follow-up, another 2 years of follow-up is estimated for accumulation of the required 440 events.

At the interim analysis, adding oxaliplatin to preoperative capecitabine-based CRT and postoperative adjuvant CT did not result in a DFS benefit for patients with locally advanced rectal adenocarcinoma.

Active Maintenance Therapy Prolongs TFS and PFS in CRC

Written by Mary Mosley

One of the current standards of care for the first-line therapy of metastatic colorectal cancer (mCRC) is combination chemotherapy with fluoropyrimidine (FP) and oxaliplatin (OX) plus the angiogenesis inhibitor, bevacizumab (BEV). However, the optimal duration of the initial induction therapy phase (with the combination regime including all compounds) and the optimal maintenance therapy (MT) have not been defined. The Phase 3 AIO KRK 0207 study [NCT00973609] showed that active MT with FP+BEV or BEV alone, compared with no treatment, prolonged the time-to-failure of strategy (TFS) and progression-free survival (PFS) in patients with mCRC after induction treatment, according to Dirk Arnold, MD, Klinik für Tumorbiologie, Freiburg, Germany [Arnold D et al. *Ann Oncol*. 2014 (abstr O-0027); *J Clin Oncol*. 2014 (abstr 3503)].

In the open-label, prospective AIO KRK 0207 study, 473 patients without disease progression after their 24-week standard induction therapy were randomized to any FP (intravenous or oral) plus BEV (n = 159), BEV monotherapy (n = 156), or no treatment (n = 158). The AIO Study Group-sponsored trial was conducted at 106 sites in Germany to determine whether BEV monotherapy or no treatment was noninferior to FP+BEV.

FP+BEV is the widely accepted standard for MT [Chibaudel B et al. *J Clin Oncol.* 2009; Tournigand C et al. *J Clin Oncol.* 2006]. Studies have evaluated whether reducing the intensity of treatment or discontinuing treatment could provide effective MT while improving quality of life for patients through reduced toxicity; however, a clear standard has not been identified [Yalcin S et al. *Oncology.* 2013; Diaz-Rubio E et al. *Oncologist.* 2012].

The primary end point of TFS, comprising MT with planned re-induction therapy, did not differ between the 3 groups. The median TFS was 6.8, 6.5, and 6.1 months in the FP+BEV, BEV monotherapy, and no-treatment groups. The risk of a shorter TFS was slightly higher in the no-treatment group as compared with the FP+BEV group (HR, 1.22; 95% CI, 0.96 to 1.57; log rank p = .11). The TFS risk was similar for the FP + BEV and BEV monotherapy groups (HR, 0.98; 95% CI, 0.76 to 1.26; Log rank p = .85). However, as the TFS definition included the planned re-induction of the initial treatment, the differences in re-induction therapy (21% of the FP+BEV, 43% BEV monotherapy, 45% no-treatment groups) contributed to this result, stated Dr. Arnold. In general, rates of re-induction therapy were surprisingly low, he stated.

The secondary end point of time to first progression (PFS1) of disease from MT initiation was longer with FP+BEV (6.2 months) and BEV monotherapy (4.8 months) as compared with no treatment (3.6 months). Compared with no treatment, the risk of disease progression was lower with FP+Bev (HR, 0.49; 95% CI, 0.38 to 0.63) and with BEV monotherapy (HR, 0.64; 95% CI, 0.50 to 0.82).

There was no significant difference among the 3 treatment groups for the secondary end point of overall survival (OS) from the start of MT (mean, 23.7 months in all patients; log rank p = .70). This OS was surprisingly long after a (not yet added) 6-month induction treatment phase before randomization, based on the current preliminary data with 200 events, stated Dr. Arnold.

The AIO KRK 207 study showed that MT with FP+BEV, BEV monotherapy, or no treatment had a similar effect on the primary end point of TFS in a protocol that included planned re-induction therapy. PFS1 improved with treatment intensity, with FP+BEV yielding better results than BEV alone, and both active MT treatments were better than no treatment. This finding of improved PFS1 confirms the standard of an active MT to exploit the maximum benefit, stated Dr. Arnold.

KRAS Mutations Predictive of Recurrence in Colon Cancer

Written by Emma Hitt Nichols, PhD

Codon 12 *KRAS* mutations are an independent predictor of time to recurrence (TTR) and disease-free survival (DFS) in patients with Stage III colon cancer who received adjuvant treatment. Julien Taieb, Assistance Publique Hôpitaux de Paris, Paris, France, presented data from a post hoc analysis of the Combination Chemotherapy With or Without Cetuximab in Treating Patients With Stage III Colon Cancer That Was Completely Removed by Surgery trial [PETACC8; Taieb J et al. *Ann Oncol* 2014 (abstr O-0024)].

KRAS mutations may be prognostic in colon adenocarcinoma, but the evidence is inconclusive. The purpose of