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Palliative head and neck radiotherapy with the RTOG 8502 regimen for incurable primary or metastatic cancers

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Abstract

Objectives—To report on our institutional experience of palliative radiotherapy (RT) of cancers in the head and neck by the RTOG 8502 ‘QUAD SHOT’ regimen.

Methods—Seventy-five patients completed at least 1 cycle of palliative RT to the head and neck for primary or metastatic disease based on the RTOG 8502 regimen (3.7 Gy twice daily over 2 consecutive days at 4 week intervals per cycle) between 2/2005 and 7/2014.

Results—Median patient age was 76 years (range 23 to 97). The most common histologies were squamous cell carcinoma (55%), non-anaplastic thyroid carcinoma (10%) and salivary gland carcinoma (9%). Thirty patients (40%) received prior RT at the palliative site. Twenty-eight patients (37%) completed at least three RTOG 8502 cycles. Sixty-five percent of all patients had a palliative response. Median overall survival was 5.67 months (range, 0.20 - 34.5). Grade 3 toxicity in 4 patients (5%) consisted of acute dermatitis and functional mucositis. Palliative response was significantly correlated with increasing number of RTOG 8502 cycles ($p=0.012$), but not KPS, prior RT, palliative chemotherapy, prior surgery, histology or stage. On survival analysis, palliative response ($p<0.001$), KPS 70 ($p=0.001$), and greater number of RTOG 8502 cycles ($p=0.022$) remained independent predictors of improved survival.

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Conclusions—For patients with incurable malignant disease in the head and neck, the palliative RTOG 8502 ‘QUAD SHOT’ regimen provides excellent rates of palliative response with minimal associated toxicity. Patients who are able to complete greater number of RT cycles have higher rates of palliative response and overall survival.

Keywords

head and neck cancer; palliative care; radiation; IMRT; RTOG 8502

Introduction

Over 40,000 cases of head and neck squamous cell carcinomas are diagnosed each year in the United States[1]. Even after continued advances in therapy, up to 15 to 50 percent of patients will develop recurrent disease[2-8]. In addition, a significant portion will present with metastatic disease or with locoregionally advanced disease not amenable to definitive therapy.

Radiotherapy (RT) for incurable head and neck cancers has been demonstrated to be an effective palliative modality, even for patients who have received prior radiation[9-13]. A cyclical hypofractionated palliative radiotherapy regimen, originally devised for advanced pelvic malignancies (RTOG 8502)[14,15], has been successfully adapted for palliative treatment of head and neck cancers[12]. This regimen consists of 3.7 Gy twice-daily fractions given over two consecutive days per cycle with a rest period of 2 to 4 weeks between the 3 prescribed cycles for a total dose of 44.4 Gy. As each cycle consists of four fractions, this regimen has become colloquially known as the ‘QUAD SHOT.’

The RTOG 8502 regimen for head and neck cancer palliation has been reported to achieve tumor response rates of 53 to 77% with palliation achieved in over 80% of patients[9,11,12]. Toxicity was reported as minimal to mild, with overall Grade 3 toxicity ranging from 0-9%, and generally related to mucositis[9,11,12].

The purpose of this study was to review a single institutional experience of palliative radiotherapy by the RTOG 8502 regimen for head and neck cancers. We also sought to analyze factors correlated with palliative response and associated with survival.

Materials and Methods

After obtaining Institutional Review Board approval, an institutional database and radiotherapy treatment records were used to identify 75 consecutive patients treated with at least one cycle of palliative RT to the head and neck by the RTOG 8502 regimen between 2005 and 2014 at our center.

Radiotherapy details and technique

Patients were simulated with computed tomography (CT) imaging in a thermoplastic five-point head and neck mask for immobilization prior to each RT cycle. The symptomatic gross disease and other concerning large volume disease were identified on available diagnostic imaging and clinical examination then contoured onto the radiation simulation CT images

by the radiation oncologist as the gross tumor volume (GTV). The clinical target volume (CTV) was equivalent to the GTV except in areas of uncertainty where additional expansions were applied.

