

Treatment Patterns and Health Care Resource Use (HCRU) Associated With Repeatedly Treated Metastatic Squamous Cell Carcinoma of the Head and Neck (mSCCHN) in the United Kingdom (UK)

Nash Smyth E,¹ La E,² Talbird S,² Li L,¹ Kaye JA,² Lin AB,¹ Bowman L¹
¹Eli Lilly and Company, Indianapolis, Indiana, USA
²RTI Health Solutions, Research Triangle Park, North Carolina, USA

ABSTRACT

OBJECTIVE
Recent data characterizing metastatic squamous cell carcinoma of the head and neck (mSCCHN) treatment patterns in the UK are limited. The current study evaluated patterns of care and HCRU in UK patients with metastatic SCCHN who received ≥3 lines of systemic therapy.

METHODS
Medical records of 220 patients with metastatic SCCHN who received ≥3 lines of systemic therapy were abstracted between 6 March 2015 – 29 April 2015. Clinical and demographic information at metastatic diagnosis as well as treatment and supportive care data were collected for patients ≥18 years initiating third-line systemic therapy between 1 January 2011 and 30 August 2014. Performance status (PS) was recorded prior to each line of therapy. SCCHN-related HCRU was captured until death or last medical record.

RESULTS
Most patients were Caucasian (90%), male (74%), current or former smokers (85%), with an initial SCCHN diagnosis of stage IVC (52%). Median age at metastatic diagnosis was 60 years and most patients had an Eastern Cooperative Oncology Group (ECOG) PS of 0 or 1 (208/217=96%). For patients with PS=0/1, the most common first-line treatment was cisplatin+5-FU (88/208=47%); docetaxel was the most common second-line (85/177=48%) and third-line treatment (30/117=26%). For patients with PS≥2, the most common first-, second-, and third-line treatments were carboplatin+5FU (5/9=56%), cetuximab (12/38=32%), and methotrexate (21/95=22%), respectively. Four patients (2%) received 4 therapy lines while no patient received ≥5 lines. Seven patients (3%) received radiation and/or surgery for metastatic disease. Most patients received supportive care during therapy (85%) and after its discontinuation (89%). SCCHN-related hospitalizations and emergency department visits were reported for 27% and 20% of patients during therapy, respectively (vs. 9% and 14% after therapy discontinuation). Median survival after metastatic diagnosis was 25.6 months.

CONCLUSIONS
Patterns of care and HCRU varied among patients with repeatedly treated metastatic SCCHN; specific systemic therapies varied by PS. Factors associated with HCRU will be examined in future multivariate analyses.

BACKGROUND

- An estimated 139,000 incident cases of head and neck cancer occur each year in Europe, approximately 90% of which are of squamous histology (Gregoire et al., 2010).
- Median overall survival for patients with metastatic squamous cell carcinoma of the head and neck (mSCCHN) is approximately 8 to 11 months (Malhotra et al., 2013; Vermorken et al., 2013; Won et al., 2011), with 1-year survival rates ranging between 38% and 44% (Adamo et al., 2004; Raguse et al., 2006; Won et al., 2011).
- Despite a wide range of treatment regimens used in third-line therapy for mSCCHN (Kantar Health, 2013), there is limited published data characterizing treatment patterns, health care resource utilization (HCRU), and survival for these patients.

OBJECTIVES

- Describe demographic and clinical characteristics among patients with mSCCHN who are treated with at least three lines of systemic therapy
- Describe specific systemic treatment regimens for each therapy line for metastatic disease by patients' Eastern Cooperative Oncology Group Performance Status (ECOG-PS)
- Describe SCCHN-associated supportive and end-of-life care
- Derive an estimate of the resource use associated with treating and managing mSCCHN
- Evaluate effects of demographic and clinical characteristics on resource use associated with treating and managing mSCCHN
- Estimate overall survival for study population from time of diagnosis and from time of starting third-line therapy

