

ORIGINAL RESEARCH

Quality of life with encorafenib plus cetuximab with or without binimetinib treatment in patients with *BRAF* V600E-mutant metastatic colorectal cancer: patient-reported outcomes from BEACON CRC

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Background: In the BEACON CRC study (NCT02928224), encorafenib plus cetuximab with binimetinib [9.3 versus 5.9 months; hazard ratio (HR) [95% confidence interval (CI)]: 0.60 [0.47-0.75]] or without binimetinib [9.3 versus 5.9 months; HR (95% CI): 0.61 (0.48-0.77)] significantly improved overall survival (OS) compared with the previous standard of care (control) in patients with *BRAF* V600E metastatic colorectal cancer (mCRC). Quality of life (QoL) was a secondary endpoint, assessed using validated instruments.

Patients and methods: BEACON CRC was a randomized, open-label, phase III study comparing encorafenib plus cetuximab with or without binimetinib and the investigator's choice of irinotecan plus cetuximab or FOLFIRI plus cetuximab (chemotherapy control) in patients with previously treated *BRAF* V600E mCRC. Patient-reported QoL assessments included the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC) and Functional Assessment of Cancer Therapy—Colorectal (FACT-C). The primary outcome for these tools was time to definitive 10% deterioration.

Results: Encorafenib plus cetuximab, both with and without binimetinib, was associated with longer median times to definitive 10% deterioration versus the control group in the EORTC Global Health Status scale [HR (95% CI): 0.65 (0.52-0.80) versus 0.61 (0.49-0.75), respectively] and the FACT-C functional well-being subscale [HR (95% CI): 0.62 (0.50-0.76) versus 0.58 (0.47-0.72), respectively]. Consistent results were observed across all subscales of the EORTC and FACT-C instruments. QoL was generally maintained during treatment for the global EORTC and FACT-C scales.

Conclusions: In addition to improving OS, encorafenib plus cetuximab with or without binimetinib delays QoL decline in previously treated patients with *BRAF* V600E-mutant mCRC.

Key words: BEACON CRC, cetuximab, colorectal cancer, encorafenib, patient-reported outcomes, quality of life

INTRODUCTION

Globally, colorectal cancer (CRC) is the second and third most commonly diagnosed cancer for women and men, respectively, with incidence rates highest in Australia, Europe, and North America.^{1,2} Although CRC represents the

second leading cause of cancer deaths worldwide, earlier detection and advances in screening and available treatments are contributing to a decreasing trend in new cases and death rates.^{2,3} In the United States, the rate of new CRC cases decreased from 56.7 per 100 000 persons in 1992 to 34.8 in 2018, with the death rate decreasing from 23.6 to 12.8 per 100 000 persons during the same time period.³

Biomarker profiling and the availability of targeted and checkpoint inhibitor therapies have resulted in an increased proportion of patients with CRC, as those surviving ≥ 5 years post-diagnosis are no longer uncommon.^{4,5} CRC survivors now represent the third largest cancer survivor group

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in developed countries, with a 5-year relative survival rate of 64.7% in the United States.^{3,6}

Initially, CRC treatment strategies focused mainly on tumor response and on prolonging progression-free survival (PFS) and overall survival (OS).^{7,8} However, with increased survivorship and more available treatment options, each with their own unique risk/benefit profiles, quality of life (QoL) has become an important and necessary complement to increasing duration of life.⁹ Unfortunately, CRC treatment options can lead to QoL challenges, such as the severe and unfavorable side-effects associated with chemotherapy that impart a substantial burden on a patient's physical and mental well-being.¹⁰⁻¹⁴ Although every effort is made by clinicians to manage treatment adverse effects,¹⁵ these adverse events (AEs) invariably have detrimental effects on patients' psychological and emotional well-being, social interactions, and ability to carry out daily activities,^{4,14,16} and, by extension, directly impact survivorship.

In patients with CRC, a higher QoL has been statistically significantly associated with all-cause mortality, even when accounting for those with metastatic disease,¹⁷ and CRC disease progression is associated with a statistically significant worsening of QoL measures.¹⁸ In addition to the relationship between patient well-being and longevity, QoL is associated as an independent predictor of response to treatment.¹⁹⁻²¹ Maisey et al. investigated baseline QoL in patients with advanced CRC in four randomized clinical trials and determined that global scores were a highly significant, independent predictor of survival.²⁰ These findings have been corroborated by numerous other studies concluding that patient-reported outcomes were better predictors of response than performance status.¹⁹ In fact, improvement in physical functioning beyond baseline assessment has been associated with increased probability of survival.²¹

Maintaining QoL in patients with CRC, especially in those with metastatic CRC (mCRC), is critical to survival and is recognized as one of the major endpoints to evaluate treatments.^{22,23} In addition, European Society of Medical Oncology Clinical Practice Guidelines for mCRC and regulatory bodies such as the European Medicines Agency recognize the value of QoL measures beyond classical efficacy endpoints by including them in their guidelines and assessments for reimbursement.⁸

The combination of encorafenib with cetuximab represents one of the targeted treatment options approved in the United States and Europe for previously treated patients with *BRAF* V600E-mutated mCRC. As the only chemotherapy-free targeted therapy for patients with *BRAF*-mutant mCRC, it is an important treatment option in the mCRC armamentarium for this patient population. In the phase III BEACON CRC study, encorafenib plus cetuximab regimens with and without binimetinib significantly improved OS compared with standard chemotherapy (irinotecan or FOLFIRI) plus cetuximab.^{15,24} Encorafenib plus cetuximab demonstrated significantly longer median OS [9.3 versus 5.9 months; hazard ratio (HR) 0.61; 95% confidence interval (CI) 0.48-0.77] and a higher objective

response rate (19.5% versus 1.8%) compared with standard chemotherapy.¹⁵ The rate of AEs of grade 3 or higher was slightly greater in the control group than in the combination group; there were few treatment discontinuations ($\leq 9\%$) due to AEs.¹⁵ The safety and tolerability of the encorafenib plus cetuximab treatment regimens were consistent with the known safety profiles of *BRAF*, *EGFR*, and *MEK* inhibitors, and AEs were manageable with standard supportive care and treatment interruptions.¹⁵

However, considering the interrelationship of efficacy measures and QoL, a more complete picture is needed to evaluate the impact of treatment with encorafenib plus cetuximab with or without binimetinib on patient's lives. Herein, we look beyond the classic clinical trial endpoints to the functional, social, and psychological well-being of patients and the impact of treatment on patient QoL in BEACON CRC.

