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Background

A phase I trial of induction cisplatin, docetaxel, 5-FU and erlotinib (TPF-E) followed by cisplatin, bevacizumab and erlotinib (PA-E) with radiotherapy (XRT) for advanced head and neck cancer (HNC) was conducted.

Methods

Eligible patients had stage IVA-C HNC, with performance status (PS) 0 or 1, good hematologic and renal reserve, and no pre-existing grade 2 cardiovascular comorbidities. Two cycles of induction q3 week TPF-E were administered, with 75 mg/m^2 cisplatin, 75 mg/m^2 docetaxel, and 750 mg/m^2 days 1-4 CI 5-FU during each cycle. Initial dose of erlotinib was 50mg daily from start of induction chemotherapy until radiotherapy completion. Dose escalation levels of erlotinib with 100mg and 150mg were performed. XRT was administered with concurrent cisplatin 30mg/m^2 weekly and bevacizumab 10 mg/kg q2 weeks. Dose limiting toxicity (DLTs) were defined as Grade 4-5 toxicity or Grade 3 toxicity attributable to erlotinib and requiring hospitalization. This trial was supported by a grant from Genentech.

Results

13 patients with previously untreated local-regionally advanced (11 patients) or previously untreated locoregional disease with oligometastatic disease (two patients) HNC were enrolled. Two patients in cohort 1 (erlotinib 50mg) did not complete XRT due to noncompliance or progression. One patient received induction Avastin with TPF-E and developed GI perforation, prompting deletion of Avastin from induction TPF-E. Four of five evaluable patients in cohort 1 completed both TPF-E and XRT with PA-E (erlotinib 50mg; erlotinib discontinued due to intractable diarrhea). Three of four patients in cohort 2 completed all therapy (100mg; patient with DLT of colonic perforation in diverticulum during induction TPF-E). Zero of one patient in cohort 3 completed all therapy (150mg; diarrhea, abscess and decreased PS). There were no Grade 5 toxicities; one patient in cohort 1 died soon after treatment with no cause on autopsy. One patient in the final regimen had significant gastrointestinal complications (perforation). At median 13.2 month follow-up, 7 patients (54%) are alive with no evidence of disease, and 2 (15%) are alive with recurrent but stable disease.

Conclusion

Erlotinib in combination with induction TPF followed by erlotinib with XRT, cisplatin and bevacizumab is active but toxic. MTD was reached at 100 mg erlotinib, but overall rates of treatment compliance were low, in part due to gastrointestinal toxicities and poor PS after induction therapy. Gastrointestinal toxicity proved to be the most frequent reason for morbidity and DLT in this study.

This trial was supported by a grant from Genentech.