Highlights of the 2011 Annual Meeting of the American Society of Clinical Oncology Gastrointestinal Cancers Symposium

January 20–22, 2011
San Francisco, California

Colorectal Cancer In Focus

Complete abstracts are available in Journal of Clinical Oncology. 2011;29(supplement 4)

362 AVANT: Results from a randomized, three-arm multinational phase III study to investigate bevacizumab with either XELOX or FOLFOX4 versus FOLFOX4 alone as adjuvant treatment for colon cancer

A De Gramont, E Van Cutsem, J Tabernero, MJ Moore, D Cunningham, F Rivera, S Im, M Makrutzki, A Shang, PM Hoff

In this international, randomized, phase III study, De Gramont and colleagues evaluated the therapeutic effect of bevacizumab administered concurrently with either the oxaliplatin, leucovorin, and 5-fluorouracil (FOLFOX4) regimen or the capecitabine and oxaliplatin (XELOX) regimen in the adjuvant setting. High-risk stage II or III colon cancer patients who had undergone surgical resection were randomized to receive 1 of 3 treatments; they were also stratified by geographic region and tumor stage. The first treatment group was given FOLFOX4 on weeks 1–24, the second group was given FOLFOX4 plus bevacizumab on weeks 1–24 followed by bevacizumab alone on weeks 25–48, and the third treatment group was given XELOX plus bevacizumab on weeks 1–24 followed by bevacizumab alone on weeks 25–48. The primary endpoint was disease-free survival (for patients with stage III disease), and secondary endpoints included overall survival (OS) and safety. A total of 3,451 patients were enrolled between December 2004 and June 2007. The final efficacy analysis, which was conducted in September 2010, showed that bevacizumab did not prolong disease-free survival or overall survival when added to either FOLFOX4 or XELOX in patients with stage III colon cancer. Furthermore, results favored the chemotherapy alone treatment group. The safety analysis found that relapses and deaths occurred more frequently in the treatment groups receiving bevacizumab; adverse events were consistent with those seen in previous studies of bevacizumab.

365 Randomized phase III study of 5-fluorouracil/folinate/oxaliplatin given continuously or intermittently with or without cetuximab, as first-line treatment of metastatic colorectal cancer: The NORDIC VII study (NCT00145314), by the Nordic Colorectal Cancer Biomodulation Group

K Tveit, T Guren, B Glimelius, P Pfeiffer, H Sorbye, S Pyrhonen, E Kure, T Ikdahl, E Skovlund, T Christoffersen

In this study, Tveit and associates evaluated the role of anti-EGFR therapy in the first-line treatment of metastatic colorectal cancer (mCRC). Patients were randomized to receive oxaliplatin 85 mg/m^2 on day 1, fluorouracil bolus 500 mg/m^2 and leucovorin 60 mg/m^2 on days 1–2 every 2 weeks (Nordic FLOX); FLOX plus cetuximab (initial dose 400 mg/m^2, then 250 mg/m^2/wk) until progression, or intermittent FLOX plus continuous cetuximab (FLOX for 16 weeks, which could be added at progression). Endpoints included progression-free survival (PFS), OS, and response. A total of 571 patients were randomized, and 566 were included in the intent-to-treat (ITT) analysis. The majority of patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 (67%); 29% of patients were ECOG 1 and 4% were ECOG 2. KRAS and BRAF mutations were obtained in 80% of patients; 40% of patients had KRAS-mutant tumors and 12% had BRAF-mutant tumors. The ITT analysis showed that response rates were similar across all 3 groups (41% in the FLOX group, 49% in the FLOX + cetuximab group, 47% in the intermittent FLOX + cetuximab group). It was noted that cetuximab plus FLOX did not significantly improve response rates, PFS, or OS compared to FLOX alone. Furthermore, overall survival in the patients treated with intermittent FLOX plus continuous cetuximab and in those treated with FLOX plus cetuximab until progression was similar (20.3 vs 19.7 months). KRAS mutation

status was not predictive for cetuximab efficacy; however, BRAF mutation was a strong negative prognostic factor.

477 Pooled safety results from SPIRITT: A multicenter, open-label, randomized, phase II study of FOLFIRI with panitumumab or bevacizumab as second-line treatment in patients with metastatic colorectal cancer

JR Hecht, SR Dakhil, MN Saleh, B Piperdi, M Cline-Burkhardt, DM Kocs, LC DeMarco, L Chen, K Krishnan, AL Cohn

A recent phase III study showed that panitumumab plus second-line leucovorin, 5-fluorouracil, and irinotecan (FOLFIRI) prolonged PFS in patients with wild-type KRAS tumors compared to chemotherapy alone. Based on this finding, Hecht and colleagues initiated a randomized, phase II, open-label study in mCRC patients whose disease progressed after or who were intolerable to 4 or more doses of first-line oxaliplatin-based chemotherapy plus bevacizumab. Patients were randomly assigned (1:1) to receive either 6 mg/kg of panitumumab every 2 weeks plus FOLFIRI or bevacizumab every 2 weeks plus FOLFIRI. Treatment was administered until disease progression, death, or study withdrawal. The primary endpoint was PFS, and secondary endpoints included objective response rate, overall survival, safety, and patient-reported outcomes. The safety analysis from this trial showed that 175 patients discontinued (81%) treatment and 39 (18%) remained on treatment. Of all enrolled patients, 38 experienced adverse events that led to study discontinuation. Serious adverse events were reported in 66 patients and included gastrointestinal disorders, infections and infestations, respiratory disorders, and metabolism and nutrition disorders. Fatal adverse events occurred in 18 patients, 9 of which were related to disease progression. The side effect profile was consistent with that seen in previous studies of FOLFIRI in combination with anti-epidermal growth factor receptor– or anti-vascular endothelial growth factor receptor–targeted therapy.