PATIENTS AND METHODS

Study design

BEACON CRC (NCT02928224) is a randomized, open-label, phase III study in patients with *BRAF* V600E-mutant mCRC that had progressed after one or two prior treatment regimens.^{15,24} Patients were randomized to encorafenib plus cetuximab with binimetinib, encorafenib plus cetuximab without binimetinib, or the investigator's choice of irinotecan or FOLFIRI plus cetuximab. Study design details and the primary endpoints have been published.^{15,24} The study was conducted in accordance with the Declaration of Helsinki, approvals obtained by regional and local institutional review boards, and informed consent obtained from all participants. The data cut-off for these analyses was 11 February 2019.

Patient-reported outcomes

Patient-reported QoL was a secondary endpoint of BEACON CRC, with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC) version 3.0 used to assess key outcomes of interest. This 30-item questionnaire consists of an overall global health status/QoL score, five functioning scores (physical, role, emotional, cognitive, and social functioning), and three composite symptom scores (fatigue, nausea, and vomiting). In addition, six single-symptom items are assessed (pain, dyspnea, insomnia, appetite loss, constipation, and diarrhea).²⁵⁻²⁷ The global health status score uses a seven-point Likert scale ranging from 'very poor' to 'excellent', and the remaining items in the EORTC use a four-point Likert scale ranging from 'not at all' to 'very much'.^{25,27,28} Items are scored 0-100 points, with a higher score representing better QoL in accordance with the scoring manual.²⁹

QoL was also assessed using the patient self-reporting Functional Assessment of Cancer Therapy—General (FACT-G) and Colorectal (FACT-C) questionnaires.^{30,31} The FACT-G is a 27-item questionnaire with a total score and four subscale QoL domains (physical, social, emotional,

Table 1. Quality of life at baseline for encorafenib plus cetuximab, with or without binimetinib, and control			
	Encorafenib plus cetuximab with binimetinib n = 224	Encorafenib plus cetuximab n = 220	Control n = 221
EORTC			
Global Health Status			
Patients, n	209	201	200
Mean (SD)	62.8 (22.2)	60.7 (21.3)	62.8 (21.8)
Median (range)	67 (0-100)	67 (0-100)	67 (0-100)
Physical functioning			
Patients, n	210	199	199
Mean (SD)	76.1 (19.4)	73.3 (20.7)	75.7 (20.5)
Median (range)	80 (13-100)	73 (0-100)	80 (13-100)
Emotional functioning			
Patients, n	209	199	200
Mean (SD)	73.7 (23.4)	74.1 (21.7)	73.7 (23.0)
Median (range)	75 (0-100)	75 (0-100)	75 (0-100)
Social functioning			
Patients, n	206	199	200
Mean (SD)	73.1 (24.9)	70.9 (27.1)	73.6 (25.0)
Median (range)	67 (0-100)	67 (0-100)	67 (0-100)
Role functioning			
Patients, n	209	201	200
Mean (SD)	70.2 (28.88)	68.2 (30.24)	72.8 (28.17)
Median (range)	67 (0-100)	67 (0-100)	67 (0-100)
Cognitive functioning			
Patients, n	209	199	200
Mean (SD)	85.4 (19.16)	84.5 (19.57)	83.3 (19.16)
Median (range)	100 (0-100)	83 (0-100)	83 (0-100)
Fatigue			
Patients, n	210	200	200
Mean (SD)	38.7 (25.12)	40.9 (25.41)	38.3 (25.39)
Median (range)	33 (0-100)	33 (0-100)	33 (0-100)
Nausea and vomiting			
Patients, n	210	199	200
Mean (SD)	9.8 (16.25)	8.4 (16.23)	11.4 (20.84)
Median (range)	0 (0-100)	0 (0-100)	0 (0-100)
Pain			
Patients, n	210	200	200
Mean (SD)	31.9 (29.85)	34.1 (30.37)	32.3 (30.54)
Median (range)	33 (0-100)	33 (0-100)	33 (0-100)
Dyspnea			
Patients, n	210	199	200
Mean (SD)	17.6 (25.92)	16.9 (25.70)	15.5 (23.12)
Median (range)	0 (0-100)	0 (0-100)	0 (0-100)
Insomnia			
Patients, n	209	200	200
Mean (SD)	27.4 (29.64)	28.3 (31.66)	31.8 (31.04)
Median (range)	33 (0-100)	33 (0-100)	33 (0-100)
Appetite loss			
Patients, n	210	199	200
Mean (SD)	23.3 (29.72)	25.6 (30.46)	24.2 (30.62)
Median (range)	0 (0-100)	33 (0-100)	0 (0-100)
Constipation			
Patients, n	210	200	199
Mean (SD)	16.2 (25.31)	17.0 (27.55)	18.1 (29.53)
Median (range)	0 (0-100)	0 (0-100)	0 (0-100)
Diarrhea			
Patients, n	208	198	200
Mean (SD)	16.0 (21.97)	17.5 (23.67)	16.3 (21.91)
Median (range)	0 (0-100)	0 (0-100)	0 (0-100)
FACT-G and FACT-C			
FACT-G total score			
Patients, n	208	200	198
Mean (SD)	74.7 (16.54)	74.8 (14.86)	75.8 (16.13)
Median (range)	77 (23-107)	76 (21-107)	77 (22-106)
FACT-C total score			
Patients, n	207	199	197
Mean (SD)	94.2 (19.82)	93.7 (18.54)	94.8 (19.66)
Median (range)	97 (36-134)	96 (27-135)	98 (29-134)

