BASELINE TREATMENT PATTERNS OF THE FIRST 277 PATIENTS IN PROMETCO: A REAL-WORLD, PROSPECTIVE, LONGITUDINAL COHORT STUDY ON THE CONTINUUM OF CARE IN METASTATIC COLORECTAL CANCER (mCRC)

J. B. Bachet,[1] C. Pinto,[2] G. Bodoky,[3] F. Marti Marti,[4] A. Mitroshkin,[5] M. Fazilleau,[6] A. Vermeire,[6] R. Fougeray,[7] R. Garcia-Carbonero,[8] M. Koopman,[9]

1. Sorbonne Université, Service d'hépato-Gastro-Entérologie, Groupe Hospitalier Pitié Salpêtrière, APHP, Paris, France; 2. Medical Oncology, Clinical Cancer Centre Azienda USL – IRCCS di Reggio Emilia – Viale Risorgimento, 80 42123 Reggio Emilia, Italy; 3. Dél-Pesti Centrumkórház Szent László Telephely Albert Flórián út 5–7 1097 Budapest, Hungary; 4. The Christie NHS Foundation Trust, Manchester, UK; 5. Klinikum Freudenstadt, akademisches Lehrkrankenhaus der Universität Tübingen, Karl-von-Hahn str. 120, 72250 Freudenstadt, Germany; 6. Global Medical and Patient Affairs Servier, Suresnes, France; 7. Institut de Recherches Internationales Servier, Suresnes, France; 8. Hospital Universitario Doce de Octubre Imas12, UCM, Av. De Córdoba s/n, 28041 Madrid, Spain; 9. Medical Centre Utrecht, Utrecht University Heidelberglaan 100 3584 CX Utrecht, the Netherlands. Corresponding email: jean-baptiste.bachet@aphp.fr

PROMETCO

ASCO Gastrointestinal Cancers Symposium

INTRODUCTION

- Tumor shrinkage and disease control with preservation or improvement in quality of life are the primary treatment goals for patients with unresectable mCRC.[1] When not possible, emphasis lies in slowing disease progression and prolonging survival.[1]
- While advances in the treatment of mCRC have improved survival to an average of 30 months in randomized clinical trials,[1] there is still a paucity of data applicable to real-world patient populations.
- 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 regardless of treatment or age.

AIM

- To present real-world patterns of treatment for metastatic disease received before PROMETCO inclusion (first 277 patients) by overall population, and stratified by bimolecular status.

RESULTS

Baseline characteristics (n=277)

Median age	
Years (range)	67 (33.9)
Male/female sex	
n (%)	155/121 (56.0/43.7)
ECOG PS 0-1[§]	
n (%)	248 (92.9)
Time between mCRC diagnosis and first metastatic treatment (months)[^]	
Median (Q1, Q3)	1.5 (0.9, 3.1)
Min, max	0.0, 68.9
Time between mCRC diagnosis and inclusion	
Median months (min, max)	22.9 (4.5, 104.9)
Total duration under treatment (months)[#^]	
Median (Q1, Q3)	13.3 (9.3, 19.2)
Min, max	0.6, 101.6
Number of metastatic sites, n (%)[‡]	
<3	243 (88.4)
≥3	32 (11.6)
Disease sidedness, n (%)	
Left (descending colon/sigmoid colon)	123 (44.4)
Right (cecum + ascending colon/traverse colon)	77 (27.8)
Rectum	93 (33.6)
***RAS/BRAF* status, n (%)[¤]**	
RAS mut	146 (53.1)
BRAF mut	8 (2.9)
RAS/BRAF WT	81 (29.5)
Unknown	40 (14.5)
MSI/MSS status, n (%)	
MSI low	2 (0.7)
MSI high	2 (0.7)
MSS	132 (47.7)
Unknown	141 (50.9)
Previous therapies for mCRC, n (%)[**]	
Fluoropyrimidine (5-FU or capecitabine)	252 (91.0)
Oxaliplatin	198 (71.5)
Irinotecan	224 (80.9)
Oxaliplatin + irinotecan	26 (9.4)
Bevacizumab	172 (62.1)
Aflibercept	60 (21.7)
Ramucirumab	2 (0.7)
Anti-EGFR (panitumumab or cetuximab)	44 (15.9)
Immunotherapy[@]	2 (0.7)
FTD/TPI	15 (5.4)
Regorafenib	3 (1.1)
Previous surgeries, n (%)	
Colorectal surgery	181 (65.3)
Liver surgery	71 (25.6)
Lung surgery	13 (4.7)
Distribution of metastatic sites, n (%)	
Liver	211 (76.2)
Lung	114 (41.2)
Peritoneal carcinosis	37 (13.4)
Other[$]	74 (26.7)

[§]n=275 due to missing data; [¤]n=267; ECOG status was undetermined in 10 patients; [*]Two patients were *RAS* and *BRAF* mutant (mut); [**]Percentages based on intention-to-treat population (n=277); [^]Length of treatment in months was calculated by converting days to months using a 30.44:1 ratio; [#]n=257; [‡]brain, skin, bone and adrenal gland metastases; [@]n=256, corresponding to the number of patients with at least one previous metastatic treatment line before PROMETCO inclusion. Only metastatic treatment lines with start and end dates completed are taken into account for global duration under treatment. A missing duration corresponds to a patient with only one metastatic treatment line for which the end date is missing; [$]Pembrolizumab, nivolumab, avelumab, atezolizumab, or encorafenib + cetuximab.

