

Real-World Outcomes of First-line and Second-line Chemotherapy with Dabrafenib and Cetuximab in BRAF V600E-Mutant Metastatic Colorectal Cancer: The Preliminary Data from a Single Center

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Abstract

Background

BRAF V600E mutation constitutes one of the crucial molecular alterations observed in metastatic colorectal cancer, occurring in roughly 10% of affected patients. This unique molecular subtype is characterized by atypical metastatic dissemination features, dismal long-term clinical prognosis, and substantial interindividual heterogeneity in survival benefits. The purpose of this analysis was to report the effectiveness and safety data of administration of chemotherapy plus dabrafenib and cetuximab as first-line and second-line treatment in BRAF V600E-Mutant mCRC from a single center.

Methods

This retrospective study screened and enrolled a total of 22 patients pathologically diagnosed with BRAF V600E-mutant metastatic colorectal cancer from November 2023 to November 2025. All patients underwent BRAF V600E genotyping before chemotherapy plus dabrafenib and cetuximab. We collected the objective response rate (ORR), progression-free survival (PFS), and adverse events (AEs). The final analysis of the database was last updated on April 10th, 2026.

Results

In the first-line group (n = 12), the ORR was 83.33%; while in the second-line group (n = 10), the ORR was 20.00%. The disease control rate was 100% in both groups. The 3-months PFS rate in the first-line group and the second-line group was 91.67% and 90.00% respectively. With a median follow-up time of 5.34 months (range, 2.69 months ~ 19.02 months), 33.33% (4/12) and 60.00% (6/10) of the patients were progression-free in the first-line group and the second-line group, respectively. In the pooled analysis, the most common grade 1–2 AEs were anemia (72.73%), fever (27.27%), neutropenia (31.82%), leukopenia (45.45%), elevated aspartate aminotransferase level (27.27%), hypoalbuminemia (36.36%), hypomagnesemia (36.36%), and hypokalemia (36.36%). In the pooled analysis, the most common grade 3–5 AEs were neutropenia (18.18%), intestinal obstruction (13.64%), and elevated alanine aminotransferase level (13.64%).

Conclusions

Our findings indicated that dabrafenib and cetuximab with chemotherapy are effective and tolerable first-line and second-line regimens for BRAF V600E-Mutant metastatic colorectal cancer patients. Furthermore, earlier use and combination with chemotherapy would achieve better response.

INTRODUCTION

Colorectal cancer (CRC), ranking as the third most prevalent malignancy in the worldwide is characterized by a high frequency of genetic alterations within the mitogen-activated protein kinase (MAPK) signaling pathway(1). Among these alterations, mutations in KRAS and NRAS are detected in approximately 50% of CRC cases, while BRAF mutations occur in roughly 10% of cases (2, 3). Previous studies have indicated that patients harboring BRAF V600E-mutated tumors exhibit higher rates of peritoneal dissemination and lymph node metastasis, derive less benefit from conventional chemotherapy regimens, and experience significantly shorter overall survival (OS)(4-6).

Recently, a lot of progress have been achieved in BRAF inhibitors. While, the response of the usage of single-agent BRAF inhibitor was very low due to the identification of adaptive feedback after BRAF inhibition, resulting in increased signaling through the epidermal growth factor receptor (EGFR) pathway in colon cancer (7, 8). This led to studies the combination use of BRAF and EGFR inhibitors, demonstrating improved activity (9-11). Encorafenib is a BRAF inhibitor that exhibits more sustained pharmacodynamic activity relative to other clinically available BRAF inhibitors (12). Combination therapy with encorafenib (a BRAF inhibitor) and cetuximab (an anti-EGFR monoclonal antibody) yielded promising findings in early clinical investigations (11, 13). The randomized, three-arm, phase III BEACON CRC trial showed that treatment with encorafenib combined with cetuximab, with or without binimetinib, resulted in significant improvements in OS and objective response rate (ORR) among patients with BRAF V600E-mutant metastatic colorectal cancer (mCRC), as compared with the current standard of care (14).