METHODS

- Medical records of 220 patients with mSCCHN who received ≥3 lines of systemic therapy were abstracted by 40 oncology physician specialists in the UK.
 - Patient inclusion criteria:
 1. Initiated third-line systemic therapy for mSCCHN (i.e., stage IVC SCCHN or recurrence with distant metastases) between 1 January 2011 and 30 August 2014
 2. Aged at least 18 years on the date of diagnosis of mSCCHN
 3. Not enrolled in treatment or interventional studies related to SCCHN at any time from the time of diagnosis of metastatic disease until the end of available medical record data; enrollment in an observational study was permitted
 4. Patients could either be dead or alive at the time of chart abstraction
- Clinical and demographic characteristics, treatment, and supportive care data were collected.
- SCCHN-related HCRU was captured until death or last medical record.

RESULTS

Table 1. Characteristics of Oncology Physician Specialists (N=40)

Number of metastatic SCCHN patients treated with at least third-line therapy in the last 12 months	Regional Distribution	N	%
Mean	North	8	20.0
Standard deviation	Midlands and East	9	22.5
Median	Greater London and Southeast	19	47.5
Range (minimum, maximum)	Southwest	4	10.0
	Scotland, Wales, and Northern Ireland	0	0.00

Number of years in practice (since oncology board certification/end of residency)	Medical specialty (N, %)
Mean	Medical Oncologist 47.5
Standard deviation	Clinical Oncologist 52.5
Median	Hematologist/Oncologist 0.00
Range (minimum, maximum)	

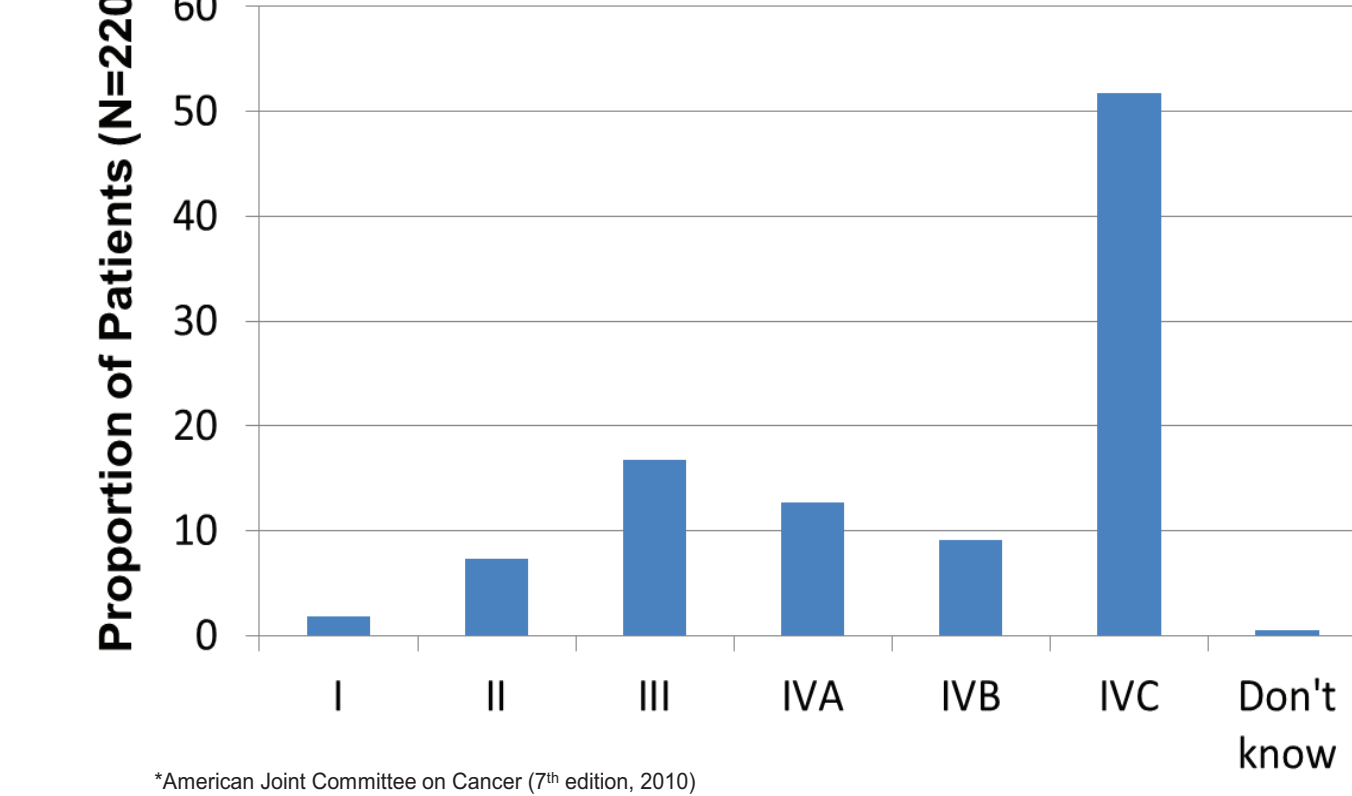
Table 2. Patient Demographic Characteristics (N=220)

