Impact of neoadjuvant chemoradiation in localised oesophageal cancer: results of a randomised controlled phase III trial FFCD 9901

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Background: Resection remains the best treatment for carcinoma of the oesophagus but poor survival due to local recurrence and distant metastatis remain an issue after surgery. Often investigated in locally advanced oesophageal tumours, impact of neoadjuvant chemoradiotherapy in patients with earlier tumours is unknown. This randomised controlled phase III trial aimed to assess whether preoperative chemoradiotherapy improves outcomes for patients with localised (stages I or II) oesophageal cancer.

Methods The primary endpoint was overall survival (OS). Secondary endpoints were progression free survival (PFS), postoperative morbidity and mortality, R0 resection rate, prognostic factors identification. Analysis was done by intention to treat. 195 patients were randomized from 06/2000 to 06/2009 in 30 centres, 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/m^2/day D1-D4 and cisplatin 75mg/m^2 D1 or D2). We report results of a planned interim analysis for primary endpoint.

Results: 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. The R0 resection rates were 85.7% (S group) vs. 88.1% (CRT group). After a median follow-up of 5.7 years, 106 deaths were observed. 3-year OS was 55.2% (S group) vs. 48.6% (CRT group) (HR 0.92, 95% CI 0.63-1.35, p=0.68). 3-year PFS was 43.9% (S group) vs. 41.2% (CRT group, p=0.98). We could stop trial for futility.

Conclusions: For stage I or II oesophageal cancers, neoadjuvant chemoradiotherapy does not improve OS, PFS or R0 resection rate but enhances postoperative mortality when compared with surgery alone.