



Associazione Italiana  
**Radioterapia Oncologica**  
Gruppo Interregionale  
Lazio/Abruzzo/Molise

# Le terapie di supporto in Radioterapia: **Verso una Guida Pratica**

**TOSSICITÀ NEI TRATTAMENTI DEL DISTRETTO TESTA-COLLO**

**MUCOSITE ORALE**

*Cenni di patogenesi e strumenti di valutazione*  
**D. Musio**

*Presidi di prevenzione e trattamento delle tossicità*  
**M. Trignani**



**SAPIENZA**  
UNIVERSITÀ DI ROMA

Roma, 4 Dicembre 2017



## *Definizione*

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La mucosite orale indotta da Radioterapia (**RIOM**) è una infiammazione della mucosa orale causata dalle radiazioni ionizzanti

Virtualmente tutti i pazienti sottoposti a radioterapia sviluppano mucosite a vario grado di severità

## *Definizione*

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**La RIOM è la più frequente ed una delle più importanti tossicità connesse con il trattamento radiante. E' causa di:**

- Difficoltà alla masticazione e deglutizione
- Dolore

Complicanze settiche

RT

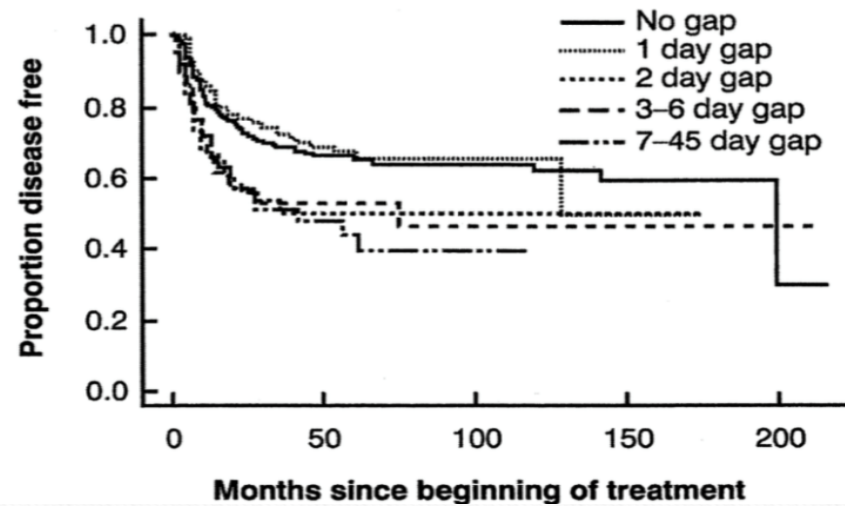
Perdita di peso

Interruzione del trattamento



## *Definizione*

- ❑ Aumento della spesa sanitaria per terapie di supporto
- ❑ Ritardo nel completamento della terapia prescritta
- ❑ Compromissione del risultato terapeutico



## *Patogenesi*

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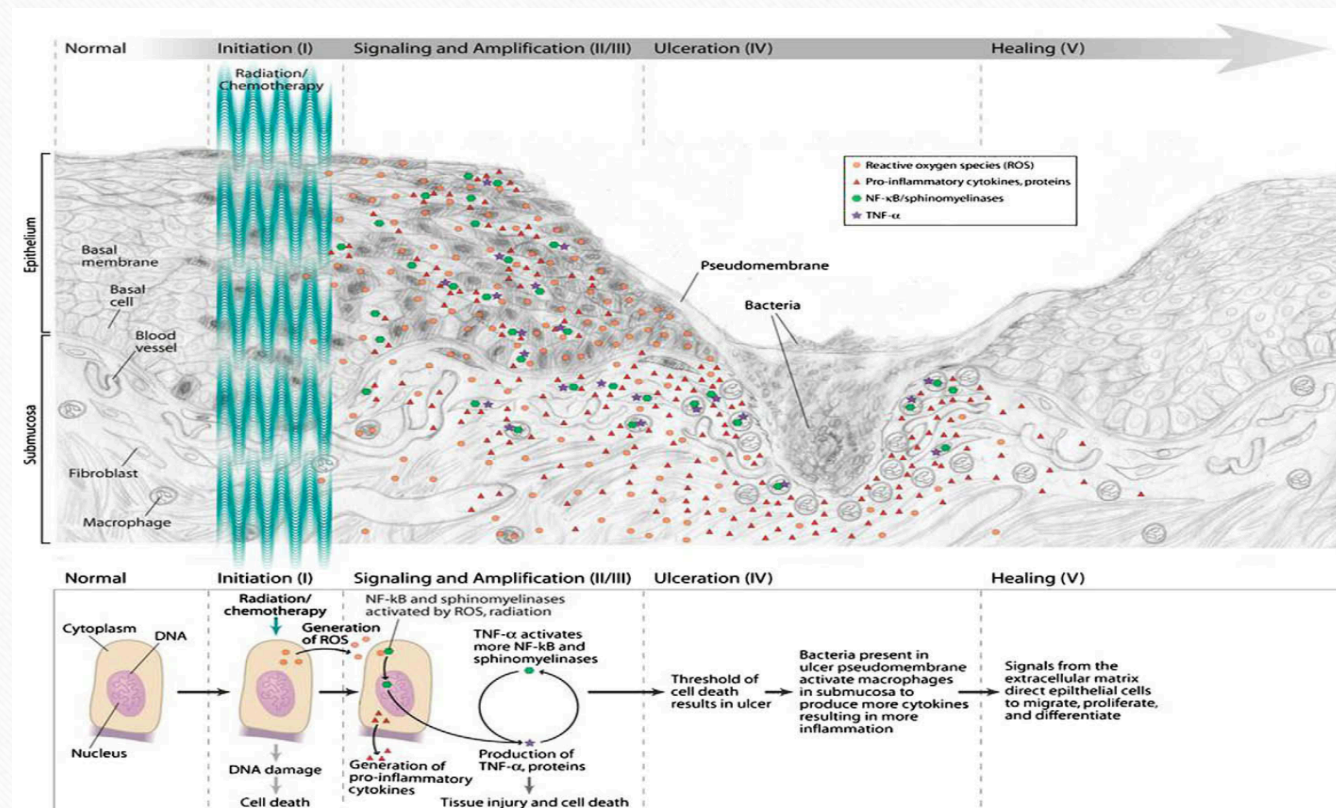
**L'eziopatogenesi della RIOM non è completamente nota**

**Meccanismo diretto:** interruzione del ciclo di rinnovamento cellulare ed apoptosi

**Meccanismo indiretto:** rilascio di mediatori dell'infiammazione, la perdita della protezione salivare, neutropenia trattamento correlata

