EFFECTIVENESS AND QUALITY OF LIFE IN PATIENTS WITH METASTATIC, BRAF^{V600E}-MUTATED, COLORECTAL CARCINOMA TREATED WITH ENCORAFENIB PLUS CETUXIMAB

DATA FROM THE EUROPEAN MULTI-CENTRIC, MULTI-NATIONAL, NON-INTERVENTIONAL STUDY – BERING^{CRC}

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INTRODUCTION

Background

BRAF^{V600E} mutations are found in 8-12% of patients with metastatic colorectal cancer (mCRC) and are linked to a poor prognosis. The standard treatment for these patients, following previous systemic therapy, is the combination of encorafenib and cetuximab (E+C). As data from controlled clinical trials are based on a selected patient population, the non-interventional study (NIS) BERING^{CRC} aims to investigate the use of E+C under real-world conditions in a broader patient population.

METHODS

Study Design

BERING^{CRC} (NCT04673955) is an ongoing multi-national, multi-centric, prospective NIS. It represents the first NIS to investigate the real-world use of E+C in BRAF^{V600E}-mutant mCRC patients from 126 sites in Germany, Austria and Switzerland. The aim of the study was to enroll up to 300 patients, who have received prior systemic therapy and who were treated according to the label.

Statistical Analysis

For the present interim analysis, data were analyzed 12 months after inclusion of 200 patients.

- Patient and disease characteristics at baseline and effectiveness outcomes were evaluated for patients who fulfilled the in-/exclusion criteria and had at least one administration of E+C documented (Full Analysis Set (FAS) = 189 patients (7 screening failures; 4 treatment not started yet)).
- Safety analyses were evaluated for patients with signed informed consent for whom at least one administration of E+C was documented and for whom at least one safety assessment was obtained while on treatment with E+C.
- Patient-reported outcomes (PROs) on QoL were assessed using the validated questionnaire EORTC QLQ-C30. These analyses were evaluated for prospectively enrolled patients in FAS having provided at least an evaluable baseline and one evaluable on-treatment PRO assessment (PRO analysis set n=54).

Table 1: Patient and disease characteristics at baseline/primary diagnosis

	FAS; n=189 (GER: 156, AUT: 26, CH: 7)
Median age, years (min – max)	66.2 (26.6-88.4)
Female gender, n (%)	90 (47.6)
ECOG Performance Status, n (%)	
• 0	66 (34.9)
• 1	89 (47.1)
• 2	27 (14.3)
• 3	2 (1.1)
• Not evaluated/missing	5 (2.6)
Location of primary tumor, n (%) *	
• Cecum and appendix	27 (14.3)
• Colon	146 (77.2)
• Rectum	23 (12.2)
Sidedness of primary tumor, n (%) #	
• Right	116 (61.4)
• Left	70 (37.0)
• Both sides	5 (2.6)
UICC stage at primary diagnosis, n (%)	
• I	3 (1.6)
• II	8 (4.2)
• III	42 (22.2)
• IV	133 (70.4)
• Missing	3 (1.6)
Localization of metastases, n (%) *	
• Liver	115 (60.8)
• Peritoneum	68 (36.0)
• Lung	41 (21.7)
• Supra-regional lymph nodes	30 (15.9)
• Other	44 (23.3)
• Missing+	1 (0.5)
Number of metastatic sites, n (%)	
• Involvement of <3 organs	158 (83.6)
• Involvement of ≥3 organs	30 (15.9)
• Missing+	1 (0.5)
Microsatellite instability at primary diagnosis and/or at baseline, n (%)	
• MSI-High	19 (10.1)
• MSI-Low	10 (5.3)
• MSS	128 (67.7)
• No test reported/missing	32 (16.9)

*Multiple answers per patient possible.
#Multiple answers due to multifocal primary tumor possible
MSI, Microsatellite Instability ; MSS, Microsatellite Stable
+ As documented in the EDC. Patient currently under query.

Table 2: Response under treatment with E+C

	FAS; n=189
Best overall response, n (%)	
Complete response (CR)	3 (1.6)
Partial response (PR)	55 (29.1)
Stable Disease (SD)	44 (23.3)
Progressive Disease (PD)	64 (33.9)
No response assessment done	23 (12.2)
Overall response rate, n (%) [95% CI for percentage]	
ORR*	58 (30.7) [24.5-37.6]
Progression-free survival	
Median PFS, months [95% CI]	5.2 [4.4-5.5]
Overall survival	
Median OS, months [95% CI]	10.3 [8.2-11.3]

*ORR is defined as proportion of patients with CR or PR as best overall response.