Continued

Table 1. Continued			
	Encorafenib plus cetuximab with binimetinib <i>n</i> = 224	Encorafenib plus cetuximab <i>n</i> = 220	Control <i>n</i> = 221
Functional well-being			
Patients, <i>n</i>	211	200	200
Mean (SD)	16.3 (6.2)	16.2 (5.9)	16.8 (6.1)
Median (range)	16 (0-28)	16 (0-28)	17 (4-28)
Physical well-being			
Patients, <i>n</i>	211	202	199
Mean (SD)	20.7 (5.7)	20.3 (5.5)	20.9 (5.4)
Median (range)	22 (4-28)	21 (3-28)	22 (6-28)
Social/family well-being subscale			
Patients, <i>n</i>	209	202	200
Mean (SD)	21.9 (5.3)	22.2 (5.2)	22.2 (5.4)
Median (range)	23 (0-28)	23 (0-28)	23 (0-28)
Emotional well-being			
Patients, <i>n</i>	210	200	199
Mean (SD)	15.9 (5.0)	16.2 (4.4)	16.0 (4.9)
Median (range)	17 (0-24)	17 (3-24)	16 (0-24)
Colorectal cancer			
Patients, <i>n</i>	210	200	200
Mean (SD)	19.3 (4.7)	18.9 (5.0)	19.0 (5.0)
Median (range)	20 (7-28)	20 (6-28)	20 (2-28)

EORTC, European Organization for Research and Treatment of Cancer Quality of Life of Questionnaire Core 30; FACT-C, Functional Assessment of Cancer Therapy—Colorectal; FACT-G, Functional Assessment of Cancer Therapy—General; SD, standard deviation.

and functional well-being) for all patients with cancer. The FACT-C includes an additional nine questions specific to CRC and with a total score and adds to the four domains of the FACT-G plus an additional CRC subscale domain. The questionnaires are based on a five-point Likert scale with a recall period of the past 7 days, with a higher score representing better QoL.

QoL assessments were carried out at screening/baseline on day 1 of each treatment cycle, at the end of treatment, and at 30-day follow-up visits. The number of patients completing the questionnaires and the number of missing or incomplete assessments were summarized by time-point. Results for each instrument were scored according to their respective scoring manuals.^{28-30,32,33} The median scores and change from baseline for each scale at the time of each assessment were summarized using descriptive statistics.

Time to definitive deterioration in the QoL domains was assessed in the three treatment arms in the full analysis set. The time to definitive deterioration is defined as the time from the date of randomization to the date of event, which is defined as at least 10% worsening relative to baseline of the corresponding scale score with no later improvement above this threshold observed during the course of the study or death due to any cause. If a patient did not have an event before either analysis cut-off or the start of another anti-cancer therapy, time to deterioration was censored at the date of the last adequate QoL evaluation. The distribution was presented descriptively using Kaplan—Meier curves. Median time to definitive deterioration along with two-sided 95% CI is reported. A Cox model was fitted with treatment arm and stratification factors as covariates to obtain an HR (95% CI) estimate of the treatment effect. The stratification factors used in the test were precisely those used for

randomization and were based on the actual randomization information (interactive web response system).

RESULTS

Patient characteristics and compliance

The study recruited 665 patients who were randomized to receive encorafenib plus cetuximab with binimetinib (*n* = 224), encorafenib plus cetuximab (*n* = 220), or control (*n* = 221).^{15,24} Full details and safety and efficacy results have been published.^{15,24} Patient characteristics were well balanced between groups at baseline (Supplementary Table S1, available at <https://doi.org/10.1016/j.esmooop.2022.100477>). At data cut-off, treatment was ongoing in 13.4% (*n* = 30) of patients in the encorafenib plus cetuximab with binimetinib group, 13.6% (*n* = 30) of patients in the encorafenib plus cetuximab group, and 3.2% (*n* = 7) in the control group.^{15,24} The most common reason for discontinuation in all three treatment groups (56%-66% of patients) was progressive disease.

Baseline QoL assessments indicated a balance across the treatment groups for each instrument and subscale (Table 1). From baseline to cycle 8, compliance with the EORTC and FACT-C instruments was 85.7%-94.3% in the encorafenib plus cetuximab with binimetinib group, 88.8%-95.7% in the encorafenib plus cetuximab group, and 83.3%-94.8% in the control group (Supplementary Table S2, available at <https://doi.org/10.1016/j.esmooop.2022.100477>).

EORTC Quality of Life Questionnaire Core 30

Baseline values for EORTC scores were similar across the groups (Table 1). EORTC global health status scores over time are shown in Figure 1A. QoL was generally maintained during treatment for both encorafenib plus