502 Patterns of maintenance treatment following first-line bevacizumab plus chemotherapy for metastatic colorectal cancer: Results from a large German community-based cohort study

D Arnold, V Petersen, M Kindler, M Schulze, J Seraphin, A Hinke, S Srock, A Kutscheidt

In this observational cohort study, Arnold and colleagues studied induction and maintenance therapy with bevacizumab combined with first-line chemotherapy regimens. A total of 1,620 patients were enrolled from 261 sites between January 2005 and June 2008. Patients were given either bevacizumab plus fluoropyrimidine/oxaliplatin (n=306) or bevacizumab plus fluoropyrimidine/irinotecan (n=1,001). After induction therapy, 271 patients received de-escalated maintenance therapy (bevacizumab alone or bevacizumab plus chemotherapy). Patients receiving bevacizumab plus maintenance chemotherapy experienced shorter induction (5.1 vs 8.7 months) but longer maintenance (4.4 vs 3.2) compared to those patients who received bevacizumab alone. Median PFS was longer for patients receiving bevacizumab plus maintenance chemotherapy compared to those receiving maintenance bevacizumab (13.5 vs 10.8 months). Currently, data are available for 161 patients who received bevacizumab and maintenance chemotherapy: 97 patients received oxaliplatin and 64 received irinotecan. The median total duration of therapy was approximately 1 month longer in patients receiving irinotecan-based induction (10.9 vs 9.6 months); the median length of induction was 4.1 and 5.5 months in the oxaliplatin and irinotecan groups, respectively. The median length of maintenance therapy was 4.3 and 4.4 months, respectively. The median PFS after induction was 12.8 and 14.1 months in patients receiving oxaliplatin- and irinotecan-based chemotherapy. The investigators concluded that the de-escalation strategies resulted in longer PFS. Also, a trend toward longer PFS was seen in patients who received bevacizumab plus chemotherapy maintenance.

510 Geriatric subgroup of AGITG MAX trial: International randomized phase III trial of capecitabine, bevacizumab, and mitomycin C in first-line metastatic colorectal cancer

TJ Price, D Zannino, K Wilson, J Simes, GA Van Hazel, BA Robinson, A Broad, V Ganju, SP Ackland, NC Tebbutt

The Australasian Gastro-Intestinal Trials Group presented data from an analysis of the MAX study, which was a 3-arm study that looked at capecitabine versus capecitabine plus bevacizumab versus capecitabine, bevacizumab, and mitomycin C in geriatric mCRC patients. The analysis evaluated the effect of adding bevacizumab to capecitabine (with/without mitomycin C) on PFS, OS, response rate, and toxicity in patients over 75 years of age. This analysis included 99 patients, of whom 37 received capecitabine, 32 received capecitabine plus bevacizumab, and 30 received the combination of all 3 drugs. Baseline characteristics across all 3 groups were balanced; comorbidities included previous and current smoking, diabetes, hypertension, ischemic heart disease, and cerebrovascular accident/transient ischemic attack. The findings showed

that PFS was 3.2 months longer in patients receiving cetuximab plus bevacizumab compared to those receiving cetuximab alone. Similarly, OS was also increased in patients receiving the cetuximab/bevacizumab combination (15.7 vs 13.4 months). Conversely, a 5% lower response rate was observed in patients receiving bevacizumab plus cetuximab. Grade 3/4 toxicities included vomiting, diarrhea, stomatitis, thrombosis/thrombus/embolism, and cardiac complications; 1 grade 5 toxicity was seen (perforation). The investigators concluded that the treatment was well tolerated with no indication of increased toxicity when compared to patients younger than 75 years.

624 Maintenance treatment with cetuximab in a series of patients treated with standard chemotherapy and cetuximab in metastatic colorectal cancer

G Quintero-Aldana, S Varela, B Campos, S Vazquez-Estevez, O Maseda, E Santos, C Iglesias, I Torres, A Lancho, J Mel

Because new therapeutic approaches are needed to improve the safety and efficacy in patients with mCRC, Quintero-Aldana and colleagues evaluated maintenance treatment with cetuximab in patients who were treated with standard chemotherapy and cetuximab in the first-line setting. They reported data on 12 patients who received standard chemotherapy plus cetuximab every 2 weeks. Cetuximab was continued until disease progression or unacceptable toxicity in those patients with response or stable disease. All patients had stage IV disease, 9 were male, and the median age was 62 years. FOLFOX4 was the most frequently administered chemotherapy; only 2 patients received FOLFIRI. Patients received a median of 12 cycles of chemotherapy and cetuximab. Seven of 12 patients achieved complete response. At the time of analysis, 7 patients continued on maintenance cetuximab therapy (median 7.5 cycles), and the remaining patients received treatment until progression. Cutaneous toxicity was the most frequently reported toxicity during maintenance treatment (grade 1 in 50% of patients). The investigators concluded that cetuximab has antitumor activity as a single-agent, in combination with chemotherapy, and as maintenance therapy after first- or second-line chemotherapy.