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598P Influence of the early stoma closure after low rectal cancer resection on completeness of adjuvant chemotherapy (CoCStom): A randomized, controlled multicentre trial of the AIO (AIO KRK 0113)

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Background: There is uncertainty whether early closure (EC) of a defunctioning stoma influences the complete administration of the adjuvant chemotherapy (CoC) after low anterior rectal resection (LAR) for rectal cancer. CoC was previously shown in retrospective analyses to improve the five-year OS and DFS.

Methods: CoCStom trial was a prospective randomized multicenter investigator-initiated study. Patients undergoing neoadjuvant therapy (chemoradiation or 5x5 Gy radiotherapy) followed by LAR for locally advanced rectal cancer were randomized in two arms. Experimental - EC, 8 to 10 days after LAR; and control - late closure of the stoma (LC), after completion of the adjuvant chemotherapy (26 weeks) which included both 5-FU- and oxaliplatin-based regimens according to local practice and tumor stage. The primary endpoint was CoC. The study was designed to show an CoC improvement of 20 % (power 80%, alpha-value 0.05). Secondary endpoints: oncological and surgical outcomes as well as quality of life.

Results: A total of 257 patients with comparable baseline characteristics and pathohistological (UICC) stages were randomized between 2013 and 2018. Of these, 233 (EC: 116 vs. LC: 117) were eligible for analysis. Median follow up was 24 months. Surgical morbidity after stoma closure was comparable (Clavien Dindo III-IV: EC vs. LC: 15.8 vs. 18.9%). The median hospitalization after LAR was 17 days in both groups. CoC was similar EC [62.9% (95% CI: 53.5 - 71.7%] and LC [65.8% (56.5 -74.3%]. Patients in the EC group started adjuvant chemotherapy (median 38 vs. 27 days after randomization) significantly later and received less oxaliplatin-based regimens (8.5 vs. 15%). DFS was numerically better in the EC group (HR 1.6; 95% CI: 0.83 — 3.06).

Conclusions: EC of the stoma was feasible and did not lead to increased surgical morbidity. CoC was not improved, however, a trend towards better DFS was observed within the EC group despite similar CoC, a later start of adjuvant therapy as well as less use of oxaliplatin-based regimens. Thus, EC of the stoma appears to be a valid option for patients undergoing LAR.

Clinical trial identification: DRKS00005113.

Legal entity responsible for the study: Flavius Sandra-Petrescu, MD, on behalf of the CoCStom Study Group.

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599P R-IMMUNE: A phase Ib/II study to evaluate safety and efficacy of atezolizumab combined with radio-chemotherapy in a preoperative setting for patients with locally advanced rectal cancer (LARC)

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Background: There is a strong rationale to combine radiotherapy with immune checkpoint inhibitors (ICIs). This study evaluates this combination before surgery in locally advanced rectal cancer (LARC).

Methods: R-IMMUNE, a multicentric phase Ib/II trial, included patients with stage II/III LARC treated with a preoperative combination of radio-chemotherapy (45-50 Gy/25 fractions, 5FU 225 mg/m2/d, 5d/w from week 1 to 5) + atezolizumab 1200 mg/infusion (ATZ). The phase Ib evaluated a single infusion of ATZ at week 3. Phase II evaluated 4 infusions of ATZ at weeks 3, 6, 9 and 12. Surgery was planned for week 15. Safety and efficacy based on the pathological complete response (pCR) rate are primary objectives. Based on a two-stage Simon design, 33 patients (+3 for the replacement of non-evaluable patients) were required in phase II to detect an increase in pCR rate from 15% to 35% ($\alpha = 0.1$, $\beta = 0.1$), with at least 8 pCRs to reject the null hypothesis.

Results: Six patients were included in phase Ib and 34 in phase II. This analysis covered 39 patients (median age 63 years, 56% male, 82% stage III, 12% MSI-H), excluding 1 phase II patient who is still undergoing treatment. A total of 193 adverse events (AEs) were reported, of which 29 (15%) were grade 3-4 and involved 19/39 (49%) of patients. Among gade 3-4 AEs, most frequent were urinary tract infections (6/29), blood disorders (5/29), post-operative anastomotic leaks/infections (4/29) and gastrointestinal disorders (4/29). Five patients presented immune-related AEs: 1 immune thrombocytopenia (grade 4), 2 endocrine disorders (grade 2) and 2 skin disorders (grade 1). So far, efficacy was assessed in 6 phase Ib patients and in 31 patients from the phase II (2 were excluded for protocol deviation). Respectively, 2/6 and 8/31 patients had a pCR. Overall, 10/37 (27%) patients had a pCR (including 2 MSI-H).

Conclusions: An analysis of the nearly complete R-immune cohort confirmed an acceptable safety profile and met study efficacy objectives. The results warrant further investigations of ICIs combined with radiotherapy in LARC eventually within a total neoadjuvant treatment and organ preservation based strategies.

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Legal entity responsible for the study: Grand Hôpital de Charleroi — Belgium.

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