Original Article

Efficacy and safety of chemotherapy combined with bevacizumab in Chinese patients with metastatic colorectal cancer: A prospective, multicenter, observational, non-interventional phase IV trial

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Abstract

Objective: Bevacizumab has an important and evolving role in improving outcomes in patients with metastatic colorectal cancer (mCRC) worldwide and was approved in China in 2010. However, there are limited real-world data on the efficacy and safety of chemotherapy regimens combined with bevacizumab in Chinese patients with mCRC. This observational, phase IV trial study aimed to obtain more experience on the efficacy and safety of bevacizumab combined with chemotherapy in Chinese mCRC patients.

Methods: Between September 2013 and November 2016, patients with histologically confirmed mCRC were enrolled in a prospective, multicenter, observational, non-interventional phase IV trial at 26 centers across China. Eligible patients received different chemotherapeutic regimens combined with bevacizumab. The efficacy and safety data in the intention-to-treat study population were analyzed.

Results: A total of 611 patients were included in the efficacy analysis. The median overall survival and median progression-free survival was 18.00 and 10.05 months, respectively. The objective response rate was 21.00% and disease control rate was 89.40%. In subgroup analyses, the survival differences were observed according to metastatic status, duration of treatment and elevation in blood pressure. A total of 613 patients were evaluable for safety assessments. And 569 (92.82%) patients reported at least one adverse event (AE), and 151 (24.63%) experienced grade 3 or higher AEs. The incidence of bevacizumab-associated AEs of special interest was reported in 31 (5.06%) patients with hypertension (n=12), abscesses and fistulae (n=7), bleeding (n=6), proteinuria (n=3), gastrointestinal perforation (n=2) and venous thrombotic events (n=1).

Conclusions: This observational phase IV trial broadens our experience and knowledge of bevacizumab in the Chinese population and provides a good indication of its overall efficacy and safety. Bevacizumab in combination

with chemotherapy offers clinical benefits to Chinese patients with mCRC and has an acceptable and manageable safety profile.

Keywords: Metastatic colorectal cancer; bevacizumab; chemotherapy; efficacy; safety

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Introduction

Colorectal cancer (CRC) is the most common gastrointestinal cancer worldwide and the second leading cause of cancer-related death (1,2). Despite improvements in screening, diagnosis, and treatment regimens, the 5-year mortality rate for patients with CRC remains high (approximately 40%−50%), and the disease represents a significant global heath burden (3). The current standard of care for patients with localized CRC includes surgical resection followed by adjuvant chemotherapy in selected patients (4,5). However, many patients experience recurrence or metastasis (6,7).

Vascular endothelial growth factor (VEGF) is considered as a key mediator of angiogenesis signaling pathways involved in both physiological and pathological conditions (8,9). Bevacizumab, a humanized monoclonal antibody targeting VEGF, is the first anti-angiogenic agent to be approved for the metastatic CRC (mCRC) treatment in combination with 5 - fluorouracil - based chemotherapy regimens (10). Several pivotal randomized clinical studies had demonstrated that the addition of bevacizumab to chemotherapy conferred clinically significant improvements in overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) (11-14). In addition, observational cohort studies have shown that bevacizumab in combination with chemotherapy was well tolerated and effective in broad western mCRC patient populations (15,16).

Bevacizumab was approved by the National Medical Products Administration (NMPA) in China in 2010. The ARTIST registration study showed that both OS and PFS were notably prolonged in Chinese mCRC patients treated with bevacizumab plus modified IFL regimen (irinotecan, leucovorin bolus, and 5-fluorouracil intravenous infusion) as first-line treatment (12). However, there are limited real-world data from large-scale phase IV clinical trials on the efficacy and safety of chemotherapy regimens combined with bevacizumab in Chinese patients with mCRC. In this prospective, multicenter, observational, non-interventional phase IV trial, we aimed to obtain more data on the efficacy and safety of bevacizumab and provide an insight into the treatment profile of this agent in Chinese unselected patients with mCRC.