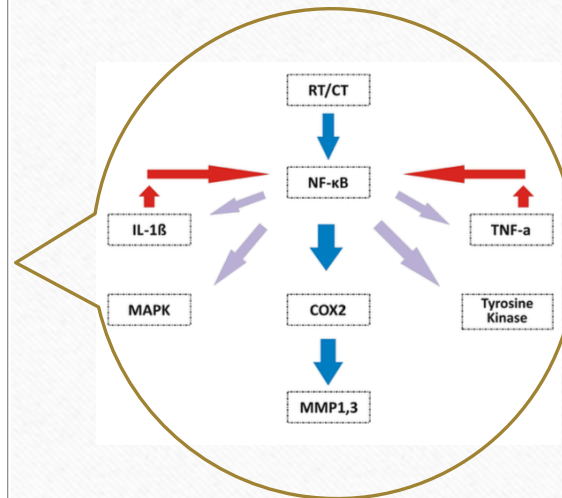
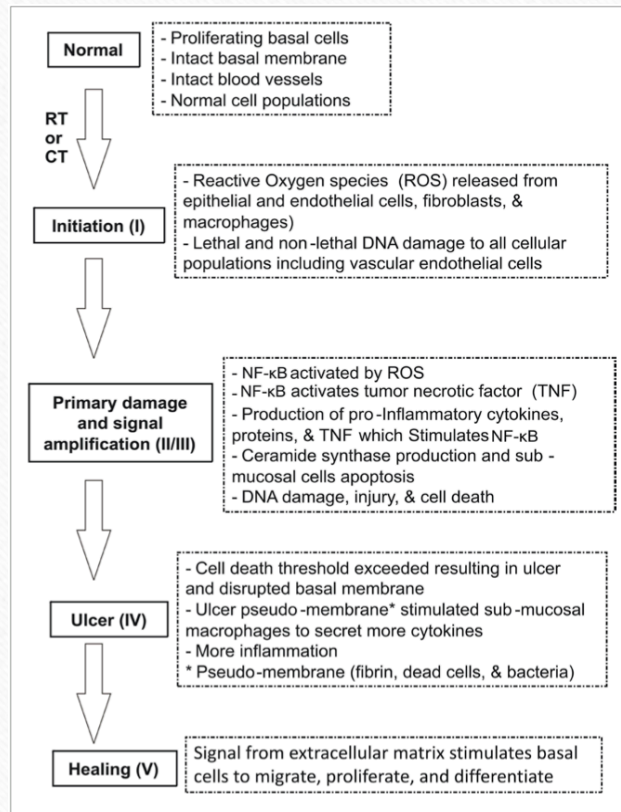
# Patogenesi

La patogenesi della RIOM non è perfettamente nota: teoria di Sonis



# Patogenesi

## La patogenesi della RIOM non è perfettamente nota: teoria di Sonis



### Signaling pathways coinvolti nello sviluppo della mucosite

- B-cells receptor signaling
- Cell cycle: G2/M DNA damage checkpoint receptor
- Death receptor signaling
- Glutamate receptor signaling
- Interleukin-6 signaling
- Integrin signaling
- Nuclear factor- $\kappa$ B signaling
- Nitrogen metabolism
- PI3K/AKT signaling
- P38 mitogen-activated protein kinase signaling
- SAPK/JNK signaling
- Toll-like receptor signaling
- Vascular endothelial growth factor signaling
- Wnt/B-catenin signaling

## *Patogenesi*

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La mucosite è una tossicità autolimitante che in genere si risolve in 2-4 settimane dalla fine della Radioterapia

In pazienti clinicamente compromessi può rivelarsi una condizione letale

**Sindrome da risposta Infiammatoria Sistemica**

SIRS





## *Decorso clinico*

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**Il decorso clinico della RIOM durante la RT con frazionamento convenzionale (2 Gy/die) è prevedibile**

Eritema associato a dolore lieve senza ulcerazioni della mucosa (>15 Gy)



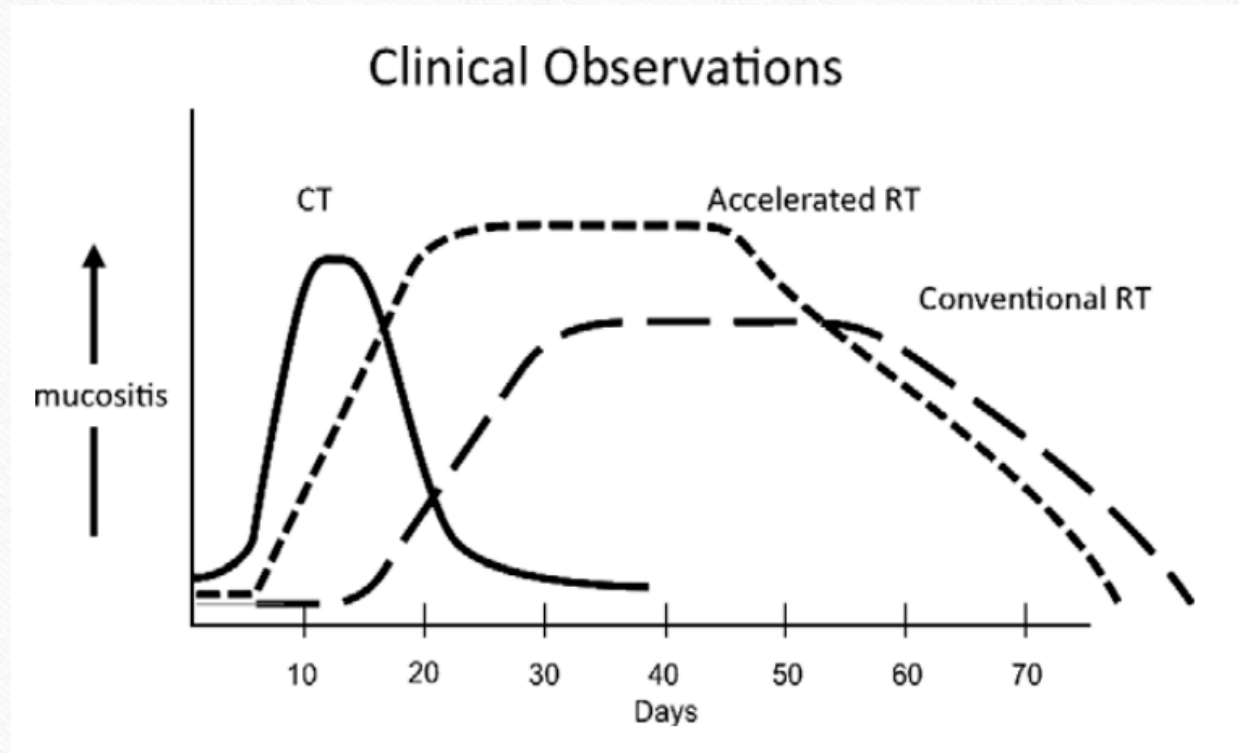
Atrofia dell'epitelio di rivestimento. Dolore lieve-moderato che necessita di terapia (16-22Gy)



Lesioni ulcerative irregolari spesso ricoperte da pseudomembrane a livello della mucosa di guance, labra, regioni ventrali e laterali della lingua. Il paziente si alimenta con difficoltà o non si alimentano (> 30 Gy,)

## *Decorso clinico*

**Variazione del decorso clinico per sola Chemioterapia o Radioterapia con frazionamento alterato/convenzionale**



## *Fattori di rischio*

**La prevalenza e la severità della RIOM dipendono da**

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**Fattori RT-correlati:** dose totale, frazionamento, volume irradiato, tecnica radioterapica, RT+CHT, target therapy.

