Lapatinib with chemotherapy for gastro-oesophageal cancer

Results from a phase 2 clinical trial of standard chemotherapy versus modified chemotherapy plus lapatinib in patients with gastro-oesophageal cancer have shown that addition of lapatinib was feasible, with an increase in toxic effects.

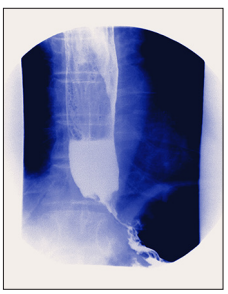
Patients with HER2-positive gastro-oesophageal adenocarcinoma were randomly assigned (1:1) to standard chemotherapy (three preoperative cycles and three postoperative cycles of 50 mg/m² epirubicin on day 1, 60 mg/m² intravenous cisplatin on day 1, and 1250 mg/m² of oral capecitabine per day) or modified chemotherapy plus lapatinib (same dose of epirubicin and cisplatin, 1000 mg/m² of capecitabine on days 1–21 of each cycle, and 1250 mg of lapatinib per day, followed by six cycles of maintenance 1500 mg lapatinib). The primary outcomes were safety and establishment of a recommended phase 3 dose, for which a cutoff of 20% of patients with grade 3 or 4 diarrhoea was deemed acceptable.

24 patients were assigned to standard chemotherapy and 22 to modified chemotherapy plus lapatinib. Two (20%) of the first ten patients given modified chemotherapy plus lapatinib had grade 3 diarrhoea, so lapatinib dose was not increased. Four (21%) of 19 in the modified chemotherapy plus lapatinib group had grade 3 or 4 diarrhoea (none in the standard chemotherapy group). One (4%) of 24 in the standard chemotherapy group and three (15%) of 20 in the modified chemotherapy plus lapatinib group stopped treatment early; four (21%) of 19 in the modified chemotherapy plus lapatinib group had a dose reduction. 11 (69%) of 16 in the standard chemotherapy group and 12 (71%) of 17 in the modified chemotherapy plus lapatinib group had R0 resection.

Study author David Cunningham (Royal Marsden NHS Foundation Trust, London, UK) said, "Targeting the HER2 pathway with trastuzumab has been shown to be successful in advanced oesophago-gastric cancer, and this study was designed to assess the feasibility and efficacy of lapatinib, which also targets the HER2 pathway. This pilot study showed that lapatinib can be safely added to chemotherapy in this setting."

Yelena Janjigian (Memorial Sloan-Kettering Cancer Center, New York, USA) said, "The most important result is the 69% to 71% R0 resection with chemotherapy plus lapatinib. These data highlight the fact that epirubicin-based therapies should be avoided as they are toxic, provide no additional efficacy, and make for a very poor back bone for addition of biologic therapy."

Robert Stirrups



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For the **study by Smyth and colleagues** see *JAMA Oncol* 2019; published online June 20. DOI:10.1001/jamaoncol.2019.1179