Materials and methods

Patient selection and study design

This was a prospective, multicenter, observational, non-interventional phase IV clinical trial conducted between September 2013 and November 2016 at 26 participating centers across China. The study protocol was approved by the institutional review boards and ethical committees of the participating centers and registered on the website (Identifier: NCT01912443; Registered 31 July 2013 https://clinicaltrials.gov/ct2/show/). The study was conducted in compliance with Good Clinical Practice procedures set out in the Declaration of Helsinki and the requirements of China's National Medical Products Administration (NMPA) and approval by the ethics committee of each participating institution [including Ethical Committees of Sun Yat-sen University Cancer Center (B2012-020-01), Ethical Committees of Chinese PLA General Hospital (C2013-061-01), Ethical Committees of the Sixth Affiliated Hospital of Sun Yat-sen University (2014ZSLYEC-007), Ethical Committees of Xinjiang Medical University Cancer Hospital (2013 010), Ethical Committees of Foshan First People's Hospital (2013 26), Ethical Committees of Shandong Cancer Hospital (201405008), Ethical Committees of West China Hospital of Sichuan University (2014 12), Ethical Committees of Jiangsu Cancer Hospital (2014NL-007), Ethical Committees of Fujian Cancer Hospital (201409), Ethical Committees of Sichuan Cancer Hospital (SCCHEC2013013), Ethical Committees of Anhui Provincial Hospital (2014 11), Ethical Committees of the First Affiliated Hospital of Soochow University (2013 309),

Ethical Committees of Henan Cancer Hospital (2013ys17), and Ethical Committees of the Second Affiliated Hospital of Zhejiang University School of Medicine (2013-048-R01)]. Written informed consent was obtained from all patients prior to their participation.

All patients scheduled to undergo treatment with bevacizumab were enrolled in this trial. The inclusion criteria were as follows: 1) histological confirmation of mCRC; 2) administration of bevacizumab in combination with chemotherapy; and 3) written informed consent provided. Patients were excluded if they did not meet the indications for bevacizumab included in bevacizumab manual (as approved by the NMPA) mainly because of: 1) evidence of bleeding diatheses or a history of hemoptysis; 2) baseline proteinuria >2 g protein/24 h; 3) major surgery or non-healing wounds within 28 d before enrollment; 4) pregnancy or lactation; or 5) known allergy to bevacizumab or any of its excipients.

Treatment regimen

All patients enrolled in the study were treated intravenously with either 5.0 mg/kg bevacizumab (Avastin®; Genentech, San Francisco, CA, USA) every 2 weeks or 7.5 mg/kg every 3 weeks, according to the different chemotherapy regimens. Bevacizumab was administered initially over 90 min; if the first infusion was well tolerated, the second infusion was delivered over no less than 60 min, and if this was well tolerated, the subsequent administration was over 30 min. Bevacizumab was temporarily or permanently withheld if serious bevacizumab-related toxicity developed.

Efficacy analysis

OS was defined as the period from the start of therapy until death. When the date of death was missing in the patients' records, the most recent date they were known to be alive was used. ORR was defined as the proportion of patients with a complete response (CR) or partial response (PR) according to the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. The disease control rate (DCR) was defined as the percentage of patients who achieved CR, PR, or stable disease (SD). PFS was defined as the interval between the start of therapy and the occurrence of disease progression or death from any cause.

Safety analysis

The safety profile of regimens containing bevacizumab was assessed from data on the incidences of all adverse events (AEs), including serious AEs (SAEs) and non-SAEs. In addition, the incidence of bevacizumab-associated AEs of special interest (AESIs) was noted, including hypertension (grade ≥3), proteinuria (grade ≥3), bleeding (grade ≥3), gastrointestinal perforations, arterial and venous thromboembolic events, wound healing complications (grade ≥3), congestive heart failure (grade ≥3), posterior reversible encephalopathy syndrome, abscesses, fistulae (grade ≥2), elevated levels of alanine transaminase or aspartate transaminase, and elevated level of bilirubin or clinical jaundice.

The National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 was used to classify the severity of AEs. All AEs were recorded up to 28 d after the last infusion of bevacizumab, whereas AESIs were recorded up to 6 months after the last bevacizumab dose.

Statistical analysis

The analysis of patient demographics and baseline characteristics was based on all enrolled patients. The analysis of safety was based on the safety set (SS), which included all patients who received at least one cycle of bevacizumab treatment and had at least one valid safety assessment. The analysis of efficacy was based on the full analysis set (FAS), which included all patients who received at least one cycle of bevacizumab and had at least one efficacy assessment. Subgroup analyses were conducted for patient age (<65 years *vs.* ≥65 years), *KRAS* status, primary tumor site (colon *vs.* rectum), primary tumor resection, peritoneal metastasis, metastatic status (synchronous *vs.* metachronous), duration of treatment (≤8 weeks *vs.* >8 weeks), blood pressure elevations (>10/5 mmHg) and treatment line (first-line *vs.* second-line).