**Fattori paziente-correlati:** sesso, età, igiene orale, abitudine al fumo, BMI, pregressa chemioterapia

## ***Fattori di rischio RT correlati***

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### **Frazionamento**

- ❑ Frazionamenti alterati (iperfrazionati o accelerati) correlano con aumento di incidenza e severità della RIOM

❖ DAHANCA 6&7Study (5 vs 6 fr/w )	➡	33% vs 53%
❖ Bentzen (conventional RT vs CHART )	➡	44% vs 75%
❖ SKLADOWSKI (5 vs 7 fr/w )	➡	53% vs 94%

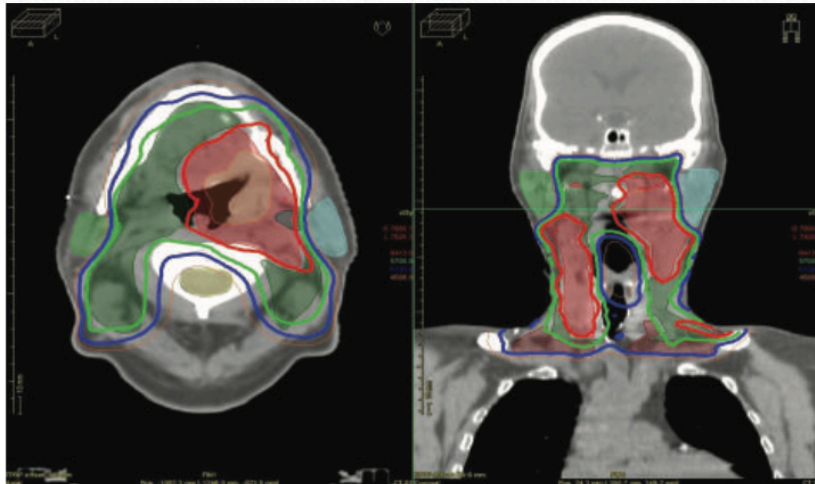
### **Radiochemioterapia**

- ❑ Aggiunta CHT aumenta incidenza severità della RIOM

❖ Mucosite severa ( G 3/4 )	➡	tra 30% - 84%
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# ***Fattori di rischio RT correlati***

## **Tecniche di radioterapia**



**Mucosa orale organo a rischio**

Dosi < 30-32 Gy ↓ RIOM

Dosi > 39 Gy ↑ RIOM

**IMRT:**

Vantaggio certo nel risparmio delle parotidi

Dati non univoci dell'impatto su incidenza e severità della RIOM

**Non sottodosare il target!!!**

## *Fattori di rischio pz. correlati*

Age	Increased risk in very young age (high cell turnover rate) and old age (slower healing rate)
Gender	Trends to increased risk in females
Oral health and hygiene	Maintaining good oral hygiene and oral health lowers radiation-induced oral mucositis (RIOM) risk
Salivary secretory function	Decreased saliva leads to increased RIOM risk
Genetic factors	Potential for high RIOM risk in certain individuals still to be identified
Body mass index	Delayed healing and increased breakdown in malnourished individuals <i>•Low body mass index (BMI &lt; 18.5)</i> <i>• Unintentional weight loss before therapy (i.e. &gt;5% weight loss over the prior month or &gt; 10% in the last 6 months),</i>
Renal function	Increased mucotoxicity linked with high serum creatinine level (poor renal function)
Smoking	Delays the healing
Previous cancer treatment	History of mucositis due to previous cancer treatment increases the risk

**Per tutti meccanismo di interazione chiaro e ben studiato.**

*Dati di letteratura non sufficienti per modificare comportamento clinico in base alla presenza di questi fattori di rischio*

# Diagnosi Differenziale

**Sospetto altre condizioni patologiche per mucosite complicata. Lesioni a livello di:**

- dorso linguale
- gengive
- palato duro

*epitelio squamoso cheratinizzante normalmente più resistente alla mucosite*

**TABLE 7 | Differential diagnosis of RIOM (20, 31).**

Disease/injury	Cause	Clinical presentation/lab findings	Severity	Treatment options
Oral mucositis	Chemotherapy and radiation therapy	Diffuse redness, ulcerations, and pain, particularly in areas where teeth abut tissue	Varies; in BMT setting up to 98% have grade 3/4	Palliative rinses, narcotics, palifermin in the BMT setting
Aphthous stomatitis	Etiology not identified	Single painful ulcer	Localized, but painful; usually grade 2	Topical
Herpetic mucositis	HSV1	Usually several spots; ulcerative	Usually grade 1–2	Acyclovir, valacyclovir, foscarnet
Oral thrush	Candida	Varies from painless to mild soreness; whitish plaques	Usually grade 0–1	Nystatin rinses; fluconazole and other azoles
Denture/oral trauma	Dentures	Common in elderly patients with loose-fitting dentures	Can limit calories	Repair, removal of dentures
Gangrenous stomatitis	Bacterial infections	Necrotic pseudomembranes	Rare, can be severe	Antibacterials that treat oral aerobes and anaerobes
Acute necrotizing stomatitis	Bacterial infections in immune-deficient patients	Pain, fever, necrotic, bloody ulcers	Grade 3/4	Control of infection

*BMT, bone marrow transplantation; RIOM, radiation-induced oral mucositis; HSV1, herpes simplex virus type 1.*

**Mandatorio eseguire esami culturali e/o citologici**

## *Scale di tossicità*

<b>Grade</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
WHO	None	Soreness ± erythema	Erythema, ulcers, and patient can swallow solid food	Ulcers with extensive erythema and patient cannot swallow solid food	mucositis to the extent that alimentation is not possible
RTOG	None	Erythema of the mucosa	Patchy reaction <1.5 cm, non-contiguous	Confluent reaction >1.5 cm, contiguous	Necrosis or deep ulceration, ±bleeding
WCCNR	Lesions: none Color: pink Bleeding: none	Lesions: 1-4 Color: slight red Bleeding: N/A	Lesions: >4 Color: moderate red Bleeding: spontaneous	Lesions: coalescing Color: very red Bleeding: spontaneous	N/A

*WHO, World Health Organization; RTOG, Radiation Therapy Oncology Group; WCCNR, Western Consortium for Cancer Nursing Research; OM, oral mucositis.*

