Committee scored percentage consensus based on three categories: "large consensus", "moderate consensus", "minimum consensus".
Results: All chapters were voted on by at least 75% of the members, and the majority was voted on by more than 85%. The total number of the voted sentences was 207. Of the 207, 86% achieved "large consensus", 13% achieved "moderate consensus", and only 3 (1%) resulted in "minimum consensus". No statement was disagreed by more than 50% of members.
Conclusions: This Consensus Conference represents an expertise opinion process that may be useful to define guidelines for staging and treatment of rectal cancer and may help to draw future programs and investigational protocols throughout Europe.

6045 POSTER

Safety analysis of starpan (star-02) study with panitumumab, 5-fluorouracil, oxaliplatin and concurrent radiotherapy in locally advanced rectal cancer

F. Di Fabio[1], C. Pinto[1], E. Maiello[2], S. Pini[1], T. Latiano[2], C. Aschele[3], C. Garufi[4], A. Bochicchio[5], D. Tassinari[6], A. Martoni[1]. [1]*Medical Oncology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy;* [2]*Medical Oncology Unit, IRCCS Casa Sollievo della Sofferenza, S. Giovanni Rotondo (FG), Italy;* [3]*Medical Oncology Unit, Galliera Hospital, Genoa, Italy;* [4]*Medical Oncology Unit, Regina Elena Institute, Rome, Italy;* [5]*Medical Oncology Unit, CROB, Rio Nero in Vulture (PZ), Italy;* [6]*Medical Oncology Unit, Degli Infermi Hospital, Rimini, Italy*

Background: The aim of this phase II study was to assess the activity of preoperative external radiotherapy combined with panitumumab, oxaliplatin and 5-fluorouracil in locally advanced rectal cancer patients (pts).
Materials and Methods: Pts entering the study had histologically-proven rectal adenocarcinoma, either cT3N+ or cT4N-/+ stage, with location <12 cm from the anal margin. Panitumumab was administered at a dose of 6 mg/kg IV, 2 weeks before the start of chemoradiotherapy, and then in combination with chemoradiotherapy, 3 times every 2 weeks. 5-fluorouracil and oxaliplatin were administered according to established schedule of STAR-01 Study (oxaliplatin 60 mg/m^2 IV weekly six times, 1 h after the panitumumab infusion, and 5-fluorouracil 225 mg/m^2/day continuous infusion IV days 1−38). Radiotherapy was delivered at a dose of 50.4 Gy in daily fractions of 1.8 Gy. Rectal surgery was performed 7−8 weeks after the end of neoadjuvant treatment. Eight courses of adjuvant chemotherapy with FOLFOX4 plus panitumumab at the dose of 6 mg/kg, every 2 weeks, were given post-surgery. The main study endpoint was complete pathological response rate.
Results: From February 2007 to April 2009 fifty-one pts were enrolled (9 too early pts). Characteristics of the 42 evaluated pts were: male 28 (66.7%), female 14 (33.3%); median age 60 (37−78); median Karnofsky PS 100 (70–100); stage: cT3N+ 31 (73.8%), cT4N− 3 (7.1%), cT4N+ 8 (19.1%). Thirty-three pts have completed neoadjuvant treatment and 30 have undergone surgery (12 pts ongoing). The most frequent grade 1−2 side effects were acneiform rash (56.7%), diarrhea (27%) and fatigue (8%). Grade 3−4 diarrhea was found in 32.4% of pts, and grade 3 cutaneous toxicity in 43.3%. No grade 3 hematological toxicity was found. The median cumulative dose of delivered radiotherapy was 50.4 Gy. The planned dose of panitumumab, 5-fluourouracil and oxaliplatin was administered in 78.8%, 63.6% and 69.6% of pts, respectively.
Conclusions: These early results demonstrate that panitumumab can be added to 5-fluorouracil/oxaliplatin-based chemoradiotherapy without compromising the concurrent radiotherapy dose. This combination treatment is associated with high incidence of grade 3−4 diarrhea.

