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ORIGINAL ARTICLE

Treatment patterns and survival outcomes for patients receiving second-line treatment for metastatic colorectal cancer in the USA

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Abstract

Background Colorectal cancer is the third most common cause of cancer death in the USA. It is important to identify patients who may experience poor outcomes from available treatments.

Methods In this retrospective observational study, treatment patterns and survival outcomes were described among adult patients from the Flatiron Health electronic medical records database who were treated with at least two lines of therapy for metastatic colorectal cancer in the USA between January 2013 and May 2018. Patients with rapid progression were defined as those whose time from start of first- to second-line therapy was ≤ 183 days.

Results A total of 14,315 patients formed the study cohort. The most common first-line treatments were FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) plus bevacizumab, received by 34.7% ($n = 4962$) of patients, followed by FOLFOX alone (17.1%, $n = 2445$). Of all patients, 6991 (48.9%) also received second-line anti-cancer therapy and of those, 3338 (47.7%) had rapid progression and 3653 (52.3%) did not. Median overall survival from the start of first- and second-line therapy was 20.8 months (95% CI 20.2–21.3) and 14.5 months (95% CI 13.9–15.0) for the entire study population, respectively. Median overall survival from the start of second-line therapy was 14.1 (95% CI 13.2–14.8) for patients with rapid progression and 14.6 months (95% CI 13.8–15.4) for patients without rapid progression.

Conclusions Patients diagnosed with metastatic colorectal cancer lived less than 2 years in this real-world database. While the time to initiation of second-line therapy was by definition longer among patients without rapidly progressing disease, survival outcomes were comparable from initiation of second-line therapy.

Keywords Observational study · Electronic medical records · Rapid progression · Colorectal cancer · Overall survival · Treatment patterns

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and is also the third leading cause of cancer death in the United States (USA), with approximately 140,250 new colorectal cases and 50,630 colon cancer deaths per year [1]. It is estimated that approximately 25% of patients present with metastatic disease at initial diagnosis and an additional 25% who presented with earlier stage disease ultimately develop metastases [2]. Patients with unresectable disease are typically initially treated with chemotherapy combinations such as FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (5-fluorouracil, leucovorin, and irinotecan), with or without a biologic agent (e.g., bevacizumab, cetuximab, panitumumab). Use of the EGFR inhibitors, cetuximab and panitumumab, is limited to patients without specific *RAS* family mutations and is recommended by National Comprehensive Cancer Network guidelines for patients with left-sided tumors [3]. Newer therapies, such as nivolumab, pembrolizumab, or nivolumab plus ipilimumab, are limited to patients with high microsatellite instability (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer among patients not appropriate for intensive therapy [3].

Microabstract
Treatment patterns and overall survival outcomes for 14,315 patients diagnosed with colorectal cancer from an electronic medical records database in the USA were studied.

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Multiple treatment options exist in the second-line setting and are based on the same agents and combinations as in the first-line setting, altered based on what was received during prior therapy. Following disease progression, patients will often switch from FOLFOX to FOLFIRI or vice versa as second-line therapies. The GERCOR study established the equivalence of outcomes regardless of order of administration: the median overall survival of patients receiving FOLFIRI followed by FOLFOX was 21.5 months for those who received the agents in the opposite order [4].

Prior retrospective observational research has identified FOLFOX as the most common first-line therapy followed by FOLFIRI; however, these data were from 2002 to 2003 and survival outcomes were not reported [5].

The goal of this retrospective observational study was to describe the current treatment patterns and survival outcomes of patients who received second-line treatment for metastatic CRC in the context of current care of patients to inform the knowledge of contemporaneous treatment patterns and outcomes in a real-world setting. .

Methods

Data source

Electronic medical records (EMR) data were obtained from the Flatiron Health database, which is a longitudinal, demographically, and geographically diverse database derived from electronic medical record (EMR) data. The Flatiron Health database at the time of this study included data from over 255 cancer clinics representing 1.7 million active cancer patients. The Flatiron Health Metastatic Colorectal Cancer Cohort is a subset of the overall Flatiron Health database that includes a geographically diverse random sample of over 18,000 patients with metastatic colorectal cancer with at least two clinical visits on or after January 1, 2013 at Flatiron community oncology and academic cancer centers in the USA. All patients in the database were diagnosed with metastatic disease on or after January 2013 and are 18 years of age or older. The data are refreshed every 30 days. Patient-level data were available through May 31, 2018 at the time of analysis.

