Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial

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Abstract

Background: Docetaxel-based chemotherapy is effective in metastatic gastric and gastro-oesophageal junction adenocarcinoma. This study reports on the safety and efficacy of the docetaxel-based triplet FLOT (fluorouracil plus leucovorin, oxaliplatin and docetaxel) as a perioperative therapy for patients with locally advanced, resectable tumours.

Methods: In this controlled, open-label, phase 2/3 trial, we randomly assigned 716 patients with histologically-confirmed advanced clinical stage cT2 or higher or nodal positive stage (cN+), or both, resectable tumours, with no evidence of distant metastases,

via central interactive web-based-response system, to receive either three pre-operative and three postoperative 3-week cycles of 50 mg/m^2 epirubicin and 60 mg/m^2 cisplatin on day 1 plus either 200 mg/m^2 fluorouracil as continuous intravenous infusion or 1250 mg/m^2 capecitabine orally on days 1 to 21 (ECF/ECX; control group) or four preoperative and four postoperative 2-week cycles of 50 mg/m^2 docetaxel, 85 mg/m^2 oxaliplatin, 200 mg/m^2 leucovorin and 2600 mg/m^2 fluorouracil as 24-h infusion on day 1 (FLOT; experimental group). The primary outcome of the trial was overall survival (superiority) analysed in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, number NCT01216644.

Findings: Between Aug 8, 2010, and Feb 10, 2015, 716 patients were randomly assigned to treatment in 38 German hospitals or with practice-based oncologists. 360 patients were assigned to ECF/ECX and 356 patients to FLOT. Overall survival was increased in the FLOT group compared with the ECF/ECX group (hazard ratio [HR] 0·77; 95% confidence interval [CI; 0.63 to 0·94]; median overall survival, 50 months [38·33 to not reached] vs 35 months [27·35 to 46·26]). The number of patients with related serious adverse events (including those occurring during hospital stay for surgery) was similar in the two groups (96 [27%] in the ECF/ECX group vs 97 [27%] in the FLOT group), as was the number of toxic deaths (two [<1%] in both groups). Hospitalisation for toxicity occurred in 94 patients (26%) in the ECF/ECX group and 89 patients (25%) in the FLOT group.

Interpretation: In locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma, perioperative FLOT improved overall survival compared with perioperative ECF/ECX.

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