6046 POSTER

Predictive role of 18f-fdg-pet in locally advanced rectal cancer patients treated with neoadjuvant chemo-radiotherapy (Bologna Project)

C. Pinto[1], F. Di Fabio[1], S. Pini[1], D. Cuicchi[2], B. Iacopino[3], P. Di Tullio[1], R. Lombardi[2], P. Castellucci[4], G. Compagnone[5], A. Martoni[1]. [1]*Medical Oncology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy;* [2]*General Surgery Unit, S. Orsola-Malpighi Hospital, Bologna, Italy;* [3]*Radiotherapy Unit, S. Orsola-Malpighi Hospital, Bologna, Italy;* [4]*Nuclear Medicine Unit, S. Orsola-Malpighi Hospital, Bologna, Italy;* [5]*Medical Physics Unit, S. Orsola-Malpighi Hospital, Bologna, Italy*

Background: The identification of predictive response factors in locally advanced rectal cancer patients (pts) treated with neoadjuvant chemo-radiotherapy (CRT) can direct the choice of therapeutic strategy. The aim of the study was to evaluate the predictive value of basal and pre-surgical 18F-FDG-PET (PET).
Materials and Methods: Pts entering the study had cT3-T4 N-/+ rectal adenocarcinoma <12 cm from the anal margin. CT consisted in 5-fluorouracil with or without oxaliplatin; RT was delivered up to a dose of 50.4 Gy in daily fractions of 1.8 Gy; rectal surgery was performed 6−8 weeks after the end of CRT. PET was performed at initial diagnosis and before the surgery. Standard Uptake Value (SUV1 = basal PET, SUV2 = pre-surgery PET) was determined from the most active tumor site. The pathological examination of surgical specimens included the Tumor Regression Grade (TRG) evaluation according to the Dworak grading. Responder pts were defined as TRG4 = complete regression, TRG3 = good regression, TRG2 = moderate regression, and non-responder pts were defined as TRG1 = minor regression, TRG0 = no regression.
Results: Eighty pts were evaluated between June 2003 and February 2009. The pt characteristics were: 55 (68.7%) males, 25 (31.3%) females; median age 65 years (33−80); stage: 36 (45%) cT3N-M0, 33 (41.3%) cT3N+M0, 6 (7.5%) cT4N-M0, 5 (6.2%) cT4N+M0. The pathological responses were: TRG1 16 (20%) pts, TRG2 28 (35%), TRG3 20 (25%), TRG4 16 (20%). The SUV1 and SUV2 cut-off related to TRG are 19 and 4.9, respectively, was identified with ROC analysis. In 53 (66.3%) pts SUV1 was $\leqslant$19 (low) and in 27 (33.7%) it was >19 (high). The low SUV1 value was significantly correlated with TRG2−4 ($p = 0.002$). In 53 (66.3%) pts the SUV2 was $\leqslant$4.9 (low) and in 27 (33.7%) it was >4.9 (high). The low SUV2 value was significantly correlated with TRG2−4 ($p < 0.0001$). In multivariate analysis, TRG2−4 was statistically correlated with SUV1 ($p = 0.010$) and SUV2 ($p = 0.018$).
Conclusions: These results suggest that a low baseline SUV value and a low pre-surgical SUV value could predict the pathological response in locally advanced rectal cancer pts treated with neoadjuvant CRT. In this pt setting, the PET evaluation should be further investigated in order to establish the treatment strategy.

6047 POSTER

Development of nomograms for prediction of pathologic complete response in locally advanced rectum cancer: a multicentric study using PET before, during and after neoadjuvant chemoradiotherapy

R. van Stiphout[1], M. Janssen[1], J. van den Bogaard[1], L. Leccisotti[2], C. Coco[3], M. Lambrecht[4], G. Lammering[1], K. Haustermans[4], V. Valentini[5], P. Lambin[1]. [1]*Department of Radiation Oncology (MAASTRO) GROW University Medical Centre Maastricht, Maastricht, The Netherlands;* [2]*Università Cattolica del S. Cuore, Nuclear Medicine Department, Rome, Italy;* [3]*Università Cattolica del S. Cuore, Surgery Department, Rome, Italy;* [4]*University Hospital Leuven, Department of Radiation Oncology, Leuven, Belgium;* [5]*Università Cattolica del S. Cuore, Radiotherapy Department, Rome, Italy*

