This difference in the time patterns of recurrence and impact of AT may ultimately explain why MMR is predictive of AT benefit.

6010 ORAL

A three-arm phase III randomized trial of FOLFOX-4 vs. FOLFOX-4 plus bevacizumab vs. XELOX plus bevacizumab in the adjuvant treatment of patients with stage III or high-risk stage II colon cancer: results of the interim safety analysis of the AVANT trial

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Background: Bevacizumab (Bev) and capecitabine (Cap) are established drugs for patients (pts) with metastatic colorectal cancer (mCRC). The AVANT trial is evaluating the efficacy and safety of Bev in combination with either intermittent Cap plus oxaliplatin (XELOX+Bev) or fluorouracil/leucovorin with oxaliplatin (FOLFOX-4+Bev) vs. FOLFOX-4 in the adjuvant treatment of pts with stage III or high-risk stage II colon cancer.
Materials and Methods: Pts were randomized to receive 12 cycles (q2 weeks) of FOLFOX-4 (Arm A), 12 cycles (q2 weeks) of FOLFOX-4+Bev (Arm B) or 8 cycles (q3 weeks) of XELOX+Bev (Arm C) followed by a further 8 cycles (q3 weeks) of Bev in Arms B and C (1 year of total Bev duration). Primary objective is to show superiority of Arm B or Arm C vs. Arm A in pts with stage III colon cancer in terms of disease-free survival (DFS). An interim safety analysis was planned 6 months after the last randomized pt ended treatment.
Results: Between December 2004 and June 2007, 3451 pts were randomized (stage III/high-risk stage II: 2867/573). Arm A, 955/192; Arm B, 960/194; Arm C, 952/187. Treatment arms were well balanced for disease stage, age, ECOG status and ethnicity. Median duration of oxaliplatin-containing chemotherapy was 5.3, 5.2 and 4.9 months, respectively, and median duration of Bev treatment was 10.6 months (Arm B) and 10.4 months (Arm C). Main toxicities of interest for Bev are shown in the table. All-cause mortality within 60 days of treatment start was 2 (0.2%) pts in Arm A, 4 (0.3%) in Arm B and 6 (0.5%) in Arm C. Number of deaths not due to colon cancer within 28 days after last drug administration were: Arm A, 8 (0.7%); Arm B, 4 (0.3%); Arm C, 10 (0.9%).
Conclusions: Bev plus fluoropyrimidine/oxaliplatin combination is safe in the adjuvant treatment of colon cancer pts. The adverse event profile is comparable to the safety profile in mCRC and in the NSABP C-08 trial (ASCO 2008–2009).

Table. Grade 3−5 AEs within 6 months of last treatment

No. (%) of pts	Arm A FOLFOX-4* n = 1126	Arm B FOLFOX-4 + Bev** n = 1145	Arm C XELOX + Bev** n = 1135
Venous thrombotic events	62 (5.5)	95 (8.3)	52 (4.6)
Hypertension	12 (1.1)	119 (10.4)	109 (9.6)
Arterial thrombotic events	11 (1.0)	18 (1.6)	17 (1.5)
Bleeding/haemorrhage	7 (0.6)	14 (1.2)	5 (0.4)
Wound healing complications	4 (0.4)	3 (0.3)	5 (0.4)
Abscess/fistula	3 (0.3)	16 (1.4)	9 (0.8)
Gastrointestinal perforations	1 (0.1)	8 (0.7)	2 (0.2)
Proteinuria	1 (0.1)	11 (1.0)	11 (1.0)

*planned treatment duration 5.5 months; ** planned treatment duration 11 months.

6011 ORAL

Calcium and magnesium (Ca/Mg) infusions to reduce oxaliplatin-induced neurotoxicity and outcome in advanced colorectal cancer (ACC) patients (pts) treated with oxaliplatin- and cetuximab-based therapy

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Background: Peripheral neurotoxicity is a potentially invalidating side effect of oxaliplatin treatment. Ca/Mg infusions are frequently used to prevent this toxicity, but the relationship with outcome is still controversial. Hypomagnesemia (hypoMg) is a frequent side effect of treatment with cetuximab (an epidermal growth factor receptor monoclonal antibody) and is associated with response to this agent. We assessed the effect of Ca/Mg infusions on toxicity and outcome.
Materials and Methods: 755 previously untreated ACC pts received capecitabine, oxaliplatin (to a maximum of 6 cycles) and bevacizumab (CB) or the same combination with the addition of cetuximab (CBC) in a phase III randomized trial (CAIRO2 study of the Dutch Colorectal Cancer Group, Tol et al., N Engl J Med 2009). Pts were divided into 2 groups: group I received Ca/Mg infusions at their first treatment cycle, group II did not. Progression-free survival (PFS), overall survival (OS), response rate (RR), and toxicity (NCI-CTC v.3.0) were assessed per treatment arm in these 2 groups and calculated using a Cox-proportional hazards model and Chi-square analysis.
Results: 732 pts were evaluable for these analyses. Group I consisted of 552 patients (75%), 269 in the CB arm and 283 in the CBC arm, of which 369 (67%) received Ca/Mg at all 6 cycles oxaliplatin. In group II, 133 out of 180 pts (74%) did not receive Ca/Mg during subsequent cycles. Baseline characteristics were comparable between group I and II. The incidence of peripheral neurotoxicity (⩾grade 2) was comparable in group I and group II (39% vs 42%; p = 0.49) in the CB and in the CBC arm. The incidence of all grade hypoMg also did not differ between groups (28% vs 24%; p = 0.32) in both treatment arms. The median PFS (95% confidence interval [CI]) in the CB arm was 10.6 (9.4−12.6) months in group I and 10.7 (9.0−12.7) months in group II (p = 0.54). In the CBC arm the median PFS was 9.2 (8.2−10.3) months in group I and 11.2 (8.6−12.6) months in group II (p = 0.15). The median OS (95% CI) was also comparable between group I and II in both the CB arm (20.0 [17.1−25.4] vs 20.4 [16.7−27.8] months; p = 0.68) and the CBC arm (18.9 [16.2−21.5] vs 20.6 [17.6−25.2] months; p = 0.20). The RR was 35% in group I vs 40% in group II in the CB arm (p = 0.45), and 36% vs 49% in the CB arm (p = 0.06).
Conclusions: Ca/Mg infusions were not correlated with a decreased incidence of peripheral neurotoxicity in pts treated with capecitabine, oxaliplatin and bevacizumab with or without cetuximab. No statistically significant differences in outcome were observed based on Ca/Mg infusions.

6012 ORAL

The FIRIS study; A Phase III trial of 5-FU/l-leucovorin/irinotecan (FOLFIRI) versus irinotecan/S-1 (IRIS) as 2nd-line chemotherapy for metastatic colorectal cancer (mCRC) [FIRIS study group]

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Background: Several phase II studies of irinotecan (IRI) plus S-1 combination therapy (IRIS) conducted in Japan have shown promising efficacy and safety for mCRC, suggesting the potential to replace FOLFIRI. We conducted a randomized phase III trial to demonstrate the