

# Real-World Quality of Life and How it Relates to Overall Survival in Metastatic Colorectal Cancer: Results from the PROMETCO Study

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## INTRODUCTION

- An increasing range of later-line therapies for metastatic colorectal cancer (mCRC), such as trifluridine/tipiracil (FTD/TPI) ± bevacizumab, has prolonged survival in clinical trial settings.<sup>1,2</sup>
- However, real-world studies of mCRC treatment in third-line (3L) and beyond have been limited to specific agents or to a single country and provide little information on real-world quality of life (QoL) outcomes and their association with survival.<sup>3,4</sup>
- PROMETCO (NCT03935763) is an international, prospective, real-world study investigating outcomes, including QoL, in patients with mCRC after two disease progressions since diagnosis. Its prospective design strengthens the collection of robust QoL data, offering high-quality evidence in a real-world setting.

## METHODS

- Inclusion criteria were: ≥18 years of age, confirmed diagnosis of mCRC, two disease progressions, and willingness to receive subsequent treatment.<sup>5</sup>
- The study consisted of retrospective medical chart data collection and a prospective observational period post-inclusion. Patients were followed up regularly, with no fixed schedule, for 18 months or until death.<sup>5</sup>
- Clinician-reported QoL was assessed using Eastern Cooperative Oncology Group Performance Status (ECOG PS) and patient-reported QoL was reported using EuroQoL five dimensions visual analogue scale (EQ-5D-5L VAS) at baseline (defined as the most recent non-missing measurement collected prior to enrolment) until end of follow up or death.
- Deterioration of ECOG PS (defined as a worsening of ECOG PS to ≥2 [from 0 or 1] or to ≥3 [from 2], or death before ECOG PS deterioration) and EQ-5D-5L VAS (defined as a decrease in score of ≥10 points) were assessed in 6 treatment groups (among patients who received 3L but not fourth-line (4L) therapy):
  - Group 1 - (first-line (1L) & second-line (2L)) doublet/ triplet + anti-vascular endothelial growth factor (VEGF) twice prior to (3L) FTD/TPI ± bevacizumab;
  - Group 2 - (1L & 2L) doublet/triplet + anti-epidermal growth factor receptor (EGFR) and doublet/triplet + anti-VEGF (any order) prior to (3L) FTD/TPI ± bevacizumab;
  - Group 3 - (1L & 2L) doublet/triplet alone twice prior to (3L) FTD/TPI ± bevacizumab;
  - Group 4 - immuno- or targeted therapy in 1L, 2L, or 3L;
  - Group 5 - (1L or 2L) doublet/triplet + anti-VEGF prior to (2L or 3L) FTD/TPI;
  - Group 6 - any other treatment.
- The impact of age on ECOG PS and EQ-5D-5L VAS deterioration was assessed using Kaplan-Meier analysis in the total population. Good and poor EQ-5D-5L VAS scores were defined as >66.7 and ≤66.7, respectively.
- A multivariable analysis was carried out in all patients to assess the impact of clinical variables and QoL on median overall survival (mOS) from 1L.

## TAKE-HOME MESSAGES

- Real-world QoL outcomes were consistent across treatment groups for patients with refractory mCRC who received three lines of therapy but did not proceed to 4L, and QoL deterioration aligns with clinical expectations. This suggests that being treated in line with guidelines not only extends survival but successfully delays the loss of patient autonomy in advanced stages.**
- Palliative chemotherapy beyond two lines of progression is feasible and safe. Patients aged <60 and ≥80 years demonstrate a slightly faster deterioration in QoL. In older patients and patients with ECOG PS ≥2, the risks and benefits of additional systemic therapy should be considered very thoroughly.**
- Patient-reported outcomes can reinforce clinical assessments. In addition to its prognostic value, EQ-5D-5L VAS serves as a critical, additional tool for shared decision-making, helping clinicians better align patient expectations with prognosis.**
- PROMETCO results in the real-world setting confirm the use of FTD/TPI monotherapy in 3L, paving the way for the use of FTD/TPI + bevacizumab as the current standard of care as recommended by ESMO guidelines.**

### Baseline characteristics – patients who received 3 lines of therapy only (n=400)

- 738 patients from 18 countries were included in PROMETCO; most patients received FTD/TPI ± bevacizumab in 3L (402/608; 66%).
- 400 patients received 3 lines of therapy and did not proceed to 4L therapy (Table 1).
- There were considerable differences between the populations in the 18 countries included in PROMETCO: for example, in Sweden patients were older (0% under 60 years' old), had highest metastatic burden and had poorer prognosis than most other countries; Greece had high rates of *RAS* mutation (76%) and MSI high (7.1%), and patients had the best perception of QoL and a more positive self-assessment; Argentina had youngest population (60% under 60 years' old) with the highest proportion of patients with just 1 metastasis (80%), compared to other countries.

