

Surgery alone versus chemoradiotherapy followed by surgery for localized esophageal cancer: Analysis of a randomised controlled phase III trial FFCD 9901.

C. Mariette, J. F. Seitz, E. Maillard, F. Mornex, P. A. Thomas, J. L. Raoul, V. Boige, D. Pezet, C. Genet, L. Bedenne, Federation Francaise de Cancerologie Digestive; Dpt of surgical oncology University Hospital of Lille, Lille, France; La Timone University Hospital, Marseille, France; Biostatistic Unit FFCD, Dijon, France; Department of radiotherapy, Pierre Benite, France; Department of thoracic surgery, Marseille, France; Departement d'Oncologie Medicale, Centre E Marquis, Rennes, France; Institut Gustave Roussy, Villejuif, France; Department of surgery, Clermond Ferrand, France; Department of Gastroenterology, Limoges, France; University Hospital, Dijon, France

Abstract Text:

Background: Resection remains the best treatment for carcinoma of the esophagus regarding local control but local recurrence, distant metastasis and poor survival remain an issue after surgery. Often investigated in locally advanced esophageal tumors, impact of neoadjuvant chemoradiotherapy in patients with small tumors is unknown. The aim of this randomised controlled phase III was to assess whether preoperative chemoradiotherapy improves outcomes for patients with localized (stages I or II) esophageal cancer.

Methods: The primary endpoint was overall survival. Secondary endpoints were progression free survival, postoperative morbidity and mortality, R0 resection rate, prognostic factors identification. Analysis was done by intention to treat. To demonstrate an increase of overall survival from 35% (S group) to 50% (CRT group) with alpha 5% and 80% power, it was required to observe 182 deaths. 195 patients were randomized from 06/2000 to 06/2009 in 30 centers, 98 were assigned to surgery alone (S group) and 97 to neoadjuvant chemoradiotherapy group (CRT group; 45Gy/25F/5weeks with 2 courses of concomitant chemotherapy 5fluorouracil 800mg/m²/day D1-D4 and cisplatin 75mg/m² D1 or D2). We report results of a planned interim analysis for primary endpoint.

Results: Patient and tumor characteristics were similar between groups. Patients were preoperatively staged I in 18%, IIA in 49.7%, IIB in 31.8%, unknown in 0.5%. Postoperative morbidity and 30 day-mortality rates were 49.5% (S group) vs 43.9% (CRT group) (p=0.17) and 1.1% (S group) vs 7.3% (CRT group) (p=0.054), respectively. After a median follow-up of 5.7 years, 106 deaths were observed. Median survivals were 43.8 (S group) vs 31.8 months (CRT group) (HR 0.92, 95% CI 0.63-1.34, p=0.66). We could stop trial for futility.

Conclusions: Neoadjuvant chemoradiotherapy with cisplatin and fluorouracil does not improve overall survival but enhances postoperative mortality rate for patients with stage I or II esophageal cancer compared with surgery alone.