Scala WHO: Descrittiva (aspetto), funzionale  
 Scala RTOG: Descrittiva (intensità della mucosite)  
 Scala WCCNR: Descrittiva



## Scale di tossicità

		<b>0</b>	<b>1</b>	<b>2</b>	Scala OMAS: Aspetti obiettivi e morfologici
	Eritema	Nessun cambiamento del colorito della mucosa	Aumento di intensità del colorito della mucosa	Mucosa di color sangue vivo	
<b>OMAS</b>		+			
	Ulcerazioni/pseudomembrane	Non lesioni	Superficie delle lesioni inferiori a 1 cm <sup>2</sup>	Superficie delle lesioni superiori a 1 cm <sup>2</sup> e pari o inferiori a 3 cm <sup>2</sup>	Superficie di lesione superiore a 3 cm <sup>2</sup>
=					

La valutazione comp sommando i punte pseudon

Scala CTCAE v4.3: sintomatica, funzionale

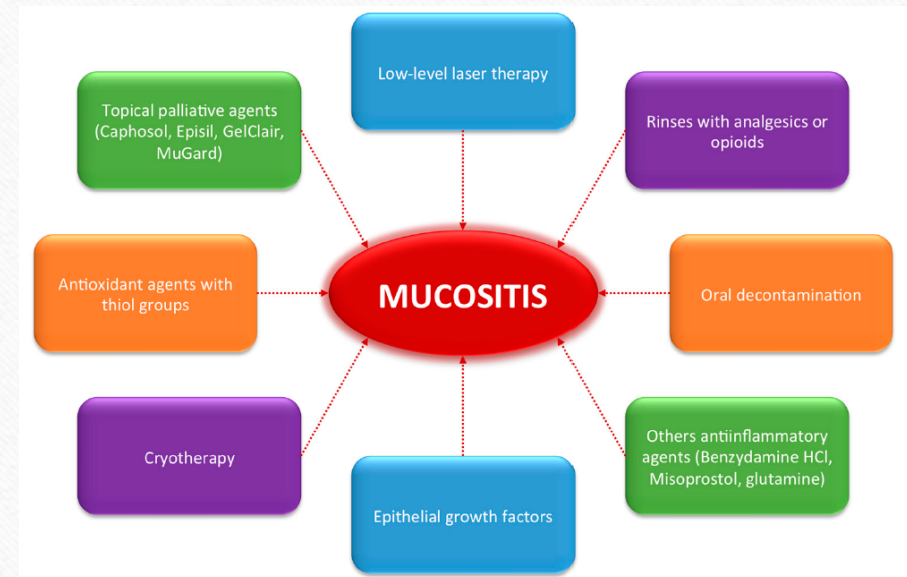
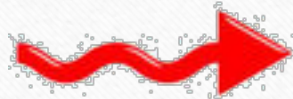
Disturbi gastrointestinali						48
Evento avverso	Grado 1	Grado 2	Grado 3	Grado 4	Grado 5	Cod. MedDRA
Mucosite del tenue	Asintomatica o sintomi lievi; intervento non indicato	Sintomatica; indicato intervento medico; limitazione delle attività quotidiane non di cura della persona (instrumental ADL, nota 1)	Dolore grave; interferisce con l'assunzione per os; nutrizione enterale, NPT o ospedalizzazione indicate; limitazione delle attività quotidiane di cura della persona (self care ADL, nota 2)	Conseguenze potenzialmente letali; è indicato un intervento urgente	Decesso	10065710
Mucosite orale	Asintomatica o sintomi lievi; intervento non indicato	Dolore moderato; non interferisce con l'assunzione orale; indicato cambiamento della dieta	Dolore grave; interferisce con l'assunzione orale	Conseguenze potenzialmente letali; è indicato un intervento urgente	Decesso	10028130

## Scale di tossicità

		WHO	RTOG	OMAS	NCI-CTCAE
<b>Gradi di mucosite e parametri di valutazione</b>	0	Nessun sintomo	Mucosa integra	Nessun cambiamento di colore della mucosa e nessuna lesione	/
	1	Dolore senza ulcere	Eritema della mucosa	Aumento intensità del colorito della mucosa e lesioni < 1cm <sup>2</sup>	Asintomatica o sintomi lievi, intervento non indicato
	2	Dolore alla mucosa con ulcere, alimentazione normale	Placche e aree di lesione < 1,5cm	Mucosa di color sangue vivo e lesioni > 1cm <sup>2</sup> e < 3cm <sup>2</sup>	Dolore moderato, non interferenza con l'assunzione orale di cibo, indicata modifica dietetica
	3	Il paziente riesce ad assumere solo dieta liquida	Aree di lesione confluenti > 1,5cm	Superficie delle lesioni > 3cm <sup>2</sup>	Dolore severo, interferenza con l'assunzione orale di cibo
	4	Il paziente non riesce né a mangiare né a bere	Necrosi o ulcerazioni profonde, +/- sanguinamento	/	Conseguenze che mettono a rischio la vita, intervento urgente indicato
	5	/	/	/	Morte

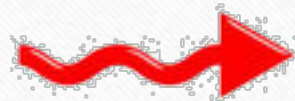
**Non vi è nessuna evidenza di superiorità di una scala rispetto ad un'altra**

# Background



# Background

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Critical Reviews in Oncology/Hematology 96 (2015) 372–384

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## Dysphagia in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus

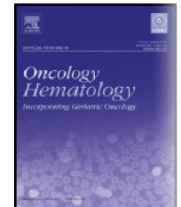
Antonio Schindler<sup>a</sup>, Nerina Denaro<sup>b</sup>, Elvio G. Russi<sup>c,\*</sup>, Nicole Pizzorni<sup>a</sup>, Paolo Bossi<sup>d</sup>,  
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Ester Orlandi<sup>i</sup>, Orietta Caspiani<sup>j</sup>, Michela Buglione<sup>k</sup>, Daniela Alterio<sup>l</sup>, Almalina Bacigalupo<sup>m</sup>,  
Vitaliana De Sanctis<sup>n</sup>, Giovanni Pa...  
Lisa Licitra<sup>e</sup>, Giuseppe Sanguineti

Critical Reviews in Oncology/Hematology 100 (2016) 147–166

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2015



2016



ELSEVIER

## Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements.

