Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Burden of Oral Mucositis: A Systematic Review and Implications for Future Research

Karin Berger[a] Dorothee Schopohl[a] Antonia Bollig[a]
Dorothea Strobach[b] Christina Rieger[a] Dale Rublee[c]
Helmut Ostermann[a]

[a]Department of Medicine III, University Hospital, Ludwig Maximilian University, Munich, Germany; [b]Department of Pharmacy, University Hospital, Ludwig Maximilian University, Munich, Germany; [c]Independent health services research, Munich, Germany

Abbreviations: OM = oral mucositis; JA = journal article; CA = conference abstracts.

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

1. Systematic literature search: incidence of OM

Supplemental Table 1. Incidence of OM

Number	Search term	Results
[1]	mucositis	28101
[2]	limit 1 to yr="2000 – 2016"	20235
[3]	stomatitis	72922
[4]	limit 3 to yr="2000 – 2016"	36383
[5]	2 or 4	53652
[6]	incidenc*	2084633
[7]	limit 6 to yr="2000 – 2016"	1319346
[8]	frequenc*	2419274
[9]	limit 8 to yr="2000 – 2016"	1498616
[10]	7 or 9	2722015
[11]	5 and 10	7141
[12]	limit 11 to article	4700
[13]	Remove duplicates from 12	3038

Database: BIOSIS Previews <1969 to 2009>, Embase <1974 to 2016 December 09>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>; date 12.12.2016

Literature selection by title, abstract and full text: Identification of 43 JA related to studies on incidence of OM in hematology/oncology patients aged ≥18 years

Exclusion criteria: JA reporting on studies conducted with the intention to compare different treatments of OM, no incidence of OM, no English language, patients <18 years of age, CA, reviews, case reports, comments, editorials, notes, brief communications, letters, animal studies

Inclusion criteria: JA reporting on studies on hematology/oncology patients aged ≥18 years with determination of incidence of OM, English language, published between January 2000 and December 2016, meta-analyses

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

2. Systematic literature search: cost/resource use of OM

Supplemental Table 2. Cost/resource use of OM

Number	Search term	Results
[1]	mucositis	28101
[2]	limit 1 to yr="2000 – 2016"	20235
[3]	stomatitis	72922
[4]	limit 3 to yr="2000 – 2016"	36383
[5]	2 or 4	53652
[6]	economic*	1230728
[7]	limit 6 to yr="2000 – 2016"	598456
[8]	cost	1282077
[9]	limit 8 to yr="2000 – 2016"	884590
[10]	7 or 9	1318978
[11]	5 and 10	1556
[12]	limit 11 to article	850
[13]	Remove duplicates from 12	586

Database: BIOSIS Previews <1969 to 2009>, Embase <1974 to 2016 December 09>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>; date 12.12.2016

Literature selection by title, abstract and full text: Identification of 17 JA related to studies on cost/resource use of OM in hematology/oncology patients aged ≥18 years

Exclusion criteria: JA reporting on studies conducted with the intention to compare different treatments of OM. The only exception made was the study of Bezinelli and colleagues [1]. No cost/resource use of OM, no English language, patients <18 years of age, CA, reviews, case reports, comments, editorials, notes, brief communications, letters, animal studies

Inclusion criteria: JA reporting on studies on hematology/oncology patients aged ≥18 years with determination of cost/resource use of OM, English language, published between January 2000 and December 2016, meta-analyses

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

3. Systematic literature search: health-related quality of life (HRQoL) and OM

Supplemental Table 3. Health-related quality of life and OM

Number	Search term	Results
[1]	mucositis	28101
[2]	limit 1 to yr="2000 – 2016"	20235
[3]	stomatitis	72922
[4]	limit 3 to yr="2000 – 2016"	36383
[5]	2 or 4	53652
[6]	quality of life	786518
[7]	limit 6 to yr="2000 – 2016"	650676
[8]	HRQoL	33464
[9]	limit 8 to yr="2000 – 2016"	30179
[10]	7 or 9	651187
[11]	5 and 10	3427
[12]	limit 11 to article	1922
[13]	Remove duplicates from 12	1372

Database: BIOSIS Previews <1969 to 2009>, Embase <1974 to 2016 December 09>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>; date 12.12.2016

Literature selection by title, abstract and full text: Identification of 17 JA related to studies on impact of HRQoL on OM in hematology/oncology patients aged ≥18 years

Exclusion criteria: JA reporting on studies conducted with the intention to compare different treatments of OM, no incidence of OM, no English language, patients <18 years of age, CA, reviews, case reports, comments, editorials, notes, brief communications, letters, animal studies

Inclusion criteria: JA reporting on studies on hematology/oncology patients aged ≥18 years with determination of the impact of OM on HRQoL, English language, published between January 2000 and December 2016, meta-analyses

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Supplemental Table 4. Incidence of oral mucositis/stomatitis in hematology/oncology patients

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
Hematopoietic Stem Cell Transplantation (HSCT)				
Wardley et al. 2000 [2]	GB	autologous and allogeneic HSCT; 365 patients: 67 allogeneic bone marrow; 62 autologous bone marrow; 236 peripheral blood progenitor cell reinfusion.	prospective observational, single-centre study; *WHO scale*	Total: 99%; G3/G4 67.4%
Grazziutti et al. 2006 [3]	US	autologous HSCT; 381 myeloma patients	retrospective, single-centre chart review study; *NCI CTCAE scale version 2.0*	Total: 75%; G3/G4 (severe OM) 21%
Vera-Llonch et al. 2007 [4]	US	allogeneic HSCT; 281 patients with hematological malignancies.	retrospective, single-centre, chart review study; *Discrete OM scale according to description in the publication*	Total: 87.9%; G1 11.7%; G2 24.9%; G3 21.4%; G4 15.3%; G5 14.6%
Jones et al. 2008 [5]	US	autologous HSCT; 8891 multiple myeloma and lymphoma inpatients.	retrospective, multicentre, database analysis; *Scale not given*	Total stomatitis: approximately 40%; Stomatitis with TBI: 66,7% vs. 36.7%; Stomatitis with age >65 years: 68.7% vs. 58.8%
McCann et al. 2009 [6]	AT, BE, CH, CZ, DE, FI, GB, IE, IT, NL, SE	autologous HSCT; 197 patients.	prospective, observational, multicentre study; *WHO scale*	Total: 86.8%; G1 22.8%; G2 19.8%; G3 30.5%; G4 13.7%
Vagliano et al. 2011 [7]	IT	autologous and allogeneic HSCT; 1579 patients >18 years: 1231 adult patients (19 - 59 years); 348 older patients (60 - 74 years).	prospective, observational, multicentre study; *WHO scale*	Total: 70%; G1 30.3%; G2 18.7%; G3 12.9%; G4 8.2%; Adults: Total: 72.7%; G1 29.6%; G2 18.7%; G3 14.8%; G4 9.6%; Older: Total: 60.7%; G1 32.5%; G2 19.0%; G3 6.0%; G4 3.2%
Gupta et al. 2012 [8]	CA	allogeneic HSCT; 115 patients: 51 MAC, 64 RIC.	prospective, observational, single-centre, study; *Bearman Toxicity Criteria*	Total: 70.4%; G1 21.7%; G ≥2 48.7%; MAC: Total: 88.2%; G1 9.8%; G ≥2 78.4%; RIC: Total: 56.3%; G1 31.3%; G ≥2 25%
Kashiwazaki et al. 2012 [9]	JP	allogeneic HSCT; 130 patients: 60 conventional HSCT (CST), 70 RIC.	retrospective, single-centre study; *NCI CTCAE scale version 3.0*	Total (CST + RIC): G1 23%; G2 23%; G3 32.3%; G4 0.7%; CST: G1 25%; G2 25%; G3 31.7%; G4 1.7%; RIC: G1 21.4%; G2 21.4%; G3 32.9%; G4 0%