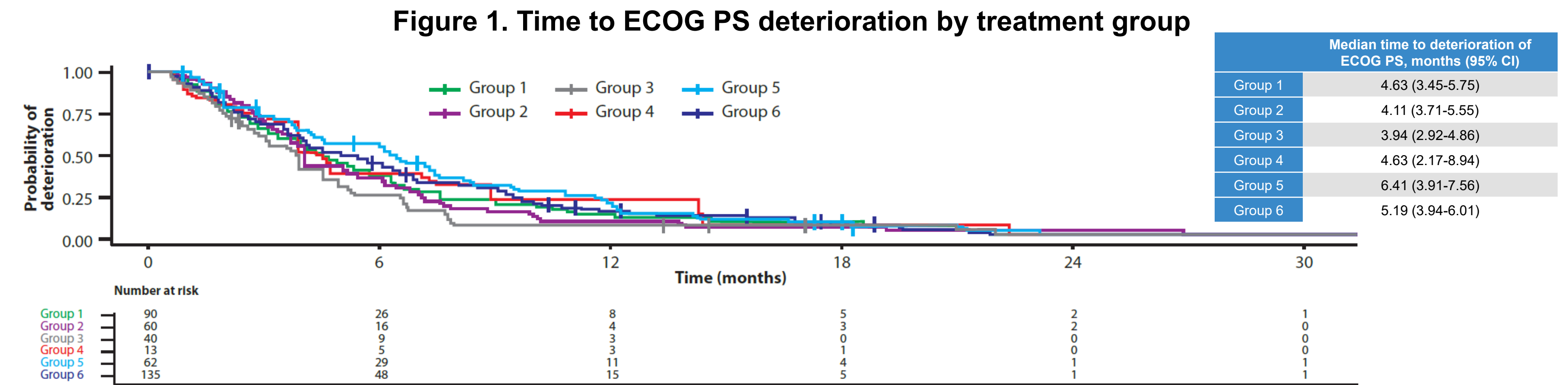
Table 1. Patient and disease characteristics at PROMETCO enrolment by treatment group

| Baseline characteristic                    | Group 1<br>(n=90) | Group 2<br>(n=60) | Group 3<br>(n=40) | Group 4<br>(n=13) | Group 5<br>(n=62) | Group 6<br>(n=135) |
|--------------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|
| Age <65 years, n (%)                       | 31 (34)           | 28 (47)           | 19 (48)           | 5 (38)            | 26 (42)           | 62 (46)            |
| Male, n (%)                                | 55 (61)           | 34 (57)           | 18 (45)           | 6 (46)            | 35 (56)           | 82 (61)            |
| ECOG PS, n (%) <sup>*</sup>                |                   |                   |                   |                   |                   |                    |
| 0                                          | 35 (40)           | 27 (45)           | 16 (41)           | 0 (0)             | 29 (47)           | 45 (34)            |
| 1                                          | 45 (51)           | 28 (47)           | 21 (54)           | 11 (100)          | 26 (42)           | 72 (55)            |
| 2                                          | 7 (8)             | 4 (7)             | 2 (5)             | 0 (0)             | 7 (11)            | 14 (11)            |
| 3                                          | 1 (1)             | 1 (2)             | 0 (0)             | 0 (0)             | 0 (0)             | 0 (0)              |
| Liver metastatic site location, n (%)      | 67 (74)           | 51 (85)           | 25 (63)           | 7 (54)            | 40 (65)           | 94 (70)            |
| Right sided disease, n (%)                 | 31 (34)           | 11 (18)           | 9 (23)            | 8 (62)            | 20 (32)           | 32 (24)            |
| <i>RAS/BRAF</i> status, n (%) <sup>*</sup> |                   |                   |                   |                   |                   |                    |
| <i>RAS</i> mutant                          | 75 (94)           | 0 (0)             | 30 (83)           | 2 (18)            | 49 (91)           | 41 (34)            |
| <i>BRAF</i> mutant                         | 4 (8)             | 0 (0)             | 2 (8)             | 8 (80)            | 3 (9)             | 6 (6)              |
| Time since diagnosis (months), mean (SD)   | 26.5 (21.7)       | 33.4 (23.0)       | 24.7 (22.1)       | 31.4 (21.0)       | 40.7 (27.9)       | 33.4 (22.9)        |
| Disease type, n (%)                        |                   |                   |                   |                   |                   |                    |
| Metachronous                               | 25 (28)           | 13 (22)           | 12 (30)           | 6 (46)            | 31 (50)           | 41 (30)            |
| Synchronous                                | 65 (72)           | 47 (78)           | 28 (70)           | 7 (54)            | 31 (50)           | 94 (70)            |

