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Real-world systemic therapy treatment patterns for squamous cell carcinoma of the head and neck in Canada

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ABSTRACT

Background In the present study, we examined real-world treatment patterns for squamous cell carcinoma of the head and neck (SCCHN) in Canada, which are largely unknown.

Methods Oncologists across Canada provided data for disease history, characteristics, and treatment patterns during May–July 2016 for 6–8 consecutive patients receiving first-line or second-line drug treatment for SCCHN (including locally advanced and recurrent or metastatic disease).

Results Information from 16 physicians for 109 patients receiving drug treatment for SCCHN was provided; 1 patient was excluded from the treatment-pattern analysis. Median age in the cohort was 63 years [interquartile range (IQR): 57–68 years], and 24% were current smokers, with a mean exposure of 26.2 ± 12.7 pack–years. The most common tumour site was the oropharynx (48%). Most patients (84%) received platinum-based regimens as first-line treatment (44% received cisplatin monotherapy). Use of cetuximab-based regimens as first-line treatment was limited (17%). Of 53 patients receiving second-line treatment, 87% received a first-line platinum-based regimen. Median time between first-line treatment with a platinum-based regimen and initiation of second-line treatment was 55 days (IQR: 20–146 days). The most common second-line regimen was cetuximab monotherapy (43%); platinum-based regimens were markedly infrequent (13%).

Conclusions Our analysis provides real-world insight into SCCHN clinical practice patterns in Canada, which could inform reimbursement decision-making. High use of platinum-based regimens in first-line drug treatment was generally reflective of treatment guidelines; cetuximab use in the second-line was higher than anticipated. Additional real-world studies are needed to understand the effect of novel therapies such as immuno-oncology agents on clinical practice and outcomes, particularly for recurrent or metastatic SCCHN.

Key Words Canada, cetuximab, head-and-neck cancer, platinum-based therapy, recurrent disease, metastatic disease, squamous cell carcinoma, SCCHN, treatment patterns

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INTRODUCTION

Head-and-neck cancers encompass neoplasms of the oral cavity, pharynx, larynx, sinuses, and salivary glands[1]. In 2012, approximately 686,000 new cases of head-and-neck cancer and 376,000 associated deaths occurred worldwide, representing the 7th leading cancer by incidence[2], with squamous cell carcinoma of the head and neck (SCCHN) accounting for approximately 90% of those cancers[3]. An estimated 4700 Canadians were diagnosed with oral cancer in 2017, resulting in 1250 deaths[4]. The most recent Canadian statistics for oropharyngeal cancer reported 180 new cases and 131 deaths in 2013[5].

Treatment for SCCHN depends on stage at diagnosis: Patients diagnosed early are treated with curative intent; patients diagnosed at advanced stages or with recurrent or metastatic disease (R/M SCCHN) are treated with the aim of prolonging remission[6]. Because of limited therapeutic options, R/M SCCHN poses a treatment challenge—particularly for the patients who present with advanced-stage disease

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(approximately 66%)[7]. Patients with locally advanced stage III or IV disease are usually treated with combined modalities, including chemotherapy, radiotherapy, and surgery (if resectable)[6,8–11]. However, approximately 50% of patients with locally advanced SCCHN subsequently develop locoregional or distant (metastatic) recurrences[7]. Median overall survival (OS) for patients with R/M SCCHN receiving treatment is 6–9 months[12].

Other treatment options for patients with R/M SCCHN commonly include chemotherapies [platinum compounds (cisplatin, carboplatin), taxanes (docetaxel, paclitaxel), fluorouracil (5FU), or methotrexate], targeted therapies (such as the anti-epidermal growth factor receptor monoclonal antibody cetuximab), and combinations of chemotherapies with targeted agents[6,13–16]. Regimen choice is governed by a number of factors, including Eastern Cooperative Oncology Group performance status, symptoms related to tumour growth, comorbidities, prior treatment (including whether chemotherapy was received in the first line), patient preference, and the need for palliation[13,16].

