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Could delayed coloanal anastomosis (DCA) without derivative stoma improve morbi-mortality after total mesorectal excision (TME) for mid and low rectal carcinoma: a feasibility study

S. Evrard, T. Razafindratsira, F. Leblanc, M. Fonck, R. Brunet, Y. Bécouarn, S. Mathoulin-Pélissier. *Institut Bergonié, Digestive Tumours Unit, Bordeaux, France*

Background: Anastomotic leakage varies between 3 and 25% after TME. Coloanal fistula may lead to the constitution of a pelvic abscess, the loss of the sphincter in case of preoperative radiotherapy. It is the main cause of postoperative mortality and should impair long term results of survival in rectal cancer. A derivative stoma is usually realised after a preoperative radiotherapy which may also bring some complications, a loss of quality of life for the patient and a financial burden for society. Hypothesis: DCA could diminish the rate of fistula without stoma.
Method: Laparoscopy was performed by default. After complete mobilisation of the left colon, a TME was realised. The rectum was cut by endoanal route. Rectum and sigmoid colon were pulled through the anus and resected at the level of the inferior mesenteric artery. 10 cm of colon were exteriorised. 6 days later, the patient was reoperated on. The exteriorised colon was cut and a direct colonanal anastomosis was performed without derivative stoma.
Results: 23 patients were enrolled in this feasibility study. Mean distance between the tumour and the anal verge was 6 cm [3– 10]. 18 (78%) patients had neoadjuvant radiochemotherapy. Laparotomy was chosen in 3 patients respectively for, a T4 tumour, a parietal dehiscence, hepatic lesions. Using laparoscopy (20), conversion rate was 10% (for bleeding). Resection was classified as R0 in 22 cases (95%), R1 in 1 case.
The two main complications were ischemic necrosis of the left colon from both part of the anus. For these two patients, a new mobilisation of the colon was followed by a new DCA with favourable outcome. One had an ischemy of the sole exteriorised colon resolved by the second step of the procedure. A bleeding of the posterior part of the prostate required haemostasis, a slippage of the small bowel behind the descending colon needed repositioning and closure of the mesenteric window; lastly a perimarginal abscess of the buttock was drained during the second step. 4 patients (17%) needed to be reoperated on for complications.
No anastomotic leakage appeared in any patient. No derivative stoma was required even in the cases needing a reoperation for complications. No patient needed a readmission to hospital after the initial discharge.
Conclusion: DCA may lead to a dramatic decrease in morbi-mortality after surgical treatment of mid and low rectal cancers without derivative stoma even after preop chemoradiotherapy. A drastic reduction of the cost may also be expected.

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Capecitabine (C), in combination with irinotecan (I) and oxaliplatin (O) (XELOXIRI) as first-line treatment of metastatic colorectal cancer (MCRC): results of a pilot study by the Gruppo Oncologico Nord-Ovest (G.O.N.O.)

S. Bursi[1], G. Masi[1], F. Loupakis[1], A. Antonuzzo[2], S. Chiara[3], E. Pfanner[4], I. Petrini[4], M.T. Barletta[1], G.G. Baldi[1], A. Falcone[5]. *[1]Az USL 6, Division of Medical Oncology, Livorno, Italy; [2]Az USL 6, Day Hospital of Medical Oncology, Piombino, Italy; [3]IST, Division of Medical Oncology, Genova, Italy; [4]S. Chiara Hospital, Division of Medical Oncology, Pisa, Italy; [5]University of Pisa, Department of Oncology, Pisa, Italy*

Background: The triple drug regimen FOLFOXIRI demonstrated improved Response Rate (RR), secondary R0-surgery on mts, PFS and OS compared to FOLFIRI in a phase III trial by the G.O.N.O. group in MCRC patients (pts). Oral C has similar efficacy compared to 5-FU and therefore it could substitute 5-FU in the FOLFOXIRI regimen thus avoiding a central venous catheter.
Methods: The G.O.N.O. started a pilot study to evaluate escalating doses of C in combination with fixed doses of I, O (XELOXIRI) in metastatic and not resectable CRC pts. The objectives of the study are the determination of the recommended dose (RD) of C in combination with I and O, safety and activity of the combination and analysis of plasma pharmacokinetics. The planned treatment in the first 3 patients was: I 165 mg/sqm over 1-h on day 1, O 85 mg/sqm over 2-h on day 1 and C 2500 mg/sqm/die from day 1 to 7, repeated every 2 weeks. C dose was increased to 3000 mg/sqm/die or decreased to 2000 mg/sqm/die in subsequent groups of 3 to 6 pts on the basis of the observed dose limiting toxicities (DLT).
Results: Up today 40 patients have been enrolled. Main patients characteristic are: gender (M/F) = 28/12, PS (0/1/2) = 34/5/1, age (median/range) = 64/42−76, sites of disease (single/multiple) = 21/19. The DLT was G3−4 diarrhea that was observed in 2 out 6 patients receiving C at 2500 mg/sqm, in 2 out 3 patients receiving C at 3000 mg/sqm and in 1 out 6 patients receiving C at 2000 mg/sqm. This last dose was defined the RD. Among the 30 patients treated at the RD main G3−4 toxicities were: diarrhea 23%, neutropenia 27%, febrile neutropenia 8%, thrombocytopenia 7%, neurotoxicity 3%. One toxic death for diarrhea and sepsis occurred. Up today 26 out of the 30 patients (4 patients too early) treated at the RD are assessable for response (ITT analysis). We observed 18 RP, 5 SD and 3 treatment failures with a response rate of 70% (95% CI: 48−86%). The median follow-up is 10.5 months and median PFS is 9.2+ months, while median OS isn't yet reached.
Conclusions: XELOXIRI is a feasible triple drug regimen with diarrhea being the DLT. The recommended dose of C is 2000 mg/sqm and at this dose-level the observed toxicities are manageable. Preliminary results on activity of XELOXIRI at the RD are promising. The study is still accruing patients and updated results will be presented. Partially supported by Fondazione ARCO.

