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Assessing the relationship between oral chronic graft-versus-host disease and global measures of quality of life

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Abstract

Chronic GVHD (cGVHD) is a frequent complication of allogeneic hematopoietic stem cell transplantation (HSCT) and affects multiple organ systems, with the oral cavity being one of the most frequently affected sites. Patients with cGVHD experience reduced quality of life (QOL), yet the specific impact of oral cGVHD on QOL is poorly understood.

OBJECTIVE—The objective of this study was to characterize the impact of oral cGVHD on global measures of QOL.

METHODS—QOL data were collected using the FACT-BMT and SF-36 instruments for 569 patients enrolled in the Chronic GVHD Consortium, with a total of 1,915 follow-up visits. At study enrollment, patients were categorized as isolated oral cGVHD (n=22), oral and concomitant extra-oral cGVHD (n=420), and only extra-oral cGVHD (n=127). Utilizing all longitudinal data, QOL scores were compared using a multivariable linear model controlling for demographic, transplant, and cGVHD characteristics.

RESULTS—Patients with isolated oral cGVHD reported better physical well-being (P=0.009), BMT well-being (P=0.01), and decreased bodily pain (P=0.01) compared to patients with oral and concomitant extra-oral cGVHD, but the differences in scores did not reach the defined threshold for clinical significance (6 points for FACT-BMT domains and 5 points for SF-36 domains).

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Conflict of Interest
None declared.

CONCLUSIONS—Global QOL scores are similar in patients with isolated oral cGVHD and patients with oral and concomitant extra-oral cGVHD.

Keywords

Oral chronic graft-versus-host disease; quality of life; stem cell transplantation

Introduction

Chronic graft-versus-host disease (cGVHD) is a frequent complication of allogeneic hematopoietic stem cell transplantation (alloHSCT) and a leading cause of long-term morbidity and non-relapse mortality.¹ Approximately 30-70% of alloHSCT recipients develop some degree of cGVHD, which can manifest in various anatomic locations including the skin, mouth, eyes, and lungs, contributing to varying degrees of morbidity and chronic disability.^{2,3,4} The oral cavity is one of the most frequently affected sites, with manifestations characterized by lichenoid mucosal inflammation with associated pain and sensitivity, difficulty eating, dry mouth and related complications.^{5,6,7,8} Long-standing oral cGVHD can be associated with daily pain and suffering, compromised nutritional intake, rampant dental decay and tooth loss, and an increased risk of oral squamous cell carcinoma.^{6,9,10}

Chronic GVHD is a major cause of reduced quality of life (QOL) after alloHSCT.^{11,12} Patients with cGVHD are more likely to report decreased global measures of QOL compared to both alloHSCT patients without a history of cGVHD as well as those with resolved cGVHD.¹³ Oral cGVHD involvement is associated with diminished oral health-related QOL, but the impact of oral or other organ-specific involvement on global QOL measures is unclear.^{14,15,16,17} The objective of this study was to characterize the impact of oral cGVHD on global measures of QOL after alloHSCT.

Methods

Chronic GVHD cohort

Subjects were enrolled in the Chronic GVHD Consortium, a prospective multi-center observational cohort of alloHSCT recipients that were ≥2 years of age and affected by cGVHD requiring systemic immunotherapy.¹⁸ Patients were classified as *incident* (enrollment ≤3 months after cGVHD diagnosis) or *prevalent* (enrollment >3 months after cGVHD diagnosis but ≤3 years after alloHSCT). Patients with relapse of primary disease or poor study compliance were excluded. Patients and clinicians reported standardized information about cGVHD involvement and symptoms at enrollment and then every six months thereafter. Incident cases had an additional follow-up visit three months after enrollment. IRB approval was obtained at each of the nine participating study sites (Fred Hutchinson Cancer Research Center, Stanford University Medical Center, Dana-Farber Cancer Institute, University of Minnesota, Vanderbilt University Medical Center, Moffitt Cancer Center, Medical College of Wisconsin, Memorial Sloan-Kettering Cancer Center, and Washington University Medical Center) and all subjects or their guardians provided informed consent in accordance with the Declaration of Helsinki.