The introduction of cetuximab in combination with platinum and 5FU chemotherapy, followed by maintenance cetuximab (the EXTREME regimen)[17], represented a significant advance in the first-line treatment of R/M SCCHN, supported by a phase III randomized trial that showed a significant survival benefit compared with platinum–5FU alone[18]. The median OS was 10.1 months for EXTREME compared with 7.4 months for platinum–5FU (hazard ratio for death: 0.80; 95% confidence interval: 0.64 to 0.99; $p = 0.04$) in patients with R/M SCCHN who had not received systemic chemotherapy within 6 months of study entry[19]. Based on published evidence, the EXTREME regimen has become a standard first-line treatment approach for R/M SCCHN in Europe[9,10] and in the United States in patients considered fit enough to tolerate the regimen[6,18]. In Canada, the Head and Neck Cancer Disease Site Group also recommends the EXTREME regimen to improve OS, progression-free survival, and response rate for "suitable" patients with R/M SCCHN[20,21].

In clinical practice, other combinations such as a taxane or cisplatin plus cetuximab are sometimes used as first-line treatment for R/M SCCHN when patients are considered too frail for the EXTREME regimen[18]; however, no randomized controlled studies have been conducted to show benefit for those treatments. Methotrexate monotherapy—which is associated with a lower response rate, but OS comparable to that with platinum–5FU[22]—is usually recommended for patients unable to tolerate combination chemotherapy[9]. Despite advances in treatment options, the prognosis for patients with SCCHN remains poor[12,18,23]. New therapies are emerging, offering a wider range of treatment options for patients with recurrent disease. Those options include the anti–PD-1 immune checkpoint inhibitors nivolumab and pembrolizumab, both of which are approved in the United States for the treatment of R/M SCCHN with disease progression on or after platinum-based therapy[24,25].

At present, there is a dearth of published evidence describing the use of therapies in real-world clinical practice, particularly for a second or later line of therapy, and to the best of the authors' knowledge, no studies have evaluated Canadian treatment patterns for SCCHN in the real-world setting. A better understanding of Canadian clinical practice patterns and clinical outcomes is needed to inform reimbursement decision-makers about treatment options in patients with SCCHN. The objective of the present study was therefore to identify real-world treatment patterns for patients with SCCHN so as to better understand the standard of care, including by line of therapy, in Canadian clinical practice.

METHODS

Study Design

This descriptive cross-sectional analysis used survey data collected from 2 May to 18 July 2016 from participating medical oncologists actively involved in the management of SCCHN across Canada. Details of the survey method, which has been used in more than 50 disease areas, have previously been published[26].

Eligible physicians who wanted to participate in the study were identified from public listings and were required to have qualified as a medical oncologist between 1981 and 2013 and to be treating a minimum of 10 patients with SCCHN per month. Participating physicians completed a detailed electronic Patient Record Form reporting data for their next 6–8 consecutively treated patients who met these eligibility criteria: SCCHN diagnosis, 18 years of age or older, receiving active drug treatment for SCCHN, not enrolled in a clinical trial (at the time of consultation), and primary tumour not located on a salivary gland or the nasopharynx. Excluded from the study were patients receiving best supportive care; those undergoing either surgery or radiotherapy (or both), but no active drug treatment; and those under a "watch and wait" treatment approach. Proportional quota sampling was used to generate a quasi-random sample evenly split between patients who were receiving first-line active drug treatment and those who were receiving second-line or later active drug treatment at the point of data collection.

Data Collection

Information extracted from the electronic Patient Record Forms included demographic and clinical characteristics of the patients and complete SCCHN drug and non-drug treatment history (including surgery and radiotherapy). Real-world treatment patterns identified in clinical practice for the participating providers included comprehensive treatment history from diagnosis to current treatment and treatment modality sequencing (that is, surgery, radiotherapy, chemotherapy, and targeted therapy, including specific agents received).

The end of a given line of drug therapy was defined by the addition, switching, or discontinuation of a drug or by repeat of the same therapy after completion of the original course. A change in dose or a treatment holiday was not considered a new line of therapy. Line of treatment was counted relative to each patient's first-line active drug treatment (either monotherapy or a combination regimen) with or without concurrent radiotherapy and regardless of disease progression (that is, for patients who had previously received drug therapy for non-recurrent or metastatic disease). Drug treatment for subsequent recurrent or metastatic disease was not considered "first line" for that disease

stage. For the purposes of the present study, radiotherapy alone and surgery alone were not counted as lines of treatment. Best supportive care was considered a line of therapy only in the third line or later. The length of time between diagnosis and treatment initiation, the duration of first-line therapy, and the time to initiation of second-line therapy also were recorded for patients receiving drug treatment.

