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Economic evaluation of capecitabine (X) vs. bolus 5-FU/LV as adjuvant chemotherapy for patients (pts) with Dukes' C colon cancer in an Italian hospital setting

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Background: In the primary analysis of the recent X-ACT adjuvant trial, X showed consistent benefits over bolus 5-FU/LV, with at least equivalent disease-free survival (DFS), and an improved safety profile [Cassidy et al. 2004]. In addition, X demonstrated superior relapse-free survival (65.5% vs. 61.9% at 3 years follow-up; p = 0.0407) and improved covariate-adjusted overall survival (p = 0.0208). In order to determine the potential economic impact of X in this setting, we used the results from X-ACT to assess the cost-effectiveness of X from the Italian hospital perspective.
Materials and methods: Trial-based data were collected on treatment period medical resource use. Unit costs for drug administration, hospitalisations, emergency room visits, and concomitant medications were considered using published sources in Italy. A health-state transition model was used to estimate incremental cost impact and the effectiveness in terms of the gains in quality-adjusted life months (QALMs). Costs and effectiveness were discounted at 3.5%.
Results: Mean duration of treatment was similar with X and 5-FU/LV, and pts received 92% and 93% of planned treatments, respectively. Administration of X required fewer clinic visits per pt (7.4 versus 28.0 with 5-FU/LV). Acquisition costs of X were higher than 5-FU/LV, approximately 2533 vs. 231 Euros, but this difference was more than fully offset by the difference in administration cost of 5-FU/LV (4338 vs. 152 Euros for X). Total hospital days for treatment-related adverse events (AEs) and medication costs for treating AEs were higher for 5-FU/LV than X. The cost of emergency room visits for treating AEs did not differ. Compared with 5-FU/LV, X is projected to increase QALMs by 6.5 months, with overall treatment period cost savings of 2234 Euros. These findings show that X is a dominant (cost-saving and more effective) treatment in this setting. Similar findings were reported from a similar analysis in UK patients [Douillard et al. 2004].
Conclusions: X as adjuvant treatment for pts with colon cancer is not only clinically effective with an improved safety profile vs. 5-FU/LV, but it is also a dominant choice from an economic perspective.

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Comparison between endorectal ultrasonography and magnetic resonance imaging in preoperative staging of rectal cancer

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Background: Preoperative staging of rectal cancer is essential for optimal therapy planning. The aim of this study was to evaluate the accuracy and clinical usefulness of endorectal ultrasonography (ERUS) and magnetic resonance imaging (MRI) in preoperative staging of rectal cancer.
Materials and methods: Between May 2003 and February 2005, 35 patients with histologically proven rectal cancer were examined with endorectal ultrasonography using 5.0–7.5 MHz endorectal probe and MR imaging (1.5 T) using a whole-body coil.
We compared results of ERUS and MRI staging with the pathology findings based on the surgical specimens.
Results: The overall accuracy of ERUS for determining depth of invasion (T stage) was 74% (26/35) and 71.4% (25/35) for MRI. Overstaging was 5.7% (2/35) by ERUS and 8.6% (3/35) by MRI. Both ERUS and MRI understaged 20% (7/35) of patients. In staging perirectal lymph node metastasis. the overall accuracy rate of ERUS was 68.5% (24/35) with 14.3% (5/35) overstaged and 17% (6/35) understaged. MRI correctly identified the N stage with an accuracy rate of 65.7% (23/35); 20% (7/35) of patients were overstaged and 14.3% (5/35) understaged.
Regarding penetration of the rectal wall (stages T1 and T2 vs stages T3 and T4). ERUS and MRI showed identical sensitivity of 72% and specificity of 90%. With regard to nodal involvement. sensitivity was 62.5 and specificity 78.9% for ERUS and 68.7% and 68.4% for MRI.
Conclusions: Both ERUS and MRI are reliable diagnostic modalities in staging rectal cancer with similar accuracy. ERUS is fast, safe and more cost-effective than MRI and therefore should be prefered while MRI has its role when ERUS is not feasibile (in stenotic and proximal rectal cancers) and in cases of advanced disease.

