Education Interventions Improve Management of irAEs, Study Shows

Since the approval of the programmed death-1 (PD-1) inhibitors pembrolizumab and nivolumab for the treatment of metastatic melanoma in 2014, the oncology community has seen a tidal wave of new approvals and indications for immunotherapies to treat cancer. This paradigm shift has been led by monoclonal antibodies targeting both sides of the PD-1 pathway, with six drugs approved by the Food and Drug Administration across dozens of indications. As PD-1 pathway blockade releases anergic T-cells to mount a robust immune response, class-specific toxicity results from autoimmune attack of self-antigens that can occur in any organ. Dubbed immune-related adverse events (irAEs), these effects have forced oncologists to learn how to optimally manage an entirely new spectrum of toxicity. Unusual and potentially serious side effects include conditions such as:

- Pneumonitis, inflammation of the lungs
- Myocarditis, inflammation of the heart muscle
- Hypophysitis, inflammation of the pituitary gland or pituitary stalk
- Guillain-Barre syndrome, a rare disorder in which your body's immune system attacks your nerves
- Myasthenia gravis, a chronic autoimmune, neuromuscular disease,
- And many others.

Treatment of irAEs often require diverse resources and expert consultation from subspecialists from all corners of the medical field.

Managing irAEs in the Community Setting

Community cancer programs have been particularly susceptible to challenges in managing irAEs, as they may have variable access to subspecialist care, limited resources compared to larger academic institutions, and/or less practice experience using anti-PD-1 pathway agents. Thus, the Association of Community Cancer Centers (ACCC) embarked on a quality improvement (QI) research study to identify barriers to optimal care of patients receiving PD-1 pathway inhibitors in community cancer programs and assess the impact of a comprehensive multidisciplinary immunotherapy educational intervention.

The project intended to assess the needs of community cancer programs administering immunotherapies, with a focus on minimizing irAE morbidity and mortality and barriers to optimal care delivery. Then, targeted educational programs were provided to faculty and staff in various formats (live and online) to educate patient-facing team members about irAE management, patient education, and care coordination strategies. The end goal was to demonstrate that targeted educational interventions offered to community oncology professionals were feasible and could improve management of irAEs.

Interested cancer programs applied for inclusion in the research study and completed a detailed questionnaire outlining specifics about their clinical practice and experience with immune checkpoint inhibitors. ACCC formed an Advisory Committee composed of two medical oncologists, an oncology nurse, and an oncology pharmacist to help select the sites included in the study, direct the project, and develop the educational materials. Site selection criteria included: adequate numbers of patients treated with checkpoint inhibitors overall and in predetermined tumor types, presence of an onsite QI or data informatics staff, and site participation in value-based payment models.

QI Methodology

The two sites selected for the project were Centra Health Alan B. Pearson Cancer Center in Lynchburg, Virginia, and Cancer and Hematology Centers of Western Michigan, in Grand Rapids, Michigan, Baseline data (see Figure 1, below) were collected from 98 patients initiating immuno-oncology (IO) therapy between December 2017 and April 2018 at both community cancer programs, including information on comorbidities, irAE development, laboratory values, emergency room visits and hospitalizations, presence or absence of patient education on said immunotherapy agent(s), and treatment adherence.

The clinicians also completed surveys designed to help understand varying immunotherapy practice patterns at each site. Some of the pertinent findings at baseline included that a majority of patients at both sites treated with IO drugs had multiple non-cancer medical co-morbidities, only 5 percent of patients had treatment-emergent irAEs graded on a standard grading system, and the majority of clinicians assessed did not feel confident managing irAEs. The advisory committee analyzed the baseline data and designed targeted educational interventions for cancer center faculty and staff to address specific gaps identified.

