A Multidisciplinary Toxicity Team for Cancer Immunotherapy–Related Adverse Events

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ABSTRACT

Background: Immune checkpoint inhibitors (ICIs) may cause immune-related adverse events (irAEs). Methods to obtain real-time multidisciplinary input for irAEs that require subspecialist care are unknown. This study aimed to determine whether a virtual multidisciplinary immune-related toxicity (IR-tox) team of oncology and medicine subspecialists would be feasible to implement, be used by oncology providers, and identify patients for whom multidisciplinary input is sought. **Patients and Methods:** Patients treated with ICIs and referred to the IR-tox team in August 2017 through March 2018 were identified. Feasibility was defined as receipt of electronic referrals and provision of recommendations within 24 hours of referral. Use was defined as the proportion of referring providers who used the team's recommendations, which was determined through a postpilot survey. Demographics and tumor, treatment, and referral data were collected. Patient features and irAE associations were analyzed. **Results:** The IR-tox team was found to be feasible and used: 117 referrals from 102 patients were received in 8 months, all providers received recommendations within 24 hours, 100% of surveyed providers used the recommendations, and 74% changed patient management based on IR-tox team recommendations. Referrals were for suspected irAEs (n=106; 91%) and suitability to treat with ICIs (n=11; 10%). In referred patients, median age was 64 years, 54% were men, 13% had prior autoimmunity, and 46% received ICI combinations versus monotherapy (54%). The most commonly referred toxicities were pneumonitis (23%), arthritis (16%), and dermatitis (15%); 15% of patients had multisystem toxicities. Multiple referrals were more common in those treated with combination ICIs (odds ratio [OR], 6.0; $P=.035$) or with multisystem toxicities (OR, 8.1; $P=.005$). The IR-tox team provided a new multidisciplinary forum to assist providers in diagnosing and managing complex irAEs. This model identifies educational and service needs, and patients with irAEs for whom multidisciplinary care is most sought. **Conclusions:** A virtual multidisciplinary toxicity team for irAEs was a feasible and used service, and facilitated toxicity identification and management.

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Background

Multidisciplinary tumor boards are a mechanism in which oncologists and subspecialists discuss challenging cases to optimize patient care. Prospective studies of these forums have demonstrated that multidisciplinary input can alter diagnosis and positively influence management across tumor types.^{1–5} More recently, specialized molecular tumor boards that interpret patient genomic data to guide clinical care have gained popularity.⁶

In the field of cancer immunotherapy, emerging immune-related toxicities require multidisciplinary management. Due to their mechanism of action, immune checkpoint inhibitors (ICIs) can cause patients to develop a variety of organ-specific immune-related adverse events (irAEs).⁷ Similarly, patients may have other processes, such as infection or progressive cancer, that mimic irAEs. Early evaluation and diagnosis is critical and associates with successful irAE outcomes.^{8,9} Diagnosis and management of selected irAEs may be challenging and often requires the input of at least one non-oncology specialist for specific physical examination, interpretation of laboratory tests or imaging, completion of a diagnostic procedure, or guidance on immunosuppression for steroid-refractory irAEs. Additionally, high-risk patients with preexisting autoimmune diseases, prior organ/bone marrow transplants, or recalcitrant irAEs may necessitate input from multiple subspecialists. Oncology physicians and nurses are central to this consultation, to

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address ICI discontinuation or suitability for future immunotherapy. Most literature regarding irAEs recommends a multidisciplinary approach but lacks practical guidance on how this can be achieved in real time. Important considerations include lack of familiarity with certain irAEs, that irAEs may occur at unpredictable times when specialists are not available, and the need for expeditious discussions to ensure medicine and oncology recommendations are not conflicting.

This study aimed to formalize the multidisciplinary collaborations between oncology and medicine subspecialists for irAE management. Our goal was to recruit oncology and medical subspecialists with expertise in irAE diagnosis and management to provide real-time input on irAEs via an electronic platform, and to test the feasibility and use of this immune-related toxicity (IR-tox) team.

