Treatment pathways and efficacy outcomes of patients with metastatic colorectal cancer (mCRC): a real-world prospective, longitudinal, cohort study (PROMETCO)

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INTRODUCTION

- Data on real-world treatment of metastatic colorectal cancer (mCRC) in third-line (3L) and beyond is limited to specific agents or to a single country.[1,2]
- With recent advances in mCRC therapies, such as trifluridine/tipiracil (FTD/TPI) ± bevacizumab, or fruquintinib, 3L treatment is no longer considered rescue therapy with prolonged survival benefits being observed in clinical trials.[3, 4] However, there is little information on real-world treatment patterns or the impact of these treatment patterns, or other variables, on survival and other outcomes.
- PROMETCO (NCT03935763) is the first international, prospective, real-world study of treatment in patients with mCRC after two disease progressions since diagnosis.

AIMS

To assess real-world treatment patterns and effectiveness in patients with mCRC

METHODS

- Enrolment in PROMETCO started in March 2019 and all eligible patients at recruiting centres were included.[5]
- Inclusion criteria were: ≥18 years of age, confirmed diagnosis of mCRC, two disease progressions, and willingness to receive subsequent treatment.[5]
- Data for lines of therapy (LoTs) were collected retrospectively before two disease progressions and prospectively during follow-up, including effectiveness data.
- Follow-up was regular, but with no fixed schedule, over an 18-month period.
- The 4 most frequently used treatment sequences were identified based on number of patients of each treatment group per line.
- Treatment patterns and median OS from first-line (1L) (mOS; calculated from 1L to remove bias of patients with pre-1L surgery) is presented here.
- A multivariable analysis was carried out from 1L and from inclusion in PROMETCO to assess variables impacting mOS.

TAKE-HOME MESSAGES

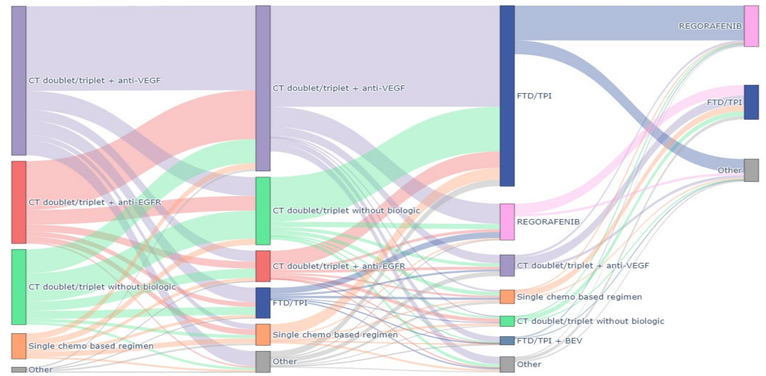
- **Patients received treatment sequences in line with guidelines, with use of chemotherapy (CT) and biologic agents in 1L and 2L, and FTD/TPI in 3L.**
- **Best mOS was observed when patients sequentially received CT + anti-VEGF/anti-EGFR in 1L/2L and 3L FTD/TPI ± bevacizumab, but selection bias cannot be excluded.**
- **Only a few patients received FTD/TPI + bevacizumab due to the timing of this study, however efficacy in these patients was consistent with the results of SUNLIGHT. [3]**
- **PROMETCO results in the real-world setting confirm the use of FTD/TPI monotherapy in 3L, paving the way to the use of FTD/TPI + bevacizumab as the current SOC in the 3L setting as recommended by ESMO guidelines (level [I,A] MCBS 4).**

RESULTS

Treatment pathway

- Overall, 736 patients were included in PROMETCO: 608 patients received ≥3 LoTs, and 400 patients received 3 LoTs and did not proceed to fourth-line (4L) treatment. Treatment sequences according to biomolecular status aligned with recommendations from ESMO.
- The most frequently used treatments at each LoT were 1L chemotherapy (CT) + biologic (505 patients, 68.6%), second-line (2L) chemotherapy (CT) + biologic (418 patients, 58.3%), 3L trifluridine/tipiracil (FTD/TPI) ± bevacizumab (402 patients, 66.1%), and 4L regorafenib (87 patients, 41.8%) (**Figure 1**).