Categorical variables were summarized in frequency tables and continuous variables were summarized with descriptive statistics. Differences in rates for qualitative factors were compared by Pearson's χ^2 contingency table analysis. The Kaplan-Meier method was used to estimate the distribution of PFS and OS. Comparisons between several factors were assessed using the log-rank test. All tests were conducted at a two-sided alpha level of 0.05, and 95% confidence intervals (95% CIs) were given at a two-sided level. All clinical data were analyzed using SAS™ (Version 9.4; SAS Institute Inc., Cary, USA).

Results

Patient characteristics and treatment

A total of 613 patients were screened for inclusion in this study. The study design is illustrated in *Figure 1*. All patients were included in the safety population and 611 patients were included in the efficacy analysis because two patients were excluded due to the absence of efficacy data. The demographic and baseline characteristics of all enrolled patients are shown in *Table 1*. The median age was 55 (range, 16–85) years, and 384 (62.64%) patients were male. The Eastern Cooperative Oncology Group performance status (ECOG PS) was 0–1 in 426 (95.30%) of the 447 patients assessed, and *KRAS* mutation was found in 98 (57.99%) of the 169 patients tested.

Patients received bevacizumab at a median dose of 33.23 (range, 2.73–328.00) mg/kg for a median of 9 (range, 1–53) cycles. There were 343 (55.95%) patients received first-line bevacizumab-based therapy and 270 (44.05%) patients received second-line bevacizumab-based therapy. Main chemotherapeutic regimens included irinotecan-based regimens (62.32%), oxaliplatin-based regimens (60.85%) and capecitabine (28.38%) (*Table 2*).

Efficacy

Patients were followed up for a median time of 9.21 (range, 0.03–33.87) months, and 280 (45.83%) of 611 patients died at the end of follow-up. The median OS was 18.00 (95% CI, 16.99–20.07) months and median PFS was 10.05 (95% CI, 9.20–11.37) months (*Figure 2*). The ORR was 21.00% and DCR was 89.40%. The median PFS in patients who received first-line therapy was longer than in those who received second-line therapy (11.04 months *vs.* 8.74 months). Higher ORR were also seen in those who