Statistical Analyses

Demographics, clinical characteristics, and antineoplastic treatment patterns are described using frequencies and proportions for categorical data and using means with standard deviation or medians with interquartile range (IQR) for numeric data. Time variables are reported as medians with IQR. The probability of time to progression from initiation of first-line therapy until initiation of second-line therapy was plotted using the Kaplan–Meier method and was calculated using the initiation dates of first-line and second-line therapy. The time-to-progression analysis included all patients in the sample, including those receiving first-line therapy only, who were censored at the time of data collection.

RESULTS

Demographic and Clinical Characteristics of the Patients

Data from 16 physicians for 109 patients with SCCHN receiving first-line or second-line drug treatment were obtained. The treatment pattern analysis ($n = 108$) excluded 1 patient whose treatment data were incomplete. Most patients (77%) were diagnosed either by a head-and-neck or ear/nose/throat surgeon (55%) or by a medical oncologist (22%). On average, patients saw a medical oncologist 6.7 times and a radiation oncologist 6.1 times annually. Most patients were receiving treatment as part of a provincial or territorial health insurance plan (75%). Participating patients were drawn predominantly from clinics in Ontario (30% of patients), Quebec (29%), and Alberta (17%).

Median patient age in the cohort was 63 years (IQR: 57–68 years), and 72% of the patients were men. Median time from diagnosis to the point of data capture was 244 days (IQR: 124–656 days). Of the 109 patients included in the study, 90% were current or former smokers, and the mean smoking exposure for the current smokers was 26.2 ± 12.7 pack–years. The most common primary tumour site was the oropharynx (48%). At the point of data capture, 76% of patients had locoregionally advanced disease (stages I–IVB), and 23% had recurrent or metastatic disease (stage IVC). Compared with their counterparts having stages I–IVB disease, patients with stage IVC disease at data capture were more likely to be treated with the aim of improving quality of life (60% vs. 41%) and symptom control (44% vs. 28%), and less likely to be treated with the aim of improving OS (32% vs. 46%). Similarly, when physicians were asked to predict the likely next treatment step, patients with stage IVC disease were deemed more likely to progress to best supportive care (40% vs. 11%) and less likely to continue with current treatment (32% vs. 46%). At data capture, almost two thirds of the patients (64%) were clinically fit, with an Eastern Cooperative Oncology Group performance status of 0 or 1. Of the 73 patients who underwent *p16* testing to determine their human papillomavirus infection status at the point of data capture, 45% tested positive (Table I).

TABLE I Demographics and clinical characteristics of the 109 study patients[a]

Characteristic	Value
Dx to data capture (days)	
Median	244
IQR	124–656
Age (years)	
Median	63
IQR[b]	57–68
Age group [*n* (%)]	
≤70 Years	92 (84)
>70 Years	17 (16)
Sex [*n* (%) men]	78 (72)
Region [*n* (%)]	
Ontario	33 (30)
Quebec	32 (29)
Alberta	19 (17)
Other	25 (23)
Diagnosing physician [*n* (%)]	
Medical oncologist	24 (22)
Radiation oncologist	8 (7)
HN or ENT surgeon	60 (55)
Pathologist	2 (2)
Primary care physician	12 (11)
Other specialist (unspecified)	2 (2)
Not reported	1 (1)
Health insurance type [*n* (%)]	
Provincial or territorial plan	82 (75)
Employer-sponsored plan	18 (17)
Private plan	5 (5)
None, other, or unknown	4 (4)
Smoking status [*n* (%)]	
Current	26 (24)
Former	72 (66)
Never	11 (10)
Cigarettes per day[c] [*n* (%)]	
<20	11 (42)
≥20	12 (46)
Don't know	3 (12)
Exposure (mean pack–years)	26.2±12.7
Primary site [*n* (%)]	
Oropharynx	52 (48)
Oral cavity (including tongue)	30 (28)
Hypopharynx	11 (10)
Larynx	8 (7)
Lip	4 (4)
Not reported	4 (4)

