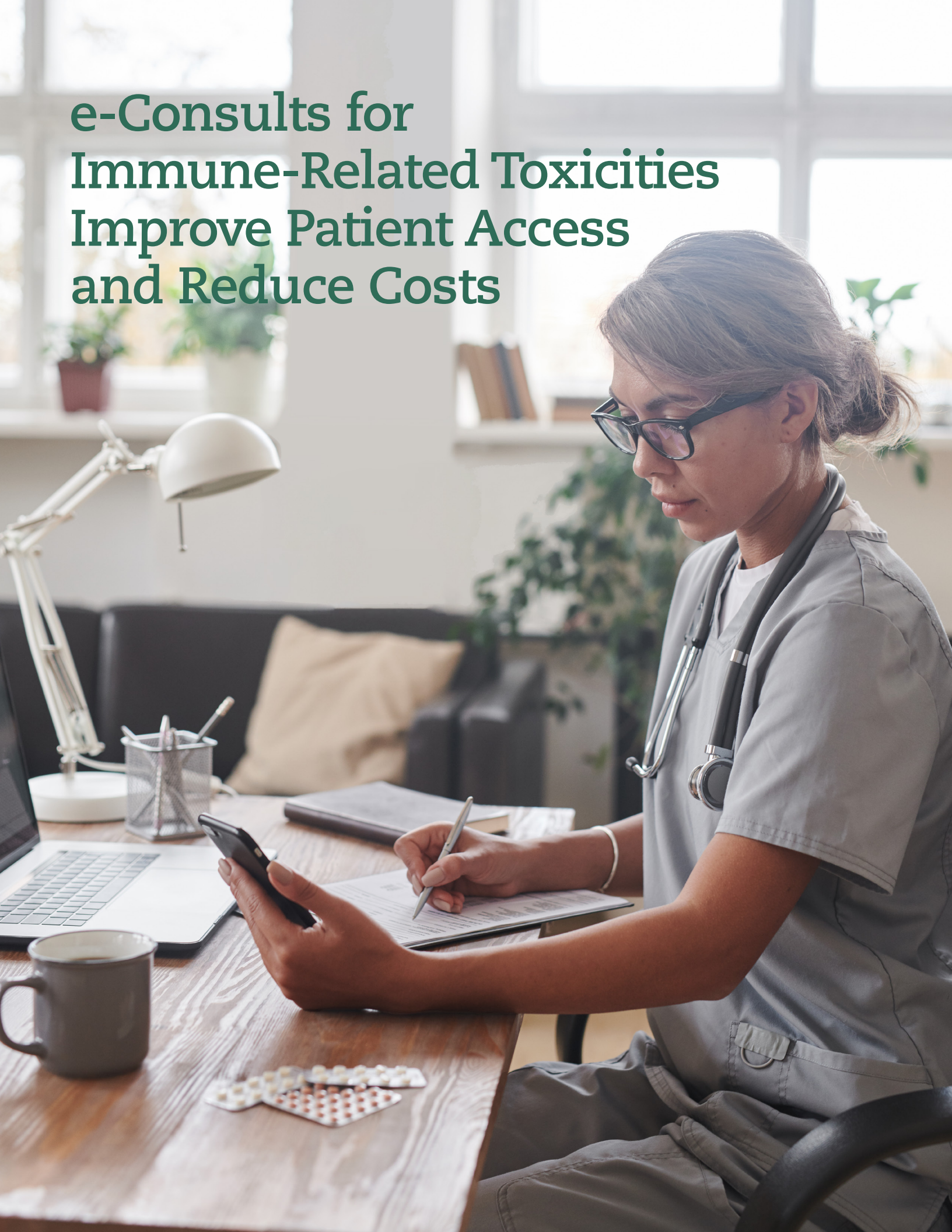
e-Consults for Immune-Related Toxicities Improve Patient Access and Reduce Costs



