

Brazilian guidelines for oral graft-*versus*-host disease: Recommendations from the Brazilian Society of Bone Marrow Transplantation

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ABSTRACT

Oral chronic graft-versus-host disease (cGVHD) is a frequent and clinically heterogeneous manifestation after allogeneic hematopoietic cell transplantation (HCT). In addition to lichenoid lesions, erythema, and ulceration, the disease can affect the salivary glands, other tissues, quality of life, and is associated with a risk of oral carcinoma. Then, the objective of this study was to update the Brazilian consensus of the Brazilian Society of Bone Marrow Transplantation (Sociedade Brasileira de Transplante de Medula Óssea—SBTMO) on oral cGVHD (2021). A narrative review was conducted including publications from 2021 onward. Evidence and strength of recommendation was graded according to the 2009 Oxford Center for Evidence-Based Medicine. The final recommendations were defined by a panel of SBTMO experts in cGVHD. The most directly applicable evidence supports the use of topical corticosteroids for symptomatic mucosal disease. Photobiomodulation, intraoral ultraviolet B phototherapy, barrier agents, and platelet lysate are promising local options, but supported mainly by small, uncontrolled studies. Ruxolitinib and belumosudil show signals of oral response in patients with refractory disease, but mouth-specific evidence remains observational, secondary or organ-specific, or partially extrapolated; both should be considered conditional second-line or salvage systemic options. Prolonged oral surveillance is necessary due to the risk of secondary oral cancer and other complications. This Brazilian consensus update supports a multidimensional assessment of oral cGVHD and favors local therapy for localized disease whenever feasible. Systemic therapies should be reserved for selected refractory or multiorgan cases, while prevention of oral complications and long-term surveillance remain integral to care.

Key words: Graft vs Host Disease. Mouth. Transplantation, Homologous. Saliva. Xerostomia. Therapeutics. Mouth Neoplasms.

INTRODUCTION

Oral chronic graft-*versus*-host disease (cGVHD) results from a complex interaction between alloreactivity, persistent inflammation, epithelial injury, salivary gland dysfunction, fibrosis, and alterations in local immunity. Clinical manifestations can include lichenoid/reticular lesions, erythema, atrophy, ulceration, superficial

mucocoeles, hyposalivation, xerostomia, sclerosis, and trismus^{1–4}. The mouth is a sentinel organ of cGVHD, but also a site where the disease may remain underdiagnosed when symptoms are attributed solely to transplant effects, medications, or infection.

The frequency of oral involvement varies according to the population, diagnostic criteria, time post-transplant, and assessment method. Clinical reviews report oral manifestations in a substantial proportion of patients with cGVHD, with repercussions on pain, eating, hygiene, speech, swallowing, and social life^{1,4}. In a Brazilian study, clinical presentation was heterogeneous, reinforcing the need for systematic examination and differentiation between active GVHD, infection, trauma, and potentially malignant lesions⁵.

Saliva should be considered an independent clinical domain. Loss of flow and qualitative alterations in saliva can compromise lubrication, buffering, remineralization, antimicrobial protection, and mucosal integrity. Consequently, xerostomia and hyposalivation can increase the risk of caries, periodontitis, candidiasis, pain, burning, difficulty chewing and swallowing, and altered taste. Recent studies also suggest that oral inflammation and dysbiosis may contribute to the maintenance or exacerbation of cGVHD, although the microbiota cannot be used as a routine clinical biomarker yet^{6,7}.

The objective of this consensus was to provide a practical and updated framework for professionals involved in the care of people undergoing allogeneic hematopoietic cell transplantation (allo-HCT), with a focus on oral cGVHD and its complications.

METHODS

Search strategy and selection

The search was organized into three dimensions: diagnosis/pathophysiology/epidemiology; treatment; and complications. PubMed, Google Scholar, Scientific Electronic Library Online (SciELO), Web of Science, and ScienceDirect were consulted, combining terms related to cGVHD, hematopoietic cell transplantation (HCT), mouth, oral mucosa, saliva, diagnosis, histopathology, treatment, and complications. References from the previous Brazilian Society of Bone Marrow Transplantation (Sociedade Brasileira de Transplante de Medula Óssea—SBTMO) consensus⁸ and the update article published for the international transplant society were also examined.

Publications between 2021 and 2026 were considered eligible. Inclusion criteria required the oral mucosa, oral cavity, salivary glands, or an oral complication to be a primary focus or a defined outcome. Clinical trials, cohort and cross-sectional studies, case series, systematic reviews, consensus statements, and narrative reviews were considered eligible if they contributed to the assessment of diagnostic criteria, safety, epidemiology, treatment, or monitoring. Publications that did not address oral cGVHD, lacked clinically relevant contributions, were not available in sufficient full text for evaluation, or were published in languages not covered by the protocol were excluded.

Data extraction and critical appraisal

We extracted design, population, definition of oral cGVHD, intervention or exposure, comparator, outcomes, instruments used, quantitative results, follow-up, adverse events, limitations, and applicability. For systemic therapies, overall cGVHD response and mouth-specific response were recorded separately. In studies of complications, we distinguished associations in allo-HCT survivors from evidence directly attributable to oral cGVHD.

Levels of evidence and grades of recommendation

The 2009 Oxford Center for Evidence-Based Medicine (OCEBM) levels of evidence were used to classify study designs⁹. Recommendations were downgraded when oral specificity was low, a comparator was absent, cointerventions were present, sample sizes were small, outcomes were not validated, or findings were extrapolated from systemic cGVHD. Thus, a high-level systemic study was not automatically interpreted as high-level evidence for the oral mucosa (Table 1).