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
Urbain et al. 2012 [10]	DE	allogeneic HSCT; 70 patients.	prospective observational, single-centre study; *WHO scale*	Total: 95.7%; G0/G1 54.3%; G2-G4 45.7%; G3/G4 20%
Legert et al. 2014 [11]	SE	allogeneic HSCT; 171 patients with mostly hematological malignancies: 99 RIC, 72 MAC.	retrospective, single-centre study; *WHO-grading, NCI CTCAE scale version 3.0*	*WHO-grading at day 11* Total: 74%; G1 18%; G2 34%; G3 15%; G4 9%; *NCI CTCAE grading at day 11* Total: 100%; G1 67%; G2 22%; G3 8%; G4 3%
Martino et al. 2014 [12]	IT	autologous HSCT; early discharge outpatient model: 382 multiple myeloma patients, 522 transplants.	retrospective, multicentre study; *WHO scale*	G3/G4 9.6% of 522 transplants
Wu et al. 2015 [13]	CN	allogeneic HSCT; 87 high-risk ALL patients; idarubicin intensified TBI–CY: 47 patients; TBI–CY regimen: 40 patients	retrospective, single-centre study; *NCI CTCAE scale version 3.0*	idarubicin intensified TBI–CY: G1/G2 55.3%, G3 6.4%; TBI–CY regimen: G1/G2 35.0%
Anand et al. 2016 [14]	US	allogeneic HSCT, CD34+ selected; MAC/age<55years 82 patients; RIC/age>55 years 23 patients.	retrospective, single-centre study; *WHO scale, Bearman RRT (regimen-related toxicity) scale*	WHO G2-G4 46.7 %, WHO G3–G4 34.3 %; Bearman G1 53.3 %, G2 15.2 %, G3–G4 0 %; MAC: WHO G0-G2 57%, WHO G3/G4 43%; RIC: WHO G0-G2 96%, WHO G3/G4 4%
Chaudhry et al. 2016 [15]	US	conditioning regimens in allogeneic HSCT: MAC 395 patients in 8 studies, RIC 245 patients in 6 studies	meta-analysis; *WHO scale, NCI CTCAE scales*	Total: MAC 73.2%, RIC 86.5%; G2-G4: MAC 79.7%, RIC 71.5%; MAC with Bu/Cy 70.5%, MAC with TBI/Cy 96.6%
Head and Neck Cancer (HNC)				
Manas et al. 2009 [16]	ES	HNC with RT; 2047 patients cross-sectional; 282 patients follow-up.	prospective, observational, multicentre study; *RTOG toxicity score*	Total: 26.4%; G3 95.7% of follow-up patients; G4 4.3% of follow-up patients
Hu et al. 2014 [17]	TW	HNC locally advanced; 170 patients: 116 split-dose (SD) cisplatin-based therapy with CCRT, 54 cetuximab with CCRT (BioRT). RT 70 Gy/35 fractions.	retrospective, single-centre study; *RTOG toxicity score*	Total: 88.2%; SD-CCRT: G1/G2 40.5%; G3/G4 48.3%; Bio-RT: G1/G2 40.7%; G3/G4 46.3%
Vatca et al. 2014	US	HNC with CCRT; 72 patients with HPV-	retrospective, single-centre study;	Total: 100%; G1 1.4%; HPV- 6.7%, HPV+ 0%;

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
[18]		associated oropharyngeal squamous cell carcinoma: HPV- 15, HPV+ 57; RT max. 70-76 Gy.	*NCI CTCAE scale version 3.0*	G2 44.4%; HPV- 73.3%, HPV+ 36.8%; G3 41.6%; HPV- 6.7%, HPV+ 50.9%; G4 12.6%; HPV- 13.3%, HPV+ 12.3%
Roy et al. 2015 [19]	IN	HNC; 60 patients: 30 hypofractionated RT (hypo) 55 Gy/20 fractions; 30 conventional RT (conv) 70 Gy/35 fractions.	retrospective, single-centre study; *RTOG toxicity score*	G0/G1 hypo, 20%; conv, 66.7%; G ≥2: hypo, 80%; conv, 33.3%; Late toxicity after 6 months (55 patients): hypo G2 29%; G3 32%; G4 18%; conv G2 11%; G3 4%; G4 0%
Tsukahara et al. 2015 [20]	JP	curative therapy for stage III, IVA, or IVB squamous-cell carcinoma of head and neck: 505 patients; UFT (Tegafur / uracil): 254 patients; S-1 (tegafur / gimeracil / oteracil potassium): 251 patients.	prospective, multicentre, randomized phase III study; *NCI CTCAE scale version 3.0*	Total mucositis/stomatitis: UFT 2.0%; S-1 12.7%; Mucositis/stomatitis G3/G4: UFT 0%; S-1 2.4%
Hoshikawa et al. 2015 [21]	JP	CCRT with Nedaplatin and S-1 for HNSCC stage III or IV without metastasis: 46 patients; RT 66-70 Gy	retrospective, observational, single-centre study; *NCI CTCAE scale version 3.0*	OM: G1 22%; G2 48%; G3 30%
Guo et al. 2015 [22]	CN	205 patients with VMAT for NPC; RT 68–70 Gy; chemotherapy in 89.8% (141/157) patients with stage III or IVa-b disease (T3–T4 or N2–N3).	prospective, observational, single-centre study; *NCI CTCAE scale version 3.0, RTOG toxicity score*	Total: 100%; OM: G1 22%; G2 50%; G3 28%; G4 0%
Xu et al. 2015 [23]	CN	stage III or IVb NPC: 44 patients; 23 patients CRT (IMRT and cisplatin); 21 patients ERT (IMRT and cetuximab); T1/T2 disease 66Gy/30 fractions, T3/T4 disease 70.4Gy/32 fractions	prospective, observational, single-centre study; *NCI CTCAE scale version 3.0*	OM G3/G4 47.8% CRT arm, 80.9% ERT arm
Romesser et al. 2016 [24]	US	PBRT median dose 60.6 Gy for locally recurrent HNC: 91 patients	retrospective, observational, multicentre study; *NCI CTCAE scale*	Total: 59.4%; G0 40.7%; G1 31.9%; G2 17.6%; G3 9.9%; G4 0%

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
			version 4.0, RTOG toxicity score	
Bonner et al. 2016 [25]	US	locally advanced HNSCC: 181 patients; RT ± cetuximab; p16-positive 74 patients; p16-negative 106 patients; RT 70 Gy-78 Gy.	prospective, multicentre, randomized phase III study; *RTOG toxicity score*	p16-positive total: RT ± cetuximab: 100 %; G3/G4: RT + cetuximab (n=40) 78%, RT (n=34) 71%; p16-negative: RT + cetuximab (n=43) total: 98%, G3/G4 65%; RT (n=63) total 95%, G3/G4 56%
Lin et al. 2016 [26]	CN	IMRT for NPC: 220 patients; mean dose 72.62 Gy (range 70.77 Gy – 74.52 Gy); RT 30 patients; CCRT 190 patients.	prospective, observational, single-centre study; *RTOG toxicity score*	Total: 99%; G1 24%; G2 47.4%; G3 27.6%; G4 0%
Xu et al. 2016 [27]	CN	non-metastatic NPC: 266 patients CCRT; 133 patients prophylactic PEG, 133 patients non-PEG; IMRT 66–80 Gy (median, 70.95 Gy)	retrospective, observational, single-centre study; *RTOG toxicity score*	PEG: G0-G2 77.5%; G3 22.5%; Non-PEG: G0-G2 63.2%; G3 36.8%;
Gupta et al. 2016 [28]	IN	locally advanced HNSCC, 5 studies: 562 patients CCRT 66-70 Gy/33-35 fractions; 557 patients AFRT 64-70 Gy/33-42 fractions.	meta-analysis; *RTOG toxicity score, NCI CTCAE scale version 2.0 and 3.0*	G3/G4: CCRT 54.3%; AFRT 66.3%
Chemotherapy				
Raber-Durlacher et al. 2000 [29]	NL	solid tumors; 150 patients.	retrospective, single-centre study; *WHO scale*	Total: 31%; G1 11%; G2 17%; G3 4%; G4 0%
Nishimura et al. 2012 [30]	JP	solid tumors; 227 patients.	prospective, observational, single-centre study; *NCI CTCAE scale version 3.0*	Total: breast cancer 76.5%; HNC 67.7%; colorectal cancer 63%; esophageal cancer 57.8%; malignant lymphoma 42.9%; G ≥3: 4.8%
Wuketich et al. 2012 [31]	AT	solid tumors; 298 outpatients.	prospective, observational, single-centre study; *WHO scale*	Total: 46.3%; G1 40.3%; G2 5.0%; G3/G4 1%
Martinez et al. 2014 [32]	PT	30 patients: 22 acute leukemia, 8 NHL; 73 episodes.	prospective, observational, single-centre study; *WHO scale*	Total: 26% of 73 episodes; G1/G2 21.9%; G3/G4 4.1%
Peric & Reeves 2015 [33]	US	chemotherapy dosing in acute myeloid leukemia; 78 patients: 12 capped doses (capped), 24 uncapped doses (uncapped), 42 low body surface area.	retrospective, single-centre study; *Documented mucositis, scale not given*	Total documented mucositis: capped 50%; uncapped 41.7%; low body surface area 42.8%
Tachi et al. 2015 [34]	JP	breast cancer; 48 outpatients.	prospective, observational, single-centre study; *NCI CTCAE scale version 4.0*	Total (47 patients): 25.5%; G1 21.3%; G2 4.3%; G3 0%

