6035 POSTER

Post-neoadjuvant anastomotic recurrence in rectal cancer: downsizing, downstaging and distal margin distance correlations

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Background: To analyze the influence of preoperative chemoradiation pelvic effects on the risk of anastomotic recurrence in rectal cancer patients.
Methods: From 4/95 to 1/05, 110 cT_{3-4} or cN+ patients treated with neoadjuvant chemoradiation had radical sphincter preserving surgery. Tumor characteristic were: adenocarcinomas; distance to the anal verge inferior to 3 mm (0.9%) or in the 4 to 6 cm segment (23, 6%); size (maximal clinical dimension) range from 2−13 cm (median 4.8 cm); cT_3 (82.7%), cN+ (44.5%). Neoadjuvant treatment included fluopirimidin modulated pelvic radiotherapy with or without induction Oxaliplatin. Pelvic radiotherapy consisted in 45−50.4 Gy followed by a 10−15 Gy intraoperative presacral electron boost. Surgical procedures performed were: anterior resection (AR) (67%), low AR (31%) ultra-low AR (4.5%).
Results: Downsizing effect was present in 80% of surgical specimens (median size of maximal residual tumor dimension 2.7 cm). T downstaging was 60% and N downstaging 30%. pT_0N_0 category rate was 12.7%. Distance from the lower limit of the residual lesion to the distal surgical margin was: 0−10 mm 26.9%, 11−20 mm 25%, 21−30 mm 25%, >31 mm 23.1%. With a median follow-up of 55.5 months (7–150 months) anastomotic recurrence was diagnosed in 7 patients (6.5%). There were no statistical correlations with downstaging (T or N) or downsizing effects, nor with distance from the lower limit of the residual lesion to the distal margin: 9.3% $\leqslant$2 cm versus 4% >2 cm. Virtual intratumoral surgical section, estimated from the pre-neoadjuvant T longitudinal dimension, was speculated in 21 patients (3 developed anastomotic recurrene 2; 12% vs 5.8%, $p = 0.21909$).
Conclusions: Anastomotic recurrence in rectal cancer patients treated with neoadjuvant chemoradiation is an exceptional event. Virtual intra-tumoral surgical section and anastomosis does not contributes to an excessive risk of recurrence. Data to further impulse the development of policies for ano-rectal complex preservation in rectal cancer patients candidates to neadjuvant treatment.

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The prognostic impact of positive lymph node number in stage III rectal cancer patients treated with surgery followed by radiochemotherapy

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Background: To investigate the prognostic impact of positive lymph node number (LNN) on disease-free survival in stage III rectal cancer patients.
Material and Methods: We retrospectively reviewed the data of 273 consecutive patients who received surgery and 5-FU based postoperative radiochemotherapy for stage III rectal cancer from 1999 to 2004. Lymph node status was evaluated as total number of lymph nodes examined (TLN), positive LNN and lymph node ratio (LNR). Positive LNN was divided into LNN1 (1−3 nodes), LLN2 (4−7 nodes), and LLN3 ($\geqslant$8 nodes). LNR was categorized into three groups, LNR1 to 3, according to cutoff points 0.2 and 0.5. The relationships between survival and clinicopathologic variables, including lymph node status were analyzed.
Results: The median values of TLN, positive LNN, and LNR were 17, 3, and 0.2, respectively. After a median follow-up of 55 months (range, 6–110 months), the disease-free survival, loco-regional failure-free survival, and distant metastasis-free survival were 54.6%, 81.7%, and 58.1%, respectively. In multivariate analysis, LNN was a significant prognostic factor for disease-free survival ($p = 0.01$), whereas TLN, LNR, pathologic tumor stage, patient's age, gender, and sequence of radiochemotherapy (chemotherapy prior to postoperative radiochemotherapy vs. immediate postoperative radiochemotherapy) were not. In patients with LNN3 showed a significant lower disease-free survival rate at 5-years than in patients with LNN2 (28.3% vs. 50.5%, $p = 0.01$), or patients with LNN1 (28.3% vs. 63.2%, $p < 0.001$).
Conclusions: Positive lymph node number was the most significant prognostic factor for the disease-free survival in stage III rectal cancer patients who had treated with surgery and postoperative radiochemotherapy.