BY CARRIE DIAMOND, BA; HARSH PATOLIA, MD;
DONNA PHINNEY; AND AFREEN IDRIS SHARIFF, MD

A challenging problem for oncology patients currently receiving immune checkpoint inhibitor therapy is immune-related adverse events (irAEs), with treatment-related deaths occurring in up to 2% of patients.[1] While irAEs occur in various Common Terminology Criteria for Adverse Events (CTCAE) grades (1-5), they are a common reason for hospital admission noted in 8.5% of patients and can lead to treatment discontinuation in up to 87% of patients after they are admitted for a high grade toxicity.[1] In recent years, Duke Cancer Institute has noted that 10% of patients receiving immune checkpoint inhibitor therapy are admitted to the hospital after less than 1 month from the initiation of therapy, and 23% of patients have been sent to the emergency department (ED), admitted to the hospital, and/or died within 6 months from therapy initiation.[2] In addition to the high risk of hospitalization and risk for treatment discontinuation, there is an added cost and utilization burden that falls on the health care system. For example, the estimated cost of admissions for irAEs at Massachusetts General Hospital was $218,700 in 2011 and skyrocketed to $1,300,000 in 2016.[3] We expect that with more common use of these agents, this number will continue to escalate, underscoring the need to prioritize effective and timely irAE management so avoidable hospitalizations can be prevented.

Among irAEs, endocrine irAEs are one of the most common toxicities with resultant endocrinopathies ranging from 4% to 14.6% of cases,[4] along with cutaneous, gastrointestinal, pulmonary, and musculoskeletal toxicities.[5] Endocrine irAEs have been noted to contribute to 12.2% of admissions related to irAEs.[6] For hospital admissions that are a result of an irAE, 87% of patients stop immune checkpoint inhibitor treatment.[7] Thus, patients stop effective therapy due to irAEs. We suspect that an important reason for these hospitalizations is delayed recognition and limited access to clinicians with expertise, resulting in delayed treatment and management. Management of irAEs is contingent upon both early recognition and prompt intervention.[8] The onset of irAEs can vary in presentation from an abrupt adverse event to, less commonly, one that is characterized by delayed onset and prolonged duration. Multidisciplinary teams and recommendations are critical for both evaluation and management guidance.[5] Access to clinical expertise in a timely manner can be challenging in both academic and community settings due to lengthy wait times. Presently at Duke Cancer Institute, for patients with cancer, the average wait time to see an endocrine specialist is 87 days.[2]

E-communication allows for professional triage and complex care facilitation. This system reduces access time to clinic, is faster, and reduces cost for the health care system via a reduction in ED visits.

One solution to this challenge is to implement expert triage from an endocrinologist who can review the case via an e-communication based platform. This platform can allow physicians to assess patients sooner and determine the need for an in-person visit. E-communication, also known as an e-consult, is an asynchronous telehealth platform that is a templated order request in an electronic health record (EHR) that allows a specialist to review a case on behalf of another provider to advise on individual patient care. E-communication allows for professional triage and complex care facilitation. This system reduces access time to clinic, is faster, and reduces cost for the health care system via a reduction in ED visits. Previous studies have demonstrated that a virtual multidisciplinary toxicity team for irAEs is easily implemented and aids in diagnosis of toxicities and recommendations for subsequent care.[1] Herein, we describe a single-institution experience with an e-communication consult platform from oncology to endocrinology and determine its effectiveness in reducing appointment access times and hospitalizations.

Methods

Patients being treated with immune checkpoint inhibitors who received an e-consult from oncology to endocrinology from the period 5/1/2020 to 11/1/2021 were eligible for inclusion in this observational study approved by the Duke Cancer Institute Institutional Review Board (IRB). All data collection was performed with manual chart abstraction

Continued on page 33

atlas

Empowering oncology teams to provide patient assistance through automation

- ✓ Reduce financial toxicity
- ✓ Improve patient experience
- ✓ Increase access to care
- ✓ Address cancer disparities

"Thank you so much for genuinely caring and doing everything you can to help me...this is such a relief and takes so much worry off of me!"

