The six immunotherapy categories listed in Table 1 have been associated with oral immune-related adverse effects (irAEs). Oral irAEs involve various tissues, including the oral mucosa, gingivae, salivary glands, taste buds, and indirectly the teeth. The most frequent oral irAEs are dysgeusia, mucosal toxicity, and xerostomia [7]. Among the oral mucosal irAEs reported are oral lichen planus (OLP)/oral lichenoid reaction (OLR), bullous pemphigoid, lichen planus pemphigoides, stomatitis, and erythema multiforme.

Oral irAEs may be severe and necessitate modifying or withholding the cancer therapy. Comprehensive evaluation, prevention, and proper treatment of adverse effects can allow continuation of cancer treatment. A working group of the Oral Care Study Group (OCSG) of the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) composed this Clinical Practice Statement (CPS) to provide a concise summary of the management of oral irAEs.

Since the clinical presentation of oral mucosal irAEs may mimic the features of well-known immune-mediated oral diseases or cancer therapy toxicities, the current approach used in treating oral irAEs is extrapolated in part from the literature as well as the clinical experience of managing these common oral diseases and conditions.

This CPS is focused primarily on management of the oral irAEs; however, it also covers diagnostic considerations that are specific for each oral irAE. Nevertheless, this CPS is not intended to be a comprehensive diagnostic tool for all oral complications in cancer patients nor for oral diseases unrelated to the cancer therapy that the patient may present.

Objective

This CPS aimed to develop a tool for practitioners that briefly summarizes the management of oral irAEs and outlines the standards of care for these oral complications.

Methods

This CPS is a compilation of expert opinions supported by quality-assessed evidence and a critical review of the literature. PubMed was searched from inception until August 1, 2024, to find literature related to oral irAEs, based on the names of drugs approved by the FDA (listed Table 1). A confirmatory search was conducted with websites of leading cancer research organizations. Some immunotherapy agents are only approved by the EU, Japan, and China, and are not covered in this CPS. The treatment approach described in this CPS is based on literature about oral irAEs and extrapolation from literature about similar oral diseases. A summary of this information was discussed by the international working group of the OCSG of MASCC/ISOO, and subsequently reviewed and approved by two independent boards: the ISOO Advisory Board and the MASCC Guidelines Committee. The CPS follows the MASCC/ISOO Guidelines Policy.

Management

Oral lichen planus/oral lichenoid reaction

- The management of oral lichen planus (OLP) or oral lichenoid reaction (OLR) may be challenging, particularly when ulcerations and erosions are present. The main goal of treatment is to reduce the severity of disease activity and its associated symptoms.
- The mainstay of treatment is topical steroids, which can be tailored to the patient's needs. These adjustments refer to the consistency and potency of the steroid as well as the frequency of use.
- Commonly used topical steroids are clobetasol (0.05%) and dexamethasone (0.01%–0.05%). Additional optional steroid preparations are listed in Table 2. Availability of commercial preparations and patient's acceptance may limit the optional agents.
- The second-line topical agent may be calcineurin inhibitors, such as tacrolimus (0.03–0.1%) and pimecrolimus (1%). Of note, the Black Box warning for topical tacrolimus and pimecrolimus indicates a risk for rare malignancies; skin malignancies and lymphoma were reported following topical calcineurin inhibitor use, and a causal relationship has not been established. Accordingly, it is advised to avoid continuous long-term use and limit its application to affected areas. Importantly, the Black Box warning refers to application on the skin; the evidence for association with oral mucosal malignancies is even weaker.
- Topical pain management may be needed with agents that provide local anesthetic effect, such as lidocaine and diphenhydramine and locally active analgesics (Table 2). Morphine solution may be prescribed for severe pain as a second line of treatment, and its use should be monitored to reduce the risk of overdose. Adjunctive pain medications targeting nociceptive and neuropathic pain may be needed.
- Non-pharmacologic pain management options may also be considered (Box 1). Of note, photobiomodulation (PBM) may help with pain management at the acute phase of the OLP/OLR. PBM protocols may vary in their efficacy and duration. It is advised to use a PBM setting that was assessed in randomized controlled trials. Some protocols that relieve pain for oral mucositis may be extrapolated for pain management in immunotherapy-