Bevacizumab continuation versus no continuation after first-line chemotherapy plus bevacizumab in patients with metastatic colorectal cancer: a randomized phase III non-inferiority trial (SAKK 41/06)


BACKGROUND
Chemotherapy plus bevacizumab is a standard option for first-line treatment in metastatic colorectal cancer (mCRC) patients. We assessed whether no continuation is non-inferior to continuation of bevacizumab after completing first-line chemotherapy.

PATIENTS AND METHODS
In an open-label, phase III multicentre trial, patients with mCRC without disease progression after 4-6 months of standard first-line chemotherapy plus bevacizumab were randomly assigned to continuing bevacizumab at a standard dose or no treatment. CT scans were done every 6 weeks until disease progression. The primary end point was time to progression (TTP). A non-inferiority limit for hazard ratio (HR) of 0.727 was chosen to detect a difference in TTP of 6 weeks or less, with a one-sided significance level of 10% and a statistical power of 85%.

RESULTS
The intention-to-treat population comprised 262 patients: median follow-up was 36.7 months. The median TTP was 4.1 [95% confidence interval (CI) 3.1-5.4] months for bevacizumab continuation versus 2.9 (95% CI 2.8-3.8) months for no continuation; HR 0.74 (95% CI 0.58-0.96). Non-inferiority could not be demonstrated. The median overall survival was 25.4 months for bevacizumab continuation versus 23.8 months (HR 0.83; 95% CI 0.63-1.1; P = 0.2) for no continuation. Severe adverse events were uncommon in the bevacizumab continuation arm. Costs for bevacizumab continuation were estimated to be ~30,000 USD per patient.

CONCLUSIONS
Non-inferiority could not be demonstrated for treatment holidays versus continuing bevacizumab monotherapy, after 4-6 months of standard first-line chemotherapy plus bevacizumab. Based on no impact on overall survival and increased treatment costs, bevacizumab as a single agent is of no meaningful therapeutic value. More efficient treatment approaches are needed to maintain control of stabilized disease following induction therapy.

CLINICAL TRIAL REGISTRATION
ClinicalTrials.gov, number NCT00544700.