Table 3: Safety

	SAF; n=189
TEAE*, n (%)	157 (83.1)
Serious TEAE, n (%)	73 (38.6)
Non-serious TEAE, n (%)	133 (70.4)
Grade 3/4 TEAE, n (%)	71 (37.6)
TEAE in ≥10% patients, any grade	
Rash, n (%)	20 (14.2)
Nausea n (%)	14 (9.9)
Fatigue n (%)	20 (10.6)

* TEAE treatment emergent adverse event

RESULTS

Patient population

On April 30, 2025, i.e. end of recruitment period, 259 patients have been enrolled in total. For the present interim analysis (data base cut January 26, 2025), 189 patients were treated with E+C and evaluable for the current analysis. For all patients who fulfilled the FAS criteria, baseline and disease characteristics are depicted in **Table 1** (n=189). Median age was 66.2 years and 82% of patients had an ECOG Performance Status of 0/1. At baseline, 99.5% of patients had distant metastases with liver (60.8%), peritoneum (36.0%) and lung (21.7%) being the most affected sites of metastasis.

The predominant reason for E+C treatment (FAS; n=189) was the presence of a BRAF mutation (53.4%) followed by remission pressure (29.1%) and physician's preference (10.6%) (**Figure 1**).

Effectiveness of E+C treatment

At database cut for this interim analysis, the median treatment duration of E+C was 4.9 months [95% CI 4.1-5.3]. Overall response rate (ORR) was 30.7% [95% CI 24.5-37.6], median progression-free survival (mPFS) was 5.2 months [95% CI 4.4-5.5] and median overall survival (mOS) 10.3 months [95% CI 8.2-11.3] (**Table 2**). The median duration of response was 4.2 months [95% CI 3.1-6.0].

Safety results showed that treatment-emergent adverse events (TEAE) were reported in 83.1% of patients (any grade), CTCAE grade 3/4 TEAEs in 37.6% of patients. Most frequent TEAEs (≥10%, any grade) were rash (14.8%), nausea (11.1%) and fatigue (10.6%) (**Table 3**).

Patient reported Outcomes during E+C treatment

In total 54 patients participated in the PRO module. The majority of patients reported to be satisfied with the E+C treatment over time (**Figure 2**).

The global health status/QoL assessed by the EORTC QLQ-C30 questionnaire remained stable for at least the first 10 months under E+C treatment (**Figure 3a**). This was also reflected in most functional and symptom scales of the EORTC QLQ-C30; change from baseline in social functioning, pain and insomnia are depicted in **Figure 3b-d**.

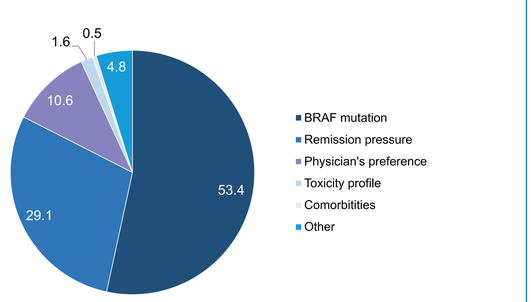

Figure 1: Treatment decision making. The reason for E+C treatment was documented in the eCRF by choosing one of the following answers: remission pressure (rapid PD, tumor load), toxicity profile, patient's preference, physician's preference, comorbidities, BRAF mutation, or other.

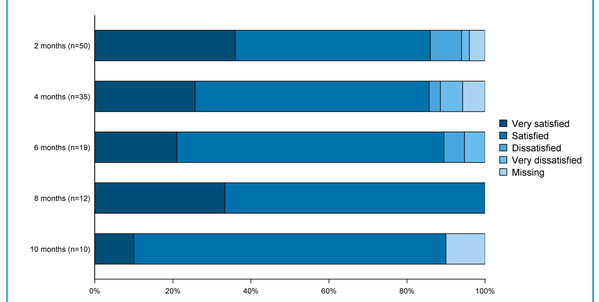

Figure 2: Patients' treatment satisfaction for patients participated in PRO analysis (n=54). Patients were asked to judge their treatment satisfaction on a 4-point scale: very satisfied, satisfied, dissatisfied, very dissatisfied. Results of months 2, 4, 6, 8 and 10 are displayed.

