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Perioperative FLOT plus ramucirumab versus FLOT alone for resectable esophagogastric adenocarcinoma— Updated results and subgroup analyses of the randomized phase II/III trial RAMSES/FLOT7 of the German AIO and Italian GOIM

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Background

Periop. FLOT has become SOC for resectable, esophagogastric adenocarcinoma (EGA). However, patient's outcome is still poor. This trial evaluates the addition of the VEGF-R2 inhibitor ramucirumab (RAM) to FLOT.

Methods

This is a prospective, international, randomized, investigator-initiated phase II/III trial. Patients (pts) with resectable, Her2-negative EGA (\geq cT2 or cN+) were randomized to 4 pre-and post-operative cycles of FLOT (docetaxel 50 mg/m²; oxaliplatin 85 mg/m²; leucovorin 200 mg/m²; 5-FU 2600 mg/m², q2w) alone (Arm A) or FLOT with RAM 8mg/kg q2w, followed by 16 cycles RAM (Arm B, FLOT-RAM). Here, we report the main results along with the subgroup analysis explaining the higher rate of R0-resection in the FLOT-RAM arm.

Results

In total, 180 pts (FLOT, 91; FLOT-RAM, 89) were randomized. Baseline characteristics were similar between arms (male, 73%; median age, 60y; cT3/T4, 83%; cN+, 78%; GEJ, 54%). The rate of signet-ring cell cancer was high (40%). As reported at ASCO, no difference in path response rates was seen (FLOT, 30%; FLOT-RAM, 27%). However, FLOT-RAM significantly improved R0-resection rate (FLOT, 82%; FLOT-RAM, 96%, p=0.0078). This difference was due to less pts in the FLOT-RAM arm with disease progression prior to operation (FLOT, 6%; FLOT-RAM, 1%), more pts proceeding to operation (FLOT, 93%; FLOT-RAM, 97%), more pts receiving resectional surgery (FLOT, 88%; FLOT-RAM, 97%), and less pts having residual tumor out of the resected pts (FLOT, 4; FLOT-RAM, 1). In the subgroup analysis, the relative benefit of FLOT-RAM in terms of R0-resection was seen in all groups but was a bit pronounced in the cT3/T4 group (FLOT, 80%; FLOT-RAM, 97%), specifically the T4 (FLOT, 1/4 [25%]; FLOT-RAM, 8/8 [100%]) and the diffuse/mixed type histology (FLOT, 77%; FLOT-RAM, 95%).

Conclusions

FLOT-RAM significantly improved R0-resection rates in a patient group enriched with diffuse type and signet cell histology, mainly because more pts proceeded to operation, more pts received resectional surgery, and less pts had residual disease. The effects were pronounced in more advanced stage and the diffuse/mixed type histology.

Clinical trial identification

NCT02661971; EudraCT: 2015-003118-26.

Legal entity responsible for the study

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Disclosure

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