—

BREAST CANCER PATIENT

Contact us + learn more at ATLAS.HEALTH

Table 1. Patient Characteristics	
TOTAL E-CONSULTS (N=102)	**N (%)**
Median age (IQR) (in years)	67.10 (14.86)
SEX	
Male (%)	55 (53.9)
Female (%)	47 (46.1)
RACE	
White/Caucasian (%)	87 (85.3)
Black/African American (%)	9 (8.8)
Asian (%)	0
Pacific Islander/Native Hawaiian (%)	0
Unknown (%)	3 (2.9)
Other (%)	3 (2.9)
ETHNICITY	
Hispanic (%)	3 (2.9)
Non-Hispanic (%)	98 (96.1)
Unknown (%)	1 (0.9)
MALIGNANCY	
Melanoma (%)	9 (8.8)
Non–small cell lung cancer (%)	31 (30.4)
Small cell lung cancer (%)	1 (1)
Head and neck cancer (%)	2 (2)
Bladder cancer (%)	4 (3.9)
Renal cell carcinoma (%)	17 (16.7)
Breast cancer (%)	4 (3.9)
Gastrointestinal cancer (%)	18 (17.5)
Gynecologic cancer (%)	16 (15.7)
Other (%)	5 (4.9)
E-CONSULT RELATED TO ENDOCRINE-RELATED IMMUNE TOXICITY?	
Yes	77 (75.5)
No	25 (24.5)

Continued from page 31

from Epic software and recorded in a secure REDCap database. Patient demographic data, including age at time of diagnosis, sex, race, and ethnicity were collected, in addition to pre-existing endocrine medical history, primary cancer diagnosis, and cancer stage (Table 1). Toxicity data regarding the type of immuno-oncology therapy, date of last dose received, diagnosis for which the patient is seeing endocrinology, and CTCAE toxicity grade were also collected and reviewed. During this period, 102 separate e-consults were ordered. Consult recommendations, including diagnostic tests and treatment recommendations, were individually analyzed in addition to the continuation of treatment throughout duration of the analysis period. A post-implementation provider questionnaire was also collected.

Results

A total of 102 e-consults were reviewed during the study period and demographic data among the included patients are outlined in Table 1. The most common diagnosis associated with an e-consult was related to thyroiditis, and the most common cancer diagnosis associated with the use of an e-consult was non–small cell lung cancer (NSCLC), as shown in Figure 1. Most cancers had progressed to stage IV by the time of the e-consult, and the most common immunotherapies were nivolumab and pembrolizumab, as shown in Figure 2. Of 102 e-consults reviewed, 88 provided diagnostic recommendations and 60 provided treatment recommendations at the time of consultation (Table 2). Seventy-four e-consults were followed by an in-person appointment (Table 2). Among the appointments that followed an e-consult, median time for follow-up was 38.50 days, which was reduced from 60.5 days in 2021 (Table 2).

In melanoma and lung cancer trials, high-grade endocrinopathies that required hospitalization and had life-threatening consequences or resulted in death have been reported more frequently than for

Table 2. Outcomes Following Implementation of the e-Consult Service	
MEDIAN INTERVAL BETWEEN CONSULT AND APPOINTMENT SCHEDULED IN DAYS (IQR)	**37 (40.25)**
VISIT PLANS FROM E-CONSULTS	
Diagnostic recommendations	88
Treatment recommendations	60
No new recommendations	4
ATTENDED FOLLOW-UP VISITS AFTER EACH E-CONSULT	
Yes	74
No	28

