Real-World Data on Overall and Progression-Free Survival for Patients (Pts) with Metastatic Colorectal Cancer (mCRC) for the United Kingdom (UK) Cohort of the PROMETCO Study (PROMETCO UK)

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INTRODUCTION

- Bowel cancer is the 4th most common cancer in the UK.[1] Treatment advances have now improved median overall survival (OS) in metastatic colorectal cancer (mCRC) to 30 months in clinical trials.[2,3]
- However, there is limited real-world evidence describing this population.
- 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.[4]
- The UK was the 4th largest recruiting country for the PROMETCO study and here we present the results for the UK cohort (PROMETCO UK).

AIMS

- To present preliminary real-world clinical characteristics and treatment patterns of 76 patients from the PROMETCO UK cohort with mCRC that have progressed twice on previous treatment.
- To show OS and progression-free survival (PFS) of the 68/76 (89%) mCRC patients that have completed the study by July 2023 (data cut-off).

METHODS

- Enrolment in PROMETCO UK took place between 19th October 2019 and 31st October 2022:
  - **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.
- Patients were assessed prospectively for up to 18 months or until withdrawal or death.
- Kaplan-Meier calculations were used for interim analysis of OS and PFS in the 68 mCRC patients that had completed the study.

TAKE-HOME MESSAGES

- **This first prospective real-world study, describing patient characteristics, survival and treatment patterns, gives us a snapshot of clinical practice in the UK during the recruitment period.**
- **In this well-defined cohort of patients who have had two progressions of disease before inclusion in PROMETCO UK, median OS was 36.47 months. These data demonstrate that the OS outcomes in the UK are comparable to the rest of recruiting countries within the study.[5]**
- **Although the treatment algorithms are in keeping with accepted international guidelines, they do reflect the funding restrictions within the National Health Service (NHS) for some drugs such as bevacizumab.**
- **National Institute for Health and Care Excellence (NICE) guidance now recommends that all patients with mCRC suitable for systemic anti-cancer therapy (SACT), are tested for *RAS* and *BRAF* mutations, including mismatch repair/microsatellite instability status, to guide clinical treatment. The molecular analysis results demonstrate the gradual adoption of testing across the UK and the lack of initial funding availability for immunotherapy in the early stages of this study.[6,7]**
- **The authors acknowledge that the data are representative of patients able to reach third-line.**
- **Since recruitment within this study, the treatment landscape has evolved and will continue to do so in terms of availability, funding and, as a consequence, additional sequencing options.**

RESULTS

Baseline characteristics

- For this analysis, baseline characteristics from 76 mCRC patients from 10 UK hospitals were collected (**Table 1**).
- Median total duration under treatment before PROMETCO UK inclusion was 11.8 (minimum 1.6, maximum 89.5) months, while median time between mCRC diagnosis and inclusion was 21.6 (minimum 6.2, maximum 92.4) months.

Table 1. Baseline characteristics

Age, years	
Median (min, max)	65.0 (39.0, 86.0)
Sex, n (%)	
Female / male	30 (39.5) / 46 (60.5)
ECOG PS¶, n (%)	
0	21 (27.6)
1	50 (65.8)
2	5 (6.6)
Time between mCRC diagnosis and PROMETCO inclusion (months)	
Median (min, max)	21.6 (6.2, 92.4)
Total duration under treatment before PROMETCO inclusion (months)	
Median (min, max)	11.8 (1.6, 89.5)
Number of metastatic sites, n (%)	
<3 / ≥3	70 (92.1) / 6 (7.9)
Type of metastasis, n (%)	
Synchronous / metachronous	46 (60.5) / 30 (39.5)
Disease sidedness, n (%)¥	
Left (descending colon/sigmoid colon)	35 (46.1)
Right (cecum + ascending colon/transverse colon)	15 (19.7)
Rectum	32 (42.1)
***RAS/BRAF* status, n (%)**	
RAS mut	30 (39.5)
BRAF mut	5 (6.6)
RAS/BRAF WT	26 (34.2)
Unknown	15 (19.7)
MSI/MSS status, n (%)	
MSI high	1 (1.3)
MSI low	7 (9.2)
MSS	23 (30.3)
Unknown	45 (59.2)
Distribution of metastatic sites, n (%)	
Liver	56 (73.7)
Lung	31 (40.8)
Peritoneal carcinosis	5 (6.6)
Bone	5 (6.6)
Adrenal gland	1 (1.3)
Other[α]	15 (19.7)

¶ Percentage based on n observed per group; ¥ patients can be in more than 1 group; 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

- During their treatment, patients received fluoropyrimidine (98.7%), irinotecan (98.7%), oxaliplatin (81.6%), anti-vascular endothelial growth factor (VEGF) therapy (2.6%) and trifluridine/tipiracil (85.5%) between mCRC diagnosis until death or withdrawal from the study (**Table 2**).
- 60.5% of the patients had colorectal surgery and 22.4% had liver surgery.

