Real-world Characterization of Immune-related Adverse Events in Nova Scotia Patients Treated with Pembrolizumab or Durvalumab and Adherence to Toxicity Management Guidelines

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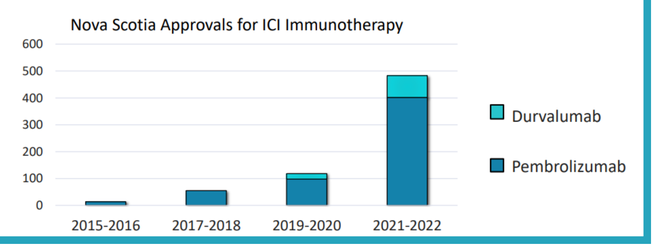
INTRODUCTION

- Pembrolizumab and durvalumab are immune checkpoint inhibitors (ICIs) indicated to treat a variety of different cancers.
- ICIs target various checkpoint proteins and enhance T-cell-mediated destruction of cancer cells.
- ICIs do not have the same cytotoxic effects as traditional chemotherapy. However, ICIs carry the risk of causing immune-related adverse events (irAEs).
- IrAEs can occur in any organ or tissue, at any point throughout treatment, and even up to a year after discontinuation.
- Prompt identification and management of irAEs is crucial to minimize risk for severe morbidity and mortality.
- As the indications for ICIs continue to expand, healthcare providers face a growing challenge in managing the increasing number of patients experiencing irAEs.

Figure 1. Total number of patients approved for immunotherapy with pembrolizumab and durvalumab in Nova Scotia, categorized by time periods.



OBJECTIVES

- The primary objectives were to characterize irAEs and describe adherence to toxicity management guidelines throughout Nova Scotia.
- The secondary objectives were to describe the change in adherence to guidelines over time and evaluate the involvement of subspecialty disciplines.

METHODS

- Multi-center retrospective chart review
- Inclusion: Adult medical oncology patients approved for pembrolizumab or durvalumab between 2010 and 2021 in Nova Scotia.
- Exclusion: ICI in combination with chemotherapy/targeted therapy, enrollment in a clinical trial.
- Categorization of irAEs by organ/system and severity/grade based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) classification and a collection of published guidelines[4-15,17].
- The likelihood of irAEs being associated with ICI treatment was classified as "definitely," "probably," or "possibly" based on clinical evidence, physician documentation, and clinical expertise.
- Management strategies were considered 'according to guidelines' if they followed any one of the current published guidelines[4-15].
- Descriptive statistics and logistic regression modelling were used for data analysis.

Table 1. Examples of current guidelines and subspecialty guidelines used in the management of immune-related adverse events caused by ICI therapy.

CCO 2020	Cancer Care Ontario. Immune Checkpoint Inhibitor Toxicity Management: Clinical Practice Guideline[6].
NCCN 2019	Journal of the National Comprehensive Caner Network. Management of Immunotherapy-Related Toxicities, Version 1.2019. NCCN Clinical Practice Guidelines in Oncology[7].
ASCO 2021	American Society of Clinical Oncology Clinical Practice Guideline. Management of Immune-Related Adverse Events in Patients Treated with Immune Checkpoint Inhibitor Therapy: Guideline Update[5].
ESMO 2017	European Society of Medical Oncology. Management of toxicities from immunotherapy. Clinical Practice Guidelines for diagnosis, treatment and follow-up[4].
AGA 2021	Clinical Practice Update on Diagnosis and Management of Immune Checkpoint Inhibitor Colitis and Hepatitis: Expert Review[15].
CDA 2020	Canadian Dermatology Association. Cutaneous Immune-Related Adverse Events to Immune Checkpoint Inhibitors: A Dermatology Perspective on Management[13].
EULAR 2021	European Alliance of Associations for Rheumatology points to consider for the diagnosis and management of rheumatic immune-related adverse events due to cancer immunotherapy with checkpoint inhibitors[12].
SE 2018	Society for Endocrinology. Endocrine emergency guidance. Acute management of the endocrine complications of checkpoint inhibitor therapy[14].

RESULTS - CHARACTERIZATION OF IMMUNE-RELATED ADVERSE EVENTS

Table 2. Baseline characteristics of Nova Scotia medical oncology patients initiated on immunotherapy with pembrolizumab or durvalumab from 2010-2021 (n = 292).