Eligibility criteria

Patients eligible for this study were adult patients in the Flatiron Metastatic Colorectal Cancer Cohort who received at least one line of anti-cancer therapy in the database. Baseline characteristics were identified from variables in the database within 45 days of the initial metastatic diagnosis of colorectal cancer, with the exception of KRAS status, which was obtained from testing at any time in the database. Patients who progressed from the start of first- to second-line therapy containing anti-cancer agents within 183 days (6 months) were defined as having rapid progression. All other patients who received two or more lines of therapy containing anti-cancer agents had disease that was not categorized as rapid progression. Regimens and lines of therapy are defined and included as variables within the Flatiron database; however, for the purposes of defining rapid progression, the lines of therapy were required to contain at least one anti-cancer agent (e.g., chemotherapy, targeted therapy or biologic therapy) to ensure supportive care or other interventions were not miscoded as a new line of therapy.

Statistical methods

Baseline characteristics were described based on the closest recorded values within ± 45 days of the initial metastatic diagnosis date. Continuous variables were reported using mean and standard deviation or median and minimum–maximum values. Categorical variables are reported as number and percent of the cohort or study subgroup. Median overall survival and 95% confidence interval (CI) were estimated by the Kaplan–Meier method. Survival analyses were conducted overall and among a priori specified subgroups based on rapid progression, treatment sequencing, and KRAS status. All analyses were intended to be non-comparative for hypothesis-generation purposes only. All study analyses were conducted using SAS Enterprise Guide (version 7.13, SAS Institute Inc., Cary, NC, USA).

Results

Study cohort and subgroups

A total of 14,315 patients met eligibility criteria and were included in this study (Fig. 1). Among patients who received additional therapy, 3338 (47.7%) had rapid progression and 3653 (52.3%) did not. Patient baseline demographic and clinical characteristics are presented in Table 1. More than half of patients were male, with a median age of 65 years (range 18–85). The Flatiron clinics are predominantly community based; only 5.7% of patients in the cohort were treated in academic practice settings. At the time of initial diagnosis, 22.1% stage III disease before developing metastases and 61.3% had stage IV disease at diagnosis. The remaining patients were diagnosed with stage 0–II disease and later progressed or recurred with metastatic disease (12.7%) or had missing stage information (3.9%). Approximately 75% of patients had KRAS status recorded; of these, 55.2% had tumors that were KRAS wild type.

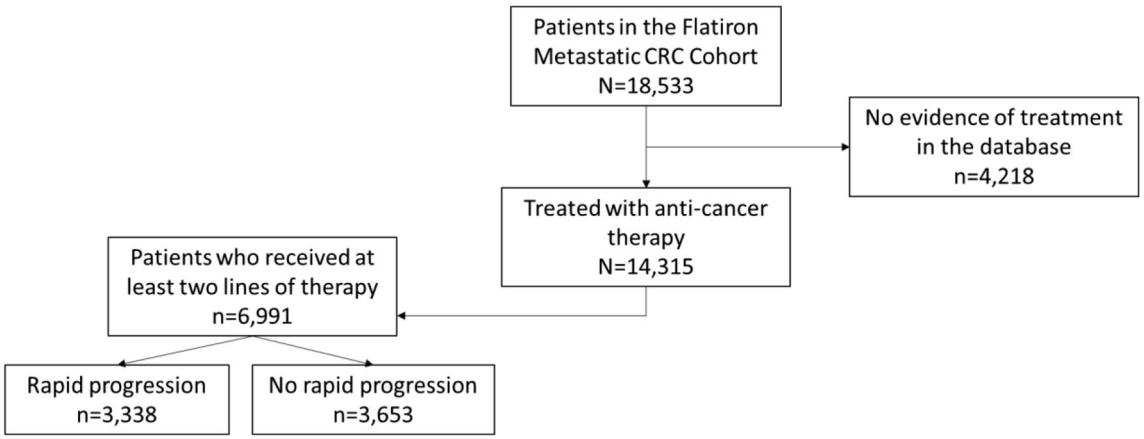

Fig. 1 Study cohort. Rapid progression defined as time from start of first- to start of second-line treatment ≤ 183 days. All other patients were categorized to no rapid progression. *CRC=colorectal cancer

