Material and Methods: The inclusion criteria were; (1) histologically proved adenocarcinoma of colon or rectum, (2) age ⩾20 years, (3) no prior treatment, (4) at least one target lesion by RECIST ver1.0 criteria, (5) ECOG Performance Status 0−1. Patients (Pts) were randomized to receive either S-1 (40−60 mg bid) and oral LV (25 mg bid) for one week and L-OHP (85 mg/m^2) on day 1, repeated every 2 weeks (SOL; Group A) or L-OHP (85 mg/m^2), *l*-LV (200 mg/m^2), and 5-FU (400 mg/m^2, bolus) on day 1, followed by 5-FU (2400 mg/m^2, ci, 46 hours), repeated every 2 weeks (mFOLFOX6; Group B). The number of the enrolled pts was set to achieve the probability that a point estimate of hazard ratio (HR) of progression free survival (PFS; primary endpoint) less than 1.0 is 80% or more. This trial was supported by Taiho Pharmaceutical CO., LTD and Yakult Honsha CO., LTD. ClinicalTrials.gov Identifier: NCT00721916.
Results: From July 2008 to July 2009, 107 pts were randomized, and 105 were eligible (56 to Group A and 49 to Group B). A cut-off date for the primary analysis was 31 March 2010. The median PFS for Group A and Group B was 9.6 and 6.9 months (HR = 0.83; 95% CI, 0.49–1.40), indicating that the primary endpoint was met. Response rate was 55.4% for Group A (31/56; 95% CI, 41.5–68.7) compared to 53.1% for Group B (26/49; 95% CI, 38.3–67.5), and disease control rate (CR + PR + SD) was 92.9% for Group A (52/56; 95% CI, 82.7–98.0) compared to 85.7% for Group B (42/49; 95% CI, 72.8–94.1). Median OS have not been reached at this time, but 1-year survival rate was 86.0% for Group A and 79.0% for Group B. The incidences of grade 3/4 adverse drug reactions were; neutropenia (19.6% Group A, 41.2% Group B), lymphopenia (14.3% and 5.9%), sensory neuropathy (19.6% and 2.0%), anorexia (12.5% and 7.8%), fatigue (10.7% and 5.9%) and diarrhea (10.7% and 3.9%).
Conclusions: SOL shows promising activity with well-tolerated toxicities compared to mFOLFOX6.

6119 POSTER

High Level of Thymidine Phosphorylase Gene Expression in Tumour Tissues is Associated With Response to Oral Uracil and Tegafur/leucovorin Chemotherapy in Patients With Colorectal Cancer

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Background: 5-Flurouracil (5-FU)/ leucovorin (LV) and oral uracil and tegafur (UFT)/LV are widely used as standard adjuvant chemotherapy for colorectal cancer (CRC). We previously reported that folylpolyglutamate synthase (FPGS) and g-glutamyl hydrolase (GGH) regulate the reduced folate levels in CRC tissue when oral LV was administered. In the present study, we examined the relationship between mRNA expressions of pyrimidine and folate metabolism-related enzymes in CRC tissues and the efficacy of UFT/LV treatment.
Material and Methods: Seventy-six well- or moderately-differentiated CRC patients without prior treatment who were scheduled to undergo surgery were enrolled. These 76 patients subsequently received oral treatment with UFT/LV for 2 weeks and underwent surgery 3 days after the final dose administration. We evaluated the tumour response on the resected specimens. We assessed pathological response based on the extent of residual cancer cells and granulation tissues, and graded on a scale from 0 to 4. A patient with scale 3 or 4 was defined as a “responder”. The mRNA expressions of pyrimidine-related enzymes (6 genes) and reduced folate-related enzymes (8 genes) were quantitatively evaluated using a RT-PCR assay. These candidate genes were evaluated based on differences in the log-transformed mRNA expression levels between responders and non-responders. A multivariate logistic regression model with a stepwise regression was used to assess the independent effect on the response to oral UFT/LV treatment.
Results: Pathological responses were observed in 19.7% (15/76) of the patients. There was no significant difference in response rates between well and moderately differentiated histologic types. The median values of relative thymidine phosphrylase (TP) mRNA expressions were 0.0019 and 0.0012 for responders and non-responders, respectively. The expression level of TP mRNA was significantly higher in responders than in nonresponders ($p = 0.011$). There were no significant differences between pathological response and other gene expressions on univariate analysis. On multivariate logistic regression analysis including clinical parameters, TP remained independent predictor of the response.
Conclusion: The TP mRNA expression levels in primary CRC tissues may be useful for predicting the efficacy of oral UFT/LV treatment in patients with CRC.

