Oral Immune-Related Adverse Events Associated with PD-1 and PD-L1 Inhibitor Therapies: A Retrospective, Single-Institution Study

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Introduction

- **Immune checkpoint inhibitors (ICI)** are effective for numerous metastatic and locally advanced cancers
- Mechanism of **PD-1/PD-L1 inhibitors**:
  - PD-1 is critical to adaptive immunity via the **binding of PD-1 to PD-L1**, suppressing T-cell receptor-mediated immune responses [1]
  - The binding suppresses T-cell receptor-mediated immune responses [1]
  - Cytotoxic T-cells attack normal cells, inducing **immune-related adverse events (irAEs)** [2]
- Previous studies estimate a low incidence [3]
  - **5% for xerostomia**
  - **3% for mucositis, dysgeusia, and oropharyngeal pain**
- **Xerostomia** and **lichenoid reactions** are the most commonly reported oral toxicities [4]
- AIM: Characterize clinical features, treatments, and outcomes of patients who developed oral irAEs on PD-1/PD-L1 inhibitors

Methods

- Retrospective chart review of 30 patients receiving PD-1 or PD-L1 inhibitors, identified based on prescriptions for dexamethasone elixir, viscous lidocaine, magic mouthwash
- Symptoms attributable to chemotherapy, radiation, surgery were excluded

Results

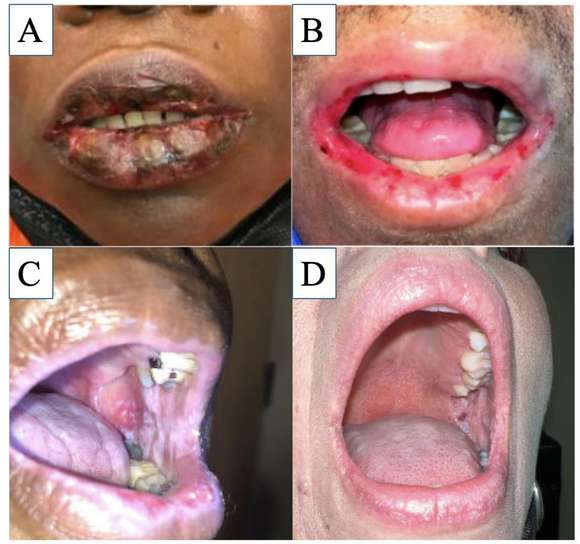
Table 1. Clinical and demographic characteristics of patients with oral irAEs on PD-1/PD-L1 inhibitors.

Oral irAE characteristics	
# of PD-1/PD-L1 inhibitor doses before oral irAEs	
Mean (count) ± SD	6.3 ± 6.8
Time between starting PD-1/PD-L1 inhibitor and oral irAEs	
Mean (days) ± SD	215.9 ± 427
Topical treatments for oral irAEs	***n***
Mucositis cocktail	19
Nystatin mouthwash	7
Viscous lidocaine	6
Topical steroid	5
Dexamethasone elixir	4
Chlorhexidine mouthwash	3
Other	4
None	5
Systemic treatments for oral irAEs	***n***
Steroids	9
Fluconazole	6
Antibiotic	4
Opioid	2
Vitamins	2
Other	3
None	13
Oral irAE clinical description	***n***
Mucositis/stomatitis/ulceration	20
Xerostomia	11
Color changes	8
Mouth pain	7
Dysphagia/odynophagia	5
Dysgeusia	3
Leukoplakia	2
Other	6
Anatomic site of oral irAE	***n***
Mucosa	14
Tongue	8
Palate	5
Lip	4
Pharynx	3
Other	9

Patient Characteristics	
Age	
Mean (years) ± SD	62.1 ± 12.3
Sex	***n (%)***
Female	18 (60%)
Male	12 (40%)
Race/Ethnicity	***n (%)***
White	4 (13.3%)
Black/African American	9 (30%)
Asian/Pacific Islander	1 (3.3%)
Hispanic/Latino	13 (43.3%)
Other/Unknown	3 (10%)
PD-1/PD-L1 inhibitor therapy	***n (%)***
Pembrolizumab	21 (70%)
Nivolumab	4 (13.3%)
Atezolizumab	3 (10%)
Durvalumab	2 (6.7%)
Cancer diagnosis	***n (%)***
Melanoma	1 (3.3%)
Urothelial/bladder cancer	3 (10%)
Lung cancer	6 (20%)
Other squamous cell carcinoma (e.g. head and neck)	4 (13.3%)
Other	16 (53.3%)
Simultaneous therapy	***n (%)***
Chemotherapy	11 (36.7%)
Targeted cancer therapy	6 (20%)
Radiation therapy	1 (3.3%)
None	12 (40%)
Responded to immunotherapy	***n (%)***
No	18 (60%)
Yes	10 (33.3%)
N/A	2 (6.7%)

- Three oral biopsies: one with ulcerated mucosa with granulation tissue, two with lichenoid mucositis
- Two skin biopsies: lichenoid dermatitis, lichenoid drug reaction

Figure 1. Clinical images of oral irAEs.



Discussion

- Most oirAEs respond well to analgesics and topical steroids—gels for mucosa, solutions for diffuse involvement, ointments for lip lesions
- Further research may aid oncologists and dermatologists in early identification, treatment, and management of these oral irAEs

References

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