TABLE I Continued

Characteristic	Value
Tumour status at diagnosis [*n* (%)]	
Resectable	33 (30)
Non-resectable or not eligible for resection	76 (70)
Disease stage at Dx [*n* (%)]	
I	11 (10)
II	26 (24)
III	32 (29)
IVA[d]	18 (17)
IVB[e]	10 (9)
IVC[f]	9 (8)
Not assessed	1 (1)
Disease stage at data capture [*n* (%)]	
I	3 (3)
II	19 (17)
III	14 (13)
IVA[d]	33 (30)
IVB[e]	14 (13)
IVC[f]	25 (23)
Not assessed	1 (1)
ECOG PS [*n* (%)]	
0	8 (7)
1	62 (57)
≥2	36 (33)
Not assessed	3 (3)
HPV p16 status [*n* (%)]	
Not tested	36 (33)
Tested	73 (67)
Positive[g]	33 (45)
Negative[g]	37 (51)
Inconclusive[g]	3 (4)

[a] At point of data capture unless otherwise specified.
[b] Two patients reported to be 90 or more years of age were assigned an age of 90 years.
[c] For current smokers.
[d] Moderately advanced locoregional disease.
[e] Very advanced locoregional disease.
[f] Distant metastatic disease.
[g] Of those tested.
Dx = diagnosis; IQR = interquartile range; HN = head-and-neck; ENT = ear, nose and throat; ECOG PS = Eastern Cooperative Oncology Group performance status; HPV = human papillomavirus.

SCCHN Treatment Overview

Median time from diagnosis to treatment initiation was 49 days (IQR: 24–131 days). At the point of data capture, 51% of the patients were receiving first-line drug treatment, 42% were receiving second-line treatment, and 6% were receiving third-line treatment (Table II).

First-Line Drug Treatment Patterns

Of the 108 patients who received first-line therapy, most (84%, *n* = 91) received a platinum-based regimen as first-line treatment (Table III), and of those patients, 26% (*n* = 24) received concomitant radiotherapy. The individual regimen most frequently received was cisplatin monotherapy (44%, *n* = 48), and of those patients, 33% (*n* = 16) received concomitant radiotherapy. Use of cetuximab-based regimens as first-line treatment was limited (17%). Use of the EXTREME regimen (cisplatin–cetuximab or carboplatin–cetuximab plus 5FU)[19] as first-line therapy was very rare (1%); however, 6% of the patients received EXTREME plus docetaxel. Docetaxel-containing regimens without cetuximab were received by 15 patients (14%), with 2 patients receiving docetaxel monotherapy.

TABLE II Time to treatment and treatment type in 109 patients at point of data capture

Variable	Value
Dx to start of first-line drug therapy (days)	
Median	49
IQR	24–131
End of 1st-line drug therapy to start of 2nd-line drug therapy (days)	
Median	49
IQR	19–149
Start of 1st-line platinum-based drug therapy to start of 2nd-line drug therapy (days)	
Median	55
IQR	20–146
Line of drug treatment at point of data capture [*n* (%)]	
First	56 (51)
Second	46 (42)
Third	7 (6)
Use of non-drug treatments[a] [*n* (%)]	
Surgery	35 (32)
Radiotherapy	82 (75)
Neither	13 (12)

[a] Before initiation of drug treatment; patients might previously have received surgery or radiotherapy, or both.
Dx = diagnosis; IQR = interquartile range.

Second-Line Drug Treatment Patterns

Median time to progression from initiation of first-line therapy to initiation of second-line therapy was 8.9 months (95% confidence interval: 6.4 months to 11.1 months; Figure 1). For the 53 patients who received second-line treatment, platinum-based therapies were used less frequently (13%) than they had been in the first line (Table IV). Few patients received concomitant radiotherapy during second-line therapy (*n* = 2). The oncologists reported a median of 49 days (IQR: 19–149) between the end of first-line and the initiation of second-line drug treatment (Table II). The second-line regimens most commonly used were cetuximab (43%), docetaxel (13%), paclitaxel (13%), and methotrexate (8%) monotherapies. Use of the EXTREME regimen remained low (2%). Of the patients who received second-line treatment, 87% (*n* = 46) had received a