6120 POSTER

Personalized Dose Management for 5-fluoruracil Based Chemotherapy Regimens to Lower Severe Toxicity by Cancer Patients

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Background: Doses of chemotherapy drugs are administered based on body surface area (BSA), determined by height and weight of the patient. This standard does not reflect the difference in absorption and metabolism by each patient, which causes big blood drug level variations. We investigated the blood level of 5-fluoruracil (5-FU) in 3 chemotherapy regiments for treatment of colorectal cancer to determine the individual dose management with less side effects for each patient compared to standard dose treatment.
Material and Methods: A group of 56 patient with colorectal cancer were first divided into two subgroups according to the stage of the disease: 21 patients receiving adjuvant chemotherapy and 35 treated for metastatic disease. Three chemotherapy regiment were chosen: 5-FU (day 1 and day 5) + leucovorin (every 21 days), FOLFOX every 21 days and FOLFIRI every 21 days. 5-FU individual plasma concentrations were determined in four different ways − once on day 1 at the end of 2 hours infusion, twice at the 20th and 46th hour of pump infusion, measuring the concentration on the first, second and third day of the infusion and on the first, second, third and fourth day of the 5-FU infusion with a chromatography method. Another group of 50 patients receiving the same standard dose chemotherapy based only on BSA (without any dose adjustment) was used as a control group to follow up toxicity, intensity of treatment and period to progression.
Results: The area under the time/concentration curve (AUC) of 5-FU (according to Gamelin FU dose adjustment table) for patients treated in adjuvant aspect: AUC 15−20 mgh/l resulted in recommendation for a 15% higher dose for 2 patients; AUC 20−24 mgh/l − 1 patient with no dose correction; AUC 30−35 mgh/l − 1 patient with a lower dose recommendation. Results for patients with metastatic disease: by AUC under 10 mgh/l − 13 patients recommended for a high dose, AUC 10−15 mgh/l − 4 patients for 15% higher dose and AUC 20−24 mgh/l − 5 patients with no dose changes. From the results without any recommendation of dose adjustment: by 7 patients plasma concentrations of 5-FU could not be measured, the other 30 results are either with too high or too low AUC values. The concentration by follow up of patients on first, second and third day was different.
Conclusions: Personalized dose management based on testing of blood drug levels has the potential to lessen severe side effects of chemotherapy drugs and to deliver the more accurate treatment to patients and a better quality of life.

6121 POSTER

Phase II Trial of Combination Therapy With Bevacizumab and S-1 in Elderly Patients With Unresectable or Recurrent Colorectal Cancer (BASIC)

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Background: Chemotherapeutic regimens for elderly patients with advanced or recurrent colorectal cancer, such as combined treatment with 5-fluorouracil, leucovorin, and bevacizumab, often do not include oxaliplatin or irinotecan, because many patients are in poor physical condition. However, treatment with 5-fluorouracil and leucovorin requires the placement of a percutaneous port as well as other precautions, causing stress for patients as well as healthcare workers. From the viewpoint of ease of treatment, it is clinically important to confirm the therapeutic effectiveness of bevacizumab combined with S-1, an oral 5-fluorouracil derivative. In this study, we evaluated the efficacy and safety of combined therapy with S-1 and bevacizumab in elderly patients who had advanced or recurrent colorectal cancer.
Materials and Methods: The study group comprised elderly patients 65 years or older who had a histologically confirmed diagnosis of advanced or recurrent colorectal cancer and were scheduled to receive first-line chemotherapy. As for the treatment regimen, bevacizumab (5 mg/kg) was given intravenously on days 1, 15, and 29, and S-1 (80 to 120 mg/day