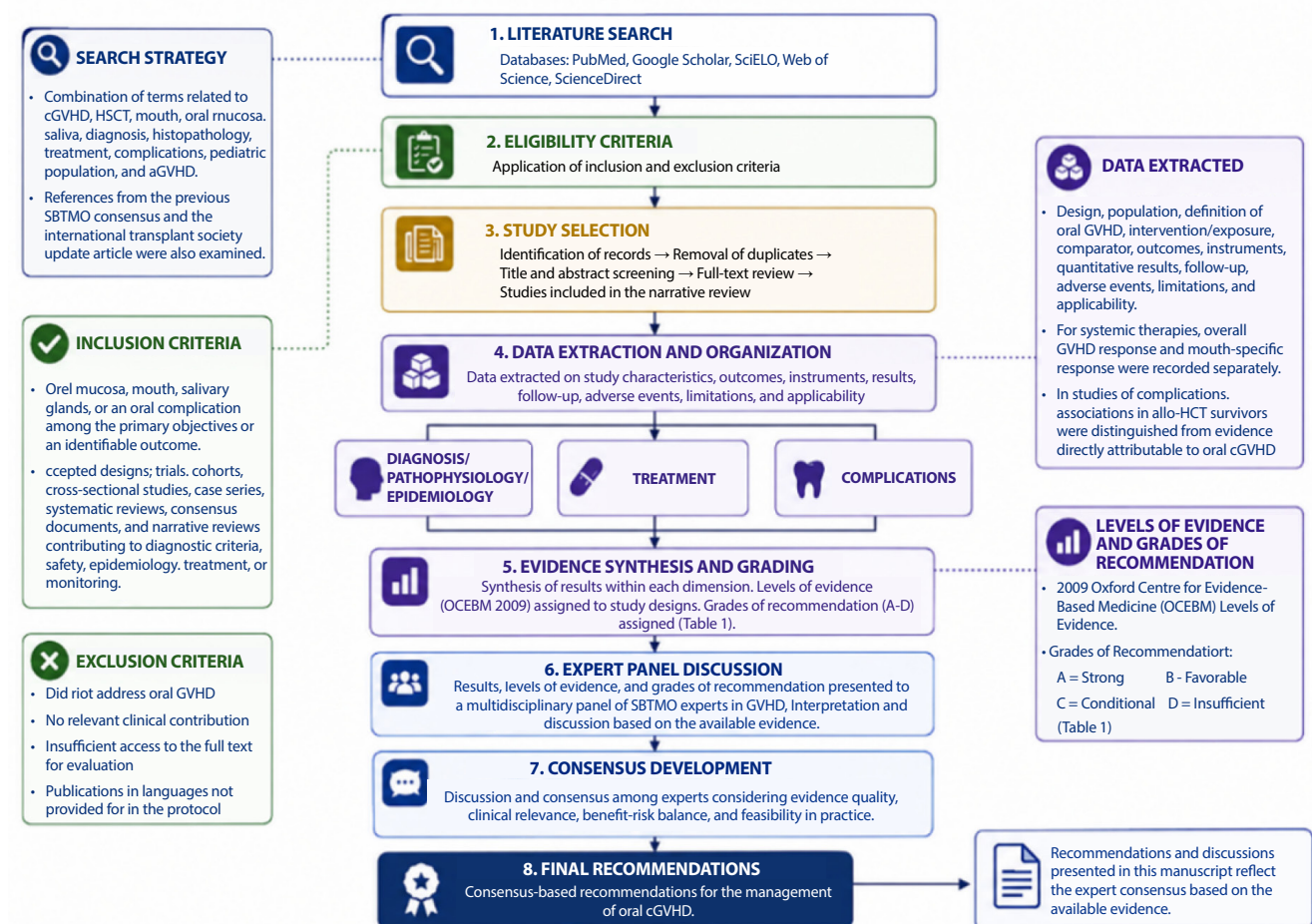
Table 1. Grades of recommendation and their interpretation used in this consensus.

Grade	Interpretation used in the consensus
A	Strong recommendation, supported by consistent evidence directly applicable to oral chronic graft-versus-host disease, with likely benefit outweighing risk. No definitive grade A was assigned to interventions in the current <i>corpus</i> .
B	Favorable or reasonable recommendation, with moderate evidence, some heterogeneity, or limited extrapolation.
C	Conditional, adjunctive, or salvage option, supported by small, observational, uncontrolled studies or good-practice consensus.
D	Insufficient, indirect, or experimental evidence; use only in the context of research, expert decision, or proposed monitoring.

Source: Adapted from Oxford Centre for Evidence-Based Medicine⁹.

DISCUSSION AND FINAL RECOMMENDATIONS

Data regarding study designs, results, levels of evidence, and grades of recommendation were presented to and discussed by a multidisciplinary panel of SBTMO experts in cGVHD. The recommendations and discussion presented in this manuscript reflect the expert consensus based on the available evidence. Figure 1 presents the methodological flowchart of the study.



cGVHD: chronic graft-versus-host disease; HSCT: hematopoietic stem cell transplantation; SBTMO: Brazilian Society of Bone Marrow Transplantation (Sociedade Brasileira de Transplante de Medula Óssea); SciELO: Scientific Electronic Library Online; OCEBM: Oxford Center for Evidence-Based Medicine; allo-HCT: allogeneic hematopoietic cell transplantation. Source: Elaborated by the authors with the assistance of generative artificial intelligence (ChatGPT, OpenAI) for visual design and layout.

The scientific content was defined and reviewed by the authors.

Figure 1. Methodological flowchart.

RESULTS

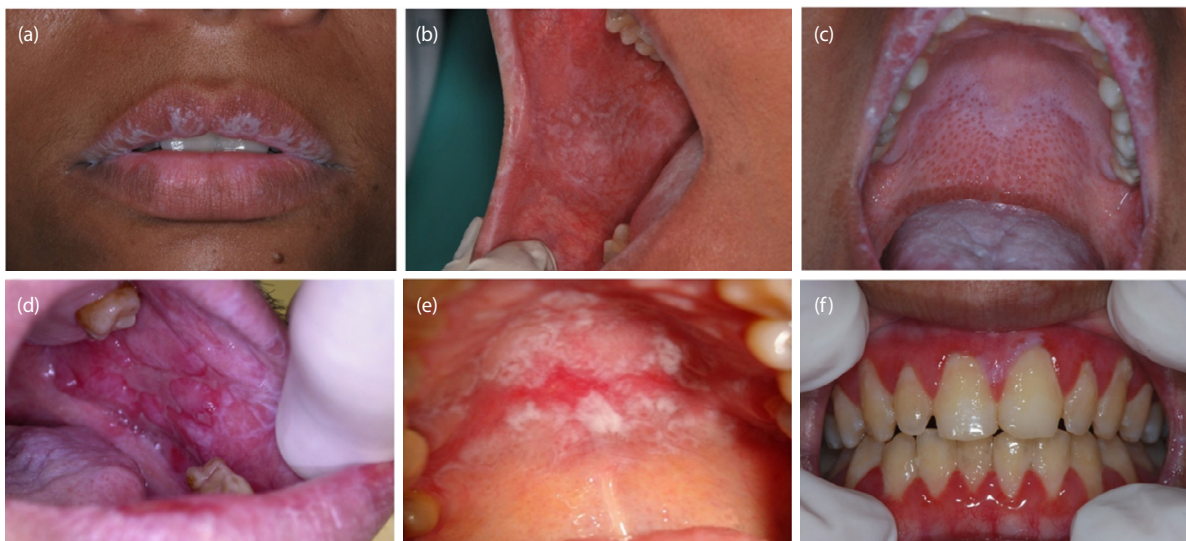
Clinical manifestations and diagnosis

The epidemiology of oral cGVHD is influenced by age, underlying disease, donor type, prophylaxis, conditioning regimen, time since transplant, National Institutes of Health (NIH) criteria, and assessment method. Variability in denominators and definitions makes it difficult to compare studies and establish a single prevalence.

The most characteristic oral manifestation is the lichenoid or reticular pattern, which may affect the buccal mucosa, tongue, lips, palate, gingiva, and other surfaces. Erythema, atrophy, ulceration, superficial mucocoeles, sensitivity, and dryness may coexist. No single manifestation should be interpreted outside the clinical context; ulcers, erythema, and xerostomia may also result from other diseases, or other treatment related complications^{1,5,10}.