On the basis of the results of the BEACON CRC trial, encorafenib plus cetuximab, was established as the standard care for previously treated BRAF V600E–mutated metastatic colorectal cancer (15, 16). In the context of first-line therapy, chemotherapy with or without a biologic agent (e.g., bevacizumab) was the standard care for BRAF V600E–mutated metastatic colorectal cancer and was associated with poorer outcomes than were seen in patients with BRAF wild-type metastatic colorectal cancer (median progression-free survival, 5.8 vs. 9.2 months; median OS, 11.1 vs. 23.7 months) (17, 18). Data have been limited with respect to first-line treatment targeting the activation pathway that can show improved effectiveness in BRAF V600E–mutated metastatic colorectal cancer.

To investigate encorafenib plus cetuximab (EC), administered with or without chemotherapy (oxaliplatin, leucovorin, and fluorouracil [mFOLFOX6]), versus standard-of-care therapy for the first-line treatment of patients with BRAF V600E-mutated metastatic colorectal cancer, the phase III BREAKWATER trial was conducted. Standard care was defined as investigator's choice of chemotherapy (mFOLFOX6; irinotecan, oxaliplatin, leucovorin, and fluorouracil [FOLFOXIRI]; or oxaliplatin and capecitabine [CAPOX]), with or without bevacizumab (19). At the data cutoff date of December 22, 2023, the proportion of patients achieving confirmed objective responses was significantly higher in the EC + mFOLFOX6 group relative to the standard care group (60.9% vs 40.0%; odds ratio = 2.44; one-sided $P < 0.001$). In addition, treatment with EC + mFOLFOX6 was associated with significantly prolonged progression-free survival (PFS) compared with standard care (median 12.8 vs 7.1 months; hazard ratio (HR) for disease progression or death = 0.53; 95% confidence interval [CI], 0.41–0.68; $P < 0.001$) (20). On the basis of these results, this investigational combination therapy was granted accelerated approval by the Food and Drug Administration as part of Project Front Runner. EC + mFOLFOX6 is currently the first-line activation pathway-targeted treatment indicated in BRAF V600E-mutated metastatic colorectal cancer. Recently, the American Society of Clinical Oncology (ASCO) - Gastrointestinal Cancers (GI) Symposium also released that the ORR in the EC + FOLFIRI group was 64.4% while the control group was 39.2% (21). The PFS was 10.7 months vs 6.0 months, HR=0.48 (95%CI: 0.32–0.72, $P < 0.001$). The OS were not immature. These data also support EC + FOLFIRI as a potential new standard of care in BRAF V600E-mutant mCRC. The Chinese Society of Clinical Oncology (CSCO) guideline recently updated the first-line use of FOLFOX with encorafenib and anti-EGFR monoclonal antibody in patients with MSS or MSI-L/pMMR status, RAS mutations and BRAF V600E mutations who eligible for intensive therapy.

Dabrafenib, another BRAF inhibitor, was more achievable and cheaper in China. Corcoran et al previously reported the ORR of the combination of BRAF, EGFR, and MEK inhibition (dabrafenib [D] + panitumumab [P] + trametinib [T]) was 20%, and this regimen had been recommended in guidelines for BRAF V600E-mutated metastatic colorectal cancer as later lines of choice (9). The preliminary results of another phase Ib study, in which dabrafenib were combined with trametinib, irinotecan and cetuximab in patients with relapsed BRAF V600E-mutated mCRC, showed 90% of disease-control rate (DCR), 7.5 months of median PFS (range 1.8-32.4 months), the median duration of response (DOR) was 5.2 months (range 0-27.7 months)(22). Data on dabrafenib combined with cetuximab and chemotherapy in the first- or second-line setting remain lacking.

In the current study, we retrospectively analyzed real-world data and compared clinical effectiveness and toxicity profiles between first-line and second-line treatment approaches for patients with BRAF V600E-mutant mCRC. This study marked the first evidence of the combination treatment of dabrafenib + cetuximab (DC) with chemotherapy and might define a new standard of care for patients and provide some evidence for further phase II and phase III study.