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Almalina Bacigalupo<sup>f</sup>, Carla Ida Ripamonti<sup>g</sup>, Michela Buglione<sup>h</sup>, Stefano Pergolizzi<sup>i</sup>,  
Johannes A. Langendjik<sup>j</sup>, Barbara Murphy<sup>k</sup>, Judith Raber-Durlacher<sup>l,m</sup>, Elvio G. Russi<sup>n,\*</sup>,  
Raiesh V. Lalla<sup>o</sup>





# DIAGNOSI E GESTIONE DELLE TOSSICITÀ IN RADIOTERAPIA ONCOLOGICA



Associazione  
Italiana

First Edition



ENDORSED  
7 APRIL 2017

## European Oral Care in Cancer Group Oral Care Guidance and Support

### Contents

- 1.0 • Introduction
- 2.0 • Assessment
- 3.0 • Care of the Oral Cavity
- 4.0 • Prevention of Oral Complications
- 5.0 • Treatment of Oral Complications
- 6.0 • Conclusion
- 7.0 • References
- 8.0 • Appendices

### Contributors

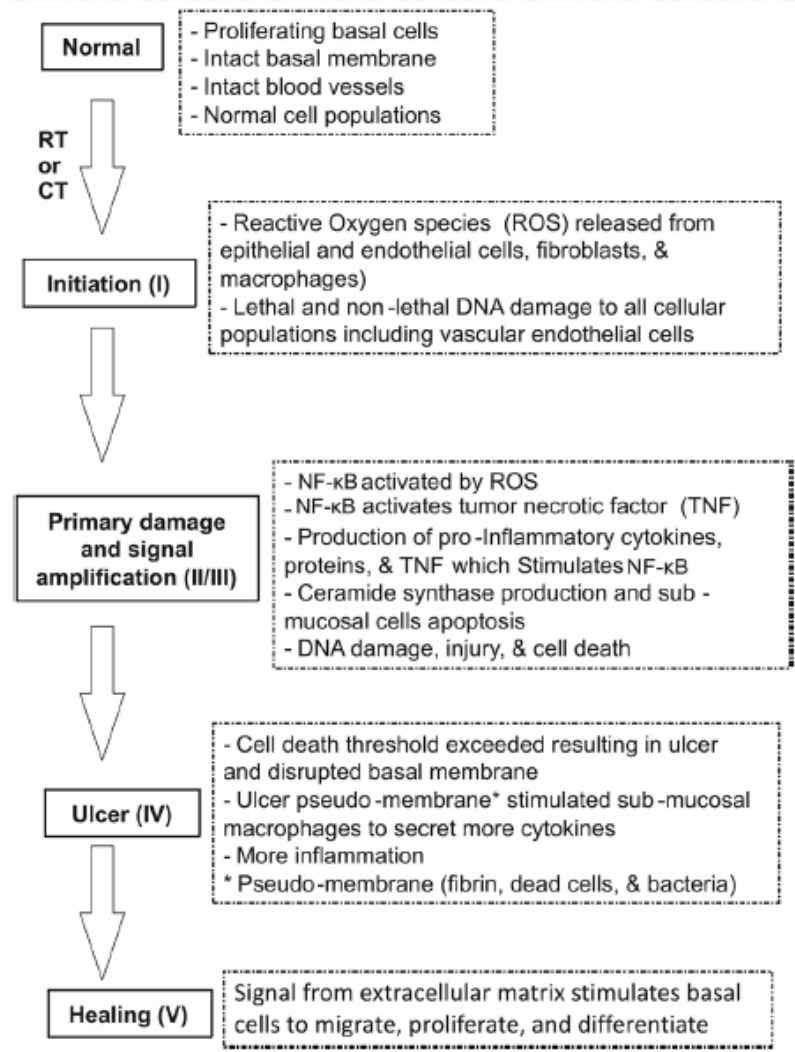
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**Task Group** S. Botti (IT), M. Kurstjens (NL), A. Margulies (CH),  
L. Orlando (IT), C. Potting (NL), D. Riesenbeck (DE), A. Sabbatini (IT),  
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**Supported by** P. Feyer (DE), A. Mank (NL), D. Kiprian (PL), M. Mravak  
Stipetic (HR)

### Expert reviewers

**Expert reviewer** N. Blijlevens (NL)



**FIGURE 1 | Pathobiology of oral mucositis (OM) (10).** Sonis has suggested five stages (phases) of OM injury induced by radiotherapy (RT) and/or chemotherapy (CT): initiation, signaling, amplification, ulceration, and healing. The pathogenesis of each phase is illustrated.

Radiation-induced oral mucositis side effects and sequels include:

- oral pain in 69% of patients;
- dysphagia in 56% of patients;
- weight loss of 3–7 kg, feeding tube insertion and hospitalization in 15% of patients.

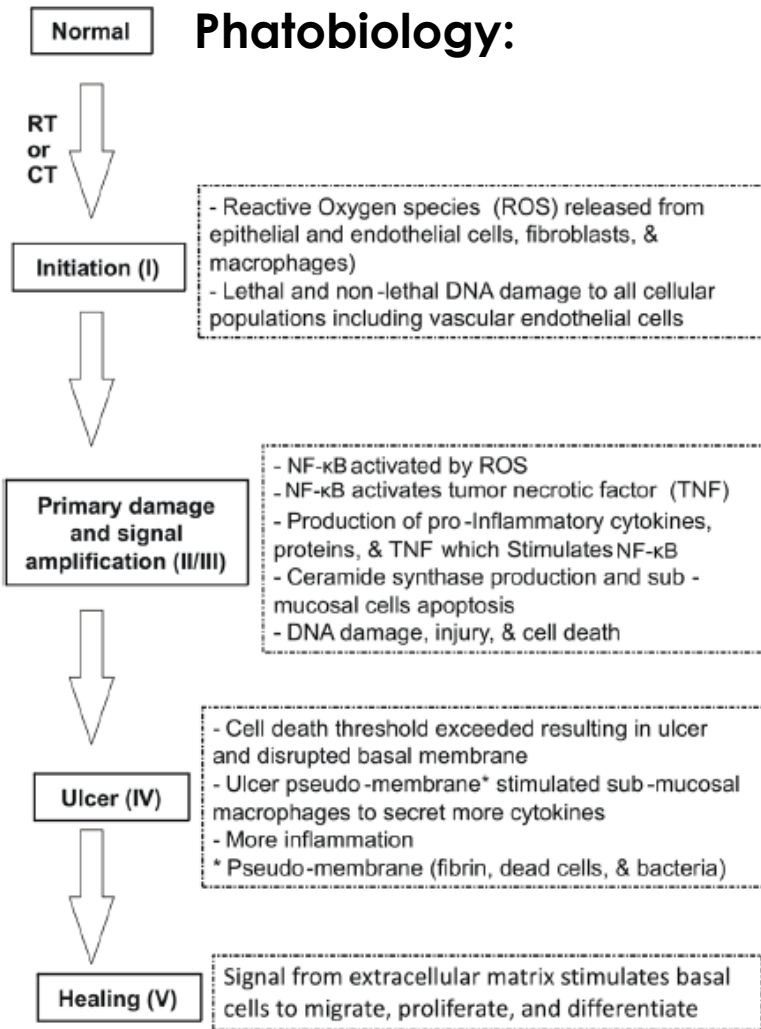
Modification or interruption of treatment in 11–16% of patients (1, 12, 16).

Maria OM, Eliopoulos N and Muanza T (2017) Radiation- Induced Oral Mucositis. *Front. Oncol.* 7:89.