Intensity-modulated radiotherapy (IMRT) was generally used for most patients with a 0.5 to 1.0 cm margin for the planning target volume (PTV) depending on setup uncertainty and available image guidance during treatment. More recently, this margin has been reduced to 0.3 cm. RT cycles with conventional opposed fields with the dose prescribed to midplane were sometimes used for the first cycle for more expeditious palliative response with margins of 2 cm around the gross disease. RT was generally delivered using a linear accelerator with 6 MV photons and occasionally by electrons for superficial lesions (e.g. scalp, lip). For patients with previous RT, the spinal cord and brainstem were prioritized as organs at risk with a constraint guideline of a total maximum point dose of 60 Gy in 2 Gy equivalents from all treatments with 70 Gy as the maximum allowable limit.

The radiotherapy prescription was for 3.7 Gy twice-daily fractions given over two consecutive days to a total of 14.8 Gy per cycle, with each cycle repeated at 4 week intervals provided no local disease progression or significant acute toxicity was appreciated. Occasionally, due to toxicity or other concerns an additional rest period of about 1-3 weeks between RT cycles was utilized. The treatment volumes were reviewed prior to each cycle of radiotherapy with reductions made for significant tumor response.

Treatment response and toxicity scoring

We defined palliative response as subjective relief of the presenting symptom(s) or objective reduction of the gross tumor by physical examination or radiographic tumor response. Toxicity was scored by the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 with acute toxicity defined as occurring up to 3 months after treatment completion.

Statistical methods and definitions

Overall survival (OS) was defined by start of palliative radiotherapy until date of death. OS was estimated by the Kaplan-Meier technique and prognostic factors were analyzed by Cox proportional hazards modeling. The Spearman's rho test was used to examine correlation between palliative response and clinical factors. Prognostic and clinical factors examined included histology, prior treatment (surgery, radiotherapy), palliative chemotherapy, concurrent chemotherapy with at least 1 cycle (defined as within 7 days of RT), KPS, T-stage, number of RTOG 8502 cycles, and palliative response.

Results

Median patient age was 76 years (range 23 to 97). Median follow-up for all and living patients was 4.35 months (range, 0.23 – 34.5) and 6.45 months (range, 0.33 – 34.5), respectively. Fifty-seven percent were male and 43% were female. The most common histology was squamous cell carcinoma (55%), followed by non-anaplastic thyroid carcinoma (10%), salivary gland carcinoma (9%), anaplastic thyroid carcinoma (7%) and sarcoma (3%). Recurrent or primary T-stage was as follows: T1 (3%), T2 (16%), T3 (20%),

T4 (47%). Forty-one patients (55%) presented with distant metastatic disease and the Karnofsky Performance Status (KPS) score was <70 in 28 patients (27%; **Table 1**).

Prior treatment

Twenty-one patients (49%) had a history of surgical resection at the primary disease site, with 30 patients (40%) having received prior RT at the palliative site, (median dose 66 Gy; range, 18 to 70 Gy). Eight patients (11%) underwent salvage surgery or palliative debulking within 4 months prior to receipt of palliative RTOG 8502 radiotherapy.

Palliative treatment

Twenty-eight patients (37%) were able to complete at least three RTOG 8502 cycles. Intensity-modulated radiation therapy (IMRT) was utilized in 73% of all patients with 55% of patients receiving IMRT at their first RTOG 8502 cycle (**Table 1**). Chemotherapy was administered at the discretion of the treating medical oncologist based on a variety of factors including medical fitness, performance status, and systemic disease status. Forty-eight patients (64%) received systemic chemotherapy as part of their palliative regimen. Of these 48 patients, concurrent systemic therapy was delivered to 22 patients (46%). Twelve of these 22 patients treated concurrently had squamous cell carcinoma and of these, 5 patients received a concurrent course of cetuximab, 4 patients received a platinum-based regimen, and 3 patients received a course of concurrent taxol monotherapy. Five patients with thyroid carcinoma received at least 1 concurrent course of doxorubicin-based chemotherapy.