METHODS

1. Study Design and Patients

This single-center retrospective observational study enrolled patients with histopathologically confirmed metastatic colorectal cancer (mCRC), including those diagnosed with synchronous or metachronous metastatic disease. Comprehensive baseline clinical data were systematically extracted from electronic medical records, covering multiple dimensions of patient characteristics. Collected baseline information consisted of demographic profiles (age and sex), clinical status (Eastern Cooperative Oncology Group (ECOG) performance status), and tumor-related pathological and molecular features. Specifically, tumor characteristics included primary tumor location, surgical history, microsatellite instability (MSI) status, pretreatment levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 199 (CA199), metastatic sites, the number of metastatic lesions, as well as the somatic mutation status of KRAS, NRAS, and BRAF genes. All participants underwent standard screening assessments. Eligibility criteria for this study included patients harboring BRAF V600E mutations, wild-type KRAS and NRAS, and microsatellite stability (MSS). Additionally, patients were required to be ≥ 18 years of age, have measurable disease as defined by the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), ECOG performance status of ≤ 2 , and adequate baseline organ function (as assessed by laboratory parameters).

This retrospective analysis was conducted based on clinical medical data of patients diagnosed with BRAF V600E-mutant metastatic colorectal cancer. All enrolled patients received first-line or second-line systemic antitumor therapy with regimens comprising FOLFIRI, FOLFOX, single-agent irinotecan, or capecitabine combined with DC.

This study was conducted in strict adherence to the ethical principles stipulated in the Declaration of Helsinki and relevant clinical practice guidelines. The research protocol was reviewed and approved by the Institutional Review Board of the Second Affiliated Hospital, Zhejiang University School of Medicine (Approval No. 2026-0371). In the present study, we compared the clinical effectiveness and toxicity profiles between the two aforementioned treatment groups.

2. Evaluation of Treatment Effectiveness and Safety

Every 3 to 4 cycles of treatment, tumor responses were evaluated using the RECIST v1.1. Throughout each cycle of antitumor treatment, treatment-related adverse events were closely monitored and graded strictly in line with the National Cancer Institute Common Terminology

Criteria for Adverse Events Version 5.0 (available at: <http://ctep.cancer.gov/reporting/ctc.html>, accessed on 15 September 2023). Progression-free survival (PFS) was defined as the time interval from the initiation of systemic treatment to the first confirmed disease progression or all-cause mortality, whichever occurred earlier. The median follow-up time was the median duration from patient enrollment (or the initiation of treatment) to the follow-up endpoint, which included the occurrence of events, the last follow-up visit, or the study closure. Tumor response evaluations were performed in strict accordance with the Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1). The objective response rate (ORR) was determined based on the combination of confirmed complete response (CR) and partial response (PR). The disease control rate (DCR) included patients who attained confirmed CR, PR, or stable disease (SD) after treatment. In this study, ORR was designated as the primary endpoint, whereas PFS and treatment-related adverse events were defined as the secondary endpoints.

3. Statistical Analysis

Patients with valid post-treatment evaluation data and complete follow-up information were ultimately included in the final statistical analysis. In this study, continuous quantitative data were expressed as mean $\pm$ standard deviation, while categorical qualitative data were presented as case numbers and corresponding percentages. All statistical computations and data visualization analyses were conducted using R software (version 4.3.0) and GraphPad Prism software (version 10.3.1). Continuous data with skewed distribution were analyzed by the Mann-Whitney U test (rank-sum test for two independent samples). Categorical data were compared using the chi-square test or Fisher's exact test. PFS was calculated via the Kaplan–Meier method. Statistical significance was set at $P < 0.05$.