The NIH/oral mucosa rating scale (OMRS)^{11,12} is useful to track activity and response but should not replace the assessment of symptoms and function. It is important to keep in mind that a low mucosal score does not exclude salivary dysfunction, dietary restrictions, impaired quality of life, or an increased risk of dental caries^{13,14}.

Biopsy is not required for every typical presentation, particularly in cases with characteristic lichenoid features, but should be considered when the pattern is atypical, unilateral, persistent, progressive, indurated, exophytic, verrucous, erythroplastic, ulcerated, or unresponsive to adequate treatment. Lesions that change or persist despite cGVHD control should not be automatically classified as cGVHD. Minor salivary gland biopsy may complement mucosal evaluation in atypical or diagnostically uncertain cases; a standardized histopathologic grading system for post-transplant salivary gland changes has recently been proposed¹⁵. The main differential diagnoses include infections, malignant lesions, and premalignant lesions. Figure 2 presents clinical manifestations of oral cGVHD.



Source: Elaborated by the authors.

Figure 2. Clinical manifestations of oral chronic graft-versus-host disease. (a and b) Reticular/lichenoid white striae on the lip and buccal mucosa-diagnostic lesions; (c) multiple mucocoeles on the soft palate and an area with a leukoplakic plaque; (d) ulcerated lesion on the buccal mucosa covered by an adherent pseudomembrane with white reticular/ lichenoid striae; (e) leukoplakic plaque with an erythematous area in palate; (f) erythema and edema in gingiva.

Saliva, microbiota, and pathophysiology

Salivary dysfunction can occur without oral mucosal involvement and may represent glandular damage, medication effects, dehydration, systemic disease, or a combination of these factors. Subjective xerostomia and objective hyposalivation are not equivalent and should be measured separately. Unstimulated and

stimulated salivary flow, standardized collection over a defined time, xerostomia inventory, medication recording, and assessment of mucosal wetness can improve phenotype characterization.

The oral microbiota can influence local and systemic inflammation. Experimental and observational data suggest that dysbiosis may accompany or exacerbate inflammation and cGVHD, but there are no sufficiently validated clinical thresholds, collection methods, or microbiota-based interventions for routine use^{6,7,16}. The microbiota should be presented as an axis for translational research.

Histopathological examination of the salivary glands reveals a periductal lymphocytic infiltrate with infiltration and damage to intralobular ducts, fibroplasia in the periductal stroma, and mixed lymphocytic and plasmacytic inflammation with destruction of acinar tissue^{10,12}.

Therapeutic options

General principles

Treatment should be selected according to the extent of oral disease, symptoms, functional impairment, risk of complications, involvement of other organs, progression, response to prior therapies, infection, cytopenias, and patient preferences^{1,10,17}. Exclusively oral and localized disease should, when possible, be treated locally to reduce unnecessary systemic exposure^{10,17}. Topical treatment may allow patients to remain off systemic immunosuppression, reduce systemic treatment intensity, or complement systemic therapy^{10,17}.

Active, progressive, extensive, disabling multiorgan disease, associated with nutritional compromise or refractory after adequate use of local therapy, requires multidisciplinary discussion. The decision to start systemic immunosuppression should not be based solely on a mucosal score or a single salivary flow value.

Topical corticosteroids and tacrolimus

The systematic review by Haas and Cruz-Pamplona¹⁷ pooled five oral clinical studies and found signals of benefit for budesonide, clobetasol, and dexamethasone, although with small samples, heterogeneous formulations, short follow-up, and methodological limitations. In a randomized double-blind trial, clobetasol produced greater clinical and symptomatic improvement than dexamethasone¹⁸. Dexamethasone also showed clinically meaningful first-line activity in a randomized phase II study, whereas the topical tacrolimus arm was terminated early for lack of activity¹⁹. Budesonide improved oral cGVHD in an open randomized multicenter phase II pilot study²⁰. The overall formal classification is baseline 1a; the practical recommendation is grade B, because certainty and applicability are lower than study design alone would suggest.

Dexamethasone, budesonide, and clobetasol can be used as first-line options for symptomatic mucosal disease. Choice should consider extent, potency, contact time, compounding feasibility, adherence, and tolerability. Mouthrinse formulations should be preferred when multiple oral sites are affected, whereas gels, ointments, or Orabase formulations should be reserved for localized lesions and/or lesions refractory to mouthrinse therapy.

Patients should be counseled on technique, contact time, and to avoid eating or drinking immediately after application. The optimal contact time for mouthrinse formulations has been reported to range from 3 to 5 minutes, with a volume of approximately 5 mL. In this context, contact time appears to be more important than the volume used. Prolonged use requires periodic reassessment, inspection for candidiasis, and tapering to the lowest intensity capable of maintaining control. Antifungal prophylaxis should be individualized, not automatic. Table 2 presents the medication options available in Brazil, some of which need to be prepared by compounding pharmacies.

Table 2. Corticosteroids and calcineurin inhibitors available in Brazil.

Class	Medication	Formulation	Concentration	Remarks
Corticosteroids	Clobetasol	Rinse/gel/paste/cream/ointment	0.05; 0.01%	Rinse should be used when multiple areas of mucosa are affected; gel, ointment, and paste for localized or refractory lesions; injection for refractory ulcerated lesions
	Dexamethasone	Rinse	0.01%	
	Triamcinolone	Rinse	0.01%	
		Ointment	0.1%	
		Injection (intralesional)	40 mg/mL / 0.5 mL/cm ²	
	Prednisolone	Rinse	0.03%	
	Budesonide	Rinse	0.03%	
Calcineurin inhibitor	Tacrolimus	Gel	0.05%	Reserved for corticosteroid-refractory cases; patients may experience intolerance, and systemic absorption can occur
		Rinse	0.1%	
		Ointment	0.03%; 0.1%	

Source: Elaborated by the authors.

Photobiomodulation, ultraviolet B, and barrier-protective products

Photobiomodulation with low power laser therapy shows a signal of benefit for pain and ulceration. In small series, there was immediate relief and clinical improvement during induction and maintenance, but recurrence after lengthening the interval between sessions was frequent^{21,22}. It should be considered a grade C adjunctive option, especially when the immediate goal is analgesia or when intensification of immunosuppression is to be avoided.

Intraoral narrowband ultraviolet B (nbUVB) phototherapy was described in a series of patients with disease refractory to conventional topical agents. All reported some degree of improvement, but there was recurrence upon discontinuation/reduction, exacerbations, and a lack of uniform comparative criteria²³. It should be reserved for experienced centers and presented as an emerging grade C therapy.

Barrier-protective gel and autologous platelet lysate showed signals of benefit in uncontrolled studies^{24,25}. These therapies can be included as adjuncts or experimental grade C interventions, contingent on infrastructure, consent, and specialized follow-up.