Purpose: The prediction of pathologic complete response (pCR) after preoperative chemoradiotherapy (CRT) might be helpful for selecting rectal cancer patients in which a less invasive surgery or a "wait and see policy" would be possible. A prediction of the pathological response already during CRT, as opposed to after CRT, would be more attractive, because it could enable response-guided modifications of the treatment protocol. In this study, data were prospectively collected at 3 different institutions. Three different imaging time points were analyzed for their predictive value: pre-CRT, during CRT and after CRT, just before surgery.
Methods: The datasets with both clinical and imaging variables from 3 different institutions were merged to have a statistical weight. A total of 64 patients were treated with long-term chemoradiotherapy (CRT). For all patients, three PET-CT scans were acquired (before CRT, during CRT, after CRT just before surgery). Clinical variables included age, sex, WHO performance status, BMI, cTNM stage. For PET-analyses, the tumors were semi-automatically contoured using standardized uptake-value (SUV) thresholding. Imaging variables consisted of tumor dimensions (GTV, maximal diameter, distance from anal verge) and metabolic activity of the tumor corrected by blood glucose (SUVmean, SUVmax). In addition, for the follow-up PET scans, all relative differences (response indices, RI) were also included in the evaluation. 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. Also, all output was converted to nomograms.
Results: For 23% of the patients, CRT resulted in a pCR. Based on the AUCs (Mean $\pm$SD) of the ROC-curves, the model containing PET variables during treatment reached the highest training performance (0.82 ± 0.07) when compared to pretreatment (0.75 ± 0.08) and pre-surgical (0.72 ± 0.10) models. For PET-imaging during treatment, these variables were predictive (ranked by their importance): response index of SUVmax during CRT (0.28), cT-stage (−0.22), cN-stage (−0.18).
Conclusion: The prediction of pCR based on both clinical variables and PET variables assessed early during treatment was found to be most accurate based on the multivariate analysis. Easy to use nomograms will be presented. A prospective validation of the model is underway and the

next step will be to use the validated model to select patients who do not need (immediate) surgery.

6048 POSTER

A comparison of efficacy of first-line chemotherapy regimens for metastatic colorectal cancer (mCRC): FOLFIRI+ bevacizumab vs. XELIRI+ bevacizumab

J. Ocvirk[1], M. Rebersek[1], M. Boc[1]. [1]*Institute of Oncology, Medical Oncology, Ljubljana, Slovenia*

Background: FOLFIRI in combination with bevacizumab (BV) is a standard treatment option in first-line Cht for mCRC. Capecitabine is an oral prodrug of 5-FU, which is converted to 5-FU by three enzymatic steps. It can maintain a constant level of 5-FU without complications. The primary endpoint was to determine the efficacy of XELIRI/BV and to compare it to FOLFIRI/BV. The secondary endpoints were overall survival (OS), time to progression (TTP) and evaluation of side effects of BV.
Methods: Pts with histologically proven, previously untreated mCRC, older than 18 years, ECOG PS 0−2 and adequate organ and hematological functions were included to receive a combination of irinotecan 180 mg/m^2 iv day 1, BV 5 mg/kg iv day 1, LV 400 mg/m^2 iv day 1, 5-FU 400 mg/m^2 bolus iv day 1and 5-FU 2400 mg/m^2 in continuosly 46-hour infusion, repeated every 2 weeks, or irinotecan 250 mg/m^2 iv day 1, BV 7.5 mg/kg iv day 1 and capecitabine 1000 mg/m^2, po twd day 1−14, repeated every 3 weeks.
Results: From February 2005 to December 2007 139 pts with mCRC were included. Median age was 58 years (31−77), M/F = 61.9%/38.1%. Of 139 44 pts were treated with FOLFIRI/BV and 95 pts with XELIRI/BV. On analysis of results, data of all pts were available. Median duration of treatment was 22 weeks (2−36 weeks) in FOLFIRI/BV group and 20.1 weeks (3−36 weeks) in XELIRI/BV group. RR were CR 15.9% (7 pts), PR 22.7% (10 pts), SD 36.4% (16 pts), PD 20.5% (9 pts) in FOLFIRI/BV group and CR 11.6% (11 pts), PR 33.7% (32 pts), SD 41.1% (39 pts), PD 7.4% (7 pts) in XELIRI/BV group. Median TTP was 13.9 months in FOLFIRI/BV group and 17.6 months in XELIRI/BV group (95% CI). Median OS was 43.3 mo in FOLFIRI/BV group and 63.6 mo in XELIRI/BV group (p = 0.112). In 40 pts, BV was discontinued because of severe side effects. Deep venous thrombosis was detected in 7 pts, pulmonary embolism in 2 pts, colon perforation in 1 pt, any hemorrhagic event in 4 pts, G 3−4 hypertension in 2 pts, proteinuria G 3−4 in 8 pts. None of pts died because of side effects.
Conclusions: XELIRI/BV is at least as effective as FOLFIRI/BV in first-line treatment of mCRC. The results of efficacy of both regimens in our pts are comparable with the results from previous phase III studies in first-line treatment of bevacizumab + chemotherapy. Median OS was longer in XELIRI/BV, but it was not statisticaly significant. The observed adverse effects of BV in our study are comparable to those previously reported in mCRC.