## Oral appearance:



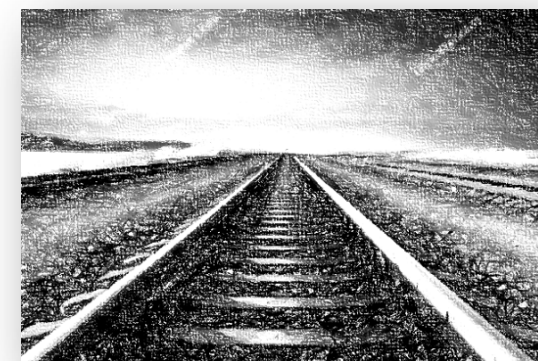
## Pathobiology:



**FIGURE 1 | Pathobiology of oral mucositis (OM) (10).** Sonis has suggested five stages (phases) of OM injury induced by radiotherapy (RT) and/or chemotherapy (CT): initiation, signaling, amplification, ulceration, and healing. The pathogenesis of each phase is illustrated.

## Mucositis effects:

- oral pain;
- dysphagia;
- weight loss;
- fatigue;
- anemia;
- anorexia;
- cachexia;
- neurocognitive alterations;
- depression.





# RIOM grading and scoring scales

TABLE 4 | Comparison of OM scoring scales (14, 21–23).

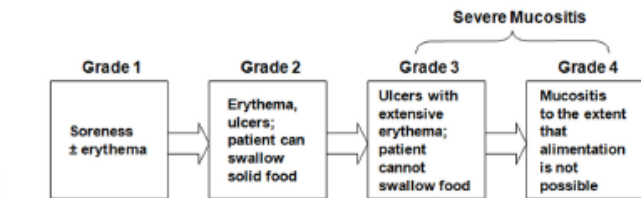
Grade	0	1	2	3	4
WHO	None	Soreness ± erythema	Erythema, ulcers, and patient can swallow solid food	Ulcers with extensive erythema and patient cannot swallow solid food	mucositis to the extent that alimentation is not possible
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WOCNR	Lesions: none Color: pink Bleeding: none	Lesions: 1–4 Color: slight red Bleeding: N/A	Lesions: >4 Color: moderate red Bleeding: spontaneous	Lesions: coalescing Color: very red Bleeding: spontaneous	N/A

TABLE 5 | Toxicity grading of oral mucositis (OM) according to World Health Organization (WHO) and National Cancer Institute Common Toxicity Criteria (NCI-CTC) criteria (2)\*.

Side effect	Grade 0 (none)	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (life threatening)
WHO oral mucositis (stomatitis)	None	Oral soreness, erythema	Oral erythema, ulcers, can eat solids	Oral ulcers, requires liquid diet only	Oral alimentation not possible
NCI-CTC chemotherapy-induced stomatitis/pharyngitis (oral/pharyngeal mucositis)	None	Painless ulcers, erythema, or mild soreness in the absence of lesions	Painful erythema, edema, or ulcers, but can eat or swallow	Painful erythema, edema, or ulcers requiring intravenous hydration	Severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation
NCI-CTC mucositis due to radiation	None	Erythema of the mucosa	Patchy pseudomembranous reaction (patches generally ≤1.5 cm in diameter and non-contiguous)	Confluent pseudomembranous reaction (contiguous patches generally > 1.5 cm in diameter)	Necrosis or deep ulceration; may include bleeding not induced by minor trauma or abrasion
NCI-CTC stomatitis/pharyngitis (oral/pharyngeal mucositis) for bone marrow transplantation studies	None	Painless ulcers, erythema, or mild soreness in the absence of lesions	Painful erythema, edema, or ulcers, but can swallow	Painful erythema, edema, or ulcers preventing swallowing or requiring hydration or parenteral (or enteral) nutritional support	Severe ulceration requiring prophylactic intubation or resulting in documented aspiration pneumonia

\*Republished with the permission of Dr. Christoph C. Zielinski.

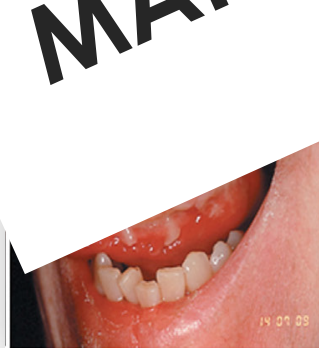
World Health Organization's Oral Toxicity Scale



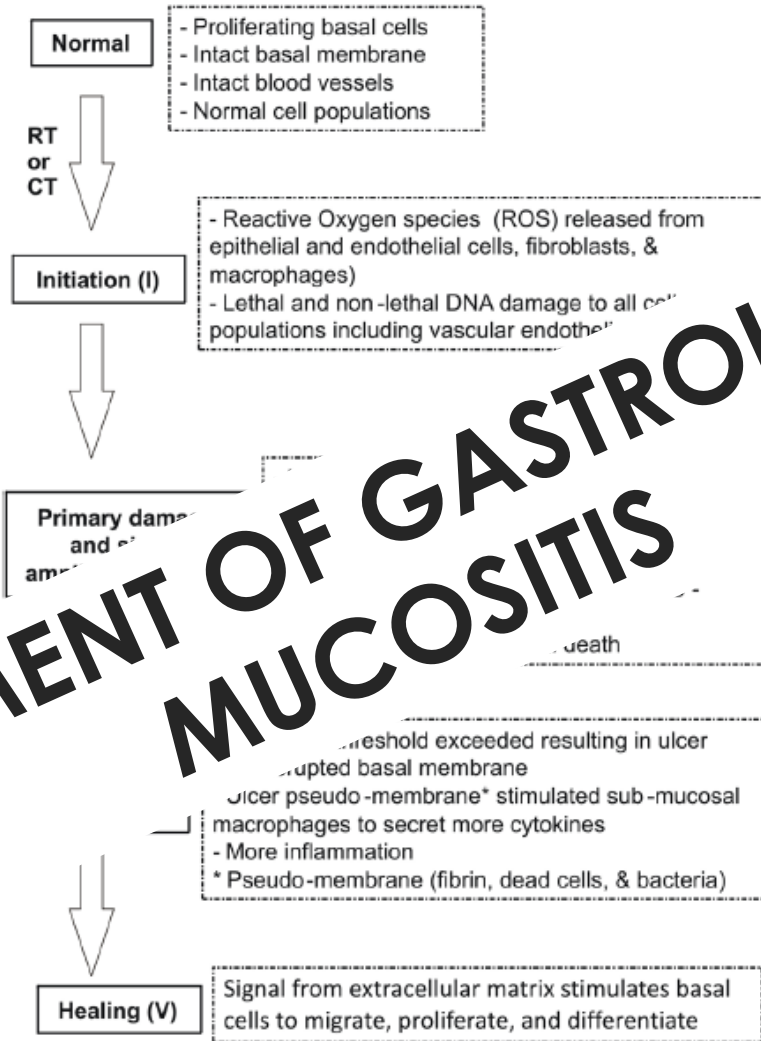
World Health Organization's Oral Toxicity Scale. Republished with the permission of Dr. Patrick Stiff, Loyola University Medical Center, IL, USA.