TABLE III First-line drug treatment patterns in 108 patients

Treatment	With radiotherapy [*n* (%)]		Overall
	No	Yes	
Treatment regimens			
Carboplatin	2 (2)	—	2 (2)
Carboplatin–docetaxel	—	1 (1)	1 (1)
Carboplatin–docetaxel–5FU	—	1 (1)	1 (1)
Carboplatin–5FU	1 (1)	—	1 (1)
Carboplatin–paclitaxel	1 (1)	—	1 (1)
Cetuximab	5 (5)	2 (2)	7 (6)
Cisplatin	32 (30)	16 (15)	48 (44)
Cisplatin–cetuximab	3 (3)	—	3 (3)
Cisplatin–docetaxel–cetuximab	1 (1)	—	1 (1)
Cisplatin–docetaxel–5FU	7 (6)	3 (3)	10 (9)
Cisplatin–docetaxel–5FU –cetuximab	5 (5)	1 (1)	6 (6)
Cisplatin–5FU	12 (11)	1 (1)	13 (12)
Cisplatin–5FU–cetuximab	—	1 (1)	1 (1)
Cisplatin–5FU –methotrexate	1 (1)	—	1 (1)
Cisplatin–other	1 (1)	—	1 (1)
Cisplatin–paclitaxel	1 (1)	—	1 (1)
Docetaxel	2 (2)	—	2 (2)
Docetaxel–5FU –methotrexate	—	1 (1)	1 (1)
5FU–other	1 (1)	—	1 (1)
Gemcitabine	1 (1)	1 (1)	2 (2)
Methotrexate	2 (2)	1 (1)	3 (3)
Other	—	1 (1)	1 (1)
Regimen class[a]			
Platinum-based	67 (62)	24 (22)	91 (84)
Cetuximab-based	14 (13)	4 (4)	18 (17)

[a] Not mutually exclusive; regimen classes overlap. "Other" regimen assumed not to contain platinum or cetuximab.

5FU = 5-fluorouracil.

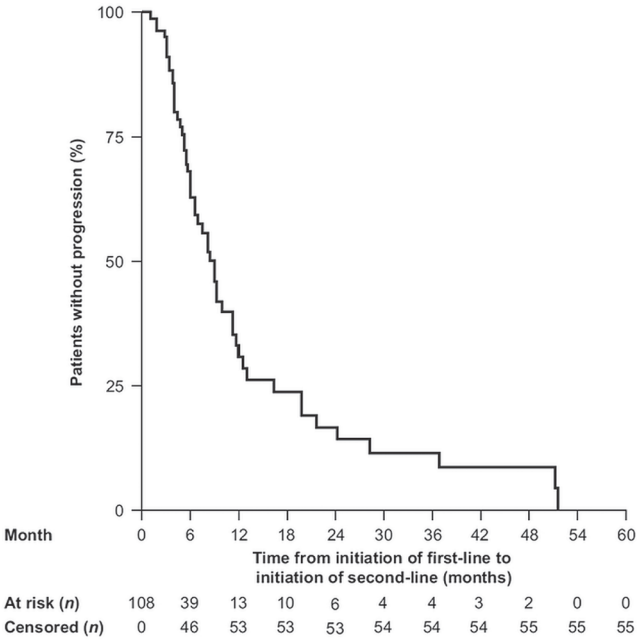

FIGURE 1 Kaplan–Meier probability of time to disease progression from initiation of first-line therapy until initiation of second-line therapy in 108 patients.

first-line platinum-based regimen. The median time between initiation of first-line treatment with a platinum-based regimen and initiation of second-line treatment was 55 days (IQR: 20–146 days; Table II). Nearly half the patients previously treated with platinum-based therapy (46%) received cetuximab monotherapy as second-line treatment; 13% received docetaxel monotherapy; 13%, paclitaxel monotherapy; 9%, methotrexate monotherapy; and 9%, another platinum-based regimen. In the patients who received platinum-based therapy in the first-line setting and who went on to receive second-line therapy, cetuximab monotherapy was the most frequently used regimen (45%, Table V).

DISCUSSION

Treatment patterns observed in this study generally reflected current treatment guidelines reported for Canada[8,20,27], with some notable deviations. Platinum-based chemotherapy (used concomitantly or postoperatively with radiotherapy) is considered the standard of care for the primary treatment of most patients with locally advanced (stages III–IVB) SCCHN[27]. Most patients (84%) received platinum-based therapies in the first-line setting. According to international guidelines[6,9], patients with an Eastern Cooperative Oncology Group performance status of 2 or greater should generally receive first-line monotherapy; accordingly, 6% of patients received cetuximab; 3%, methotrexate; and 2%, docetaxel. No patient received paclitaxel, carboplatin, 5FU, or capecitabine monotherapy. Docetaxel–cisplatin–5FU was received by 9% of the patients receiving first-line drug therapy. For larynx preservation, Canadian guidelines recommend either that regimen followed by radiation and surgery, or concurrent chemoradiotherapy, in preference to radiotherapy alone[27]. Cetuximab (as monotherapy or in combination with other agents) was received by 17% of patients in the first line; practice guidelines suggest the use of cetuximab in addition to intensified radiotherapy as an alternative to chemoradiotherapy for patients with stages III–IVB SCCHN who are ineligible for concurrent platinum-based chemotherapy or those more than 70 years of age[27].