Presenting symptoms and palliative response

The most common presenting symptoms were pain (51%), dysphagia/odynophagia (23%), hemorrhage (12%), or vision changes (9%). Sixty-five percent of all patients had a palliative response. Of the 28 patients receiving 3 or more cycles of the RTOG 8502 regimen, 89% achieved a palliative response. Palliative response by presenting symptom ranged from 53% for dysphagia/odynophagia (total n = 17) to 100% for trismus or epistaxis (total n = 3 each; **Table 2**). By Spearman's rank correlation coefficient, achieving a palliative response was significantly correlated with increasing number of RTOG 8502 cycles ($p = 0.012$), but not KPS, prior RT, prior surgery, palliative chemotherapy, concurrent chemotherapy, histology or stage (**Table 3**). Though there was no statistical difference in response by histology, due to small numbers, the range of response varied from 38% for thyroid carcinoma (total n = 13) to 100% for sarcoma (total n = 2; **Table 2**).

Overall survival

Median OS was 5.67 months (range, 0.20 - 34.5). On univariate analysis, palliative chemotherapy ($p = 0.018$), palliative response ($p < 0.001$), KPS ≥ 70 ($p = 0.004$), and greater number of RTOG 8502 cycles ($p = 0.027$) were significantly associated with OS. These significant variables were included in a multivariate Cox proportional hazard model and the remaining independent factors were palliative response ($p < 0.001$), KPS ≥ 70 ($p = 0.001$), and greater number of RTOG 8502 cycles ($p = 0.022$; **Table 4** and **Figure 1**).

Toxicity

Grade 3 acute toxicity was observed in 4 patients (5%), and consisted of functional mucositis (n = 3) and acute dermatitis (n = 1). The rate of overall Grade 2 acute toxicity was 28%, with the most common being fatigue (n = 8) and mucositis (n = 6). No late Grade 3 or higher toxicities have been reported. See **Table 5** for a summary of the most common acute toxicities observed.

Discussion

One of the most difficult situations for a head and neck clinician is discerning which patients are not suitable for radical curative therapy. Generally, these patients either exhibit significant medical comorbidities hindering their ability to undergo an extended course of radical treatment or have incurable advanced or metastatic disease. However, even in these situations many patients present with significant symptoms from their advanced local disease such as intractable pain, tumor hemorrhage or asphyxiation that have dramatic effects on their quality of life[16]. Palliative radiotherapy for incurable head and neck cancers can be an effective option and is deliverable by a variety of fractionation schedules. We sought to review our experience of the RTOG 8502 regimen for these patients.

In this retrospective cohort of 75 consecutively treated patients at a single institution, palliative radiotherapy for cancers of the head and neck by the RTOG 8502 'QUAD SHOT' regimen was an effective approach with 65% of patients experiencing a palliative response. Limited toxicity was observed with Grade 3 or higher toxicity occurring in only 5% of treated patients.

The RTOG 8502 regimen has been studied in other prospective and retrospective series. Paris et al. treated 37 patients with 39 lesions on a Phase I/II study where 85% of lesions achieved palliation with minimal acute toxicity and no late complications in this population with a limited life expectancy of 4.5 months on average. Corry et al. reported on a Phase II study of 30 patients who received 14 Gy over 4 fractions in 2 consecutive days repeated at 4 week intervals to a maximum of 3 cycles, which differed slightly from than the traditional RTOG 8502 dose of 14.8 Gy per cycle. The median survival was 5.7 months with quality of life improvements reported in 44% of patients. No Grade 3 or higher toxicity was reported[9]. In addition, there have been efforts to combine systemic therapy with this palliative regimen[17]. Carrascosa and colleagues reported on 20 patients with advanced pelvic (n = 13) or head and neck malignancies (n = 7) who underwent the RTOG 8502 regimen concurrently with low dose paclitaxel 60 mg/m² with each cycle of RT. They reported that 89.5% of treated patients had palliation of their presenting symptoms. Only 2 patients experienced a Grade 2 allergic reaction to paclitaxel with no other reported toxicity but the authors acknowledged that the small cohort may not be an accurate representation of expected toxicity in a larger population.

