

Management of Oral Mucositis

General Information

- The content included in this material refers to published international results. Although detailed, this instrument is not intended or designed as an exhaustive review. The absence of errors, omissions or inaccuracies is not guaranteed. For more complete information and details regarding the described studies, the reader is invited to consult the quoted original documents.
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Introduction

The oral mucositis therapeutics market includes several kinds of drug formulations and treatments such as:

- Cryotherapy
- Growth factors
- Antioxidants
- Anti-inflammatory agents
- Low-level laser therapy (LLLT)
- Mouthwashes
- Barriers
- Coating agents

Management of Oral Mucositis

International Guidelines and Recommendations

The European Society for Medical Oncology (ESMO)

- *Oral and gastrointestinal mucositis due to cancer therapies continues to be an important clinical problem¹*
- *Strategic advances over the past decade relative to understanding the molecular basis of the injury led to opportunities for development of drugs and devices to prevent or treat the toxicity¹*
- *The presented guidelines are a summary of the 2015 publication Management of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up¹*
- *They represent updates to Peterson (2011)¹ and they were based on guidelines produced by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society for Oral Oncology (MASCC/ISOO)²*

1. Peterson et al. *Ann Oncol* 2015; 26 Suppl 5:v139-51
2. Lalla RV et al. *MASCC/ISOO Cancer* 2014; 120:1453–1461.

Basic oral care and good clinical practice - 1

- *ESMO Guidelines recommendation (example of a Basic Oral Care Protocol):¹*
- *Basic oral care is key in preventing and reducing oral injury*
- *Two key strategies for mitigation of oral mucosal injury before and during treatment*
 - Maintenance of optimal nutritional support throughout the entire period of cancer therapy
 - Developing a daily oral hygiene routine, including brushing teeth and the gums four times a day with a soft brush and using mouth rinses. This approach can contribute to the reduction and, ideally, prevention of oral tissue injury and associated pain, nutritional compromise, and related adverse outcomes

Basic oral care and good clinical practice - 2

•*ESMO Guidelines recommendation (example of a Basic Oral Care Protocol):¹*

The following information is presented as a portfolio of patient-based instructions for which health professional guidance is recommended

General measures

- Inspect your oral mucosa daily
- Have your dental team eliminate sources of trauma (e.g. ill-fitting prostheses; fractured teeth)
- Lubricate lips with (sterile) Vaseline/white paraffin (petrolatum), lip balm, or lip cream. Be aware that Vaseline/white paraffin (petrolatum) should not be used chronically on the lips, as this promotes mucosal cell dehydration and is occlusive leading to risk of secondary infection
- Drink ample amount of fluids to keep the mouth moist

Brushing teeth and gums

- Use a soft toothbrush or swab (as tolerated) after meals and before sleep. Brushing with a soft toothbrush reduces risk of bleeding. Each month you should utilise a new soft toothbrush
- Clean the dentition and gingiva with a mild fluoride-containing, non-foaming toothpaste
- Brush teeth twice a day (after meals and at bedtime) according to the Bass or modified Bass method. If using an electric toothbrush, utilise the techniques cited in the product description instead
- Rinse the brush thoroughly after use with water and store the toothbrush in a cup with the brush head facing upward
- If you are used to do so, clean the area between the teeth once a day. Consult a dental hygienist/dentist about the most appropriate interdental cleaner (floss, toothpick, brushes). In case you are not used to use interdental cleaners on a regular base, do not start with it while on cancer therapy, since it can break the epithelial barrier, visible through gingival bleeding

Basic oral care and good clinical practice - 3

ESMO Guidelines recommendation (example of a Basic Oral Care Protocol):¹

The following information is presented as a portfolio of patient-based instructions for which health professional guidance is recommended

Rinse mouth

- Rinse mouth with an alcohol-free mouthwash upon awakening and at least four times a day after brushing, for ~1 min with 15 ml mouthwash; gargle; and then spit out. During the first half hour after rinsing, avoid eating and drinking

Denture care

- Remove dentures before performing oral care. Brush dentures with toothpaste and rinse with water; clean the gums
- Defer wearing dental prostheses as much as possible until the lining tissues of your mouth are healed. If in the hospital, soak the denture for 10 min in an antimicrobial solution (e.g., chlorhexidine 0.2% if available) before inserting in your mouth

Avoid painful stimuli

- Smoking
- Alcohol
- Certain foods such as tomatoes, citrus fruits, hot drinks and spicy, hot, raw, or crusty foods

Basic oral care and good clinical practice - 4

Pain management¹

Adequate pain management, e.g. anesthetic mouthwashes (viscous lidocaine 2%), coating agents, or systemic analgesics following the WHO pain management ladder may be provided to treat pain from stomatitis

- If patients find the mouthwash painful, they should be advised to use one of these approaches beforehand

With persistent severe pain, more aggressive pain management may be considered to treat severe pain from stomatitis

- Since oral complaints can complicate administration of drugs by mouth, one should consider other kinds of administration routes, such as transdermal or intranasal routes

ESMO Mucositis Guidelines: Radiation therapy - 1

RECOMMENDATIONS FOR PREVENTION (ORAL CAVITY MUCOSITIS GUIDELINE) ¹

Cancer of any kind

- Oral care protocols should be used to prevent oral mucositis in all age groups and across all cancer treatment modalities

