PROMETCO: real-world characteristics and safety outcomes of patients with metastatic colorectal cancer (mCRC) after two disease progressions, including patients with ECOG PS ≥2

[1]Rocio Garcia-Carbonero, [2]Jean-Baptiste Bachet, [3]Carmine Pinto, [4]György Bodoky, [5]Kalena Marti, [6]Andrey Mitroshkin, [7]Tomas Buchler, [8]Patrick Stuebs, [9]Ana Maria Lopez Munoz, [10]Rakesh Raman, [11]Elias Choucair, [11]Bénédicte Chevallier, [12]Jessica Azzi, [13]Adam Sullivan, [14]Miriam Koopman

[1]Oncology Department, Hospital Universitario Doce de Octubre, Imas12, Facultad y Departamento de Medicina, Universidad Complutense de Madrid (UCM), Avenida De Córdoba s/n, 28041 Madrid, Spain. [2]Sorbonne Université, Service d'hépato-Gastro-Entérologie, Groupe Hospitalier Pitié Salpêtrière, APHP, Paris, France. [3]Medical Oncology, Comprehensive Cancer Centre, AUSL – IRCCS di Reggio Emilia – Viale Risorgimento, 80 42123 Reggio Emilia, Italy. [4]Dél-Pesti Centrumkórház Szent László Telephely Albert Flórián út 5–7 1097 Budapest, Hungary. [5]Department of Medical Oncology, The Christie NHS Foundation Trust, Wilmslow Road, Manchester, M20 4BX, UK. [6]Klinikum Freudenstadt, Akademisches Lehrkrankenhaus der Universität Tübingen, Karl-von-Hahn-Strasse, 100, 72250 Freudenstadt, Germany. [7]Department of Oncology, First Faculty of Medicine, Charles University and Thomayer University Hospital, Videnska 800, 140 59 Prague, Czech Republic. [8]DRK Kliniken Berlin Köpenick, Salvador-Allende-Straße 2 – 8, 12559 Berlin. [9]Oncology Department, Hospital Universitario de Burgos, Avenida Islas Baleares 3, 09006. Burgos, Spain. [10]Kent Oncology Centre, Kent, UK. [11]Servier, 35 rue Verdun, 92284 Suresnes, France. [12]Institut de Recherches Internationales Servier, Gif-sur-yvette, France. [13]Servier Pharmaceuticals, 200 Pier 4 Blvd, Boston, MA 02210, USA. [14]Department of Medical Oncology, University Medical Centre Utrecht, Utrecht University Heidelberglaan 100 3584 CX Utrecht, the Netherlands

Presented at ESMO-GI Congress,
July 2-5, 2025
Barcelona, Spain

Final publication number: 64P

INTRODUCTION

- Median overall survival (OS) for patients with metastatic colorectal cancer (mCRC) has been improved to 30 months in clinical trials[1] and data on third-line and beyond treatments suggest OS can be prolonged further.[2,3]
- Data on real-world treatment of mCRC in third-line and beyond is available; however, studies with a follow-up of recruited patients were limited to specific agents or to a single country.
- PROMETCO (NCT03935763) is the first international, prospective, real-world study of treatment in patients with mCRC after two disease progressions since diagnosis.
- PROMETCO provides an opportunity to assess safety outcomes at third-line treatment and beyond in the real-world setting.

METHODS

- Enrolment in PROMETCO started in March 2019 and all eligible patients at recruiting centres were included. Inclusion/exclusion criteria have been described previously.[4]
- Inclusion criteria were: ≥18 years of age, confirmed diagnosis of mCRC, two disease progressions, and willingness to receive subsequent treatment.
- Electronic case report forms and the ClinInfo electronic data capture system[4] were used to collect retrospective data for all patients at enrolment.
- Patients were then assessed prospectively for up to 18 months or until withdrawal or death.
- Data were analysed in the overall population and in the subgroup of patients with the most frequently administered treatment schedule (FTD/TPI mainly in monotherapy, before FTD/TPI + bevacizumab was recognized as standard of care in third-line)
- Data were also stratified by Eastern Cooperative Oncology Group performance status (ECOG PS) at FTD/TPI initiation (0-1 or ≥2).
- Baseline data at diagnosis, including patient and disease characteristics, and safety data, including adverse events (AEs) are presented here. Disease progression was presented as an AE.