Other hypofractionated palliative regimens have been reported for head and neck cancers[18-22]. The "Hypo Trial" conducted by Porceddu and colleagues treated 35 incurable head and neck cancer patients with the goal of 30 Gy in 5 fractions with 2 fractions per week. Thirty-one (88%) of the patients received at least 30 Gy. Overall 80% of

patients experienced an overall objective response with Grade 3 mucositis and dysphagia developing in 25% and 11%, respectively[22]. Monnier et al. reported on a series of 78 patients treated with a concurrent hypofractionated regimen dubbed the Irradiation HypoFractionnée 2 Séances Quotidiennes (IHF2SQ) that delivered 3Gy twice daily on the first, third, fifth and seventh week of treatment with concurrent platinum-based chemotherapy with a response rate of 54% and 1% of patients developing acute Grade 3 or 4 toxicity[18].

In examining the comparisons between diverse palliative fractionation schemes, Chen et al. reviewed the University of California Davis School of Medicine experience in 60 patients who underwent a variety of hypofractionated palliative regimens for recurrent or incurable head and neck cancers including the RTOG 8502, 70 Gy in 35 fractions, 30 Gy in 10 fractions, 37.5 Gy in 15 fractions, and 20 Gy in 5 fractions. The most common regimen, which was based on the RTOG 8502 regimen demonstrated a high rate of palliative response (83%) and low Grade 3 or higher toxicity (9%). These results were generally superior to the other fractionation schedules reviewed which reported palliative response ranging from 60 – 86% with markedly greater Grade 3 or higher toxicity ranging from 20 – 42%[11].

A practical consideration is the flexibility offered by this cyclical RTOG 8502 regimen. Patient comorbidities and treatment tolerability in this population with advanced disease and other comorbidities can limit delivery of protracted radiation schedules. Furthermore, assessment of response and tolerability with respect to the first cycle of radiotherapy can be incorporated into decision making as the treating physician and patient consider the risk and benefit of additional cycles of radiotherapy. Indeed, in our study, we found that certain patients were unable to tolerate additional cycles of RT after delivery of the first cycle. However, even a single cycle of RTOG 8502 can still provide benefit in some patients. In our study, a slight majority of patients who received only 1 RTOG 8502 cycle achieved a palliative response (55%). Yet, for patients who received at least 3 cycles of RT, they achieved a much greater rate of palliative response (88%).

As with any palliative approach, careful patient selection is necessary. Recurrent patients who are fit for salvage re-irradiation can achieve durable locoregional control with a conventionally fractionated regimen[13,23,24].

In conclusion, in patients with cancers of the head and neck not suitable for curative treatment and with limited life expectancy, the RTOG 8502 palliative RT regimen offers an overall high palliative response rate and is well tolerated. It is an effective palliative approach that minimizes the burden of longer protracted courses of treatment that is vital in a palliative setting. For appropriately selected patients, this regimen is our current institutional standard for patients requiring palliation for incurable cancers of the head and neck.

References

1. Society AC. Cancer Facts & Figures 2014. American Cancer Society. 2014
2. Bourhis J, Le Maitre A, Baujat B, et al. Individual patients' data meta-analyses in head and neck cancer. Current opinion in oncology. May; 2007 19(3):188–194. [PubMed: 17414635]