The participants received ACCC immunotherapy wallet cards (see Figure 2, page 66) for patient distribution and National Comprehensive Cancer Network (NCCN) pocket guides on management of irAEs as a clinician resource. In addition, members of the advisory committee held on-site educational workshops that included didactic presentations focusing on irAE

Figure 1. A Schema Depicting an Overview of the Study Activities

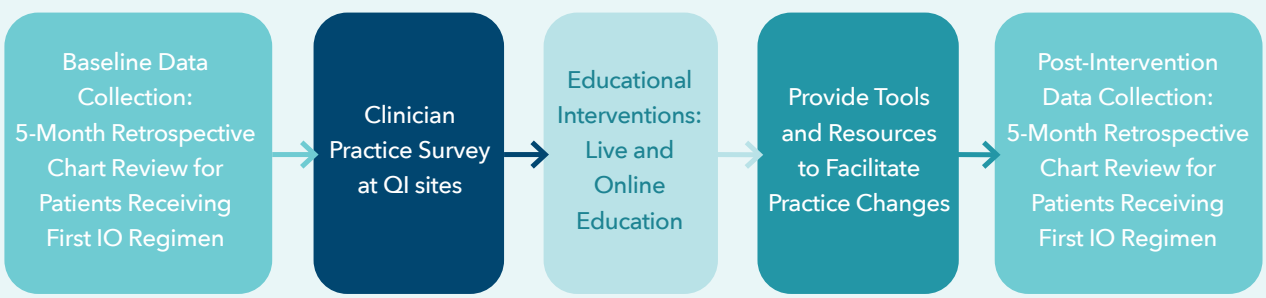


Figure 2. ACCC Immunotherapy Wallet Card

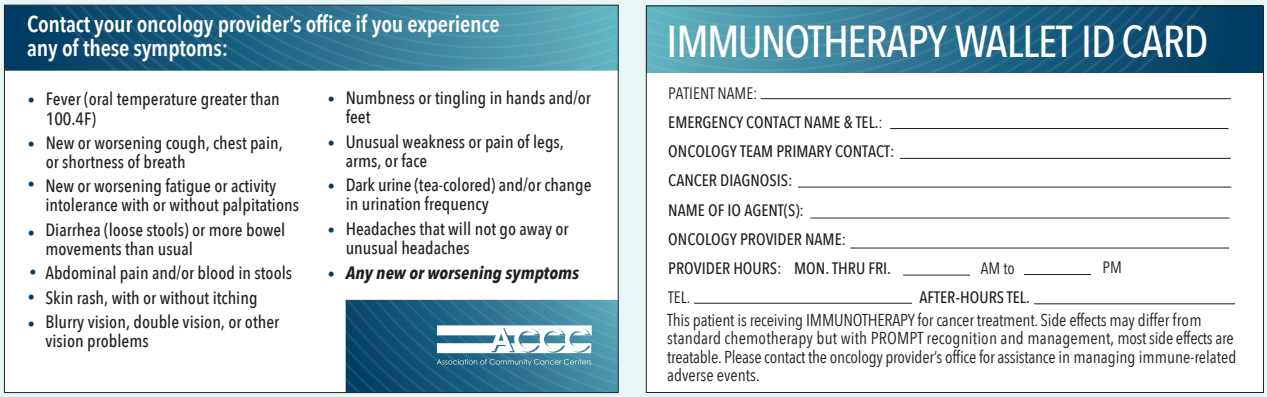
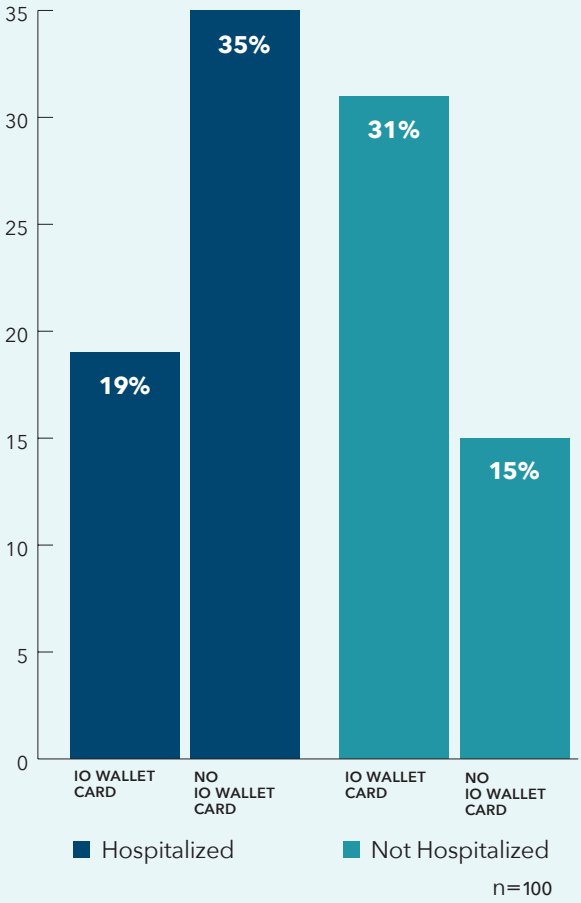