Patients and Methods

IR-Tox Team Operations

The IR-tox team was proposed as a collaboration between medical oncology (J.N., Co-Chair) and medicine subspecialists (L.C.C., Co-Chair). This multidisciplinary group consisted of subspecialists with expertise in irAE management, including medical oncologists (n=8), oncology nurses (n=4), and subspecialists from rheumatology (n=4), pulmonology (n=3), gastroenterology (n=3), neurology (n=2), endocrinology (n=2), dermatology (n=2), ophthalmology (n=2), cardiology (n=1), infectious diseases (n=1), and hematology (n=1). The co-chairs proposed a pilot program for oncology providers (faculty, fellows, nurses) who administer ICIs to patients in a tertiary cancer center to electronically consult the IR-tox team for assistance in the diagnosis and management of suspected irAEs or related issues. An electronic referral template was provided (supplemental eFigure 1A, available with this article at JNCCN.org). Patient referral information included demographics, tumor type, immunotherapy regimen, clinical course, specific referral questions, and request for subspecialist consultation. Members of the IR-tox team discussed cases in real time via a password-protected electronic messaging forum. After 24 hours, a summary of recommendations was sent to referring providers via email, and may have been added to the patient's electronic medical record at the discretion of the referring provider (supplemental eFigure 1B). Further discussion and recommendations beyond 24 hours were used at the discretion of the referring provider and were not included in the 24-hour summary. Members of the IR-tox team met monthly to discuss referrals and identify new clinical, educational, or research needs. Feasibility of the team was defined as receipt of electronic referrals and provision of

recommendations within 24 hours of referral. Use of the team was assessed as the proportion of referring providers who used the team's recommendations, collected in a postpilot survey.

Inclusion and Exclusion Criteria, Data Collection

Patients were included if they were referred to the IR-tox team and were treated at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Hospital (JHH). Included patients had a pathologically confirmed solid tumor or hematologic malignancy and were either receiving, had received, or were due to receive an ICI as standard-of-care or part of a clinical trial. Patients were excluded if they were not treated at JHH and had not received or were not due to start ICIs. Patient, referral, irAE management, and outcome data were collected from electronic referrals, IR-tox team meetings, or extracted from the electronic medical record and collected in an IRB-approved database (IRB00144013). Patients were deemed to have confirmed irAEs if competing diagnoses were excluded, multidisciplinary consensus was reached, and they had either pathologic evidence of irAE or showed clinical improvement with corticosteroid/irAE-based management. Confirmed irAEs were graded according to CTCAE, version 5.0.¹⁰ Patients with no or unconfirmed irAEs included those for whom an alternative diagnosis was confirmed or for whom no multidisciplinary consensus could be reached. A flare of a known autoimmune condition was not coded as an irAE. Patients who developed irAEs involving ≥ 2 organs/systems were defined as having multisystem irAEs. Patients with prior autoimmune conditions or solid organ/bone marrow transplants were defined as having prior autoimmunity or high-risk conditions. Reason for referral was coded as suspected irAE or suitability for ICI. Referral data also included whether diagnostic or management recommendations were sought by referring providers.

Postpilot Survey

After the first 8 weeks of the pilot program, an anonymous electronic survey was sent to all members of the cancer center, including oncology providers, nurses, and allied staff, to assess the use and utility of the team, types of questions posed to the team, and future suggestions (supplemental eAppendix 1). Providers were asked about their area of practice in oncology, ICI prescribing patterns, and experience in managing irAEs. Providers were unaware they would be surveyed before the postpilot survey was administered.

Statistical Analysis

Patient, tumor, and treatment characteristics; referral data; and the spectrum of suspected and confirmed irAEs were summarized in frequency and percentage. Patient

characteristics were compared by irAE grade using the Wilcoxon rank-sum test for continuous variables and Pearson chi-square test for categorical variables. Univariate and multivariate logistic regression were used to obtain odds ratios (ORs) for the effects of treatment, sex, smoking status, age, prior autoimmunity/high-risk conditions, multisystem irAEs, and ICI dose on development of selected irAEs. Clinical factors associated with increased referral (>1 referral/patient) were explored. Statistical analyses were performed using STATA 14.1 (StataCorp LP). Statistical tests were 2-sided with a *P* value <.05 considered to indicate statistical significance.

