6106 POSTER

Immune-boost Treatment With Gemcitabine, Oxaliplatin, Levofolinate, 5-flurouracil, Granulocyte/macrophage Colony-stimulating-factor (GM-CSF) and Aldesleukine Enhances Progression-free and Overall-survival Over FOLFOX Chemotherapy in Metastatic Colorectal Cancer Patients − Early Results From the GOLFIG-2 Phase III Trial

P. Correale[1], M.S. Rotundo[2], C. Botta[1], A. Guglielmo[1], A. Licchetta[1], R. Conca[1], P. Tassone[2], R. Ridolfi[3], E. Mini[4], P. Tagliaferri[2]. [1]*"S. Maria alle Scotte" Siena University Hospital, Department of Oncology, Siena, Italy;* [2]*Magna Græcia University and Tommaso Campanella Cancer Center Catanzaro, Medical Oncology, Catanzaro, Italy;* [3]*"Morgagni-Pieranton" Hospital of Forlì, Oncology Unit, Forlì, Italy;* [4]*"Careggi" University Hospital of Florence, Department of Preclinical and Clinical Pharmacology, Florence, Italy*

Background: Previous translational studies demonstrated the safety, the immunological and anti-tumour activity of a newest chemo-immunotherapy boost with gemcitabine + FOLFOX followed by sc. GM-CSF and low dose aldesleukine (GOLFIG regimen) in largely pretreated metastatic colorectal cancer (mCRC) patients. We designed a phase III trial to compare the efficacy of this regimen with standard FOLFOX-4 chemotherapy in frontline treatment of mCRC.
Material and Methods: GOLFIG/2 is a multicenter open label/randomized phase III trial (EUDRACT#457/05) designed test the hypothesis of a two months advantage of GOLFIG over FOLFOX-4 regimen in term of progression-free-survival (PFS). Patients were randomized in a 1:1 ratio in the two arms to receive FOLFOX-4 or GOLFIG regimen [gem-citabine (1000 mg/m^2, day-1); oxaliplatin (85 mg/m^2, day-2); levofolinate (100 mg/m^2, days 1−2), 5-FU (400 mg/m^2 in bolus followed by 24 h infusion at 800 mg/m^2, days 1−2), sc. GM-CSF (100 μg, days 3−7); sc. aldesleukine (0.5 MIU bi-daily, days 8−14)]. Kaplan–Meier, Log-rank test and cox analysis were used for statistical comparisons.
Results. The study was prematurely terminated on January 2010 for outcome imbalance in favor of the experimental arm at the first preplanned interim analysis at 130 patients. No differences were observed in term of frequency of adverse events, with the exception of a higher frequency of fever, and self-limiting signs of autoimmunity in experimental arm. The GOLFIG regimen showed significant superiority over FOLFOX in term of response-rate [63.1 vs. 33.8%, P = 0.001], PFS [16.5 (95% CI;11.18–21.81) vs. 7.43 (95% CI;5.72–9.15) months, P = 0.001; HR = 0.372, P < 0.001] and overall-survival (OS) [30.51 (95% CI 22.86–38.16) vs. 21.51 (95% CI 16.17–26.84) months, P = 0.049; HR = 0.37, P = 0.001]. Several treatment-related changes in different lymphocyte subsets and myeloid-lineage cells were observed in patients enrolled in the GOLFIG arm, however, none of these was predictive of positive outcome with exception of a baseline neutrophil-count ⩽5,500 cell/μl (HR = 3.693 in term of OS, P = 0.001). In this group of patients, sex, age, primary tumour and metastatic sites, histotype, grading and k-ras-status did not achieve statistical predictive value.
Conclusion: The results of this trial provide the first proof of efficacy for a chemo-immunological regimen as first line treatment of mCRC.

6107 POSTER

Improved Overall Survival in the Patients With Metastatic Colorectal Cancer Associated With Ant-VEGF Antibody Drug and Anti-EGFR Antibody Drug Administration

T. Denda[1], N. Nakamura[1], K. Sudo[1], K. Nakamura[1], K. Minashi[2], S. Hironaka[2], T. Hara[3], H. Soda[4], N. Takiguchi[4], T. Yamaguchi[1]. [1]*Chiba Cancer Center Hospital, Division of Gastroenterology, Chiba, Japan;* [2]*Chiba Cancer Center Hospital, Department of Cllinical Trial Promotion, Chiba, Japan;* [3]*Chiba Cancer Center Hospital, Division of Endoscopy, Chiba, Japan;* [4]*Chiba Cancer Center Hospital, Division of Gastroenterological Surgery, Chiba, Japan*