Treatment patterns

First-line regimens used by at least 1% of the study cohort are shown in Table 2. FOLFOX-based therapy was common in the first-line setting: FOLFOX + bevacizumab (34.7%), FOLFOX (17.1%), FOLFOX + panitumumab (1.3%), and FOLFOX + cetuximab (1.0%), whereas FOLFIRI-based therapy was less commonly used (e.g., FOLFIRI + bevacizumab, 10.9%; FOLFIRI, 3.7%; FOLFIRI + cetuximab, 1.9%; FOLFIRI + panitumumab, 0.8%). Conversely, FOLFIRI-based regimens were more common on the second-line setting (Table 3), with FOLFIRI + bevacizumab being the most common regimen (25.3%), followed by FOLFIRI (8.6%), FOLFIRI + cetuximab (4.6%), FOLFIRI + panitumumab (2.5%), FOLFIRI + aflibercept (2.4%), and FOLFIRI + ramucirumab (1.5%). The number of regimens used in the third-line is shown in Table 4 and contains a wider variety of chemotherapy backbones. At least 29.2% of third-line regimens are FOLFIRI-based and at least 10.9% are FOLFOX-based.

Anti-angiogenic therapy with FOLFOX, FOLFIRI, or other chemotherapy backbones is common: 53.7%, 55.0%, and 35.6% of patients receive these agents in the first-, second-, or third-line settings, respectively. The continued use of anti-angiogenic therapy across multiple lines of therapy is observed as well. Among patients receiving FOLFOX + bevacizumab in the first line setting, 62.6% continue to receive anti-angiogenic therapy (bevacizumab, ramucirumab or aflibercept), and 20.8% received EGFR inhibitors (cetuximab or panitumumab) in the second line. Among the full study cohort, EGFR inhibitors were used by 7.9%, 20.3%, and 25.9% of patients in the first-, second-, and third-line settings, respectively. The use of checkpoint inhibitors was low (0.3%, 1.1%, and 2.0% in the first-, second-, and third-line settings, respectively).

Treatment sequencing followed similar patterns. Among patients receiving FOLFOX with or without bevacizumab in the first-line setting, second-line regimens were primarily FOLFIRI-based (Table 5), and first-line FOLFIRI regimens tended to be followed by FOLFOX-based therapy (data not shown).

Overall survival

The median overall survival (OS) outcomes are described in Table 6 for each of the individual cohorts included in this study. From the time of metastatic diagnosis, median OS for the study cohort was 25.0 months (95% CI 24.5–25.5) and from the initiation of first-line therapy was 20.8 months (95% CI 20.2–21.3). For all patients who received second-line therapy, median OS from the initiation of second-line therapy was 14.5 months (95% CI 13.9–15.0). As would be expected, survival from the start of first-line therapy was shorter (17.1 months; 95% CI 16.2–18.0) for those with rapid progression than for those without rapid progression (29.8 months; 95% CI 28.9–30.9). However, little difference in OS was evident after progression, as median OS from the start of second-line therapy was 14.1 months (95% CI 13.2–14.8) for patients who experienced rapid progression and 14.6 months (95% CI 13.8–15.4) for those who did not. Median OS of those initiating FOLFOX followed by FOLFIRI was 25.4 months (95% CI 24.5–26.6) and 24.1 months (95% CI 21.6–26.1) for those initiating FOLFIRI followed by FOLFOX.