Results

Feasibility of the IR-Tox Team

Data were collected from August 1, 2017, through March 30, 2018. The IR-tox team received 122 referrals concerning 107 patients over an 8-month period. Five patients were excluded (did not receive ICIs, *n*=4; not managed at JHH, *n*=1). A total of 117 referrals concerning 102 patients were included in the analysis. For all referrals, the IR-tox team responded with recommendations within 24 hours.

Patient Demographics and Oncologic History

CONSORT diagrams of referrals and individual patients are provided in Figure 1 and supplemental eFigure 2, respectively. Indications for referrals included suspected irAE (*n*=106; 91%) and suitability for ICIs (*n*=11; 10%). Of 106 referrals for suspected irAEs, these included 118 potential irAEs. Of the 11 patients referred for suitability for ICIs, 10 (91%) were for pre-immunotherapy assessment and 1 (9%) for ICI rechallenge. Of the 10 pre-immunotherapy referrals, 7 had prior autoimmune conditions (rheumatoid arthritis, *n*=3; inflammatory bowel disease, *n*=1; immune thrombocytopenia purpura/Evans syndrome, *n*=1; myasthenia gravis, *n*=1; Sjögren syndrome, *n*=1), 1 had a prior high-grade irAE (hepatitis), and 2 had other clinical conditions wherein suitability for ICI was questioned (live vaccination, *n*=1; splenectomy/increased infection risk, *n*=1). Most patients were referred to the team once (*n*=87/102; 85%) and some were referred twice (*n*=15/102; 15%).

Patient, treatment, and tumor features of referred patients are summarized in Table 1. The median age was 64 years (range, 21–91 years), 54% of patients were male (*n*=55), and 13% had prior autoimmunity/high-risk conditions (*n*=13; 9 autoimmune conditions, 1 solid

Figure 1. CONSORT diagram of referrals received by the IR-tox team.

Abbreviations: IR-tox, immune-related toxicity; irAE, immune-related adverse event.

^aThere were 118 total potential irAEs and 79 confirmed irAEs.

Table 1. Total Patient Cohort: Demographics and Oncologic History (N=102)

Patient Characteristic	n (%)
Median age (range), y	64 (21–91)
Sex	
Male	55 (53.9)
Female	47 (46.1)
Smoking status	
Former/Current	39 (38.6)
Never	63 (61.8)
Race	
White	83 (81.4)
Black/African American	11 (10.8)
Asian	7 (6.9)
Other	1 (1.0)
Prior autoimmunity/high-risk conditions ^a	
Yes	13 (12.7)
No	89 (87.3)
Malignancy type	
Thoracic	34 (33.3)
Gastrointestinal	18 (17.6)
Melanoma/Skin	17 (16.7)
Genitourinary	7 (6.9)
Gynecologic	8 (7.8)
Head and neck	6 (5.9)
Breast	4 (3.9)
Hematologic	7 (6.9)
Sarcoma	1 (1.0)
Treatment setting	
Inpatient	37 (36.3)
Outpatient	65 (63.7)
Immune checkpoint inhibitor therapy	
Monotherapy	55 (53.9)
Combination therapy	
+ Other immunotherapy	34 (33.3)
+ Chemotherapy	5 (4.9)
+ Targeted therapy	4 (3.9)
+ Other agent	4 (3.9)
Median number of doses at referral (range)	3 (0–40)
Receipt of therapy	
Standard of care	50 (49.0)
Clinical trial	52 (51.0)

^aAutoimmune conditions (n=9); solid organ transplant (n=1); bone marrow transplant (n=2); prior immune-related adverse event (n=1).

organ transplant, 2 bone marrow transplant, 1 prior irAE). The most common malignancies in referred patients were thoracic (n=34; 33%), gastrointestinal (n=18; 18%), and

melanoma/skin malignancies (n=17; 17%). Patients received either ICI monotherapy (n=55; 54%) or combinations (n=47; 46%), either as standard-of-care (n=49; 49%) or in clinical trials (n=52; 51%). Most referrals were received from the outpatient (n=65; 63%) rather than the inpatient setting (n=37; 36%). The median number of ICI doses received before referral was 3 (range, 0–40).

