2 cm is given. Small bowel dose is not to exceed 50 Gy point dose. A 3 or 4 field box technique is utilized. All patients receive prolonged venous infusion 5 Fluorouracil with the RT, followed by postoperative chemotherapy for 4 cycles.
Results: 22 of 30 patients have been accrued. Preoperative stage shows 14 T3N0 and 8 T3N1 patients. One patient did not complete chemotherapy due to Grade 3 GI toxicity. Postoperative pathology of the first 18 patients shows 3 complete responses − T0N0, 1 T1N0, 5 T2N0, 4 T3N0, 3 T3N1. One patient developed distant metastases and did not have surgery. One patient declined recommended surgery and had local excision alone, which showed no residual disease. One patient whose pathology showed incomplete TME has had a local recurrence. In total, two patients have developed distant liver metastases.
Conclusions: Involved field rectal RT is feasible. The dose to small bowel and bladder is reduced. Data from the remainder of the patients will be presented with discussion of dosimetric and clinical toxicity data.

	Mean Dose			
	Small Bowel (cGy)		Bladder (cGy)	
Patient	Involved Field	Standard	Involved Field	Standard
2	36.4	387.0	1,575.1	3,550.8
3	1,179.3	2,357.6	2,804.1	4,028.1
4	973.2	2,644.9	3,754.9	4,052.0
5	338.5	388.2	3,458.9	4,183.3
6	2,289.3	3,146.5	3,942.6	4,273.9
7	352.0	225.0	3,808.0	3,796.0
8	2,998.6	3,118.4	3,785.0	3,872.0
9	2,105.8	2,241.4	4,009.9	4,534.9
10	187.7	1,102.4	3,601.3	4,394.1
11	1,231.6	1,562.6	4,205.5	4,415.4
12	270.4	1,030.6	4,076.1	4,353.4
13	912.2	4,722.9	3,289.0	3,988.8
14	272.5	1,369.4	3,694.9	4,346.6
15	279.1	253.3	3,931.5	4,302.1
16	2,237.5	2,084.6	3,518.4	4,489.4
17	1,015.4	1,295.2	3,946.6	4,398.4
18	788.2	755.5	4,890.7	5,062.9
20	407.0	2,078.4	4,508.3	4,458.4
Average	993.0	1,709.1	3,711.2	4,250.0

6039 POSTER

Pathologic Complete Response (pCR) after preoperative radiochemotherapy in cT3M0 rectal cancer patients: an analysis from a large database

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Background: Many studies reported that patients responding with a pathologic complete response (pCR) after preoperative radiochemotherapy have very good long-term outcome. Predicting a pCR at diagnosis will be important in an attempt to modulate the treatment for each patient (i.e. less invasive surgery).
The purpose of this analysis is to retrospectively evaluate the impact of progressive intensified schedules of preoperative radiochemotherapy on pT0N0 in rectal cancer patients treated in our institution since 1985.
Matherial 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 chemoradiotherapy (CRT: 45−55 Gy, 1 or 2 drugs). Surgery was performed 6−10 weeks after treatment and pathologic reports were reviewed for complete response (ypT0N0). 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), and concomitant chemo type. Post-treatment were collected for 408 patients: the volume index and the relative difference between pre- and post treatment evaluations of tumor distance, Qrt, tumor length and volume index. 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 from the model output.
Results: CRT resulted in a ypT0N0 for 20% of the patients. Based on the AUCs (Mean ±SD) of the ROC-curves we found that the pre+post-treatment model has the highest performance (AUC = 0.65±0.04) compared to pretreatment alone (AUC = 0.62±0.03). Predictive pretreatment variables ranked to importance (i.e. weights): chemo type (0.11), cT (−0.097), tumor length (−0.065) and cN-stage (−0.053). Post-treatment the volume index was most important (−0.17).
Conclusions: the analysis shows the presence of predictive pT0N0 risk factors related to the intensification of the treatments, to some tumor characteristics at the diagnosis (cT, tumor length and cN-stage), and to the response to radiochemotherapy. A nomogram to predict pCR in cT3M0 patients after radiochemotherapy will be proposed.

6040 POSTER

A pilot study of neoadjuvant chemoradiation with higher dose enteric-coated tegafur/uracil plus leucovorin for locally advanced rectal cancer

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Background: Neoadjuvant chemoradiation (CRT) with tegafur/uracil (UFT) 200–350 mg/m^2/day plus leucovorin (LV) 25−75 mg/day for 5 days a week with 45 Gy radiation (RT) for locally advanced rectal cancer (LARC) was known to be efficacious and tolerable, but higher dose UFT/LV and RT may improve pathologic response rate. We have performed a pilot study to evaluate pathologic response rate and toxicity profile of neoadjuvant CRT with higher dose enteric-coated tegafur-uracil (UFT-E)/LV.
Materials and Methods: Patients (pts) were planned to be treated with UFT-E 400 mg/m^2/day plus LV 90 mg/day for 7 days a week during RT 50.4 Gy. Main eligibility criteria were histologically proven rectal adenocarcinoma; T2−4 lesions; age >18 years; ECOG PS 0−1; no prior chemotherapy or pelvic irradiation. Total mesorectal excision was planned to be performed 4−8 weeks after completion of CRT.
Results: Between June 2008 to January 2009, 39 pts were enrolled; median age 57 years (40−92); M/F 26/13; PS 0/1 37/1; cT2/T3 2/33; N0/N+ 6/29; median tumor location from anal verge 6.0 cm (2.0−9.0). The median relative dose intensity of UFT-E was 95.0% (51.6–111.7). Three pts were given reduced dose RT (1 with 27 Gy, 2 with 45 Gy) due to grade 3/4 diarrhea; 5 pts needed UFT-E dose interruption due to toxicities. Grade 3/4 toxicities included leucopenia (2, 5.1%), neutropenia (3, 7.7%), hyperglycemia (4, 10.3%), elevated transaminase level (2, 5.1%), diarrhea (4, 10.3%), nausea (2, 5.1%), and pain (2, 5.1%). Of 36 pts who underwent surgery (all R0 resection), 22 (91.7%) were treated with sphincter saving procedure. Pathologic T0 and N0 were observed in 8 (22.2%) and 29 (80.6%) pts, respectively. Downstaging in T stage was achieved in 24 pts (66.6%). Pathologic complete responses were observed in 8 (22.2%) pts and another 7 (19.4%) pts had only minimal microscopic residual tumor.
Conclusions: Neoadjuvant CRT with higher dose UFT-E/LV showed favorable efficacy and tolerability. A phase II trial of CRT with higher dose UFT-E/LV is ongoing.

6041 POSTER

Evaluation of folate derivates in the neoadjuvant treatment of resectable rectal cancer with the antifolate pemetrexed

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Background: Understanding the role of different folate derivates is essential in the understanding of the physiology of tumor growth. To our knowledge this is the first study introducing a sensitive liquid chromatography-mass spectrometry (LC-MS/MS) method to analyze folate levels in tumor and adjacent mucosa.
Methods: Between June 06 and January 08, 37 patients with a histologically proven diagnosis of operable rectal adenocarcinoma were enrolled. Pemetrexed was dosed at 500 mg/m^2 every 3 weeks, during

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