Chemotherapy with Modified Docetaxel, Cisplatin, and 5-Fluorouracil in Patients with Metastatic Head and Neck Cancer

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ABSTRACT

Introduction: This retrospective study evaluates the efficacy of palliative chemotherapy with a modified docetaxel, cisplatin, 5-fluorouracil (5-FU; “TPF” regimen) regimen (mTPF; reduced doses of docetaxel, cisplatin, and 5-FU with reduction of intravenous 5-FU from 4 days to 2 days) in Asian patients with recurrent and metastatic squamous cell carcinoma of head and neck (HNSCC) after surgery and adjuvant chemoradiation. Methods: The mTPF regimen was used in this study. Fifty-five patients (from January 2007 to October 2009) received docetaxel on day 1, followed by cisplatin and 5-FU administered continuous infusion on day 2 for another 48 hours every 3 weeks for three to six cycles. Results: The disease control rate was 81%. The overall response rate was 56%. Five patients achieved complete remission; 26 patients had partial remission; 14 patients had stable disease. Ten patients had disease progression. The metastatic sites that responded well to mTPF regimen (either complete or partial remission) were: neck lymph node, lung, liver, and skin. The median follow-up was 15 months (range 1-28 months). The median overall survival was 10 months (range 2-28 months). The common nonhematological toxicity was alopecia and the most common hematological adverse event was neutropenia. Thirty-one patients (56%) had grade 3-4 neutropenia. Conclusion: The mTPF chemotherapy regimen is efficacious for the palliative treatment of recurrent and metastatic HNSCC in Asian patients.

Keywords: chemotherapy; head and neck cancer; metastatic squamous cell carcinoma

INTRODUCTION

Until now, treatment has been difficult for patients with metastatic HNSCC. In fact, the prognosis of
patients with metastatic squamous cell carcinoma of head and neck (HNSCC) is extremely poor. The choice of palliative chemotherapy includes single agent, two-agent combination therapy, and target agents with or without chemotherapy. The response rates with conventional chemotherapeutic agents range from 15% to 30% with a response duration of 3-5 months. Docetaxel is able to induce response rates ranging between 20% and 40%, and has been used with good efficacy in treating head and neck cancer, especially in neoadjuvant settings. Much of the progress in recent years has been done for induction chemotherapy followed by concurrent chemoradiation for local advanced HNSCC. In addition, docetaxel is also important in treating recurrent HNSCC. Docetaxel and cisplatin have also shown overall response rates (OR) of 30%-50% with a median duration of 5 months in several phase 2 studies. In addition, weekly chemotherapy with docetaxel may have efficacy with less toxicity. In fact, it has been shown that in patients with recurrent HNSCC who received second-line chemotherapy with a weekly low dose of docetaxel (35 mg/m²) and cisplatin (25 mg/m²) every 3 weeks, only 10% of the patients had greater than grade 3 toxicities. Recently, for patients with hypopharynx and larynx carcinomas, the docetaxel, cisplatin, 5-fluorouracil (5-FU; “TPF” regimen) induction chemotherapy was better than the PF (cisplatin and 5-FU) chemotherapy. The response rate was 80% in the TPF group and was 59% in the PF group. In the TAX 323 clinical trial, induction chemotherapy with TPF was compared with PF in stage III/IV unresectable locally advanced HNSCC. The TPF group had a median progression-free survival (PFS) of 11 months, whereas it was only 8.2 months in the PF group. Moreover, the TPF group had a median survival of 71 months, whereas it was 30 months in the PF group. Moreover, the efficacy of induction chemotherapy with paclitaxel added to PF has also been proven to have a better PFS and overall survival rate as compared to the PF regimen in one phase 3 trial.

The prognosis is ominous for patients with metastatic HNSCC and the current palliative chemotherapy only provides limited benefit. Moreover, the information regarding the use of the TPF regimen for metastatic HNSCC is also limited. According to the authors’ experience, the standard TPF regimen is too toxic for Asian patients due to severe bone marrow suppression; therefore, the present retrospective study was undertaken to examine the use of an modified TPF (mTPF) regimen for patients with metastatic HNSCC to investigate whether this regimen could be beneficial for Asian patients.

MATERIALS AND METHODS

From January 2007 and October 2009, 55 patients were recruited. All patients had received prior therapy with surgery followed by adjuvant chemoradiation with weekly cisplatin at 40 mg/m² and were clinically in remission after the previous treatment. Patients with confirmed recurrent and metastatic HNSC were included in this study. All patients were gave written consent before any treatment. To be included for mTPF chemotherapy, patients had Eastern Cooperative Oncology Group (ECOG) performance status ≤2; blood count with absolute neutrophil count ≥2×10⁹/L and platelet count ≥100×10⁹/L; serum levels of total bilirubin ≤2 mg/dL; and creatinine ≤1.6 mg/dL were also required. Treatment with the mTPF regimen consisting of intravenous docetaxel (60 mg/m²) on day 1, followed by cisplatin (50 mg/m²) on day 2, and 5-FU at 500 mg/m² with continuous infusion for 24 hours for another 2 days (days 2 to 4). Carboplatin at a