OVERALL AND PROGRESSION-FREE SURVIVAL OF PATIENTS WITH METASTATIC COLORECTAL CANCER: A REAL-WORLD PROSPECTIVE, LONGITUDINAL COHORT STUDY ON THE CONTINUUM OF CARE (PROMETCO)

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INTRODUCTION

- The primary treatment goal for patients with unresectable metastatic colorectal cancer (mCRC) is tumour shrinkage and disease control with preservation or improvement of quality of life[1]
- Clinical emphasis lies in avoidance of rapid disease evolution, and prolonging survival[1]
- Advances in mCRC treatment have now improved median overall survival (OS) to 30 months in clinical trials[1]
- PROMETCO (NCT03935763) is the first international, prospective real-world study to investigate the continuum of care in the mCRC patient population, collecting data on all patients with two disease progressions, regardless of treatment or age

AIMS

- To present preliminary real-world clinical characteristics and treatment patterns of 738 patients with mCRC that have progressed twice on previous treatment
- To show OS and progression-free survival (PFS) of the 655/738 mCRC patients that have completed the study

METHODS

- Enrolment in PROMETCO started in March 2019:
  - **Inclusion criteria**: adult patients with two disease progressions since the first diagnosis of mCRC, who were willing to receive subsequent treatment, were included
  - **Exclusion criteria**: patients enrolled in other clinical trials, receiving treatment for other cancers or those with reduced mental capacity were excluded
- At enrolment, patient data such as clinical characteristics, medical history and treatment from first mCRC diagnosis were collected retrospectively using electronic case report forms and the ClinInfo electronic data capture system[2]
- Patients were assessed prospectively for up to 18 months or until withdrawal or death
- Kaplan-Meier calculations were used for analysis of OS and PFS in the 655 mCRC patients that had completed the study

TAKE-HOME MESSAGES

- **These data describing patient characteristics, survival and treatment patterns in the real world, are consistent with clinical trial observations and current ESMO guidelines**
- **In this well-defined cohort of patients who have had two progressions of disease before inclusion in PROMETCO, median OS was 36.4 months**
- **Recent clinical trial data suggest that further improvements in OS compared to those observed in PROMETCO are possible with third-line combination therapy[3]**
- **The difference in duration between mCRC diagnosis and PROMETCO inclusion, and treatment before PROMETCO inclusion, suggests the use of treatment breaks in the real world**

RESULTS

Baseline characteristics

- For this analysis, baseline characteristics from 738 mCRC patients from 18 countries were collected (**Table 1**)
- Median total duration under treatment before PROMETCO inclusion was 13.2 (minimum 0.5, maximum 101.6) months, while median time between mCRC diagnosis and inclusion was 22.3 (minimum 3.4, maximum 214.9)

Table 1. Baseline characteristics

Age, years	
Median (min, max)	67.0 (31.0, 87.0)
Sex, n (%)	
Female / male	302 / 433 (41.1 / 58.9)
ECOG PS¶, %	
0-1	92.3
Time between mCRC diagnosis and PROMETCO inclusion (months)	
Median (min, max)	22.3 (3.4, 214.9)
Total duration under treatment before PROMETCO inclusion (months)	
Median (min, max)	13.2 (0.5, 101.6)
Number of metastatic sites, n (%)‡	
<3 / ≥3	659 (89.8) / 75 (10.2)
Type of metastasis, n (%)	
Synchronous / metachronous	480 (65.3) / 255 (34.7)
Disease sidedness, n (%)¥	
Left (descending colon/sigmoid colon)	311 (42.4)
Right (cecum + ascending colon/transverse colon)	207 (28.2)
Rectum	262 (35.7)
RAS/BRAF* status, n (%)	
RAS mut	361 (48.9)
BRAF mut	37 (5.0)
RAS/BRAF WT	236 (32.0)
Unknown	95 (12.9)
MSI/MSS status, n (%)	
MSI high	12 (1.6)
MSI low	26 (3.5)
MSS	405 (54.9)
Unknown	295 (40.0)
Distribution of metastatic sites, n (%)	
Liver	541 (73.3)
Lung	285 (38.6)
Peritoneal carcinosis	105 (14.2)
Bone	29 (3.9)
Adrenal gland	22 (3.0)
Other$^{\alpha}$	159 (21.4)

¶Percentage based on n observed per group (i.e., not including ND values; n=716); ‡n=734 due to missing data; *9 patients had RAS & BRAF mutations; α, brain and skin metastases included in 'other'; **Abbreviations**: ECOG PS, Eastern Cooperative Oncology Group performance status; max, maximum; mCRC, metastatic colorectal cancer; min, minimum; MSI, microsatellite instability; MSS, microsatellite stable; mut, mutant; WT, wild-type.

Treatment/surgery during treatment pathway

- Most patients were exposed to fluoropyrimidine (98.5%), irinotecan (96.2%), oxaliplatin (88.4%), anti-VEGF therapy (78.7%) and trifluridine/tipuracil (75.2%) between mCRC diagnosis until death or withdrawal from the study (**Table 2**)
- 64.6% of the patients had colorectal surgery, and 22.9% had liver surgery