Use of the EXTREME regimen[19] was low, with only 1% of patients receiving the regimen in the first line, and only 2% receiving it in the second line, although an additional 6% of patients received EXTREME–docetaxel as first-line treatment. Based on observations of increased survival[18],

TABLE IV Second-line drug treatment patterns in 53 patients

Treatment	With radiotherapy [*n* (%)]		Overall
	No	Yes	
Treatment regimens			
Capecitabine–cetuximab	1 (2)	—	1 (2)
Carboplatin	1 (2)	—	1 (2)
Carboplatin–5FU	1 (2)	—	1 (2)
Carboplatin–paclitaxel	—	1 (2)	1 (2)
Cetuximab	22 (42)	1 (2)	23 (43)
Cisplatin	1 (2)	—	1 (2)
Cisplatin–5FU	2 (4)	—	2 (4)
Cisplatin–5FU–cetuximab	1 (2)	—	1 (2)
Docetaxel	7 (13)	—	7 (13)
Docetaxel–cetuximab	1 (2)	—	1 (2)
Erlotinib	2 (4)	—	2 (4)
5FU	1 (2)	—	1 (2)
Methotrexate	4 (8)	—	4 (8)
Paclitaxel	5 (9)	—	7 (13)
Regimen classes			
Platinum-based regimens	6 (11)	1 (2)	7 (13)
Cetuximab-based regimens	25 (47)	1 (2)	26 (49)

[a] Not mutually exclusive; regimen classes overlap.
5FU = fluorouracil.

TABLE V Second-line treatment in 46 patients receiving first-line platinum

Treatment	Value [*n* (%)]
Monotherapy	
Cetuximab	20 (43)
Cetuximab + RT	1 (2)
Docetaxel	6 (13)
Docetaxel + RT	0
5FU ± RT	1 (2)
Gemcitabine ± RT	0
Methotrexate	4 (9)
Methotrexate + RT	0
Paclitaxel	4 (9)
Paclitaxel + RT	2 (4)
Other ± RT	2 (4)
Platinum	2 (4)
Platinum + RT	0
Combination therapy	
EXTREME regimen[a] ± RT	1 (2)
Platinum–5FU ± RT	0
Platinum–taxane ± RT	1 (2)
Other ± RT	2 (4)

[a] Platinum–5FU–cetuximab.
5FU = fluorouracil; RT = radiotherapy.

Canadian practice guidelines recommend the EXTREME regimen to improve survival and response rate in "suitable" untreated patients with R/M SCCHN[20,21]. However, few patients in the present study had metastatic disease at diagnosis. Additionally, EXTREME and other existing platinum-based treatment options are associated with severe toxicity and adverse effects on health-related quality of life[28]. It is unclear whether the low rates of use of EXTREME or other cetuximab–platinum–5FU–containing regimens observed in our study reflect such concerns.

Optimal first-line treatment selection is crucial to ensure that patients remain sufficiently healthy to receive subsequent treatments (that is, second-line and beyond)[18]—particularly those with locoregional progression. In the present study, second-line drug treatment regimens varied and primarily used monotherapies—namely, cetuximab (43%), taxanes (docetaxel, 13%; paclitaxel, 13%), and methotrexate (8%). Of the patients who progressed to second-line treatment, a high proportion (87%) had received platinum-based first-line treatment; only 9% of patients who received first-line platinum-based therapy subsequently received platinum-based therapy in the second-line setting. Given the poor response rates with existing therapies for R/M SCCHN and disease progression during or after platinum-based chemotherapy[18], the substantial health care and economic burden represented by those patients is driven largely by hospitalizations and anticancer therapy costs[10,29]. That observation has led to suggestions to limit the use of combination regimens for metastatic cancers and to restrict chemotherapy on the basis of performance status[30].