Age at diagnosis of mSCCHN* (years)	Mean (Standard Deviation [SD]) 59.0 (8.0) Median (minimum, maximum) 60.0 (31.5, 77.3)
Age at initiation of third-line systemic therapy for mSCCHN (years)	Mean (SD) 60.7 (8.0) Median (minimum, maximum) 61.9 (32.3, 80.5)
Gender (n, %)	Male 162 (73.6) Female 58 (26.4)
Ethnic origin (n, %)	White/Caucasian 199 (90.5) African/Black 3 (1.4) Asian/Pacific Islander 9 (4.1) Middle Eastern 4 (1.8) Indian Subcontinent (Indian, Pakistani, Bangladeshi) 5 (2.3)
Supplemental private insurance at time of diagnosis of metastatic disease (n, %)	Yes 4 (1.8) No 204 (92.7) Don't know 12 (5.5)
Smoking status (n, %)	Current 59 (26.8) Former 128 (58.2) Non-smoker 27 (12.3) Don't know 6 (2.7)

*metastatic squamous cell carcinoma of the head and neck

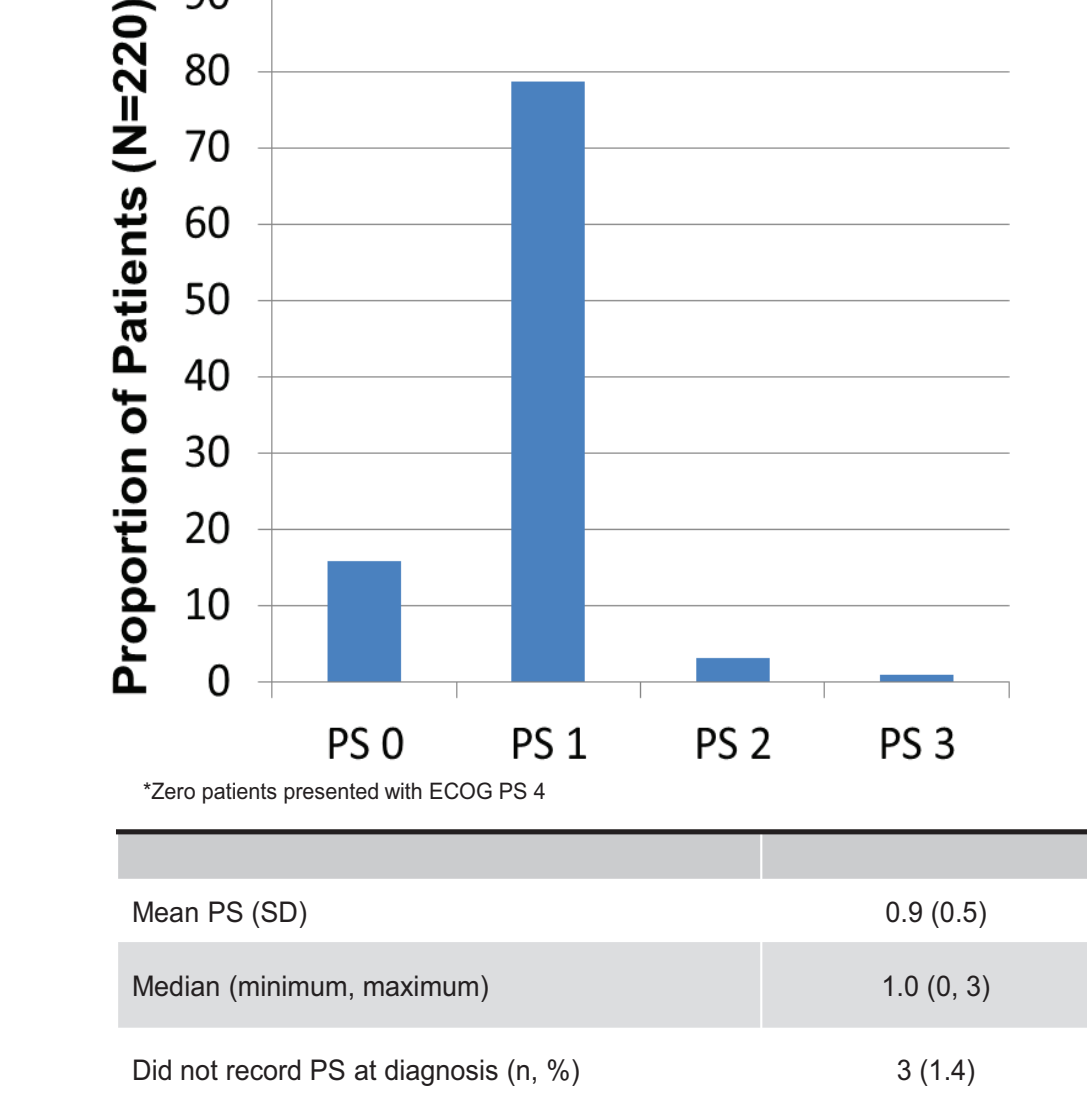
RESULTS (continued)

