

Meeting the Challenge of Immune-Related Adverse Events With Optimized Telephone Triage and Dedicated Oncology Acute Care

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

Immune checkpoint inhibitors (ICIs) have improved outcomes for many patients with advanced cancers. However, managing the immune-related adverse events (irAEs) associated with these agents is challenging. Late recognition and/or inadequate irAE management can result in ICI discontinuation or termination, negatively impacting patient outcomes and increasing unplanned emergency department visits, hospital admissions, and costs of care. Improved clinician training and infrastructure development are needed to adequately address irAEs and maximize the potential benefits of ICIs. Advanced practice providers (APPs) are well positioned to drive these improvements. Two aspects of care may reduce the burden of irAE management: improved telephone triage and the implementation of dedicated oncology acute care services. Evidence-based protocols should be used for telephone triage. Protocol development may benefit from an evaluation of current irAE management guidelines together with resources from the Melanoma Nursing Initiative and Immuno-Oncology Essentials. Patients and their caregivers must be educated to recognize and report early symptoms suggestive of an irAE, thereby supporting triage efforts. Advanced practice providers should also advocate for the development of dedicated oncology acute care facilities staffed with clinicians well trained to recognize, grade, and manage irAEs. This manuscript reviews multiple existing models of telephone triage and dedicated oncology acute care. Oncology APPs are poised to lead the staffing, infrastructure, and educational changes necessary to reduce the burden of irAEs in patients receiving ICI therapy.

Optimization of triage and acute care for immune-related adverse events (irAEs) associated with immune checkpoint inhibitor (ICI) therapy represents both a challenge and opportunity for the advanced practice provider (APP) community. As the number of oncology patients receiving ICI therapy grows and the complexity of therapy increases (particularly with the anticipated availability of myriad combination approaches), irAE management will become an essential competency in oncology. Advanced practice providers have demonstrated strength and expertise in irAE management and should continue leading the charge to address this growing challenge. This article serves as a call to action for APPs to appreciate the burden associated with inadequate irAE triage/acute care, evaluate the models for addressing this issue, and plan for education and resource allocation to optimize irAE management across clinic settings.

This article is part of a supplement highlighting the resources of the Immuno-Oncology (IO) Essentials and Melanoma Nursing Initiative (MNI; Rubin, 2017). Companion articles included in this supplement review the optimal incorporation of these resources, some of which are discussed herein. This supplement includes an article addressing ICI use in non-small cell lung cancer (Davies, 2019), another focused specifically on ICI use in head and neck squamous cell cancer (Fazer, 2019), and a final article that reviews irAE management across tumor subtypes (Wood, 2019).

RATIONALE FOR IMPROVED TRIAGE AND ACUTE CARE

Immuno-oncology is a rapidly developing field that has given rise to a number of new immunotherapies, including several ICIs, with additional agents in clinical development (Cousin, Seneschal, & Italiano, 2018; Zhu, Zhao, Li, & Yu, 2018). The result is expanded treatment options and significantly improved outcomes for many cancer patients in both the adjuvant and metastatic setting (AstraZeneca Pharmaceuticals LP, 2018; Khan et al., 2018; Zhu et al., 2018). However, ICIs differ in important ways from traditional cytotoxic chemotherapy and require specialized management strategies and collaborative approaches for the

oncology care team. This is particularly crucial in the setting of irAE management (Brahmer et al., 2018; Postow, Sidlow, & Hellmann, 2018). The situation is likely to be further complicated as current and emerging immunotherapies are increasingly used in combination with cytotoxic chemotherapy or other anticancer therapies (Yan et al., 2018). Strong foundational knowledge of ICIs and their associated irAEs is essential for providing optimal care of patients receiving these therapies.

Maximizing the effectiveness and lowering the health-care costs associated with irAEs requires corresponding improvements in training and infrastructure development. Currently, many health-care providers (HCPs) are insufficiently trained on the differences between irAEs associated with ICIs and chemotherapy-related AEs (Association of Community Cancer Centers, 2016). Moreover, irAEs may be difficult to distinguish from symptoms of disease progression (e.g., in the case of liver dysfunction from an irAE vs. disease progression). Delayed identification and treatment of irAEs can lead to ICI discontinuation or termination, resulting in reduced therapeutic benefit, increased morbidity and mortality, and impaired quality of life.