RESULTS

1. Population and Disposition

We retrospectively identified 23 patients who had received a diagnosis of the BRAF mutation between October 2023 and November 2025. Of them, one patient without tumor assessment and follow-up was excluded from the analysis. Finally, 22 patients were included in the analysis. In the first-line group, approximately 91.67% (11/12) of the patients received FOLFOX with DC. In the second-line group, 80.00% (8/10) of the patients received FOLFOX or FOLFIRI with DC, significant statistical difference was observed ($P < 0.001$). Of the patients, the median age was 53.09 years old and 27.27% were women. When comparing the baseline characteristic between the first-line and second-line group, the detailed chemotherapy and location of primary tumor showed statistically significance ($P < 0.05$). The final analysis of this database was last updated on April 10th, 2026. The detailed baseline demographics and characteristics of the two groups could be seen in **Table 1**.

2. Treatment effectiveness

In the first-line group ($n=12$), the ORR was 83.33%; while in the second-line group ($n=10$), the ORR was 20.00% (**Table 2**). The DCR were both 100.00% in the first-line and second-line group. As of the analysis cutoff point, the median follow-up duration was 6.07 months in the first-line group and 5.26 months in the second-line group. We further compared the clinical effectiveness between the two treatment regimens by evaluating 3-month PFS. No significant difference was noted in 3-month PFS (HR, 0.75, 95% CI, 0.071~7.945; $P = 0.879$; **Figure 1**). The 3-months PFS rate in the first-line group and the second-line group was 91.67% (11/12) and 90.00% (9/10), respectively. With a median follow-up time of 5.34 months (range, 2.69 months ~ 19.02 months), 33.33% (4/12) and 60.00% (6/10) of the patients were progression-free in the first-line group and the second-line group, respectively (**Table S1**).

Table 1. Clinical characteristic of patients.

Characteristics	Total (n = 22)	First line(n=12)	Second line(n=10)	Statistic	P
Age (Mean ± SD)	53.09 ± 13.24	55.83 ± 13.28	49.80 ± 13.10	t=1.07	0.298
Median follow-up time (Mean ± SD)	5.40 ± 3.90	5.36 ± 3.06	5.46 ± 4.90	t=-0.06	0.950
Chemotherapy, n (%)				-	<.001
Capecitabine + DC	1 (4.55)	0 (0.00)	1 (10.00)		
FOLFIRI + DC	6 (27.27)	0 (0.00)	6 (60.00)		
FOLFOX + DC	13 (59.09)	11 (91.67)	2 (20.00)		
Irinotecan + DC	2 (9.09)	1 (8.33)	1 (10.00)		
Primary tumor resection, n (%)				-	0.073
Complete	6 (27.27)	2 (16.67)	4 (40.00)		
None	5 (22.73)	5 (41.67)	0 (0.00)		
Partial	11 (50.00)	5 (41.67)	6 (60.00)		
Location of primary tumor, n(%)				-	0.031
Left side of colon	14 (63.64)	5 (41.67)	9 (90.00)		
Right side of colon	8 (36.36)	7 (58.33)	1 (10.00)		
Liver metastasis, n(%)				-	0.391
No	10 (45.45)	4 (33.33)	6 (60.00)		
Yes	12 (54.55)	8 (66.67)	4 (40.00)		
Organs involved, n(%)				-	1.000
Less than 2(<=2)	15 (68.18)	8 (66.67)	7 (70.00)		
More than 3(>=3)	7 (31.82)	4 (33.33)	3 (30.00)		
CA199 level, n(%)				-	1.000
>=37	17 (77.27)	9 (75.00)	8 (80.00)		
<37	5 (22.73)	3 (25.00)	2 (20.00)		
ECOG, n(%)				-	0.670
0	11 (50.00)	5 (41.67)	6 (60.00)		
1	11 (50.00)	7 (58.33)	4 (40.00)		
Dose of dabrafenib, n(%)				-	0.323
Standard dose	17 (77.27)	8 (66.67)	9 (90.00)		
Reduced dose	5 (22.73)	4 (33.33)	1 (10.00)		
Sex, n(%)				-	0.056
Male	16 (72.73)	11 (91.67)	5 (50.00)		
Female	6 (27.27)	1 (8.33)	5 (50.00)		
Initial stage, n(%)				-	0.135
3	5 (22.73)	1 (8.33)	4 (40.00)		
4	17 (77.27)	11 (91.67)	6 (60.00)		
CEA level, n(%)				-	0.192
>=5	9 (40.91)	3 (25.00)	6 (60.00)		

<5	13 (59.09)	9 (75.00)	4 (40.00)
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Note: DC, dabrafenib and cetuximab.