Figure 3. Impact of IO Wallet Card on Hospitalization Rates at One Participating Site



management within the context of case scenarios and an open discussion period intended to uncover institution-specific challenges to implementing irAE management and provide strategies to improve care. Live discussions were attended by clinicians as well as nurses, pharmacists, advanced practice providers, and other team members.

During the open discussion sections, the site participants and Advisory Committee members had an opportunity to discuss specific barriers encountered that they felt affected irAE management and worked with the Advisory Committee members for guidance. A common refrain was lack of subspecialty support and understanding of irAEs. The clinicians also reported inadquate training in diagnosing irAEs, as well as insufficient standardized guidelines on management. The Advisory Committee members provided information on up-to-date practice resources, as well as reviewed their experiences in engaging and involving subspecialists in complex cases. In addition to the live events, the cancer care teams were also included in four webinars designed and led by the Advisory Committee members:

1. Clinical Advances in Immunotherapy
2. Rare irAEs
3. Common irAEs
4. Challenges with Implementing Immunotherapy.

Study Findings

Following the live workshops and online webinars, ACCC surveyed the participating sites at three and six months to assess the status of their progress and patient outcomes. Data was collected from 100 patients initiating IO therapy between January 2019 and April 2019 and compared to baseline using Fisher's exact test. Surveys were also performed before and after participating in the live and online workshops to understand clinician perspectives of the value of these educational programs.

Results of the study were presented in abstract form at the 2020 ASCO-SITC Clinical Immuno-Oncology Symposium. The study found that the educational interventions were, in fact, feasible and well-received by faculty and staff, with pre- and post-surveys revealing perceived improvements in several areas. Clinicians from both sites reported handing out more patient-centered education materials after the workshops, although only one site utilized the immunotherapy wallet card provided by ACCC. Clinician participants also reported improved understanding of how to manage specific irAEs. Notably, there was consistent reporting of improvements in care coordination and communication both among inter-office team members, as well as with outside specialists. Although these were not statistically significant (primarily due to the overall total numbers of respondents among only two sites), there did appear to be a trend toward perceived care improvements owing to the workshops.

As noted above, one institution elected to utilize the ACCC-designed immunotherapy wallet card while the other did not. There was a statistically significantly lower rate of hospitalization among IO-treated patients at the cancer program that adopted the wallet card in comparison to the site that did not (19% vs 35%, $p = 0.0024$; Figure 3, left). While many factors could have contributed to this difference in the hospitalization rate, these data are hypothesis-generating and lends credence to the idea that simple educational initiatives have the potential to dramatically impact patient outcomes.

Cancer programs and practices that want to use this education tool with their IO patients can download a print-ready PDF of the IO Wallet Card at accc-cancer.org/io-walletcard. Limited print quantities are available. Please contact Janelle Schrag, Senior Program Manager, at jschrag@accc-cancer.org for these and other inquiries.

In summary, this ACCC-initiated QI research study successfully provided educational materials and targeted learning to faculty and staff at two community cancer programs and demonstrated clearly that this approach was feasible and valued by faculty and staff alike. The study design utilized relatively little time or resources to provide educational interventions, thus it would likely be possible to design a similar enduring program that would be portable and provide perceived value at other community cancer programs. The finding of a marked decline in hospitalizations at the site that adopted the ACCC IO wallet card for patients suggests the possibility that this intervention could have tangible value but requires further research to confirm its significance. ■

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