All these scoring scales are validated and are required in assessing RIOM and the therapeutic benefits of any new treatment of RIOM.

## Oral appearance:



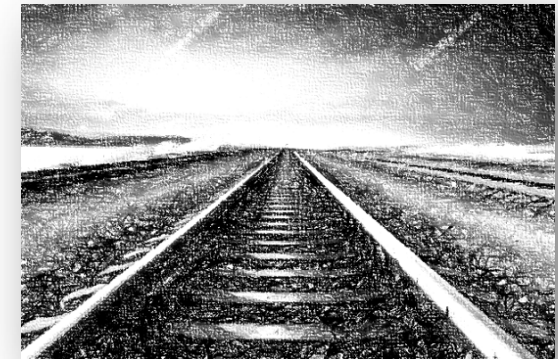
# MANAGEMENT OF GASTROINTESTINAL MUCOSITIS



**FIGURE 1 | Pathobiology of oral mucositis (OM) (10).** Sonis has suggested five stages (phases) of OM injury induced by radiotherapy (RT) and/or chemotherapy (CT): initiation, signaling, amplification, ulceration, and healing. The pathogenesis of each phase is illustrated.

## Mucositis effects:

- anemia;
- anorexia;
- cachexia;
- neurocognitive alterations;
- depression.



# MANAGEMENT OF GASTROINTESTINAL MUCOSITIS:

- PREVENTION
- TREATMENT

$$\text{M.C.D.}(48; 42; 66) =$$

48 2	42 2	66 2
24 2	21 3	33 3
12 2	7 7	11 11
6 2	1	1
3 3		
1		

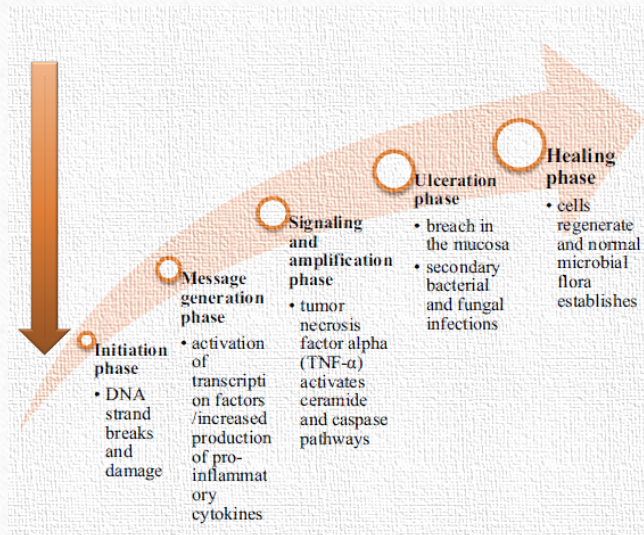
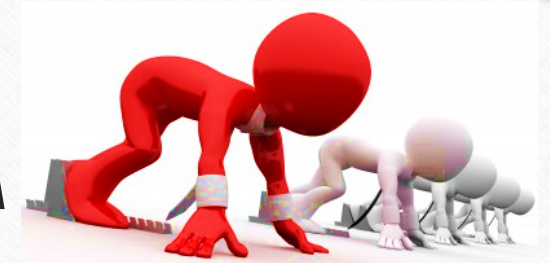
$48 = 2^4 \cdot 3$     $42 = 2 \cdot 3 \cdot 7$     $66 = 2 \cdot 3 \cdot 11$

prendiamo una sola volta quello con il minimo esponente, quindi il 2, senza esponenti.

Although the quality of **evidence derived from clinical studies** is somewhat **limited** (Worthington et al., 2011), MASCC and ESMO have developed guidelines which offer potential strategies for managing mucositis (Lalla et al., 2014).

Cinausero M, (2017) New Frontiers in the Pathobiology and Treatment of Cancer Regimen-Related Mucosal Injury. Front. Pharmacol. 8:354.

# PREVENTION of RIOM



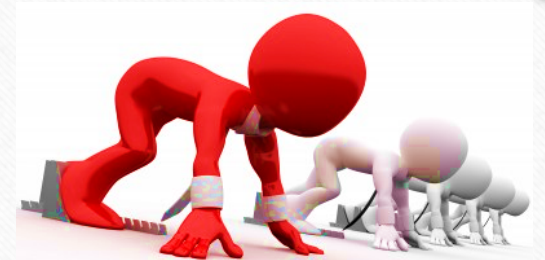
## ORAL HYGIENE

- Patient **education in oral hygiene techniques** is of utmost importance.
- Using a **soft toothbrush and floss or an interproximal brush**, and **fluoridated toothpaste** to be continued on a lifelong basis.
- The use of oral care products not containing alcohol without intense flavor is suggested.
- No superiority of one mouthwash over saline or bicarbonate rinses has been demonstrated.
- Oral prostheses should be kept clean with an antimicrobial solution and their use should be discouraged during night time and in presence of overt oral mucositis.

## DENTAL EXAMINATION

- The control of the pre-existing periodontal and dental disease and a pretreatment professional dental cleaning may allow a better control of RIOM.
- It is recommended that a qualified oral health care team be integrated in a multidisciplinary approach on the basis of well-defined protocols from pre-treatment phase, during treatment, and follow-up

# PREVENTION of RIOM



**Oral care has been often recommended to reduce the incidence and severity of OM.**

Recommendations regarding oral care based on systematic reviews are available and have been regularly updated (Eilers and Million, 2011; Lalla et al., 2008; Rubenstein et al., 2004; Bensinger et al., 2008; Keefe et al., 2007; Niscola et al., 2012; Lalla et al., 2014, Keefe et al., 2007), although the evidence for the use of oral care protocols is weak and the amount of data is limited.