Figure 1: Sankey diagram showing first 4 lines of treatment



*Analysis of 717/736 patients with ≥2 LoTs. Other: grouping treatment categories with fewer than 10 patients. Abbreviations: FTD/TPI + BEV, trifluridine/tipiracil + bevacizumab; n, number; CT, chemotherapy; VEGF, vascular endothelial growth factor; EGFR, epidermal growth factor receptor; 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line.

Overall survival

- Use of CT and biologic agents in 1L and 2L, followed by FTD/TPI ± bevacizumab in 3L, led to a mOS from 1L of >23 months, and mOS was lower when a biologic was not used in 1L/2L (**Table 1**).
- In patients who received 4L treatment, most patients received CT and biologics in 1L/2L, 3L FTD/TPI ± bevacizumab, and 4L regorafenib, and these patients had a mOS of 29.9 months (anti-vascular endothelial growth factor (VEGF) twice in 1L/2L) and 34.7 months (anti-VEGF + anti-epidermal growth factor receptor (EGFR) in 1L/2L) (**Table 1**).

Table 1: Overall survival by treatment sequence from first-line in patients who received 3 or 4 lines of treatment

Treatment pathway	Patients (n)	mOS (95% CI)
Treatment pathway in patients with 3 lines of therapy		
1L/2L doublet/triplet CT + **anti-VEGF** → 3L **FTD/TPI ± BEV**	90	23.8 (21.6–28.6)
1L/2L CT + **anti-EGFR**/CT + **anti-VEGF** (any order) → 3L **FTD/TPI ± BEV**	60	28.6 (26.4–37.9)
1L/2L doublet/triplet CT without biologic → 3L **FTD/TPI ± BEV**	40	20.6 (15.7–24.7)
1L/2L/3L at least one immunotherapy / targeted therapy	13	23.8 (20.4–NR)
Doublet/triplet CT + **anti-VEGF** only once → **FTD/TPI ± BEV** (2L or 3L) after 'doublet/triplet CT + anti-VEGF' And not in groups 1-4	62	34.8 (27.2-43.9)
All other treatment pathways with at least three LoTs	135	30.7 (26.6–35.9)
Treatment pathway in patients with 4 lines of therapy		
1L/2L doublet/triplet CT + **anti-VEGF** → 3L **FTD/TPI ± BEV** → 4L **regorafenib**	35	29.9 (24.0–43.1)
1L/2L CT + **anti-EGFR**/CT + **anti-VEGF** (any order) → 3L **FTD/TPI ± BEV** → 4L **regorafenib**	16	34.7 (31.0–40.9)
1L/2L/3L/4L at least one **immunotherapy / targeted therapy**	9	26.8 (16.5–NR)
Doublet/triplet CT + **anti-VEGF** prior to '**FTD/TPI** (at 2L, 3L, or 4L)' Not included in groups 6–8	48	39.7 (31.9–46.9)
Any patient who received four LoTs and is not included in groups 6–9	58	33.9 (31.6–38.4)

Abbreviations: mOS, median overall survival; CI, confidence interval; FTD/TPI ± BEV, trifluridine/tipiracil + bevacizumab; n, number; CT chemotherapy; VEGF vascular endothelial growth factor; EGFR, epidermal growth factor receptor; NR, not reached; 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line.

Focus on patients treated with FTD/TPI + bevacizumab

- 23 patients were treated with FTD/TPI + bevacizumab in the PROMETCO study, and of these, 1 patient received FTD/TPI + bevacizumab as 2L therapy, 18 patients received it as 3L therapy, and 5 patients received it as 4L therapy.
- Due to the timing of the study only 4.1% of patients received FTD/TPI + bevacizumab, however efficacy outcomes in these patients were consistent with the SUNLIGHT trial.[3]
- Median (95% confidence interval [CI]) progression-free survival and OS from diagnosis was 2.89 (1.64–3.78) months and 39.1 (27.2–75.1) months, respectively. Median OS (95% CI) from PROMETCO inclusion was 13.6 (7.43-21.2) months.