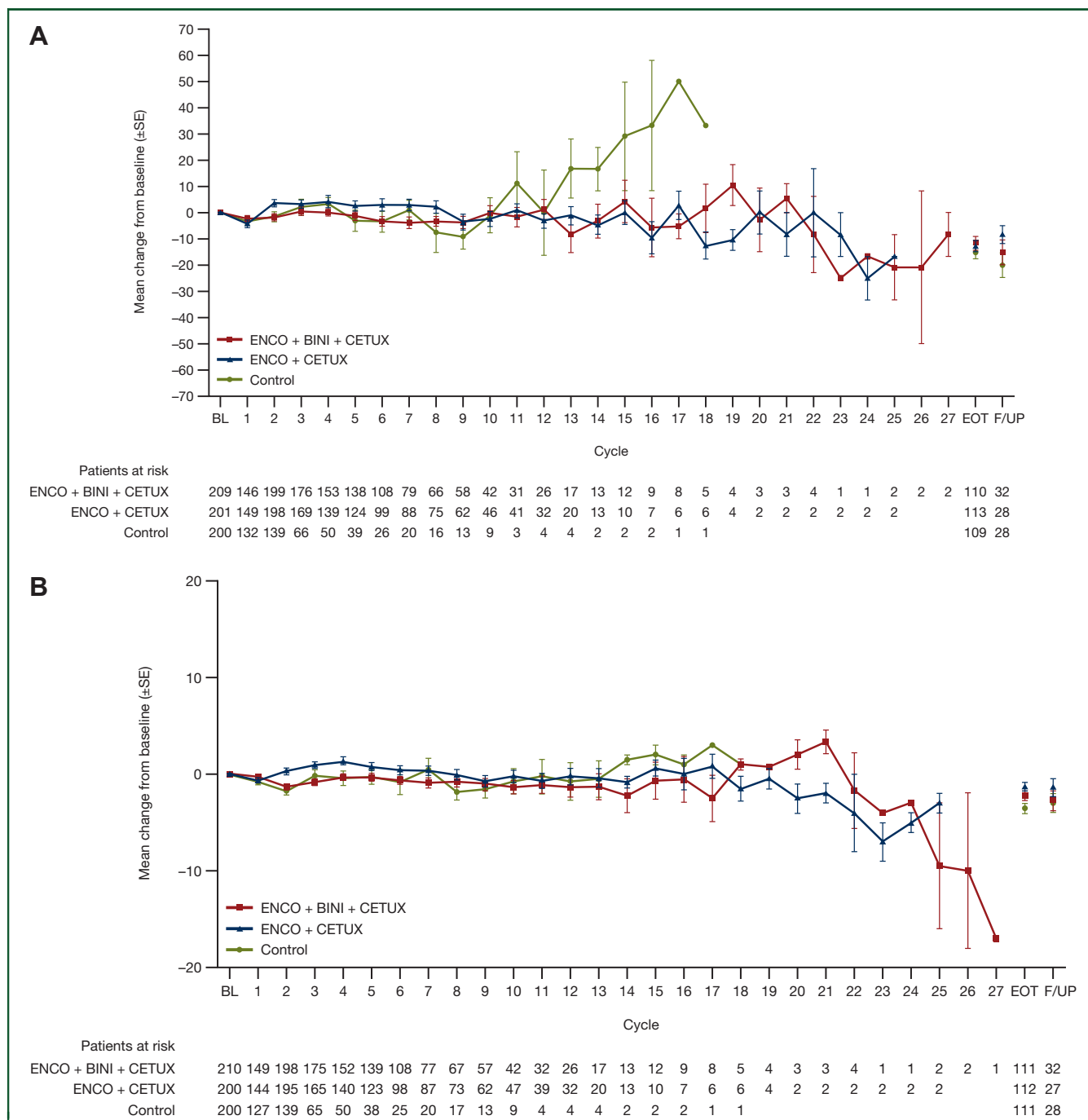


Figure 1. Scores over time for (A) EORTC global health status and (B) FACT-C colorectal cancer. Mean change of baseline (\pm SE) over time for (A) EORTC global health status and (B) FACT-C colorectal cancer by visit for patients treated with encorafenib plus cetuximab with or without binimetinib, or control. Baseline was defined as the last assessment carried out on or before the date of the first dose of study treatment.

BINI, binimetinib; BL, baseline; CETUX, cetuximab; FACT-C, Functional Assessment of Cancer Therapy—Colorectal; ENCO, encorafenib; EORTC, European Organization for Research and Treatment of Cancer Quality of Life of Questionnaire Core 30; EOT, end of treatment; F/UP, follow-up; SE, standard error.

cetuximab with or without binimetinib regimens compared with control.

Time to deterioration: EORTC

Encorafenib plus cetuximab, with or without binimetinib, was associated with longer median times to definitive 10% deterioration in the EORTC Global Health Status scale relative to the control group [5.6 and 6.2 versus 2.8 months, respectively; HR

(95% CI): 0.65 (0.52-0.80) versus 0.61 (0.49-0.75), respectively; Figure 2A]. Similar findings were observed for the EORTC physical functioning, emotional functioning, and social functioning subscales (Figure 3). For the emotional functioning subscale, the encorafenib plus cetuximab with binimetinib group was associated with a longer median time to deterioration compared with the encorafenib plus cetuximab group: 7.7 versus 5.9 months [HR (95% CI): 0.76 (0.60-0.95)] (Figure 3B).