Figure 1. Clinical Stage* of SCCHN at Initial Diagnosis



*American Joint Committee on Cancer (7th edition, 2010)

Figure 2. ECOG PS at Diagnosis of Metastatic Disease*



*Zero patients presented with ECOG PS 4

Mean PS (SD)	0.9 (0.5)
Median (minimum, maximum)	1.0 (0, 3)
Did not record PS at diagnosis (n, %)	3 (1.4)

Table 3. Top 3 Systemic Therapy Treatments, Overall and by PS*

First Line of Therapy	Overall N=220* (100.0)	ECOG* PS 0 N=35	ECOG PS 1 N=173	ECOG PS 2+ N=9
	n (%)	n (%)	n (%)	n (%)
Cisplatin + 5-FU ^b	102 (46.4)	20 (57.1)	78 (45.1)	3 (33.3)
Cisplatin + Cetuximab + 5-FU	36 (16.4)	5 (14.3)	31 (17.9)	-
Carboplatin + 5-FU	26 (11.8)	3 (8.6)	16 (9.3)	5 (55.6)
Cisplatin + Capecitabine	-	3 (8.6)	-	-
Cisplatin + 5-FU + Paclitaxel	-	-	-	1 (11.1)

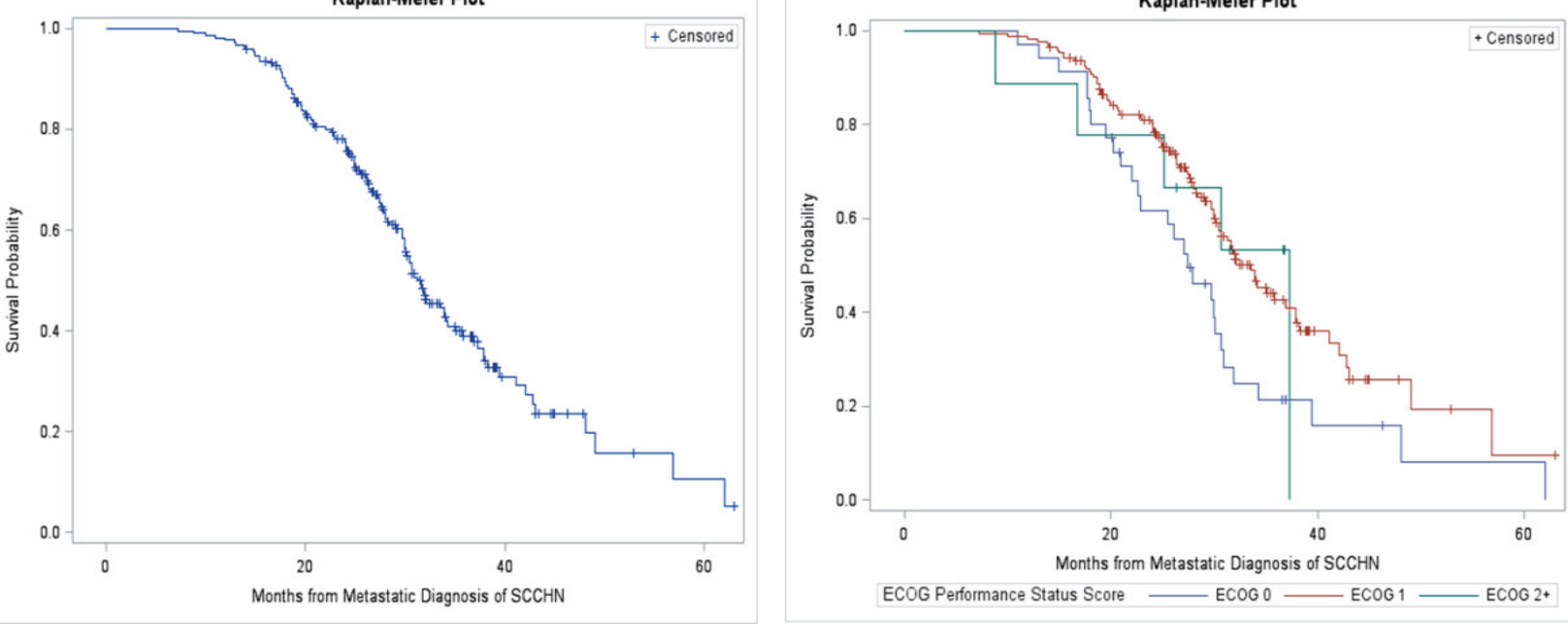
Second Line of Therapy	Overall N=220 (100.0)	ECOG PS 0 N=5	ECOG PS 1 N=172	ECOG PS 2+ N=38
	n (%)	n (%)	n (%)	n (%)
Paclitaxel	28 (12.7)	2 (40.0)	18 (10.5)	8 (21.1)
Docetaxel	99 (45.0)	1 (20.0)	84 (48.8)	10 (26.3)
Carboplatin + Gemcitabine	-	1 (20.0)	16 (9.3)	-
Cetuximab + 5-FU	-	1 (20.0)	-	-
Carboplatin + Paclitaxel	19 (8.6)	-	16 (9.3)	-
Cetuximab	19 (8.6)	-	-	12 (31.6)

Third Line of Therapy	Overall N=220 (100.0)	ECOG PS 0 N=1	ECOG PS 1 N=116	ECOG PS 2+ N=95
	n (%)	n (%)	n (%)	n (%)
Docetaxel	40 (18.2)	1 (100.0)	29 (25.0)	-
Cetuximab	43 (19.6)	-	27 (23.3)	15 (15.8)
Methotrexate	43 (19.6)	-	22 (19.0)	21 (22.1)
Gemcitabine	-	-	-	16 (16.8)

Fourth Line of Therapy	Overall N=4	ECOG PS 0 N=0	ECOG PS 1 N=2	ECOG PS 2+ N=1
	n (%)	n (%)	n (%)	n (%)
Docetaxel	1 (25.0)	-	1 (50.0)	-
Gemcitabine	1 (25.0)	-	1 (50.0)	-
Capecitabine	1 (25.0)	-	-	1 (100.0)
Carboplatin + Etoposide	1 (25.0)	-	-	-