Figure 1. Cancer Diagnoses Associated With e-Consults

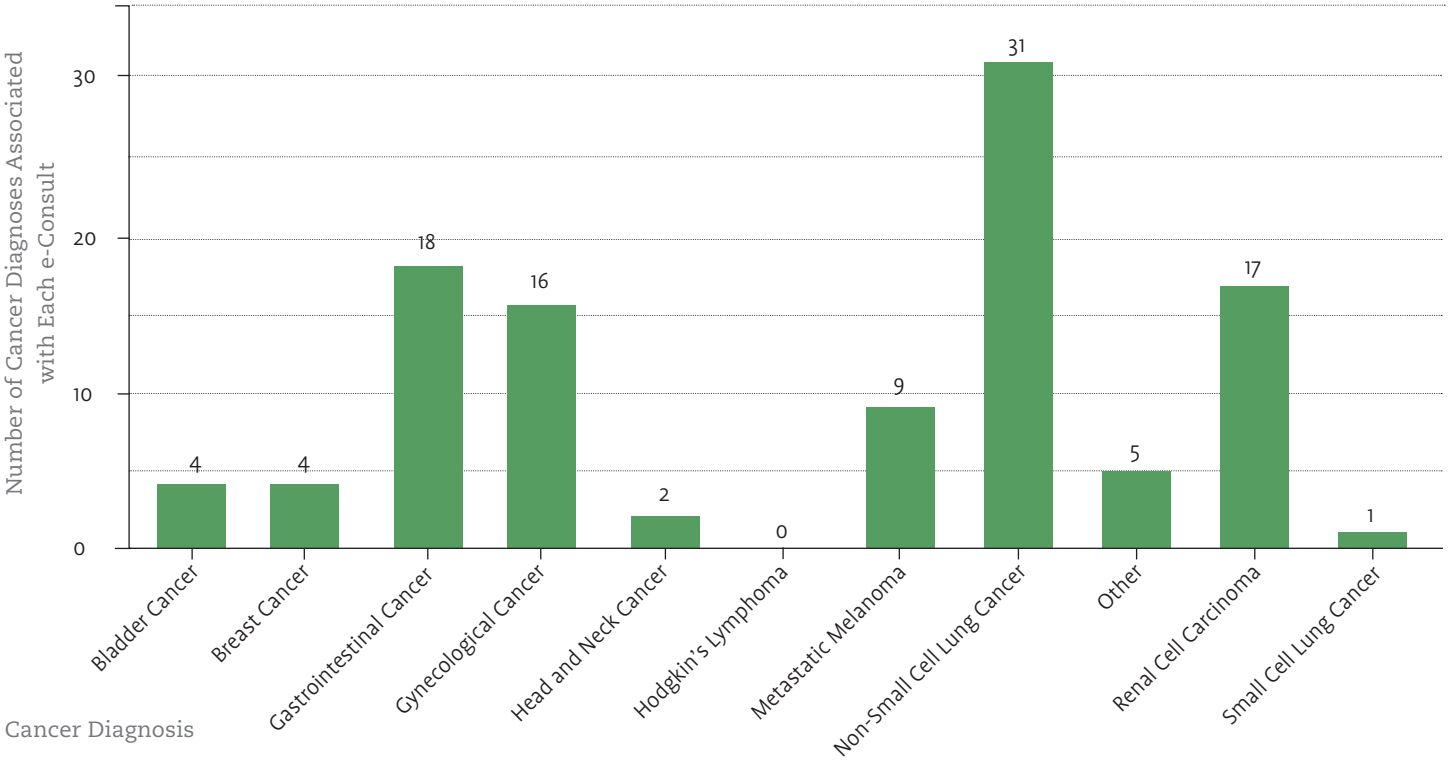
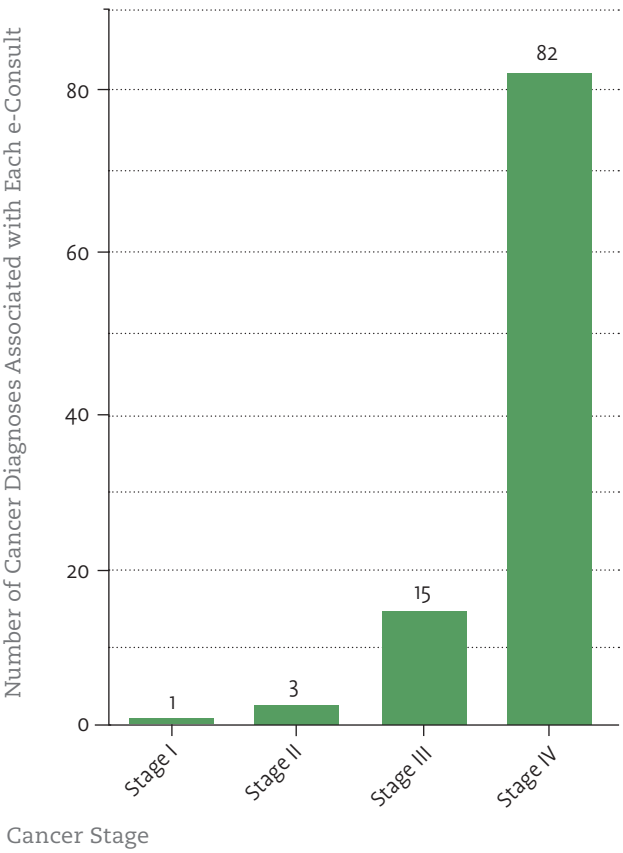