6049 POSTER

Phase II trial of combined chemotherapy with irinotecan, S-1, and bevacizumab in patients with metastatic colorectal cancer

K. Hatanaka[1], Y. Komatsu[2], S. Yuki[3], M. Nakamura[4], T. Miyagishima[5], M. Kudo[6], M. Munakata[7], Y. Sakata[7], M. Asaka[3]. [1]*Hakodate Municipal Hospital, Gastroenterology, Hakodate, Japan;* [2]*Hokkaido University Hospital Cancer Center, Cancer Chemotherapy, Sapporo, Japan;* [3]*Hokkaido University Hospital, Gastroenterology, Sapporo, Japan;* [4]*Sapporo City General Hospital, Gastroenterology, Sapporo, Japan;* [5]*Kushiro Rosai Hospital, Internal Medicine, Kushiro, Japan;* [6]*Sapporo Hokuyu Hospital, Gastroenterology, Sapporo, Japan;* [7]*Misawa City Hospital, Medical Oncology, Misawa, Japan*

Background: A study comparing the effectiveness and safety of irinotecan plus S-1 (IRIS) with that of a combination of 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) as second-line treatment in patients with advanced, recurrent colorectal cancer (FIRIS trial) is ongoing in Japan. We previously reported that IRIS is very effective as first-line treatment (33rd ESMO in 2008). Bevacizumab, a molecular targeted agent, is positioned as a standard regimen for the treatment of advanced colorectal cancer. We examined the effectiveness and safety of the IRIS regimen combined with bevacizumab.
Materials and Methods: Eligible patients had to have mCRC with a confirmed diagnosis of adenocarcinoma, an age of $\geqslant$20 years, a ECOG performance status (PS) of 0−1, and no history of prior chemotherapy. S-1 40−60 mg twice daily p.o. was given on days 1−14 and irinotecan 100 mg/m^2 and bevacizumab 5 mg/kg i.v. were given on days 1 and 15 of a 28-day cycle. The primary endpoint was safety. The secondary endpoints included overall response (OR), progression-free survival (PFS), and overall survival (OS).
Results: The target number of 53 patients was enrolled as of March 2009. The results are reported for 45 patients with evaluable lesions. The clinical characteristics of the patients were as follows. The median age was 63 years (interquartile range, 48 to 82). The male:female ratio was 3:2. The performance status on the Eastern Cooperative Oncology Group scale was 0. At interim analysis, median follow-up was 162 days. On safety analysis, the incidence of grade 3 or 4 neutropenia was 27%. The incidences of other grade 3 or 4 adverse reactions were as follows: diarrhea, 13%; anorexia, 7%; stomatitis, 2%; hypertension, 11%; and gastrointestinal perforation, 0%. The overall response rate was 53%. Twenty-four patients (53%) had a partial response, 17 (38%) had stable disease, none had progressive disease, and 4 (9%) were not evaluable. Median progression-free survival and overall survival were not reached.
Conclusions: Our results suggest that IRIS plus bevacizumab is a well-tolerated, highly effective chemotherapeutic regimen that is easy to administer. The latest data will be reported at this meeting.