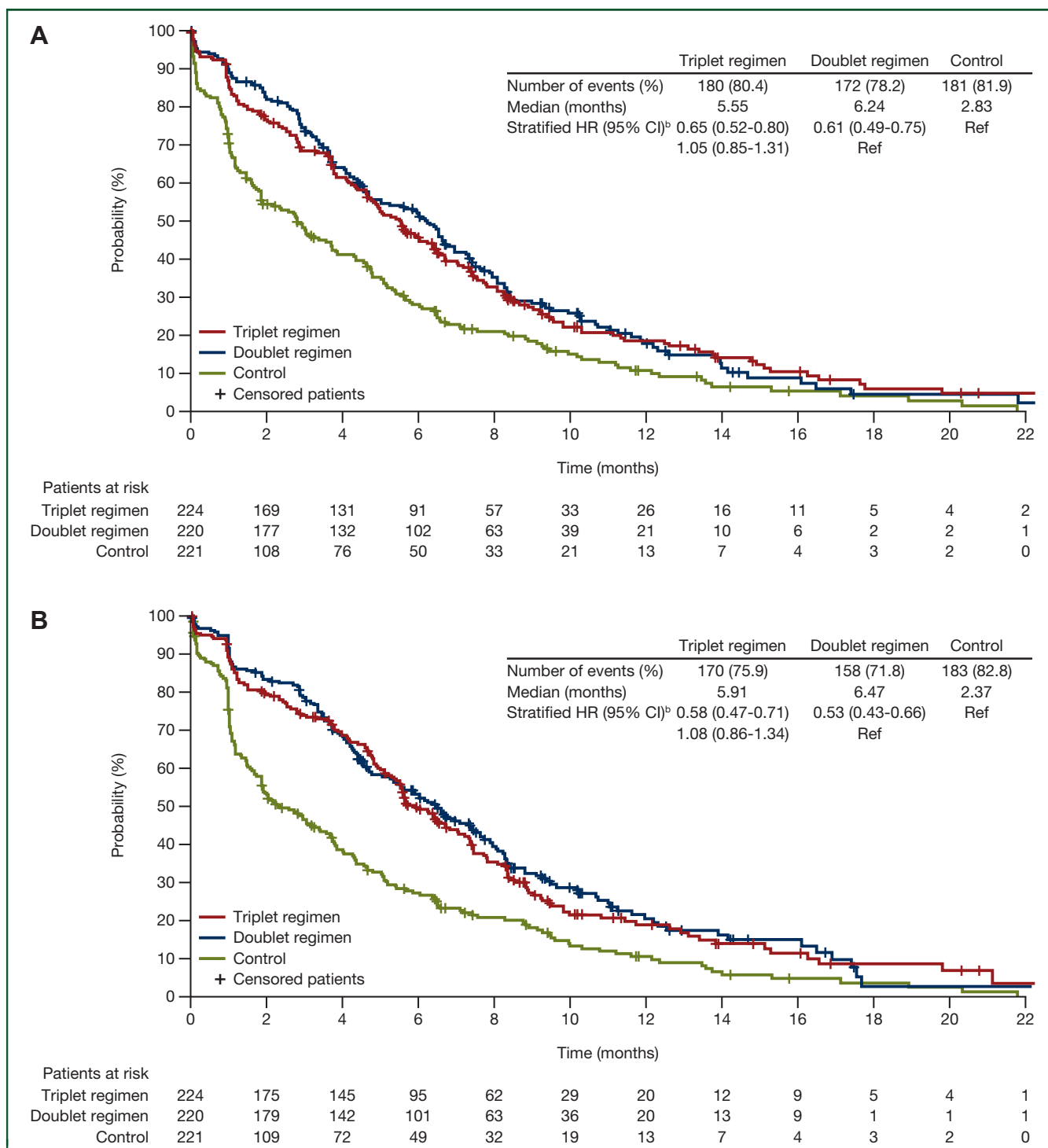


Figure 2. Median time to definitive deterioration^a for encorafenib plus cetuximab with or without binimetinib compared with control: (A) EORTC global health status; (B) FACT-C colorectal cancer. Probability (%) of median time to definitive 10% deterioration in (A) EORTC global health status or (B) FACT-C colorectal cancer for patients treated with encorafenib plus cetuximab with or without binimetinib (triplet and doublet, respectively) compared with the control.

CI, confidence interval; FACT-C, Functional Assessment of Cancer Therapy—Colorectal; HR, hazard ratio; EORTC, European Organization for Research and Treatment of Cancer Quality of Life of Questionnaire Core 30.

^aDefinitive deterioration is at least 10% worsening relative to baseline with no later improvement above this threshold, or death due to any cause.

^bStratified by Eastern Cooperative Oncology Group performance status, source of cetuximab, and prior irinotecan use at randomization.

FACT-C

Baseline values for FACT-C scores were similar across the groups (Table 1). FACT-C CRC subscale scores over time are shown in Figure 1B. QoL was generally maintained during treatment for the encorafenib plus cetuximab with or without binimetinib regimens compared with control.

Time to deterioration: FACT-C

For the FACT-C CRC subscale, median times to deterioration were 5.9 months for encorafenib plus cetuximab with binimetinib, 6.5 months for encorafenib plus cetuximab, and 2.4 months for control. HR (95% CI) was 0.58 (0.47-0.71) for encorafenib plus cetuximab with