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
Rashid et al 2015 [35]	US	metastatic breast cancer; 1682 patients	retrospective, multicentre, database analysis; *ICD-9 diagnosis code for stomatitis*	Stomatitis 3.4%
Miroddi et al. 2015 [36]	IT, GB	colorectal cancer, ± anti-Epidermal Growth Factor Receptor monoclonal antibodies (anti-EGFR MoAbs): 9 double arm comparisons, 7470 patients	meta-analysis; *NCI CTCAE scale version 2.0 and 3.0*	G3/G4: with anti-EGFR MoAbs 7.1%; without anti-EGFR MoAbs 2%
Shameem et al. 2015 [37]	US	mTOR (rapamycin) inhibitors for solid tumors; 2725 patients: 1967 everolimus, 758 temsirolimus.	meta-analysis; *NCI CTCAE scale version 2.0 or 3.0*	Total (all-grade stomatitis): 33.5%; High-grade stomatitis: 4.1%; everolimus 5.4%, temsirolimus 1.2%
Rugo et al. 2016 [38]	US, DE, FR, CH	everolimus (mTOR inhibitor) in solid tumors: 5 double arm comparisons, 2526 patients: 1455 everolimus, 1071 placebo.	meta-analysis; *NCI CTCAE scale version 3.0*	Total stomatitis: everolimus 67% (range 59% - 71%, thereof 89% first episodes), rate of second episode in patients with first episode 40%; placebo 19% (range 11% - 29%); everolimus: G3/G4 9%, G4 0.1%
Zhang et al. 2016 [39]	CN	chemotherapy regimens for metastatic/advanced breast cancer: 5 double arm comparisons, 1141 patients.	meta-analysis; *Scales not given*	Total stomatitis: cyclophosphamide+methotrexate+5-fluorouracil 14.5%/5.5%; doxorubicin 10%/7.6%; doxorubicin+paclitaxel 4.3%/0.8%; capecitabine 2.6%/0.9%; fluorouracil+doxorubicin+cyclophosphamide 1.6%/0.8%
Marschner et al. 2016 [40]	DE	250 patients with signal transduction inhibitors for advanced/ metastasized renal cell carcinoma.	prospective, observational multi-centre registry-based study; *NCI CTCAE scale version 3.0*	Total mucositis/stomatitis: 14.4%, G3/4 1.4%; bevacizumab + interferon 0%; sorafenib 12.0%, G3/G4 4.0%; sunitinib 23.2%, G3/G4 1.6%; temsirolimus 11.4% G3/G4 0%
Al Ibraheemi et al. 2016 [41]	JO	breast cancer; 75 female patients.	prospective, observational single-centre study; *WHO scale*	Total OM: 81.3%; G1 31.3%, G2 52.4%, G3 16.3%
Mixed tumor types and treatment				
Cheng et al. 2010 [42]	HK	chemotherapy, RT or CCRT for cancer; 137 patients.	prospective, observational, multicentre study; *WHO scale*	Total: 89.8%; G1/G2 40.1%; G3/G4 49.6%
Palliative Care				
Mercadante et al. 2015 [43]	IT	669 patients with advanced cancer.	prospective, observational, multicentre study; *WHO scale, NCI*	Total mucositis: 22.3% (146 patients);

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Incidence/frequency of oral mucositis/stomatitis
			CTCAE scale version 4.0	WHO grading: G1 63.1%, G2 26.2%, G3/G4 10.7%; CTCAE grading: G1 45.9%, G2 38.5%, G3/G4 15.6%
Nakajima et al. 2016 [44]	JP	Terminal stage of cancer: 115 patients good oral intake group, 158 patients poor oral intake group.	retrospective, observational, single-centre study; *Scale not given*	Total stomatitis: 13.9%; Good oral intake group: 10.4%; Poor oral intake group: 16.5%

Supplement Table 4. Incidence of oral mucositis/stomatitis in hematology/oncology patients

Data on incidence of oral mucositis/stomatitis were extracted from 43 JA describing 43 studies.

Mucositis assessment: WHO-scale = grading scale for OM developed by the World Health Organization; *NCI-CTCAE* = National Cancer Institute – Common Terminology Criteria for Adverse Events; *RTOG* = Radiation Therapy Oncology Group Criteria to score acute radiation morbidity.

G = Grade of oral mucositis; HSCT = hematopoietic stem cell transplantation; TBI = total body irradiation;CY = cyclophosphamide; RIC = reduced-intensity conditioning; MAC = myeloablative conditioning; RT = radiotherapy; CCRT = concurrent chemoradiotherapy; HPV = human papillomavirus; NPC = nasopharyngeal carcinoma; head and neck squamous cell carcinoma = HNSCC; VMAT = volume-modulated arc therapy; PBRT = proton beam radiation therapy; IMRT = intensity-modulated radiotherapy; AFRT = altered fractionation radiotherapy; PEG = percutaneous endoscopic gastrostomy; NHL = non-Hodgkin's lymphoma.

GB=United Kingdom; US=United States; AT=Austria; BE=Belgium; CH=Switzerland; CZ=Czech Republic; DE=Germany; FI=Finland; IE=Ireland; IT=Italy; NL=Netherlands; SE=Sweden; CA=Canada; JP=Japan; CN=China; ES=Spain; TW=Taiwan; IN=India; PT=Portugal; FR=France; JO=Jordan; HK=Hong Kong.

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Supplemental Table 5. Cost/resource use associated with oral mucositis/stomatitis in hematology/oncology patients

Author Year Source	Country	Patients	Study design *Mucositis assessment*	Cost perspective	Cost / resource use associated with oral mucositis/stomatitis
Hematopoietic Stem Cell Transplantation (HSCT)					
Sonis et al. 2001 [45]	US, NL	HSCT, 92 patients.	prospective observational and retrospective multicentre study and database analysis; *OMAS scale*	provider perspective	**Cost:** Incremental costs: USD42,749 of mean hospital charges; One point increase in OMAS score is followed by additional hospital charges of USD25,405
Vera-Llonch et al. 2007 [4]	US	allogeneic HSCT, 281 patients.	retrospective, single-centre study; *Discrete OM scale according to description in the publication*	provider perspective	**Cost:** Incremental costs of total charges: OM G1 USD37,810; OM G2 USD98,570; OM G3 USD65,774; OM G4 USD91,373; OM G5 USD223,426 **Resource use:** Mean days with TPN 6.7 G0, 7.7 G1, 8.8 G2, 10.2 G3, 13.2 G4, 14.0 G5; with parenteral narcotic therapy 7.6 G0, 10.8 G1, 10.7 G2, 11.5 G3, 14.0 G4, 17.2 G5; mean LOS (days) 28.1 G0, 30.3 G1, 34.5 G2, 32.7 G3, 35.9 G4, 42.4 G5.
Jones et al. 2008 [5]	US	autologous HSCT, 8,891 patients.	retrospective, multicentre database analysis; *ICD-9 diagnosis codes*	payer perspective	**Cost:** Increased hospital costs range USD15,000 to USD50,000; Medicare cost-to-charge ratios for urban centers (2003)
McCann et al. 2009 [6]	AT, BE, CH, CZ, DE, FI, GB, IE, IT, NL, SE	autologous HSCT; 197 patients, 109 MM, 88 NHL.	prospective observational multicentre study; *WHO scale*		**Resource use:** Mean days with opioid use 0.3 G0, 0.9 G1, 2.6 G2, 6.5 G3, 4.8 G4; with TPN 2.2 G0, 2.4 G1, 2.9 G2, 5.4 G3, 4.9 G4; with antibiotic use 4.8 G0, 5.5 G1, 8.7 G2, 9.1 G3, 8.3 G4; mean LOS (days): MM 17.0 G0, 19.8 G1, 19.7 G2, 21.5 G3, 21.5 G4; NHL 21.1 G0, 23.1 G1, 24.1 G2, 22.2 G3, 23.8 G4.
Bezinelli et al. 2014 [1]	BR	autologous and allogeneic HSCT, 167 patients (91 LLLT, oral care; 76 no LLLT, no oral care).	retrospective, single-centre study; *WHO scale*	provider perspective	**Cost:** Mean incremental cost for HSCT with need for parenteral nutrition and opioids due to OM: autologous HSCT, USD10,558; allogeneic HSCT, USD16,297 **Resource use:** No LLLT: percent of patients with TPN 0.0% G1, 0.0%

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

					G2, 100% G3/G4; with opioid prescription 1.7% G1, 20.0% G2, 78.3% G3/G4; with fever >37.8°C 4.5% G1, 27.3% G2, 68.2% G3/G4, with infection confirmed by culture 100% G3/G4.
Head and Neck Cancer (HNC)					
Peterman et al. 2001 [46]	US	HNC, 45 patients.	retrospective, single-centre study; *Scale not given*	low: payer perspective; high:provider perspective	**Cost:** Estimates of incremental costs as range of low mean - high mean (low: Medicare reimbursement; high: hospital billing) Incremental professional time USD122-194; Outpatient support USD534-828; Prescription medications USD452-1,049; Hospitalizations USD1,840-1,966; Total costs USD2,949-4,037
Elting et al. 2007 [47]	US	HNC with RT with or without chemotherapy; 204 patients.	retrospective, single-centre study; *NCI CTCAE scale version 2.0*	provider perspective	**Cost:** Average increase in costs (2006 USD): G1/G2 USD1,700; G3/G4 USD3,600; mean incremental cost with OM: RT: USD5,678; CCRT: USD6,046; incremental cost of care: RT no OM/G1-G2 USD1,900; G1-G2/G3-G4 USD2,100-2,200; CCRT no OM/G1-G2 USD2,200-2,400; G1-G2/G3-G4 USD2,400-2,500 **Resource use:** Mean LOS (days) RT 3.6 G1/G2, 6.8 G3/G4, CCRT 3.0 G0, 7.4 G1/G2, 7.8 G3/G4; mean ED visits RT 0.1 G0, 0.3 G1/G2, 0.5 G3/G4, CCRT 0 G0, 0.9 G1/G2, 0.9 G3/G4; mean days with opioids RT 15.9 G0, 27.6 G1/G2, 28.6 G3/G4, CCRT 14.5 G0, 33.9 G1/G2, 34.3 G3/G4; mean days antimicrobials oral RT 0.8 G0, 1.4 G1/G2, 0.8 G3/G4, CCRT 0 G0, 7.5 G1/G2, 6.3 G3/G4, intravenous RT 0 G0, 0.7 G1/G2, 0.4 G3/G4, CCRT 0 G0, 1.0 G1/G2, 1.3 G3/G4; gastrostomy tube mean days during RT (all patients) RT 1.3 G0, 7.4 G1/G2, 8.5 G3/G4, CCRT 0.5 G0, 17.2 G1/G2, 16.3 G3/G4.
Murphy et al. 2009 [48]	US	HNC with RT with or without chemotherapy; 75 patients	prospective, longitudinal, multicentre, study; *Oral Mucositis Weekly Questionnaire-HNC (OMWQ-HN) 5-point scale to quantify the degree of mouth and throat soreness (MTS)*		**Resource use:** Maximum pain score (0=none n=2; 1=a little n=5; 2=moderate n=11; 3=quite a lot n=38; 4=extreme n=19): mean LOS in days 1.5 G0, 1.0 G1, 1.2 G2, 1.6 G3, 2.3 G4; Feeding tube in percent of patients 0% G0, 0% G1, 9% G2, 26% G3, 32% G4; mean TPN in days 0 G0, 0 G1, 0 G2, 0.1 G3, 1.2 G4; Mean nutritional visits 2.0 G0, 1.6 G1, 1.8 G2, 2.4 G3, 3.6 G4. 30% of hospital admissions due to mucositis.
Chemotherapy					