Overall study population

- 20 (7.2%) patients had no/undocumented previous treatment.
- Some patients received third- and/or fourth-line treatment before PROMETCO inclusion.

Length of treatment, overall population

Overall population

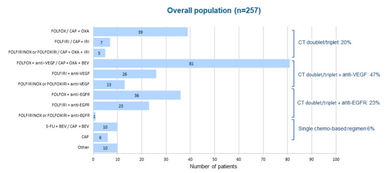
Length of treatment (months)[^]	Treatment line			
	Line 1 (n=257[¤])	Line 2 (n=209)	Line 3 (n=30[#])	Line 4 (n=4[#])
Median (Q1, Q3)	8.0 (4.9, 13.2)	5.2 (2.7, 9.2)	3.4 (1.9, 7.9)	1.5 (0.5, 14.8)
Min, max	0.03, 87.4	0.03, 55.1	0.03, 18.0	0.5, 14.8

[#]Missing data = 1; a patient can have multiple treatments for each treatment line; [^]Length of treatment in months was calculated by converting days to months using a 30.44:1 ratio.

- The majority of patients analyzed received first- and second-line treatment.
- Duration of treatment decreases with each successive line.

Treatments by line (first, second)

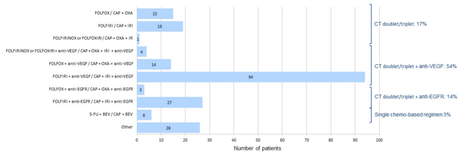
Overall population (n=257)



First line

- At first line after mCRC diagnosis, patients were mainly receiving CT doublet/triplet + anti-VEGF/EGFR therapies (70%).
- However, 20% were receiving CT alone, which is not in accordance with the international/ESMO guidelines.

Overall population (n=209)



Second line

- At second line after mCRC diagnosis, 68% of patients received CT doublet/triplet + anti VEGF/EGFR therapy.
- The proportion of CT doublet/triplet given alone is stable between first and second line.

RAS/BRAF status

- Due to patients with no/undocumented previous treatment, and the low number of patients in some groups, only *RAS* mut and *RAS/BRAF WT* groups are presented.

Length of treatment, *RAS/BRAF*

***RAS* mut**

Length of treatment (months)[^]	Treatment line			
	Line 1 (n=135)	Line 2 (n=110)	Line 3 (n=14)	Line 4 (n=3[#])
Median (Q1, Q3)	8.0 (4.7, 12.1)	4.8 (2.8, 9.2)	3.8 (2.3, 8.2)	7.6 (0.5, 14.8)
Min, max	0.03, 87.4	0.1, 35.4	1.2, 18.0	0.5, 14.8

***RAS/BRAF* WT**

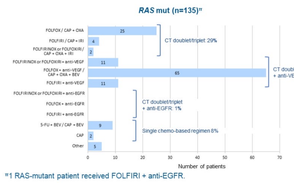
Length of treatment (months)[^]	Treatment line			
	Line 1 (n=76)	Line 2 (n=67)	Line 3 (n=14[#])	Line 4 (n=1)
Median (Q1, Q3)	8.4 (5.6, 14.3)	4.4 (2.4, 8.1)	2.2 (1.0, 7.0)	1.5 (1.5, 1.5)
Min, max	1.9, 36.0	1.2, 32.0	0.03, 12.2	1.5, 1.5

[#]Missing data = 1; a patient can have multiple treatments for each treatment line; [^]Length of treatment in months was calculated by converting days to months using a 30.44:1 ratio.

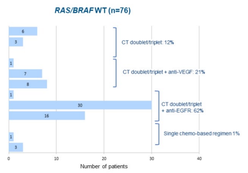
- There was no difference between the groups.
- Duration of treatment decreases with each successive line, in line with the overall population.

Treatments by line (first, second)

***RAS* mut (n=135)[¤]**



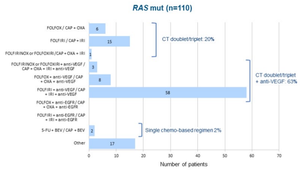
***RAS/BRAF* WT (n=76)**



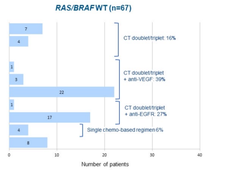
[¤]1 RAS-mutant patient received FOLFIRI + anti-EGFR.

- The *RAS* mut group received a higher proportion of CT doublet/triplet therapy in first line compared to the *RAS/BRAF* WT group.
- *RAS* mut patients received (as per international guidelines) mainly CT doublet/triplet + anti-VEGF therapy (59%).