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Tolerability of yttrium-90 chemoradiation treatment of liver metastases from colorectal cancer: international clinical trial

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Background: Liver metastases are detected in over 70% of patients with advanced colorectal cancer and represent the principal cause of death in this patient population. Surgical resection of hepatic disease may improve survival, but this strategy is not feasible in the majority of patients with metastatic disease. Selective internal radiation therapy (SIRT) involves the injection of SIR-Spheres® (which contain the beta-emitter, yttrium-90) into the arterial supply of the liver resulting in preferential lodgement in malignant microvasculature, delivering approximately 200 Gy to tumour tissue. In a Phase 2 feasibility trial, the combination of SIRT with systemic 5-fluorouracil (5-FU) and folinic acid (LV) improved median survival by 16 months compared to systemic chemotherapy alone (van Hazel et al. J Surg Oncol 2004; 88: 78–85). Oxaliplatin is a radiosensitising diaminocyclohexane-platinum compound. Th ombination of 5-FU/LV and oxaliplatin (FOLFOX4) appears synergistic in the treatment of advanced colorectal cancer. We tested the hypothesis that FOLFOX4 with concomitant SIRT is well tolerated.
Methods: A 2-centre Phase I study of Sir-spheres® with modified FOLFOX4 systemic chemotherapy was conducted in patients with inoperable liver metastases from colorectal carcinoma who had not received prior chemotherapy for metastatic disease. In the context of full-dose 5-FU and LV, inter- and intra-patient dose escalation was performed with oxaliplatin (30 to 85 mg/m^2). SIRT was administered on day 3 or 4 of the first cycle of chemotherapy. The primary endpoint was toxicity.
Results: Seventeen patients were entered into the study. The mean dose of SIRT administered was 1.7 GBq (range 0.9 to 3.1 GBq). Six patients received 85 mg/m^2 of oxaliplatin from cycle 1. Of the 169 cycles administered, the total dose delivered was 91% of the protocol chemotherapy dose. Six patients required chemotherapy dose reduction; this occurred after the 9th cycle for 5 patients. Five patients required up to 7 days of treatment delay per cycle due to myelosuppression. Eight patients experienced NCI grade 1–3 abdominal pain within 48 hours of SIRT. Grade 3/4 neutropenia was seen in 10 patients. The nadir in mean leukopaenia levels was observed 2 months from SIRT. Grade 3 anaemia was observed in 1 patient. No significant thrombocytopenia was recorded. Peripheral neuropathy and gastrointestinal system adverse events were common, with grade 3/4 diarrhoea in 2 patients and grade 1/2 nausea in 12 patients. Grade 1 toxicity was observed in liver function tests measured in serum from 6 patients. Complete responses were measured by RECIST criteria in 2 of 17 patients, partial responses in 13 patients and stable disease in 2 patients, with no evidence of radiation hepatitis on contrast-enhanced computed tomography scans.
Conclusions: SIRT administration in combination with systemic FOLFOX4 is well tolerated by this patient group. The results suggest that studying the effect of chemoradiation with SIRT on response rate, local control and overall survival in patients with liver metastases from colorectal cancer is timely.

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Local lymphocyte infiltration as a major prognostic factor in rectal cancer patients

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Background: In order to evaluate the relevance of various prognostic factors on the onset of relapse after radical resection of rectal cancer, the clinical history of 203 patients were analyzed.
Materials and methods: All the patients were affected with a low rectal cancer and all underwent a total rectal resection in combination with a complete mesorectal excision and a coloendoanal anastomosis.
Results: The pathological examination identified 43 Astler Coller B_1, 64 B_2, 21 C_1, and 75 C_2. patients. Despite the presence of lymphocyte infiltration