<sup>\*</sup>Percentages calculated based on number of patients with known values (excluding missing data). Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; *BRAF*, B-Raf proto-oncogene, serine/threonine kinase; *RAS*, rat sarcoma.

### Time to ECOG PS deterioration – patients who received 3 lines of therapy only (n=400)

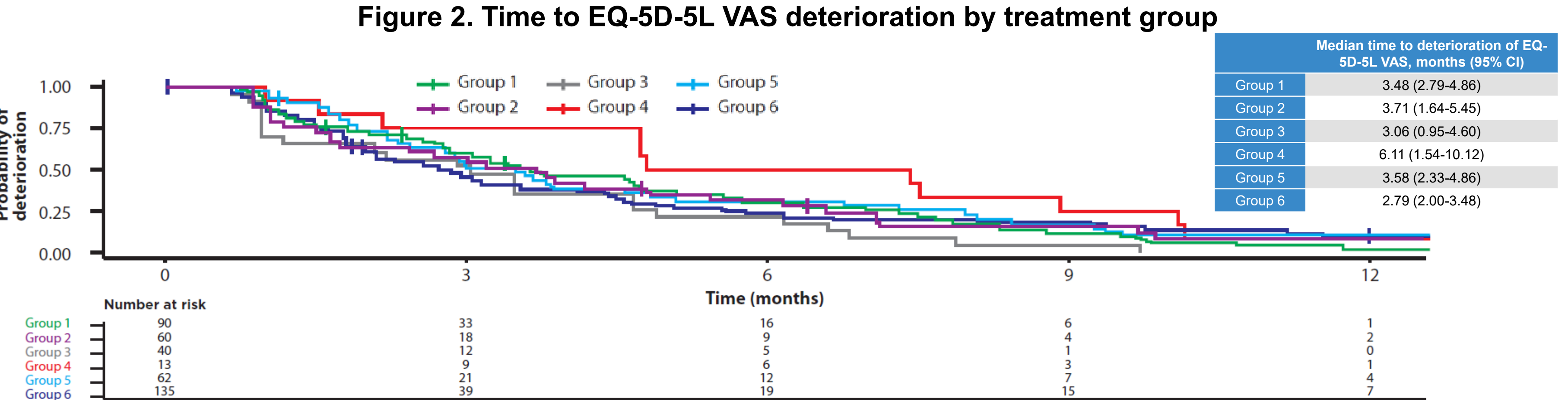
- The median time to ECOG deterioration varied slightly depending on the treatment sequence but differences were not significant (**Figure 1**).
- ECOG deterioration in the real-world setting was consistent with available clinical data.



Abbreviations: CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status.

### Time to EQ-5D-5L VAS deterioration – patients who received 3 lines of therapy only (n=400)

- No major differences in time to EQ-5D-5L VAS deterioration between groups were observed; medians ranged from 2.79 to 6.11 months (**Figure 2**).
- In this real-world setting EQ-5D-5L VAS deterioration was consistent with available clinical data.