Discussion

This study provides current insights into the treatment patterns and survival outcomes of patients diagnosed with metastatic colorectal cancer in primarily community-based practices in the USA. The most common treatment strategy is FOLFOX-based therapy followed by FOLFIRI-based

Table 1 Demographic and clinical characteristics

Characteristics	Overall study cohort $N = 14,315$	Patients with rapid progression, $N = 3338$	Patients without rapid progression, $N = 3653$
Year of metastatic diagnosis, *n* (%)			
2013	2532 (17.69)	626 (18.75)	846 (23.16)
2014	2740 (19.14)	663 (19.86)	874 (23.93)
2015	2961 (20.68)	739 (22.14)	900 (24.64)
2016	2918 (20.38)	656 (19.65)	761 (20.83)
2017	2510 (17.53)	596 (17.86)	272 (7.45)
2018	654 (4.57)	58 (1.74)	0 (0.00)
Gender, *n* (%)			
Female	6345 (44.32)	1468 (43.98)	1597 (43.72)
Male	7970 (55.68)	1870 (56.02)	2056 (56.28)
Age at diagnosis (years)			
Mean (SD)	63.8 (12.33)	62.5 (12.25)	62.4 (11.99)
Median	65	63	63
Min, max	18.0, 85.0	22.0, 85.0	18.0, 84.0
Body weight (kg)			
N	11,518	2719	3050
Mean (SD)	82.7 (26.75)	83.1 (25.82)	84.9 (28.20)
Median	78.5	79.5	79.7
Min, Max	31.0, 297.8	34.5, 245.4	34.9, 297.8
Practice type, *n* (%)			
Academic	819 (5.72)	190 (5.69)	193 (5.28)
Community	13,496 (94.28)	3148 (94.31)	3460 (94.72)
Geographic region, *n* (%)			
Northeast	2674 (18.68)	586 (17.56)	716 (19.60)
Midwest	2350 (16.42)	506 (15.16)	641 (17.55)
South	5567 (38.89)	1327 (39.75)	1421 (38.90)
West	2413 (16.86)	607 (18.18)	559 (15.30)
Unknown/missing	1311 (9.16)	312 (9.35)	316 (8.65)
Race, *n* (%)			
White	9453 (66.04)	2177 (65.22)	2472 (67.67)
Black/African-American	1496 (10.45)	356 (10.67)	431 (11.80)
Asian	380 (2.65)	99 (2.97)	126 (3.45)
Other	1533 (10.71)	375 (11.23)	360 (9.85)
Unknown/missing	1453 (10.15)	331 (9.92)	264 (7.23)
Ethnicity, *n* (%)			
Hispanic	1226 (8.56)	319 (9.56)	315 (8.62)
Non-Hispanic	13,089 (91.44)	3019 (90.44)	3338 (91.38)
ECOG performance status, *n* (%)			
0	2920 (20.40)	699 (20.94)	818 (22.39)
1	2484 (17.35)	597 (17.88)	620 (16.97)
2	724 (5.06)	138 (4.13)	128 (3.50)
3	142 (0.99)	22 (0.66)	15 (0.41)
4	12 (0.08)	0 (0.00)	1 (0.03)
Unknown/missing	8033 (56.12)	1882 (56.38)	2071 (56.69)
Cancer stage at initial diagnosis*, *n* (%)			
Stage 0	2 (0.01)	0 (0.00)	1 (0.03)
Stage I	373 (2.61)	78 (2.34)	81 (2.22)
Stage II	1448 (10.12)	312 (9.35)	353 (9.66)

Table 1 (continued)

Characteristics	Overall study cohort $N = 14,315$	Patients with rapid progression, $N = 3338$	Patients without rapid progression, $N = 3653$
Stage III	3159 (22.07)	823 (24.66)	804 (22.01)
Stage IV	8770 (61.26)	1998 (59.86)	2290 (62.69)
Unknown/missing	563 (3.93)	127 (3.80)	124 (3.39)
Cancer site, *n* (%)			
Colon	10,589 (73.97)	2400 (71.90)	2712 (74.24)
Rectum	3441 (24.04)	873 (26.15)	869 (23.79)
Colorectal NOS	285 (1.99)	65 (1.95)	72 (1.97)
KRAS mutation status, *n* (%)			
Wild type	5904 (41.24)	1562 (46.79)	1866 (51.08)
Mutant	4787 (33.44)	1265 (37.90)	1446 (39.58)
Unknown/missing	3624 (25.32)	511 (15.31)	341 (9.33)