Spectrum of irAEs Referred to the IR-Tox Team

The spectrum of suspected and confirmed irAEs by organ system and individual event is depicted in Figure 2. Of 118 suspected irAEs, 79 irAEs from 68 patients were confirmed by the team (CTCAE grade 1: 13 [16%]; grade 2: 34 [43%]; grade ≥3: 32 [41%]). The most frequent irAE referral was for suspected pneumonitis (n=28; 24%). However, 36% of suspected pneumonitis referrals were deemed not irAEs (progressive non-small cell lung cancer, n=5; pulmonary infection, n=4; myasthenia gravis, n=1). This occurred in other suspected irAEs, wherein subsequent imaging, laboratory studies, or clinical features determined that a referral was not for an irAE or consensus was not achieved and attribution was coded as unknown. Aside from pulmonary medicine, referrals were received most frequently for rheumatology (n=21; 18%), gastroenterology (n=15; 13%), dermatology (n=15; 13%), endocrinology (n=14; 13%), and neurology (n=10; 8%).

The most common confirmed irAEs included pneumonitis (n=18; 23%), arthritis (n=13; 16%), dermatitis (n=12; 15%), and diarrhea/colitis (n=8; 10%) (Figure 2B). One new case of osteitis was identified that had not previously been reported in the literature. A total of 58 patients (85%) had irAEs involving 1 organ/system, whereas 10 patients (15%) had multisystem irAEs. The spectrum of irAEs stratified by treatment type, organ system, and grade is depicted in Figure 3. In multivariate analyses, receipt of combination ICIs (n=34) was associated with an increased risk of grade ≥3 irAEs (OR, 6.5; 95% CI, 1.70–24.6; *P*=.018) and colitis (OR, 12.9; 95% CI, 1.2–143.7; *P*=.037) and a trend toward multisystem irAEs (OR, 3.0; 95% CI, 0.9–9.3; *P*=.06). Patients with prior autoimmunity/high-risk conditions (n=13) were more likely to develop pneumonitis (OR, 27.2; 95% CI, 1.9–385.9; *P*=.015), and trended toward a higher risk for grade ≥3 irAEs (OR, 8.9; 95% CI, 0.8–95.8; *P*=.07). Importantly, an increased risk for multiple referrals (n=13) to the IR-tox team was seen in patients with multisystem irAEs (OR, 8.1; 95% CI, 1.9–34.8; *P*=.005) and/or those receiving combination ICIs (OR, 6.0; 95% CI, 1.1–32.6; *P*=.035).

Recommendations by the IR-Tox Team

IR-tox team referral data and recommendations are depicted in Table 2. Referrals were received from

Figure 2. Spectrum of irAE referrals by (A) frequency of suspected and confirmed irAE by organ system and (B) specific suspected and confirmed irAE.

Abbreviation: irAE, immune-related adverse event.

attending physicians (n=81; 69%), fellows (n=12; 10%), and nurses (n=24; 21%). In patients being treated as part of clinical trials, specific irAE management recommendations outlined in the study protocol were adhered to. Among referrals received regarding suitability for ICIs, 45% of referring providers (n=5/11) sought management recommendations. For the 118 suspected irAEs, the IR-tox team was mostly asked for diagnostic recommendations (n=110; 93%); in 95%

(n=75/79) of confirmed irAEs, the team was asked for management recommendations.

In the 17 patients with no/unknown irAEs in whom a management recommendation was sought, the team advised supportive care only in 94% (n=16) and immunosuppression in 1 patient with a flare of known inflammatory bowel disease. Subspecialist consultations were obtained for referred patients regardless of whether they had a confirmed irAE, with 51% of

Figure 3. irAEs confirmed by IR-tox team by (A) grade and organ system and (B) grade and specific irAE. Abbreviations: irAE, immune-related adverse event; IR-tox, immune-related toxicity.

non-irAEs/unknown and 35% of confirmed irAEs requiring more than one medicine consultation.