Figure 2. Stage of Cancer at the Time of e-Consult



other cancer types,[9] with rates ranging from 0.3% to 1.3%.[10] Among our data, most e-consults pertaining to irAEs were stratified to CTCAE grades 1 and 2 (86 out of 88 coded irAEs). Of the irAEs documented in the study, 2 (2.23%) were severe enough to warrant hospitalization for further evaluation and management. Among graded irAEs, 99% (87 of 88) received diagnostic or treatment recommendations for further management—all within 48 hours.

Thoracic oncology was the highest utilizer of this service and NSCLC was the most common cancer noted. From the provider satisfaction survey, 9/12 (75%) of providers felt the e-consult to endocrinology changed the management of their patient and 83% reported a 5/5 experience with the consult service. From the 12 providers who completed the survey, 3/12 (25%) felt the e-consult prevented a hospital or emergency department visit for their patient. We also noted that these e-consults were poorly reimbursed by all payers; average reimbursement ranged from $15 to $32 per consult.[3]

Limitations

As this is a retrospective and observational study from a single-center institution, there are limitations to our data. Due to variations in documentation by different providers, faithfully classifying and recording irAEs was challenging. For example, because the diagnosis of irAEs requires clinical suspicion, conveying and capturing symptoms from EHRs is subject to interobserver variation and bias. Future improvements include the possibility of implementing a documentation template so that details are abstracted and captured in a consistent manner.

Discussion

Immune checkpoint inhibitor therapy has transformed care for millions of patients and continues to be actively studied with regard to progression-free survival and overall survival. However, toxicities, especially severe toxicities, result in treatment holidays and treatment termination that can affect these outcomes in the long term.[2] Endocrine toxicities are common and often treatable with hormone replacement. The challenge, however, is to diagnose and treat adrenal insufficiency, hypothyroidism and hyperthyroidism, and new-onset type 1 diabetes when the concern is raised by oncologists and before patients progress to severe presentations like adrenal crisis, diabetic ketoacidosis, or thyroid storm. As with our institution, many organizations face access delays of weeks or months to see a specialist, and this delay can result in the progression of CTCAE from grade 2 or 3 to grade 4 or 5.

With our e-consult model we have demonstrated a care framework that improves access, mitigates gaps in specialty care, and can be scalable across other specialties that provide services to patients with cancer. We have shown a drop in appointment wait time from a median of 60.5 days to 38.5 days and a drop from 60.5 days to less than 2 days for diagnostic and treatment recommendations. We have also been successful in reducing hospitalization rates from endocrine irAEs from 11% at our institution (between 2007 and 2017) to 2.23% in e-consulted patients between 2020 and 2021. During our study, we also collected billing and reimbursement information for these e-consults and the results show an effort-reimbursement mismatch, which we anticipate will be an important factor to address before considering scalability. The demonstration of reduced health care utilization and reduced access times is ideally placed in a value-based health care system, and we anticipate that health systems and payers will consider these important variables when considering e-consult reimbursement.