Patient Characteristics, n=292	
Age, mean (±SD)	
Age (years)	67 (± 10)
Gender, n (%)	
Male	175 (60)
Female	117 (40)
Drug, n (%)	
Pembrolizumab	237 (81.2)
Durvalumab	55 (18.8)
Indication/Cancer diagnosis, n (%)	
Pembrolizumab	
Metastatic Melanoma	58 (19.9)
Adjuvant Melanoma	37 (12.7)
1st Line -NSCLC	74 (25.3)
2nd Line- NSCLC	30 (10.3)
Metastatic Urothelial	33 (11.3)
Head & Neck SCC	5 (1.71)
Durvalumab	
NSCLC	55 (18.8)
Geographical zone, n (%)	
Central Zone (CZ)	180 (61.6)
Eastern Zone (EZ)	39 (13.4)
Western Zone (WZ)	36 (12.3)
Northern Zone (NZ)	37 (12.7)

SD, standard deviation; NSCLC, non-small cell lung cancer; HNSCC, head and neck squamous cell carcinoma

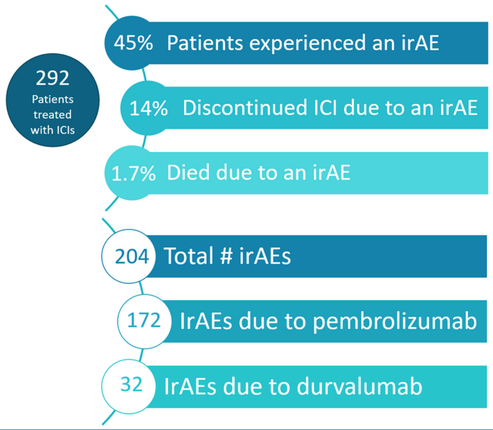


Figure 2. Total frequency of immune-related adverse events experienced by medical oncology patients in Nova Scotia, categorized by organ/system and by drug (pembrolizumab or durvalumab).

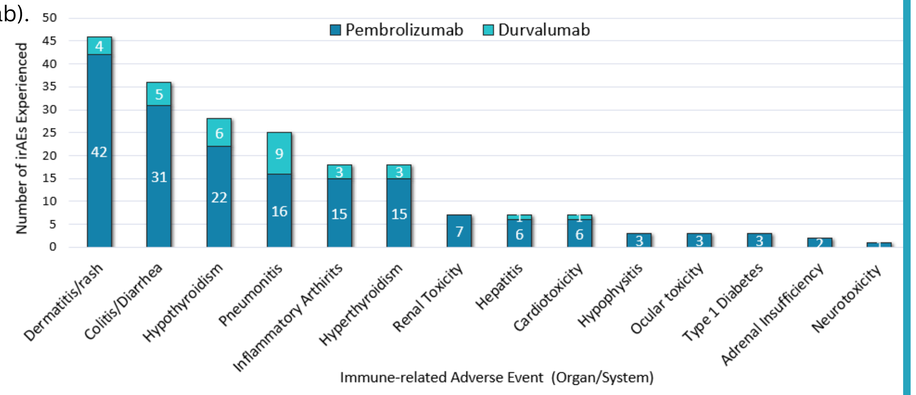
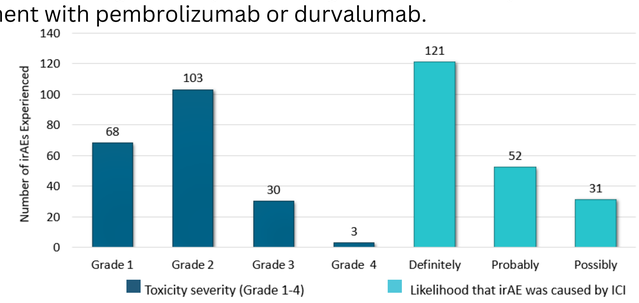


Figure 3. The number of immune-related adverse events experienced by medical oncology patients in Nova Scotia categorized by severity (grades 1-4) and by likelihood that the irAE was caused by treatment with pembrolizumab or durvalumab.



RESULTS - ADHERENCE TO GUIDELINES

Figure 4. The proportion of immune-related adverse events that were 'managed according to guidelines', 'not managed according to guidelines' and 'not documented' based on current published guidelines[4-15].