Systemic therapies for refractory disease

Ruxolitinib

Ruxolitinib is a systemic option for cGVHD refractory to corticosteroids and other lines, especially in the presence of multiorgan disease. The oral cohort by Kaurinovic et al.²⁶ observed a reduction in mucosal score and oral response at four and 12 weeks, with an overall oral response of 81% at 12 weeks, but without a control group, with cointerventions and selection bias. The prospective publication by Bellido et al.²⁷ reinforced a signal of oral response, but there was a discrepancy between the abstract and detailed analysis; for prudence, the more conservative rate should be used. Long-term systemic follow-up studies suggest that response may be maintained in some patients, but do not substitute for controlled mouth-specific outcomes²⁸. The systemic meta-analysis by Fan et al.²⁹ supports global activity, but application to the mouth remains secondary and heterogeneous.

For oral cGVHD, ruxolitinib should be considered grade C, level 2b in oral studies and 2a with caveats in the aggregate review. Its use requires monitoring for cytopenias, infections, viral reactivation, interactions, and cumulative immunosuppression. It is not first-line treatment for localized oral disease.

Belumosudil

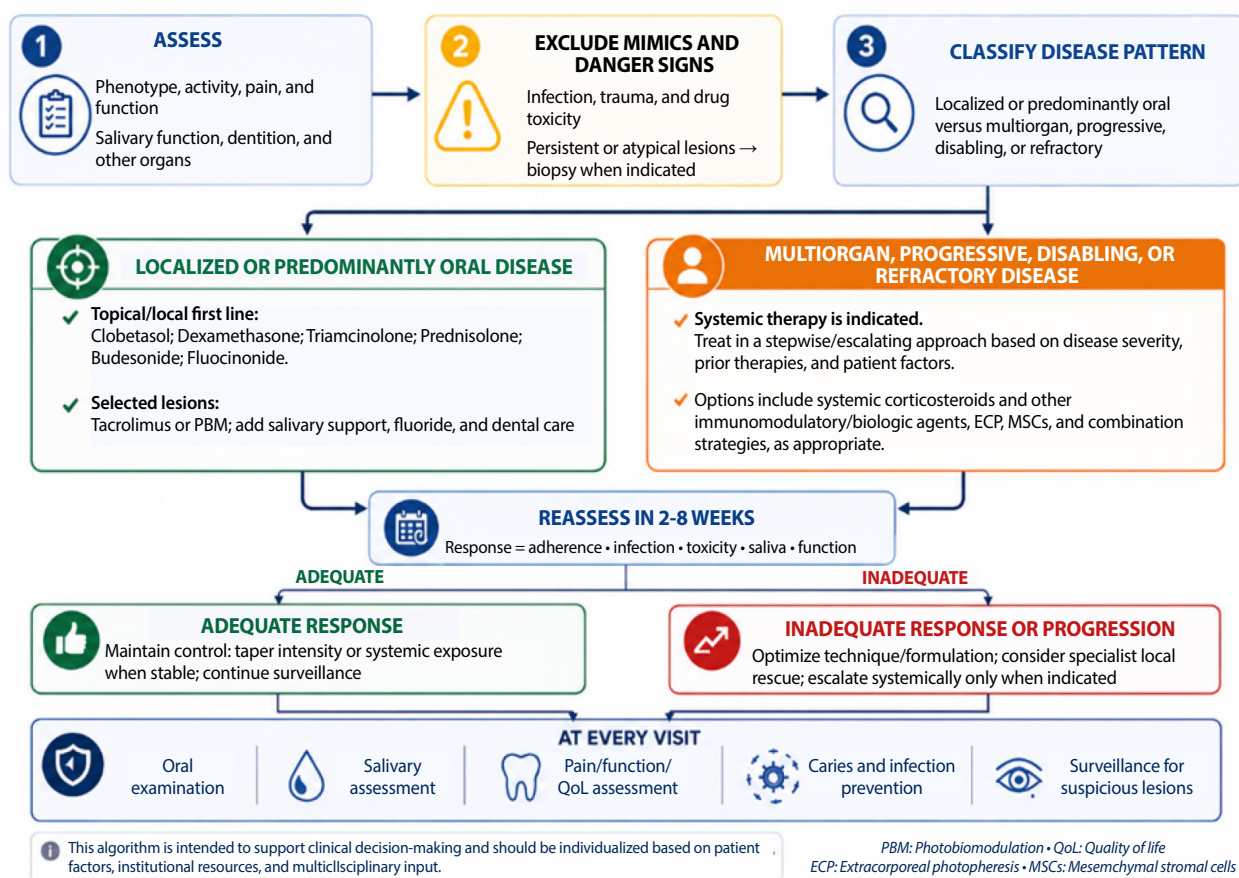
Belumosudil adds a systemic option with antifibrotic and anti-inflammatory plausibility. In the ROCKstar companion study³⁰, 20 patients with persistent, multi-refractory oral cGVHD showed a classifiable oral response in 65%, in addition to reductions in collagen, interleukin-17-producing cells, and salivary transforming growth factor (TGF)- β 1. French and Italian real-world cohorts also suggest organ-specific activity, but are observational and without mouth-specific controls^{31,32}.

Belumosudil may be considered in refractory, fibrosing, or multiorgan oral disease after multiple lines, with grade C and level 2b for oral substudy. Histological and salivary changes should not be presented as proof of restoration of salivary flow or glandular function. Dose, interactions, toxicity, and availability should follow the label and institutional protocol.

Other therapies

Extracorporeal photopheresis can be used in systemic cGVHD refractory to or dependent on corticosteroids, but the submitted evidence does not present separate oral outcomes³³. Topical ruxolitinib was studied in skin and should not be recommended for the oral mucosa based on extrapolation from another organ^{34,35}.

Figure 3 presents a proposed algorithm for the treatment of oral chronic GVHD. Table 3 provides an overview of the level of evidence and grade of recommendation.



PBM: photobiomodulation; ECP: extracorporeal photopheresis; MSC: mesenchymal stromal cells. Source: Elaborated by the authors with the assistance of generative artificial intelligence (ChatGPT, OpenAI) for visual design and layout. The scientific content was defined and reviewed by the authors.

Figure 3. Treatment algorithm for oral chronic graft-versus-host disease.

Table 3. Levels of evidence and grades of recommendation for interventions in oral chronic graft-versus-host disease.

Area	Recommendation	Level	Grade
Topical corticosteroid	Use clobetasol, dexamethasone, triamcinolone, prednisone, budesonide, or fluocinonide as first-line options for symptomatic disease	Baseline 1a	B
Topical tacrolimus	Consider for localized or refractory lesions	3b	C
Photobiomodulation	Consider as an adjunct for persistent pain and ulceration	4	C
Intraoral ultraviolet B	Reserve for refractory disease in specialized centers	4	C
Platelet lysate/barrier	Consider only as adjunctive or experimental	3b–4	C
Ruxolitinib	Consider in refractory oral chronic graft-versus-host disease, mainly multiorgan, with specialized monitoring	2a–2b	C
Belumosudil	Consider after multiple lines in refractory/fibrosing or multiorgan disease	2b–3b	C
Xerostomia	Measure symptoms and flow; combine dental prevention and symptomatic treatment	2b–4	C
Sialagogues	Individualized trial of pilocarpine/cevimeline when there is glandular reserve	4	C
Caries	Fluoride, adapted hygiene, diet control, and dental follow-up	2b–5	C
Taste/smell	Actively inquire and assess nutrition when there is functional impact	2c	C
Secondary cancer	Prolonged oral surveillance and early biopsy of suspicious lesions	2a–2b	B–C
Salivary monitoring	Propose a prospective protocol with sialometry, symptoms, oral health, and quality of life	4–5	D

Source: Adapted from Oxford Centre for Evidence-Based Medicine⁹.