Oncol Res Treat
DOI: 10.1159/000487085

Elting et al. 2003 [49]	US	chemotherapy for solid tumors, 599 patients with mucositis in 37% of 1,236 chemotherapy cycles.	retrospective, single-centre study; *NCI CTCAE scale for mucositis not due to radiation*	payer perspective	**Cost:** Incremental costs: Hospitalization USD2384; Per chemotherapy cycle USD2,725 (G1/G2); USD5,565 (G3/G4); mean Medicare payments per day of hospitalization **Resource use:** mean LOS (days) 3.9 no OM, 6.3 any grade OM, 8.16 G3/G4; Mean ED visits 0.8 no OM, 1.0 any grade OM, 1.1 G3/G4; percent of patients with TPN 0 no OM, 3% any grade OM, 10% G3/G4; with opioids <1% no OM, 7% any grade OM, 17% G3/G4; with antibacterial antibiotics 36% no OM, 68% any grade OM, 87% G3/G4.
Gatzemeier et al. 2008 [50]	DE	NSCLC, based on 2 trials: erlotinib, 485 patients; docetaxel, 276 patients; pemetrexed, 265 patients.	piggy-back analysis; *NCI CTCAE scale version 2.0*	payer perspective	**Cost:** Hospitalization EUR2,014.95 (USD2,231; 27.07.2015); German statutory health insurance perspective (2008)
Mickisch et al. 2010 [51]	DE	renal cell carcinoma, based on 2 trials: bevacizumab/interferon-α2a, 325 patients; sunitinib, 375 patients.	piggy-back analysis; *NCI CTCAE scale version 3.0*	payer perspective	**Cost:** Mucosal inflammation: EUR45 (G2) (USD50; 27.07.2015), EUR1,713 (G3/G4) (USD1,896; 27.07.2015); Stomatitis: EUR65 (G2) (USD72; 27.07.2015), EUR1,614 (G3/G4) (USD1,787; 27.07.2015); German DRG funding system catalogue (2008)
Mittmann et al. 2010 [52]	CA	breast cancer, based on one trial, 1,491 women.	retrospective, multicentre cost data (Ontario Case Costing Initiative: patient-level costs for inpatient and ambulatory care cases in Ontario); *NCI CTCAE scale version 1.0*	payer perspective	**Cost:** G3/G4 stomatitis: CAD3,151.18 (USD2,298.44; 15.12.2015); Canadian provincial government costs
Banz et al. 2011 [53]; Nuijten et al. 2012 [54];	DE, FR, IT, ES	NSCLC, based on 2 trials: erlotinib, 433 (438) patients; pemetrexed, 441 patients.	piggy-back analysis; *NCI CTCAE scale version 3.0*	payer perspective	**Cost:** G3/G4 mucositis/stomatitis: Germany EUR312 (USD354; 30.03.2016), France EUR441 (USD500;30.03.2016), Italy EUR45 (USD51; 30.03.2016), Spain EUR102 (USD116; 30.03.2016)
Rashid et al. 2016 [55]	US	metastatic breast cancer; 1682 patients	retrospective cohort database analysis; *ICD-9*	total of plan paid plus patient paid amounts for each	**Cost:** Single episodes of stomatitis (per episode): outpatient EUR85 (USD91; 07.12.2016), hospital EUR4,313 (USD4,630; 07.12.2016);

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

			diagnosis code for stomatitis	episode	Multiple episodes of stomatitis (per episode): hospital plus emergency room EUR8,349 (USD8,963; 07.12.2016); 2013 US dollars
Mixed tumor types and treatment					
Elting & Shih 2004 [56]	US	cancer patients	combined meta-analysis and population-based estimates of cost from the Texas Hospital Discharge Database; *ICD-9 diagnosis codes*	payer and provider perspective	**Cost:** Mean inpatient cost USD7,985 (based on 557,281 inpatient claims from statewide registry; 2002 Medicare costs); Range out- and inpatient cost USD3,053-4,179 (based on reports in the literature)
Nonzee et al. 2008 [57]	US	CCRT for HNC, 99 patients; NSCLC, 40 patients.	retrospective, multicentre study; *Grading type not given, mucositis / pharyngitis defined as toxicity that resulted in documentation in physician chart notes*	provider perspective	**Cost:** Incremental costs: Total cost USD18,515; Hospitalization USD12,600; Supportive care pharmaceuticals USD111; 2005 costs **Resource use:** mean LOS (days): HNC 5 no OM, 15 severe OM; NSCLC 5 no OM, 13 severe OM; median number of clinic visits: 18 (range 1-33) no OM, 25 (range 17-35) severe OM.

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Supplement Table 5. Cost/resource use associated with oral mucositis/stomatitis in hematology/oncology patients

Data on cost and/or resource use related to oral mucositis/stomatitis were extracted from 17 JA describing 16 studies.

Mucositis assessment: OMAS = The Oral Mucositis Assessment Score; *WHO-scale* = grading scale for OM developed by the World Health Organization; *NCI-CTCAE* = National Cancer Institute – Common Terminology Criteria for Adverse Events.

G = Grade of oral mucositis; HSCT = hematopoietic stem cell transplantation; LLLT = low-level laser therapy; RT = radiotherapy; CCRT = concurrent chemoradiotherapy; NSCLC = non-small-cell lung cancer; TPN = total parenteral nutrition; LOS = length of hospital stay; MM = multiple myeloma; NHL = Non-Hodgkin`s lymphoma; ED = emergency department.

US=United States; NL=Netherlands; AT=Austria; BE=Belgium; CH=Switzerland; CZ=Czech Republic; DE=Germany; FI=Finland; GB=United Kingdom; IE=Ireland; IT=Italy; SE=Sweden; BR=Brazil; CA=Canada; FR=France; IT=Italy; ES=Spain.

Supplemental Table 6. Impact of oral mucositis/stomatitis on health-related quality of life (HRQoL) in hematology/oncology patients

Author Year Source	**Country**	**Patients**	**Study design** ***Mucositis assessment***	**Measurement of patient reported outcomes (PROs)**	**Influence of OM on HRQoL**
Hematopoietic Stem Cell Transplantation (HSCT)					
Sakellari et al. 2015 [58]	GR	autologous HSCT; 39 patients	prospective, observational, multicentre study; *WHO scale*	HRQoL: FACT-G; OM pain: MTS, MTS activity limitations questionnaire (MTS-AL)	Mean total **FACT-G** score: 78.8±19.1 on day 1, 70.5±21.3 on day +7, 80.9±15.8 on discharge (p=0.006 between day 1 and day+7); decrease in physical well-being domain between day 1 (19.6±6.7) and day +7 (14.8±6.8) (p<0.001); on the day of discharge, all scores recovered. Median **MTS** score among patients with OM was 0 on day 1, 2.5 on day +7, and 0 on discharge. 25 % of the patients reported a score ≥6 on day +7.
Head and Neck Cancer (HNC)					