6050 POSTER

Clinical features of interstitial lung disease induced by FOLFOX or FOLFIRI for colorectal cancer

T. Shimura[1], N. Fuse[1], T. Yoshino[1], K. Minashi[1], M. Tahara[1], T. Doi[1], T. Joh[2], A. Ohtsu[1]. [1]*National Cancer Center Hospital East, Division of Gastrointestinal Oncology and Digestive Endoscopy, Kashiwa, Japan;* [2]*Nagoya City University Graduate School of Medical Sciences, Department of Gastroenterology and Metabolism, Nagoya, Japan*

Background: Either infusional fluorouracil, leucovorin and oxaliplatin (FOLFOX) or infusional fluorouracil, leucovorin and irinotecan (FOLFIRI) has been recognized as one of the standard chemotherapy for colorectal cancer. Chemotherapy-induced interstitial lung disease (ILD) is rare, and few patients with ILD following FOLFOX or FOLFIRI have been reported. The aims of this study are to clarify and evaluate the clinical features of ILD after treatment of FOLFOX or FOLFIRI for colorectal cancer.
Material and Methods: We identified 734 patients with colorectal cancer treated with FOLFOX or FOLFIRI from April 2005 to December 2008 at National Cancer Center East Hospital by using computerized data base of the institution. ILD was defined when a chest computed tomography revealed interstitial infiltrates and the other pulmonary disease was clinically excluded. We categorized patients with ILD into improved ones and dead ones.
Results: Of 734 patients, 449 (92) received FOLFOX (with bevacizumab), 55 (18) FOLFIRI (with bevacizumab) and 230 (93) both FOLFOX and FOLFIRI (with bevacizumab). Eleven (1.5%) patients developed ILD, which consisted of 7 improved ones and 4 dead ones. All patients with ILD were men, and 10 of 11 patients were heavy smoker. Of 11 patients, 10 patients had any pulmonary shadows except lung metastases before chemotherapy. FOLFOX has been ever administered for all of the ILD patients. Six patients developed ILD during FOLFOX therapy, one occurred on the 137th day after completion of adjuvant chemotherapy with FOLFOX, and four developed ILD during the other regimens (FOLFIRI in three patients and fluorouracil/leucovorin plus bevacizumab in one). Median Brinkman Index was 700 (range, 0–1000) in the improved patients and 1085 (range, 380–1380) in the dead ones. Median days from the last dose of any chemotherapy to the episode were 8 days (range, 0–137 days) in the improved patients and 1.5 days (range, 0−10 days) in the dead ones. Median days from the episode to start of the treatment were 8.5 days (range, 0−14 days) in the improved patients and 13 days (range, 5−21 days) in the dead ones.
Conclusions: This study was the first systemic analysis to investigate the incidence of ILD induced by FOLFOX or FOLFIRI. The incidence of ILD was not so common, but it is life-threatening complication. We should be careful to the onset of ILD not only during, but also after chemotherapy for colorectal cancer.

6051 POSTER

Balancing pros and cons of the addition of Bevacizumab (BEVA) to first-line chemotherapy (CT) for advanced/metastatic colorectal cancer (MCRC): Meta-analysis of randomized clinical trials exploring absolute benefits

F. Cuppone[1], V. Vaccaro[1], F. Loupakis[2], M. Milella[1], P. Carlini[1], C. Nisticò[1], A. Falcone[2], D. Giannarelli[1], F. Cognetti[1], E. Bria[1]. [1]*Regina Elena National Cancer Institute, Medical Oncology, Roma, Italy;* [2]*Istituto Toscano Tumori, Medical Oncology, Livorno, Italy*

Background: Although the addition of BEVA to CT has provided a significant survival benefit for MCRC, the magnitudes of both the advantages and the drawbacks (with particular regard to vascular toxicities) have not been extensively weighted. With these perspectives, a literature-based meta-analysis was conducted.