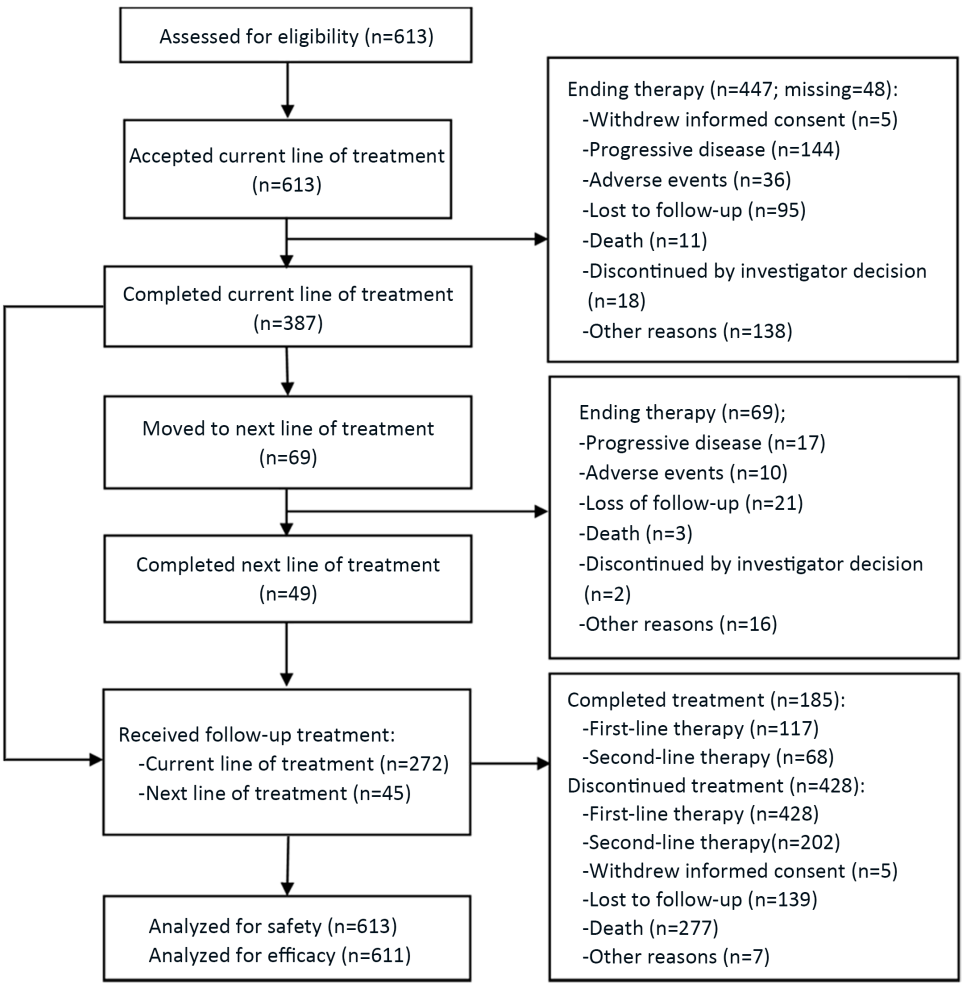

Figure 1 Flowchart of study design.

Table 1 Summary of patient demographics and baseline characteristics

Parameter	All enrolled patients (N=613) [n (%)]
Age (year) [median (range)]	55 (16–85)
Sex: male	384 (62.64)
Time since diagnosis of CRC (month) [median (range)]	10.23 (0.03–164.62)
Site of disease at the first diagnosis	
Colon	359 (58.56)
Rectum	254 (41.44)
Tumor stage	
Tx	184 (30.02)
T0	3 (0.49)
Tis	8 (1.31)
T1	17 (2.77)
T2	18 (2.94)
T3	129 (21.04)
T4	254 (41.44)
Node stage	
Nx	220 (35.89)
N0	100 (16.31)
N1	129 (21.04)
N2	164 (26.75)
Therapy line	
Started with first-line therapy	343 (55.95)
Started with second-line or later	270 (44.05)
Previous treatment	
Surgery	453 (73.90)
Local radiation	89 (14.52)
ECOG performance status (N=447)	
0	113 (25.28)
1	313 (70.02)
≥2	21 (4.70)
KRAS mutation (N=169)	
No	69 (40.83)
Yes	98 (57.99)
Unknown	2 (1.18)

CRC, colorectal cancer; ECOG, Eastern Cooperative Oncology Group.

Table 2 Summary of chemotherapy regimens combined with bevacizumab during the study (N=613)

Therapy regimens	n (%)
Irinotecan-based regimen	382 (62.32)
Oxaliplatin-based regimen	373 (60.85)
Capecitabine	174 (28.38)
5-Fluorouracil/folinic acid	29 (4.73)
mFOLFOXIRI	85 (13.87)
Other regimens*	106 (17.29)

*, Other regimens included raltitrexed-based regimens, gemcitabine-based regimens, pemetrexed-based regimens, and tegafur-based regimens. FOLFOXIRI, folinic acid, 5-fluorouracil, oxaliplatin, and irinotecan.

received first-line therapy (27.08% *vs.* 13.45%) (*Table 3*).

In subgroup analyses of FAS population, no significant interactions were observed for age, *KRAS* mutation status, primary tumor site, or primary tumor resection and different chemotherapy regimens. However, survival differences were observed according to metastatic status, duration of treatment and elevation in blood pressure (*Table 4*). Patients with metachronous metastasis showed a shorter median PFS than those with synchronous metastasis (9.20 months *vs.* 10.97 months; P=0.044). The longer duration of treatment was significantly associated with better survival. With a cut-off of 8 weeks, patients receiving more than 8 weeks of treatment had a significantly improved median OS compared with those receiving ≤8 weeks of treatment (19.15 months *vs.* 17.81 months; P<0.001). Patients with elevated blood pressure had a longer median OS than those without elevated blood pressure (20.80 months *vs.* 16.66 months; P=0.002).