SCOPE OF THE PROBLEM

Oncology HCPs are generally aware of the large management burden associated with cytotoxic chemotherapy for cancer. Patients undergoing chemotherapy experience an average of one hospital admission and two emergency department (ED) visits per year, and 40% to 50% of these visits are prompted by chemotherapy-related side effects (Daly et al., 2018). Moreover, these visits come at a high cost and are primarily driven by reliance on acute hospital care, which accounts for roughly half (48%) of total cancer expenditures (Brooks et al., 2014). In 2010, the average cost of a chemotherapy-related hospitalization was \$22,000 (Daly et al., 2018). In addition to elevating health-care costs, an acute-care hospital visit delays treatment, reduces patients' quality of life, adds to caregiver burden, and increases risk of nosocomial infections. A recent study reported a regional spending variance in Medicare cancer patients that was chiefly driven by acute-care hospital usage (Brooks et al., 2014). This suggests that reducing the reli-

ance of cancer patients on traditional acute care facilities such as EDs can go a long way to improving cancer care and reducing cost.

The scope of this problem may be magnified in cancer patients receiving ICI therapy. Immune checkpoint inhibitor therapy is associated with a large number of diverse irAEs (Sznol et al., 2017a, 2017b). The onset of irAEs may vary widely, sometimes occurring long after ICI therapy has ended. This contrasts with cytotoxic chemotherapy, in which the onset of treatment-related AEs is more predictable and closely tied with time from infusion. As a consequence, irAEs are more likely to be experienced outside a health-care setting. Couple this with their sometimes subtle presentation, and irAEs can easily be missed by both the patient and HCP unless they are both vigilant and know what to look for. The management of irAEs is further complicated by the often simultaneous presentation of clinical signs and symptoms of irAEs that can have different origins (e.g., symptoms and signs of hormonal irAEs and gastrointestinal irAEs at the same time). A recent paper reported that 25% of the visits by ICI-treated cancer patients to the ED of a comprehensive cancer center were related to irAEs (El Majzoub et al., 2018).

Figure 1 illustrates the time to onset of grade 3/4 select irAEs in a pooled analysis involv-

ing patients with advanced melanoma receiving nivolumab/ipilimumab combination therapy, highlighting the wide variation in onset of irAEs (Sznol et al., 2017a). The pooled analysis from which this figure was drawn showed 95% of patients experienced at least 1 irAE, and 55% experienced at least 1 grade 3/4 irAE (Sznol et al., 2017a). The onset of grade 1 or 2 irAEs also varies significantly (McGettigan & Rubin, 2017). These data illustrate that a large number of patients receiving ICIs can be expected to experience irAEs of varying intensity and at varying timepoints.

Reimbursement Ramifications

There is also a financial impetus for better management. The United States Centers for Medicare & Medicaid Services (CMS) recently proposed a change to its Hospital Outpatient Quality Reporting (Hospital OQR) Program that could impact hospitals' outpatient Medicare payments for cancer patients beginning in 2020 (Miller, 2016; U.S. Centers for Medicare & Medicaid Services, 2019). This financial consequence serves as a further impetus to improve cancer care and to take action to limit potentially preventable treatment-related ED/acute care or hospital visits.

The CMS identified 10 conditions in hospital patients receiving chemotherapy that are poten-