***RAS* mut (n=110)**



***RAS/BRAF* WT (n=67)**



- There was no difference between the *RAS* mut and *RAS/BRAF* WT groups at second line.

MSI status

- Due to patients with no/undocumented previous treatment, and the low number of patients in some groups, only the MSS group is presented.

Length of treatment, MSI

MSS

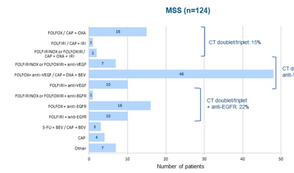
Length of treatment (months)[^]	Treatment line			
	Line 1 (n=124)	Line 2 (n=102)	Line 3 (n=14[#])	Line 4 (n=1)
Median (Q1, Q3)	8.0 (4.6, 12.2)	4.6 (2.8, 7.5)	5.8 (2.9, 8.5)	–
Min, max	0.03, 43.9	0.1, 55.1	0.8, 18.0	–

[#]Missing data = 1; a patient can have multiple treatments for each treatment line; [^]Length of treatment in months was calculated by converting days to months using a 30.44:1 ratio.

- Duration of treatment decreases with each successive line, in line with the overall population.

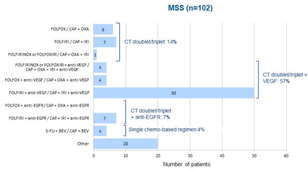
Treatments by line (first, second)

MSS (n=124)



- The treatment distribution in MSS patients follows a similar trend to the overall population.

MSS (n=102)



- The distribution of treatments received after first disease progression is similar in MSS patients and the overall population.

Reference: 1. Van Cutsem E, Cervantes A, Adam R, et al. Ann Oncol. 2016;27(8):1386–1422. **Regimens:** Anti-VEGF, bevacizumab, aflibercept and ramucirumab; anti-EGFR, cetuximab and panitumumab.

Abbreviations: 5-FU, fluorouracil; BEV, bevacizumab; CAP, capecitabine; CI, confidence interval; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FOLFIRI, folinic acid + 5-FU + irinotecan; FOLFIRINOX/ FOLFOXIRI, folinic acid + 5-FU + irinotecan + oxaliplatin; FOLFOX, folinic acid + 5-FU + oxaliplatin; FTD/TPI, trifluridine/ tipiracil; IRI, irinotecan; max, maximum; min, minimum; MSI, microsatellite instability; MSS, microsatellite stable; Mut, mutant; OXA, oxaliplatin; PRO, patient-reported outcomes; Q, quartile; SD, standard deviation; VEGF, vascular endothelial growth factor; WT, wild-type.

METHOD

- Enrollment in PROMETCO began in March 2019. On 1 October 2020, systemic treatment characteristics from 277 mCRC patients (of the 1,000 expected) from 16 countries were analyzed:
  - **Inclusion** criteria**:** adult patients with two disease progressions since the first diagnosis of metastatic disease, who were willing to receive subsequent treatment, were included.
  - **Exclusion** criteria**:** patients enrolled in other clinical trials, those receiving treatment for other cancers or those with insufficient mental capacity.
- Treatments started prior to study inclusion were analyzed by line and by patients' molecular status (*RAS/BRAF* and MSI).
- Systemic treatment characteristics separated by line/regimen of treatment were summarized for the efficacy population. Treatment characteristics were analyzed using descriptive statistics. Continuous variables are summarized using mean, median and range. Categorical variables are reported as number and percentage of patients.

TAKE-HOME MESSAGES

- Preliminary data from the PROMETCO trial provide key insights as to the treatment patterns of real-world mCRC patients.
- **Overall population:** first- and second-line treatment was CT doublet/triplet + anti-VEGF/EGFR therapy, in line with the guidelines. However, 20% of the population received CT doublet/triplet therapy at first line, not in accordance with the European guidelines. Some patients received third- and fourth-line treatment before PROMETCO inclusion. These observations are to be monitored further in a larger cohort analysis.
- ***RAS/BRAF* population**: the *RAS* mut group received a higher proportion of CT doublet/triplet therapy at first line compared to *RAS/BRAF* WT; thus, there is scope to explore this observation further in later analyses. In addition, *RAS* mut patients received (as per the guidelines) mainly CT doublet/triplet + anti-VEGF therapy (59%). Fifteen percent of the population had unknown *RAS/BRAF* status at inclusion; thus, there is interest to further evaluate the differences in testing/reimbursement between countries in a larger cohort.
- **MSS/MSI population**: the treatment distribution in MSS patients follows a similar trend to the overall population, in line with the guidelines. Fifty percent of the population had unknown MSI status at inclusion; thus, again, there is interest to further evaluate the differences in testing/reimbursement between countries in a larger cohort.
- It is anticipated that PROMETCO will provide valuable data on overall survival, treatment patterns, effectiveness, safety, adherence to treatment guidelines, healthcare resource utilization and PROs in this patient population.