± PS prior to receipt of 1st, 2nd, 3rd, and 4th line therapy
*PS was not recorded at the start of each therapy line for all patients
^a Eastern Cooperative Oncology Group; ^b 5-fluorouracil

Figure 3. Estimated Survival from Diagnosis of mSCCHN, Overall and by PS



	Total n	% censored	Estimated Survival (in months)	
			Median	95% CI
Overall	220	45.0	31.2	29.9 34.1

ECOG PS	Total n	% censored	Estimated Survival (in months)	
			Median	95% CI
ECOG PS=0	35	20.0	27.4	22.0 30.6
ECOG PS=1	173	50.3	33.5	30.4 37.8
ECOG PS≥2	9	44.4	37.3	8.7 37.3

References:

- Grégoire V, et al. Ann Oncol. 2010;21(Suppl 5):v184-6
- Kantar Health. Treatment architecture: Western Europe Head and Neck Cancer. CancerMPact Western Europe, 2013. December 2013
- Malhotra B, et al. Head Neck 2014 Dec;36(12):1712-7
- Raguse JD, et al. Oral Oncol. 2006;42(6):614-8
- Vermorken JB, et al. Eur J Cancer. 2013;49(13):2877-83
- Won YW, et al. Ann Oncol. 2011;22(2):417-23

Figure 4. Estimated Survival from Initiation of Third-Line Therapy for mSCCHN, Overall