Table 2. The comparison of effectiveness between the First line and Second line group

Effectiveness	Total (n = 22)	First line (n = 12)	Second line (n = 10)	P
Response, n (%)				0.001
CR	1 (4.55)	0 (0.00)	1 (10.00)	
PR	11 (50.00)	10 (83.33)	1 (10.00)	
SD	10 (45.45)	2 (16.67)	8 (80.00)	
ORR, n (%)				0.008
CR + PR	12 (54.55)	10 (83.33)	2 (20.00)	
SD + PD	10 (45.45)	2 (16.67)	8 (80.00)	
Dose of dabrafenib, n (%)				0.323
Standard	17 (77.27)	8 (66.67)	9 (90.00)	
Reduced	5 (22.73)	4 (33.33)	1 (10.00)	

Note: CR, complete response; PR, partial response; SD, stable disease; PD, progressed disease; ORR, objective response ratio.

3. Treatment Safety

As shown in **Table 3**, the most common AEs were anemia (91.67%), fever (50.00%), leukopenia (58.33%), elevated aspartate aminotransferase level (50.00%), elevated alanine aminotransferase level (50.00%), and hypomagnesemia (50.00%) in the first-line group. In the second-line group, the most common AEs were anemia (50.00%), leukopenia (50.00%), neutropenia (50.00%), hypokalemia (50.00%) and hypoalbuminemia (40.00%) in the second-line group. In the pooled analysis, the most common grade 1-2 AEs were anemia (72.73%), fever (27.27%), neutropenia (31.82%), leukopenia (45.45%), elevated aspartate aminotransferase level (27.27%), hypoalbuminemia (36.36%), hypomagnesemia (36.36%) and hypokalemia (36.36%). In the pooled analysis, the most common grade 3-5 AEs were neutropenia (18.18%), intestinal obstruction (13.64%), and elevated alanine aminotransferase level (13.64%).

