Immune-Related Adverse Events in Patients on Immunotherapy Presenting to the Emergency Department: A Retrospective Cohort Study

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Background

Immunotherapy is a preferred line of treatment for a wide array of hematologic and solid-tumor malignancies, despite the risk of dangerous complications. Immune related adverse events (irAEs), including colitis, pneumonitis, hypophysitis, and hepatitis, among others, comprise the most common of these potentially life-threatening treatment-related toxicities.[1,2] Treatment-related toxicity must be identified early in the course and managed with systemic steroids, usually in the hospital.[3] As such, a thorough understanding of the presentation of irAEs in the ED, as well as variables that may contribute to their successful identification, is essential to minimizing irAE-related morbidity and mortality.

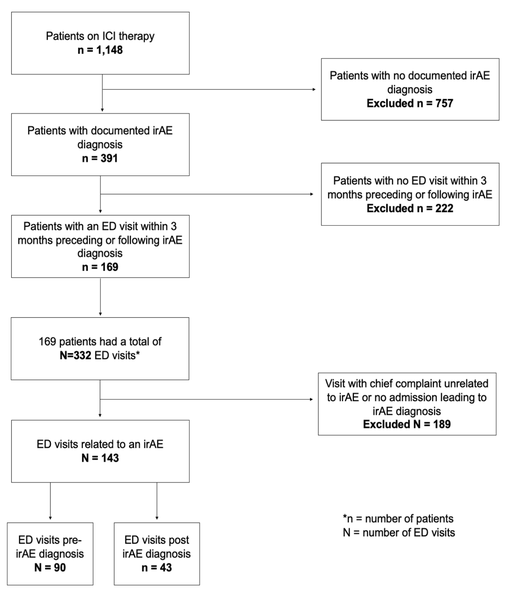
Study objectives

- To describe the incidence, timing, type, rates of misdiagnosis, and relevant clinical characteristics of immune-related adverse events (irAEs) in patients on immunotherapy presenting to the emergency department (ED) at a large, academic medical center associated with a comprehensive cancer center.
- To identify factors predicting early identification of irAEs by ED clinicians.

Methods

We performed a retrospective chart review as a secondary analysis of a registry of 1,148 patients treated with immune checkpoint inhibitors between January 1, 2010 – June 1, 2017.[4] Descriptive statistics were performed using Stata15 (StataCorp LLC, College Station TX). Data management utilized REDCap.[5]

Figure 1. Patient selection process.



Results

Table 1. Malignancy Types.

Cancer Type	n	%
Non-Small Cell Lung Cancer	69	17.7
Small Cell Lung Cancer	4	1.02
Melanoma	137	35.0
Renal Cell Carcinoma	45	11.5
Head and Neck Carcinoma	25	6.4
Merkel Cell Carcinoma	3	0.8
Hodgkin's Lymphoma	11	2.8
Breast Cancer	3	0.8
Colon Cancer	7	1.8
Pancreatic Cancer	2	0.5
Sarcoma	19	4.9
Prostate Cancer	2	0.5
Bladder Cancer	18	4.6
Other	46	11.8

Table 2. Immunotherapy Agents.

Agent	n	%
Nivolumab (Nivo)	157	40.2
Pembrolizumab	76	19.4
Atezolizumab	11	2.8
Ipilimumab (Ipi)	69	17.7
Nivo + Ipi	52	13.3
Tremelimumab	1	0.3
Nivo + Chemotherapy	3	0.8
Other	22	5.6

Table 3. irAE Subtype.

Type	n	%
Pneumonitis	46	11.8
Colitis/Diarrhea	113	28.9
Thyroid Abnormality	109	27.9
Hepatitis/LFT Abnormality	74	18.9
Dermatitis/Rash/Pruritis	140	35.8
Myalgia/Arthralgia	33	8.4
Neurological	43	11.0
Hypophysitis	26	6.7
Other (pyrexia, cardiac, etc.)	83	21.2

- In our cohort of 1,148 patients on ICIs, 391 had at least one irAE (34.1%).
- Among patients with irAEs, 169 presented at least once to the ED during the 3 months preceding or following the diagnosis of an irAE (43.2%).
- 124 unique patients had a median of 1 visit (range 1-4) prior to irAE diagnosis.
- 99 unique patients had a median of 1 visit (range 1-5) post irAE diagnosis.
- The most common irAEs included dermatitis/rash/pruritis (n=140, 35.8%), colitis/diarrhea (n=113, 28.9%), and thyroid abnormality (n=109, 27.9%).
- IrAEs were suspected by the ED treating team in 47.8% and 53.5% of irAE-related encounters preceding and following an oncologist's irAE diagnosis, respectively.
- Providers initiated treatment for irAE in 39.1% of ED encounters.

Conclusions

- IrAEs frequently present in the acute setting.
- Identification of irAEs in the ED remains poor, despite an ED's association with a large, academic medical center affiliated with comprehensive cancer center.
- Further analysis is required to determine specific factors associated with improved irAE identification by emergency clinicians.

References

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