Highlights of the 2010 Annual Meeting of the American Society of Clinical Oncology

June 4–8, 2010
Chicago, Illinois

Colorectal Cancer In Focus

Complete abstracts are available in Journal of Clinical Oncology. 2010;28(15S)

E14112 Cetuximab/Irinotecan in Wild-type KRAS Patients With Irinotecan-refractory mCRC

Y Hong, M Kang, J Baek, J Lee, H Chang, S Jang, Y Kang, T Kim

Previous analyses have shown that cetuximab plus irinotecan is effective in KRAS wild-type, epidermal growth factor receptor (EGFR)+ and EGFR- patients with irinotecan-refractory metastatic colorectal cancer (mCRC). Hong and colleagues conducted a prospective, nonrandomized, multicenter phase II study of 40 patients (20 EGFR+ and 20 EGFR-). Patients with histologically-proven adenocarcinoma expressing wild-type KRAS who had failed first-line irinotecan-containing chemotherapy were enrolled. Patients received biweekly cetuximab 500 mg/m^2 and irinotecan 150–180 mg/m^2. The primary endpoint was response rate, and secondary endpoints included toxicity, progression-free survival (PFS), and overall survival (OS). Study findings demonstrated an overall response rate (ORR) of 45% (55% in EGFR+ arm and 35% in EGFR- arm). The overall median PFS was 7.1 months (8.3 months in EGFR+ arm and 5.8 months in EGFR- arm), with a 1-year survival rate of 81.1% (86.6% in EGFR+ and 78.7% in EGFR- arm). Safety analysis found that neutropenia (n=5) was the most common grade 3/4 toxicity, followed by febrile neutropenia/asthenia (n=2). Incidence of grade 2/3 skin rash was slightly higher in EGFR+ patients compared to EGFR- patients (14 vs 11 patients). The study findings showed that biweekly cetuximab and irinotecan was well tolerated as a second-line treatment for mCRC.

3528 Randomized, Open-label, Phase III Study of Panitumumab With FOLFOX4 Versus FOLFOX4 Alone for mCRC: Efficacy by Skin Toxicity

J Douillard, J Cassidy, J Jassem, F Rivera, I Kocáková, W Rogowski, JR Canon, EP Yanez, F Xu, JL Gansert

Skin toxicity is one of the most common drug-related adverse events in patients receiving anti-EGFR antibodies. In this study, Douillard and colleagues examined the efficacy and safety of panitumumab, a fully human anti-EGFR antibody, plus 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with mCRC. A total of 1,183 patients with metastatic adenocarcinoma of the colon or rectum who had no prior chemotherapy for mCRC or oxaliplatin exposure and a European Cooperative Oncology Group (ECOG) score of 0–2 were randomized 1:1 to receive panitumumab plus FOLFOX4 (n=593) or FOLFOX4 alone (n=590). Of 1,096 patients with evaluable KRAS, 656 were wild type and 440 were mutant. In patients with wild-type KRAS, an improvement in PFS was observed with panitumumab (9.6 vs 8.0 months; 95% confidence interval, 0.66–0.97; *P*=.02). Skin toxicity was observed in 97% and 95% of patients with wild-type and mutated KRAS, respectively. Median PFS and OS were higher in wild-type KRAS patients with grade 2–4 toxicity compared to those with grade 1 toxicity. A similar trend was seen in patients who had mutant KRAS. Since a PFS and OS benefit was seen in wild-type patients and also in mutant KRAS patients (who typically do not respond to panitumumab) with grade 2–4 skin toxicity, it is possible that there may be confounding prognostic factors that were not taken into consideration.

3565 Phase III Study of Panitumumab With FOLFIRI Versus FOLFIRI Alone as Second-line Treatment of mCRC: Analysis by EGFR Staining

M Peeters, A Cervantes-Ruiperez, A Strickland, T Ciuleanu, PN Mainwaring, VI Tzekova, A Santoro, CW Johnson, A Zhang, JL Gansert

Panitumumab plus 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) versus FOLFIRI alone has been examined in studies as second-line therapy for mCRC by KRAS status. In this phase III study, efficacy analysis by EGFR status was performed. Patients (N=1,186) were randomized 1:1 to panitumumab 6 mg/kg every 2 weeks plus FOLFIRI (arm 1) or FOLFIRI alone (arm 2). Primary endpoints included PFS and OS, which were prospectively analyzed by KRAS status. EGFR was not required for study entry, and tumor tissue had to be

sectioned within 2 months prior to testing. Of all patients, 1,083 were evaluable for KRAS and 719 were evaluable for EGFR staining. In those patients with wild-type KRAS, median PFS was higher in arm 1 compared to arm 2 (5.9 vs 3.9 months). A 2-month difference was also seen in OS (14.5 vs 12.5 months, respectively). Of the 1,083 patients with KRAS, 391 with wild-type KRAS also had EGFR results; 295 were EGFR positive. Adverse event rates were similar in both arms. Panitumumab significantly improved PFS and was well tolerated when added to FOLFIRI in patients with wild-type KRAS mCRC.

