Title of the Article:
Lapatinib versus lapatinib plus capecitabine as second-line treatment in human epidermal growth factor receptor 2-amplified metastatic gastro-oesophageal cancer: a randomised phase II trial of the Arbeitsgemeinschaft Internistische Onkologie.

Abstract:
Human epidermal growth factor receptor 2 (HER2) amplification is present in a subgroup of gastro-oesophageal cancers (GCs). HER2 inhibition with trastuzumab has shown to improve outcomes in advanced disease. Lapatinib ditosylate (LAP), a dual anti-epidermal growth factor receptor (EGFR) and anti-HER2 tyrosine kinase inhibitor with preclinical activity against GC, has been approved in HER2-positive breast cancer. We aimed to study the activity of LAP in HER2-amplified GC. Patients (pts) with HER2-positive (gene amplification or increased copy numbers based on predefined criteria) advanced GC were randomly allocated 1:1 to receive LAP 1250mg per day 1-21 plus capecitabine (CAP) 2000mg/m² on days 1-14 of a 21-day cycle or LAP 1500mg monotherapy day 1-21 after having failed on a platinum-based first-line therapy. HER2 status was assessed centrally. The primary end-point was the objective response rate (ORR) as assessed by the investigator using Response Evaluation Criteria in Solid Tumors.
We aimed to include 38 pts per arm to show an interesting response rate of >20% in either of the two arms. 37 pts were enrolled (18 to LAP+CAP, 19 to LAP). Pts had received a median of three prior treatment lines. 12 pts in the LAP+CAP group (67%) and 12 pts in the LAP group (63%) had received prior trastuzumab. Only two pts (11.1%; 95% confidence interval (CI): 1.37-34.7), both in the LAP+CAP arm, achieved an objective response. The study was closed prematurely for futility. Median time to progression was 42 (95% CI: 38-61) days in the LAP group and 83 (95% CI: 42-86) days in the LAP+CAP group. Other secondary efficacy end-points (progression-free and overall survival) were comparable in the two treatment groups. Rates of diarrhoea were higher with LAP+CAP (61%; 95% CI: 35-83) compared to 26% (95% CI 9-51) with LAP mono, whereas other adverse events were mostly similar between the groups (18 [100%] versus 17 [90%]). Lapatinib showed insufficient activity in HER2-amplified pretreated advanced GC. The safety profile of LAP or LAP+CAP was as expected with some more toxicity in the combination arm. (ClinicalTrials.gov Identifier, NCT01145404).