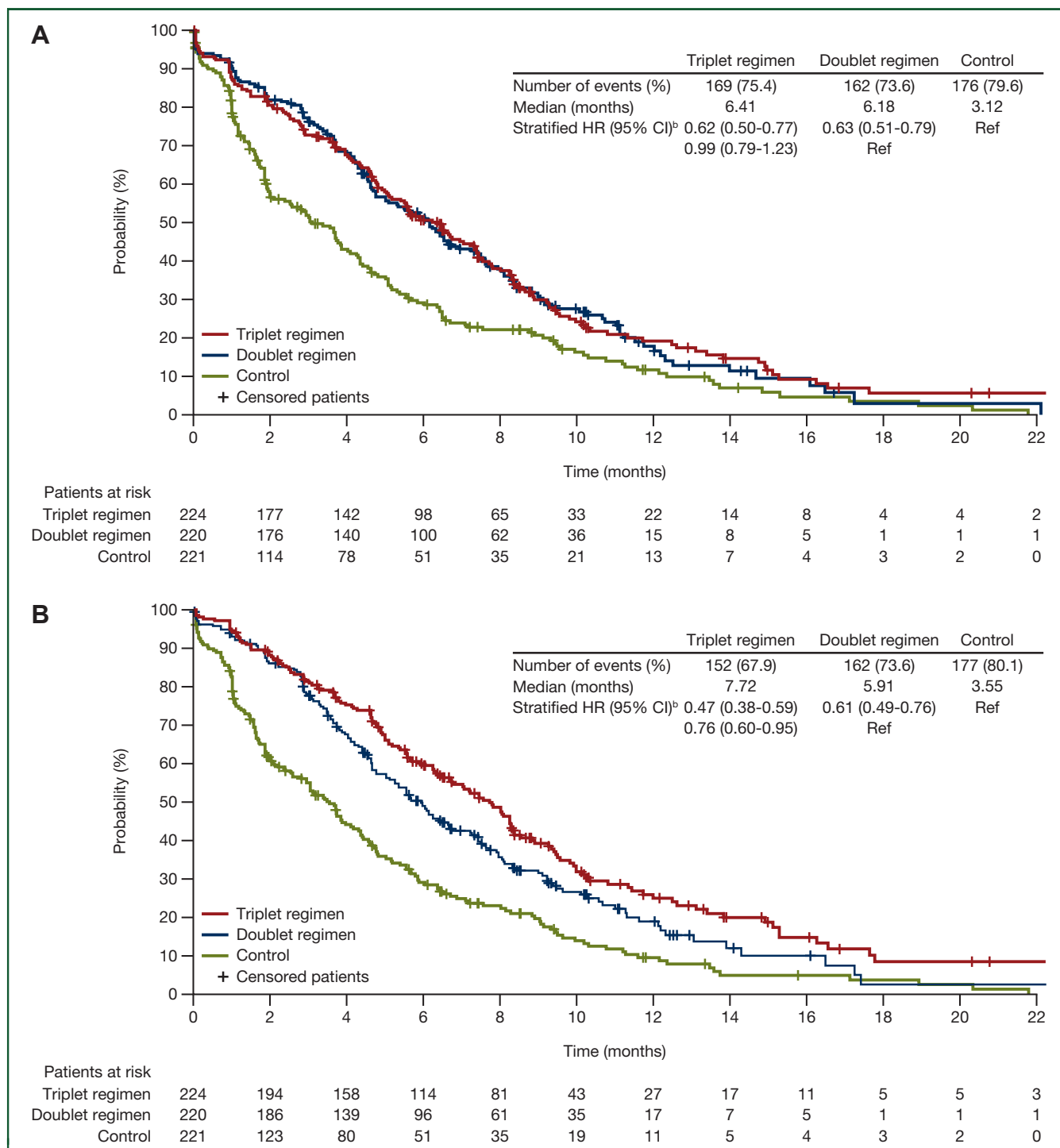


Figure 3. Median time to definitive deterioration^{a,b} in EORTC for encorafenib plus cetuximab with or without binimetinib compared with control: (A) Physical functioning; (B) emotional functioning; (C) social functioning. Probability (%) of median time to definitive 10% deterioration in EORTC global health status subscales (A) physical functioning, (B) emotional functioning, and (C) social functioning for patients treated with encorafenib plus cetuximab with or without binimetinib (triplet and doublet, respectively) compared with the control.

CI, confidence interval; HR, hazard ratio; EORTC, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

^aDefinitive deterioration is at least 10% worsening relative to baseline with no later improvement above this threshold, or death due to any cause.

^bStratified by Eastern Cooperative Oncology Group performance status, source of cetuximab, and prior irinotecan use at randomization.

binimetinib versus control, and 0.53 (0.43-0.66) for encorafenib plus cetuximab versus control (Figure 2B). With respect to the other FACT-C subscales, the median times to deterioration were longer for encorafenib plus cetuximab, with and without binimetinib, compared with control (Figure 4).

DISCUSSION

Tumor-related endpoints, such as PFS, OS, or overall response rate, do not inevitably translate into significant improvements in the quality of survival. The US Food and Drug Administration and the American Society of Clinical Oncology have stated that

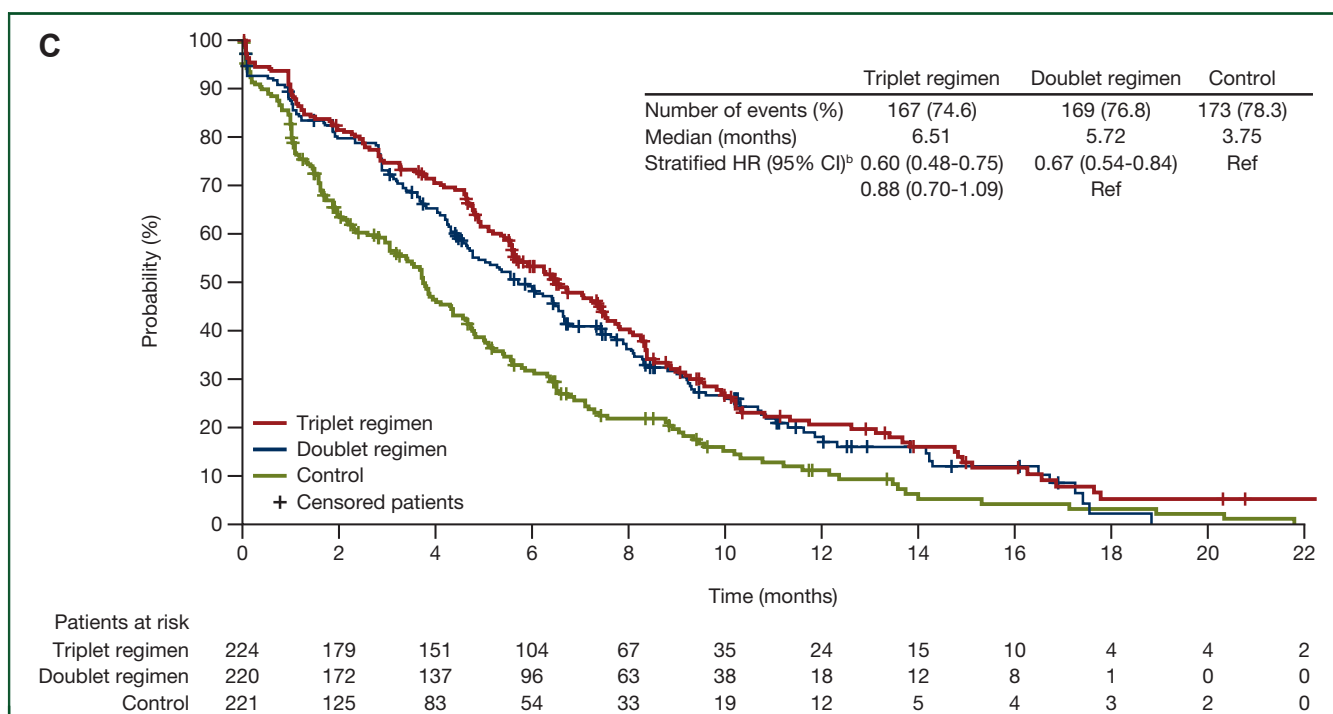


Figure 3. Continued.