Multivariable analysis

- Being fitter and having a lower disease burden (Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0-1, good prognosis characteristics (GPCs), and Microsatellite Stability (MSS)) led to a significantly increased OS after two progressions of disease (**Table 2**).
- Other factors that led to significantly improved OS from PROMETCO inclusion were having surgery and being more than 65 years old (**Table 2**). Time since diagnosis, and tumor sidedness (left or right) did not influence OS from PROMETCO inclusion.

Table 2: Multivariable analysis of factors influencing overall survival from PROMETCO inclusion

Characteristic	n (%)	HR (multivariable) (95% CI, p)
Age		
<65 years	223 (40.0)	-
≥65 years	335 (60.0)	0.71 (0.56-0.90, p=0.005)
ECOG PS		
0/1	504 (92.6)	-
≥2	40 (7.4)	2.31 (1.53-3.47, p<0.001)
Prognostic sub-group*		
GPC	330 (59.1)	-
PPC	228 (40.9)	1.68 (1.30-2.16, p<0.001)
MSI status		
MSI-high	9 (2.7)	-
MSS	326 (97.3)	0.39 (0.19-0.79, p=0.009)
Surgery		
No	185 (33.2)	-
Yes**	373 (66.8)	0.64 (0.50-0.83, p=0.001)

Abbreviations: HR, hazard ratio; MSI, microsatellite instability; MSS, microsatellite stable; ECOG PS, eastern cooperative oncology group performance status; GPC, good prognosis characteristics; PPC, poor prognosis characteristics; CI, confidence interval.
*Good prognosis characteristics [GPC], defined as having <3 metastatic sites at study entry and ≥18 months from diagnosis of metastatic disease to study entry, best prognosis characteristics and the remaining patients had poor prognosis characteristics [PPC].[6] **At least one colorectal, liver or lung surgery

- For OS from 1L, as expected, having surgery, being ECOG PS 0-1, and having GPCs were positive prognostic factors and significantly increased OS (**Table 3**).
- Having a longer time since diagnosis positively and significantly impacted OS from 1L but not after two progressions of disease.

Table 3: Multivariable analysis of factors influencing overall survival from first-line

Characteristic	n (%)	HR (multivariable) (95% CI, p)
Time since diagnosis at baseline (5 months change), months	6.5 (5.0)*	0.85 (0.82-0.87, p<0.001)
ECOG PS		
0/1	504 (92.6)	-
≥2	40 (7.4)	2.22 (1.58-3.12, p<0.001)
Prognostic sub-group*		
GPC	330 (59.1)	-
PPC	228 (40.9)	4.73 (3.62-6.18, p<0.001)
Surgery		
No	185 (33.2)	-
Yes**	373 (66.8)	0.74 (0.60-0.91, p=0.005)

Abbreviations: HR, hazard ratio; MSI, microsatellite instability; MSS, microsatellite stable; ECOG PS, eastern cooperative oncology group performance status; GPC, good prognosis characteristics; PPC, poor prognosis characteristics; CI, confidence interval.
*Reported as mean (SD), not n (%); *Good prognosis characteristics [GPC], defined as having <3 metastatic sites at study entry and ≥18 months from diagnosis of metastatic disease to study entry, best prognosis characteristics and the remaining patients had poor prognosis characteristics [PPC].[6]; **At least one colorectal, liver or lung surgery

References

1. Taieb J, Price T, Vidot L, et al. BMC Cancer. 2023;23(1): 94.
2. Weiss L, Karthaus M, Rierà-Knorrenschild J, et al. ESMO Open. 2022;7(1): 100391.
3. Prager GW, Taieb J, Fakih M, et al. N Engl J Med. 2023;388(18):1657-67.
4. Dasari A, Lonardi S, Garcia-Carbonero R, et al. The Lancet. 2023;402(10395): 41-53.
5. Koopman M, Pinto C, Bodoky G, et al. Future Oncol. 2022;18(11):1313-1320.
6. Tabernero J, Argiles G, Sobrero AF, et al. ESMO Open. 2020;5(4).

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