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Final results and subgroup analysis of the PETRARCA randomized phase II AIO trial: Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2 positive resectable esophagogastric adenocarcinoma

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Background

Perioperative FLOT is a standard of care for resectable, esophagogastric adenocarcinoma (EGA). This trial evaluates the addition of trastuzumab (tras) and pertuzumab (per) to FLOT for HER2-positive patients (pts).

Methods

PETRARCA is a multicenter, randomized, investigator initiated trial planned as a phase II/III study. We report the phase II part of this trial. Pts with HER2+ resectable EGA (≥ cT2 or cN+) were randomized 1:1 to 4 pre- and post-operative cycles of FLOT (Docetaxel 50 mg/m^2; Oxaliplatin 85 mg/m^2; Leucovorin 200 mg/m^2; 5-FU 2600 mg/m^2, q2w) (Arm A) or the same regimen with tras 8/6 mg/kg and per 840 mg q3w, followed by 9 cycles tras/per (arm B). Primary endpoint for the phase II part was the rate of pathological complete remission (pCR). Main secondary endpoints were DFS, OS and safety.

Results

The trial closed prematurely and did not proceed to phase III. In total, 81 pts were randomized (A, 41; B, 40). Baseline characteristics were balanced (overall, male 79%; median age 60; cT3/T4 86%; cN+ 85%; GEJ 75%). 93% in arm A and 90% in arm B completed pre-OP treatment as planned. More pts had at least one dose modification in arm B (A, 44%; B, 70%). pCR rate was significantly improved with tras/per (A, 12%; B, 35%; p = 0.02). Likewise, the rate of pathological lymph node negativity was higher with tras/per (A, 39%; B, 68%). R0-resection rate (A, 90%; B, 93%) and surgical morbidity (A: 43%; B, 44%) were comparable. Moreover, in-house mortality was equal in both arms (overall 2.5%). Median DFS was 26 months in arm A and not yet reached in arm B (HR 0.58, p = 0.14). After a median follow-up of 22 months median OS was not yet reached. DFS and OS rates [with 95% CI] at 24 months were 54% [38-71%] and 77% [63-90%] in arm A and 70% [55-85%] and 84% [72-96%] in arm B, respectively. More ≥ grade 3 adverse events were reported with tras/per (75% vs. 85%), especially diarrhea (5% vs. 41%) and leukopenia (13% vs 23%).

Conclusions

The addition of tras/per to perioperative FLOT significantly improved pCR and nodal negativity rates in pts with Her2+ resectable EGA at the price of higher rates of diarrhea and leukopenia. Subgroup analyses will be presented.

Clinical trial identification

NCT02581462; EudraCT: 2014-002695-86.

Legal entity responsible for the study

Institut für Klinische Krebsforschung IKF GmbH.

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Disclosure

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