TAKE-HOME MESSAGES

- **Safety outcomes in the real-world were consistent with expected outcomes for patients with refractory mCRC.**
- **No new safety signals were observed in patients treated with FTD/TPI (the most frequent 3L treatment). Less neutropenia was observed in this real-world population compared to clinical trials.**
- **Patients with an ECOG PS ≥2 at FTD/TPI initiation showed a safety profile consistent with the known safety profile of FTD/TPI.**
- **The high incidence of anaemia observed in FTD/TPI-treated patients with ECOG PS ≥2 can likely be explained by older age and more advanced disease.**

RESULTS

Patient and disease characteristics at baseline

- 736 patients from 18 countries were included in this analysis, most patients (59.0%) were ≥65 years old, most had ECOG PS 0-1 (89.9%), 65.5% of patients had synchronous disease, and median time since first metastasis was 22 months.
- In the total population, 560 patients received FTD/TPI, of whom 469 had ECOG PS 0-1, 50 had ECOG PS ≥2 at FTD/TPI initiation, and ECOG PS for 41 patients was not recorded.
- Patients with ECOG PS ≥2 at FTD/TPI initiation were older and were more likely to have a right-sided primary tumour, had a numerically higher median number of metastases, and were more likely to have metastases located in the liver, than FTD/TPI-treated patients with ECOG PS 0-1 (**Table 1**).

Table 1. Patient and disease characteristics at PROMETCO enrolment

Baseline characteristic	Overall (n=736)	FTD/TPI* (n=560)	FTD/TPI ECOG PS 0-1 (n=469)	FTD/TPI ECOG PS ≥2 (n=50)
Age, years, n (%)				
Mean (SD)	65.9 (10.7)	65.9 (10.5)	65.9 (10.4)	68.9 (9.5)
Sex, n (%)				
Female	303 (41.2)	229 (40.9)	191 (40.7)	22 (44.0)
Male	433 (58.8)	331 (59.1)	278 (59.3)	28 (56.0)
Number of metastatic sites, n (%)				
Median (Q1-Q3)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-3.0)
Time since CRC initial diagnosis to enrollment, months				
Median (Q1-Q3)	25.0 (17.0-40.0)	25.0 (17.0-40.0)	24.0 (17.0-40.0)	26.0 (16.0-47.0)
CRC stage at initial diagnosis, n (%)				
Localized or resectable	183 (24.9)	146 (26.1)	127 (27.1)	9 (18.0)
Locally advanced or potentially resectable disease after downsizing	71 (9.6)	53 (9.5)	39 (8.3)	7 (14.0)
Metastatic or non-resectable	482 (65.5)	361 (64.5)	303 (64.6)	34 (68.0)
Metastatic site location, n (%)				
Liver	545 (74.0)	426 (76.1)	353 (75.3)	42 (84.0)
Lung	187 (39.0)	230 (41.1)	186 (39.7)	27 (54.0)
Peritoneal carcinomatosis	106 (14.4)	69 (12.3)	53 (11.3)	9 (18.0)
Bone	29 (3.9)	23 (4.1)	16 (3.4)	6 (12.0)
Disease sidedness, n (%)				
Left	535 (72.7)	413 (73.8)	353 (75.3)	31 (62.0)
Right	207 (28.1)	151 (27.0)	120 (25.6)	19 (38.0)
***RAS/BRAF* status, n (%)**				
RAS mut	370 (50.3)	302 (53.9)	259 (55.2)	23 (46.0)
RAS wild-type	296 (40.2)	207 (37.0)	171 (36.5)	17 (34.0)
BRAF mut	47 (6.4)	29 (5.2)	25 (5.3)	3 (6.0)
BRAF wild-type	464 (63.0)	355 (63.4)	297 (63.3)	28 (56.0)
MSI/MSS status, n (%)				
MSI high	12 (1.6)	6 (1.1)	4 (0.9)	1 (2.0)
MSS	405 (55.0)	297 (53.0)	243 (51.8)	30 (60.0)

*All patient's who received FTD/TPI (± bevacizumab) at least once. Abbreviations: FTD/TPI, trifluridine/tipiracil: SD, standard deviation: CRC, colorectal cancer: Q, quartile: MSI, microsatellite instability: MSS, microsatellite stable: *RAS*, rat sarcoma: *BRAF*, B-Raf proto-oncogene, serine/threonine kinase.

Summary of AEs

- Most patients experienced at least one AE during follow-up, with 96.1% and 97.3% of patients experiencing AEs in the overall and FTD/TPI populations, respectively (**Table 2**).

