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Real-world (RW) sequential regorafenib and trifluridine/tipiracil ± bevacizumab (BEV) treatment for 3L+ metastatic colorectal cancer (mCRC) in the US community oncology setting: A post-hoc analysis of the SEQRT2 study

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BACKGROUND

- In the US, colorectal cancer (CRC) is the third most diagnosed cancer and the second leading cause of cancer-related deaths, with 50%–60% of patients eventually developing metastatic disease (mCRC).[1-4]
- Regorafenib (R) and trifluridine/tipiracil (T) ± bevacizumab (BEV) are both indicated for patients with mCRC who have failed prior standard therapies and have been shown to extend overall survival, but there is no specific guidance on the optimal sequencing.[5,6]
- The SEQRT2 study (NCT04450836) evaluated the sequencing of regorafenib (R) and trifluridine/tipiracil (T) ± bevacizumab (BEV) in patients with metastatic CRC after prior therapies.[7]

RESEARCH OBJECTIVE

- This post hoc analysis of a real-world subgroup from the SEQRT2 study evaluated clinical outcomes and treatment sequencing patterns among patients with metastatic CRC who received regorafenib and trifluridine/tipiracil ± bevacizumab in third- to sixth-line (3L+) therapy within US community oncology practices. Safety information was not collected as part of the study.

METHODS

- **Data Source:** Electronic medical records from The US Oncology Network
- **Study Design:** Retrospective analysis of adult patients with metastatic CRC receiving sequential R and T ± BEV
- **Study Cohort:** Patients receiving R and T ± BEV in third to sixth lines of therapy (LOT 3–6), between 09/01/2015–11/30/2022, with follow-up until 05/31/2023
- **Statistical Analysis:** Treatment patterns and overall survival (OS) assessed by sequence (R-T vs T-R)

Table 1. Characteristics of mCRC patients by treatment

Variable	R – T(± BEV) (n=119)	T(± BEV) – R (n=119)
Treatment Type, n (%)		
R and T only	107 (89.9%)	108 (90.8%)
R and T(+BEV)	12 (10.1%)	11 (9.2%)
Age at baseline, mean (SD)		
Years	64.5 (10.6)	62.4 (10.1)
Sex, n (%)		
Male	63 (52.9%)	70 (58.8%)
Race, n (%)		
Asian	6 (5.0%)	10 (8.4%)
African American	10 (8.4%)	11 (9.2%)
White	81 (68.1%)	76 (63.9%)
Not documented	15 (12.6%)	17 (14.3%)
Initial cancer diagnosis, n (%)		
Colon cancer	78 (65.5%)	88 (74.0%)
Rectal cancer	41 (34.5%)	31 (26.1%)
Stage at initial colorectal cancer diagnosis, n (%)		
≤ II	20 (16.8%)	12 (10.1%)
III	16 (13.4%)	25 (21.0%)
IV	78 (65.5%)	81 (68.1%)
Distant metastatic site, n (%)		
Lymph Node	17 (14.3%)	11 (9.2%)
Liver	79 (66.4%)	79 (66.4%)
Lung	37 (31.1%)	35 (29.4%)
ECOG at baseline (± 30 days from index date), n (%)		
0 -1	75 (63.1%)	71 (59.7%)
2	9(7.6%)	7(5.9%)

Table 2. Sequence duration

Variable	R – T(± BEV) (n=119)	T(± BEV) – R (n=119)
Sequence Duration, months		
Median (Min, Max)	7.0 (1.6, 27.3)	6.4 (0.6, 67.5)
IQR	5.1, 10.0	4.7, 8.7

Figure 1. Overall Survival estimate in 3L+ patients

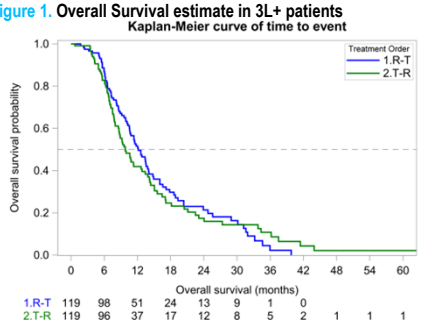

Table 3. Overall Survival outcomes

Variable	R – T(± BEV) (n=119)	T(± BEV) – R (n=119)
Median Survival		
Months (95% CI)	12.2 (10.6,14.0)	9.8 (8.6,12.8)
Survival at 12 Months		
% (95% CI)	51.6% (41.8,60.6)	41.9% (32.4,51.2)
Events		
n (%)	89 (74.8%)	89 (74.8%)

RESULTS

- Among 238 patients with metastatic colorectal cancer receiving third- to sixth-line therapy, R-T and T-R sequences were equally represented; approximately 10% and 9% of patients, respectively, received bevacizumab.
- Baseline characteristics were balanced (mean age 63.5 years; 56% <65; 55% male; 70% colon cancer; ECOG 0–1: 61%).Overall mortality was 74.8% across sequences.
- Median sequence duration was 7.0 months (IQR 5.1–10) for R-T cohort versus 6.4 months (IQR 4.7–8.7) for the reverse.
- Median overall survival and 12-month survival favored R-T (12.2 months, 52%) versus T-R (9.8 months, 42%).

LIMITATIONS

- Retrospective, post hoc design limits causal interpretation of treatment sequencing and outcomes.
- Findings are derived from a subset of patients within The US Oncology Network and may not be fully generalizable.
- Variability in prior lines of therapy and treatment practices could influence observed outcomes.

CONCLUSIONS

- Patients initiating treatment with regorafenib first in the third to sixth line of therapy appeared to have a longer duration of treatment and survival, although not statistically significant.
- The one-year median duration of survival in this real-world setting for the regorafenib followed by trifluridine/tipiracil ± bevacizumab sequence confirms the importance of access to these treatments in patients with metastatic colorectal cancer and can inform physicians regarding the choice of medications while sequencing therapies in metastatic colorectal cancer.

Acknowledgments

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