The algorithm should be interpreted as a clinical framework and not as a mandatory sequence. At all levels, infection, trauma, and malignancy must be excluded, and dental care, caries prevention, salivary management, and functional assessment must be maintained.

COMPLICATIONS

Saliva and xerostomia

Xerostomia can cause difficulty speaking, chewing, and swallowing, in addition to increasing the risk of caries, candidiasis, and trauma. In a retrospective study of 70 adults, pilocarpine and cevimeline produced modest subjective improvement in dryness score, without demonstration of objective restoration of salivary flow, caries prevention, or comparative benefit³⁶. Sialagogues may be individually trialed when there is glandular reserve, with attention to cholinergic effects and contraindications.

A recent narrative review explored the therapeutic potential of photobiomodulation for salivary function recovery across different conditions, highlighting its potential to mitigate inflammatory-phase damage in diseases such as Sjögren's syndrome. However, its efficacy and role in salivary gland dysfunction in cGVHD remain to be established³⁷.

CARIES, DENTITION, AND ORAL HEALTH

Dental health depends on saliva, diet, hygiene, access to dental care, periodontal disease, medications, and the intensity of immunosuppression. In a late cohort of 70 survivors, current oral cGVHD was associated with worse quality of life, greater difficulty with dry foods, and greater dietary limitation, but there was no statistically demonstrated difference in mean tooth loss between groups³⁸. Therefore, the consensus should recommend prevention and surveillance, without attributing independent causality to oral GVHD.

Fluoridated dentifrice is recommended, with additional fluoride measures in high-risk individuals, hygiene adapted to pain and sensitivity, reduction of fermentable sugars, hydration, lubrication, and dental follow-up. The clinical practice review reinforces pre-transplant dental assessment—including extraction of non-restorable or infected teeth, periodontal stabilization, and endodontic evaluation, infection prevention, caries control, and specialized referral, although its basis is narrative^{39,40}.

For a comprehensive, phase-specific approach to dental management before, during, and after hematopoietic cell transplantation, readers are referred to the companion Brazilian dental consensus series^{40–42}.

Pain, function, taste, and quality of life

Pain and sensitivity may impact quality of life more intensely than the extent of mucosal involvement. In a study of 56 patients, pain and sensitivity correlated with Oral Health Impact Profile-14, whereas mucosal severity alone showed no significant correlation¹³. In an objective study of taste and smell, hypogeusia occurred in 68.9% of participants, although some patients did not subjectively recognize the deficit⁴³.

Follow-up should include questions about pain, avoided foods, chewing, swallowing, speech, taste, smell, weight, and intake. Patients with nutritional impact should be referred to nutrition and functional rehabilitation. There is insufficient basis to recommend a specific pharmacologic treatment for dysgeusia as standard.

Infections, fibrosis, trismus, and osteonecrosis

Candidiasis and reactivated herpes simplex virus may mimic or worsen oral cGVHD, particularly in the presence of hyposalivation, topical corticosteroid use, or systemic immunosuppression; evaluation should be guided by the clinical phenotype and response to therapy. These risk factors warrant vigilance and targeted treatment when infection is suspected, but do not justify universal prophylaxis^{1,44–46}.

Orofacial fibrosis and trismus should be monitored by measuring mouth opening and initiating early stretching exercises when restriction develops. Jaw osteonecrosis should be considered in relation to antiresorptive exposure, corticosteroids, radiotherapy, infection, and other risk factors, rather than attributed directly to oral cGVHD; invasive procedures require individualized hematologic, infectious-disease, and dental/oral-surgery assessment^{1,45–48}.

Secondary oral cancer and potentially malignant lesions

Available evidence suggests that oral cGVHD may be associated with an increased risk of secondary oral cancer, although the magnitude and causality of this association remain uncertain because studies are heterogeneous, denominators are inconsistent, and the number of events is often small^{49–52}. Persistent cGVHD, prolonged immunosuppression, previous radiotherapy, and host or behavioral factors may modify this risk.

Patients with Fanconi anemia constitute a very-high-risk subgroup because of their inherited DNA-repair defect and predisposition to aggressive head and neck squamous cell carcinoma, including oral cancer; this risk may be further compounded after allo-HCT⁵³. Lifelong and more intensive oral surveillance (every six months or less) should therefore be considered mandatory, beginning early after transplantation and coordinated with hematology/transplantation, oral medicine or dentistry, and otorhinolaryngology when indicated. For other allo-HCT recipients, specialized oral examination every 6–12 months is recommended, with shorter intervals and prompt specialist evaluation or biopsy for persistent or clinically discordant lesions⁵⁴.

Table 3 summarizes the levels of evidence and grades of recommendation for treatments related to oral cGVHD.

Perspectives: early monitoring of salivary function

Salivary gland dysfunction is a clinically significant component of oral cGVHD and can progress even in the presence of stable or minimally symptomatic mucosal disease. Reduced salivary flow can compromise lubrication, swallowing, speech, and mucosal integrity, in addition to increasing the risk of dental caries, opportunistic infections, and a decreased quality of life. However, it has not been established yet whether early detection of glandular hypofunction alters clinical outcomes. We therefore propose an exploratory and longitudinal salivary function assessment that is feasible in clinical practice and can be performed by physicians, nurses, dentists, and other trained members of the transplant team. Unstimulated total saliva could be collected at predefined time points, after 5 minutes of rest, in a pre-weighed container, allowing for the gravimetric calculation of salivary flow in mL/min. The interpretation of sialometry should be integrated with symptoms of xerostomia, clinical examination, dental and periodontal health, the occurrence of oral infections, and the impact on quality of life^{55,56}.

Serial evaluation may allow for the identification of trajectories of reduction, stability, or recovery of salivary function and their association with cGVHD activity, oral complications, and patient-reported outcomes. Salivary gland scintigraphy can provide additional functional information but should remain a complementary test, preferably performed at specialized centers or as part of research protocols.

A low flow result alone should not trigger systemic immunosuppression or other disease-modifying treatment; confirmation of the change, repeat measurement, review of reversible factors, preventive oral care, and appropriate referral should precede any therapeutic escalation. This proposal is therefore an SBTMO exploratory perspective, intended to support future trials of early gland-preserving interventions rather than to recommend preemptive treatment.

CONCLUSION

This Brazilian update recognizes oral cGVHD as a disease affecting mucosa, saliva, and oral function. Topical corticosteroids remain the main strategy for symptomatic, localized oral disease, with potential to reduce systemic exposure. Ruxolitinib and belumosudil can be options for refractory disease, but with conditional recommendations because oral-specific evidence remains limited. Prevention and surveillance for xerostomia, caries, infection, functional impairment, and secondary oral cancer should accompany treatment.