Table 2. Treatment/surgery during treatment pathway

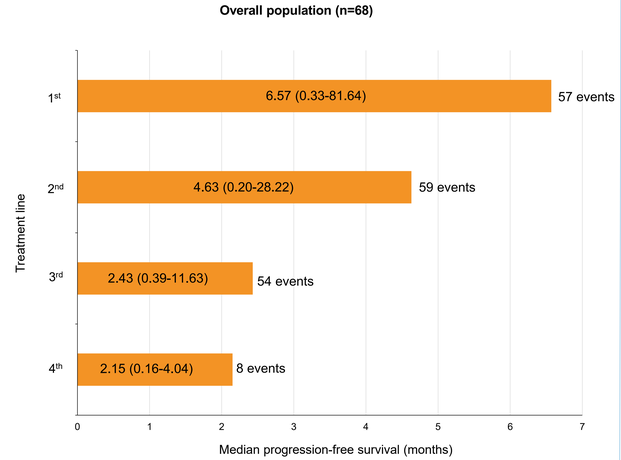
All therapies for mCRC, n (%)	
Fluoropyrimidine (5-FU or capecitabine or tegafur)	75 (98.7)
Irinotecan	75 (98.7)
Oxaliplatin	62 (81.6)
Anti-VEGF (bevacizumab, aflibercept, ramucirumab)	2 (2.6)
Anti-EGFR (panitumumab or cetuximab)	34 (44.7)
FTD/TPI	65 (85.5)
Immunotherapy (nivolumab)	1 (1.3)
Regorafenib	1 (1.3)
All surgeries for mCRC, n (%)	
Colorectal surgery	46 (60.5)
Liver surgery	17 (22.4)
Lung surgery	6 (7.9)

Abbreviations: 5-FU, fluorouracil; EGFR, epidermal growth factor receptor; FTD/TPI, trifluridine/tipiracil; mCRC, metastatic colorectal cancer; VEGF, vascular endothelial growth factor.

PFS

- 59/68 of the mCRC patients enrolled in PROMETCO UK completed the study.
- A range of 0.16-81.64 months PFS was seen across the four treatment lines.

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

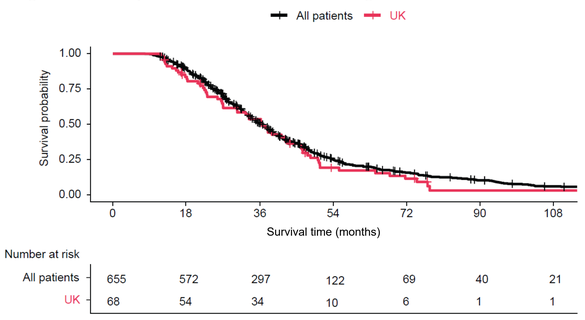


Progression free survival (PFS) definition: Start, start date of treatment line; End, Event (date of PD)/Event (date of death)/Censor (end of line of treatment)/Censor (end of line of treatment)/Censor (end of last available day). **Abbreviations:** min, minimum; max, maximum.

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 36.5 months (95% CI: 26.94-42.15), which is similar to the main PROMETCO study cohort of 36.4 months (95% CI: 33.7-37.8), and higher than the median OS seen in clinical trials.[2,5]

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



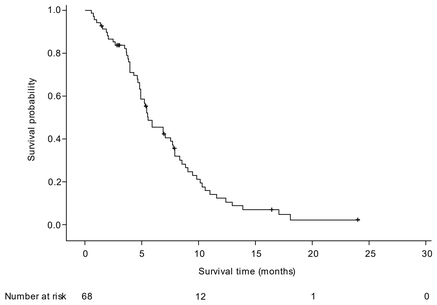
OS	All
Event, n (%)	59 (87.0)
Censored, n (%)	9 (7.5)
Median (95% CI), months	**36.5** (26.94-42.15)
Min-max, months	11.66-151.25

N=68. **Abbreviations**: CI, confidence interval; min, minimum; max, maximum; OS, overall survival

OS from inclusion into PROMETCO UK

- OS was calculated for patients from inclusion into PROMETCO UK, i.e., after second disease progression, to the end of the study (**Figure 3**).
- The median OS from second disease progression was 5.52 months (95% CI: 4.89-7.69).

Figure 3. OS in patients with mCRC from inclusion in PROMETCO UK to the end of the study



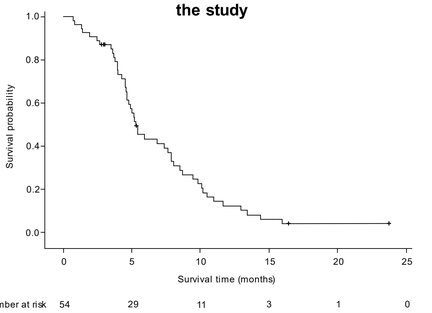
OS	All
Event, n (%)	59 (87.0)
Censored, n (%)	9 (7.5)
Median (95% CI), months	**5.52** (4.89-7.69)
Min-max, months	0.56-23.95

N=68. **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 5.29 months (95% CI: 4.66-7.88), which is shorter than the median OS of 5.52 months (95% CI: 4.89-7.69) from inclusion in PROMETCO UK, 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 (%)	48 (70.6)
Censored, n (%)	6 (9)
Median (95% CI), months	**5.29** (4.66-7.88)
Min-max, months	0.72-23.72

N=54. **Abbreviations**: CI, confidence interval; min, minimum; max, maximum; OS, overall survival

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