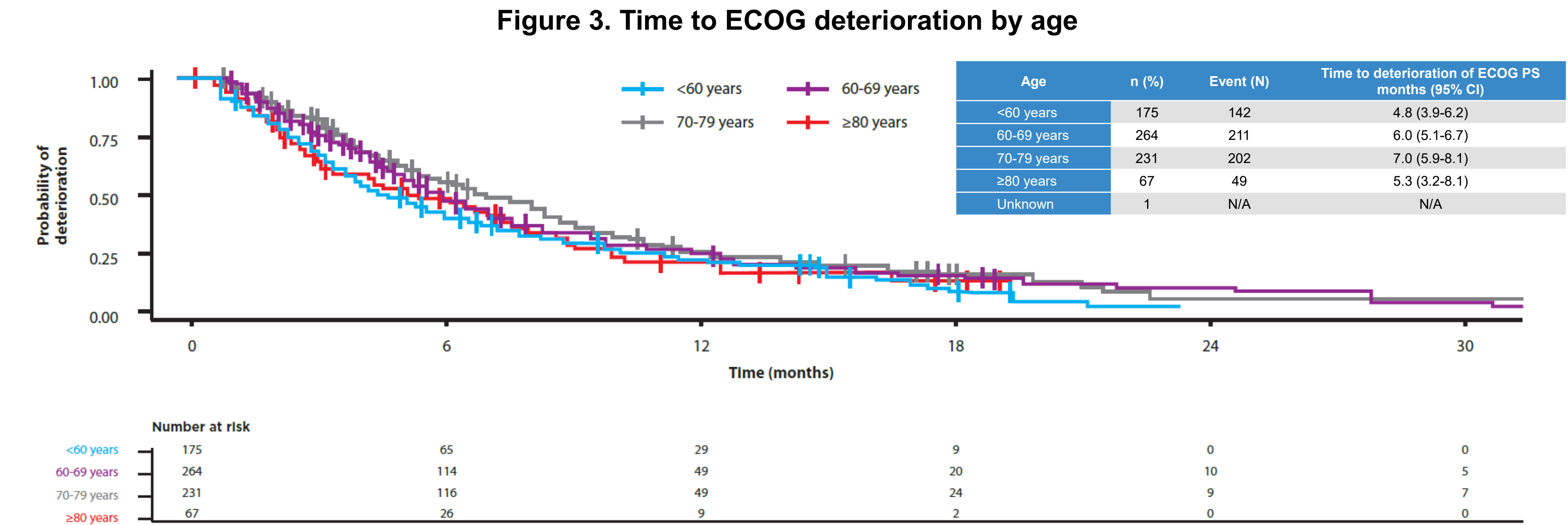


Abbreviations: CI, confidence interval; EQ-5D-5L VAS, EuroQoL five dimensions visual analogue scale.

## RESULTS

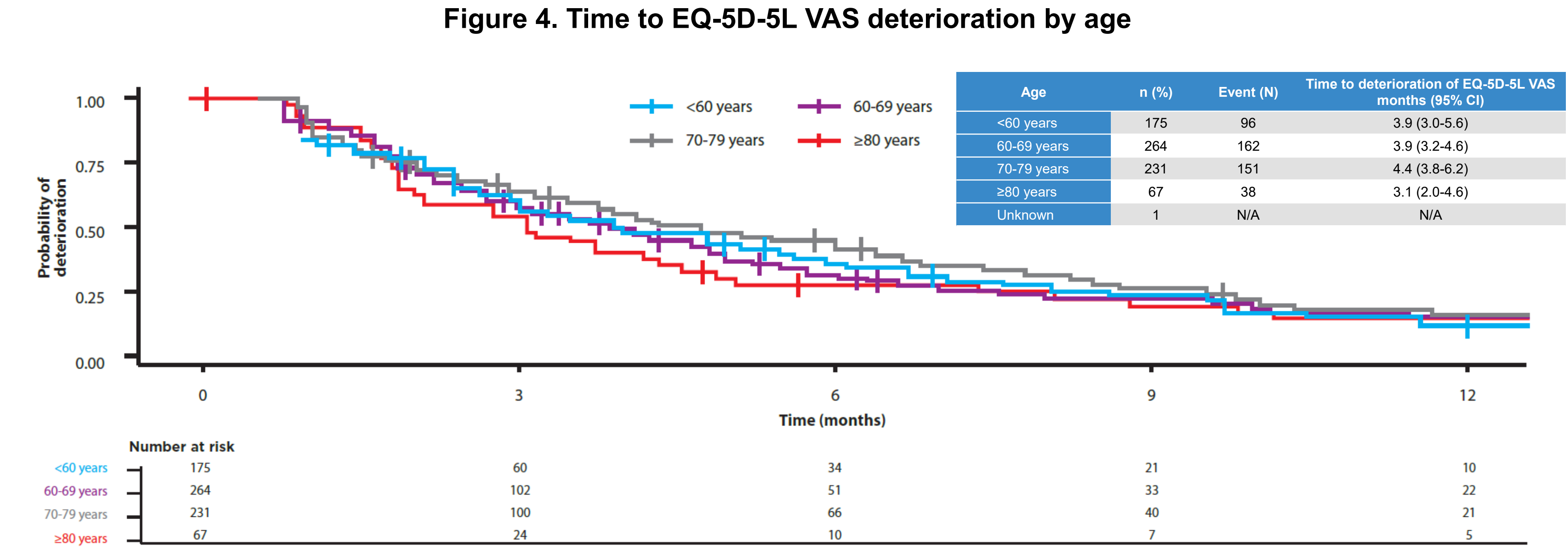
### Impact of age on time to ECOG PS and EQ-5D-5L VAS deterioration – all patients (n=738)

- The longest median time to ECOG PS deterioration was observed in patients aged 70-80 years, while the shortest was observed in patients aged <60 years and ≥80 years (**Figure 3**).



