Real-world biomarker prevalence and treatment patterns among metastatic colorectal cancer patients who underwent NGS testing

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Introduction

- Colorectal cancer (CRC) is the second most common cause of cancer-related deaths in the United States,[1,2] accounting for an estimated 7.8% of all new cancer cases and 8.6% of all cancer-related deaths in 2023[2]
- The survival rate for colorectal cancer decreases with disease progression, with the 5-year survival rate dropping from 90.9% for patients with localized colorectal cancer to only 15.6% for patients with metastatic colorectal cancer (mCRC)[2]
- Management of mCRC is challenging and treatment strategies vary by tumor-, disease-, and patient-related factors.[3] However, biomarker testing has driven the growth of targeted therapy for mCRC and may help identify mutations that predict the efficacy of therapies[3]
- The current study aims to evaluate biomarker prevalence, demographic and clinical characteristics, and treatment patterns by line of therapy among mCRC patients who have undergone next-generation sequencing (NGS)

Methods

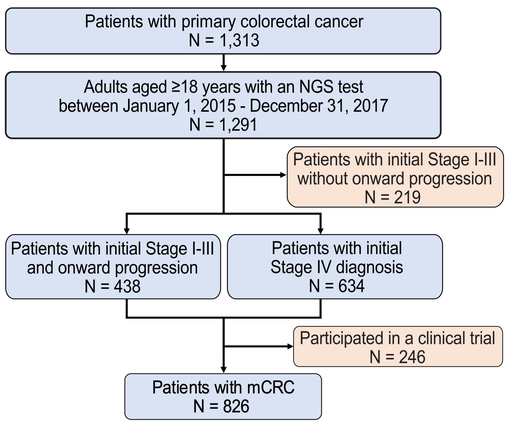
Study design

- This was a retrospective observational analysis using data from the American Association for Cancer Research Project Genomics Evidence Neoplasia Information Exchange-Biopharma Collaborative (AACR Project GENIE: Biopharma Collaborative)
- Eligible subjects were ≥18 years of age at the time of sequencing, with a primary diagnosis of colorectal cancer who were included in the AACR Project GENIE-Biopharma Collaborative Phase 1 colorectal cancer cohort, had undergone NGS testing between January 1, 2015 and December 31, 2017
- Patients participating in clinical trials were excluded from the analysis
- A line of therapy (LOT) algorithm was applied to define each LOT.[4] Briefly, initiation of a LOT was defined after mCRC diagnosis or progression from prior treatment. All drugs initiated within 30 days were considered a part of the treatment regimen in that line. The end of line was defined as the earliest date of:
  1. A treatment gap of 120 days, or
  2. Initiation/addition of a new antineoplastic therapy, or
  3. End of follow-up
- Descriptive statistics were used to describe biomarker prevalence, patient characteristics, and treatment patterns

Results

- A total of 826 adults with mCRC met the study inclusion criteria (**Figure 1**)

Figure 1. Study attrition diagram



- A majority of patients were male (56.2%), White (78.9%), with a median (IQR) age of 54 (46-64) years (**Table 1**)
- Over half (58.1%) of subjects were diagnosed with mCRC at their initial diagnosis

Table 1. Demographic and clinical characteristics[a]

Demographic and clinical characteristics	Study population (N = 826)
Age at diagnosis in years, mean (SD)	**54 (12)**
Age at diagnosis in years, median [IQR]	**54 [46-64]**
Age group	
≥65	183 (22.2)
<65	643 (77.8)
Sex	
Male	464 (56.2)
Female	362 (43.8)
Ethnicity	
Non-Hispanic or Latino	769 (93.1)
Hispanic or Latino	28 (3.4)
Other	4 (0.5)
Unknown	25 (3.0)
Race	
White	652 (78.9)
Black	62 (7.5)
Asian	49 (5.9)
Other	22 (2.7)
Unknown	41 (5.0)
Initial diagnosis stage	
I-III	346 (41.9)
IV	480 (58.1)
Histology	
Adenocarcinoma	660 (79.9)
Carcinoma	23 (2.8)
Other histology/mixed tumor	4 (0.5)
Unknown	139 (16.8)
Number of metastatic sites	
0	347 (42.0)
1-2	400 (48.4)
3-4	63 (7.6)
≥5	16 (1.9)

SD, standard deviation.
[a]Values presented as N (%) unless indicated otherwise.

- Hotspot mutations in RAS were identified in 48.3% of the study population while V600E BRAF mutation was reported in 7.0% of the study population. Other mutations were present in less than 2.0% of the study population (**Table 2**)
- A total of 664 patients had known MSI/MMR status, with 75.2% having MSS/pMMR and 5.2% having MSI-H/dMMR

Table 2. Biomarkers[a]

Biomarker	Study population[b] (N = 826)
RAS (hotspot mutation)	399 (48.3)
BRAF (V600E mutation)	58 (7.0)
HER2 (amplification)	13 (1.6)
HER2 (activating mutation)	12 (1.5)
POLE	7 (0.8)
NTRK fusion	1 (0.1)
ROS1 fusion	0 (0)
MSI/MMR status	
MSI-H/dMMR	43 (5.2)
MSS/pMMR	621 (75.2)
Unknown	162 (19.6)

dMMR, deficient mismatch repair; MMR, mismatch repair; MSI, microsatellite instability; MSI-H, high microsatellite instability; MSS, microsatellite stability; pMMR, proficient mismatch repair.
[a]Values presented as N (%).
[b]CRC subjects with unknown biomarker status are 28 (3.4%) for HER2 (amplification) and 161 (19.5%) for POLE.