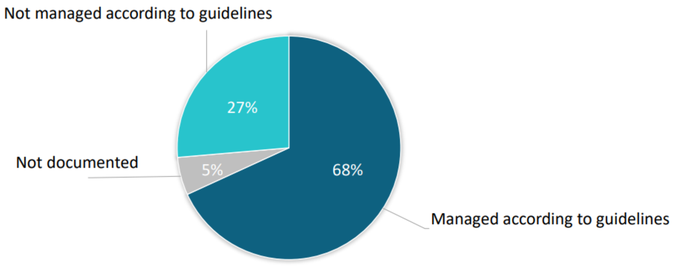
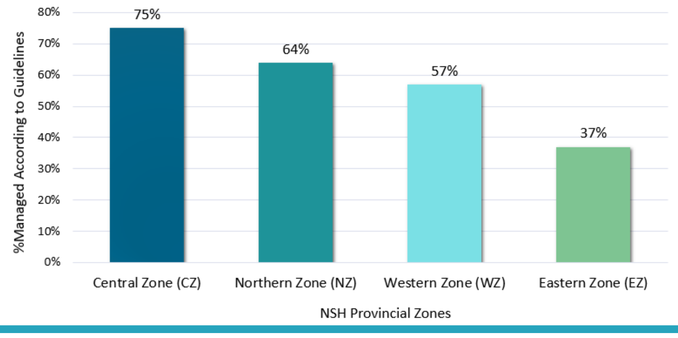
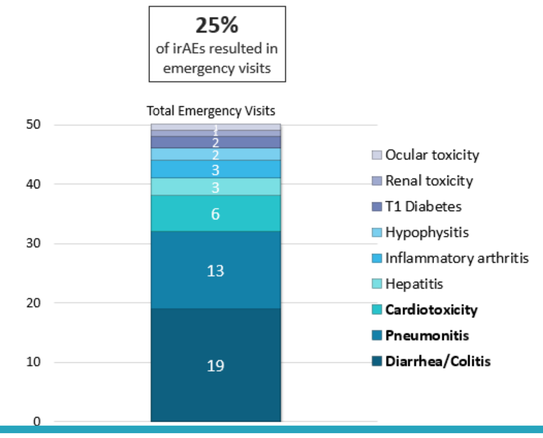


Figure 5. The proportion of immune-related adverse events experienced by patients who received pembrolizumab or durvalumab that were managed according to guidelines, categorized by provincial healthcare zones in Nova Scotia.



RESULTS - EMERGENCY VISITS

Figure 6. The proportion of documented irAE-related emergency department visits across Novia Scotia.



RESULTS - MANAGEMENT STRATEGIES

Table 3. Management of immune-related adverse events in Nova Scotia patients treated with pembrolizumab or durvalumab.

Total irAEs (n=204)	n (%)
Topical steroids	36 (17.6)
Transdermal cream or ointment	34 (16.7)
Ophthalmic drops	2 (0.98)
Intra-articular steroids	4 (1.9)
Systemic steroids (PO/IV)	96 (47.0)
Prednisone 10-20 mg/day (PO)	13 (6.4)
Prednisone 0.5-1 mg/kg/day (PO/IV)	55 (26.9)
Prednisone 1-2 mg/kg/day (PO/IV)	17 (8.3)
Methylprednisolone 1-2 mg/kg/day (IV)	7 (3.4)
Methylprednisolone 2-4 mg/kg/day (IV)	3 (1.5)
Methylprednisolone 1 g/day (IV)	1 (0.5)
Life-long HRT - Hydrocortisone TID (IV)	5 (2.5)
Add MMF or infliximab	5 (2.5)
Levothyroxine	27 (13.2)
Subspecialty consult	56 (27.5)
Admit to hospital	33 (16.2)
Hold ICI	72 (35.5)
Permanently discontinue ICI	41 (20.1)

IrAEs, immune-related adverse events; PO, oral; IV, intravenous; HRT, hormone replacement therapy; TID, three times a day; MMF, mycophenolate mofetil; ICI, immune checkpoint inhibitor

DISCUSSION & CONCLUSION

- Approximately half of patients receiving ICIs experienced at least one irAE[18,19].
- Of the 204 irAEs evaluated, 55 (27.0%) were 'not managed according to guidelines'.
- Deviations from guidelines may be intentional based on individual patient characteristics and risk-benefit assessments.
- Lower rates of guideline adherence were observed in more rural areas of Nova Scotia.
- The limited sample sizes in our evaluations of guideline adherence across provincial zones underscore the necessity for larger studies to validate these findings.
- Data was limited by the available information documented in health records.

Future Research & Implications for Practice

- Compare guideline adherence between oncologists and non-oncology physicians.
- Explore interventions such as pharmacist-led toxicity screening clinics[27] and irAE-specific toxicity management order sets.
- Establishing a specialized committee with irAE expertise could enhance outcomes and reduce the healthcare burden[26].
- This study's findings can guide clinical decision-making, enhance education, and encourage innovative changes to optimize irAE management and patient care.

REFERENCES & DISCLOSURES

Authors of this poster have the following to disclose concerning possible personal or financial relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
Tara Di Costanzo - Nothing to disclose, Arezou Teimouri - Nothing to disclose, Dr. Susan Bowles - Nothing to disclose, Amanda Daniels - Nothing to disclose, Samantha Scott - Noting to disclose, Dr. Stephanie Snow- Nothing to disclose, Dr. Laura V Minard - Nothing to disclose.

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References