Our conclusion: a framework of e-consults revealed early signs of effectiveness in triaging consult questions and thus expediting receipt of appropriate and high-quality care while ameliorating the patient experience in a care milieu that is fraught with protracted wait times and preventable hospital admissions. To support e-consults, the effort-payment mismatch must be addressed by health systems and payers that can propel integration and scalability of these effective services across oncology and other subspecialty practices to enhance access and mitigate gaps in specialty care provided to cancer patients. OI

Carrie Diamond is an upcoming graduate of Duke University School of Medicine who will be starting her first year of dermatology residency at Duke University Hospital. Harsh Patolia is currently a fellow in cardiovascular disease at the Cleveland Clinic Foundation who completed his internal medicine residency at Duke University Hospital. Donna Phinney is current director, Duke Telehealth Office and Virtual Care Center. Afreen Idris Shariff, MD, is an endocrinologist; associate professor of medicine; director, Duke Endo-Oncology Program; and associate director, Cancer Therapy Toxicity Program, Center for Cancer Immunotherapy at Duke Cancer Institute.

References

1. Naidoo J, Zhang J, Lipson EJ, et al. A multidisciplinary toxicity team for cancer immunotherapy-related adverse events. *J Natl Compr Canc Netw*. 2019;17(6):712-720. doi:10.6004/jnccn.2018.7268

2. Duke University Hospital. Duke Cancer Institute Performance Services Data (2022).

3. Chu JN, Choi JG, Ostvar S, et al. (2018). Cost of inpatient admissions for immune-related adverse effects from immune checkpoint inhibitor therapy: a single center experience. *J Clin Oncol*. 2018;36(15):3060. doi:10.1200/JCO.2018.36.15_suppl.3060

4. Chiloiro S, Bianchi A, Giampietro A, Milardi D, De Marinis L, Pontecorvi A. The changing clinical spectrum of endocrine adverse events in cancer immunotherapy. *Trends Endocrinol Metab*. 2022;33(2):87-104. doi:10.1016/j.tem.2021.10.009

5. Puzanov I, Diab A, Abdallah K, et al. Managing toxicities associated with immune checkpoint inhibitors: consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group. *J Immunother Cancer*. 2017;5(1):95. doi:10.1186/s40425-017-0300-z

6. Molina GE, Zubiri L, Cohen JV, et al. Temporal trends and outcomes among patients admitted for immune-related adverse events: a single-center retrospective cohort study from 2011 to 2018. *Oncologist*. 2021;26(6):514-522. doi:10.1002/onco.13740

7. Balaji A, Zhang J, Wills B, et al. Immune-related adverse events requiring hospitalization: spectrum of toxicity, treatment, and outcomes. *J Oncol Pract*. 2019;15(9):e825-e834. doi:10.1200/JOP.18.00703

8. Spain L, Diem S, Larkin J. Management of toxicities of immune checkpoint inhibitors. *Cancer Treat Rev*. 2016;44:51-60. doi:10.1016/j.ctrv.2016.02.001

9. Manne A, Mulekar MS, Escobar DE, et al. Clinical and hematological predictors of high-grade immune-related adverse events associated with immune checkpoint inhibitors. *J Clin Med Res*. 2021;13(5):268-275. doi:10.14740/jocmr4511

10. Wang DY, Salem JE, Cohen JV, et al. Fatal toxic effects associated with immune checkpoint inhibitors: a systematic review and meta-analysis. *JAMA Oncol*. 2018;4(12):1721-1728. doi:10.1001/jamaoncol.2018.3923