Patients with rapid progression were defined as those whose time from start of first- to second-line therapy was ≤ 183 days

ECOG Eastern Cooperative Oncology Group, *NOS* not otherwise specified, *SD* standard deviation

*All patients in the cohort were either diagnosed metastatic or had progressed to metastatic disease after initial early-stage diagnosis

therapy; however, variability in the regimens used appears to increase by line of therapy, with greater numbers of regimens being used as the disease progresses. Overall survival was 20.76 months from the start of first-line therapy (95% CI 20.20–21.25) and 14.47 months (95% CI 13.88–15.00 months) from the start of second-line therapy. Randomized trial data have demonstrated similar efficacy regardless of the order of FOLFIRI and FOLFOX regimens [4], a finding that these descriptive data support. While it is important to note that the survival outcomes are not adjusted for any baseline differences between groups and, therefore, direct comparisons cannot be made, the outcomes observed in this study are consistent with those from the randomized trial. The primary survival findings in this study are descriptive in nature and show interesting observations of median overall survival from the start of second-line therapy of 14.1 months (95% CI 13.2–14.8) for patients with rapid

Table 2 First-line regimens ($n = 14,315$)

Regimen[a]	Number	Percent
FOLFOX + bevacizumab	4962	34.7
FOLFOX	2445	17.1
Fluoropyrimidine	1873	13.1
FOLFIRI + bevacizumab	1554	10.9
Fluoropyrimidine + bevacizumab	574	4.0
FOLFIRI	526	3.7
FOLFIRI + cetuximab	265	1.9
FOLFOX + panitumumab	188	1.3
FOLFOX + cetuximab	147	1.0

FOLFOX fluoropyrimidine, leucovorin, and oxaliplatin, *FOLFIRI* fluoropyrimidine, leucovorin, and irinotecan

[a] All other regimens not listed were each used by < 1% of the study cohort

Table 3 Second-line regimens ($n = 7034$)[a]

Regimen[a]	Number	Percent
FOLFIRI + bevacizumab	1780	25.3
FOLFOX + bevacizumab	1013	14.4
FOLFIRI	603	8.6
FOLFOX	338	4.8
Fluoropyrimidine + bevacizumab	332	4.7
FOLFIRI + cetuximab	327	4.6
Irinotecan + cetuximab	220	3.1
Regorafenib	200	2.8
FOLFIRI + panitumumab	179	2.5
FOLFIRI + aflibercept	168	2.4
Trifluridine/tipiracil	156	2.2
Panitumumab	127	1.8
FOLFOX + panitumumab	112	1.6
FOLFIRI + ramucirumab	103	1.5
Irinotecan + bevacizumab	100	1.4
Irinotecan + panitumumab	86	1.2
Irinotecan	83	1.2
Cetuximab	81	1.2

Number is higher than the count used to determine rapid progression due to some regimens as defined within the Flatiron database not containing anti-cancer agents

FOLFOX fluoropyrimidine, leucovorin, and oxaliplatin, *FOLFIRI* fluoropyrimidine, leucovorin, and irinotecan

[a] All other regimens not listed were each used by < 1% of the study cohort

Table 4 Third-line regimens ($n = 3232$)

Regimen[a]	Number	Percent
FOLFIRI + bevacizumab	393	12.2
Regorafenib	375	11.6
Trifluridine/tipiracil	345	10.7
FOLFOX + bevacizumab	250	7.7
FOLFIRI	151	4.7
Irinotecan + cetuximab	144	4.5
FOLFIRI + cetuximab	143	4.4
Panitumumab	106	3.3
FOLFOX	103	3.2
Fluoropyrimidine + bevacizumab	102	3.2
FOLFIRI + panitumumab	100	3.1
FOLFIRI + aflibercept	90	2.8
FOLFIRI + ramucirumab	67	2.1
Cetuximab	62	1.9
Irinotecan + panitumumab	61	1.9
Irinotecan + bevacizumab	40	1.2
Fluoropyrimidine	38	1.2
Pembrolizumab	33	1.0