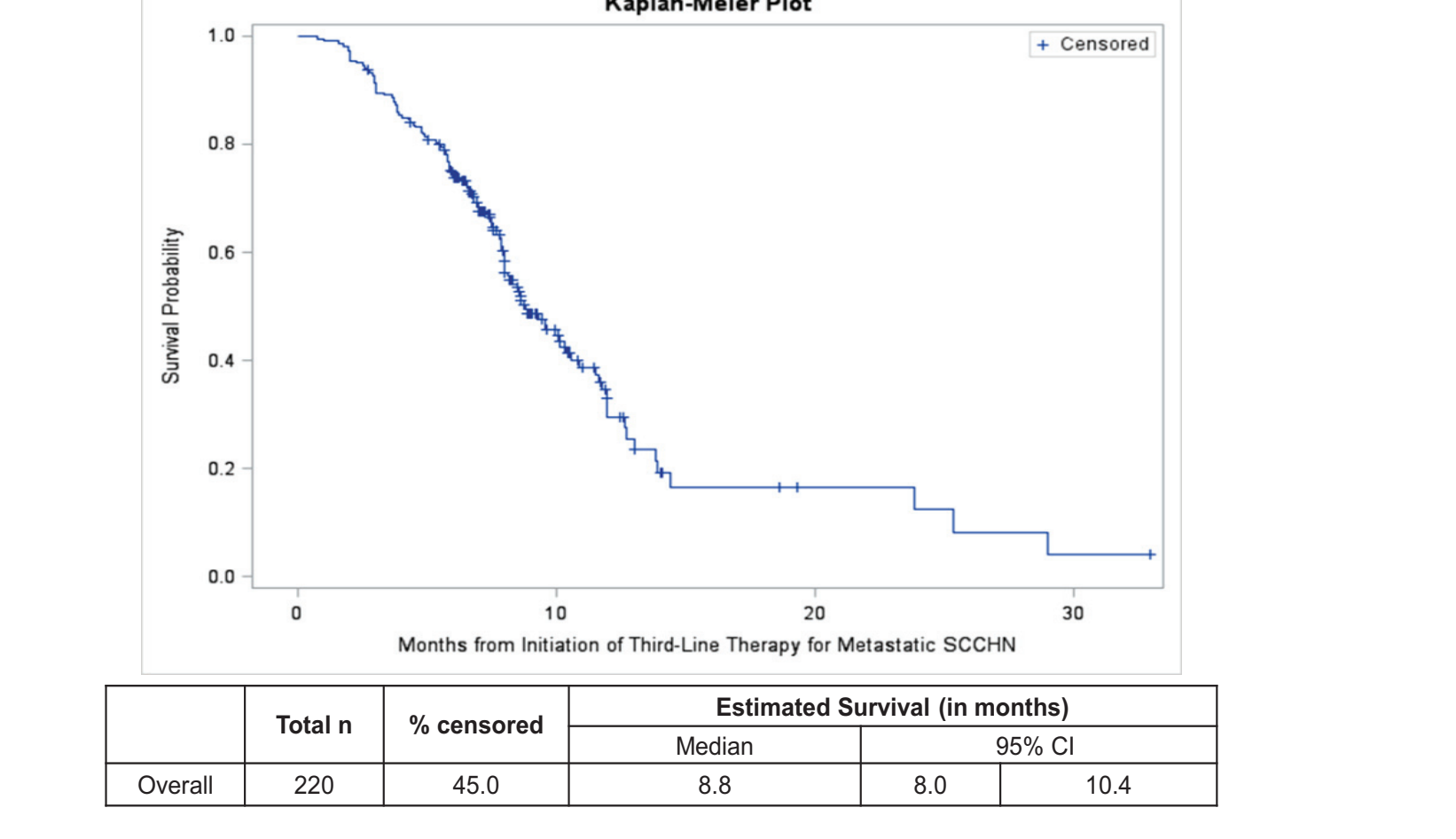


Table 4. Frequency of Select Supportive Care Measures for mSCCHN Patients^b

	Prior to Metastatic Disease Diagnosis (N=105)	After Metastatic Diagnosis and Before Discontinuation of Systemic Therapy (N=220)	After Discontinuation of Systemic Therapy for Metastatic Disease Until Death (N=164) ^a
	n (%)	n (%)	n (%)
Audiology	27 (25.7)	3 (1.4)	1 (0.6)
Dental care for radiotherapy effects	65 (61.9)	49 (22.3)	16 (9.8)
Depression assessment and management	13 (12.4)	28 (12.8)	18 (11.0)
Nutritional support	77 (73.3)	129 (58.6)	81 (49.4)
Pain and symptom management	63 (60.0)	117 (53.2)	95 (57.9)
Speech and swallowing therapy	47 (44.8)	49 (22.3)	15 (9.2)
Tracheostomy care	10 (9.5)	3 (1.4)	1 (0.6)
Wound management	18 (17.1)	8 (3.6)	3 (1.8)
Xerostomia management	28 (26.7)	53 (24.1)	23 (14.0)
Antiemetics	NC ^c	131 (59.6)	65 (39.6)
Management of oral and gastrointestinal mucositis	NC ^c	65 (29.6)	27 (16.5)
Hematologic growth factor/transfusions	NC ^c	57 (25.9)	19 (11.6)
Any supportive care	96 (91.4)	186 (84.5)	146 (89.0)
None	1 (1.0)	6 (2.7)	5 (3.1)
Don't know	8 (7.6)	28 (12.7)	13 (7.9)

^aNC = not collected
^b56 patients still receiving systemic therapy at the time of data collection
^cpatients could have received multiple types of supportive care

Table 5. Health Care Resource Utilization Related to mSCCHN, Overall

	During Systemic Therapy (N=220)	After Discontinuation of Therapy until Death (N=164) ^a
	n (%)	n (%)
Outpatient office visits/consults at responding physician's office	154 (70.0)	83 (50.6)
Outpatient visits in a hospital clinic or cancer center	77 (35.0)	60 (36.6)
Emergency department	45 (20.5)	23 (14.0)
Palliative care	98 (44.6)	59 (36.0)
Hospitalization	59 (26.8)	14 (8.5)

^a56 patients were still receiving systemic therapy at the time of data collection