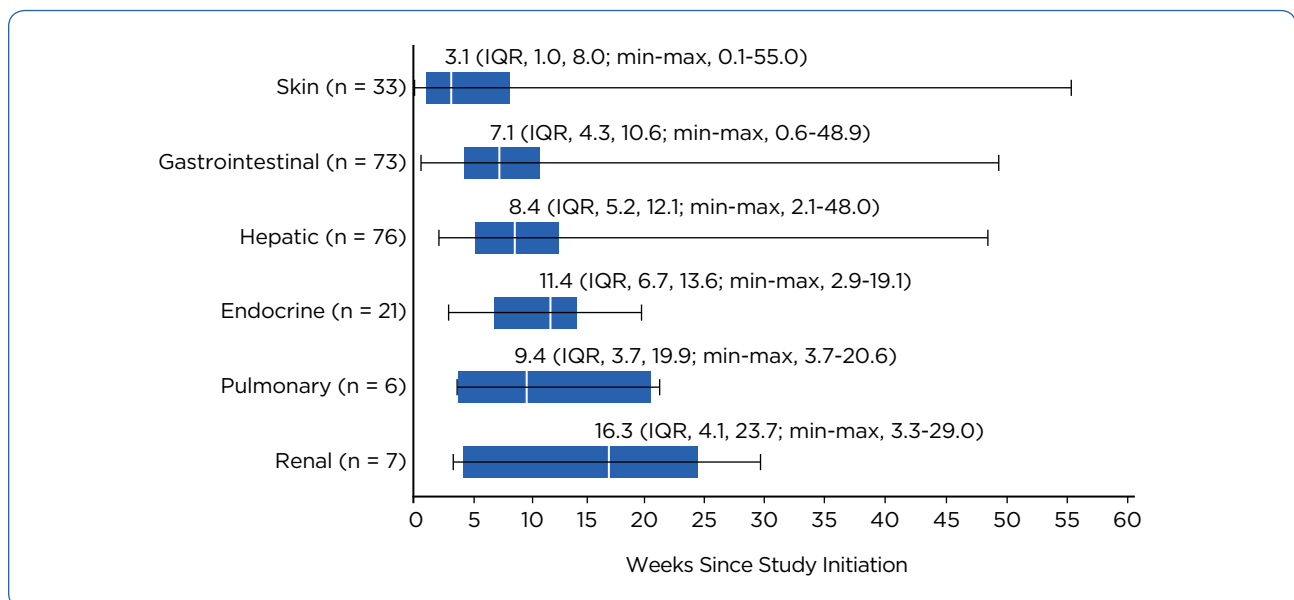


Figure 1. Onset of grade 3/4 treatment-related select adverse events in a pooled analysis of nivolumab and ipilimumab combination therapy in advanced melanoma patients. IQR = interquartile range. Adapted from Sznol et al. (2017a).

tially preventable through appropriately managed outpatient care: anemia, dehydration, diarrhea, emesis, nausea, neutropenia, fever, pain, pneumonia, and sepsis (Battaglia, 2018; Miller, 2016). The CMS plans to measure cancer hospitals' performance on the basis of frequency of ED visits and admissions. Beginning in 2020, hospitals may be penalized financially if patients receiving anticancer drugs visit the ED or are admitted to the hospital. Because of the newness of ICIs, ICI-associated irAEs were not specifically incorporated in the CMS reimbursement changes proposed to take place in 2020, but subsequent changes that incorporate ICI irAEs are expected in the near future. To reiterate, there is a strong financial incentive to limit unnecessary ED visits and hospital admissions for irAE management.

Overall Approach to Reduce Hospital-Based Acute Care in Oncology

Table 1 presents select strategies to reduce general hospital acute care use by cancer patients that are relevant to this article (Handley, Schuchter, & Bekelman, 2018). One strategy is to standardize clinical pathways for symptom (AE/irAE) management, which includes the development and implementation of phone triage systems and standardized symptom management pathways for use in the outpatient or ED/acute care setting. Optimizing the care of cancer patients treated with ICIs will likely require building a framework within one's institution to better handle irAEs. This process would benefit from an evaluation of

current irAE management guidelines (Brahmer et al., 2018; National Comprehensive Cancer Network [NCCN], 2018), together with resources at the IO Essentials/MNI websites. This entails ensuring clinicians are suitably knowledgeable and/or trained to identify, grade, and manage irAEs, both over the telephone and in person. Standardized irAE management education is critically important (Handley, Schuchter, & Bekelman, 2018). Each institution must decide how they will assess irAEs via telephone triage and how to standardize their approach to irAE management. Otherwise, given the variation in different irAE management guidelines (Brahmer et al., 2018; NCCN, 2018), inconsistency and confusion is likely to emerge among the different participants.

There is also a need for institutions caring for ICI-treated patients to develop methods for establishing care continuity. Plans should be developed to maximize close communication between patients and oncology HCPs and between different oncology HCPs involved in the management of irAEs in these patients. As Table 1 suggests, access and coordination of care can be enhanced by developing reliable mechanisms for the patient to contact the care team and for standardized care transitions, both within the institution and with ED or urgent/acute care clinics that are embedded with providers trained to manage irAEs (Handley et al., 2018).