3. Brockstein B, Haraf DJ, Rademaker AW, et al. Patterns of failure, prognostic factors and survival in locoregionally advanced head and neck cancer treated with concomitant chemoradiotherapy: a 9-year, 337-patient, multi-institutional experience. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO*. Aug; 2004 15(8):1179–1186. [PubMed: 15277256]
4. Bernier J, Dompé C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *The New England journal of medicine*. May 6; 2004 350(19):1945–1952. [PubMed: 15128894]
5. Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *The New England journal of medicine*. May 6; 2004 350(19):1937–1944. [PubMed: 15128893]
6. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *The New England journal of medicine*. Nov 27; 2003 349(22):2091–2098. [PubMed: 14645636]
7. Hall SF, Groome PA, Irish J, O'Sullivan B. The natural history of patients with squamous cell carcinoma of the hypopharynx. *The Laryngoscope*. Aug; 2008 118(8):1362–1371. [PubMed: 18496152]
8. Setton J, Caria N, Romanyszyn J, et al. Intensity-modulated radiotherapy in the treatment of oropharyngeal cancer: an update of the Memorial Sloan-Kettering Cancer Center experience. *International journal of radiation oncology, biology, physics*. Jan 1; 2012 82(1):291–298.
9. Corry J, Peters LJ, Costa ID, et al. The 'QUAD SHOT'--a phase II study of palliative radiotherapy for incurable head and neck cancer. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. Nov; 2005 77(2):137–142. [PubMed: 16260054]
10. Stevens CM, Huang SH, Fung S, et al. Retrospective study of palliative radiotherapy in newly diagnosed head and neck carcinoma. *International journal of radiation oncology, biology, physics*. Nov 15; 2011 81(4):958–963.
11. Chen AM, Vaughan A, Narayan S, Vijayakumar S. Palliative radiation therapy for head and neck cancer: toward an optimal fractionation scheme. *Head & neck*. Dec; 2008 30(12):1586–1591. [PubMed: 18798313]
12. Paris KJ, Spanos WJ Jr, Lindberg RD, Jose B, Albrink F. Phase I-II study of multiple daily fractions for palliation of advanced head and neck malignancies. *International journal of radiation oncology, biology, physics*. Mar 15; 1993 25(4):657–660.
13. Lee N, Chan K, Bekelman JE, et al. Salvage re-irradiation for recurrent head and neck cancer. *International journal of radiation oncology, biology, physics*. Jul 1; 2007 68(3):731–740.
14. Spanos WJ Jr, Clery M, Perez CA, et al. Late effect of multiple daily fraction palliation schedule for advanced pelvic malignancies (RTOG 8502). *International journal of radiation oncology, biology, physics*. Jul 30; 1994 29(5):961–967.
15. Spanos WJ Jr, Guse C, Perez C, Grigsby P, Doggett RL, Poulter C. Phase II study of multiple daily fractionations in the palliation of advanced pelvic malignancies: preliminary report of RTOG 8502. *International journal of radiation oncology, biology, physics*. Sep; 1989 17(3):659–661.
16. Sciubba JJ. End of life considerations in the head and neck cancer patient. *Oral oncology*. Apr-May; 2009 45(4-5):431–434. [PubMed: 18804409]
17. Carrascosa LA, Yashar CM, Paris KJ, Larocca RV, Faught SR, Spanos WJ. Palliation of pelvic and head and neck cancer with paclitaxel and a novel radiotherapy regimen. *Journal of palliative medicine*. Aug; 2007 10(4):877–881. [PubMed: 17803408]
18. Monnier L, Touboul E, Durdux C, Lang P, St Guily JL, Huguet F. Hypofractionated palliative radiotherapy for advanced head and neck cancer: the IHF2SQ regimen. *Head & neck*. Dec; 2013 35(12):1683–1688. [PubMed: 23359352]
19. Agarwal JP, Nemade B, Murthy V, et al. Hypofractionated, palliative radiotherapy for advanced head and neck cancer. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. Oct; 2008 89(1):51–56. [PubMed: 18649963]
20. Al-mamgani A, Tans L, Van rooij PH, Noever I, Baatenburg de jong RJ, Levendag PC. Hypofractionated radiotherapy denoted as the "Christie scheme": an effective means of palliating