In all confirmed irAEs, invasive diagnostic testing was more likely to be undertaken in high-grade versus low-grade irAEs (59% vs 37%; $P = .006$). In addition, 39% of patients ($n = 31$) with high-grade irAEs were managed with corticosteroids $\pm$ additional immunosuppression, and significant differences in management

recommendations were seen in low- versus high-grade irAEs ($P < .001$).

Outcomes of Confirmed irAEs

Clinical outcomes of confirmed irAEs referred to the IR-tox team are summarized in supplemental eAppendix 2. All low-grade irAEs completely resolved/improved (39/47; 83%) or stabilized (17%; 8/47), whereas 13% of

Table 2. IR-Tox Team Referral Data and Recommendations

Reason for Referral	Suspected irAE (N=118)		Suitability for Immunotherapy, n (%) (N=11)
	Not irAE/Unknown, n (%) (N=39)	Confirmed irAE, n (%) (N=79)	
Question for the IR-tox team			
Suitability for immunotherapy			
Yes	0 (0)	0 (0)	11 (100)
No	39 (100)	79 (100)	0 (0)
Diagnostic			
Yes	38 (97)	72 (91)	1 (9)
No	1 (3)	7 (9)	10 (91)
Management			
Yes	17 (44)	75 (95)	5 (45)
No	22 (56)	4 (5)	6 (55)
IR-tox team recommendations			
Total diagnostic recommendations	38	72	1
No further diagnostic tests required	6 (15)	0 (0)	0 (0)
Noninvasive diagnostic tests	24 (62)	44 (56)	1 (9)
Invasive diagnostic test	8 (20)	28 (35)	0 (0)
Total management recommendations	17	75	5
Supportive care only	16 (41)	14 (18)	2 (18)
Corticosteroids only	0 (0)	46 (58)	1 (9)
Additional immunosuppression only	0 (0)	4 (5)	2 (18)
Steroids + additional immunosuppression	1 (3)	11 (14)	0 (0)
IR-tox team general recommendations			
Medicine consultation			
One	12 (31)	47 (59)	4 (36)
Multiple	20 (51)	28 (35)	1 (9)
None	6 (8)	4 (6)	6 (55)

Abbreviations: irAE, immune-related adverse event; IR-tox, immune-related toxicity.

high-grade irAEs (4/32) worsened. Of the 4 patients whose irAEs worsened, 3 died of their irAEs (nephritis: 1; pneumonitis: 1; encephalitis: 1).

Use of the IR-Tox Team: Postpilot Survey by Users

Among 57 respondents to the postpilot survey at JHH (physician, n=35; nurse practitioner/physician's assistant, n=7; registered nurse, n=15; other, n=4), the frequency of irAE evaluation varied: 3.6% evaluated them daily, 8.9% two to three times per week, 25% once per week, and 51.8% once per month. A total of 34 respondents used the IR-tox team service (59.7%), whereas 23 did not (40.3%). Of those who contacted the team, 100% of providers used all (n=19; 55.9%) or some (n=15; 44.1%) of the recommendations. Importantly, 73.5% (n=25) of referring providers said the IR-tox team recommendations changed their diagnostic evaluation or management

of immune-related toxicity. Overall, most respondents who used the IR-tox team rated it as definitely or probably helpful (n=33; 97%) (supplemental eFigure 3); 39 respondents (72.2%) thought a regular irAE tumor board-style meeting, in addition to the electronic referral system, would definitely or probably be beneficial.

Discussion

This is the first report of a multidisciplinary team for immune-related toxicity. We demonstrated the feasibility of an electronic referral system for patients with irAEs and related issues to multiple subspecialists. We also demonstrated use of the IR-tox team, because all surveyed providers who contacted the team used all or some of the recommendations, and most changed their management based on team recommendations. These data highlight important functions an IR-tox team

can provide in guiding clinical care and disseminating knowledge to providers less familiar with irAEs, and standardizing irAE management across an institution. We also identified toxicities that require subspecialist input, of which pneumonitis, arthritis, and dermatitis were the most common. Results of our program highlight patient populations more likely to use this service, such as those receiving combination ICIs and those with multisystem irAEs. With expanding use of combination ICIs in multiple tumor types,^{11–14} the absolute number of patients treated with these regimens is likely to increase, supporting the need for an IR-tox team.

