

Clinical outcomes of adjuvant treatment strategies in locally advanced gastroesophageal and gastric adenocarcinoma with poor pathological response to neoadjuvant FLOT: A Turkish Oncology Group (TOG) study.

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Background: Perioperative FLOT is the standard of care for locally advanced gastroesophageal adenocarcinoma. However, the clinical benefit of continuing the same regimen or employing alternative strategies (regimen switch, addition of radiotherapy) in patients with poor pathological response (TRG 2–3) remains unclear. **Methods:** This multicenter retrospective study included 380 patients with poor pathological response (Ryan TRG 2–3) after neoadjuvant FLOT. Patients with TRG 0–1 and those receiving non-FLOT neoadjuvant therapy were excluded. The impact of R0 resection status, perioperative treatment completion rates, and adjuvant treatment modalities on disease-free survival (DFS) and overall survival (OS) were analyzed. **Results:** R0 resection was achieved in 83.4% of patients (median age 58.7, 75% male). The perioperative FLOT completion rate was 65.7%. In the adjuvant setting, 82% received FLOT, 10.2% received doublet (FOLFOX/CAPOX) regimens, and 16.2% received adjuvant radiotherapy (RT). For the entire cohort, median OS was 33.0 months (95% CI: 29.6–36.4) and median DFS was 17.0 months (95% CI: 13.8–20.2). OS was longer in the R0 group compared to R1 (34 vs 27 months, $p = 0.161$). No significant difference was found between adjuvant FLOT and doublet regimens for DFS (18 vs 19 months, $p = 0.729$) or OS ($p = 0.515$). The addition of adjuvant RT did not provide additional benefit for DFS (20 vs 18 months, $p = 0.436$) or OS ($p = 0.97$) compared to those who did not receive RT. **Conclusions:** In patients with poor response to neoadjuvant FLOT, continuing FLOT in the adjuvant setting, switching to doublet regimens, or adding radiotherapy did not result in significant survival differences. Novel biomarker-driven studies are needed to determine the optimal adjuvant approach in this high-risk subgroup. Research Sponsor: None.