Effectiveness Outcomes in Patients With Recurrent or Refractory Head and Neck Cancers: Retrospective Analysis of Data From a Community Oncology Database

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ABSTRACT

Purpose: The purpose of this study was to provide an understanding of the effectiveness of existing therapies in patients with advanced head and neck cancer (HNC), particularly in clinical practice.

Methods: Data from the electronic medical records of adult patients diagnosed with locally advanced or metastatic (Stage III-IVc) HNC between January 1, 2007, and October 1, 2015, were retrospectively collected from a network of community oncology practices in the United States. Eligible patients experienced disease progression despite having received prior systemic therapy. Kaplan-Meier and Cox regression analyses of progression-free survival (PFS) and overall survival (OS) were conducted. Patient-reported outcomes were also collected.

Findings: The study included 462 patients (median age 61.0 years; 80.7% male; 77.1% white). Most patients had a history of tobacco use (41.8% current, 41.8% past), and human papillomavirus testing was infrequent overall (11.0%). The median overall duration of follow-up was 16.4 months (range, 2.3–85.2 months). Median PFS values were 8.45 months with first-line treatment and 5.33 months with second-line treatment. PFS with first-line treatment was significantly associated with primary tumor location, performance status, and tobacco use. Performance status was a predictor of PFS in second-line treatment. Median OS values were 21.04 and 9.53 months from the start of the first and second lines of therapy, respectively. Abuse/excessive use of alcohol, older age, and impaired performance status were associated with a significantly increased risk for death in outcomes analyses. Outcomes were worse among patients initially diagnosed with Stage IVc disease versus those who progressed to Stage IVc. Past tobacco use and alcohol abuse were associated with worse patient-reported symptoms such as dry mouth and sore throat (smoking) and trouble swallowing (alcohol).

Implications: This study of data from clinical practice shows that there remains a large unmet need for effective therapeutic options in advanced HNC. Patients' characteristics such as alcohol use and performance status were statistically significant predictors of PFS and OS in Stage III-IVc HNC. (*Clin Ther.* 2018;■:1–16) © 2018 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Key words: head and neck cancer, OS, outcomes, PFS, PRO.

INTRODUCTION

Head and neck cancers (HNCs) comprise a diverse group of oral cavity, pharyngeal, and laryngeal cancers. Squamous cell carcinoma is the predominant histologic subtype. Approximately 4% of all new cancers (n = 64,690) and 2% of cancer-related deaths (n = 13,740) each year in the United States are attributable to HNC.[1] HNC is often curable using surgery and radiotherapy, particularly if diagnosed at Stage I or II when the 5-year survival rate is >80%.[1,2] Unfortunately, more than half of all diagnosed patients eventually experience local,

Accepted for publication July 19, 2018.
https://doi.org/10.1016/j.clinthera.2018.07.016
0149-2918/$ - see front matter

regional, or metastatic recurrence.[2] The prognosis is typically poor in patients with locoregional/metastatic recurrent disease, with median overall survival (OS) ranging from 5 to 10 months.[3] Platinum-based chemotherapy regimens or other chemotherapy regimens such as gemcitabine + vinorelbine are some recommended first-line treatment options in patients with metastatic or recurrent disease, depending on a patient's performance status, goals of therapy, and distal metastases.[4] Cetuximab, which targets the epidermal growth factor receptor pathway, in combination with platinum- or taxane-based chemotherapy regimens, also provides a survival benefit in patients with advanced disease.[5,6]

Patients who have resistant or progressive disease despite platinum-based chemotherapy can present a treatment challenge. For example, in one study, the addition of cetuximab to a docetaxel regimen did not appear to provide the same added benefit in this patient population, compared with the benefit seen with cetuximab as a first-line treatment in patients with advanced disease.[7] Similarly, other combination therapies (eg, docetaxel + gefitinib, vandetanib + methotrexate + 5-fluorouracil, everolimus + erlotinib) did not improve OS or progression-free survival (PFS) in the second-line setting.[8–11] In 2016, 2 agents that target programmed cell death-1, pembrolizumab and nivolumab, received approval from the US Food and Drug Administration for use in the treatment of patients with recurrent or metastatic HNC that had progressed after the administration of platinum-based chemotherapy.[12–15] Afatinib is also an option in these patients, based on results from a Phase III study that showed improvement in median PFS versus that with methotrexate (2.6 vs 1.7 months; $P = 0.030$).[4,16]

Our study aimed to characterize the demographic and clinical characteristics, effectiveness outcomes, and health-related quality of life (HRQOL) in patients with Stage III-IVc HNC who experienced disease progression in the advanced HNC setting. Although this study ended before the approval of immunotherapy options, it adds to the limited clinical-practice data on patients with difficult-to-treat HNC, both for outcomes and HRQOL, using retrospective data from a community oncology setting. This research lays the groundwork for future studies to evaluate the emerging treatment paradigm shift to immuno-oncology therapies.

PATIENTS AND METHODS

Study Design, Patients, and Setting

This retrospective, observational study used electronic data from a network of US community oncology practices. The database included electronic medical records, patient-reported outcomes (PROs) data from patient care monitors (PCMs), and notes from health care providers. Experienced clinical research nurses abstracted key information not otherwise available from structured data fields (eg, tumor location, performance status). Eligible patients were those diagnosed with advanced (Stage III-IVc) HNC between January 1, 2007, and October 1, 2015. Diagnoses included codes from the *International Statistical Classification of Diseases and Related Health Problems, Ninth Revision* (ICD-9) ranging from 140.x to 149.x or 161.x, or the corresponding ICD-10 codes (C00.x to C14.x or C32.x). Additional eligibility criteria included age ≥18 years at diagnosis and prior use of systemic anticancer therapy in the advanced care setting (in any line), with evidence of at least one disease progression. The protocol for this study was approved by IntegReview Institutional Review Board (Austin, Texas).

Procedures

Data were extracted using computerized queries of structured data fields and manual review of providers' notes by clinical research nurses. Qualifying diagnosis, staging, and details for other inclusion criteria were verified and documented. Data from patients who met all of the eligibility criteria were accrued. Relevant study data were abstracted and entered into electronic case-report forms. Protected health information and patients' identifiers were not collected. An independent quality-assurance review of the data was performed to confirm accuracy and completeness.

Study Measures

Study measures included demographic characteristics (age, sex, and race) and clinical disease characteristics (stage at diagnosis, primary tumor location, human papillomavirus [HPV] status, tobacco/alcohol use history, performance status, and comorbidities). The date of advanced-HNC diagnosis and date of disease progression were recorded. Date of death, from either the clinical record or Social Security Death Index records, was also recorded. Medical records provided information on surgeries and radiation received, and