How would improvements in triage and the use of dedicated oncology urgent care improve outcomes? The key is to prevent unplanned pre-

Table 1. Select Strategies to Reduce Acute Care for Patients With Cancer

Strategy	Example interventions (in order of increasing complexity)
Enhance access and care coordination	<ul style="list-style-type: none"> • Reliable mechanisms for patients to contact the care team • Improved and standardized care transitions • Patient navigator programs • Automated hovering
Standardize clinical pathways for symptom management	<ul style="list-style-type: none"> • Outpatient symptom management and phone triage systems • Supportive care incorporated into standardized disease management pathways • ED symptom management pathways
Develop urgent cancer care tactics	<ul style="list-style-type: none"> • Flexible scheduling and embedded urgent care clinics • Cancer providers embedded in the ED • Dedicated acute cancer treatment clinics • Dedicated cancer EDs

Note. ED = emergency department. Adapted from Handley, Schuchter, & Bekelman (2018).

presentations to hospitals for acute care. These are relatively common for chemotherapy-treated cancer patients; one retrospective study reported 43% within 90 days after chemotherapy infusion (Aprile et al., 2013). Although not as well studied, unplanned presentations are likely to be even more common for patients treated with ICIs, and especially for those receiving combination therapy, where overlapping symptom (AE/irAE) clusters that are difficult to disentangle may predominate (Daly et al., 2018). As has been noted, “The management of unscheduled presentations of cancer outpatients is becoming crucial to avoid inappropriate selection for hospital admission and interference with the ordinary work plan, improving quality of oncology services” (Aprile et al., 2013). We will now explore the telephone triage and acute care models in more depth.

OPTIMIZING TELEPHONE TRIAGE

The importance of the early identification of an irAE cannot be overemphasized. The general goal of triage is to create a hierarchy of patient needs to better manage them while minimizing the use of scarce health-care resources, including providers’ time, infusion or urgent chairs, and hospital beds. In the setting of ICIs, patients with a serious irAE would be appropriately directed to a suitable facility for further workup and management, while those with a less serious (lower grade) irAE would receive appropriate treatment to prevent the escalation of the irAE. The impact of irAEs should be minimized so they do not (1) progress and lead to poor clinical outcomes by themselves; (2) lead to poor outcomes owing to premature or unnecessary treatment discontinuation; and (3) cause excessive or unnecessary health-care utilization and costs.

In terms of personnel, optimal irAE triage requires an HCP experienced in irAE recognition and management, with the ability to ask appropriate questions, promptly formulate a differential diagnosis, and when necessary, involve appropriate subspecialty care. Typically, effective telephone triage relies on nurses or APPs well versed and trained to rapidly recognize and grade irAEs as well as established protocols for prioritizing patients according to their immediate needs. Nurses and APPs who have participated in ICI clinical tri-

als or who have significant standard-of-care experience are generally prepared to deal with irAEs, but many other oncology nurses or APPs may require additional support and guidance. Having ready access to an established multidisciplinary team (composed of various subspecialists) is also helpful in streamlining the process when additional experts are needed for formulating the differential diagnosis or for management.

Principles and Models

The telephone triage clinician must be able to distinguish which patients can be instructed to manage their symptoms at home, which need to come into an acute care clinic in an urgent fashion, which need to come in less urgently, and which need to go directly to the ED. These clinicians need to be skilled to effectively triage these often complex patients. A challenge for the triaging clinician is that patient assessment and clinical decisions need to be made without the physical presence of the patient (i.e., without visual inputs; Frisone, 2016; Hickey & Newton, 2012). Hence, when triaging patients via telephone, the clinician should use methodical, open-ended, probing questions and should listen acutely—not only to the words, but for additional clinical clues such as labored breathing, slurred speech, voice tone or confusion, and whether the patient sounds anxious or depressed. The nature and onset of the symptom are important, and the severity should be graded, if possible. As illustrated in the side-effect search function of the MNI symptom tracker (themelanomanurse.org/side-effect-search-section), during the call, the triage clinician should assess for information beyond that related to the symptom itself, including how accurate a “historian” the patient is, language barriers, cognitive defects, and alcohol or substance abuse issues. Additional factors should be considered during the interaction, including how far the patient lives from care facilities, available patient support and resources outside the clinic, and additional comorbidities.

The Care Step Pathways (CSPs) and other IO Essentials materials at aimwithimmunotherapy.org may be useful in developing guidelines for irAE assessment via telephone. Benefits of the CSPs are that they align with the standardized irAE management guidelines, provide advice on how to grade

different irAEs, and suggest which questions to ask. The latest Oncology Nursing Society (ONS) Telephone Triage guidelines are another valuable tool but are not grade based (Hickey & Newton, 2019). They represent a standardized resource for the management of chemotherapy-related AEs and now include a section on irAE management. However, they may be expensive to implement in the electronic medical record. The side-effect search function of the MNI website provides guidance on a wide variety of irAEs associated with ICI therapy, including recommendations for office vs. ED visits. By way of example, Figure 2 illustrates the telephone triage guidance for management for “Blood/Mucus in the Stool.” The side-effect search function provides additional links on a range of symptoms associated with irAEs.