Patient-reported quality of life measures

Quality of life was assessed using the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) v4.0 and the Short-Form Health Survey (SF-36) v2.0. The FACT-BMT is a 37-item patient-reported questionnaire that assesses the impact of cancer therapy on several QOL domains including functional well-being, physical well-being, social/family well-being, emotional well-being, and bone marrow transplant well-being.^{19,20} Baseline mean, minimum, and maximum QOL scores were reported for each QOL domain, with higher scores indicating better QOL.

The SF-36 v2.0 is a 36-item patient-reported questionnaire that assesses overall health status and functioning by examining the following QOL domains: vitality, physical functioning, bodily health perceptions, physical role functioning, emotional role functioning, social role functioning, bodily pain, and mental health.²¹ In addition to individual scores for each QOL domain, the SF-36 also provides summary physical and mental component scores. Baseline mean, minimum, and maximum QOL scores were reported for all SF-36 domain and component scores, with higher scores indicating better QOL.

Chronic GVHD assessment

Chronic GVHD was assessed by a trained clinician using the NIH Chronic GVHD Consensus criteria, which describes involvement according to measures specific to each organ, as well as general overall measures of cGVHD activity.²² Included were clinician- and patient-reported assessments of oral cavity involvement, conducted at enrollment and all serial follow-up visits. Clinician-reported measures included the NIH oral mucosal score and oral pain score. Patient-reported clinical assessments of the oral cavity included NIH oral symptom scores for pain, sensitivity, and dryness.²³

Statistical methods

Subjects were categorized into three groups based on cGVHD features at cGVHD cohort enrollment: isolated oral involvement, oral and concomitant extra-oral involvement, and only extra-oral involvement. Oral involvement was defined by the presence of any clinician-reported criteria (severity score ≥ 1 , erythema, lichenoid changes, ulcers, mucocelles, or oral pain). Extra-oral involvement was defined as a severity score of ≥ 1 in one or more extra-oral sites. Summary statistics of baseline QOL data were reported by patient groups, including mean, minimum, and maximum scores.

Utilizing all longitudinal data, the difference in QOL scores between patients with isolated oral cGVHD and those with either oral and concomitant extra-oral cGVHD or only extra-oral cGVHD were calculated for each domain using linear mixed models with random intercept to account for within patient correlations. Models included covariate adjustment for study site (Fred Hutchinson Cancer Research Center vs. other), education (high school, college, graduate school), income ($< \$75,000$ vs. greater), months from alloHSCt to enrollment (< 12 months vs. greater), primary diagnosis, graft source, CMV status, donor type (matched related, matched unrelated, mismatched), platelet count ($< 100k$ vs. higher), total bilirubin (> 2 vs. higher), overlap v. classic cGVHD, and visit time since enrollment. A positive difference in QOL scores indicated higher QOL scores and a negative difference in

QOL scores indicated lower QOL domain scores in the isolated oral cGVHD group. Minimum clinically meaningful differences in QOL scores were defined as one-half of the population standard deviation (5 points for SF-36 domains and 6 points for FACT-BMT domains).^{24,25} Given multiple testing, $P = 0.01$ was considered to be statistically significant.

Results

Chronic GVHD cohort

The Chronic GVHD Consortium enrolled 569 subjects that met the inclusion criteria and completed all follow-up visits prior to March 2014 (Table 1). Subjects were 58% male, approximately two-thirds had prior acute GVHD, and the majority (88%) received peripheral blood stem cells. Approximately half of the study subjects were enrolled at the Fred Hutchinson Cancer Research Center ($n=253$). Clinician-reported cGVHD severity was predominantly mild (46%) and moderate (43%), and the majority of cases were incident cases (60%). Median follow-up time from enrollment to date of last visit was 52.9 months for patients with isolated oral cGVHD, 45.6 months for patients with oral and concomitant extra-oral cGVHD, and 39.2 months for only extra-oral cGVHD. No associations were observed between the three patient groups and patient education, income, months from alloHSCT to enrollment, primary diagnosis, CMV status, platelet count, total bilirubin, overlap v. classic cGVHD, and visit time since enrollment.