3566 PRIME Trial Analysis by EGFR Staining

S Siena, J Tabernero, D Cunningham, P Koralweski, P Ruff, M Rother, CW Johnson, A Zhang, JL Gansert, J Douillard

In an analysis of the PRIME (Panitumumab Randomized Trial in Combination With Chemotherapy for Metastatic Colorectal Cancer to Determine Efficacy) study, Siena and coworkers evaluated outcomes according to EGFR positivity, which was determined by immunohistochemistry on tumor tissue that had been sectioned within 2 months prior to testing. EGFR staining results were not required for study entry but were available in 69% of all patients and 68% of patients with KRAS wild-type tumors. Tissue section age exceeding 2 months was the most common reason for lack of an EGFR result. A total of 1,183 patients were randomized 1:1 to receive panitumumab plus FOLFOX4 or FOLFOX4 alone. PFS and OS were study endpoints. For wild-type KRAS patients, median PFS was 9.6 months in arm 1 and 8.0 months in arm 2. Median OS was 23.9 months and 19.7 months in arms 1 and 2, respectively. A multivariate Cox model did not demonstrate treatment effect by EGFR staining in KRAS wild-type patients. The authors concluded that, in first-line therapy of mCRC, the addition of panitumumab to FOLFOX4 significantly improved PFS and was well tolerated in patients with KRAS wild-type tumors. This effect of panitumumab on PFS and OS was seen in both EGFR+ and EGFR– patients.

3570 Final Data from the CRYSTAL Study: Association of KRAS and BRAF Biomarker Status With Treatment Outcome

E Van Cutsem, I Lang, G Folprecht, M Nowacki, C Barone, I Shchepotin, J Maurel, D Cunningham, I Celik, C Kohne

Previous findings from the CRYSTAL (Cetuximab Combined With Irinotecan in First-line Therapy for Metastatic Colorectal Cancer) trial have showed that KRAS wild-type patients benefited from the addition of cetuximab to FOLFIRI as first-line treatment for mCRC. In this analysis, Van Cutsem and colleagues evaluated the KRAS and BRAF mutation status of an expanded patient population by using polymerase chain reaction and melting curve assays and compared treatment arms based on mutation status. The primary analysis population comprised 1,198 patients, 1,063 of which were evaluable for KRAS testing. Of the 666 patients with KRAS wild-type tumors, 625 were evaluable for BRAF testing. There were 566 patients who were KRAS and BRAF wild type and 59 patients who were KRAS wild-type and BRAF mutated. In patients with KRAS wild type tumors, median OS, median PFS, and ORR were significantly higher in patients receiving cetuximab plus FOLFIRI compared to those receiving FOLFIRI alone. BRAF mutation suggested poor prognosis in both groups, with significantly lower efficacy endpoints compared to patients with wild-type BRAF status. The investigators concluded that the findings corroborated the value of KRAS tumor status as a predictor of outcome in patients with mCRC receiving first-line cetuximab plus FOLFIRI.

3594 Resection of CRC Metastases After First-line Treatment With Bevacizumab: Results of the ETNA Study

E Terrebonne, D Smith, Y Becouarn, P Michel, R Guimbaud, D Auby, A sa Cunha, A Ravaud, M Rouyer, A Fourrier-Réglat

In this ETNA cohort study, Terrebonne and colleagues evaluated secondary resection of metastases from CRC that were initially unresectable. ETNA was conducted in 28 French centers and included 411 patients who were treated with bevacizumab from January 2006 to December 2007. Of the 411 patients treated with first-line bevacizumab, 347 were evaluable after 24 months of follow-up; 67 patients had resection of metastasis. In those patients who underwent resection, mean age was 61.6 years, 46.3% were male, 91% had an ECOG performance status of 0–1, and 58.2% had 1 metastatic site. Those patients who did not undergo resection had a mean age of 64 years, 60% were male, 77.5% had an ECOG score of 0–1, and 55.7% had 1 metastatic site. The main resection site was liver (n=44), followed by lung (n=10), and the median time from commencement of bevacizumab to first resection was 207 days. In resected patients, the objective response rate was 85.7% (32.8% complete response); 14.9% of patients had stable disease. Bevacizumab treatment was given for a median of 6.9 months. Median PFS in patients who received resection was 13.6 months compared to 9 months in those who did not receive resection. The 1-year and 2-year OS rates in resected patients were 94.0% and 81.7%, respectively, compared to 75.2% and 44.5% in those who did not have resection of metastasis. Evaluation of morbidity and longer follow-up are needed.