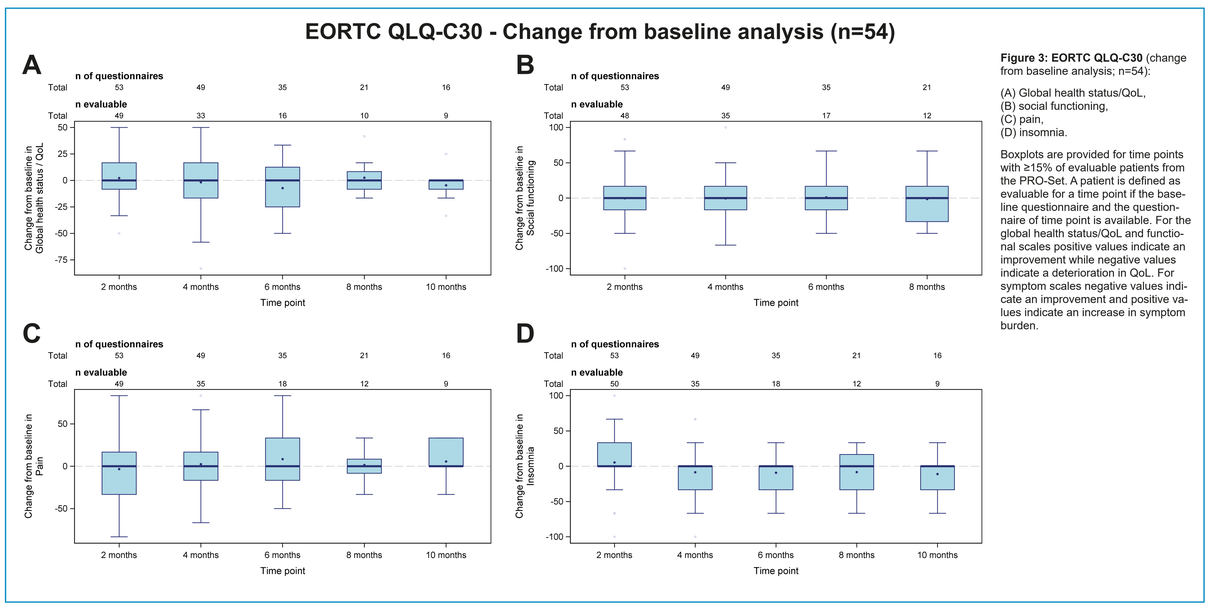

Figure 3: EORTC QLQ-C30 (change from baseline analysis; n=54):

(A) Global health status/QoL,
(B) social functioning,
(C) pain,
(D) insomnia.

Boxplots are provided for time points with ≥15% of evaluable patients from the PRO-Set. A patient is defined as evaluable for a time point if the baseline questionnaire and the questionnaire of time point is available. For the global health status/QoL and functional scales positive values indicate an improvement while negative values indicate a deterioration in QoL. For symptom scales negative values indicate an improvement and positive values indicate an increase in symptom burden.

CONCLUSION

This interim analysis of the BERING^{CRC} study showed that QoL was maintained during E+C treatment in patients participating in the PRO module. The data confirm the effectiveness and safety profile of E+C in an older and broader real-world patient population compared to the pivotal BEACON CRC trial.

LIMITATIONS

Considering the exploratory nature of this interim analysis, with a limited number of patients and a short observational period, these results are considered preliminary and the data as well as differences between interim analyses should be interpreted with caution.

INFORMATION

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Contact

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Conflicts of Interest S. Stintzing:

Consulting or Advisory Role: Merck, Roche, Amgen, Pierre Fabre, MSD, AstraZeneca, Servier, GlaxoSmith Kline, TERUMO, Nordic Bioscience, Seagen, Daiichi Sankyo, CV6 Therapeutics, Isofol Medical; Travel, Accomodations, Expenses, Honoraria: Merck, Roche, Amgen, Servier, MSD, Pfizer, Pierre Fabre, Bristol-Myers Squibb, Nordic Bioscience, Astra Zeneca, Daiichi Sankyo, Merck, Roche, Sanofi, Bayer, Sirtex Medical, Amgen, Lilly, Takeda, Pierre Fabre, Astra Zeneca; Research Funding: Pierre Fabre, Roche, Merck, Amgen, MSD; Other: Board member of the AIO within DKG.

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