Table 6. Association of mSCCHN-Related HCRU and Select Covariates

Select Covariates Represented by Odds Ratio and 95% Confidence Interval	Dependent variables of interest				
	SCCHN-related hospitalization visit	SCCHN-related ED visit	SCCHN-related office visit/consult visit	SCCHN-related outpatient visit in a hospital clinic	SCCHN-related outpatient palliative care visit
PS at diagnosis (referent group: ECOG ^b PS 0)					
ECOG 1	0.51 (0.22-1.21) p=.13	0.61 (0.26-1.45) p=.26	0.23 (0.07-0.77) p=.02 ^a	0.72 (0.32-1.63) p=.43	0.82 (0.34-1.94) p=.65
ECOG 2+	0.42 (0.07-2.41) p=.33	0.13 (0.01-1.41) p=.09	0.21 (0.03-1.41) p=.11	0.08 (0.01-0.77) p=.03 ^a	0.07 (0.01-0.73) p=.03 ^a
Comorbidity burden ^c	1.42 (1.13-1.79) p<.01 ^a	1.29 (1.02-1.63) p=.04 ^a	1.82 (1.30-2.55) p<.01 ^a	0.94 (0.76-1.16) p=.56	1.81 (1.40-2.33) p<.01 ^a
Received surgery for non-metastatic disease (referent group: did not receive surgery for non-metastatic disease)	0.80 (0.30-2.16) p=.66	1.31 (0.47-3.64) p=.60	4.80 (1.54-14.91) p=.01 ^a	4.63 (1.71-12.51) p<.01 ^a	0.66 (0.25-1.72) p=.39
Received radiotherapy (RT) for metastatic disease (referent group: did not receive radiotherapy for metastatic disease)	2.27 (0.58-8.95) p=.24	7.39 (1.91-28.55) p<.01 ^a	6.21 (0.71-54.27) p=.10	12.90 (1.92-86.56) p=.01 ^a	1.56 (0.39-6.17) p=.53
Received systemic therapy for non-metastatic disease (referent group: did not receive systemic therapy for non-metastatic disease)	0.32 (0.11-0.99) p=.05 ^a	0.75 (0.23-2.43) p=.64	4.23 (1.18-15.20) p=.03 ^a	3.55 (1.12-11.26) p=.03 ^a	0.65 (0.21-1.99) p=.45

^aCount of the number of comorbidities recorded, ranging from 0 to 28
^bstatistically significant in any of the logistic regression; other covariates evaluated but not statistically significant include: age at metastatic disease diagnosis, female sex, supportive care received prior to metastatic disease diagnosis, non-stage IVC at diagnosis, received RT for non-metastatic disease
^cEastern Cooperative Oncology Group; ^dsquamous cell carcinoma of the head and neck

LIMITATIONS

- Survival estimates apply to our study population only, and are not estimates of survival for all patients in the general population diagnosed with mSCCHN. This study's eligibility criteria required that patients had to have received at least three lines of therapy for mSCCHN, causing immortal time bias (upward bias) for our population as compared with all patients diagnosed with SCCHN
- Patients selected for study inclusion represent a convenience sample, in that the records were obtained from physicians who were willing to participate in the study. Our findings may therefore not be generalizable to the overall mSCCHN population in the UK
- The data collected is potentially subject to data entry errors as it was directly entered by physicians; the study team did not review actual chart data of patients to confirm accuracy of information collected
- Physicians reported data based on patients' medical records to which they had access. Information pertinent to the patient's SCCHN condition and study objectives but not captured in the patient's chart to which the participating physician had access was not included in our analysis
- The data collection form was designed to prioritize collection of key information in support of study objectives while balancing physician time burden. There could be additional measures that would be useful in understanding variations in treatment and outcomes that were not captured

CONCLUSIONS

- To our knowledge, this is the first study to characterize demographic and clinical characteristics, metastatic treatments by PS, and HCRU for mSCCHN patients who have received multiple lines of therapy in the UK
- The majority of mSCCHN patients transitioned from good to poorer levels of PS during the observation period
- For patients with PS=0/1, the most common first-line treatment was cisplatin+5-FU; docetaxel was the most common second-line and third-line treatment. For patients with PS≥2, the most common first-, second-, and third-line treatments were carboplatin+5FU, cetuximab, and methotrexate, respectively
- Of covariates evaluated, PS and comorbidity burden were most consistently associated with select measures of HCRU
- The proportion of patients utilizing specific health care resources decreased in the period after discontinuation of systemic therapy (with the exception of outpatient visits in a hospital clinic or cancer center)
- Supportive care utilization by study participants varied throughout the course of disease, from non-metastatic disease until death