Subjects were categorized into three groups based on oral involvement at the time of enrollment: isolated oral involvement ($n=22$), oral and concomitant extra-oral involvement ($n=420$), and only extra-oral involvement ($n=127$). The three groups were otherwise similar with respect to demographic and transplant characteristics (Table 1). Overall cGVHD severity differed between the three groups, with greater proportions of patients with moderate and severe disease in the oral and concomitant extra-oral and only extra-oral groups (57% and 51% respectively) compared to the isolated oral group (9%). Oral cGVHD features and patient-reported oral symptoms were similar among patients with isolated oral cGVHD and those with oral and concomitant extra-oral cGVHD (Table 2). Extra-oral features (e.g. skin, liver, eye, GI, and genital involvement) were largely similar in subjects with oral and concomitant extra-oral cGVHD and those with only extra-oral cGVHD (Table 2).

Impact of oral cGVHD involvement on global measures of quality of life

Baseline QOL data from FACT-BMT and SF-36 instruments were available at least in part for 83% and 85% of subjects, respectively. Baseline SF-36 physical and mental component scores were available partly or in full for 82% of study subjects at the time of enrollment. Subjects with isolated oral cGVHD reported greater baseline mean QOL scores prior to adjustment for covariates for all FACT-BMT domains and all but one SF-36 domain (social/family well-being) compared to subjects with oral and concomitant extra-oral cGVHD and only extra-oral cGVHD, but QOL was still worse than population normative values (for SF-36 domains), particularly in physical functioning scales (Figure 1).²⁶

Multivariable analysis using all QOL data from patients with isolated oral cGVHD (156 visits), oral and concomitant extra-oral cGVHD (1481 visits), and only extra-oral cGVHD (728 visits) detected statistically significant differences in two out of six FACT-BMT domains and one out of ten SF-36 domains when comparing subjects with isolated oral cGVHD to subjects with oral and concomitant extra-oral cGVHD, and failed to detect statistically significant differences when comparing subjects with isolated oral cGVHD to those with only extra-oral cGVHD (Table 3). Patients with isolated oral cGVHD reported better physical well-being ($P=0.009$, difference in scores = 1.09), better FACT-BMT bone marrow transplant (BMT) well-being ($P=0.01$, difference in scores = 1.10), and decreased bodily pain ($P=0.01$, difference in scores = 2.26) compared to patients with oral and concomitant extra-oral cGVHD. While these differences were statistically significant, the magnitudes of the differences in scores did not exceed the previously defined threshold for clinical significance (6 points for FACT-BMT domains and 5 points for SF-36 domains).

Discussion

This study attempted to characterize the impact of oral cGVHD on global measures of QOL using data from the Chronic GVHD Consortium. As all patients in this study underwent comprehensive and standardized clinical evaluation, we were able to clearly define the population according to oral and extra-oral features. We failed to identify any clinically meaningful differences in QOL among patients with isolated oral, oral and concomitant extra-oral, or only extra-oral cGVHD, suggesting that we should not overlook the impact that even isolated oral cGVHD involvement may have on QOL.

This study revealed several important findings. First, no clinically meaningful differences in QOL were observed when comparing patients with isolated oral cGVHD to patients with oral and concomitant extra-oral cGVHD. This finding is particularly noteworthy as overall disease severity was considerably greater in patients with oral and concomitant extra-oral cGVHD compared to those with isolated oral cGVHD. Moderate or severe global NIH cGVHD severity was reported in 57% of patients with oral and concomitant extra-oral cGVHD, compared to only 9% of patients with isolated oral. This observation was expected given that, in patients with isolated oral cGVHD, the global NIH cGVHD severity classification can only be driven by oral cavity involvement, whereas patients with extra-oral involvement may have multiple organs contributing to this classification. However, it remains possible that the difference in global NIH cGVHD disease severity reduced QOL scores in patients with oral and concomitant extra-oral cGVHD relative to scores reported by patients with isolated oral cGVHD, making the similarities in QOL scores between these two patients groups even more noteworthy. There are several possible explanations for why QOL scores were as low as they were in patients with isolated oral cGVHD. Inclusion in the Chronic GVHD Consortium required systemic immunotherapy, which may have selected for isolated oral cGVHD cases with more burdensome forms of oral involvement. However, the prevalence of oral ulcers, which are thought to be a significant contributor to oral cGVHD symptom burden, was similar in patients with isolated oral cGVHD and patients with oral and concomitant extra-oral cGVHD, although specifics regarding the extent and severity of oral ulcers were not collected in this study. Our findings are also limited by the sensitivity of the FACT-BMT and SF-36 instruments and the accuracy of the clinical data, much of which