Safety

All patients (n=613) were evaluable for safety assessments, and observed AEs are summarized in *Table 5*. A total of 569 (92.82%) patients reported at least one AE, and 151 (24.63%) experienced grade 3 or higher AEs. The most common AEs were leukopenia (39.97%), nausea (39.31%), neutropenia (29.04%), vomiting (27.24%), loss of appetite (23.16%), hypertension (19.25%), diarrhea (18.76%), and anemia (17.78%). Incidences of SAEs were reported in 27 (4.40%) patients and included neutropenia, death, leukopenia, diarrhea, pulmonary infection, and stoma-related bleeding. And 288 (46.98%) patients had bevacizumab-related AEs. AESIs were reported in 31 (5.06%) patients with hypertension (n=12), abscesses and fistulae (n=7), bleeding (n=6), proteinuria (n=3), gastrointestinal perforation (n=2), and venous thrombotic events (n=1). AEs leading to treatment discontinuation occurred in 31 (5.06%) patients. Dose adjustments were done in 76 patients (12.40%).

Across age, *KRAS* status, chemotherapy regimen, tumor

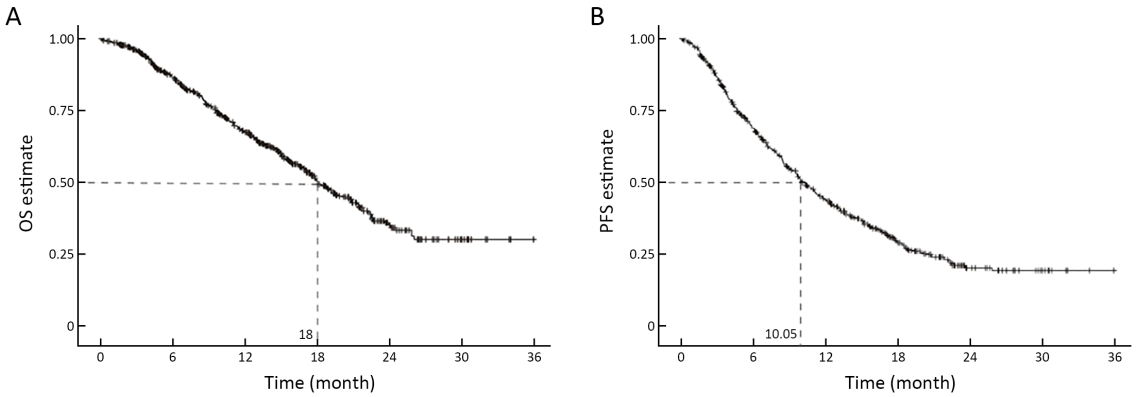

Figure 2 Kaplan-Meier plots of OS [median OS: 18.00 (95% CI: 16.99–20.07) months] (A) and PFS [median PFS: 10.05 (95% CI: 9.20–11.37) months] (B) in FAS population. OS, overall survival; PFS, progression-free survival; 95% CI, 95% confidence interval; FAS, full analysis set.

Table 3 Efficacy according to administered treatment in evaluable patients

Efficacy	FAS population (N=611)	First-line therapy (N=342)	Second-line therapy (N=269)
Median OS (95% CI) (month)	18.00 (16.99–20.07)	18.00 (17.08–21.82)	17.45 (14.72–20.07)
Median PFS (95% CI) (month)	10.05 (9.20–11.37)	11.04 (9.66–13.34)	8.74 (7.49–10.58)
ORR (%)	21.00	27.08	13.45
SD (%)	68.40	65.70	71.75
PD (%)	10.60	7.22	14.80
DCR (%)	89.40	92.78	85.20

OS, overall survival; 95% CI, 95% confidence interval; PFS, progression-free survival; ORR, objective response rate; SD, stable disease; PD, progressive disease; DCR, disease control rate; FAS, full analysis set.

Table 4 Subgroup analysis of efficacy according to patients' metastasis status, duration of treatment, blood pressure elevation, and peritoneal metastasis

Population	Subgroup analysis	Efficacy	P
FAS	Metastasis status	Median PFS (95% CI) (month) Synchronous metastatic lesions: 10.97 (9.59–13.01) Metachronous metastatic lesions: 9.20 (7.59–10.58)	0.044
	Duration of treatment	Median OS (95% CI) (month) ≤8 weeks: 17.81 (15.77–19.48) >8 weeks: 19.15 (17.02–23.92)	<0.001
	Elevated blood pressure*	Median OS (95% CI) (month) No: 16.66 (14.72–18.00) Yes: 20.80 (17.74–23.92)	0.002
First-line therapy	Peritoneal metastasis	Median OS (95% CI) (month) No: 19.48 (17.54–22.37) Yes: 10.84 (8.05–25.82)	0.001
		Median PFS (95% CI) (month) No: 11.70 (9.99–14.95) Yes: 6.90 (5.42–10.84)	0.008
	Duration of treatment	Median PFS (95% CI) (month) ≤8 weeks: 12.32 (10.05–14.95) >8 weeks: 8.87 (6.90–10.55)	0.004
Second-line therapy	Duration of treatment	Median OS (95% CI) (month) ≤8 weeks: 15.38 (11.86–18.99) >8 weeks: 21.45 (16.49–not reached)	<0.001