Head and neck cancer

- Benzylamine mouthwash can be used to prevent oral mucositis in patients receiving moderate dose radiation therapy (up to 50 Gy), without concomitant chemotherapy
- Chlorhexidine or misoprostol mouthwashes should not be used to prevent oral mucositis in patients receiving radiation therapy
- Systemic pilocarpine, administered orally, should not be used to prevent oral mucositis in patients receiving radiation therapy
- PTA (polymyxin, tobramycin, amphotericin B) and BCoG antimicrobial lozenges and PTA paste should not be used to prevent oral mucositis in patients receiving radiation therapy
- Iseganan antimicrobial mouthwash should not be used to prevent oral mucositis in patients receiving radiation therapy or concomitant chemoradiation
- Sucralfate mouthwash should not be used to prevent oral mucositis in patients receiving radiation therapy (I) or concomitant chemoradiation (II)
- Low-level laser therapy (wavelength ~632.8 nm) be used to prevent oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy

ESMO Mucositis Guidelines: Radiation therapy - 2

RECOMMENDATIONS FOR PREVENTION (ORAL CAVITY MUCOSITIS GUIDELINE)¹

Hematological malignancy

- Recombinant human keratinocyte growth factor-1 (KGF-1/palifermin) can be used to prevent oral mucositis (60 µg/kg per day for 3 days before conditioning treatment and for 3 days after transplant)
- Oral cryotherapy can be used to prevent oral mucositis in patients receiving high-dose melphalan, with or without total body irradiation, as conditioning for HSCT

Oral cancer

- Systemic zinc supplements administered orally may be of benefit to prevent oral mucositis in oral cancer patients receiving radiation therapy or chemoradiation

ESMO Mucositis Guidelines: Radiation therapy - 3

RECOMMENDATIONS FOR TREATMENT¹

Cancer of any kind

- Sucralfate mouthwash should not be used to treat oral mucositis in patients receiving radiation therapy

Head and neck cancer

- 0.2% morphine mouthwash may be effective to treat pain due to oral mucositis in patients receiving chemoradiation therapy

*ESMO 2015: “Expert opinion suggests that other treatments, such as **coating agents**, topical analgesic or anti-inflammatory agents, topical anesthetics, and alternative mouthwashes may be considered to treat stomatitis.”¹*

ESMO Mucositis Guidelines: Standard Dose Chemotherapy - 1

*RECOMMENDATIONS FOR PREVENTION*¹

Cancer of any kind

- **Sucralfate mouthwash** should not be used to prevent oral mucositis in patients receiving chemotherapy for cancer
- 30 min of **oral cryotherapy** can be used to prevent oral mucositis in patients receiving bolus 5-fluorouracil chemotherapy

ESMO Mucositis Guidelines: Standard Dose Chemotherapy - 2

RECOMMENDATIONS FOR TREATMENT ¹

Cancer of any kind

- 0.5% doxepin mouthwash may be effective to treat pain due to oral mucositis (for all cancer treatment modalities)
- Transdermal fentanyl may be effective to treat pain due to oral mucositis in patients receiving conventional and high-dose chemotherapy, with or without total body irradiation
- Due to inadequate and/or conflicting evidence, no guidelines for the prevention or treatment of oral mucositis were possible for the interventions of dental care, normal saline, sodium bicarbonate, mixed medication mouthwash, chlorhexidine in patients receiving chemotherapy

*ESMO 2015: "Expert opinion suggests that other treatments, such as **coating agents**, topical analgesic or anti-inflammatory agents, topical anesthetics, and alternative mouthwashes may be considered to treat stomatitis."*¹

ESMO Mucositis Guidelines: High Dose Chemotherapy - 1

*RECOMMENDATIONS FOR PREVENTION*¹

In favour of an intervention

- **Recombinant human keratinocyte growth factor-1 (KGF-1/palifermin)** can be used to prevent oral mucositis (60 µg/kg per day for 3 days before conditioning treatment and for 3 days after transplant) in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous stem cell transplantation, for a hematological malignancy
- **Low-level laser therapy** (wavelength at 650 nm, power of 40 mW, and each square cm treated with the required time to a tissue energy dose of 2 J/cm²), be used to prevent oral mucositis in patients receiving HSCT conditioned with high-dose chemotherapy, with or without total body irradiation
- **Oral cryotherapy** can be used to prevent oral mucositis in patients receiving high-dose melphalan, with or without total body irradiation, as conditioning for HSCT

ESMO Mucositis Guidelines: High Dose Chemotherapy - 2

RECOMMENDATIONS FOR PREVENTION ¹

Against an intervention

- **Iseganan antimicrobial mouthwash** should not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT, or in patients receiving radiation therapy or concomitant chemoradiation for head and neck cancer
- **Intravenous glutamine** should not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT
- **Granulocyte–macrophage colony-stimulating factor (GM-CSF) mouthwash** should not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, for autologous or allogeneic stem cell transplantation
- **Pilocarpine**, administered orally, should not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer, or in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT

UK Oral Mucositis Guidelines

- Indications for assessment and care of the oral cavity
- Risk classification following WHO scale



RISK	LOW	MODERATE	SEVERE
INTERVENTION	<ul style="list-style-type: none"> • Self-reporting of any oral changes • Good oral hygiene • Regular Fluid intake • Salt water mouthwash • Nutritional assessment and referral to a dietician where appropriate 	<p><i>Low intervention +:</i></p> <ul style="list-style-type: none"> • Increase frequency of saline mouthwashes • Ice chips • Oral rinses: Benzydamine 0.15% oral solution, Caphosol (4-10 times a day) • Consider mucosal protectants, including Episil, Gelclair, Oralife Gel, Mugard 	<p><i>Moderate intervention +:</i></p> <ul style="list-style-type: none"> • HSCT & H&N patients should be reviewed prior to commencing treatment • Low Level Laser Therapy • Anti-infective prophylaxis • Palifermin HSCT +/- TBI • Daily Vitamin B supplements for patients with alcohol misuse issues

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