- patients with head and neck cancers not suitable for curative treatment. *Acta oncologica*. 2009; 48(4):562–570. [PubMed: 19373698]
21. Mohanti BK, Umapathy H, Bahadur S, Thakar A, Pathy S. Short course palliative radiotherapy of 20 Gy in 5 fractions for advanced and incurable head and neck cancer: AIIMS study. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. Jun; 2004 71(3):275–280. [PubMed: 15172142]
22. Porceddu SV, Rosser B, Burmeister BH, et al. Hypofractionated radiotherapy for the palliation of advanced head and neck cancer in patients unsuitable for curative treatment--"Hypo Trial". *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. Dec; 2007 85(3):456–462. [PubMed: 18036689]
23. Riaz N, Hong JC, Sherman EJ, et al. A nomogram to predict loco-regional control after re-irradiation for head and neck cancer. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. Jun; 2014 111(3):382–387. [PubMed: 24993329]
24. Tanvetyanon T, Padhya T, McCaffrey J, et al. Prognostic factors for survival after salvage reirradiation of head and neck cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. Apr 20; 2009 27(12):1983–1991. [PubMed: 19289616]

Highlights

- We reviewed our experience with the RTOG 8502 regimen for incurable head and neck cancers.
- Overall palliative response: 65%.
- Grade 3 toxicity in 5% of patients, most commonly mucositis.
- Greater number of RT cycles correlated with higher palliative response and survival.

Log-rank $p = 0.073$.

Figure 1.
Overall survival stratified by number of RTOG 8502 cycles received.

Table 1

Baseline Clinical and Treatment Characteristics

Total patients	75		Palliative chemotherapy	n	%
			Yes	48	64%
Age			No	27	36%
Median	72				
Min	23		Prior radiotherapy to RTOG 8502 site	n	%
Max	97		Yes	30	40%
			No	45	60%
Gender	n	%	Median dose (Gy)	66	range 18 - 70
Male	43	57%			
Female	32	43%	IMRT for first RTOG 8502 cycle	n	%
			Yes	41	55%
KPS	n	%	No	34	45%
70 or greater	55	74%			
50 to 60	20	27%	IMRT for any RTOG 8502 cycle	n	%
			Yes	55	73%
Histology	n	%	No	20	27%
SCC	41	55%			
Salivary gland	7	9%	IMRT for patients who received >1 RTOG 8502 cycle	n	%
Thyroid	13	17%	Yes	38	83%
Sarcoma	2	3%	No	8	11%
Other	12	16%			
			Cycles of RTOG 8502	n	%
T-stage	n	%	1 (14.8 Gy)	29	36%
T0/TX	9	12%	2 (29.6 Gy)	18	27%
T1	2	3%	3 (44.4 Gy)	24	32%
T2	12	16%	4 (59.2 Gy)	3	4%
T3	15	20%	5 (74.0 Gy)	1	1%
T4	35	47%			
			Surgery for primary disease	n	%
N-stage			Yes	37	49%
N0	11	15%	No	38	51%
N1	10	13%			
N2	37	49%	Salvage surgery prior to RTOG 8502	n	%
N3	2	3%	Yes	10	13%
NX or unknown	15	20%	No	65	87%

Abbreviations: KPS, Karnofsky Performance Status; IMRT, intensity-modulated radiation therapy; RTOG, Radiation Therapy Oncology Group

Table 2

Presenting symptoms and palliative response by number of completed RTOG 8502 cycles.

			Palliative response	
Presenting symptoms prior to RTOG 8502 ^a	n	%	# of responders	% of responders
Pain	38	51%	25	66%
Dysphagia/odynophagia	17	23%	9	53%
Hemorrhage	9	12%	6	67%
Visual blurriness/deficits	7	9%	4	57%
Airway compromise	4	5%	2	50%
Trismus	3	4%	3	100%
Epistaxis	3	4%	3	100%
Response by histology				
Squamous cell carcinoma	41	55%	30	73%
Salivary gland	7	9%	5	71%
Thyroid (all)	13	17%	5	38%
<i>Anaplastic thyroid carcinoma</i>	7	54%	2	29%
<i>Non-anaplastic thyroid carcinoma</i>	6	46%	3	50%
Sarcoma	2	3%	2	100%
Other	12	16%	7	58%
Overall palliation achieved				
Yes	49	65%		
No (symptoms persisted, worsened)	7	9%		
No (patient expired shortly after treatment)	19	25%		
Number of completed cycles of RTOG 8502				
1	29	36%	16	55%
2	18	27%	8	44%
3	24	32%	21	88%
4	3	4%	3	100%
5	1	1%	1	100%
Total	75	100%	49	65%

