cancer. Secondary objective was to establish treatment related variables which correlate with oncological prognosis.
Methods: From 1994 until 2004, 203 patients with locally advanced and 117 patients with locally recurrent rectal cancer underwent multimodality treatment. All patients have been staged by MRI for the rectal cancer and by CT of the thorax and abdomen in order to rule out metastatic disease. In all primary cases the circumferential margin was involved or less than 2 mm free according to MRI. All pelvic locally recurrent cases were eligible. Multimodality treatment consisted of neoadjuvant radio-(chemo) therapy, resection, extended if necessary and Intraoperative Electron Radiotherapy (IOERT) at the area of risk. Concomitant chemotherapy was added to the radiotherapy since 1999.
Patients were referred from over forty different hospitals in the Netherlands. However, surgery and IOERT were performed in one institution.
Results: Five-year survival rate and local recurrence rate were 55% and 17% for locally advanced rectal cancer and 32% and 39% for locally recurrent rectal cancer respectively. After radical resection (R0) with negative circumferential margins, 5 year survival and local recurrence rate were 60% and 10% for locally advanced (n = 168) and 48% and 24% in locally recurrent cases (n = 68). Response to neoadjuvant treatment, and type of neoadjuvant treatment were statistically significant variables for obtaining radical resections. In primary advanced cases 30% showed poor response to neoadjuvant treatment, but were responsible for 86% of all irradical resections (30/35) In primary advanced rectal cancer cases R0 resection rate was 72% after neoajuvant radiotherapy only, and 89% after combined radiochemotherapy. In locally recurrent cases these figures were 56% and 68% respectively.
Conclusion: Combined multimodality treatment is effective in the treatment of locally advanced primary rectal cancer and can be used as salvage strategy for patients with locally recurrent rectal cancer. Treatment related factors: response to neoadjuvant treatment and the ability to perform a radical R0 resection strongly correspond with oncological outcome.

634 POSTER

Post-study treatment does not influence outcome in the X-ACT phase III trial of capecitabine (X) vs. bolus 5-FU/LV as adjuvant therapy for patients (pts) with Dukes' C colon cancer

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Background: The X-ACT trial evaluated adjuvant X vs. 5-FU/LV in pts with resected Dukes' C colon cancer. Between Nov 1998 and Nov 2001, 1987 pts were randomised to receive either oral X (1250 mg/m^2 bid d1–14, q3w) or i.v. bolus 5-FU/LV (Mayo Clinic regimen: LV 20 mg/m^2 + 5-FU 425 mg/m^2 d1–5, q4w) for 24 weeks. X was at least equivalent to 5-FU/LV in terms of disease-free survival (DFS; HR 0.87, 95% CI 0.75–1.00, $p < 0.0001$), with a strong trend towards superior DFS ($p = 0.053$). X significantly improved relapse-free survival (HR 0.86, 95% CI 0.74–0.99, $p = 0.041$), with a trend towards improved overall survival (HR 0.84, 95% CI 0.69–1.01, $p = 0.071$). The primary safety endpoint was met with fewer key grade 3/4 adverse events and later onset with X vs. 5-FU/LV ($p < 0.001$).
Materials and methods: In a separate analysis, we looked at post-study treatment in both arms of the X-ACT trial to determine whether there were any differences that could influence survival outcome.
Results: At the time of this analysis, 632 pts in the X and 579 in the 5-FU/LV arms are alive and disease-free, with 131 and 142 pts alive with relapse/new recurrence in the X and 5-FU/LV arms, respectively. Of the pts receiving post-study chemotherapy, 25 in the X and 10 in the 5-FU/LV arm received other adjuvant chemotherapy following randomisation into X-ACT either because they never received study treatment or at the investigator's discretion (after early termination of study treatment for any reason). In addition, 13 pts in the X and 16 pts in the 5-FU/LV arm received post-study chemotherapy for new occurrences of cancer other than colon cancer (breast, prostate, lung) prior to relapse. Pts meeting the entry criteria (free of disease at study entry and receiving $\geqslant$1 doses of study treatment) who were treated according to the protocol and experienced relapse formed the largest group receiving post-study chemotherapy. There were no major imbalances in post-study chemotherapy for metastatic disease (see table) or radiotherapy (6% in both arms).
Conclusions: These data suggest that there are no differences in post-study chemotherapy that could influence survival outcome in pts who received either X or 5-FU/LV as adjuvant therapy in the X-ACT trial. Efficacy, safety and pharmacoeconomic findings indicate that X should replace 5-FU/LV as adjuvant treatment for colon cancer.

% of pts receiving post-study chemotherapy for metastatic disease

	X (n = 372)	5-FU/LV (n = 404)
Irinotecan-based	39	35
5-FU-based	17	16
Oxaliplatin-based	32	29
X single agent	4	10
Other chemotherapy	9	6

635 POSTER

Arterial thromboembolic events in a pooled analysis of 5 randomized, controlled trials of bevacizumab with chemotherapy

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Background: Bevacizumab (Avastin^{TM}) is a monoclonal antibody to VEGF with demonstrated survival benefit when combined with chemotherapy in metastatic colorectal cancer (mCRC). Individual safety data from several randomized controlled trials suggested that adding bevacizumab to chemotherapy may increase the risk of arterial thromboembolic events. We conducted a pooled analysis to evaluate this potential safety signal.
Methods: Data from 1745 pts with metastatic carcinomas (breast, colorectal, and non-small-cell lung) pooled from 5 randomized controlled trials of bevacizumab with chemotherapy were analyzed to assess arterial thromboembolic event risk and identify predisposing factors in the context of overall clinical effect. Clinical parameters, including age, gender, development of proteinuria on study, and history of hypertension, diabetes, atherosclerosis, arterial thromboembolic events, venous thromboembolic events, and use of aspirin or a statin, were assessed for relationship to arterial thromboembolic event occurrence by univariate analysis and a Cox proportional hazards regression model.
Results: Within this pooled population, the addition of bevacizumab to chemotherapy increased the risk of arterial thromboembolic events compared to chemotherapy alone (3.8% vs 1.7%, $p < 0.01$ by Chi-square test). In addition to bevacizumab treatment, history of arterial thromboembolic events and age $\geqslant$65 years were identified as independent risk factors by multivariate analysis (hazard ratios of 1.9, 2.9, and 2.2 respectively).
Conclusion: The addition of bevacizumab to chemotherapy is associated with an increased risk of arterial thromboembolic events in patients with metastatic carcinoma, especially those $\geqslant$65 years old with a prior history of arterial thromboembolic events. The risk/benefit of bevacizumab in mCRC by arterial thromboembolic event-risk group will be presented.

636 POSTER

Initial safety findings from a phase III study of capecitabine (X) plus oxaliplatin (XELOX) vs. infusional 5-FU/LV plus oxaliplatin (FOLFOX-6) in first-line treatment of patients (pts) with metastatic colorectal cancer (MCRC)

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Background: The oral fluoropyrimidine X is replacing 5-FU/LV as the backbone of colorectal cancer therapy, in both the metastatic and adjuvant settings. The combination of X and 3-weekly oxaliplatin (XELOX) has demonstrated good efficacy and safety in phase II clinical trials in MCRC. We initiated a phase III trial to compare XELOX with FOLFOX-6 as first-line therapy in pts with MCRC. This abstract provides the initial safety findings from a planned interim analysis.