QoL can be considered a co-primary endpoint besides OS if no effect of treatment is observed.³⁴ Furthermore, in Europe, health assessments to determine reimbursement decisions require both clinical and patient-reported endpoints (such as QoL assessments); treatments are generally considered for reimbursement based on the added value that these treatments provide in terms of QoL.^{18,35,36}

To optimize treatment approaches for mCRC, it has been suggested that treatment algorithms should be tailored according to three major themes: (1) patient characteristics, which include patient preferences/life-quality indices and acceptance of toxicities and expectations; (2) tumor features; and (3) the molecular profile of the disease.³⁷ Differences in mechanisms of action and the distinct safety profiles of chemotherapeutic agents and treatment goals during later lines of treatment may guide treatment selection for individual patients. Management of AEs to maintain QoL is also a key consideration and is crucial to best practice in the setting of mCRC.³⁸ The main consideration for many patients is generally to maintain QoL for as long as possible; on that basis, QoL becomes more important with successive lines of treatment.³⁹

The findings from this study showed that encorafenib plus cetuximab with or without binimetinib consistently demonstrated longer maintenance of QoL as measured by EORTC and FACT-C as well as across the individual subscales such as physical, functional, social, and emotional functioning compared with chemotherapy in patients with previously treated *BRAF* V600E-mutant mCRC in the BEACON CRC study. This manuscript includes a plain language summary explaining the significance of these QoL results in a concise, easy-to-understand format as a tool to

communicate to a broad audience and assist with engagement between medical professionals, patients, and others (Supplemental Figure S1, available at <https://doi.org/10.1016/j.esmooop.2022.100477>). Consequential changes in QoL may alert practitioners to disease progression and increased risk of mortality, but these changes can be challenging to detect.²² In the BEACON CRC study, the median time to definitive deterioration was longer for encorafenib plus cetuximab, with or without binimetinib, compared with control (EORTC and FACT-C). Time until definitive deterioration has been used to analyze changes in QoL^{22,40} and may provide an approach that yields meaningful, accessible results that are more easily evaluated by clinicians than patient-reported outcome scales alone, facilitating vital and timely clinical decision making.²²

Possible limitations include limited data beyond the early treatment cycles due to the lower number of assessable patients. Additional data evaluating the impact of encorafenib plus cetuximab with or without binimetinib on QoL and its relationship to classical parameters such as OS in mCRC would be of value. Although the EORTC and FACT-C are widely used, they do not give a complete picture of a patient's QoL due to limitations of memory recall and time between instrument administration. This analysis did not assess QoL in terms of financial burdens associated with mCRC as well as other mitigating life-quality factors such as socioeconomic status, access to health care, and presence or quality of a support system. As with all open-label studies, there is a risk of bias.

Previous clinical reports on targeted agents in patients with mCRC have shown that treatment can provide survival benefits without diminishing QoL.⁴¹⁻⁴⁸ This includes studies