Improving Telephone Triage

Telephone triage is best accomplished when the triaging clinician is well prepared to deal with irAEs, and patients and caregivers have been educated before or at the beginning of ICI therapy about possible irAEs (Battaglia, 2018). Patients and their caregivers should learn about the full range of possible irAEs and about the importance of reporting *any* unusual signs or symptoms at first occurrence—no matter how inconsequential they may seem, and no matter when they occur in relation to the last infusion, including months after completing or discontinuing treatment. The patient action plans found on the IO Essentials site provide key education and anticipatory guidance that can be shared with patients so they know what to do and how to direct themselves should they experience symptoms associated with an irAE (Figure 3). Further patient education may also be accomplished during a telephone triage call (Hickey & Newton, 2012). Advanced practice providers often lead such patient education efforts.

Advanced practice providers may also be involved in the training of clinicians for telephone triage. It is important that an institution providing care to patients receiving ICI therapy have an evidence-based telephone triage protocol that includes how to search for, recognize, grade (when possible), and manage irAEs. Ideally, the triage protocol should include prompts for a baseline review of symptoms

that can be easily located. Because irAEs affect a range of organ systems, they may produce a variety of overlapping symptoms that are difficult to recognize and understand. In some cases, APPs may be brought in to handle more complex calls. It is important that protocols include red flags (see Figure 2) that serve as reminders for rapid intervention at the recognition of signs/symptoms of a more serious, life-threatening nature.

In our experience, when patients and caregivers receive directed IO education prior to starting therapy, they are more likely to report symptoms early, when intervention can be more effective in preventing symptom elaboration and treatment discontinuation as well as hospital or ED admission.

The patient's ability or likelihood to carry out a treatment recommendation is another crucial component of telephone triage. This may be affected by their sense of urgency as well as issues related to transportation, caregiver support, and needs of dependents. When the triaging clinician suspects the patient is unlikely to follow a recommendation for self-management or to seek further help at an urgent care facility or ED, he/she should take action to motivate the patient by emphasizing the seriousness of the situation and the harm that is likely to occur if the advice is not acted upon in a prompt manner (Frisone, 2016). If there are transportation issues, a member of the multidisciplinary team should not only set up an appointment with a suitable clinic or hospital (if required) but also arrange appropriate transportation when able (Hickey & Newton, 2012).

EMERGENCY DEPARTMENT AND ACUTE/URGENT CARE

For more acute side effects, in many cases an irAE can be quickly identified and effectively managed by dedicated oncology professionals working in an acute care setting, thereby preventing an exacerbation that requires hospital admission and withdrawal or termination of ICI therapy. Of course, sometimes hospitalization will be necessary. In such cases, it is of critical importance to have ready access to an inpatient team that knows how to assess (identify and grade) and manage irAEs.

Patients with cancer may present to the urgent care facility, acute care clinic, or ED via self-referral or via referral from the oncology practice.



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Symptom: Blood/Mucus in the Stool

Initial Grading Reminder

CTCAE grading of blood in stool (bowel movement changes):

Grade 1 (Mild): Asymptomatic; clinical or diagnostic observations only; intervention not indicated

Grade 2 (Moderate): Abdominal pain; mucus or blood in stool

Grade 3 (Severe): Severe abdominal pain; change in bowel habits; medical intervention indicated; peritoneal signs

Grade 4 (Life-threatening): Life-threatening consequences; urgent intervention indicated

Assessment and Grading

Characterize the symptom (onset, pace)

Ask the patient:

Do you have a history of hemorrhoids? Of hard stools/constipation? Is this a new or worsening symptom? When did it start or get worse? Has it developed gradually or suddenly? Have you had a change in diet in the past day or so?

“Suddenly” would be more consistent with peritoneal signs.

Grade the symptom

Ask the patient:

How much blood and mucus is in the stool? Do you see blood on the toilet paper or actually in your stool? Have your bowel movements been different in other ways?

Patient Query Regarding Other Symptoms/Red Flags

Ask the patient:

Do you have any abdominal (belly) pain/tenderness, nausea, fever, or decreased appetite?

Patient Factors to Consider That Affect the Approach to Intervention

Consider the following in individualizing the intervention: Is the patient a good or poor historian? Any language barriers or cognitive deficits? Is the patient reliable (able to carry out treatment recommendations)? Does this patient have alcohol/substance abuse issues? Does the patient have transportation? Is there sufficient caregiver support?