Oncol Res Treat
DOI: 10.1159/000487085

Weymuller et al. 2000 [59]	US	HNC; 210 patients with different therapies.	prospective, observational, single-centre study; *No grading of OM available*	UWQOL	TNM stage I-IV influenced composite QoL scores significantly ($p < 0.001$); Site of tumor (oral cavity, oropharynx, hypopharynx, or larynx) affected composite QoL scores by 3 months ($p < 0.05$).
Epstein et al. 2001 [60]	CA	HNC with RT; 20 patients; mean total dose 52.17 Gy (range 35 Gy-60 Gy), mean 24 fractions (range 20 – 30 fractions).	prospective, longitudinal, observational, single-centre study; *EORTC QLQ-C30 with addendum to assess oral symptoms and function*	EORTC QLQ-C30	Mean **EORTC QLQ-C30** scores before cancer therapy / 1 month / 6 months after treatment: Overall physical: 5.5 / 3.4 / 4.3, $p < 0.0005$; Overall QoL: 5.65 / 3.40 / 4.45, $p < 0.0005$; Physical: 96.0 / 51.0 / 78.0, $p < 0.0005$; Role: 95.0 / 45.0 / 80.0, $p < 0.0005$; Emotional: 76.3 / 52.9 / 65.4, $p = 0.002$; Cognitive: 85.0 / 67.5 / 79.2, $p = 0.003$; Social: 86.7 / 53.3 / 74.2, $p < 0.0005$; Global: 76.3 / 40.0 / 56.7, $p < 0.0005$.
Elting et al. 2008 [61]	AU, DE, ES, FR, GB, IT, NL, US	HNC with RT; 191 patients: 126 patients with oral cavity or oropharynx tumors, 65 patients with tumors of the larynx or hypopharynx.	prospective, observational, multicentre study; *Patient-reported mouth and throat soreness (MTS)*	OMDQ with MTS, FACT-G, FACIT	Mean **FACT-G** scores at baseline / week 6: Total: 85.1 / 69; Functional well-being domain: 18.3 / 12.3; Mean MTS scores and FACIT-fatigue scores are shown in figures, only baseline values are available: MTS: Oral or Oropharynx 0.84; Larynx or Hypopharynx 0.79; FACIT: Oral or Oropharynx 41.4; Larynx or Hypopharynx 42.2; The reduction in QOL associated with MTS was significant, and there was a correlation between severity of MTS and drop in QOL.
Citak & Tulek 2013 [62]	TR	HNC with RT; 54 out-patients; average dose 54 Gy-70 Gy in 5 or 6 weeks	prospective, single-centre, longitudinal observational study; *RTOG toxicity score*	EORTC QLQ-C30 (version 3.0), EORTC QLQ-H&N35	Mean **EORTC QLQ-C30** scores before / after /1 month after / 3 months after RT: Physical: 73.95 / 68.88 / 83.08 / 90.24, $p = 0.000$; Role: 79.93 / 71.60 / 88.27 / 95.67, $p = 0.000$; Emotional: 75.92 / 71.29 / 88.42 / 95.21, $p = 0.000$; Cognitive: 89.19 / 88.58 / 94.75 / 96.91, $p = 0.000$; Social: 72.53 / 63.27 / 82.40 / 90.12, $p = 0.000$; Global: 62.65 / 46.14 / 61.26 / 77.31, $p = 0.000$; Correlation of RTOG toxicity and EORTC QLQ-C30 scores: Global: mucosa $p = 0.003$; salivary gland $p = 0.011$. Mean **EORTC QLQ-H&N35** scores before / after /1 month after / 3 months after RT:

Oncol Res Treat
DOI: 10.1159/000487085

					Pain: 17.43 / 38.27 / 15.12 / 4.62, p = 0.000; Swallowing: 20.98 / 39.19 / 12.65 / 3.70, p = 0.000; Social eating: 23.45 / 38.27 / 12.80 / 4.62, p = 0.000; Opening mouth: 18.51 / 36.41 / 9.87 / 7.40, p = 0.000; Dry mouh: 27.16 / 50.61 / 35.80 / 25.92, p = 0.000; Sticky saliva: 31.71 / 48.76 / 31.48 / 24.69, p = 0.000; Feeling ill: 35.18 / 40.74 / 13.58 / 3.08, p = 0.000.
Xu et al. 2015 [23]	CN	stage III or IVb NPC: 44 patients; 23 patients CRT (IMRT and cisplatin); 21 patients ERT (IMRT and cetuximab); T1/T2 disease 66Gy/30 fractions, T3/T4 disease 70.4Gy/32 fractions	prospective, observational, single-centre study; *NCI CTCAE scale version 3.0*	EORTC QLQ-H&N35	Mean **EORTC QLQ-H&N35** scores during RT and 3 months after RT: Pain: 25.6 / 23.7 CRT, 40.1 / 16.7 ERT (p = 0.003 / 0.775); Swallowing: 22.6 / 12.2 CRT, 40.2 / 18.3 ERT (p = 0.000 / 0.633); Speech: 11.0 / 12.8 CRT, 28.4 / 17.8 ERT (p = 0.003 / 0.443); Eating: 18.4 / 21.7 CRT, 32.8 / 19.5 ERT (p = 0.003 / 1.000); Feeling ill: 24.8 / 30.8 CRT, 40.8 / 33.3 ERT (p = 0.004 / 0.633); Overall: 21.5 /31.3 CRT, 31.8 / 35.9 ERT (p = 0.002 / 0.566).
Chemotherapy					
Dodd et al. 2001 [63]	US	solid tumors; 77 outpatients, 28 mucositis (OM), 49 no mucositis (no OM).	prospective, comparative, longitudinal, observational, multicentre study; *Oral Assessment Guide (OAG)*	MQOLS-CA, POMS	Comparison start of chemotherapy / start of mucositis or end of study: Mean **MQOLS-CA** score: OM 69.92 / 62.24; no OM 75.33 / 69.44; Mean **POMS** score (p for significant differences between OM vs. no OM): Anxiety: OM 5.46 / 6.79, no OM 4.89 / 4.58, not statistically significant; Depression: OM 3.43 / 7.57, no OM 3.69 / 4.31, p < 0.001; Anger: OM 2.50 / 5.07, no OM 3.21 / 3.53, p < 0.01; Vigor: OM 7.89 / 5.36, no OM 9.76 / 8.29, not statistically significant; Fatigue: OM 7.54 / 11.54, no OM 5.19 / 7.69, not statistically significant; Confusion: OM 4.22 / 4.57, no OM 2.75 / 3.15, not statistically significant; Total Mood Disturbance: OM 15.26 / 30.18, no OM 9.98 / 14.97, p = 0.03.
Kim et al. 2012 [64]	KR	solid tumors; 322 patients: 458 CT cycles OM-negative, 175 CT	prospective, observational, single-centre study; *interviews, OM diaries on*	FACT-G version 4	Mean **FACT-G** score OM-negative /OM-positive CT cycles: Physical: 22.47 / 19.09, p<0.001; Social / family: 18.04 / 18.33, p = 0.569;

Oncol Res Treat
DOI: 10.1159/000487085

		cycles OM-positive.	*OM-related symptoms*		Emotional: 17.97 / 16.74, p<0.001; Educational: 16.55 / 15.90, p = 0.216; Total: 75.09 / 70.26, p<0.001.
Martinez et al. 2014 [32]	PT	30 patients: 22 AL, 8 NHL.	prospective, longitudinal, observational, single-centre study; *WHO scale*	OMDQ, UK Oral Mucositis in Cancer Group analog pain scale	The results of **OMDQ** showed some limitations in QoL of patients with mucositis related with the ability to eat, drink, and with mouth pain (p<0.001). The higher the grade of mucositis, the more likely the patients (with AL and NHL) experience **pain** (p<0.001).
Tachi et al. 2015 [34]	JP	breast cancer; 48 outpatients.	prospective, observational, single-centre, study; *NCI CTCAE scale version 4.0*	EQ-5D, QOL-ACD	Mean **EQ-5D** utility values before CT / after CT: OM G0: 0.84 / 0.74, OM G1-3: 0.84 / 0.68, p = 0.237; Oral pain G0: 0.85 / 0.74, Oral pain G1-3: 0.78 / 0.66, p = 0.927; Mean **QOL-ACD** total score before CT / after CT: OM G0: 88.54 / 84.46, OM G1-3: 88.58 / 84.92, p = 0.885; Oral pain G0: 88.62 / 85.21, Oral pain G1-3: 88.00 / 79.20, p=0.309. Mean **QOL-ACD** subscale score before CT / after CT: Activity: OM G0: 4.56 / 4.12, OM G1-3: 4.60 / 4.24, p = 0.793; Oral pain G0: 4.58 / 4.21, Oral pain G1-3: 4.50 / 3.63, p = 0.255; Physical condition: OM G0: 4.34 / 3.96, OM G1-3: 4.32 / 3.93, p = 0.959; Oral pain G0: 4.33 / 4.02, Oral pain G1-3: 4.37 / 3.37, p = 0.014 (p<0.05); Psycological condition: OM G0: 4.04 / 3.78, OM G1-3: 3.83 / 3.70, p = 0.602; Oral pain G0: 3.94 / 3.73, Oral pain G1-3: 4.36 / 4.00, p = 0.655; Social relationships: OM G0: 2.31 / 2.68, OM G1-3: 2.48 / 2.82, p = 0.875; Oral pain G0: 2.40 / 2.72, Oral pain G1-3: 1.96 / 2.68, p = 0.160.
Al-Batran et al. 2015 [65]	DE	doxetaxel toxicities with metastatic cancer: 2659 patients, prostate cancer 48.1%, breast cancer 17.1%, NSCLC 15.8%	prospective, observational, multicentre study; *NCI CTCAE scale version 3.0*	EORTC QLQ-C30	Mean **EORTC QLQ-C30** scores (pooled over week 4 to 40): Stomatitis G3/G4 yes 36.41, no 50.88 (p = 0.01854).
Goebell et al. 2016 [66]	DE	metastatic renal cell carcinoma: 60 patients	prospective, observational multicentre study; *NCI*	FACIT-F (FACT-G plus subscale for	Mean overall **FACT-G** total score 75.9 ± 16.7 points (possible maximum 108 points);