There are several unique features of the IR-tox team program. The multidisciplinary nature of the group facilitated identification of newly recognized irAEs and multisystem events. Similarly, the CAR-T-cell-therapy-associated TOXicity (CARTOX) Working Group leverages oncologists and subspecialists across institutions¹⁵ to guide management of CAR T-cell toxicities. We envisage that IR-tox teams across institutions and countries, treating diverse populations with ICIs, may collaborate to guide research and refine current irAE guidelines.

The prospective nature of irAE data collection through the IR-tox team created an opportunity to identify alternative diagnoses for suspected irAEs. For example, patients not deemed to have pneumonitis by the team had progressive cancer or respiratory infection, and in one case a different irAE (myasthenia gravis). Likewise, only 30% of suspected neurologic irAE referrals were found to be irAEs. In contrast, all patients with suspected colitis had this diagnosis confirmed. This emphasizes the diagnostic dilemma that exists for pneumonitis and neurologic irAEs in particular.

Another unique feature of the IR-tox team program was its electronic platform to engage multiple specialists. This format reduces administrative burden and could be leveraged for telemedicine, to provide irAE expertise to patients being managed in limited-access settings.¹⁶ Although other immune-related toxicity initiatives have been proposed as part of inpatient oncology services, this virtual team allowed for specialist input for outpatients, which may be more applicable. Lastly, more than half of IR-tox team referrals were for patients enrolled in clinical trials, to ascertain an irAE diagnosis, or for management advice when specific guidance was not outlined in the study protocol. This was especially relevant for rare toxicities that may not have been addressed individually in study protocols. Attribution of toxicity to a study drug has important implications for cancer drug development, and may identify a unique and important use for a multidisciplinary team. Electronic or in-person IR-tox teams could serve as independent adjudicators of

irAE attributions, and resolve relative discrepancies in irAE attribution between study sites, noted in irAE publications.¹⁷

One limitation of this study was the lack of a control group (ie, patients for which the IR-tox team was not available for consultation). Future studies might aim to evaluate time to referral, time to irAE treatment, or time to irAE resolution in patients referred to the IR-tox team versus not. During the time period of our study, there were likely patients who were directly referred to medicine subspecialists and therefore not captured in this dataset. These patients may have had lower grade or less complex irAEs. Additionally, known areas of interest for members of the IR-tox team may have influenced referral patterns (eg, pneumonitis and arthritis are areas of interest of the co-chairs). Although we were able to bring together a large team of irAE subspecialists at our institution, this may be more challenging to re-create outside of academic medicine. In addition, although an electronic platform allowed access to a variety of specialists without an unacceptable wait time, some clinical scenarios warrant emergent management. We attempted to account for this with an immediate response message, urging providers to direct patients to the emergency room in urgent situations.

Conclusions

This pilot program demonstrates that an electronic referral system for immune-related toxicities was feasible, used, and informative about patterns of irAEs requiring subspecialist care. These data lay the foundation for the development of local, national, and international IR-tox teams with the goal of optimizing multidisciplinary clinical care, supporting irAE education, leveraging virtual expertise to limited access settings, and applying to clinical trials. Further research in this area is likely to be fostered by a comprehensive irAE database, and future studies aimed at evaluating whether an IR-tox team approach versus ad hoc specialist referral could influence important patient outcomes, such as hospitalization rates, time on corticosteroid treatment, or time to restarting immunotherapy, in patients who develop irAEs.

