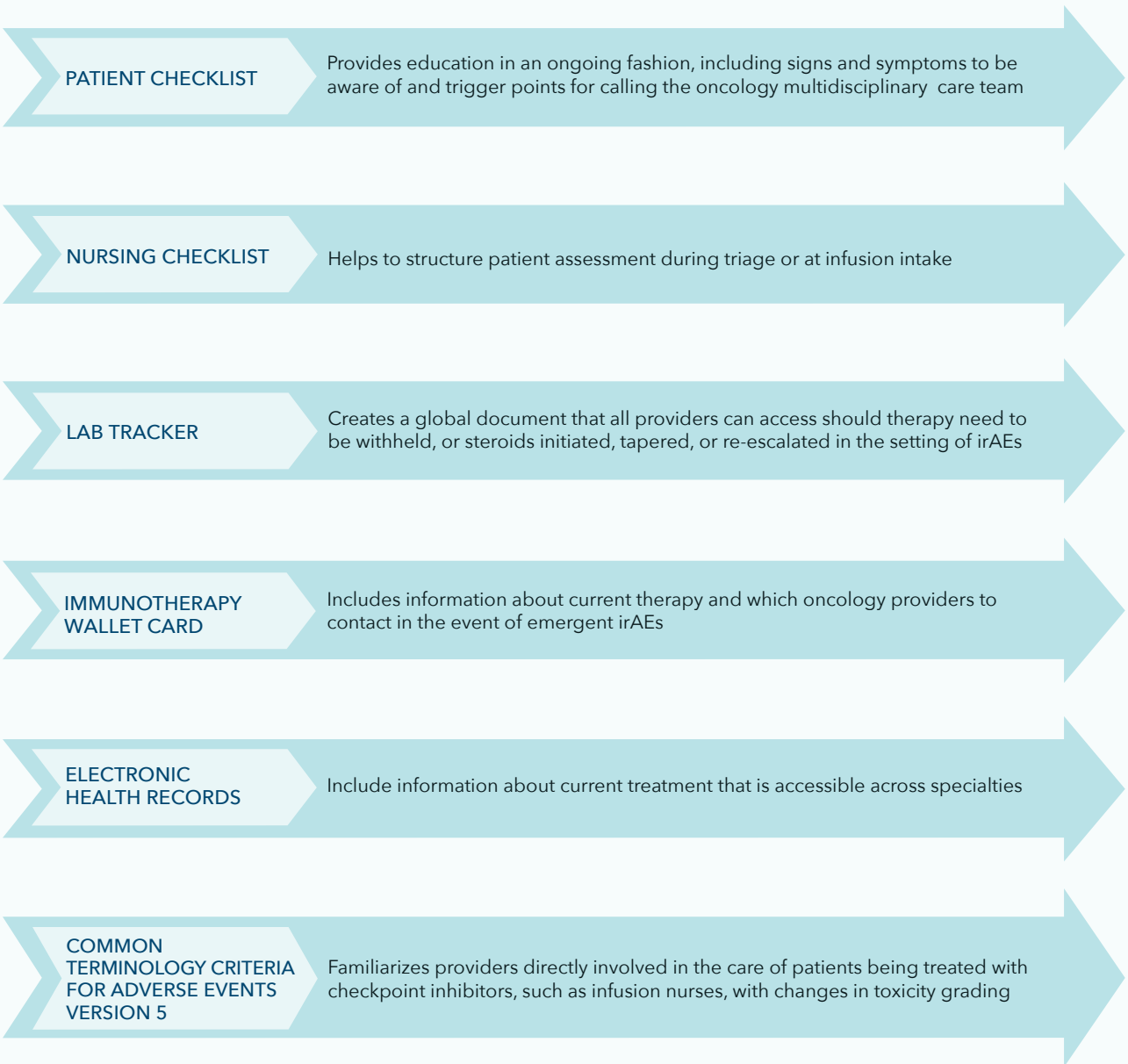
Optimizing Immunotherapy Reimbursement

Precertification for immunotherapy is resource and time intensive and many challenges persist. For instance, while payer policies lag behind new indications and medication approvals, payer

Figure 1. Biomarkers for Immunotherapy Response

PD-L1	MSI	TMB
Programmed death ligand-1 (PD-L1) expression correlates with response to checkpoint inhibitor therapy and is conducted via immunohistochemistry. Several studies are ongoing to answer questions about the role of biomarkers in therapy selection.	DNA mismatch repair system (MMR) failure causes microsatellite instability (MSI). MSI occurs most commonly in colorectal or endometrial cancer but can occur in every malignancy. MSI-high as measured by fragment analysis correlates to an increased neoantigen burden, which may respond more favorably to checkpoint inhibitor therapy.	Tumor mutational burden (TMB) measures the total number of somatic mutations identified per megabase of the genome coding area. Tumors with high TMB are likely to harbor neoantigens and might respond more favorably to immune checkpoint inhibitors.

Figure 2. Tools for Multidisciplinary Team Communication and Education



authorization requirements are continually expanding. Revenue work queues (e.g., JW modifiers) can streamline prior authorization practices, and trigger collation of the data necessary to support precertification as soon as immunotherapy is prescribed, including:

- Documentation of disease state
- Payer policies and practices
- Prior therapies received by patients
- Biomarker findings if required
- Concurrent indications that might preclude authorization.

Pharmacy staff should be armed with the most recent clinical data, published guidelines, insurance provider clinical policies, compendia, and national/local coverage determinations (NCD/LCD) in order to support precertification claims. It can also be useful to include guideline recommendations and FDA approvals as part

of a prior authorization claim, as well as any information on changes in therapy dosing and administration. Patients should be aware of their financial obligations before therapy initiation, and pharmacy staff can identify patients in need of assistance and access resources such as assistance programs for uninsured and/or underinsured patients. In order to optimize waste management, it is important to clarify if payers will allow for wastage billing.

Unfortunately, denials are common, and payers have strict guidelines and timelines about the appeals process. A denial management process that works with the revenue cycle can support routing claims in a timely fashion and ensure staff have access to the resources they will need to support an appeal (e.g., guidelines, NCD/LCD, clinical policies). Finally, it is important for oncology pharmacy staff to monitor trends with payers and hold them accountable if immunotherapy denials become an established pattern.

Conclusion

As part of the learning workshops process, the expert faculty collaborated with the participants at each cancer center to develop action plans for incorporating short-term and long-term changes in their practice aimed at improving the quality of patient care. The action plans drafted at these workshops covered creation of educational resources for the clinical staff and patients and information cards that can be used for patients going to the emergency room or for referring providers. Several changes are currently underway at the participating cancer centers including addition of immunotherapy information to an existing Oncologic Emergency Card that patients can present at the emergency room and the development of education materials for nurses and other healthcare providers on how to recognize and manage irAEs. Immediate changes like these demonstrate the effectiveness of onsite CME designed to identify solutions to local needs. ■

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