

## gastrointestinal tumours, non-colorectal

### 629P LAPATINIB VERSUS LAPATINIB PLUS CAPECITABINE AS SECOND-LINE TREATMENT IN HER2-OVEREXPRESSING METASTATIC GASTRO-ESOPHAGEAL CANCER (GC): A RANDOMIZED PHASE II TRIAL OF THE ARBEITSGEMEINSCHAFT INTERNISTISCHE ONKOLOGIE (AIO)

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**Aim:** Her2 amplification is present in a subgroup of gastroesophageal cancers (GCs). Her2 inhibition with Trastuzumab has shown to improve clinical outcomes in metastatic disease. Lapatinib ditosylate (LAP), a dual anti 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.

**Methods:** Patients (pts) with Her2 positive (FISH ratio  $\geq 2.0$  or IHC3+ if ratio was between 1.8 and  $<2.0$ ) advanced GC were randomly allocated 1:1 to receive LAP 1250 mg per day 1-21 plus capecitabine (CAP) 2000mg/m<sup>2</sup> on days 1-14 of a 21-day cycle or LAP 1500 mg monotherapy day 1-21 after having failed on a platinum-based first-line therapy. Her2 status was assessed centrally. The primary endpoint was the objective response rate (complete or partial response) as assessed by the investigator using RECIST 1.1 criteria. We aimed to include 38 pts per arm to show an interesting response rate of  $>20\%$  in either of the two arms.

**Results:** 37 pts were enrolled (18 to LAP + CAP, 19 to LAP mono). Pts received a median of three treatment cycles. 10 pts in the LAP + CAP group (56%) and 7 pts in the LAP mono group (37%) had received prior Trastuzumab. Only two pts (11.1%; 95% CI: 1.37 – 34.7), both in the LAP + CAP arm, achieved an objective response. Therefore, the study was closed prematurely. Median time to progression was 42 (95% CI: 38 to 61) days in the LAP group and 83 (95% CI: 42 to 86) days in the LAP + CAP group ( $p = 0.07$ ). The other secondary efficacy endpoints (progression-free [median 41 and 47 days] and overall survival [median values not yet mature]) were comparable in the two treatment groups. Rates of diarrhea (all grades) were higher with LAP + CAP (61%; 95% CI: 35 to 83) compared to 26% (95%CI 9 to 51) with LAP mono, while other adverse events were mostly similar between the groups (18[100%] vs. 17[90%]). Slightly more pts in the LAP-CAP group experienced serious adverse events (44 vs. 32%).

**Conclusions:** Lapatinib showed insufficient activity, especially as monotherapy, in HER2 amplified pretreated advanced GC. This led to premature study termination. The safety profile of LAP or LAP + CAP was as expected with some more toxicity in the combination arm.

**Disclosure:** P.C. Thuss-Patience: Research support by GSK; F. Lordick: GSK. All other authors have declared no conflicts of interest.