			CTCAE scale version 3.0	fatigue)	Mucositis: 16 patients with FACT-G global score ≤75 points, severity of OM 2.8 ± 1.3; 18 patients with FACT-G global score ≥76 points, severity of OM 1.6 ± 0.8; statistically significant effect ($p < 0.05$) on physical subscale ($r = -0.508$).
Mixed tumor types and treatment					
Öhrn et al. 2001 [67]	SE	HNC, 18 patients; haematological malignancies, 23 patients; RT in HNC 30 Gy-70 Gy in 5 to 7 weeks (25 to 35 fractions).	prospective, observational, single-centre study; *Visual Analogue Scale (VAS), Oral Symptom Summary Score (OSSS),Oral Mucositis Index (OMI)*	EORTC QLQ-C30, EORTC QLQ-H&N35	HNC patients: mean **EORTC QLQ-H&N35** scores before / during / end of / 1 month after RT: Pain: 21.4 / 31.7 / 44.8 / 24.9, p = 0.0077; Swallowing: 15.6 / 25.4 / 46.3 / 27.6, p = 0.0046; Social eating: 14.6 / 33.2 / 49.1 / 34.3, p<0.0001; Open mouth: 14.6 / 12.4 / 20.8 / 14.5, not statistically significant; Dry mouth: 14.4 / 52.1 / 54.2 / 52.0, p<0.0001; Sticky saliva: 7.1 / 66.6 / 78.6 / 57.1, p<0.0001; Feeling ill: 4.1 / 18.6 / 31.2 / 29.1, p = 0.0025. HNC patients: mean **EORTC QLQ-C30** scores before / during / end of / 1 month after RT: Physical: 90.7 / 86.3 / 75.5 / 81.1, p = 0.0003; Role: 53.7 / 56.9 / 38.0 / 53.7, not statistically significant; Emotional: 77.5 / 85.2 / 72.8 / 81.0, not statistically significant; Cognitive: 88.8 / 90.7 / 76.8 / 84.3, not statistically significant; Social: 79.7 / 79.7 / 64.8 / 81.5, p = 0.0431; Global: 72.3 / 62.0 / 46.3 / 60.2, p = 0.0003; Summary of Oral Symptoms Scores (OSSS): 132.5 / 408.3 / 509.7 / 389.3, p<0.0001. Patients with haematological malignancies: mean **EORTC QLQ-C30** scores before / after two weeks / end of CT cycle: Physical: 86.6 / 84.6 / 87.8, not statistically significant; Role: 63.1 / 58.0 / 69.6, not statistically significant; Emotional: 86.7 / 90.1 / 89.9, not statistically significant; Cognitive: 89.0 / 89.8 / 92.0, not statistically significant; Social: 74.6 / 73.9 / 80.4, not statistically significant; Global: 75.5 / 65.3 / 71.4, not statistically significant; Summary of Oral Symptoms Scores (OSSS): 66.6 / 92.8 / 68.6, not

Oncol Res Treat
DOI: 10.1159/000487085

					statistically significant.
Cheng et al. 2007 [68]; Cheng et al. 2007 [69];	HK	chemotherapy, RT or CCRT for solid tumors; 88 patients, 38 in-patients, 50 out-patients.	prospective, observational, single-centre study; *WHO scale*	Chinese version-FACT-G	Mean **Ch-FACT-G** score by severity of OM Slight / Moderate / Severe / Very severe: Physical: 8.64 / 19.00 / 17.00 / 11.44, p = 0.124; Social / family: 18.25 / 15.53 / 14.21 / 15.67, p = 0.013 (p<0.05); Emotional: 16.46 / 16.37 / 13.93 / 12.89, p = 0.052; Functional: 12.79 / 11.07 / 10.14 / 10.33, p = 0.519; Mean **Ch-FACT-G** score by type of cancer therapy CT / RT / CRT: Physical: 16.12 / 15.00 / 13.54, p = 0.28; Social / family: 16.19 / 15.21 / 17.46, p = 0.21; Emotional: 15.83 / 15.06 / 15.69, p = 0.49; Functional: 15.12 / 10.53 / 10.79, p = 0.02 (p<0.05).
Cheng et al. 2010 [42]	HK	chemotherapy, RT or CCRT for cancer; 137 patients.	prospective, observational, multicentre study; *WHO scale*	OMQoL	Mean **OMQoL** scores by OM severity no OM / mild OM (G1 and G2) / severe OM (G3 and G4): Symptom subscale: Peak scores: 97.1 / 89.3 / 60, p<0.01; AUC scores: -7.9 / -8 / -28, p<0.01; Diet subscale: Peak scores: 92.5 / 82.1 / 47.9, p<0.01; AUC scores: -6 / -14.5 / -40.1, p<0.01; Social subscale: Peak scores: 98.9 / 93.6 / 62.1, p<0.01; AUC scores: -1.2 / -5.7 / -25.8, p<0.01; Swallowing subscale: Peak scores: 97.6 / 89.1 / 52.4, p<0.01; AUC scores: -1.9 / -9.1 / -34.5, p<0.01.
Chaitanya et al. 2016 [70]	IN	455 cancer patients with OM: Group I chemotherapy, Group II CCRT, Group III RT within 14 days of initiation, Group IV RT after 14 days of initiation	prospective, observational, multicentre study; *no scale given, division in mild, moderate, severe OM*	Hospital Anxiety and Depression Scale (HADS)	OM severe 44.4%, moderate 32.5%, mild 23.1%; Severe OM group III > Group I > Group IV > Group II; Severe OM and established anxiety: Group III 58.8% , Group IV 47.5%; Mild OM and borderline anxiety: Group I 47.2%, Group II 40% (p = 0.01); Severe OM and established depression: Group III 56.4%, Group IV 39.6%; Mild OM and abnormal depression, moderate OM and established depression: association in Group I and Group II (p = 0.02)

Oncology Research and Treatment

Systematic Review

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental Material

Supplement Table 6. Impact of oral mucositis/stomatitis on health-related quality of life (HRQoL) in hematology/oncology patients

Data on the influence of oral mucositis/stomatitis on HRQoL were extracted from 17 JA describing 16 studies.

Mucositis assessment: WHO-scale = grading scale for OM developed by the World Health Organization; *RTOG* = Radiation Therapy Oncology Group Criteria to score acute radiation morbidity; *NCI-CTCAE* = National Cancer Institute – Common Terminology Criteria for Adverse Events.

Measurement of patient reported outcomes (PROs): EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality-of-Life Questionnaire; EORTC QLQ-H&N35 = European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire for Head and Neck cancer patients; EQ-5D = European Quality of Life Utility Scale; FACIT = Functional Assessment of Chronic Illness Therapy-Fatigue subscale questionnaire; FACT-G = Functional Assessment of Cancer Therapy-General score; MTS = patient-reported mouth and throat soreness; MQOLS-CA = Multidimensional Quality of Life scale Cancer version; OMDQ = Oral Mucositis Daily Questionnaire; OMWQ-HN = Oral Mucositis Weekly Questionnaire-Head and Neck; UWQOL = University of Washington Quality-of-Life questionnaire; OMQoL = OM-specific QoL measure; POMS = Profile of Mood States; QOL-ACD = QOL Questionnaire for Cancer Patients Treated with Anticancer Drugs.

G = Grade of oral mucositis or oral pain; RT = radiotherapy; CT = chemotherapy; IMRT = intensity-modulated radiotherapy; NPC = nasopharyngeal carcinoma; AL = acute leukemia; NHL = Non-Hodgkin`s lymphoma; NSCLC = non-small-cell lung cancer; AUC = area under the curve.

GR=Greece; US=United States; CA=Canada; AU=Australia; DE=Germany; ES=Spain; FR=France; GB=United Kingdom; IT=Italy; NL=Netherlands; TR=Turkey; CN=China; KR=Republic of Korea; PT=Portugal; JP=Japan; SE=Sweden; HK=Hong Kong; IN=India.

Oncol Res Treat
DOI: 10.1159/000487085

Supplemental References

1. Bezinelli LM, de Paula Eduardo F, da Graca Lopes RM, Biazevic MG, de Paula Eduardo C, Correa L, *et al.* Cost-effectiveness of the introduction of specialized oral care with laser therapy in hematopoietic stem cell transplantation. *Hematol Oncol* 2014; **32:** 31-9.

2. Wardley AM, Jayson GC, Swindell R, Morgenstern GR, Chang J, Bloor R, *et al.* Prospective evaluation of oral mucositis in patients receiving myeloablative conditioning regimens and haemopoietic progenitor rescue. *Br J Haematol* 2000; **110:** 292-9.

3. Grazziutti ML, Dong L, Miceli MH, Krishna SG, Kiwan E, Syed N, *et al.* Oral mucositis in myeloma patients undergoing melphalan-based autologous stem cell transplantation: incidence, risk factors and a severity predictive model. *Bone Marrow Transplant* 2006; **38:** 501-6.

4. Vera-Llonch M, Oster G, Ford CM, Lu J, Sonis S. Oral mucositis and outcomes of allogeneic hematopoietic stem-cell transplantation in patients with hematologic malignancies. *Support Care Cancer* 2007; **15:** 491-6.

5. Jones JA, Qazilbash MH, Shih YC, Cantor SB, Cooksley CD, Elting LS. In-hospital complications of autologous hematopoietic stem cell transplantation for lymphoid malignancies: clinical and economic outcomes from the Nationwide Inpatient Sample. *Cancer* 2008; **112:** 1096-105.

6. McCann S, Schwenkglenks M, Bacon P, Einsele H, D'Addio A, Maertens J, *et al.* The Prospective Oral Mucositis Audit: relationship of severe oral mucositis with clinical and medical resource use outcomes in patients receiving high-dose melphalan or BEAM-conditioning chemotherapy and autologous SCT. *Bone Marrow Transplant* 2009; **43:** 141-7.