Table 2. Treatment/surgery during treatment pathway

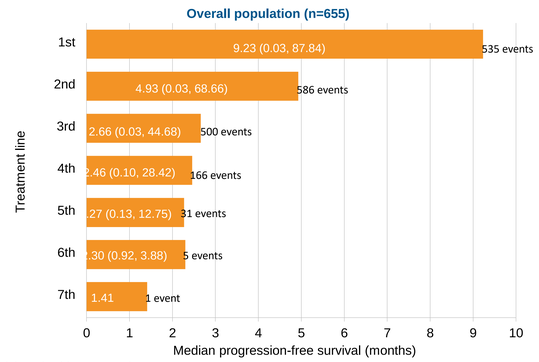
All therapies for mCRC, n (%)	
Fluoropyrimidine (5-FU or capecitabine or tegafur)	727 (98.5)
Irinotecan	706 (96.2)
Oxaliplatin	649 (88.4)
Anti-VEGF (bevacizumab, aflibercept, ramucirumab)	578 (78.7)
Anti-EGFR (panitumumab or cetuximab)	294 (40.1)
FTD/TPI	552 (75.2)
Immunotherapy$^{\theta}$	30 (4.1)*
Regorafenib	186 (25.3)
All surgeries for mCRC, n (%)	
Colorectal surgery	474 (64.6)
Liver surgery	168 (22.9)
Lung surgery	37 (5.0)

θ pembrolizumab, nivolumab, avelumab, atezolizumab or encorafenib + cetuximab; * to be confirmed; **Abbreviations**: 5-FU, fluorouracil; EGFR, epidermal growth factor receptor; FTD/TPI, trifluridine/tipiracil; mCRC, metastatic colorectal cancer; VEGF, vascular endothelial growth factor.

PFS

- 655/738 of the mCRC patients enrolled in PROMETCO completed the study and were included in subsequent survival analyses
- A range of 0.03-87.84 months PFS was seen across seven treatment lines
- As expected, the median PFS decreased significantly from 1st treatment line (9.23 months [95% CI: 8.61;10.15]) to 7th treatment line (1.41 months [95% CI: not calculable]) (**Figure 1**)
- The PFS was similar between the third- and sixth-line treatment, ranging between 2.27 and 2.66 months

Figure 1. Median (min, max) PFS in patients at each line of treatment

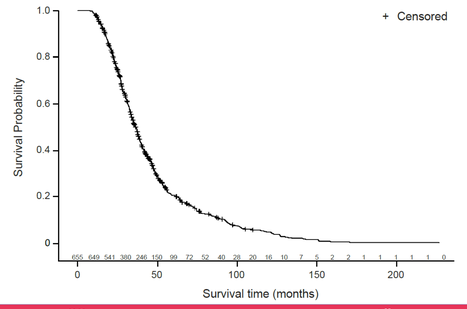


Abbreviations: min, minimum; max, maximum
Progression free survival definition: Start, start date of treatment line; End, Event (date of PD)/Event (date of death)/Censor (end of line of treatment)/Censor (end of line of treatment)/Censor (end of last available day)

OS from mCRC diagnosis

- OS was calculated for patients from mCRC diagnosis to the end of the study (**Figure 2**)
- The median OS from mCRC diagnosis was 36.4 months (95% CI: 33.7-37.8), which is higher than the median OS seen in clinical trials[1]

Figure 2. OS in patients with mCRC from diagnosis to the end of the study



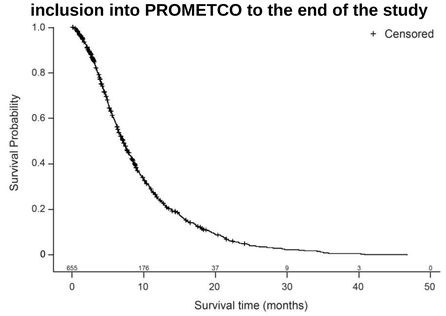
OS	All
Event, n (%)	550 (84)
Censored, n (%)	105 (16)
Median (95% CI), months	**36.4** (33.7-37.8)
Min, max, months	7.8, 226.9

N=655. **Abbreviations**: CI, confidence interval; min, minimum; max, maximum; OS, overall survival

OS from inclusion into PROMETCO

- OS was calculated for patients from inclusion into PROMETCO, i.e., after second disease progression, to the end of the study (**Figure 3**)
- The median OS from second disease progression was 7.06 months (95% CI: 6.5-7.6)

Figure 3. OS in patients with mCRC from second disease progression and inclusion into PROMETCO to the end of the study



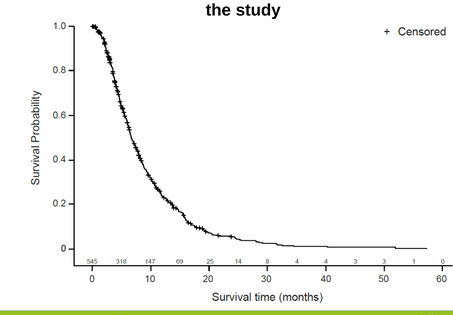
OS	All
Event, n (%)	550 (84)
Censored, n (%)	105 (16)
Median (95% CI), months	**7.06** (6.5-7.6)
Min, max, months	0.1, 46.6

N=655. **Abbreviations:** CI, confidence interval; min, minimum; max, maximum; OS, overall survival

OS from 3rd treatment line

- OS was calculated for patients from the start of third-line treatment to the end of the study (**Figure 4**)
- The median OS after starting third-line therapy was 6.64 months (95% CI: 6.2-7.4), which is shorter than the median OS from inclusion in PROMETCO, reflecting the time difference between second progression and the start of third-line treatment

Figure 4. OS in patients with mCRC from third treatment line to the end of the study



OS	All
Event, n (%)	446 (86)
Censored, n (%)	79 (14)
Median (95% CI), months	**6.64** (6.2-7.4)
Min, max, months	0.1, 46.6

N=655. **Abbreviations**: CI, confidence interval; min, minimum; max, maximum; OS, overall survival

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