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Supplemental online content for:

A Multidisciplinary Toxicity Team for Cancer Immunotherapy–Related Adverse Events

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eFigure 1: Representative Templates to and From IR-Tox Team

eFigure 2: CONSORT Diagram

eFigure 3: Selected Results of the Electronic Postpilot Survey

eAppendix 1: Postpilot Questionnaire About the IR-Tox Team

eAppendix 2: Clinical Outcomes of Confirmed irAEs

<p>A</p> <p>Referral to IR-Tox Team</p> <p>Patient initials:</p> <p>Medical record number:</p> <p>Referring provider:</p> <p>Primary provider:</p> <p>Name of immunotherapy agent(s):</p> <p>Duration of immunotherapy: x months (y doses)</p> <p>Tumor type:</p> <p>Diagnostic evaluation ordered/completed:</p> <p>Brief summary:</p> <p>Specific question:</p> <p>Request for medicine referral:</p>	<p>B</p> <p>IR-Tox Team Email Recommendation Template</p> <p>Recommendation:</p> <ul style="list-style-type: none"> - Summary of recommendations <p>Request for medicine referral:</p> <ul style="list-style-type: none"> - Name of provider - Provider cc'ed <p>Disclaimer: Recommendations from the IR-tox team will be provided within 24 hours of referral. The IR-tox team provides recommendations; however, decisions regarding the diagnostic evaluation and management of referred patients will be made by the patient's primary provider.</p>
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eFigure 1. Representative templates of information included for (A) referral to IR-tox team and (B) recommendations provided by IR-tox team 24 hours after referral.

Abbreviation: IR-tox, immune-related toxicity.

eFigure 2. CONSORT diagram of patients referred to the IR-tox team.

Abbreviations: IR-tox, immune-related toxicity; irAE, immune-related adverse event.

eFigure 3. Selected results of the electronic postpilot survey sent to oncology providers in the cancer center, after the IR-tox team pilot program. Abbreviations: IR-tox, immune-related toxicity; irAE, immune-related adverse event.

eAppendix 1. Postpilot Questionnaire About the IR-Tox Team

Q1	What area of oncology do you primarily work in?
Q2	What type of provider are you?
Q3	How often do you prescribe immunotherapy for cancer treatment/evaluate patients on immunotherapy?
Q4	What kind of immunotherapy do you prescribe? (check all that apply)
Q5	How often do you encounter suspected immune-related toxicity?
Q6	How often do you encounter immune-related toxicity that requires an intervention?
Q7	Have you contacted the IR-tox team?
Q8	What topic(s) did you ask the team about? (check all that apply)
Q9	Did you use the specific suggestions provided by the IR-tox team?
Q10	Did the IR-tox team recommendations change your approach to evaluation or management of immune-related toxicity?
Q11	Did you find the IR-tox team service to be helpful?
Q12	What format would you prefer to contact the IR-tox team? (choose one)
Q13	What other resources could the IR-tox team provide that would be helpful? (check all that apply)
Q14	How would you prefer to access information on IR-tox?
Q15	Do you think there would be a benefit to a regular tumor board–style meeting about IR-tox?
Q16	How often should a tumor board–style meeting for IR-tox take place?
Q17	Would you support an immune-related toxicity registry/enrollment of patients with irAEs for research purposes?
Q18	Do you want a separate irAEs outpatient clinic?
Q19	Do you want a separate irAEs urgent care?
Q20	Would you attend an irAEs masterclass if offered?
Q21	Please provide any additional feedback

Abbreviations: IR-tox, immune-related toxicity; irAE, immune-related adverse event.

eAppendix 2. Clinical Outcomes of Confirmed irAEs

Clinical Outcomes	Grade 1–2 (n=47; 60%) n (%)	Grade ≥3 (n=32; 40%) n (%)
irAE1^a		
Completely resolved	2 (4)	3 (9)
Improved	32 (68)	20 (63)
Stabilized	6 (13)	3 (9)
Worsened	0 (0)	3 (9)
irAE2^b		
Completely resolved	3 (7)	0 (0)
Improved	2 (4)	1 (3)
Stabilized	2 (4)	1 (3)
Worsened	0 (0)	1 (3)

Abbreviation: irAE, immune-related adverse event.

^aFirst irAE prompting referral.

^bSecond irAE prompting referral.