is subjective patient-reported data. Despite these explanations, it cannot be ruled out that oral cGVHD, even in isolation, is associated with a disease burden that is comparable to that of extra-oral cGVHD.

This study also demonstrated that vitality and social/family well-being scores were markedly similar in patients with isolated oral cGVHD and patients with oral and concomitant extra-oral cGVHD. The similarity in vitality scores, which measure one's feelings of energy, might be explained by previous work that suggests oral cGVHD manifestations are directly or indirectly related to malnutrition and weight loss.^{6,27} Higher mouth NIH scores are associated with malnutrition and cGVHD-related salivary dysfunction is associated with significantly greater difficulty with swallowing solid foods.^{14,28} With respect to the relationship between oral cGVHD and social/family well-being, oral cGVHD is associated with inferior social/family well-being.¹⁶ Additionally, patients with chronic mucosal diseases may experience discomfort in social settings and reluctance to participate in social activities.²⁹ Collectively, this suggests that oral cGVHD involvement might be a significant contributing factor in determining the social/family well-being of patients with cGVHD.

A major strength of this study was our ability to define distinct patient populations based on organ-specific cGVHD involvement, which provided the basis for the study design. Another strength was the comprehensive serial collection of QOL data using multiple instruments (FACT-BMT and SF-36), both of which provide global assessments of QOL and are not confined to the direct effects of oral cGVHD. This study also had several limitations. The total sample size of patients was robust (n=569), yet the number of patients with isolated oral involvement (n=22) was small, with the majority (82%) of these patients enrolled at a single center (Fred Hutchinson Cancer Research Center). While this was not surprising given the inclusion criteria of systemic immunosuppression, it diminished our ability to detect statistically significant differences in QOL scores in our cohort and to comment on oral cGVHD of lesser severity. Lastly, the 2014 NIH chronic GVHD consensus criteria recommendation that mucocels no longer be used for cGVHD studies may make our isolated oral and oral and concomitant extra-oral patient populations less relevant in the future, given that mucocels were included in our definition of oral cGVHD involvement.³⁰

In summary, global QOL scores are similar in patients with isolated oral cGVHD and patients with oral and concomitant extra-oral cGVHD. Additional work is needed to better understand the influence of oral cGVHD on global as well as oral health-related measures of QOL, in particular with respect to severity and management outcomes. Future studies addressing the relationship between oral health and global QOL measures will better define the influence of oral cavity disease, with the ultimate goal of identifying more targeted approaches to improving cGVHD-associated morbidity and improving QOL after alloHSCT.