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Bevacizumab – Capecitabine – Oxaliplatin – Radiation – REctal Cancer Trial (A-CORRECT) for locally advanced and low rectal cancers

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Background: Capecitabine (Cap) and oxaliplatin (Ox) have been given safely in phase I/II trials concurrently with radiation with promising pathological complete response (pCR) rates of 15−24% compared with historical rates of 8−14% with 5-FU alone. The aim of this multicenter phase II trial is to evaluate the efficacy and safety of bevacizumab (Bev), Cap and Ox given concurrently with radiotherapy in patients (pts) with locally advanced or low-lying rectal cancer.
Materials and Methods: Pts with histologically confirmed locally advanced mid, upper (fixed/tethered T3/4 or bulky N+) or low ($\geqslant$T3NX) rectal adenocarcinomas received i.v. Bev 5 mg/kg (d −14, 1, 15, 29), oral Cap 825 mg/m^2 bid (d1−14, 22−35), i.v. Ox 50 mg/m^2 (d1, 8, 22, 29) and radiation 50.4 Gy/28 fractions (d1−35, Mon-Fri). Surgery was performed 7−9 weeks after completion of radiation. Study endpoints are: pCR rate, rate of sphincter-sparing surgery, complete resection (R0) rate, safety, 1-month post-surgical complication rates. The planned sample size is 37 evaluable pts.
Results: As of 16 April 2009, 37 pts have been enrolled. Baseline data is available for 30 pts: M/F 23/7; median 59 (range 38−84) years; ECOG 0/1 22/8; T3/4 23/7; median distance from anal verge 5 cm (range 0.4−18 cm). 29 pts are evaluable for toxicity and 16 pts are evaluable for response. *Preoperatively:* the most common adverse events (# of pts: all grades/grade 3+) were pain 22/1, fatigue 19/1 and diarrhea 19/4. 4 infection/abscess, 1 fistula and no bleeding complications or perforations reported. *Postoperatively:* the most common adverse events were pain 13/1, fatigue 12/1, hypertension 6/1 and insomnia 6/0. Pre-defined post operative toxicities, including Serious Adverse Events, were infection/abscess 4/1, anastomotic leaks 4/2, wound healing complications 4/1, fistula 1and no bleeding complications or perforations. Treatment modification was required in 12/74 cycles (16%). 22 of 24 pts who completed radiation received full dose radiation, 50.4 Gy/28. At cut-off, postoperative data were available for 16 pts: sphincter-sparing surgery ($n = 9$); R0 ($n = 14$); pathological staging pT0/1/2/3/4: 3/2/3/7/1 with 3 pts (19%) achieving a pCR.
Conclusions: Pre-operative therapy with Cap, Ox and Bev was well tolerated allowing planned delivery of radiation. 38% of pts (6/16) had post-operative complications grade 3+ consistent in frequency with other studies.
Funding provided by grants from Hoffman La Roche and Sanofi Aventis. Clinical trials management by Ozmosis Research Inc.

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Pilot study of preoperative involved field radiotherapy in rectal cancer

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Background: The success of total mesorectal excision (TME) surgery in reducing local recurrence rates in rectal cancer, suggests that the majority of cells leading to local recurrence reside within the mesorectal fascia. If correct, RT to the entire pelvis in rectal cancer patients may not be needed. We hypothesize that preoperative RT to the rectal tumor with a margin to encompass the mesorectal tissue and adjacent lymph nodes (involved field) will lead to equivalent local control as the standard RT volume but with less morbidity and improved quality of life.
Methods and Materials: Thirty MRI or endorectal ultrasound staged T3 and/or N1/M0 rectal cancer patients accrued. Preoperative RT to a dose of 45 Gy to PTV1 (GTV+ mesorectum + presacral space + lateral lymph nodes + 3.5 cm superior and inferior) +/− a boost of 9 Gy to the GTV +