Higher-than-expected cetuximab use was identified in the second line. A formal comparison of observed treatment patterns with guideline recommendations was not the purpose of our study, because guidelines might not reflect currently approved indications or preferred clinical practice in a given country. Additionally, physician prescribing preferences are likely to be influenced by familiarity and personal preferences. For example, chemotherapy often incorporates a combination of drugs, each of which might have already been on the market for a long time. The label might therefore not reflect the combinations used for the treatment of cancer in a particular setting, oncologists might individualize therapy, and institutional protocols might allow for flexibility. The practice patterns identified in the present study illustrate the importance of real-world evidence in describing clinical practice and informing reimbursement decision-makers.

The increasing availability of novel therapies with better adverse event profiles could potentially change the Canadian treatment algorithm for SCCHN. A new therapy class—immune checkpoint inhibitors—has shown promising os results as monotherapy, with tolerable toxicities[31–34] and improvements in health-related quality of life[32,35] in patients with R/M SCCHN. However, our analysis was conducted before Canadian approval of those therapies. Subsequent real-world treatment-pattern studies are needed to understand the effects of novel therapies on clinical

practice and the outcomes of patients with R/M SCCHN and platinum-refractory disease. To the best of the authors' knowledge, few studies have examined real-world treatment patterns for patients with SCCHN. A real-world study of patients with R/M SCCHN conducted between 2006 and 2013 in the Netherlands provided insight into local drug usage patterns[10]; however, its reported findings cannot be compared directly with our results because of geographic differences in treatment guidelines, clinical practice, and reimbursement policies. The SCCHN treatment patterns presented here provide the most reliable evidence of Canadian clinical practice to date.

Several study limitations should be noted. With respect to the study's methods and the selection of participating physicians, a cross-sectional rather than a longitudinal approach was taken; the data therefore reflect the population with SCCHN at the time of data collection and cannot be used for causal inference or to project treatment patterns beyond the reporting period, because new agents have become available and clinical practice patterns could have changed. In addition, although some data were available at the time of diagnosis, most of the included data were available only at the time of capture; the study findings might therefore not have reflected the comprehensive clinical or treatment characteristics of the patients at the time of diagnosis. Furthermore, although disease stage and treatment could be identified at data capture, we could not elucidate the disease stage of the patients during prior lines of therapy. Physician inclusion was influenced by willingness to participate, resulting in a convenience sample that might not be representative of the overall population of Canadian physicians treating patients with SCCHN. In terms of patient selection, the patients included in the study represent a quasi-random sample because physicians were asked to select, from study initiation, the first 6–8 consecutive patients meeting the entry criteria. Providers were more likely to collect data from patients seen more frequently, who thus might have been overrepresented. Additionally, physician preferences could, in part, be influenced by provincial variations in reimbursement policy and patient access to relevant clinical trials. However, the systematic approach to recruitment was designed to reduce selection bias. No formalized diagnostic checklist was mandated in the study methods; instead, diagnosis of the target patient group was based on the judgment and diagnostic skills of the responding physicians, as being reflective of routine real-world clinical practice. With regard to treatment data, patients were selected on the basis of receiving drug therapy and only general first-line and second-line drug treatments were included. Information such as dose, frequency of therapy, or receipt of therapy by stage or tumour site was not reported. In addition, the classifications used in our analysis for line of therapy were based on receipt of drug therapy rather than on receipt of any therapy (for example, surgery or radiation) and could be open to interpretation. Consequently, it is not possible to differentiate between "line of any type of therapy" (that is, drug or non-drug treatment) and "line of drug therapy." Finally, as in any study based on chart review, data quality relied on the accurate reporting of information by physicians.

CONCLUSIONS

The published literature contains little information about clinical practice patterns in SCCHN. This Canadian real-world study revealed high use of platinum-based regimens as first-line treatment. Although some variation in second-line treatment patterns was noted, cetuximab-based regimens were used most frequently. Monotherapies were used more often in the second-line than in the first-line setting, with cisplatin being the monotherapy in highest use in the first line, and cetuximab being the most common monotherapy agent in the second line. The study findings generally support the view that there is no standard second-line treatment for SCCHN in Canada. Management strategies are expected to evolve with the emergence of the new immuno-oncology treatment options for patients with SCCHN, which could lead to improved outcomes for patients in Canada.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare the following interests: KB and PH were employees of Adelphi Real World at the time of the study; AATM is a full-time employee of Bristol–Myers Squibb Canada; AM is a full-time employee of Bristol–Myers Squibb Canada and received nonfinancial support from Bristol–Myers Squibb during the conduct of the study; JWS is a full-time employee and stockholder of Bristol–Myers Squibb.

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