Abbreviations: RTOG, Radiation Therapy Oncology Group

^a Sum of percentages exceeds 100% as some patients presented with multiple symptoms.

Table 3

Spearman's rho correlation of palliative response with patient and clinical factors Palliation achieved? (0=no, 1=yes)

	n	Correlation Coefficient	Sig. (2-tailed)
Age (years)	75	0.10	0.383
KPS	75	−0.10	0.414
Histology (SCC, salivary, thyroid, sarcoma, other)	75	−0.17	0.141
T1-2 vs T3-4	65	−0.03	0.834
N0-1 vs N2-3	75	0.01	.952
Prior RT to treated site	75	−0.03	0.77
Surgery to primary site	75	−0.13	0.287
Chemotherapy as part of palliative treatment	75	0.15	0.187
Chemotherapy concurrently with at least 1 cycle of RTOG 8502	75	0.04	0.743
Additional palliative RT to primary site	72	−0.03	0.836
Cycles of RTOG 8502	75	0.29	0.012^a

Abbreviations: KPS, Karnofsky Performance Status; RT, radiotherapy; RTOG, Radiation Therapy Oncology Group;

^a p<=0.05

Table 4

Univariate and multivariate analysis of overall survival

			UVA	MVA	
	n	%	p-value	p-value	HR
Palliation Achieved			<0.001	<0.001	0.236
No (referent)	26	35%			
Yes	49	65%			
Age (years, continuous variable)			0.639	-	-
KPS			0.003	0.001	0.288
<70 (referent)	20	27%			
70	55	73%			
Histology			0.772	-	-
Squamous cell carcinoma	41	65%			
Salivary gland	7	11%			
Thyroid carcinoma	13	21%			
Sarcoma	2	3%			
Other (basal cell, Merkel cell, neuroendocrine, lymphoma, multiple myeloma)	12	19%			
T-stage			0.159	-	-
T1-2 (referent)	18	28%			
T3-4	47	72%			
T0 or X, or Unknown* (not analyzed)	10	15%			
N-stage			0.577		
N0-1 (referent)	21	28%			
N2-3	39	52%			
Unknown	15	20%			
Prior radiotherapy to RTOG 8502 site			0.446	-	-
No (referent)	45	100%			
Yes	30	67%			
Surgery at initial presentation			0.92	-	-
No (referent)	41	100%			
Yes	34	83%			
Surgery at palliative presentation			0.509	-	-
No (referent)	65	100%			
Yes	10	15%			
Chemotherapy use as part of palliative treatment			0.017	0.677	0.872
No (referent)	27	42%			
Yes	48	74%			
Chemotherapy concurrent with at least 1 cycle of RTOG 8502			0.887	-	-

			UVA		MVA	
	n	%	p-value		p-value	HR
No (referent)	53	82%				
Yes	22	34%				
Cycles of RTOG 8502 (continuous variable)			0.021		0.018	0.687
1	29	39%				
2	18	24%				
3	24	32%				
4	3	4%				
5	1	1%				

Abbreviations: KPS, Karnofsky Performance Status; RTOG, Radiation Therapy Oncology Group

Table 5

Acute toxicity

Toxicity (CTCAE)	Grade 1		Grade 2		Grade3	
	No.	%	No.	%	No.	%
Mucositis	11	15%	6	8%	3	4%
Skin	24	32%	1	1%	1	1%
Fatigue	25	33%	8	11%	0	0%
Xerostomia	26	35%	1	1%	0	0%

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events