[Click Here for Telephone Triage](#)

Suggested Intervention

If the blood in the stool is moderate/severe, the patient should be seen.

If patients have any of the red-flag symptoms, they should be seen for GI workup or referred to the ED.

[Click Here for In-Office Triage](#)

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Figure 2. Grading reminder, assessment and grading criteria, query regarding red flags, patient factors to consider, and telephone triage recommendations for the symptom “Blood/Mucus in the Stool” on the side-effect search function for the Melanoma Nursing Initiative (MNI) website (themelanomanurse.org/side-effect-search-section). Used with permission from Melanoma Nursing Initiative.



LUNG AND BREATHING PROBLEMS

KEYTRUDA® (pembrolizumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in breathing
- Dry cough
- Chest pain
- Worsening of existing breathing symptoms
- Increased shortness of breath when you walk or exercise
- Shortness of breath when you are resting

What you should tell your oncology team member:

- When you first noticed the changes in your breathing or cough
- If you are feeling very tired, are wheezing (making a whistling sound when you breathe), or have a fever
- If the symptoms are interfering with your daily activities
- If you've ever had breathing problems before and if your existing symptoms are worse
- If you have respiratory allergies to pollen, trees, pets, or other things or food allergies and if you've recently been exposed to these allergens
- If you think you've been exposed to cold or flu viruses
- Interventions you've tried at home (eg, inhaler, cough medicine, etc)

Red flag(s):

- If you are having any trouble breathing, new or worsening cough, and particularly if symptoms come on suddenly
- Any chest pain

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your lungs:

- Avoid environments that can irritate your lungs or make it hard to breathe. For instance, if you work outdoors, pollen or chemicals may affect you. If you have a hobby like painting, use of certain chemicals might be a problem
- Wear a pollen mask or a respirator when you are around things that may irritate your lungs
- Adhere to any pre-existing asthma or allergy treatment plans during your cancer therapy
- Check with your HCP before using any steroid-based inhalers

Figure 3. An individual adverse event education page on lung problems from an Immuno-Oncology (IO) Essentials Patient Action Plan for gastric cancer. Note how the page provides an overview of symptoms, information the patient should keep track of, red flags, and instructions on where to go based on the severity of the symptom. Retrieved from aimwithimmunotherapy.org/wp-content/uploads/2018/10/KEYTRUDA_ACTIONPLAN_GastricGEJ-Final.pdf. Used with permission from the IO Essentials Initiative.

In the clinic setting, HCPs provide a more directed, focused assessment, with the goal of evaluating the seriousness of the condition and either managing it or sending the patient for hospital admission. The clinician in this setting is able to record relevant physical parameters and initiate appropriate tests to guide future decision-making (Hickey & Newton, 2012). There is also available dedicated infrastructure and space in the ED and urgent care settings to administer fluids or intravenous medications.

As in the telephone triage situation, it is important that the clinician(s) in the acute care setting be suitably trained to identify, grade, and manage irAEs associated with ICI therapy. In the typical outpatient oncology clinic, the management of irAEs may be challenging due to lack of space as a result of an increased volume of patient visits as well as the time requirement necessary to adequately assess symptoms. In the case of standard urgent care clinics, providing patient support can be difficult if the patient needs care for the irAE outside of normal business hours. Moreover, most standard urgent care and ED clinicians lack oncology-specific medical training and, in particular, familiarity with irAEs associated with newer IO drugs (Ayers, 2018). As a result, these visits too often lead to poor outcomes from either unnecessary hospital admissions, failure to appropriately hospitalize for management, or inadequate work-up of symptoms felt to be progressive cancer. In contrast, oncology providers working in the acute setting often see the big picture and can direct the patients appropriately.

As suggested in Table 1, one possible strategy to reduce unnecessary inpatient acute care/hospital admissions may be to create dedicated, cancer-focused urgent care treatment centers (Handley et al., 2018). However, this might not be realistic for all centers. Different strategies for dedicated oncologic approaches to acute care that can be used to improve outcomes include implementing flexible scheduling at embedded urgent care centers, setting up dedicated acute cancer treatment clinics, having trained oncology personnel available within the ED, or by creating dedicated cancer EDs with cancer providers trained in managing irAEs and other cancer-related issues (Table 1).

Clinic Models

An example of an oncology-based symptom management clinic is the University of Colorado's Clinical Assessment and Rapid Evaluation (CARE) Clinic, which was developed in 2015 based on a needs assessment. At that time, 48% of inpatient admissions at University of Colorado came from the emergency department, 20% from an oncology outpatient clinic, and the rest from a variety of other referring clinics. When the staff reviewed the disposition of the cases, they estimated that approximately 68% of the unscheduled inpatient admissions could have been handled by an urgent symptom management clinic (Brianna Hoffner, personal communication).