Table 3. Adverse Events during Treatment

Adverse effect	Total			First line (n=12)					Second line(n=10)					
				Grade					Grade					
	Grade 1-2(%)	Grade 3-5(%)	Total (%)	1	2	3	4	5	Total (%)	1	2	3	4	5
Nausea	1(4.55%)	0(0.00%)	0(0.00%)	0	0	0	0	0	0(0.00%)	1	0	0	0	0
Anemia	16(72.73%)	0(0.00%)	11(91.67%)	2	9	0	0	0	5(50.00%)	2	3	0	0	0
Diarrhea	2(9.10%)	0(0.00%)	1(8.33%)	1	0	0	0	0	1(10.00%)	1	0	0	0	0
Decreased appetite	1(4.55%)	0(0.00%)	1(8.33%)	1	0	0	0	0	0(0.00%)	0	0	0	0	0
Rash	1(4.55%)	0(0.00%)	0(0.00%)	0	0	0	0	0	1(10.00%)	1	0	0	0	0
Fever	6(27.27%)	0(0.00%)	6(50.00%)	2	4	0	0	0	0(0.00%)	0	0	0	0	0
Peripheral sensory neuropathy	3(13.64%)	0(0.00%)	2(16.67%)	0	2	0	0	0	1(10.00%)	1	0	0	0	0
Fatigue	1(4.55%)	0(0.00%)	1(8.33%)	1	0	0	0	0	0(0.00%)	0	0	0	0	0
Neutropenia	7(31.82%)	4(18.18%)	6(50.00%)	3	1	2	0	0	5(50.00%)	1	2	2	0	0
Leukopenia	10(45.45%)	2(9.09%)	7(58.33%)	3	4	0	0	0	5(50.00%)	1	2	2	0	0
Platelet count decreased	4(18.18%)	1(4.55%)	5(41.67%)	3	1	1	0	0	0(0.00%)	0	0	0	0	0
Intestinal obstruction	0(0.00%)	3(13.64%)	1(8.33%)	0	0	1	0	0	2(20.00%)	0	0	2	0	0
Elevated alanine aminotransferase (ALT) levels	5(22.73%)	3(13.64%)	6(50.00%)	3	0	2	1	0	2(20.00%)	2	0	0	0	0
Elevated aspartate aminotransferase (AST) levels	6(27.27%)	2(9.09%)	6(50.00%)	3	1	1	1	0	2(20.00%)	2	0	0	0	0
Vaginal bleeding	1(4.55%)	1(4.55%)	1(8.33%)	0	1	0	0	0	1(10.00%)	0	0	1	0	0
Bleeding gums	2(9.09%)	0(0.00%)	1(8.33%)	1	0	0	0	0	1(10.00%)	0	1	0	0	0
Hypoalbuminemia	8(36.36%)	0(0.00%)	4(33.33%)	2	2	0	0	0	4(40.00%)	4	0	0	0	0
Hypokalemia	8(36.36%)	0(0.00%)	3(25.00%)	3	0	0	0	0	5(50.00%)	3	2	0	0	0
Mouth ulcers	2(9.09%)	0(0.00%)	0(0.00%)	0	0	0	0	0	2(20.00%)	0	2	0	0	0
Venous thrombosis	1(4.55%)	0(0.00%)	0(0.00%)	0	0	0	0	0	1(10.00%)	1	0	0	0	0
Bloody stools	3(13.64%)	0(0.00%)	2(16.67%)	2	0	0	0	0	1(10.00%)	1	0	0	0	0
Hypomagnesemia	8(36.36%)	0(0.00%)	6(50.00%)	3	3	0	0	0	2(20.00%)	2	0	0	0	0
Allergic Reaction	1(4.55%)	0(0.00%)	1(8.33%)	0	1	0	0	0	0(0.00%)	0	0	0	0	0
Renal insufficiency	1(4.55%)	0(0.00%)	1(8.33%)	1	0	0	0	0	0(0.00%)	0	0	0	0	0
Elevated blood sugar	1(4.55%)	0(0.00%)	1(8.33%)	0	1	0	0	0	0(0.00%)	0	0	0	0	0

DISCUSSION

Up to now, clinical data of dabrafenib combined with anti-EGFR monoclonal antibody and chemotherapy in colorectal cancer remains limited. Previous triplet targeted therapy (dabrafenib + trametinib + cetuximab) achieved an ORR of 20%, and has been recommended by relevant guidelines for later-line treatment (9). Another Phase Ib study, in which dabrafenib, trametinib, irinotecan and cetuximab were performed in BRAF V600E–mutated metastatic colorectal cancer patients who were failed to standard treatments, showed the DCR was 90%, the median PFS was 7.5 months (22). Previous BREAKWATER study reported that the ORR in the EC + mFOLFOX6 and the EC + FOLFIRI was 60.9% and 64.4%,

respectively (19, 21). In our study, there was significant differences to be observed between the first-line and second-line groups in terms of ORR (83.33% vs. 20.00%). The DCR were both 100.0% in the first-line and second-line group. When compared with BREAKWATER study, our first-line use of DC and chemotherapy showed higher ORR, which indicated that dabrafenib can also be used in the first-line setting. As for second-line setting, the ORR was obviously lower than the first-line use, maybe due to that drugs were more effective in tumor naïve patients. Thus, we may indicate that if patients had not used the BRAF inhibitor, such as dabrafenib in the first line, they could also choose the dabrafenib in the second-line due to the 100% DCR observed in our study. Also, different chemotherapy combination may also show differed response. In our center, FOLFOX is more commonly used in the first-line which is more tolerable. FOLFIRI with EC may achieve slightly better response according to the BREAKWATER study. And no significant difference was noted in 3-month PFS rate in our study. The first-line and second-line use both showed high good response in short time. While there were more patients in the second-line group remain progression-free at the final follow-up, maybe due to shorter follow-up time and more patients with left side of colon in the second-line group. Longer follow-up and larger sample size may be needed in the future. And the combination of DC with FOLFIRI could show persistent tumor control than the combination of FOLFOX, which head-to-head randomized clinical trial is demanded to confirm this.