Background: In Japan, new anti-cancer drug oxaliplatin was approved for the treatment of metastatic colorectal cancer (CRC) in 2005. Subsequently, anti-vascular endothelial growth factor (VEGF) antibody bevacizumab was approved in 2007, anti-Epidermal growth factor receptor (EGFR) antibody cetuximab in 2008, and anti-EGFR antibody panitumumab in 2010. Indirect evidence suggests that the introduction of anti-VEGF antibody drug and anti-EGFR antibody drugs is improving patient-outcomes; however, the gain has not yet been quantified.
Material and Methods: We performed a retrospective review of patients newly diagnosed with metastatic CRC treated at our institution from 2005 to 2010. Landmark analysis evaluated the association between diagnosis year and administration of molecular-targeted drugs with overall survival.
Results: Three hundred eighty patients who were diagnosed with metastatic CRC received primary treatment at our institution during this period. The median overall survival for patients diagnosed from 2005 to 2011 was 27.9 months that appeared to increase over time and was 25.7 and 28.8 months for patients diagnosed from 2005 to 2006 and 2007 to 2008, respectively. The median survival had not yet been reached for those diagnosed from 2009 to 2011. There were significant differences ($p < 0.05$) between each time period. The rate of bevacizumab use among patients diagnosed from 2005 to 2011 was 51%; it was 39%, 67%, and 78% among patients diagnosed from 2005 to 2006, 2007 to 2008, and 2009 to 2011, respectively, showing a gradual increase. The rate of anti-EGFR antibody use among patients diagnosed from 2005 to 2011 was 24%; it was 20%, 36%, and 17% among patients diagnosed from 2005 to 2006, 2007 to 2008, and 2009 to 2011, respectively, not showing a gradual increase. Thus, the improved outcomes from 2005 to 2011 appeared to be as a result of increased bevacizumab administration.
Conclusions: Profound improvements in outcomes in metastatic CRC appear to be associated with increased bevacizumab administration at present. If more patients with K-ras wild type CRC will be administered with anti-EGFR antibody drugs, there is a possibility of improvement of overall survival of patients with CRC.

6108 POSTER

Adjuvant Chemotherapy for Colon Cancer in the Netherlands: Who Are We Treating Actually?

N. van Leersum[1], K. van der Hoeven[2], R. Tollenaar[3], M. Wouters[4]. [1]*Leiden University Medical Center, Surgery K6−50, Leiden, The Netherlands;* [2]*Medisch Centrum Alkmaar, Surgery, Alkmaar, The Netherlands;* [3]*Leiden University Medical Center, Surgery, Leiden, The Netherlands;* [4]*Antonie van Leeuwenhoek, Surgery, Amsterdam, The Netherlands*

Background: According to Dutch guidelines, chemotherapy should be considered in all patients with stage III and high-risk stage II colon carcinoma. The definition of high-risk stage II and the benefit of chemotherapy for these patients is subject of debate in literature. In an ageing population with a large number of patients with comorbid conditions, weighing of the risks and benefits of adjuvant chemotherapy may therefore lead to less use of chemotherapy. We evaluated the use of adjuvant chemotherapy in the Netherlands.
Materials and Methods: Analysis was based on data of 11.000 patients with primary colon cancer enrolled in the Dutch Surgical Colorectal Audit between 2009–2010. Multivariate logistic regression was performed on the risk of not applying adjuvant chemotherapy in patients in who treatment is indicated.
Results: 3391 patients had stage III (31%) and 1507 patients had high risk stage II colon carcinoma (14%). Mean age was 71 years and 19% had substantial concomitant disease (Charlson >1). Chemotherapy was administered in 59% of patients with stage III and 18% of patients with high risk stage II. In patients aged over 80 years with high risk stage II, only 2% received chemotherapy. The most recognized risk factor in stage II patients was T4 tumour, treated with chemotherapy in 30% of patients. Only a quarter of patients with stage III disease who did not receive chemotherapy had substantial comorbidity. In multivariate analysis, age was most frequently associated with lower probability of receiving chemotherapy (OR 25.1). The correlation with both ASA score IV-V and Charlson score >1 was less robust (resp. OR 3.8 and OR 1.6). Severe complications after surgery had a substantial contribution (OR 2.2) to the risk of not receiving chemotherapy as well.
For patients younger than 75 years with stage III, a large variation in administration of chemotherapy between individual hospitals was observed, ranging from 18 to 89% in the whole group and from 18 to 100% in patients with only minor comorbidities (ASA I-II or Charlson 0−1).
Conclusions: In the Netherlands, high-risk stage II colon cancer is not always recognized as an indication for adjuvant chemotherapy. Age seems a more important factor than comorbidity when considering chemotherapy. This may imply undertreatment of a large group of healthy old patients, who might benefit from chemotherapy. There is large variation in the use of chemotherapy between hospitals, even in patients with a favourable casemix.

6109 POSTER

Difference in Overall Survival in Colorectal Cancer Patients With the KRas P.G13D and Other KRas Mutations After the Failure of 5-fluorouracil, Oxaliplatin, and Irinotecan

K. Suyama[1], T. Yoshino[2], Y. Kawamoto[2], H. Bando[2], T. Doi[2], H. Baba[3], A. Ohtsu[2]. [1]*National Cancer Center Hospital East, Medical Oncology, Kashiwa Chiba, Japan;* [2]*National Cancer Center Hospital East, GI Oncology, Kashiwa Chiba, Japan;* [3]*Kumamoto University, Gastroenterological Surgery, Kumamoto, Japan*

Background: Metastatic colorectal cancer (mCRC) patients with *KRAS* codon 12 or 13 mutations are currently not treated with cetuximab (Cmab).