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Clinical Trial Results

Adding Preoperative Radiotherapy Plus Cetuximab to Perioperative Chemotherapy for Resectable Esophageal Adenocarcinoma: A Single-Center Prospective Phase II Trial

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Author Summary

Abstract

Background. Local and systemic recurrence are important sources of treatment failure following surgical resection of esophageal adenocarcinoma. We hypothesized that adding preoperative cetuximab and radiotherapy (cetux-RT) to perioperative chemotherapy would increase treatment efficacy with acceptable toxicity.

Methods. In this prospective phase II trial, patients were treated with three cycles of epirubicin, cisplatin, and capecitabine (ECX), followed by cetux-RT. After surgery with curative intent, patients received three more cycles of ECX. Primary endpoints were efficacy, determined by histopathological complete response (pCR) rate, and safety, which was assessed with resectability rate.

Results. Of the 12 patients enrolled in this trial, six received at least one dose of cetux-RT. In five patients, cetux-RT was not started because of adverse events (AEs) related to preoperative chemotherapy; one patient had progressive disease. Addition of cetux-RT was well tolerated and did not interfere with the resectability rate (100%). However, the pCR rate was 0, and 50% of patients experienced serious adverse events (SAEs) postoperatively.

Conclusion. With 12 patients enrolled, the lack of initial signs of efficacy and a high incidence of postoperative SAEs prompted us to end this study prematurely. Perioperative ECX was associated with considerable toxicity, and further treatment intensification is problematic. ***The Oncologist*** 2014;19:32–33

Discussion

Long-term survival in patients with resectable esophageal adenocarcinoma remains poor, with a 5-year survival rate of only 20%–42% [1]. Perioperative ECX chemotherapy has improved survival rates but failed to deliver a significant proportion of pathologic complete responses. Since better locoregional control would probably improve survival rates, we added cetux-RT preoperatively (Fig. 1).

We found that intensification of the preoperative treatment was poorly feasible, as 42% of patients discontinued treatment because of toxicity of preoperative ECX. Addition of cetux-RT was well tolerated (Table 1) and did not interfere with the resectability rate; however, the extension of the preoperative treatment led to a high postoperative complication rate. The combination of an extensive surgical procedure, the type of disease, a prolonged preoperative period, and high preoperative toxicity may have contributed to the postoperative toxicity of this regimen.

Although we did not complete full accrual, analysis of the six evaluable patients showed disappointing efficacy, as none of the resected tumors showed pCR. Previous studies with

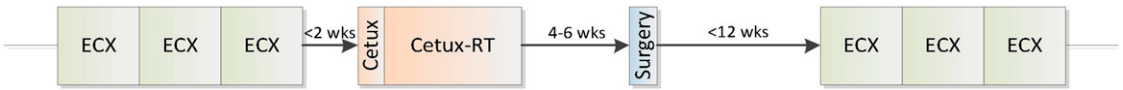

Figure 1. Treatment schedule. ECX: epirubicin (day 1, 50 mg/m^2), cisplatin (day 1, 60 mg/m^2), capecitabine (days 1–21, 1,250 mg/m^2); Cetux: cetuximab (day 1, 400 mg/m^2); Cetux-RT: cetuximab 250 mg/m^2 weekly, radiotherapy 45 Gy (25 × 1.8 Gy).

Abbreviations: Cetux, cetuximab; Cetux-RT, cetuximab plus radiotherapy; ECX: epirubicin, cisplatin, and capecitabine; wks, weeks.

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Table 1. Adverse events related to cetux-RT

Name	*NC/NA	1	2	3	4	5	All Grades
Rash: acne/acneiform	16%	33%	50%	0%	0%	0%	83%
Fatigue (asthenia, lethargy, malaise)	50%	16%	33%	0%	0%	0%	50%
Nail changes	83%	0%	16%	0%	0%	0%	16%
Dysphagia (difficulty swallowing)	83%	0%	16%	0%	0%	0%	16%
Hypertension	83%	0%	16%	0%	0%	0%	16%
Rash: hand-foot skin reaction	83%	0%	16%	0%	0%	0%	16%
Dry skin	66%	33%	0%	0%	0%	0%	33%
Cough	66%	33%	0%	0%	0%	0%	33%
Nausea	66%	33%	0%	0%	0%	0%	33%
Pain in irradiated area	66%	33%	0%	0%	0%	0%	33%

*No Change from Baseline/No Adverse Event

cetux-RT in patients with esophageal cancer did show an increase in pCR to 27%–33% [2–4]. However, cetux-RT efficacy appears to be limited to squamous cell carcinomas [4, 5].

Since there were no preliminary signs of efficacy, we feel that our study does not warrant further investigation of cetux-RT for resectable esophageal adenocarcinoma. Furthermore, since intensification of ECX will be problematic, alternative multimodality neoadjuvant schedules need to be identified.

Author disclosures and references available online.