The safety profiles of our study of the combination regimens were almost consistent with that known for each agent. In the pooled analysis of the most common grade 3–5 AE were neutropenia, intestinal obstruction, and elevated alanine aminotransferase level. During the follow-up period, no treatment interruption due to intolerance was observed. This may be attributed to the relatively short follow-up duration, and adverse events were temporarily controllable. Up to now, the regimen of DC with chemotherapy was also tolerable.

In our study, some patients received non-standard dosing due to economic reasons. Owing to our limited sample size, no correlation between dose and effectiveness was observed. Thus, further studies with an expanded sample size are warranted to demonstrate the correlation with dose and effectiveness. In addition, one patient in our study received successful conversion therapy and obtained no evidence of disease (NED) after surgical treatment and achieved relative long PFS. In the past, surgeons were more conservative in the surgical treatment of patients with BRAF mutations. With the promotion of the BREAKWATER study and similar regimen like our study, more and more patients may achieve unexpected successful conversion. Under the condition of stable disease, they will have the opportunity to receive complete surgery, obtain NED status, and achieve better OS. However, there is currently no standard for the subsequent treatment of patients after NED, which requires further clinical research to explore.

LIMITATIONS

Our study still has several limitations that need to be improved and verified in subsequent studies. Firstly, this study was a small-sample, single-center, retrospective study. It lacked the support of data from multi-center, randomized controlled phase III clinical trials, which might lead to limited representativeness and extrapolatability of the research results, making it difficult to fully reflect the effectiveness and safety characteristics of the treatment regimen in a broad population. Secondly, the follow-up time of this study was relatively short, 6-month PFS and complete median OS data have not yet been collected, which made it impossible to fully evaluate the impact of this treatment strategy on the long-term survival prognosis of patients and difficult to clarify its long-term benefits and potential risks. Thirdly, among AE data collected in this study, hematological-related adverse events accounted for a relatively high proportion, while the collection and analysis of non-hematological adverse events were not comprehensive enough, which might lead to bias in the evaluation of adverse events and failure to fully present the safety profile of the treatment regimen. Finally, the PFS in some of the patients were short in our study, mutation-related drug resistance mechanism warranted further investigation. In the near future, we may enlarge the sample size, collect fresh tumor samples, and perform multi-omics sequencing to discover the mechanism of resistance.

CONCLUSION

In conclusion, our study found that the combination of DC and chemotherapy has good effectiveness and safety. Dabrafenib combined with chemotherapy and anti-EGFR monoclonal antibody may become the standard first-line and second-line treatment regimen for BRAF-mutated colorectal cancer.

Abbreviations

CRC = Colorectal cancer; MAPK = mitogen-activated protein kinase; OS = overall survival; ORR = objective response rate; EGFR = epidermal growth factor receptor; EC = encorafenib + cetuximab; PFS = progression-free survival; HR = hazard ratio; CI = confidence interval; ASCO = American Society of Clinical Oncology; GI = Gastrointestinal Cancers; DCR = disease-control rate; DOR = duration of response; DC = dabrafenib + cetuximab; ECOG = Eastern Cooperative Oncology Group; MSI = microsatellite instability; CEA = carcinoembryonic antigen; CA199 = Carbohydrate antigen199; MSS = microsatellite stability; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1; AE = adverse event; NCI-CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; CR = complete response; PR = partial response; SD = stable disease; NED = no evidence of disease.