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References

1. Lee SJ, Vogelsang G, Flowers ME. Chronic graft-versus-host disease. *Biol Blood Marrow Transplant.* 2003; 9(4):215–233. [PubMed: 12720215]
2. Socié G, Salooja N, Cohen A, et al. Nonmalignant late effects after allogeneic stem cell transplantation. *Blood.* 2003; 101(9):3373–3385. [PubMed: 12511420]
3. Flowers ME, Inamoto Y, Carpenter PA, et al. Comparative analysis of risk factors for acute graft-versus-host disease and for chronic graft-versus-host disease according to National Institutes of Health consensus criteria. *Blood.* 2011; 117(11):3214–3219. [PubMed: 21263156]
4. Baird K, Pavletic SZ. Chronic graft versus host disease. *Curr Opin Hematol.* 2006; 13(6):426–435. [PubMed: 17053454]
5. Schubert MM, Correa ME. Oral graft-versus-host disease. *Dent Clin North Am.* 2008; 52(1):79, 109, viii–ix. [PubMed: 18154866]
6. Woo SB, Lee SJ, Schubert MM. Graft-vs.-host disease. *Crit Rev Oral Biol Med.* 1997; 8(2):201–216. [PubMed: 9167093]
7. Meier JK, Wolff D, Pavletic S, et al. Oral chronic graft-versus-host disease: report from the International Consensus Conference on clinical practice in cGVHD. *Clin Oral Investig.* 2011; 15(2): 127–139.
8. Treister N, Duncan C, Cutler C, Lehmann L. How we treat oral chronic graft-versus-host disease. *Blood.* 2012; 120(17):3407–3418. [PubMed: 22898605]
9. Imanguli MM, Alevizos I, Brown R, Pavletic SZ, Atkinson JC. Oral graft-versus-host disease. *Oral Dis.* 2008; 14(5):396–412. [PubMed: 18593456]
10. Bassim CW, Ambatipudi KS, Mays JW, et al. Quantitative salivary proteomic differences in oral chronic graft-versus-host disease. *J Clin Immunol.* 2012; 32(6):1390–1399. [PubMed: 22806177]
11. Pallua S, Giesinger J, Oberguggenberger A, et al. Impact of GvHD on quality of life in long-term survivors of haematopoietic transplantation. *Bone Marrow Transplant.* 2010; 45(10):1534–1539. [PubMed: 20228854]
12. Lee SJ, Kim HT, Ho VT, et al. Quality of life associated with acute and chronic graft-versus-host disease. *Bone Marrow Transplant.* 2006; 38(4):305–310. [PubMed: 16819438]
13. Fraser CJ, Bhatia S, Ness K, et al. Impact of chronic graft-versus-host disease on the health status of hematopoietic cell transplantation survivors: a report from the Bone Marrow Transplant Survivor Study. *Blood.* 2006; 108(8):2867–2873. [PubMed: 16788100]
14. Imanguli MM, Atkinson JC, Mitchell SA, et al. Salivary gland involvement in chronic graft-versus-host disease: prevalence, clinical significance, and recommendations for evaluation. *Biol Blood Marrow Transplant.* 2010; 16(10):1362–1369. [PubMed: 20353829]
15. Bassim CW, Fassil H, Mays JW, et al. Validation of the National Institutes of Health chronic GVHD Oral Mucosal Score using component-specific measures. *Bone Marrow Transplant.* 2014; 49(1):116–121. [PubMed: 23995099]
16. Fall-Dickson JM, Mitchell SA, Marden S, et al. Oral symptom intensity, health-related quality of life, and correlative salivary cytokines in adult survivors of hematopoietic stem cell transplantation with oral chronic graft-versus-host disease. *Biol Blood Marrow Transplant.* 2010; 16(7):948–956. [PubMed: 20139026]
17. Daikeler T, Mauramo M, Rovó A, et al. Sicca symptoms and their impact on quality of life among very long-term survivors after hematopoietic SCT. *Bone Marrow Transplant.* 2013; 48(7):988–993. [PubMed: 23292241]
18. Consortium CG. Rationale and design of the chronic GVHD cohort study: improving outcomes assessment in chronic GVHD. *Biol Blood Marrow Transplant.* 2011; 17(8):1114–1120. [PubMed: 21664473]
19. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol.* 1993; 11(3):570–579. [PubMed: 8445433]
20. McQuellon RP, Russell GB, Cella DF, et al. Quality of life measurement in bone marrow transplantation: development of the Functional Assessment of Cancer Therapy-Bone Marrow