*, Defined as an elevation in systolic BP of 10 mmHg or diastolic BP of 5 mmHg within 60 d of starting bevacizumab treatment. FAS, full analysis set; PFS, progression-free survival; 95% CI, 95% confidence interval; OS, overall survival.

Table 5 Summary of adverse events (N=613)

AEs	n	%
Overall AEs	569	92.82
Grade ≥3 AEs	151	24.63
SAEs	27	4.40
AESIs	31	5.06
Proteinuria	3	0.49
Hypertension	12	1.96
Bleeding	6	0.98
Abscesses and fistulae	7	1.14
Gastrointestinal perforation	2	0.33
Venous thrombotic events	1	0.16
AEs leading to discontinuation of treatment	31	5.06
AEs leading to dose adjustment	76	12.40
AEs leading to death	15	2.45
AEs associated with bevacizumab	288	46.98

AE, adverse event; SAE, serious adverse event; AESI, adverse event of special interest.

position, and metastasis status subgroups, patients had similar incidences of AEs and SAEs. However, patients with *KRAS* mutation and primary tumor locating in rectum had higher incidences of AESIs.

Discussion

In the prospective, multicenter, observational, non-interventional phase IV study, we reported the efficacy and safety profile of bevacizumab combined with chemotherapy in patients with mCRC and provides valuable information on bevacizumab that the safety profile of bevacizumab in Chinese patients is comparable with that observed in other patient populations.

In terms of the response of bevacizumab-containing regimens, the reported ORR of 21.00% in this study (first-line: 27.08% and second-line: 13.45%) was comparable to that of previous randomized phase III trials, such as E3200 trial (11) and ML18147 trial (17). The E3200 trial compared three different regimens (FOLFOX4 with bevacizumab *vs*. FOLFOX4 *vs*. bevacizumab) in previously treated mCRC. The ORRs were 22.7%, 8.6% and 3.3%, respectively (11). The ML18147 trial assessed the continued use of bevacizumab plus standard second-line chemotherapy in patients with mCRC progressing after standard first-line bevacizumab-based treatment, and the response rate was found to be 22% with bevacizumab-containing chemotherapy (17). However, it was lower than that of other previously reported phase II–IV trials (11-14, 17-22) (*Table 6*). One explanation to note is the different methods assessing ORR. For example, in the study of Saltz *et al*. (13), ORR with bevacizumab plus chemotherapy assessed by investigators was 47%, but 38% by the independent response committee review. Another explanation is that our trial is non-interventional and enrolls different patients with no strict selection.

In terms of survival, patients in this trial had a median OS of 18.00 months and a median PFS of 10.05 months. Median OS between patients with first-line therapy and second-line therapy was comparable (18.00 *vs.* 17.45 months), but median PFS of patients with first-line therapy was longer than those with second-line therapy (11.04 *vs.* 8.74 months). In both first- and second-line therapy settings, previous randomized trials have demonstrated improvements in OS or PFS in patients with mCRC treated with bevacizumab in combination with cytotoxic chemotherapy (11,14). The ML18147 trial showed that the benefits of bevacizumab continued beyond disease progression and that switching chemotherapy was beneficial for patients with mCRC who were previously treated with bevacizumab in the first-line setting. The continued use of bevacizumab beyond disease progression led to a significant improvement in OS and PFS compared with post-progression chemotherapy alone (17). Our observational study confirmed this result as the use of bevacizumab after disease progression was also associated with survival benefits. The findings from our subgroup analyses were generally consistent with those in the overall study population. The unfavorable prognostic impact of *KRAS* mutations in patients with mCRC has been reported previously (23). The exploratory analysis of the *KRAS* subgroup in our study showed that there was no evidence to suggest a difference between the overall population and subgroups based on the *KRAS* mutational status.