A look at the evolution of the clinic reveals some key strategies and resources for successful implementation. The CARE Clinic was initially staffed by two dedicated APPs and located in the Cancer Center's infusion clinic. It was poorly utilized during the first 2 years due to a variety of issues, including hours, location, and provider resources. A revised CARE Clinic model was launched in July 2017, with dedicated space separate from infusion and service provided by six rotating oncology APPs, with trained medical assistants, oncology nurses (including a CARE charge nurse), and schedulers. The Clinic currently offers priority imaging and is able to perform procedures such as skin biopsies and paracentesis. The CARE Clinic is closely associated with palliative care, facilitating collaboration between the two teams for patients presenting with cancer-related pain. Recent changes to the clinic include the addition of a part-time diabetes educator and establishment of a separate department in the electronic medical record system. Service hours were expanded in September 2018, with the eventual goal of providing 24/7 care for patients with advanced cancer. Figure 4 shows the continued growth of visits to the CARE Clinic in 2018 vs. 2017.

Other models of cancer-based urgent care centers include (but are not limited to) those at the University of Texas Southwestern Medical Center, Penn Medicine Abramson Cancer Center, and Johns Hopkins (Battaglia, 2018). Each of these models have been demonstrated to provide better care while also lowering costs as compared with the ED. With the Johns Hopkins model, patients call

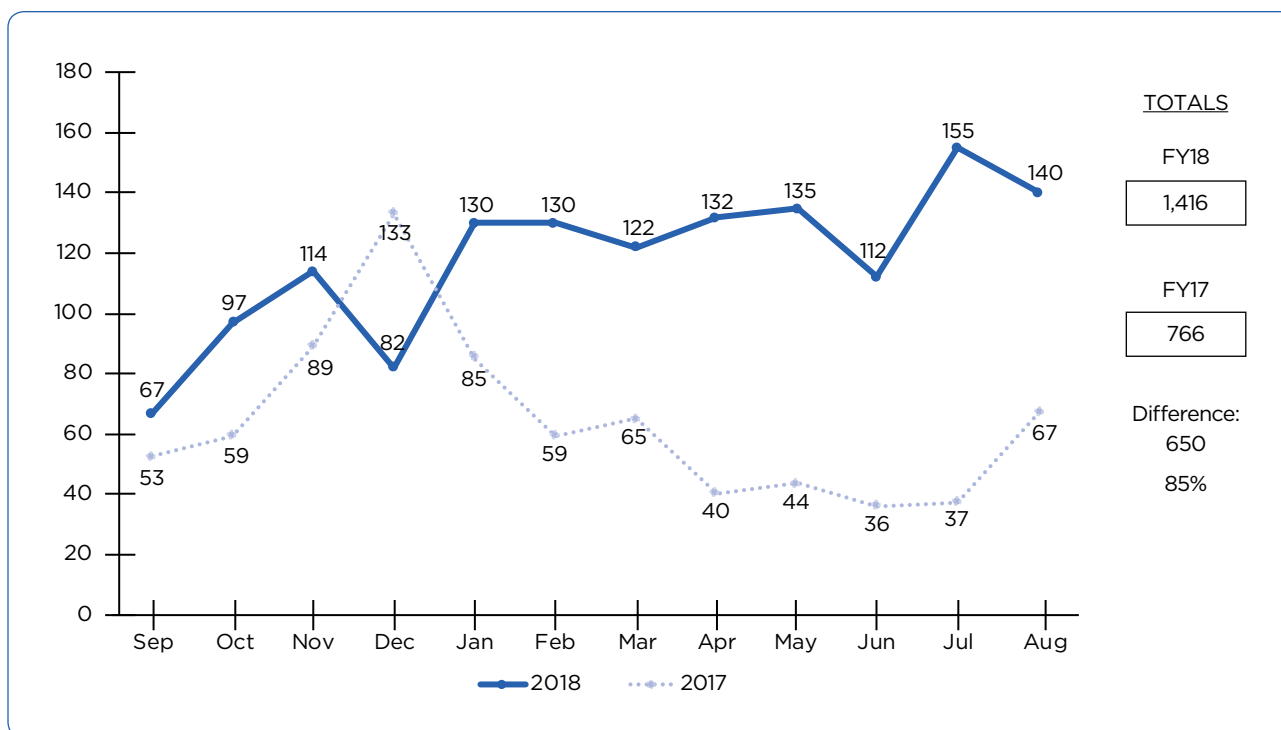


Figure 4. Patient volume by month at the University of Colorado Care Clinic, 2018 vs. 2017. Courtesy of Brianna Hoffner.

the center's hotline to determine whether the problem can be triaged over the phone or if the patient should come into clinic (Advisory Board, 2016). Patients spend less than 3.5 hours at the clinic and 81% are discharged home from the center, saving many patients from hospital admissions (Ughetta, n.d.).