- Transplant (FACT-BMT) scale. Bone Marrow Transplant. 1997; 19(4):357–368. [PubMed: 9051246]
21. McHorney CA, Ware JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care. 1993; 31(3):247–263. [PubMed: 8450681]
 22. Filipovich AH, Weisdorf D, Pavletic S, et al. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. Diagnosis and staging working group report. Biol Blood Marrow Transplant. 2005; 11(12):945–956. [PubMed: 16338616]
 23. Pavletic SZ, Martin P, Lee SJ, et al. Measuring therapeutic response in chronic graft-versus-host disease: National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: IV. Response Criteria Working Group report. Biol Blood Marrow Transplant. 2006; 12(3):252–266. [PubMed: 16503494]
 24. Norman GR, Sloan JA, Wywrich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care. 2003; 41(5):582–592. [PubMed: 12719681]
 25. Pidala J, Kurland BF, Chai X, et al. Sensitivity of changes in chronic graft-versus-host disease activity to changes in patient-reported quality of life: results from the Chronic Graft-versus-Host Disease Consortium. Haematologica. 2011; 96(10):1528–1535. [PubMed: 21685473]
 26. Ware, J.; Kosinski, M.; Bjorner, J.; Turner-Bowker, D.; Gandek, B.; Maruish, M. User's Manual for the SF- 36v2 Health Survey. 2nd ed.. Quality Metric Incorporated; Lincoln, RI: 2007.
 27. Lenssen P, Sherry ME, Cheney CL, et al. Prevalence of nutrition-related problems among long-term survivors of allogeneic marrow transplantation. J Am Diet Assoc. 1990; 90(6):835–842. [PubMed: 2345257]
 28. Bassim CW, Fassil H, Dobbin M, et al. Malnutrition in patients with chronic GVHD. Bone Marrow Transplant. 2014; 49(10):1300–1306. [PubMed: 25029231]
 29. Riordain RN, Meaney S, McCreary C. Impact of chronic oral mucosal disease on daily life: preliminary observations from a qualitative study. Oral Dis. 2011; 17(3):265–269. [PubMed: 20860762]
 30. Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant. 2015; 21(3):389–401. e381. [PubMed: 25529383]

Highlights

- Chronic GVHD is associated with diminished quality of life but the contribution of oral cavity involvement remains unclear.
- Isolated oral cGVHD is not associated with clinically significant better quality of life compared to oral and concomitant extra-oral cGVHD.
- Organ-specific cGVHD involvement can influence various quality of life measures and outcomes.

Figure 1.

Baseline QOL scores for cohort members at enrollment according to oral involvement group and prior to adjustment for covariates. Mean values are shown and error bars indicate maximum and minimum values for each subscale. Greater QOL scores indicate better QOL. BMT= bone marrow transplant. PCS= physical component score. MCS= mental component score.

Table 1

Patient characteristics at Chronic GVHD Cohort enrollment.

	All (N=569) N (%)	cGVHD involvement			p-value
		isolated oral (N=22) N (%)	oral and extra-oral (N=420) N (%)	only extra-oral (N=127) N (%)	
site					<0.001
FHCRC	253 (44)	18 (82)	223 (53)	12 (9)	
other	316 (56)	4 (18)	197 (47)	115 (91)	
gender					0.16
male	329 (58)	17 (77)	238 (57)	74 (58)	
female	240 (42)	5 (23)	182 (43)	53 (42)	
case type					0.05
incident	340 (60)	8 (36)	259 (62)	73 (57)	
prevalent	229 (40)	14 (64)	161 (38)	54 (43)	
stem cell source					0.03
peripheral blood	501 (88)	20 (91)	375 (89)	106 (83)	
bone marrow	40 (7)	2 (9)	30 (7)	8 (6)	
cord blood	28 (5)	0 (0)	15 (4)	13 (10)	
conditioning intensity					0.62
myeloablative	294 (52)	10 (45)	215 (51)	69 (55)	
non-myeloablative	271 (48)	12 (55)	203 (49)	56 (45)	
donor match					0.71
match unrelated	243 (43)	12 (55)	181 (43)	50 (40)	
match related	234 (41)	8 (36)	170 (41)	56 (44)	
mismatch	90 (16)	2 (9)	68 (16)	20 (16)	
prior acute GVHD					0.84
yes	375 (66)	15 (68)	279 (66)	81 (64)	
no	194 (34)	7 (32)	141 (34)	46 (36)	
Global NIH cGVHD severity					<0.001
none	1 (<1)%	1 (5)	0 (0)	0 (0)	
mild	265 (46)	19 (86)	182 (43)	63 (50)	
moderate	242 (43)	2 (9)	192 (46)	48 (38)	
severe	61 (11)	0 (0)	45 (11)	16 (13)	

FHCRC= Fred Hutchinson Cancer Research Center. cGVHD= chronic graft-versus-host disease.