CONFLICT OF INTEREST

Nothing to declare

DATA AVAILABILITY STATEMENT

All datasets were generated and analyzed in the current study.

AUTHORS' CONTRIBUTIONS

Conception and design: Macedo LD and Correa MEP; **Acquisition of data:** Macedo LD, Costa MA, Eduardo FP, Bezinelli LM, Santos PSS, Antunes HS and Correa MEP; **Analysis and interpretation of data:** Macedo LD, Costa MA, Eduardo FP, Bezinelli LM, Santos PSS, Antunes HS and Correa MEP; **Manuscript preparation:** Macedo LD, Costa MA, Eduardo FP, Bezinelli LM, Santos PSS, Antunes HS and Correa MEP. **Final approval:** Macedo LD.

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DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

Chat GPT, Open AI was used as a design-support tool in the development of Figures 1 and 2. The authors reviewed, edited, and take full responsibility for the scientific content and final version of the figure.

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REFERENCES

1. Elad S, Aljitawi O, Zadik Y. Oral graft-versus-host disease: a pictorial review and a guide for dental practitioners. *Int Dent J*. 2021;71(1):9-20. <https://doi.org/10.1111/idj.12584>
2. Al Masri B, Perry LM, Stoopler ET. Palatal superficial mucocoeles associated with chronic graft-versus-host disease. *Hematol Transfus Cell Ther*. 2023;45(1):140. <https://doi.org/10.1016/j.htct.2021.09.014>
3. Tollemar V, Legert KG, Sugars RV. Perspectives on oral chronic graft-versus-host disease from immunobiology to morbid diagnoses. *Front Immunol*. 2023;14:1151493. <https://doi.org/10.3389/fimmu.2023.1151493>
4. Dean D, Sroussi H. Oral chronic graft-versus-host disease. *Front Oral Health*. 2022;3:903154. <https://doi.org/10.3389/froh.2022.903154>
5. Scaraficci AC, Fernandes PM, Alves FA, Schmidt Filho J, Jaguar GC. Oral manifestations of graft-versus-host disease in patients submitted to allogeneic hematopoietic stem cell transplantation: the experience of a Brazilian Cancer Center. *Support Care Cancer*. 2022;30:567-73. <https://doi.org/10.1007/s00520-021-06349-9>
6. Kambara Y, Fujiwara H, Yamamoto A, Gotoh K, Tsuji S, Kunihiro M, Oyama T, Terao T, Sato A, Tanaka T, Peltier D, Seike K, Nishimori H, Asada N, Ennishi D, Fujii K, Fujii N, Matsuoka KI, Soga Y, Reddy P, Maeda Y. Oral inflammation and microbiome dysbiosis exacerbate chronic graft-versus-host disease. *Blood*. 2025;145(8):881-96. <https://doi.org/10.1182/blood.2024024540>
7. Yamamoto A, Kambara Y, Fujiwara H. Impact of oral microbiota on pathophysiology of GVHD. *Front Immunol*. 2023;14:1132983. <https://doi.org/10.3389/fimmu.2023.1132983>
8. Correa MEP, Eduardo FP, Macedo LD, Bezinelli LM, Santos PSS, Antunes HS. Oral graft-versus-host diseases. *J Bone Marrow Transplant Cell Ther*. 2021;2(1):181-6. <https://doi.org/10.46765/2675-374X.2021v4n1p181-186>
9. Oxford Centre for Evidence-Based Medicine. Levels of Evidence [Internet]. Oxford: Centre for Evidence-Based Medicine, University of Oxford; 2009 [cited 2026 Aug 16]. Available from: <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009>
10. Nguyen JT, Jessri M, Costa-da-Silva AC, Sharma R, Mays JW, Treister NS. Oral chronic graft-versus-host disease: pathogenesis, diagnosis, current treatment, and emerging therapies. *Int J Mol Sci*. 2024;25(19):10411. <https://doi.org/10.3390/ijms251910411>
11. Bassim CW, Fassil H, Mays JW, Edwards D, Baird K, Steinberg SM, Williams KM, Cowen EW, Mitchell SA, Cole K, Taylor T, Avila D, Zhang D, Pulanic D, Grkovic L, Fowler D, Gress RE, Pavletic SZ. Validation of the National Institutes of Health chronic GVHD Oral Mucosal Score using component-specific measures. *Bone Marrow Transplant*. 2014;49(1):116-21. <https://doi.org/10.1038/bmt.2013.137>

12. Treister N, Chai X, Kurland B, Pavletic S, Weisdorf D, Pidala J, Palmer J, Martin P, Inamoto Y, Arora M, Flowers M, Jacobsohn D, Jagasia M, Arai S, Lee SJ, Cutler C. Measurement of oral chronic GVHD: results from the Chronic GVHD Consortium. *Bone Marrow Transplant*. 2013;48(8):1123-8. <https://doi.org/10.1038/bmt.2012.285>
13. Stolze J, Boor M, Hazenberg MD, Brand HS, Raber-Durlacher JE, Laheij AMGA. Oral health-related quality of life of patients with oral chronic graft-versus-host disease. *Support Care Cancer*. 2021;29:6353-60. <https://doi.org/10.1007/s00520-021-06197-7>
14. DePalo J, Chai X, Lee SJ, Cutler CS, Treister N. Assessing the relationship between oral chronic graft-versus-host disease and global measures of quality of life. *Oral Oncol*. 2015;51(10):944-9. <https://doi.org/10.1016/j.oraloncology.2015.07.009>
15. Tollemar V, Arvidsson H, Häbel H, Tudzarovski N, Legert KG, Le Blanc K, Warfvinge G, Sugars RV. Grading of minor salivary gland immuno-histopathology post-allogenic hematopoietic cell transplantation. *Heliyon*. 2023;9(4):e15517. <https://doi.org/10.1016/j.heliyon.2023.e15517>
16. Sato S, Shimizu E, He J, Ogawa M, Asai K, Yazu H, Rusch R, Yamane M, Yang F, Fukuda S, Kawakami Y, Tsubota K, Ogawa Y. Positive effects of oral antibiotic administration in murine chronic graft-versus-host disease. *Int J Mol Sci*. 2021;22(7):3745. <https://doi.org/10.3390/ijms22073745>
17. Haas L, Cruz-Pamplona M. Topical treatment of oral chronic graft-versus-host-disease in hematopoietic stem cell transplant recipients: A systematic review. *J Clin Exp Dent*. 2023;15(5):e420-7. <https://doi.org/10.4317/jced.60138>
18. Noce CW, Gomes A, Shcaira V, Corrêa MEP, Moreira MCR, Silva Júnior A, Gonçalves LS, Garnica M, Maiolino A, Torres SR. Randomized double-blind clinical trial comparing clobetasol and dexamethasone for the topical treatment of symptomatic oral chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2014;20(8):1163-8. <https://doi.org/10.1016/j.bbmt.2014.04.009>
19. Treister N, Li S, Kim H, Lerman M, Sultan A, Alyea EP, Armand P, Cutler C, Ho V, Koreth J, Antin JH, Soiffer R. An open-label phase II randomized trial of topical dexamethasone and tacrolimus solutions for the treatment of oral chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2016;22(11):2084-91. <https://doi.org/10.1016/j.bbmt.2016.08.020>
20. Elad S, Zeevi I, Finke J, Koldehoff M, Schwerdtfeger R, Wolff D, Mohrbacher R, Levitt M, Greinwald R, Shapira MY. Improvement in oral chronic graft-versus-host disease with the administration of effervescent tablets of topical budesonide-an open, randomized, multicenter study. *Biol Blood Marrow Transplant*. 2012;18(1):134-40. <https://doi.org/10.1016/j.bbmt.2011.06.001>
21. Epstein JB, Raber-Durlacher JE, Epstein GL, Hazenberg MD, Tzachanis D, Spielberger RT. Chronic oral graft-versus-host disease: induction and maintenance therapy with photobiomodulation therapy. *Support Care Cancer*. 2021;29:1387-94. <https://doi.org/10.1007/s00520-020-05626-3>
22. Finfter O, Avni B, Grisariu S, Haviv Y, Nadler C, Rimón O, Zadik Y. Photobiomodulation (low-level laser) therapy for immediate pain relief of persistent oral ulcers in chronic graft-versus-host disease. *Support Care Cancer*. 2021;29:4529-34. <https://doi.org/10.1007/s00520-021-05997-1>
23. Choi E, Lenga M, Nguyen CV, Zheng L, Froelich A, Centanni E, Choi JN. Treatment of oral graft-versus-host disease with intraoral nbUVB phototherapy. *Support Care Cancer*. 2024;32:438. <https://doi.org/10.1007/s00520-024-08642-9>
24. Cao J, Ye L, Li X, Song Q, Chai Y. Early intervention with oral mucosal barrier protective agents in chronic oral graft-versus-host disease: a retrospective cohort study. *BMC Oral Health*. 2024;24:958. <https://doi.org/10.1186/s12903-024-04724-6>