Table 2. AEs in the overall population and in patients who received FTD/TPI

	Overall (N=736)	FTD/TPI* (n=560)
Any AE, n (%)	707 (96.1)	545 (97.3)
Any grade ≥3 AE, n (%)	640 (87.0)	504 (90.0)
Any serious AE**, n (%)	602 (81.8)	471 (84.1)
AE with causal relationship with FTD/TPI, n (%)	282 (38.3)	282 (50.4)
Grade ≥3 AE with causal relationship with FTD/TPI, n (%)	126 (17.1)	126 (22.5)
Serious AE with causal relationship with FTD/TPI, n (%)	35 (4.8)	35 (6.3)
AE with causal relationship with another medicinal product, n (%)	280 (38.0)	189 (33.8)
Grade ≥3 AE with causal relationship with another medicinal product, n (%)	69 (9.4)	49 (8.8)
Serious AE with causal relationship with another medicinal product, n (%)	25 (3.4)	19 (3.4)

*All patient's who received FTD/TPI (± bevacizumab) at least once. **Defined as a medical occurrence that results in death, is life-threatening, requires hospitalization, causes significant disability, leads to a birth defect, or necessitates medical intervention to prevent serious outcomes. Abbreviations: FTD/TPI, trifluridine/tipiracil: N, number of patients: AE, adverse event.

- The most frequently reported AEs were disease progression (reported as an AE), diarrhoea, fatigue, nausea, anaemia, asthenia, and neutropenia (**Table 3**).

Table 3. Most frequently occurring AEs overall

	Overall (N=736)	
	Any AE	Serious AE
Patients with any AE	707 (96.1)	602 (81.8)
Haematologic		
Neutropenia*	165 (22.4)	15 (2.0)
Anaemia	159 (21.6)	12 (1.6)
Non-haematologic		
Disease progression	426 (57.9)	420 (57.1)
Fatigue	181 (24.6)	0 (0.0)
Nausea	179 (24.3)	7 (1.0)
Diarrhoea	189 (25.7)	7 (1.0)
Asthenia	160 (21.7)	9 (1.2)
Decreased appetite	140 (19.0)	0 (0.0)
Abdominal pain	119 (16.2)	16 (2.2)
Vomiting	101 (13.7)	11 (1.5)

*Some patients may have received granulocyte colony-stimulating factor (G-CSF), however G-CSF prophylaxis was not recorded in the electronic case report form.
Abbreviations: N, number of patients: AE, adverse event.

AEs in patients treated with FTD/TPI according to ECOG PS

- Patients with ECOG PS ≥2 had a numerically higher incidence of AEs during FTD/TPI treatment and within 30 days after, compared to patients with ECOG PS 0-1 (**Table 4**), in alignment with previous studies in solid tumours that indicated that a poorer performance status is associated with an increased likelihood of experiencing AE.
- Patients treated with FTD/TPI with ECOG PS ≥2 had a higher incidence of AE's compared to patients treated with FTD/TPI with ECOG PS 0-1, including anaemia (**Table 4**).
- In FTD/TPI-recipients, 184 (39.2%) and 26 (52%) had serious AE on FTD/TPI therapy + 30 days, in patients with ECOG PS 0-1 and ≥2, respectively (**Table 4**).
- There were no AEs related to FTD/TPI that lead to death.
- The most frequently occurring AE (≥15%) were disease progression, neutropenia, anaemia, fatigue, nausea and diarrhoea (**Table 4**).

Table 4. AEs in patients who received FTD/TPI, by ECOG PS

	FTD/TPI* (N=560)	FTD/TPI with ECOG PS 0–1 (n=469)	FTD/TPI with ECOG PS ≥2 (n=50)
Any AE, n (%)	545 (97.3)	455 (97.0)	50 (100.0)
Any AE on FTD/TPI + 30 days, n (%)	490 (87.5)	411 (87.6)	47 (94.0)
AE with causal relationship with FTD/TPI, n (%)	282 (50.4)	236 (50.3)	28 (56.0)
Any serious AE on FTD/TPI + 30 days, n (%)	227 (40.5)	184 (39.2)	26 (52.0)
Serious AEs with causal relationship with FTD/TPI, n (%)	35 (6.3)	28 (6.0)	5 (10.0)
Haematologic			
Neutropenia**	139 (24.8)	118 (25.2)	9 (18.0)
Anaemia	125 (22.3)	102 (21.7)	16 (32.0)
Non-haematologic			
Disease progression	112 (20.0)	95 (20.3)	11 (22.0)
Fatigue	107 (19.1)	99 (21.1)	5 (10.0)
Nausea	100 (17.9)	86 (18.3)	9 (18.0)
Diarrhoea	86 (15.4)	81 (17.3)	3 (6.0)
Asthenia	78 (13.9)	65 (13.9)	6 (12.0)
Decreased appetite	74 (13.2)	63 (13.4)	6 (12.0)
Abdominal pain	66 (11.8)	57 (12.2)	3 (6.0)
Vomiting	61 (10.9)	53 (11.3)	4 (8.0)