7. Vagliano L, Feraut C, Gobetto G, Trunfio A, Errico A, Campani V, *et al.* Incidence and severity of oral mucositis in patients undergoing haematopoietic SCT--results of a multicentre study. *Bone Marrow Transplant* 2011; **46:** 727-32.

8. Gupta V, Panzarella T, Li L, Khan J, Sharma A, Lipton JH, *et al.* A prospective study comparing the outcomes and health-related quality of life in adult patients with myeloid malignancies undergoing allogeneic transplantation using myeloablative or reduced-intensity conditioning. *Biol Blood Marrow Transplant* 2012; **18:** 113-24.

9. Kashiwazaki H, Matsushita T, Sugita J, Shigematsu A, Kasashi K, Yamazaki Y, *et al.* A comparison of oral mucositis in allogeneic hematopoietic stem cell transplantation between conventional and reduced-intensity regimens. *Support Care Cancer* 2012; **20:** 933-9.

10. Urbain P, Raynor A, Bertz H, Lambert C, Biesalski HK. Role of antioxidants in buccal mucosa cells and plasma on the incidence and severity of oral mucositis after allogeneic haematopoietic cell transplantation. *Support Care Cancer* 2012; **20:** 1831-8.

11. Legert KG, Remberger M, Ringden O, Heimdahl A, Dahllof G. Reduced intensity conditioning and oral care measures prevent oral mucositis and reduces days of hospitalization in allogeneic stem cell transplantation recipients. *Support Care Cancer* 2014; **22:** 2133-40.

12. Martino M, Montanari M, Ferrara F, Ciceri F, Scortechini I, Palmieri S, *et al.* Very low rate of readmission after an early discharge outpatient model for autografting in multiple myeloma patients: an Italian multicenter retrospective study. *Biol Blood Marrow Transplant* 2014; **20:** 1026-32.

13. Wu Q, Zhang R, Wang H, You Y, Zhong Z, Hong M, *et al.* Comparison of outcomes of idarubicin intensified TBI-CY and traditional TBI-CY conditioning regimen for high-risk acute lymphoblastic leukemia undergoing allogeneic hematopoietic stem cell transplantation: A single center experience. *Leuk Res* 2015.

14. Anand A, Anandi P, Jain NA, Lu K, Dunavin N, Hourigan CS, *et al.* CD34+ selection and the severity of oropharyngeal mucositis in total body irradiation-based allogeneic stem cell transplantation. *Support Care Cancer* 2016; **24:** 815-22.

15. Chaudhry HM, Bruce AJ, Wolf RC, Litzow MR, Hogan WJ, Patnaik MS, *et al.* The Incidence and Severity of Oral Mucositis among Allogeneic Hematopoietic Stem Cell Transplantation Patients: A Systematic Review. *Biol Blood Marrow Transplant* 2016; **22:** 605-16.

16. Manas A, Palacios A, Contreras J, Sanchez-Magro I, Blanco P, Fernandez-Perez C. Incidence of oral mucositis, its treatment and pain management in patients receiving cancer treatment at Radiation Oncology Departments in Spanish hospitals (MUCODOL Study). *Clin Transl Oncol* 2009; **11:** 669-76.

17. Hu MH, Wang LW, Lu HJ, Chu PY, Tai SK, Lee TL, *et al.* Cisplatin-based chemotherapy versus cetuximab in concurrent chemoradiotherapy for locally advanced head and neck cancer treatment. *Biomed Res Int* 2014; **2014:** 904341.

18. Vatca M, Lucas JT, Jr., Laudadio J, D'Agostino RB, Waltonen JD, Sullivan CA, *et al.* Retrospective analysis of the impact of HPV status and smoking on mucositis in patients with oropharyngeal squamous cell carcinoma treated with concurrent chemotherapy and radiotherapy. *Oral Oncol* 2014; **50:** 869-76.

19. Roy S, Mallik C, Ghorai S, Hazra A, Majumdar A. Hypofractionated versus conventional radiotherapy with or without chemotherapy in head and neck cancer: a comparative study. *Clinical Cancer Investigation Journal* 2015; **4:** 140-6.

20. Tsukahara K, Kubota A, Hasegawa Y, Takemura H, Terada T, Taguchi T, *et al.* Randomized phase III trial of adjuvant chemotherapy with S-1 after curative treatment in patients with squamous-cell carcinoma of the head and neck (ACTS-HNC). *PLoS One* 2015; **10:** e0116965.

21. Hoshikawa H, Kishino T, Mori T, Indo K, Inamoto R, Akiyama K, *et al.* Clinical outcomes of nedaplatin and S-1 treatment with concurrent radiotherapy in advanced head and neck cancer. *Acta Otolaryngol* 2015; **135:** 103-8.

22. Guo R, Tang LL, Mao YP, Zhou GQ, Qi ZY, Liu LZ, *et al.* Clinical Outcomes of Volume-Modulated Arc Therapy in 205 Patients with Nasopharyngeal Carcinoma: An Analysis of Survival and Treatment Toxicities. *PLoS One* 2015; **10:** e0129679.

23. Xu T, Liu Y, Dou S, Li F, Guan X, Zhu G. Weekly cetuximab concurrent with IMRT aggravated radiation-induced oral mucositis in locally advanced nasopharyngeal carcinoma: Results of a randomized phase II study. *Oral Oncol* 2015; **51:** 875-9.

24. Romesser PB, Cahlon O, Scher ED, Hug EB, Sine K, DeSelm C, *et al.* Proton beam reirradiation for recurrent head and neck cancer: multi-institutional report on feasibility and early outcomes. *International Journal of Radiation Oncology Biology Physics* 2016; **95:** 386-95.

25. Bonner JA, Giralt J, Harari PM, Baselga J, Spencer S, Bell D, *et al.* Association of human papillomavirus and p16 status with mucositis and dysphagia for head and neck cancer patients treated with radiotherapy with or without cetuximab: Assessment from a phase 3 registration trial. *Eur J Cancer* 2016; **64:** 1-11.

26. Lin L, Yao JJ, Zhou GQ, Guo R, Zhang F, Zhang Y, *et al.* The efficacy and toxicity of individualized intensity-modulated radiotherapy based on the tumor extension patterns of nasopharyngeal carcinoma. *Oncotarget* 2016; **7:** 20680-90.

27. Xu Y, Guo Q, Lin J, Chen B, Wen J, Lu T, *et al.* Benefit of percutaneous endoscopic gastrostomy in patients undergoing definitive chemoradiotherapy for locally advanced nasopharyngeal carcinoma. *Onco Targets Ther* 2016; **9:** 6835-41.

28. Gupta T, Kannan S, Ghosh-Laskar S, Agarwal JP. Systematic Review and Meta-analysis of Conventionally Fractionated Concurrent Chemoradiotherapy versus Altered Fractionation Radiotherapy Alone in the Definitive Management of Locoregionally Advanced Head and Neck Squamous Cell Carcinoma. *Clin Oncol (R Coll Radiol)* 2016; **28:** 50-61.

29. Raber-Durlacher JE, Weijl NI, Abu Saris M, de Koning B, Zwinderman AH, Osanto S. Oral mucositis in patients treated with chemotherapy for solid tumors: a retrospective analysis of 150 cases. *Support Care Cancer* 2000; **8:** 366-71.

30. Nishimura N, Nakano K, Ueda K, Kodaira M, Yamada S, Mishima Y, *et al.* Prospective evaluation of incidence and severity of oral mucositis induced by conventional chemotherapy in solid tumors and malignant lymphomas. *Support Care Cancer* 2012; **20:** 2053-9.

31. Wuketich S, Hienz SA, Marosi C. Prevalence of clinically relevant oral mucositis in outpatients receiving myelosuppressive chemotherapy for solid tumors. *Support Care Cancer* 2012; **20:** 175-83.

32. Martinez JM, Pereira D, Chacim S, Mesquita E, Sousa I, Martins A, *et al.* Mucositis care in acute leukemia and non-Hodgkin lymphoma patients undergoing high-dose chemotherapy. *Support Care Cancer* 2014; **22:** 2563-9.

33. Peric KM, Reeves DJ. Tolerability of induction chemotherapy dosing practices in acute myeloid leukemia patients. *Leuk Res* 2015; **39:** 173-6.

34. Tachi T, Teramachi H, Tanaka K, Asano S, Osawa T, Kawashima A, *et al.* The impact of outpatient chemotherapy-related adverse events on the quality of life of breast cancer patients. *PLoS One* 2015; **10:** e0124169.

35. Rashid N, Koh HA, Baca HC, Li Z, Malecha S, Abidoye O, *et al.* Clinical Impact of Chemotherapy-Related Adverse Events in Patients with Metastatic Breast Cancer in an Integrated Health Care System. *J Manag Care Spec Pharm* 2015; **21:** 863-71.

36. Miroddi M, Sterrantino C, Simonelli I, Ciminata G, Phillips RS, Calapai G. Risk of grade 3-4 diarrhea and mucositis in colorectal cancer patients receiving anti-EGFR monoclonal antibodies regimens: A meta-analysis of 18 randomized controlled clinical trials. *Crit Rev Oncol Hematol* 2015; **96:** 355-71.