25. Torrent-Rodríguez A, Lizondo-López T, Charry P, Suárez-Lledó M, Mestre-Ribot MM, Cremades-Artacho C, Salas MQ, Muñoz CM, Rovira M, Fernández-Avilés F, López-Cabezas C, Aranda-Cortés L, Cid J, Lozano M. Effectiveness of oral platelet lysate gel to treat oral mucosal manifestations associated with chronic graft versus host disease. *Blood Transfus.* 2025;23(5):461-8. <https://doi.org/10.2450/BloodTransfus.880>
26. Kaurinovic M, Delli K, Jonk A-ME, Biswana A, Hazenberg CLE, Choi G, Groot MR, Morsink LM, Vissink A, Bellido M. Effect of ruxolitinib on the oral mucosa of patients with steroid-refractory chronic Graft-versus-Host disease and oral involvement. *Clin Oral Investig.* 2022;26:4209-16. <https://doi.org/10.1007/s00784-022-04393-1>
27. Bellido M, Jonk A-ME, Kaurinovic M, Biswana A, Hazenberg CLE, Choi G, Morsink LM, Huls G, Vissink A, Delli K. Effect of ruxolitinib on the oral mucosa in steroid-refractory graft-versus-host disease: a prospective observational exploratory study. *Clin Oral Investig.* 2025;29:552. <https://doi.org/10.1007/s00784-025-06604-x>
28. Sanli NM, Karakus E. Long-term follow-up results of ruxolitinib as salvage therapy for chronic graft-versus-host disease. *Hematol Transfus Cell Ther.* 2025;47(3):103835. <https://doi.org/10.1016/j.htct.2025.103835>
29. Fan S, Huo W-X, Yang Y, Shen M-Z, Mo X-D. Efficacy and safety of ruxolitinib in steroid-refractory graft-versus-host disease: A meta-analysis. *Front Immunol.* 2022;13:954268. <https://doi.org/10.3389/fimmu.2022.954268>
30. Sharma R, Holtzman NG, Pusic I, Cutler C, Treister N, Mehta RS, Alousi AS, Vigneswaran N, Javaid A, Boksa F, Mody DP, Costa-da-Silva AC, Schueller O, Macé S, Yao Y, Ji R, Hu B, Marshall K, Blazar BR, Lee SJ, Pavletic SZ, Mays JW. Belumosudil reduces oral chronic graft-versus-host disease tissue inflammation and fibrosis: a ROCKstar companion study. *Blood Adv.* 2025;9(14):3479-94. <https://doi.org/10.1182/bloodadvances.2025016170>
31. Bonifazi F, Roberto M, Lupo Stanghellini MT, Chiusolo P, Polverelli N, Geromin A, Prezioso L, Algeri M, Mancini G, Prunotto G, Algarotti A, Nozzoli C, Malagola M, Mordini N, Fedele M, Santoro L, Zallio F, Castagna L, Picardi A, Busca A, Giaccone L, Skert C, Elice F, Facchini L, Mariotti J, Pierini A, Spina A, Marchi R, Salvatore D, Martino M, Tumino M, Rambaldi A, Locatelli F. Real-world outcomes in refractory chronic graft-versus-host disease: the Italian multicenter experience with belumosudil. *Haematologica.* 2026;111(6). <https://doi.org/10.3324/haematol.2025.289302>
32. Michonneau D, Malard F, Le Grand S, Magro L, D'Aveni M, Tudesq JJ, Villate A, Meunier M, Maillard N, Castilla-Llorente C, Marçais A, Cabrera Q, Huynh A, Menard A-L, Forcade E, Labussière-Wallet H, Raus N, Loschi M. Efficacy and safety of belumosudil for treatment of cGVHD: multicenter retrospective analysis of the French cohort of the compassionate use program, on behalf of the French Society of Bone Marrow Transplantation and Cellular Therapy. *Bone Marrow Transplant.* 2025;60:779-86. <https://doi.org/10.1038/s41409-025-02554-w>
33. Vargas DF, Pereira MP, Silva TS, David CN, Paz AA, Astigarraga CC. Extracorporeal photopheresis in chronic graft-versus-host disease: clinical description and economic study. *Hematol Transfus Cell Ther.* 2023;45(2):182-7. <https://doi.org/10.1016/j.htct.2021.08.014>
34. Hudda Z, Flannery A, Teusink-Cross A, Davies SM, Khandelwal P. Topical ruxolitinib is promising as sole or adjunctive therapy in treating maculopapular rash of acute and chronic skin GVHD. *Bone Marrow Transplant.* 2024;59:425-7. <https://doi.org/10.1038/s41409-023-02181-3>
35. Sarmiento M, Jara V, Soto K, Uribe P, Ocqueteau M, Bertin P, Pereira J. A real life use of ruxolitinib in patients with acute and chronic graft versus host disease refractory to corticosteroid treatment in Latin American patients. *Hematol Transfus Cell Ther.* 2021;43(3):303-8. <https://doi.org/10.1016/j.htct.2020.06.015>