The Cancer Urgent Care Clinic at Southwestern Medical Center in Dallas was opened when providers observed that their ED was not adequately equipped to treat AEs associated with cytotoxic chemotherapy, including mouth sores, fevers, dehydration, and nausea (Battaglia, 2018). Patients at the center are cared for by APPs trained in the management of chemotherapy-related AEs and who have easy access to the patient's oncologist, when necessary. Patients can bypass the ED and be admitted directly into the hospital there, when required. The Penn Medicine Abramson Cancer Center recently opened the Oncology Evaluation Center within their outpatient clinic (Battaglia, 2018). The Oncology Evaluation Center is staffed by oncologists and nurse practitioners with extensive experience in managing various cancer treatment-related complications, thereby providing acute care specifically for cancer patients. Consistently, around 80% of

patients are able to be discharged home following intervention (Suzanne McGettigan, personal communication). The remainder are evaluated in the ED or directly admitted to the hospital.

Other centers, including Memorial Sloan Kettering Cancer Center, University of Nebraska Medical Center, Siteman Cancer Center, and the Froedtert Clinical Cancer Center at the Medical College of Wisconsin, have established cancer care clinics that are open to patients 24 hours a day, 7 days a week. Such comprehensive availability and expertise sets an important benchmark for the management of cancer care-related issues.

FINAL THOUGHTS AND THE ROLE OF THE APP

Cancer care, and specifically the management of irAEs associated with ICIs, can be improved at multiple levels within the current health-care delivery system. At each level, there is a need for an increased awareness of irAEs and how their presentation, severity, and management may differ from the chemotherapy-related AEs most HCPs are currently more familiar with. Improved training is required to support telephone triaging and in-clinic

(urgent care center or ED) triaging, and to provide HCPs with the tools they need when further managing irAEs in the clinic or—when necessary—in an acute care center or hospital. Developing cancer-specific urgent/acute care centers and EDs with clinicians well-versed in the assessment and management of irAEs is part of this process. The goal is to improve patient outcomes via the skillful management of irAEs and reduce inpatient admissions. Such improvements will maximize benefits from treatment (decreasing morbidity and mortality), enhance the quality of life of patients and caregivers, and make better use of scarce health-care resources, thereby lowering health-care costs.

Many HCPs recognize the importance of having acute care/hospital personnel prepared to effectively treat irAEs from ICI therapy. Some patients will require inpatient care, and if managing clinicians are ill-prepared to deal with these irAEs, the benefits of ICI are likely to be reduced or lost and the risk of hospital readmission increased. However, the importance of telephone triage is often underestimated or lost in the mix. Telephone triage is a critical component of the infrastructure of ICI therapy. The authors have been surprised to learn that not all institutions have devoted efforts to formalize telephone triage algorithms. Barriers are likely multifaceted, including financial considerations, indeterminate outcomes, and a lack of a full understanding of the need for triage algorithms.

It is imperative that administration and management support the unique needs of ICI management and recognize the need for well-trained, dedicated specialty nurses and APPs for telephone triage. Without dedicated personnel, the risk of disjointed care and poor communication increases.

In some cases, changes in institutional infrastructure may be warranted. Institutional leaders should ask important questions about the management of ICI patients, including: “Are we ready to do this?” “Are we doing it effectively now, and are we ready for the future?” “How do we advocate to ensure our administration provides the resources needed to deal with the problem and better address unmet needs?” “Do we have adequate staff and resources to deal with the demand (i.e., do we have enough chairs and clinicians)? But also, do we have nurses and APPs who are experienced with irAE management and who can effectively triage?”

Answers to these questions are urgently needed. Moreover, additional questions and issues are likely to arise over time as newer immunotherapies make their way to the market and are increasingly used with other anticancer options. The APP is in the ideal position to assess the situation and advocate for the resources and education needed to adequately address irAE management now and in the future. ●

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