Abbreviations: CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; N/A, not available.

- The longest median time to EQ-5D-5L VAS deterioration was observed in patients aged 70-80 years, and the shortest was observed in patients aged ≥80 years (**Figure 4**).



Abbreviations: CI, confidence interval; EQ-5D-5L VAS, EuroQoL five dimensions visual analogue scale; N/A, not available.

### Impact of ECOG PS and EQ-5D-5L VAS on OS from 1L – all patients

- mOS was 33.5 months and 30.6 months in patients with ECOG PS 0 and 1, respectively, and was 22.2 months in patients with ECOG PS ≥2.
- An ECOG PS score ≥2 was associated with a significantly higher risk of death (hazard ratio = 1.62) compared to ECOG PS 0 (**Table 2**).
- A poor EQ-5D-5L VAS score at baseline was an independent predictor of shorter mOS (27.4 months with a poor EQ-5D-5L VAS score versus 35.1 months for a good score), with a hazard ratio of 1.23.
- A longer (>18 months) time between mCRC diagnosis and inclusion in PROMETCO was associated with a lower risk of death than a shorter time from diagnosis to PROMETCO inclusion (≤18 months) (**Table 2**). A shorter time from diagnosis to inclusion may be an indicator of more aggressive disease.

Table 2. Impact of QoL and time between diagnosis and PROMETCO inclusion on OS from 1L (Cox model)

|                                                                    | N <sup>*</sup> | Hazard ratio (multivariable)           |
|--------------------------------------------------------------------|----------------|----------------------------------------|
| EQ-5D-5L VAS at baseline                                           |                |                                        |
| Good (>66.7)                                                       | 210            |                                        |
| Poor (≤66.7)                                                       | 358            | 1.23 (1.00-1.51, p=0.051)              |
| ECOG PS at baseline                                                |                |                                        |
| 0                                                                  | 282            |                                        |
| 1                                                                  | 374            | 1.04 (0.85-1.28, p=0.687)              |
| 2                                                                  | 53             | 1.62 (1.13-2.33, p=0.009) <sup>^</sup> |
| Time between mCRC diagnosis and inclusion in PROMETCO <sup>+</sup> |                |                                        |
| > 18 months                                                        | 506            |                                        |
| ≤ 18 months                                                        | 221            | 6.16 (4.90-7.74, p<0.001)              |

Abbreviations: 1L, first-line; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EQ-5D-5L VAS, EuroQoL five dimensions visual analogue scale; mCRC, metastatic colorectal cancer; OS, overall survival. <sup>\*</sup>Duration between mCRC diagnosis and inclusion in the PROMETCO study. <sup>^</sup>All evaluable PROMETCO patients were included per OS analysis. <sup>+</sup>Cox analysis of ECOG 0 versus ≥2.

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**Disclosures:** **AM:** Received honoraria or grants from Servier, Pierre Fabre, Merck, Bayer, Lilly, BMS, Takeda. **JBB:** Received personal fees from Abbvie, Amgen, Bristol Myers Squibb, GlaxoSmithKline, Incyte, Merck Serono, Merck Sharp & Dohme, Novocure, Nutricia, Pierre Fabre, Sanofi, Servier, and Takeda. **RGC:** Has provided scientific advice and/or received honoraria or funding for continuous medical education from Advanz Pharma, Amgen, Astellas, Bayer, BMS, Boehringer, Cipla, Esteve, Hutchmed, Ipsen, Merck-Serono, MSD, Novartis, Novocure, PharmaMar, Servier, Takeda. Has received research grants from MSD. Honoraria received by spouse for advisory board or invited speaker roles: AstraZeneca, Genentech, Lilly, Merck, Pfizer, Roche, Sanofi. **GP:** 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 member or speaker from Amgen, AstraZeneca, Roche, Bayer, Pfizer, Janssen, Novartis, Lilly, Servier, Nordic Pharma, Taiho, **FM:** Honoraria from Servier. **EC, BC:** Are employees of Servier. **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 (PGD), Pierre Fabre, Roche, Sirnex, Servier.

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