FOLFOX fluoropyrimidine, leucovorin, and oxaliplatin, *FOLFIRI* fluoropyrimidine, leucovorin, and irinotecan

[a] All other regimens not listed were each used by < 1% of the study cohort

Table 5 Treatment sequences

	Number	Percent
Second-line regimens after first-line FOLFOX + bevacizumab ($N = 2470$)		
FOLFIRI + bevacizumab	1176	47.6
FOLFIRI	262	10.6
FOLFIRI + cetuximab	159	6.4
FOLFIRI + Ziv-aflibercept	114	4.6
FOLFIRI + panitumumab	91	3.7
Irinotecan + cetuximab	85	3.4
FOLFIRI + ramucirumab	74	3.0
Irinotecan + bevacizumab	53	2.1
Regorafenib	33	1.3
Irinotecan	30	1.2
Panitumumab	27	1.1
Second-line regimens after first-line FOLFOX ($N = 1249$)		
FOLFOX + bevacizumab	373	29.9
FOLFIRI	235	18.8
FOLFIRI + bevacizumab	210	16.8
Fluoropyrimidine + bevacizumab	85	6.8
FOLFIRI + cetuximab	43	3.4
FOLFOX + panitumumab	37	3.0
Irinotecan + cetuximab	24	1.9
FOLFIRI + panitumumab	23	1.8
FOLFOX + cetuximab	22	1.8
Bevacizumab	17	1.4
Irinotecan	15	1.2
Panitumumab	15	1.2
FOLFOXIRI + bevacizumab	14	1.1

Limited to second-line regimens used in > 1% of the cohort

FOLFOX fluoropyrimidine, leucovorin, and oxaliplatin, *FOLFIRI* fluoropyrimidine, leucovorin, and irinotecan, *FOLFOXIRI* fluoropyrimidine, leucovorin, irinotecan, and oxaliplatin

progression and 14.6 months (95% CI 13.8–15.4) for patients without rapid progression. While statistical comparisons were not conducted, future research should consider obtaining a comprehensive dataset to enable adjustments for baseline confounders to make formal comparisons between groups. Additionally, these findings warrant further research regarding the treatment sequencing and factors associated with rapid progression.

Prior research has suggested that obtaining an early response or delaying progression leads to improved survival [6]. While progression was estimated based on time to second-line therapy, the OS outcomes from initiation of first-line therapy are consistent with this prior research; however, there appeared to be similar outcomes after progression to second-line therapy, regardless of whether progression was early or late (OS was 14.1 months or 14.6 months from the start of second-line therapy, respectively). There is a need to investigate this observation, as tumor response data and reason for treatment change were not available in this EMR dataset.

Findings from randomized data related to continuation of anti-angiogenic therapy across multiple lines of therapy [7] appear to have been incorporated into clinical practice. The data from this study show that more than half of patients receiving anti-angiogenic therapy will do so across lines of therapy. However, the EGFR inhibitors appear to be used primarily in later lines of therapy. While analyses were not conducted specifically among patients with KRAS-wild type tumors, the proportion of patients receiving the EGFR inhibitors cetuximab or panitumumab was less than 10% in the first-line setting, but more than a quarter of all patients received them in the third-line setting. This analysis did not evaluate treatment by tumor sidedness as these data are not recorded in the database, but this observation could be due to the lack of perceived value or awareness of the effectiveness of EGFR agents in this population. Additional work is needed to ensure targeted therapies are used at the time point where they can provide the optimal outcomes for patients.

