3 cycles with standard co-medication (vitamin B_{12}, folic acid, and dexamethasone) on an outpatient base. If radiotherapy was used, minimum interval between start of radiotherapy and last dose of pemetrexed were 2 weeks. A LC-MS/MS method has been used for the determination of 5,10-methyleneTHF, THF, and 5-methylTHF levels. The folate extraction method involved homogenization, heat treatment and folate conjugate treatment to hydrolyze polyglutamyl folates to monoglutamyl folates. Biopsies of tumor and mucosa were taken before the patient received any vitamine supplementation.
Results: Mean methyleneTHF levels (1018±506 pmol/g) were significantly higher in tumor compared with mucosa (830±610 pmol/g), p = 0.013. Mean THF levels were also significantly higher in tumor (584±257 pmol/g) compared with mucosa (463±256 pmol/g), p = 0.013. Mean 5methylTHF levels were not significantly higher in tumor (436±316/g) compared with mucosa (352±199 pmol/g), p = 0.34.
Conclusions: These explorative data suggest that this unique method leads to understand intra- and inter-patient influence of folates during the course of the treatment and may help to identify patients who do profit from antifolate therapies.

6042 POSTER

Metastases prediction after preoperative radiochemotherapy in cT3M0 rectal cancer patients: an analysis of a large database

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Background: the last randomized trials showed that preoperative radiochemotherapy (CRT) has a local recurrence rate of 4−8% and distant metastases rate of 25−30%, in stage II-III rectal cancer patients.
Many of these studies focused on the subgroup analysis to identify risk factors correlated to local recurrence; few data are available to identify risk factors for distant metastases, and adjuvant postoperative chemotherapy after pre-operative chemoradiation is still far from consensus based on the available evidences.
At the Università Cattolica del Sacro Cuore of Rome a multidisciplinary rectal cancer database is available since 1980. We reviewed our clinical data to identify the metastases prediction risk factors in cT3M0 patients treated with preoperative radiochemotherapy.
Materials and Methods: from a large database containing 1420 patients, a group of 405 patients between 1985–2008 was collected retrospectively. The patients were diagnosed with rectal cancer with cT-stage 3 and cM-stage 0 and were treated with preoperative CRT (45−55 Gy, 1 or 2 drugs). Surgery was performed 6−10 weeks after treatment and metastasis presence (M^+) was evaluated at follow-up. Collected pre-treatment variables included sex, age, cN-stage, tumor distance from the anorectal ring, number of involved rectum quartiles (Qrt), tumor length, volume index (Qrt × tumor length), chemo type. Post-treatment were collected: the volume index and the relative difference between pre- and post treatment evaluations of tumor distance, Qrt, tumor length and volume index. Surgery variables included type of surgery, ypT-stage, ypN-stage, TRG score and adjuvant chemo. Multivariate analysis was performed with a 2-norm support vector machine (SVM). Performance of the model was expressed as the Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curves and assessed with leave-one-out (LOO) cross-validation. A nomogram was build based on the model output.
Results: CRT resulted in M^+ for 19% of the patients. Based on the AUCs (Mean ±SD) of the ROC-curves we found that the model performs with AUC 0.69±0.04. Predictive variables ranked to importance (i.e. weights): pN-stage (0.18), relative difference of volume index (−0.08), pT-stage (0.07), and type of surgery (0.06).
Conclusions: the analysis shows the presence of predictive risk factors of distant metastases mainly related to the different response to the treatment. A nomogram to tailor the adjuvant treatment in cT3M0 patients after radiochemotherapy will be proposed.

6043 POSTER

Late adverse effects of preoperative hyperfractionated radiation therapy (RT) for advanced rectal cancer

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Background: To analyze the occurrence of late adverse effects in patients (pts) treated with preoperative hyperfractionated RT for LARC with or without gemcytabine or gefitinib (Iressa).
Materials and Methods: Between 1997 to 2006, 109 pts accepted to participate in the present study in three centers. All patients were enrolled in three successive phase I-II trials and treated preoperatively with 50 Gy in 40 fractions of 1.25 Gy over 4 weeks without (52 pts) or with concomitant gemcitabine (37 pts) or gefitinib (20 pts). Rectal surgery was scheduled 6 weeks after completion of RT. Fifty four pts received adjuvant chemotherapy (CT), according to local policy. Late adverse effects were defined as occurring at >3 months, according to RTOG criteria. Concomitant CT, age, sex, tumor location and field size were assessed for potential correlation with adverse late effects.
Results: The median age of the pts was 60 years (range: 30−88 years). One hundred and one patient had stages cT3−4 and cN+ in 56 pts. Surgery consisted in low anterior resection in 79 pts, abdominoperineal resection in 25 pts and other surgery in 5 pts. With a median follow-up of 55 months (range: 3–105 months), severe late complications (grade 3−4) occurred in 12 pts (11%). Erectile dysfunction was described by 14 pts. Neither CT, nor age or gender influenced the rate of late adverse effects. Field dimension (>15 cm) and distal location showed a trend (p = 0.07 and 0.13).
Conclusions: Although this small cohort size precludes detailed risk factor analysis, the rate of severe late complications was not influenced by the addition of gemcytabine or gefitinib to preoperative RT. Refinements in the RT (field size) and surgical techniques to reduce late sequela, particularly operative procedures allowing preservation of sexual function merit further investigation.

6044 POSTER

Multidisciplinary rectal cancer treatment: 'Looking for an European Consensus' (EURECA-CC2)

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Background: During the last two decades some important results from European randomized studies have been published. In order to conform the clinical practice to the best scientific evidence from the literature, the International Conference on 'Multidisciplinary Rectal Cancer Treatment: 'Looking for an European Consensus' (EURECA-CC2) was organized in Italy under the endorsement of European Society of Medical Oncology (ESMO), European Society of Surgical Oncology (ESSO), and European Society of Therapeutic Radiation Oncology (ESTRO).
Materials and Methods: The Delphi method was used to achieve the consesus. All Committee members had a document customized for the consensus process, available on the web. Eight chapters were identified: epidemiology, diagnostics, pathology, surgery, radiotherapy and chemotherapy, treatment toxicity and quality of life, follow-up, and research questions. Each chapter was subdivided by topic, and a series of statements were developed. Each sentence was voted and commented by all members three times. During the Consensus Conference held in Perugia (Italy) from 11 December through 13 December 2008, the sentences which did not reach agreement after voting round #2 were openly debated. After each debate the opinion of both the Committee members and the audience were collected by a hand-held televoting system. The Executive