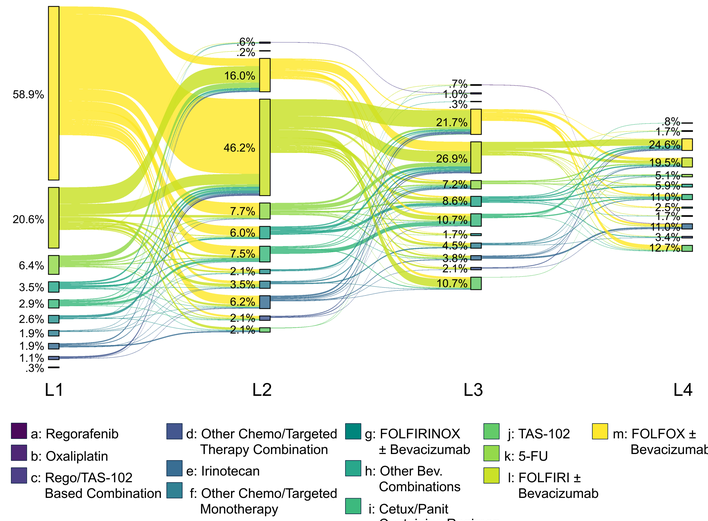
- A majority (88.9%) of subjects received 1L therapy, 63.0% received 2L therapy, 35.1% received 3L, and 14.3% received 4L+ (**Table 3**)
- For 1L, the most commonly used therapy was FOLFOX-based therapy (58.9% of 1L therapy) followed by FOLFIRI-based therapy (20.6% of 1L therapy; **Table 3** and **Figure 2**)
- Increasing usage of TAS-102 monotherapy was observed in later LOTs, increasing from 0.3% in 1L to 12.7% in 4L+

Table 3. Treatment patterns[a]

Class	1L (N = 734)	2L (N = 520)	3L (N = 290)	4L+ (N = 118)
Combination therapy				
FOLFOX ± bevacizumab	432 (58.9)	83 (16.0)	63 (21.7)	29 (24.6)
FOLFIRI ± bevacizumab	151 (20.6)	240 (46.2)	78 (26.9)	23 (19.5)
Other bevacizumab combinations[b]	26 (3.5)	31 (6.0)	25 (8.6)	7 (5.9)
Cetuximab/panitumumab -containing regimen	21 (2.9)	39 (7.5)	31 (10.7)	13 (11.0)
FOLFIRINOX ± bevacizumab	19 (2.6)	11 (2.1)	5 (1.7)	3 (2.5)
5-FU	9 (1.2)	15 (2.9)	4 (1.4)	4 (3.4)
Regorafenib/TAS-102-based combination	–	3 (0.6)	3 (1.0)	1 (0.8)
Other chemotherapy/ targeted therapy combination	8 (1.1)	11 (2.1)	6 (2.1)	4 (3.4)
Monotherapy				
5-FU	38 (5.2)	25 (4.8)	17 (5.9)	2 (1.7)
Irinotecan	12 (1.6)	32 (6.2)	11 (3.8)	13 (11.0)
TAS-102	2 (0.3)	11 (2.1)	31 (10.7)	15 (12.7)
Oxaliplatin	–	–	2 (0.7)	–
Regorafenib	–	1 (0.2)	1 (0.3)	2 (1.7)
Other chemotherapy/ targeted monotherapy	14 (1.9)	18 (3.5)	13 (4.5)	2 (1.7)

[a]Values presented as N (%).
[b]Excludes TAS-102 + Bevacizumab combination therapy.

Figure 2. Sankey diagram, by line-of-therapy



Limitations

- Although data for the current analysis are from real-world data, the study population was based on patients sequenced from one of the four academic centers contributing to the AACR Project GENIE: Biopharma Collaborative and therefore may not be representative of the general mCRC patient population in the United States
- Patients included in the study underwent NGS sequencing between 2015 and 2017 and were followed until the end of 2019. Therefore, treatment patterns reported here may not represent current treatment patterns
- Depending on the time of sample collection for sequencing during the course of disease, biomarker results may not be reflective of the biomarker status of mCRC

Conclusions

- Just over 15% of subjects included in this study have an actionable biomarker (BRAF, MSI-H/dMMR, HER2, NTRK) that could help guide their treatment strategies
- Real-world treatment patterns indicate mCRC patients often use FOLFOX- or FOLFIRI-based therapy with substantial recycling of chemotherapies in relapsed/refractory setting

References

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