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Neoadjuvant bevacizumab plus XELOX is feasible in patients with potentially curable metastatic colorectal cancer receiving synchronous resection

B. Gruenberger[1], W. Scheithauer[1], D. Tamandl[2], C. Zielinski[1], J. Schueller[1], T. Gruenberger[2]. *[1]Medical University Vienna, Dept. Oncology, Vienna, Austria; [2]Medical University Vienna, Dept. General Surgery, Vienna, Austria*

Background: Bevacizumab (Avastin®) in combination with standard first-line chemotherapy regimens has become the standard of care in patients (pts) with metastatic colorectal cancer (mCRC). The side effect profile of bevacizumab in pts with metastatic CRC is well established; however, there are limited data on the effect on surgical wound-healing and hepatic regeneration following liver resection.
Methods: Pts with mCRC and liver metastases potentially curable by resection were eligible for this single-centre, non-randomised phase II trial. Eligibility criteria: pts at high risk of early recurrence; synchronous liver metastases; primary non-optimally resectable disease, multiple liver metastases; lymph node-positive primary CRC. Pts received six cycles (3 months) of neoadjuvant XELOX (capecitabine 3500 mg/m^2/day days 1–7 plus oxaliplatin 85 mg/m^2 day 1) plus bevacizumab 5 mg/kg every 2 weeks. The sixth cycle did not include bevacizumab resulting in a gap of 5 weeks between last bevacizumab dose and surgery. The same regimen was reinitiated 5 week after surgery for additional 3 months.
Results: In total, 56 pts have been enrolled and are evaluable having received 6 cycles of therapy and undergone surgery. Ten evaluable pts (4 male, 6 female) with a median age 55 (49–67) years and ECOG PS 0/1 (100%/0%) received synchronous resection of their primary (2 rectum, 8 colon) and the liver metastases. Assessments following neoadjuvant therapy found that all pts with synchronous resection responded, with 4 (40%) complete responses and 6 (60%) partial responses in the liver. All pts underwent potentially curative resection; one pt required a second liver resection due to recurrence. Peri- and post-operative complications are consistent with pts with liver resection only. No pts experienced wound-healing or bleeding complications and no pts required perioperative blood transfusion; median length of hospitalisation was 8 (7–18) days. Only three pts experienced postoperative complications: wound infection, sepsis and anastomotic leak (all n = 1). Eight pts have received adjuvant bevacizumab plus XELOX as scheduled.
Conclusions: These data provide further evidence that bevacizumab in the neoadjuvant setting can be safely administered in pts with metastatic CRC, including those with synchronous bowel and liver resection, without increasing the rate of surgical or wound healing complications or severity of bleeding.

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Safety and efficacy of sunitinib and FOLFIRI in combination in treatment-naive metastatic colorectal cancer (mCRC): a phase I study

F. Vazquez[1], A. Carrato[1], N. Starling[2], I. Chau[2], P. Hill[3], M.J. Lechuga[4], J. Tursi[4], R. Chao[5], D. Cunningham[6]. *[1]Elche University Hospital, Medical Oncology Service, Alicante, Spain; [2]Royal Marsden Hospital, Cancer Therapeutics, Sutton, United Kingdom; [3]Pfizer Ltd, Sandwich, Sandwich, United Kingdom; [4]Pfizer Italia Srl, Clinical Research Oncology, Milan, Italy; [5]Pfizer Inc., Global Research and Development, La Jolla, USA; [6]Royal Marsden Hospital, Gastrointestinal Unit, Sutton, United Kingdom*

Background: Sunitinib malate (SUTENT®; SU), an oral, multitargeted inhibitor of VEGFRs and other tyrosine kinases, is approved for the treatment of advanced RCC and imatinib-resistant or -intolerant GIST. Inhibition of VEGF in combination with chemotherapy has been shown to improve survival of patients (pts) with mCRC. Thus, the antiangiogenic