36. Mousavian M, Sroussi H, Villa A, Cutler C, Treister N. Use of prescription sialagogues for management of xerostomia in chronic graft-versus-host-disease. *Transplant Cell Ther.* 2021;27(6):480.e1-e5. <https://doi.org/10.1016/j.jtct.2021.02.020>
37. Calarga CC, Brito CBT, Cotomácio CC, Simões A. Photobiomodulation for salivary gland dysfunction: aligning clinical expectations with etiology-dependent treatment responsiveness. *Lasers Med Sci.* 2026;41:196. <https://doi.org/10.1007/s10103-026-04991-5>
38. Treister NS, Liang L, Lee SJ, Cutler C, Gooley TA, Hujoel P, Gbujie D, Oh UY, Bennett-Johnson L, Hagstrom MK, Rothen M, Lloid M, Dean D, Sroussi H. Tooth loss and oral health-related quality of life in a sub-cohort within the Chronic Graft-Versus-Host Disease Consortium. *Transplant Cell Ther.* 2026;32(7):893.e1-e10. <https://doi.org/10.1016/j.jtct.2026.03.004>
39. Johnson LB, Oh U, Rothen M, Sroussi HY, Dean DR, Lloid CM, Cintron K, Lee SJ, Cutler CS, Treister NS. A review of oral chronic graft-versus-host disease: considerations for dental hygiene practice. *J Dent Hyg.* 2022;96(2):6-17. <https://jdh.adha.org/content/96/2/6>
40. Correa MEP, Granzotto FCN, Innocentini LMAR, Reis TC, Lima EM, Varanda RF, Santos PSS, Soares Junior LAV, Bezinelli LM, Eduardo FP, Melo WR, Antunes HS, Macedo LD. Brazilian dental consensus on dental management in hematopoietic stem cell transplantation - Part I - pre-HCT. *Hematol Transfus Cell Ther.* 2023;45(3):358-67. <https://doi.org/10.1016/j.htct.2023.04.001>
41. Gobbi MF, Ferreira MH, Carvalho DLC, Silva GBL, Macari KSM, Neves LJ, Santos PSS, Soares Junior LAV, Melo WR, Antunes HS, Macedo LD, Eduardo FP, Bezinelli LM. Dental consensus on HCT - Part II: dental care during HCT. *Hematol Transfus Cell Ther.* 2023;45(3):368-78. <https://doi.org/10.1016/j.htct.2023.04.003>
42. Santos PSS, Granzotto FCN, Antunes HS, de Lima EM, Varanda RF, Maccari K, Bezinelli LM, Melo WR, Soares Junior LAV, Macedo LD, Eduardo FP. Dentistry consensus on HCT - Part III: special topics - dentistry on HCT. *Hematol Transfus Cell Ther.* 2023;45(3):379-86. <https://doi.org/10.1016/j.htct.2023.04.004>
43. Boor M, Raber-Durlacher JE, Hazenberg MD, Rozema FR, Laheij AMGA. Taste and smell disturbances in patients with chronic oral graft vs. host disease: An observational study. *Front Oral Health.* 2022;3:934607. <https://doi.org/10.3389/froh.2022.934607>
44. Treister N, Duncan C, Cutler C, Lehmann L. How we treat oral chronic graft-versus-host disease. *Blood.* 2012;120(17):3407-18. <https://doi.org/10.1182/blood-2012-05-393389>
45. Zadik Y, Raber-Durlacher JE, Epstein JB, Majorana A, Laheij A, Bardellini E, Blijlevens N, Elad S. MASCC/ISOO Clinical Practice Statement: Management of oral manifestations of chronic graft-versus-host-disease. *Support Care Cancer.* 2024;32:546. <https://doi.org/10.1007/s00520-024-08686-x>
46. Laheij AMGA, Fregnani ER, Macedo LD, Treister NS. Oral chronic graft-versus-host disease and oral health after allogeneic hematopoietic cell transplantation—what the care team needs to know. *Transplant Cell Ther.* 2024;30(9 Suppl.):S548-58. <https://doi.org/10.1016/j.jtct.2024.07.006>
47. Haverman TM, Raber-Durlacher JE, Raghoobar II, Rademacher WMH, Rozema FR, Hazenberg MD, Epstein JB, Treister NS. Oral chronic graft-versus-host disease: What the general dental practitioner needs to know. *J Am Dent Assoc.* 2020;151(11):846-56. <https://doi.org/10.1016/j.adaj.2020.08.001>
48. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' position paper on medication-related osteonecrosis of the jaws-2022 update. *J Oral Maxillofac Surg.* 2022;80(5):920-43. <https://doi.org/10.1016/j.joms.2022.02.008>
49. Gervazio TC, Silva JK, Evangelista K, Cavalcanti MGP, Silva MAGSS, Yamamoto-Silva FP, Silva BSF. Risk of oral cancer in patients with graft-vs-host disease: A systematic review and meta-analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2022;133(6):650-62. <https://doi.org/10.1016/j.oooo.2022.02.002>

50. Santarone S, Natale A, Angelini S, Papalinetti G, Vaddinelli D, Di Bartolomeo A, Di Bartolomeo P. Secondary oral cancer following hematopoietic cell transplantation. *Bone Marrow Transplant.* 2021;56:1038-46. <https://doi.org/10.1038/s41409-020-01147-z>
51. Janowiak-Majeranowska A, Osowski J, Mikaszewski B, Majeranowski A. Secondary oral cancer after systemic treatment of hematological malignancies and oral GVHD: a systematic review. *Cancers.* 2022;14(9):2175. <https://doi.org/10.3390/cancers14092175>
52. Cantile T, Coppola N, Canfora F, Adamo D, Ruoppo E, Mignogna MD, Leuci S. Oral cancer in HCT pediatric patients arising on GVHD: a comprehensive review. *Cancers.* 2022;14(23):5775. <https://doi.org/10.3390/cancers14235775>
53. Fanconi Anemia Research Fund. Head and neck cancer in patients with Fanconi anemia. Clinical Care Guidelines [Internet]. Fanconi Anemia Research Fund [cited 2026 Aug 16]. Available at: <https://fanconi.org/clinical-care-guidelines/head-and-neck-cancer-in-patients-with-fanconi-anemia/>
54. Raber-Durlacher JE, Treister NS, Zadik Y, Dean DR, Miranda-Silva W, Fregnani ER, Epstein JB, Elad S. MASCC/ISOO Clinical Practice Statement: The risk of secondary oral cancer following hematopoietic cell transplantation. *Support Care Cancer.* 2024;32:545. <https://doi.org/10.1007/s00520-024-08685-y>
55. Navazesh M, Kumar SK. Measuring salivary flow: challenges and opportunities. *J Am Dent Assoc.* 2008;139(Suppl. 2):35S-40S. <https://doi.org/10.14219/jada.archive.2008.0353>
56. Fontana M, Zunt S, Eckert GJ, Zero D. A screening test for unstimulated salivary flow measurement. *Oper Dent.* 2005;30(1):3-8. <https://operative-dentistry.kglmeridian.com/downloadpdf/view/journals/odnt/30/1/article-p1.pdf>