*All patient's who received FTD/TPI (± bevacizumab) at least once. **Some patients may have received granulocyte colony-stimulating factor (G-CSF), however G-CSF prophylaxis was not recorded in the electronic case report form. Abbreviations: FTD/TPI, trifluridine/tipiracil: N, number of patients: AE, adverse event.

References

1. Van Cutsem E, Cervantes A, Adam R, et al. Ann Oncol. 2016;27(8):1386-1422.
2. Prager GW, Taieb J, Fakih M, et al. N Engl J Med. 2023;388(18):1657-67.
3. Dasari A, Lonardi S, Garcia-Caronero R, et al. Lancet. 2023;402(10395):41-53.
4. Koopman M, Pinto C, Bodoky G, et al. Future Oncol. 2022;18(11):1313-1320.

Acknowledgements

This study is sponsored by Servier Affaires Médicales, France.
Editorial assistance was provided by Emily Eagles of ESP Medical Communications Ltd, and supported by Servier.

Corresponding Author & Disclosures

Corresponding email: rgcarbonero@gmail.com

Disclosures: **RGC**: has provided scientific advice and/or received honoraria or funding for continuous medical education from AAA-Novartis, Advanz Pharma, Amgen, Astellas, Bayer, BMS, Boehringer, Esteve, GSK, Hutchmed, Ipsen, Midatech, MSD, PharmaMar, Servier, Sanofi, Takeda; has received research grants from BMS, MSD, and Pfizer, has Leadership Role, Global PI of investigator-initiated clinical trials (AXINET, NICENEC, PEMBRO-A). BMS, MSD, Pfizer, other - Honoraria received by spouse for advisory board or invited speaker roles: AbbVie, AstraZeneca, Genomica, Lilly, Merck, Pfizer, Roche, Sanofi. **JBB**: Received personal fees from Abbvie, Amgen, Bayer, Bristol Myers Squibb, Danone, GlaxoSmithKline, Merck Serono, Merck Sharp & Dohme, Pierre Fabre, Sanofi, Servier, Takeda and non-financial support from Amgen, Merck Serono, and Sanofi. **CP**: Received honoraria for acting as an advisory board member or speaker for Amgen, Astellas, AstraZeneca, Bayer, BMS, Daiichi Sankyo, Janssen, Lilly, Merck Serono, MSD, Novartis, Pfizer, Roche, Sandoz, Sanofi and Servier. **GB**: Received honoraria as an advisory board mentar or speaker from Amgen, Astra Zeneca, Roche, Bayer, Pfizer, Janssen, Novartis Lilly, Servier, Nordic Pharma, Taiho. **KM**: Honoraria from Servier. **AM**: Received honoraria or grants from Bayer, Servier, Pierre Fabre, Merck, Lilly and BMS. **TB**: Invited speaker for Roche, Astellas, Janssen, Bristol Myers Squibb, and Merck; advisory board member for Bayer, Bristol Myers Squibb, Ipsen, Merck, Servier, Eli Lilly, Pfizer, and Accord; institutional support from Bristol Myers Squibb, Astra Zeneca, Merck, Bayer, Exelixis, Eisai, Eli Lilly, Roche, and MSD. **PS**: Declares no conflict of interest. **AMLM**: Honoraria received for speaker roles: Amgen, Astra Zeneca, Bayer, BMS, Eisai, Merck Serono, Pierre Fabre, Roche, Servier, Astellas. **RR**: Declares no conflict of interest **MK**: Reports having an advisory role for Eisai; Nordic Farma. Merck-Serono, Pierre Fabre, Servier (paid to institution), Institutional scientific grants from Bayer, Bristol Myers Squibb, Merck, Personal Genome Diagnostics (PGDx), Pierre Fabre, Roche, Sirtex, Servier.