Table 2

Organ involvement at enrollment.

	cGVHD involvement					
	isolated oral (N=22)		oral and extra-oral (N=420)		only extra-oral (N=127)	
	N (%)	mean (SD)	N (%)	mean (SD)	N (%)	mean (SD)
Oral cavity	22 (100)		420 (100)		0 (0)	
clinician severity score 1	18 (72)		330 (79)		-	
erythema	12 (55)		225 (54)		-	
lichenoid changes	20 (91)		327 (78)		-	
ulceration	6 (27)		80 (19)		-	
mucocelles	9 (41)		158 (38)		-	
clinician mouth pain	13 (59)		234 (56)		-	
total mucosal score		3.6 (2.9)		3.1 (2.6)		-
patient mouth pain ^a		1.8 (2.5)		2.5 (3.0)		-
sensitivity ^a		2.5 (2.8)		3.2 (3.0)		-
dryness ^a		2.9 (3.2)		4.0 (3.0)		-
Liver	-		219 (52)		74 (58)	
Skin	-		278 (66)		79 (62)	
GI tract	-		150 (36)		35 (28)	
Eyes	-		230 (55)		54 (43)	
Joint and fascia	-		115 (27)		55 (43)	
Genital	-		52 (13)		6 (5)	
Lung	-		229 (55)		46 (36)	

Organ system involvement is defined as a clinician-reported organ score 1. GI= gastrointestinal.

^aIndicates patient-reported clinical measures. Scores range from 0-10 for all patient-reported clinical measures.

Table 3

Multivariable analysis comparing quality of life scores.

		isolated oral vs. oral and extra-oral		isolated oral vs. only extra-oral	
		difference in QOL scores between groups (95% CI)	p-value	difference in QOL scores between groups (95% CI)	p-value
FACT-BMT					
	total	3.14 (0.34, 5.94)	0.03	1.58 (−1.53, 4.70)	0.32
	physical well-being	1.09 (0.27, 1.92)	0.009	1.09 (0.17, 2.00)	0.02
	social/family well-being	0.17 (−0.53, 0.87)	0.63	−0.13 (−0.91, 0.65)	0.75
	emotional well-being	0.45 (−0.14, 1.05)	0.14	0.07 (−0.59, 0.72)	0.85
	functional well-being	0.88 (0.004, 1.76)	0.05	0.29 (−0.68, 1.26)	0.56
	BMT well-being	1.10 (0.22, 1.97)	0.01	0.81 (−0.16, 1.78)	0.10
SF36					
	PCS	1.20 (−0.41, 2.80)	0.14	1.08 (−0.69, 2.86)	0.23
	MCS	0.17 (−1.59, 1.92)	0.85	−0.67 (−2.61, 1.26)	0.50
	physical functioning	0.96 (−0.68, 2.60)	0.25	0.79 (−1.02, 2.61)	0.39
	physical role functioning	−0.29 (−2.17, 1.59)	0.76	−0.52 (−2.60, 1.56)	0.62
	bodily pain	2.26 (0.45, 4.07)	0.01	2.43 (0.43, 4.44)	0.02
	general health perceptions	1.62 (0.03, 3.21)	0.05	0.22 (−1.55, 1.98)	0.81
	vitality	0.07 (−1.64, 1.77)	0.94	−0.50 (−2.39, 1.39)	0.60
	social role functioning	1.29 (−0.71, 3.29)	0.21	0.81 (−1.40, 3.01)	0.47
	emotional role functioning	0.46 (−1.65, 2.56)	0.67	−0.72 (−3.03, 1.60)	0.54
	mental health	0.27 (−1.37, 1.91)	0.75	−0.43 (−2.25, 1.39)	0.64

Difference in QOL scores estimates the difference in QOL scores between the two groups. A positive difference in QOL scores indicates higher QOL scores and a negative difference in QOL scores indicates lower QOL domain scores in the isolated oral cGVHD group. BMT= bone marrow transplant. CI= confidence interval. PCS= physical component score. MCS= mental component score.