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Resection of the primary tumour as an independent prognostic factor for survival in patients with advanced colorectal cancer. CAIRO study of the Dutch Colorectal Cancer Group (DCCG)

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Background: Frequently used stratification factors in trials for patients (pts) with advanced colorectal cancer (ACC) are LDH, prior adjuvant treatment, performance status (PS), number of affected organs, and predominant localization of metastases (mets). Few data are available on the prognostic value of metachronous versus synchronous mets and resection of the primary tumour. Therefore we studied these parameters in a large phase III trial for pts with ACC.
Methods: 803 eligible previously untreated ACC pts were randomized between sequential (arm A) and combination therapy (arm B) with capecitabine, irinotecan, and oxaliplatin (Koopman et al, Ann Oncol 2006). Pts were divided into 3 groups: metachronous mets, and synchronous mets with or without resection of the primary tumour. Metachronous mets were defined as occurring >12 months after resection of the primary tumour as used in previous studies.
Results: All 284 pts with metachronous mets (group 1) underwent resection of the primary tumour. Of 539 pts with synchronous mets, a resection of the primary tumour was performed in 368 pts (group 2) and not in 151 pts (group 3). Median age of pts in group 1, 2, 3 was 65 yrs (36−84), 60 yrs (27−82), and 63 yrs (31−83), respectively. Multivariate analysis (table 1) showed a significant difference in overall survival in favour of group 2 vs 3: 16.8 (95% CI 14.8−18.9) vs 12.2 months (95% CI 10.2−14.5, p = 0.01), of group 1 vs 3: 19.7 months (95% CI 17.9−21.7) vs 12.2 (95% CI 10.2−14.5, p = 0.003), and a trend in favour of group 1 vs 2: 19.7 (95% CI 17.9−21.7) vs 16.8 months (95% CI 14.8−18.9, p = 0.3). The prognostic value of serum LDH and PS was confirmed, however not for prior adjuvant treatment and predominant site of mets.
The probability of response (PR/CR) was in favour of group 2 vs 1 by multivariate analysis (p = 0.03), and a trend towards an increased response rate was noted in group 2 vs 3 (p = 0.07).
Conclusion: In our study resection of the primary tumour is an independent prognostic factor for the overall survival in pts treated with chemotherapy for ACC. If confirmed, resection of the primary tumour (yes vs no) should be considered as a stratification factor in future studies in ACC pts.

Table 1 Multivariate analysis of clinical parameters in ACC for overall survival

Clinical parameters	P-value
Synchronous mets	
without resection vs synchronous mets with resection (+)	0.01
without resection vs metachronous mets (+)	0.003
with resection vs metachronous mets (+)	0.30
Sequential vs combination treatment (+)	0.10
Performance status PS2 vs PS0−1 (+)	0.05
Serum LDH abnormal vs normal (+)	<0.0001
Predominant site extrahepatic vs liver (+)	0.66
Prior adjuvant therapy yes vs no (+)	0.20
Colon vs rectum (+)	0.21
Rectum vs rectosigmoid (+)	0.15
Colon vs rectosigmoid (+)	0.08

+ = increased survival.

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Safety and effectiveness of bevacizumab (BV) plus chemotherapy (CT) in elderly patients with mCRC: results from the BRiTE registry

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Background: Bevacizumab (BV, Avastin®) prolongs overall survival (OS) and progression-free survival (PFS) when added to standard CT for 1st-line and 2nd-line treatment of patients with metastatic colorectal cancer (mCRC). In phase III trials of BV in mCRC, the efficacy (PFS/OS) of BV was similar in patients <65yr and ⩾65yr. However, across clinical trials of BV, certain safety issues, e.g. arterial thromboembolic events (ATE), appear more frequently in the older population. This analysis describes safety and efficacy of BV in patients ⩾65yr in a large community-based BV treatment registry (BRiTE) for patients with mCRC.
Materials and Methods: Population and methods have been described previously (Kozloff, ASCO 2006;A3537). Multiple regression analyses (Cox and logistic regression models for PFS and safety events, respectively) were performed.
Results: Of 1953 evaluable patients, 896 (45.9%) were ⩾65yr at baseline. In contrast, 32% of patients were ⩾65yr in the mCRC pivotal trial AVF2107, and the general population estimate from SEER for mCRC is 60%. FOLFOX and FOLFIRI were the most frequently used 1st-line regimens; 5-FU bolus/LV was more frequent in the ⩾65yr subgroup (10.9% patients ⩾65yr versus 3.2% patients <65yr). Table 1 shows selected BV-associated safety events, median PFS, 1-year survival rates, and median OS for patients <65yr versus ⩾65yr in BRiTE. Multiple regression analyses adjusted for various baseline factors showed age was not a significant factor for predicting incidence of GI perforation, bleeding/wound healing complications or ATE, nor for predicting PFS.
Conclusions: In BRiTE, a large community-based registry, the safety and effectiveness (PFS and 1-year survival) of BV in patients ⩾65yr and <65yr were similar and comparable with results from controlled BV trials in mCRC. On the basis of a small number of events available for model-based analyses, age was not a significant factor for predicting targeted BV-related safety events.

Table 1. Safety and efficacy measures

	<65 (n = 1057)	⩾65 (n = 896)
GI Perforations	2.3%	1.1%
Bleeding/wound healing complications	2.1%	1.0%
Grade 3/ 4 bleeding	2.1%	2.9%
ATE	1.3%	2.2%
Estimated median PFS, months (95% CI)	10.3 (9.7, 11.3)	9.9 (9.3, 10.3)
Estimated 1-year survival rate	77.3%	71.6%
Estimated median OS (months)	NE	21.8

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Management of hypertension (HTN) in patients (pts) with metastatic colorectal cancer (mCRC) treated with bevacizumab (BV) plus chemotherapy (CT)

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Introduction: Bevacizumab (BV, Avastin®) prolongs overall survival (OS) and progression-free survival (PFS) when added to standard CT for 1st- or 2nd-line treatment of patients with mCRC. Following FDA approval of BV, a large community-based registry (BRiTE) was initiated in patients receiving BV in combination with 1st-line CT to evaluate BV-targeted safety events and the effectiveness of BV in combination with various commonly used CT regimens. Grade 3 HTN has been identified in all BV clinical trials as a related toxicity. However, the outcome and effective management of BV-associated HTN have not been determined. The experience from BRiTE