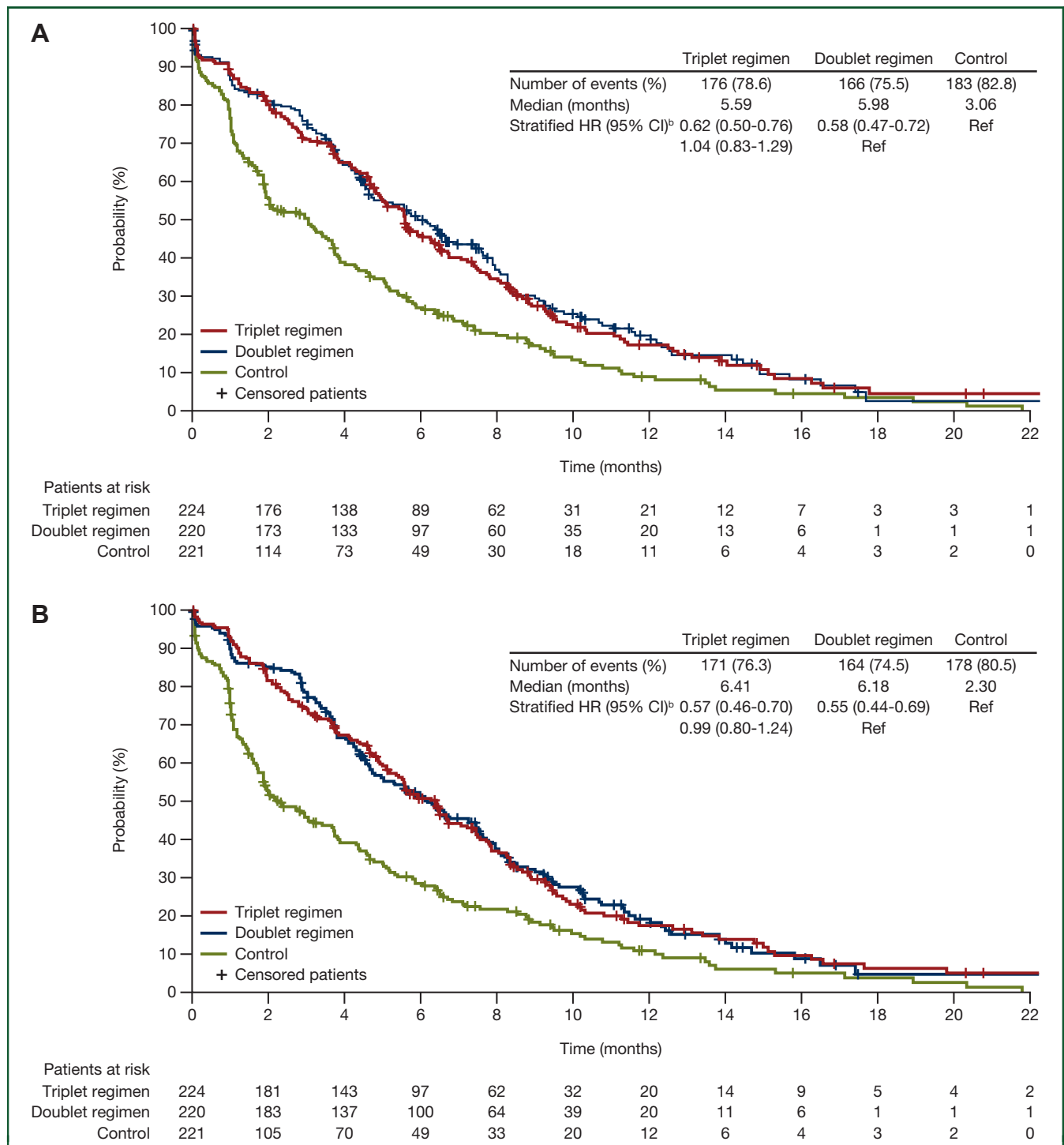


Figure 4. Median time to definitive deterioration^a in FACT-C subscales for encorafenib plus cetuximab with or without binimetinib compared with control: (A) Functional well-being; (B) physical well-being; (C) social/family well-being; (D) emotional well-being. Probability (%) of median time to definitive 10% deterioration in FACT-C colorectal cancer subscales (A) functional well-being, (B) physical well-being, (C) social/family well-being, and (D) emotional well-being for patients treated with encorafenib plus cetuximab with or without binimetinib (triplet and doublet, respectively) compared with the control.

CI, confidence interval; FACT-C, Functional Assessment of Cancer Therapy—Colorectal; HR, hazard ratio.

^aDefinitive deterioration is at least 10% worsening relative to baseline with no later improvement above this threshold, or death due to any cause.

^bStratified by Eastern Cooperative Oncology Group performance status, source of cetuximab, and prior irinotecan use at randomization.

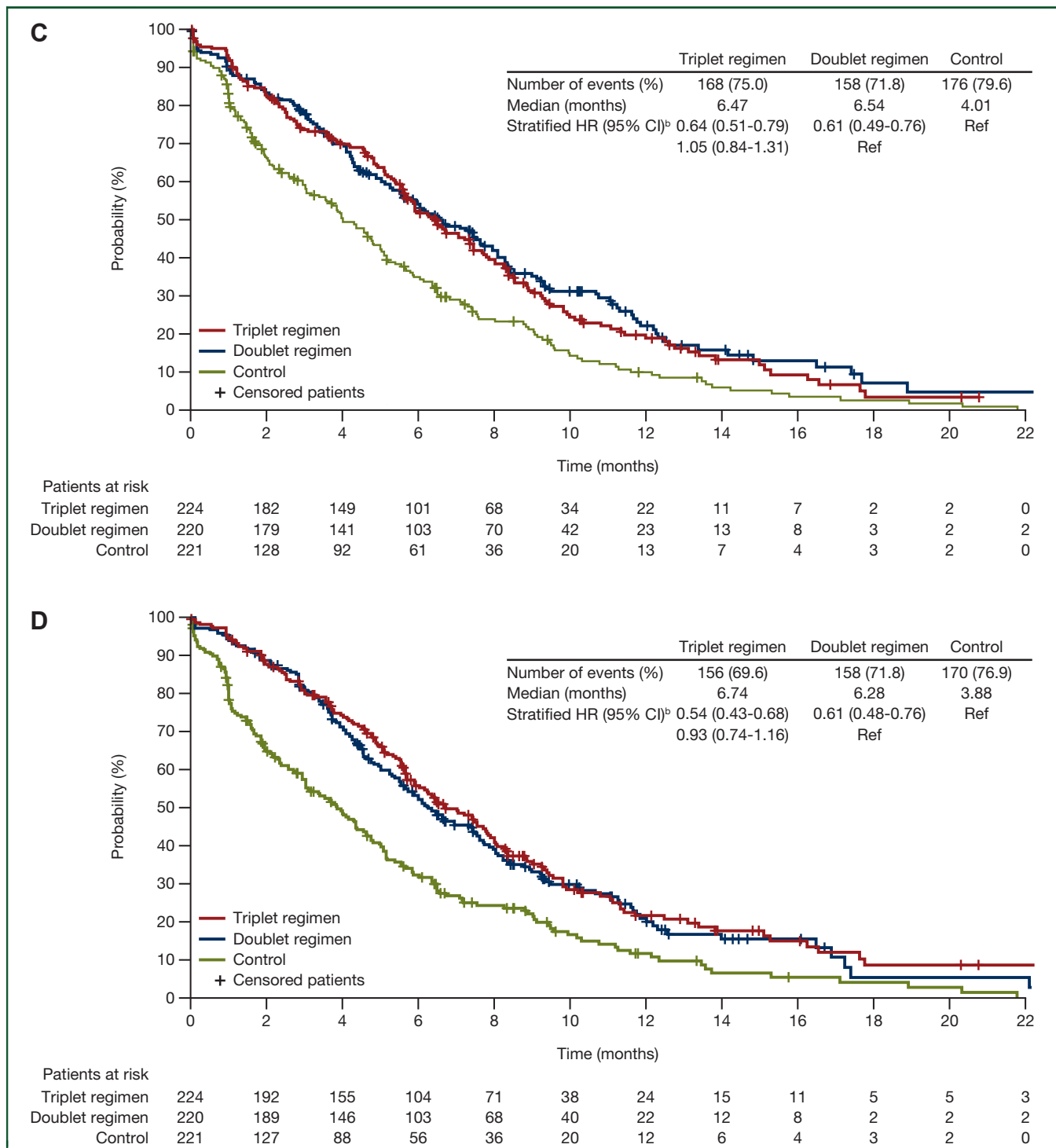


Figure 4. Continued.

indicating that adding cetuximab to chemotherapy for mCRC does not negatively impact QoL relative to chemotherapy alone.⁴¹⁻⁴³ Similar findings have been reported for bevacizumab, panitumumab, aflibercept, and regorafenib.⁴⁴⁻⁴⁸

In addition to improving OS as reported previously, encorafenib plus cetuximab with or without binimetinib delays QoL decline in previously treated patients with *BRAF* V600E-mutant mCRC.

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DATA SHARING

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See <https://www.pfizer.com/science/clinical-trials/trial-data-and-results> for more information.

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