Novel therapies, such as ramucirumab, checkpoint inhibitors, and trifluridine/tipiracil were relatively infrequently used, but this could be due to the recency of these approvals. This study included all data from 2013 to 2018, and these drugs were only approved for a portion of this time period. Future studies of these specific agents may require additional time until a sufficient number of cases for study are available in

Table 6 Overall survival (OS), median, and 95% confidence interval (CI)

Cohort	Median OS [95% CI] from start of first-line therapy *n*	Median OS [95% CI] from start of second-line therapy *n*
Overall population	20.76 [20.20, 21.25]	14.47 [13.88, 15.00]
	N = 14,315	*N* = 7033
KRAS-wild type	23.32 [22.40, 24.24]	15.49 [14.93, 16.41]
	N = 5904	*N* = 3440
KRAS-mutant	21.32 [20.63, 22.30]	13.39 [12.80, 14.47]
	N = 4787	*N* = 2726
Any FOLFOX-containing first-line regimens followed by any second-line FOLFIRI-containing regimen*	25.39 [24.47, 26.64]	13.68 [12.96, 15.07]
	N = 2602	*N* = 2602
Any FOLFIRI-containing first-line regimens followed by any second-line FOLFOX-containing regimen*	24.05 [21.64, 26.12]	12.37 [10.69, 14.01]
	N = 385	*N* = 385
Patients with rapid progression	17.07 [16.18, 17.96]	14.11[13.19, 14.80]
	N = 3338	*N* = 3338
Patients without rapid progression	29.77 [28.88, 30.89]	14.64 [13.75, 15.36]
	N = 3653	*N* = 3652

FOLFOX fluoropyrimidine, leucovorin, and oxaliplatin, *FOLFIRI* fluoropyrimidine, leucovorin, and irinotecan

*Excluding patients ever using EGFR inhibitors, cetuximab, or panitumumab

real-world datasets and restrict the time period to that in which the drug was consistently available to patients.

It is important to point out that a retrospective descriptive study is, by design, intended to be hypothesis generating, and it would not be appropriate to draw substantive conclusions from these findings. The data from a descriptive retrospective study are intended to help guide future research by exploring a variety of patterns and outcomes in modern-day clinical practice in the USA. It is possible that additional patients that would have been classified as non-rapid progressors could be included in the original cohort but had not reached the point in time during the database period to have reached a subsequent line of therapy; patients initiating therapy late in the study time period may have been excluded due to the lack of sufficient follow-up time. As with all retrospective analyses, there are additional limitations that must be taken into account. The data used for this study were collected as part of routine clinical practice at the oncologist office and not specifically for research purposes. As a result, data are not recorded and could not be included in this study (e.g., surgical details, comorbid conditions) and other data may be underreported (e.g., KRAS status, ECOG performance status). The Flatiron database does not contain data on either tumor response or progression; therefore, the definitions of rapid progression are purely based on timing of therapy, which may not accurately reflect disease progression. As a result, this study did not include progression-free survival or tumor response outcomes. Therapies may change due to other reasons, such as patient choice or toxicity, which are similarly not recorded in EMR data.

Despite these limitations, this study provides insights into the current practice patterns and survival outcomes of patients diagnosed with metastatic colorectal cancer in the USA and provides a range of data to guide the development of subsequent hypothesis-driven research. Patients in this study lived less than 2 years from the start of first-line therapy, demonstrating the need to further improve these outcomes, perhaps through improved treatment selection and treatment sequencing. While the time to initiation of second-line therapy was longer among patients without rapidly progressive disease, outcomes were comparable from initiation of second-line therapy for both patients considered to be rapid progressors and for those who were not.

Clinical practice points

- Of patients, 53.7% received anti-angiogenic therapy and 7.9% received EGFR inhibitors in the first line setting
- FOLFOX + bevacizumab was the most common first-line chemotherapy regimen (34.7%)
- Of patients receiving first-line FOLFOX + bevacizumab, 20.8% subsequently received an EGFR inhibitor and 62.6% received additional anti-angiogenic therapy in the second line
- Median survival outcomes were less than 2 years from the start of first-line therapy and slightly longer than 1 year from the start of second-line therapy

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Compliance with ethical standards

Disclosure All authors were employees of Eli Lilly and Company at the time this work was conceptualized and initiated; DM retired from Eli Lilly and Company prior to submission of this work to the journal.

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