37. Shameem R, Lacouture M, Wu S. Incidence and risk of high-grade stomatitis with mTOR inhibitors in cancer patients. *Cancer Invest* 2015; **33:** 70-7.

38. Rugo HS, Hortobagyi GN, Yao J, Pavel M, Ravaud A, Franz D, *et al.* Meta-analysis of stomatitis in clinical studies of everolimus: incidence and relationship with efficacy. *Ann Oncol* 2016; **27:** 519-25.

39. Zhang XH, Hao S, Gao B, Tian WG, Jiang Y, Zhang S, *et al.* A network meta-analysis for toxicity of eight chemotherapy regimens in the treatment of metastatic/advanced breast cancer. *Oncotarget* 2016.

40. Marschner N, Muller L, Munch A, Blumenstengel K, Hutzschenreuter U, Busies S. Adverse reactions in mRCC patients documented in routine practice by German office-based oncologists and uro-oncologists. *J Oncol Pharm Pract* 2016.

41. Al Ibraheemi AA, Shamoun S. Incidence and Risk Factors of Oral Mucositis in Patients with Breast Cancer Who Receiving Chemotherapy in Al-Bashir Hospital. *Int J Hematol Oncol Stem Cell Res* 2016; **10:** 217-23.

42. Cheng KK, Leung SF, Liang RH, Tai JW, Yeung RM, Thompson DR. Severe oral mucositis associated with cancer therapy: impact on oral functional status and quality of life. *Support Care Cancer* 2010; **18:** 1477-85.

43. Mercadante S, Aielli F, Adile C, Ferrera P, Valle A, Fusco F, *et al.* Prevalence of oral mucositis, dry mouth, and dysphagia in advanced cancer patients. *Support Care Cancer* 2015; **23:** 3249-55.

44. Nakajima N. Characteristics of oral problems and effects of oral care in terminally ill patients with cancer. *American Journal of Hospice & Palliative Medicine* 2016**:** 1-5.

45. Sonis ST, Oster G, Fuchs H, Bellm L, Bradford WZ, Edelsberg J, *et al.* Oral mucositis and the clinical and economic outcomes of hematopoietic stem-cell transplantation. *J Clin Oncol* 2001; **19:** 2201-5.

46. Peterman A, Cella D, Glandon G, Dobrez D, Yount S. Mucositis in head and neck cancer: economic and quality-of-life outcomes. *J Natl Cancer Inst Monogr* 2001**:** 45-51.

47. Elting LS, Cooksley CD, Chambers MS, Garden AS. Risk, outcomes, and costs of radiation-induced oral mucositis among patients with head-and-neck malignancies. *Int J Radiation Oncology Biol Phys* 2007; **68:** 1110-20.

48. Murphy BA, Beaumont JL, Isitt J, Garden AS, Gwede CK, Trotti AM, *et al.* Mucositis-related morbidity and resource utilization in head and neck cancer patients receiving radiation therapy with or without chemotherapy. *J Pain Symptom Manage* 2009; **38:** 522-32.

49. Elting LS, Cooksley C, Chambers M, Cantor SB, Manzullo E, Rubenstein EB. The burdens of cancer therapy. Clinical and economic outcomes of chemotherapy-induced mucositis. *Cancer* 2003; **98:** 1531-9.

50. Gatzemeier U, Pirk O, Gabriel A, Kotowa W, Heigener D. Second-Line-Therapy for Non-Small Cell Lung Cancer (NSCLC) - a Retrospective Cost Analysis [Second-Line-Therapie des nichtkleinzelligen Lungenkarzinoms (NSCLC) - eine retrospektive Kostenanalyse]. *TumorDiagnostik und Therapie* 2008; **29:** 211-7.

51. Mickisch G, Gore M, Escudier B, Procopio G, Walzer S, Nuijten M. Costs of managing adverse events in the treatment of first-line metastatic renal cell carcinoma: bevacizumab in combination with interferon-alpha2a compared with sunitinib. *Br J Cancer* 2010; **102:** 80-6.

52. Mittmann N, Verma S, Koo M, Alloul K, Trudeau M. Cost effectiveness of TAC versus FAC in adjuvant treatment of node-positive breast cancer. *Curr Oncol* 2010; **17:** 7-16.

53. Banz K, Bischoff H, Brunner M, Chouaid C, de Castro Carpeno J, de Marinis F, *et al.* Comparison of treatment costs of grade 3/4 adverse events associated with erlotinib or pemetrexed maintenance therapy for patients with advanced non-small-cell lung cancer (NSCLC) in Germany, France, Italy, and Spain. *Lung Cancer* 2011; **74:** 529-34.

54. Nuijten MJ, de Castro Carpeno J, Chouaid C, Vergnenegre A, Grossi F, Bischoff H, *et al.* A cross-market cost comparison of erlotinib versus pemetrexed for first-line maintenance treatment of patients with locally advanced or metastatic non-small-cell lung cancer. *Lung Cancer* 2012; **76:** 465-71.

55. Rashid N, Koh HA, Baca HC, Lin KJ, Malecha SE, Masaquel A. Economic burden related to chemotherapy-related adverse events in patients with metastatic breast cancer in an integrated health care system. *Breast Cancer (Dove Med Press)* 2016; **8:** 173-81.

56. Elting LS, Shih YC. The economic burden of supportive care of cancer patients. *Support Care Cancer* 2004; **12:** 219-26.

57. Nonzee NJ, Dandade NA, Patel U, Markossian T, Agulnik M, Argiris A, *et al.* Evaluating the supportive care costs of severe radiochemotherapy-induced mucositis and pharyngitis : results from a Northwestern University Costs of Cancer Program pilot study with head and neck and nonsmall cell lung cancer patients who received care at a county hospital, a Veterans Administration hospital, or a comprehensive cancer care center. *Cancer* 2008; **113:** 1446-52.

58. Sakellari I, Angelopoulou M, Tsopra O, Dervenoulas I, Tsirigotis P, Spyridonidis A, *et al.* A prospective study of incidence, clinical and quality of life consequences of oral mucositis post palifermin prophylaxis in patients undergoing high-dose chemotherapy and autologous hematopoietic cell transplantation. *Ann Hematol* 2015; **94:** 1733-40.

59. Weymuller EA, Yueh B, Deleyiannis FW, Kuntz AL, Alsarraf R, Coltrera MD. Quality of life in patients with head and neck cancer: lessons learned from 549 prospectively evaluated patients. *Arch Otolaryngol Head Neck Surg* 2000; **126:** 329-35; discussion 35-6.

60. Epstein JB, Robertson M, Emerton S, Phillips N, Stevenson-Moore P. Quality of life and oral function in patients treated with radiation therapy for head and neck cancer. *Head Neck* 2001; **23:** 389-98.

61. Elting LS, Keefe DM, Sonis ST, Garden AS, Spijkervet FK, Barasch A, *et al.* Patient-reported measurements of oral mucositis in head and neck cancer patients treated with radiotherapy with or without chemotherapy: demonstration of increased frequency, severity, resistance to palliation, and impact on quality of life. *Cancer* 2008; **113:** 2704-13.

62. Citak E, Tulek Z. Longitudinal quality of life in Turkish patients with head and neck cancer undergoing radiotherapy. *Support Care Cancer* 2013; **21:** 2171-83.

63. Dodd MJ, Dibble S, Miaskowski C, Paul S, Cho M, MacPhail L, *et al.* A comparison of the affective state and quality of life of chemotherapy patients who do and do not develop chemotherapy-induced oral mucositis. *J Pain Symptom Manage* 2001; **21:** 498-505.

64. Kim JW, Cha Y, Kim SJ, Han SW, Oh DY, Lee SH, *et al.* Association of oral mucositis with quality of life and symptom clusters in patients with solid tumors receiving chemotherapy. *Support Care Cancer* 2012; **20:** 395-403.

65. Al-Batran SE, Hozaeel W, Tauchert FK, Hofheinz RD, Hinke A, Windemuth-Kieselbach C, *et al.* The impact of docetaxel-related toxicities on health-related quality of life in patients with metastatic cancer (QoliTax). *Ann Oncol* 2015; **26:** 1244-8.

66. Goebell PJ, Muller L, Hurtz HJ, Koska M, Busies S, Marschner N. A Cross-Sectional Investigation of Fatigue, Mucositis, Hand-Foot Syndrome and Dysgeusia in Advanced Renal Cell Carcinoma Treatment: Final Results From the FAMOUS Study. *Clin Genitourin Cancer* 2016; **14:** 63-8.

67. Öhrn KE, Sjödén PO, Wahlin YB, Elf M. Oral health and quality of life among patients with head and neck cancer or haematological malignancies. *Support Care Cancer* 2001; **9:** 528-38.

68. Cheng KK. Oral mucositis and quality of life of Hong Kong Chinese patients with cancer therapy. *Eur J Oncol Nurs* 2007; **11:** 36-42.

69. Cheng KK. Oral mucositis, dysfunction, and distress in patients undergoing cancer therapy. *J Clin Nurs* 2007; **16:** 2114-21.

70. Chaitanya NC, Garlapati K, Priyanka DR, Soma S, Suskandla U, Boinepally NH. Assessment of Anxiety and Depression in Oral Mucositis Patients Undergoing Cancer Chemoradiotherapy: A Randomized Cross-sectional Study. *Indian J Palliat Care* 2016; **22:** 446-54.