The safety profile of bevacizumab-based therapy in this trial was similar to that observed in previous clinical trials (15,16). We did not detect any new safety signals concerning the use of bevacizumab in mCRC, and all observed AEs in our patient population have a well-known association with either bevacizumab or chemotherapy. Our results showed that bevacizumab was well-tolerated and associated with a relatively low incidence of severe AEs (4.4%). In addition, the rates of treatment discontinuation and death were lower than those reported in other studies (11,17,19,20). Guan *et al*. (12) showed that compared with chemotherapy alone, the administration of a combination

Table 6 Reported trials of bevacizumab in combination with chemotherapy in treatment of mCRC

Study	Phase	No. of patients	Regimen(s)	Efficacy			Safety (%)				
				ORR (%)	PFS (month)	OS (month)	Discontinued due to AEs	Deaths due to AEs	Hypertension (grade ≥3)	Proteinuria (grade ≥3)	Gastro-intestinal perforation
E3200 (11)	III	286	FOLFOX4/Bev (2nd line)	22.70	7.30	12.90	23.40	5.00	6.20	0.70	NR
ARTIST (12)	III	141	mIFL/Bev (1st line)	35.30	8.30	18.70	10.00	1.00	2.80	0.70	0.70
Saltz *et al*. (13)	III	699	FOLFOX4 or XELOX/Bev (1st line)	38.00	10.40	21.30	30.00	2.00	4.00	<1.00	NR
Hurwitz *et al*. (14)	III	402	IFL/Bev (1st line)	44.80	10.60	20.30	8.40	2.60	11.00	0.80	1.50
ML18147 (17)	III	409	oxaliplatin-based or irinotecan-based/Bev (2nd line)	22.00	5.70	11.20	16.00	6.00	2.00	NR	2.00
ITACa (18)	III	176	FOLFIRI or FOLFOX4/Bev (1st line)	50.60	9.60	20.80	17.00	2.30	27.80	22.20	NR
Kabbinavar *et al*. (19)	II	104	5-FU/LV/Bev (1st line)	26.00	9.20	16.60	10.00	4.00	16.00	1.00	2.00
AVEX (20)	III	140	Capecitabine/Bev (1st line)	27.00	9.10	20.70	25.00	7.00	2.00	1.00	0
TREE-2 (21)	II	223	mFOLFOX6 /Bev bFOL/Bev CapeOx/Bev (1st line)	52.00 39.00 46.00	9.90 8.30 10.30	26.10 20.40 24.60	NR	2.70	13.00	NR	NR
Sobrero *et al.* (22)	IV	209	FOLFIRI or IFL/Bev (1st line)	53.10	11.10	22.20	24.00	2.40	5.00	2.00	2.00

mCRC, metastatic colorectal cancer; ORR, objective response rate; PFS, progression-free survival; OS, overall survival; AE, adverse event; FOLFOX, infused 5-fluorouracil, folinic acid, and oxaliplatin; Bev, bevacizumab; XELOX, capecitabine plus oxaliplatin; IFL, irinotecan, folinic acid (Leucovorin) bolus, and 5-fluorouracil; 5-FU/LV, 5-fluorouracil and folinic acid (Leucovorin); NR, not reported.

of bevacizumab and chemotherapy in Chinese patients with mCRC resulted in a slightly higher incidence of AEs, especially chemotherapy-associated AEs, such as neutropenia, diarrhea, and nausea. According to previous reports, the most frequent AEs associated with bevacizumab are hypertension and proteinuria, with gastrointestinal perforation being the most serious (24-26). Hypertension and proteinuria are likely directly related to the inhibition of VEGF, which results in vasoconstriction and regulated glomerular vascular permeability (27,28). In our study, we noted relatively low rates of hypertension (1.96%) and proteinuria (0.94%), and only two patients experienced gastrointestinal perforation. Most cases of hypertension and proteinuria were asymptomatic. According to the summary of product characteristics for bevacizumab, minor bleeding events have been observed in approximately 30% of patients with mCRC who received bevacizumab (29). Only 6 (0.98%) patients experienced bleeding events in this study. The rates of thromboembolic events were also consistent with those findings from previous trials of bevacizumab in patients with mCRC, as providing further evidence of the safety of bevacizumab in Chinese patients.

Conclusions

The real-world data from the phase IV trial broaden our experience and knowledge of bevacizumab in the Chinese population and provide a good indication of its overall efficacy and safety. The study showed that bevacizumab in combination with chemotherapy has an acceptable and manageable safety profile, with no new safety signals reported, and it offers clinical benefits to patients with mCRC.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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