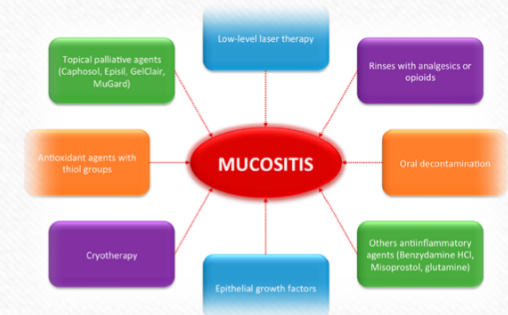


However, considering the lack of evidence on the choice of one product over another, normal saline and sodium bicarbonate mouth washes or oral mouthwashes not containing alcohol and without intense flavor are considered helpful for oral care

# PREVENTION of RIOM: OFFER



1. Barrier agents such as sucralfate, GelClair®, MuGard® and Mucotrol®  
Allopurinol gel
2. Chlorhexidine digluconate mouth rinse
3. Povidone-iodine
4. Triclosan mouth washes
5. Iseganan mouth washes
6. Aloe vera
7. Granulocyte macrophage colony-stimulating factor
8. Pure natural honey
9. Misoprostol and Prostaglandin E2
10. Antibiotic + antifungal pastilles (containing polymixin, tobramycin and amphotericin orbacitracin, clotrimoxazole and gentamicine)
11. Benzydamine mouthwashes
12. Cryotherapy
13. Amifostine
14. Glutamine



# PREVENTION of RIOM



1

As a minimum to keep the mouth clean, bland gargles and rinses with water, normal saline (0.9% NaCl) or saltwater are recommended at least four times a day (Level-III)

2

Mucosal protectants/barrier rinses licensed to use as preventative to reduce pain: Mugard® (Level-I)

3

Consider oral rinses (Benzydamine®) (Level-I)

4

Low Level Laser therapy (Level-III)

**High Risk: Patients with previous moderate or severe oral problems, high risk agents, high dose chemotherapy and/or radiation prior to stem cell transplantation, radical radiation to the head and neck**

# TREATMENT of RIOM



## Radiation-Induced Oral Mucositis

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**No single agent has been approved by the US-FDA for the treatment of RIOM.** Symptoms reduction and complications prevention of RIOM, including nutritional support, pain control, prophylaxis, and/or treatment of secondary infections, are considered the main cornerstone in the management of RIOM



# TREATMENT of RIOM

2<sup>nd</sup> week

- Grade I
- Erythema



TOP 3

# TREATMENT of RIOM: G1

1

Benzydamine mouthwash to prevent oral mucositis without concomitant chemotherapy (Level-I)

2

Mucosal protectants/barrier rinses licensed to use as reduce pain: Mugard® (Level-I)

3

Gargles and rinses with water, normal saline (0.9% NaCl) or saltwater are recommended at least four times a day (Level-III)

4

Low Level Laser therapy

Low level laser therapy (wavelength around 632.8 nm) to prevent oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, vigilance remains necessary and no recommendation is possible. (Level-III)

# TREATMENT of RIOM

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3<sup>rd</sup> week

- Grade II
- Focal areas of desquamation



TOP 3

# TREATMENT of RIOM: G2

NO PREVENTIVE ANTIMICOTIC, ANTIBIOTIC  
ANTIVIRAL THERAPIES

4

Low Level Laser therapy

No recommendation is possible (Level-III)

# TREATMENT of RIOM

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# TREATMENT of RIOM: G3-G4

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## Severe Mucositis/Oral Complications

- increase oral rinses and care

There is insufficient evidence that many products reduce the severity of mucositis but comfort can be provided for the patient.

- increase pain medication following patient needs

- increase nutritional support

pain medication following the WHO recommendations where applicable

[http://www.who.int/medicines/areas/quality\\_safety/guide\\_on\\_pain/en/](http://www.who.int/medicines/areas/quality_safety/guide_on_pain/en/)

TOP 3

# TREATMENT of RIOM: G3-G4

1

Benzydamine mouthwash to prevent oral mucositis without concomitant chemotherapy  
(Level-I)

2

INCREASE ↑

Mucosal protectants/barrier rinses licensed to use as reduce pain: Mugard® (Level-I)  
**Gelclair® EOCC guidelines**  
(Level-III)

3

INCREASE ↑

2 % morphine mouthwash (Level-III)  
**Oral, transdermic, iv pain medication (sec WHO)**  
**paracetamolo, codeina**

Introduce/Increase nutritional support

No recommendation can be given about the use of GM-CSF

**TREATMENT OF RIOM SPECIFIC COMPLICANCE**

# TREATMENT RIOM SPECIFIC COMPLICANCE

1

BLEENDING

4

INFECTION



# TREATMENT RIOM SPECIFIC COMPLICANCE

1

## BLEENDING

- Continue mouth gargling.
- Gargling/swishing with tranexamic acid (TRANEX 500mg) as a mouthwash.

- Antimicotic Loramyc (Miconazolo)
- Antibiotic
- Antiviral

# Cost of RIOM

RIOM treatment adds an economic cost that was estimated to increase up to 17,000.00 USD per patient treated for head and neck cancers.



## Evaluating the Supportive Care Costs of Severe Radiochemotherapy-Induced Mucositis and Pharyngitis

TABLE 2  
Median Direct Costs for the Treatment of Patients With Head and Neck or Nonsmall Cell Lung Cancer According to the Presence/Absence of Severe Mucositis/Pharyngitis

Sources of Direct Medical Cost	Median Cost (Range), \$								
	Patients With HNC, n=99			Patients With NSCLC, n=40			All Patients, n=139		
	Without Mucositis/Pharyngitis, N=29	With Mucositis/Pharyngitis, N=70	Incremental Cost for Patients With Mucositis/Pharyngitis, n=99	Without Mucositis/Pharyngitis, n=25	With Mucositis/Pharyngitis, n=15	Incremental Cost for Patients With Mucositis/Pharyngitis, n=40	Without Mucositis/Pharyngitis, n=54	With Mucositis/Pharyngitis, n=85	Incremental Cost for Patients With Mucositis/Pharyngitis, n=139
Inpatient hospitalization	7000 (0-28,000)	21,000 (3850-42,000)	14,000*	7000 (2800-19,600)	18,200 (0-37,800)	11,200	7000 (0-23,100)	19,600 (3500-40,600)	12,600*
Tests and procedures	924 (61-2833)	3150 (887-10,139)	2226*	3756 (790-7022)	4536 (2623-11,022)	780	1094 (685-5111)	3419 (1136-10,195)	2325*
Imaging procedures	3510 (2157-6746)	5602 (3392-13,616)	2092*	10,102 (4807-16,031)	14,248 (8138-23,974)	4146	5900 (2678-10,225)	7 019 (3954-14,817)	1119
Clinic visits	960 (660-1530)	1170 (885-1920)	510	1320 (730-2880)	2280 (1200-3510)	960	1080 (660-1980)	1500 (1020-2100)	420
Mucositis/pharyngitis-related medication†	105 (14-299)	196 (77-432)	90	11 (0-134)	14 (0-205)	3	84 (2-195)	195 (53-306)	110*
Laboratory diagnostic tests	463 (221-715)	553 (314-887)	90	517 (262-971)	725 (451-1028)	208	494 (239-864)	595 (342-908)	101
Total	18,512 (7312-39,030)	35,756 (17,952-70,210)	17,244*	21,187 (14,787-62,108)	46,246 (28,565-68,700)	25,060	20,798 (9898-48,596)	39,313 (18,961-69,290)‡	18,515*

Nonzee N, Cancer 2008

# Grazie dell'attenzione

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Cost of RIOM  
Treatment?



Cost of RIOM  
sequels treatment?