Declarations

Ethics approval and consent to participate: The study protocol was reviewed and approved by Institutional Review Board of the Second Affiliated Hospital, Zhejiang University School of Medicine. The need for informed consent was waived due to the retrospective nature of the study and the use of the anonymized data.

Consent for publication: Not applicable.

Availability of data and materials: The data and materials analyzed in the current study are available from the corresponding author on reasonable requests.

Competing interests: Not applicable.

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Authors' contribution: SSW and YY conceptualized and designed the study. CHZ, FLH, and YH collected the patients' information. CHZ and DL performed formal analysis including bioinformatics and statistical. CHZ, DL, KJ, YY and SSW were involved in critical review of the data and interpretation of results. CHZ and FLH created the manuscript figures and Supplemental materials. CHZ and FLH drafted the manuscript. CHZ, DL and YY acquired funding for the study. All authors edited, reviewed, revised, and approved the manuscript text.

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Figures

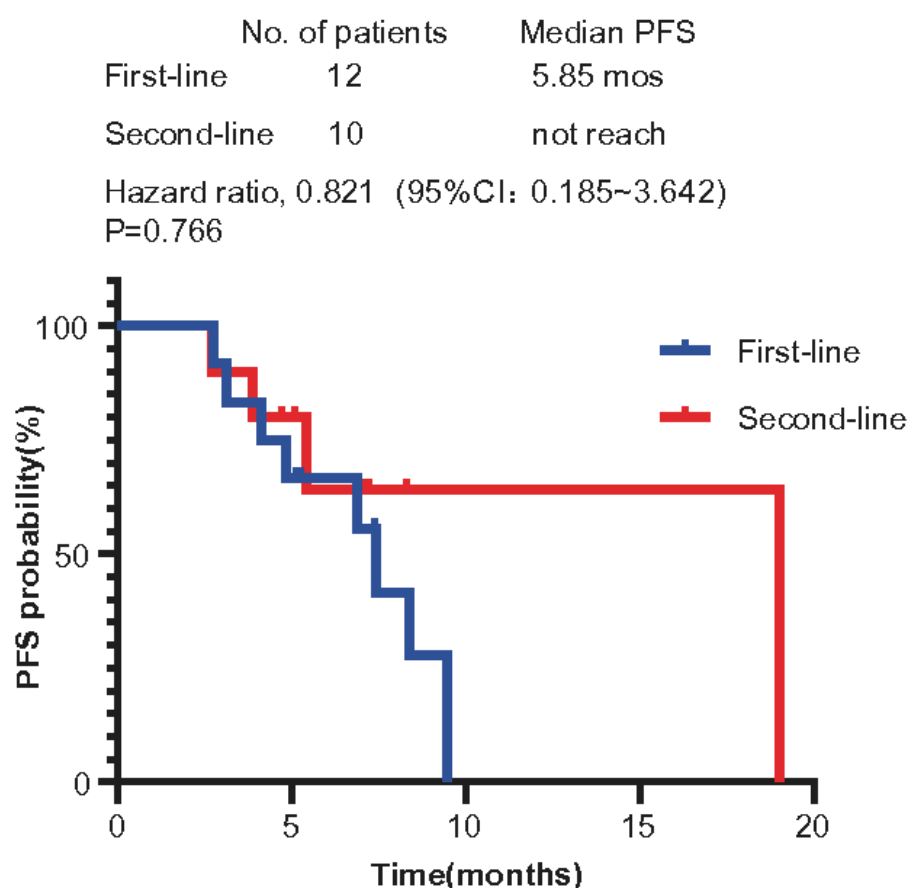


Figure 1

Kaplan–Meier survival curves for three-month PFS rates in the 22 included patients with BRAF V600E-mutant metastatic colorectal cancer.
 Note: Differences in 3-month PFS was analyzed using a log-rank test. Three-month PFS did not significantly vary between the two treatment arms (P = 0.380). PFS, progression-free survival.

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