RESULTS OF THE ONGOING NON-INTERVENTIONAL STUDY VALIDATE

QUALITY OF LIFE IN PATIENTS WITH RAS WILD-TYPE METASTATIC COLORECTAL CANCER RECEIVING 1ST-LINE PANITUMUMAB PLUS FOLFIRI OR FOLFOX

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BACKGROUND

Panitumumab, a recombinant, fully human monoclonal anti-EGFR antibody, is approved, including but not limiting as first-line therapy in combination with FOLFIRI (5-FU + Folinic acid + Irinotecan) or FOLFOX (5-FU + Folinic acid + Oxaliplatin) for adult patients with RAS wild-type metastatic colorectal cancer (mCRC). The approval was based on several clinical trials[1,2].

Quality of life (QoL), however, has not been formally assessed in real-world so far and real-world data in general are scarce. To address the effect of panitumumab plus FOLFIRI or FOLFOX on QoL, patient-reported outcomes (PROs) were assessed in a large mCRC cohort. The present analysis shows first data on QoL during first-line treatment with panitumumab + FOLFIRI or FOLFOX of the satellite project of VALIDATE.

METHODS

VALIDATE (NCT03043950) is an ongoing, multicentric, non-interventional study prospectively observing patients with RAS wild-type mCRC who are treated with first-line panitumumab plus FOLFIRI or FOLFOX according to SmPC. The primary focus of VALIDATE is to prospectively validate the five-factor mCRC prognostic score (mCCS)[3] in a large real-world cohort of patients by evaluating overall survival in three different risk groups (low / intermediate / high risk) based on the mCCS. Moreover, a prospectively planned satellite project to assess PROs on QoL using the validated questionnaires EORTC QLQ-C30 and QLQ-CR29 was established. Questionnaires were distributed at baseline and thereafter three-monthly during first-line treatment until end of treatment (EOT). Scores were calculated according to the respective EORTC manuals for each scale or single item. Summary tables with descriptive statistics were used to display questionnaire results. A clinically relevant deterioration of a scale/single item was defined as deterioration (increased symptoms/ decreased functionality) of the median score by at least 10 points (minimal important difference, MID) compared to baseline at a post-baseline questionnaire timepoint. At data-base cut (March 15, 2022), first-line therapy was still ongoing in 16 patients. The present analysis presents QoL regardless of the mCSS risk group.

RESULTS

In total, 613 patients were enrolled in VALIDATE. Of those, 316 patients consented to participate in the PRO module and were subject of the present analysis. The median age was 66.1 years (range: 32.3-87.0), 70.6% of patients were male and 87.3% had an ECOG performance status of 0/1. 59.8% of patients had a tumor of the colon and in 86.1% of all patients the tumor was left-sided. Further patient and disease characteristics are shown in **Table 1**. 25.6% of patients received FOLFOX and 74.4% received FOLFIRI as chemotherapy backbone.

Of all 316 patients who consented to participate in the PRO module, 264 patients were evaluable, i.e., filled out a questionnaire before start of treatment with panitumumab + FOLFIRI or FOLFOX (=baseline) . The questionnaire return rate per questionnaire timepoint is depicted in **Figure 1**.

The median EORTC QLQ-C30 global health status did not show any clinically relevant changes at all time points during panitumumab treatment and at the patients' individual end of treatment as compared to baseline (**Figure 2**).

Overall, 24 functional and symptom scales of the QLQ-C30 and QLQ-CR29 did not show any clinically relevant changes during first-line panitumumab treatment as compared to baseline. In total, clinically relevant deteriorations were reported for two EORTC QLQ-C30 functional scale scores (role and social functioning), for two EORTC QLQ-C30 symptom scale scores (fatigue and dyspnoea) and for eight EORTC QLQ-CR29 scale scores (body image, dry mouth, dyspareunia, hair loss, impotence, stool frequency, trouble with taste, urinary frequency). Scores that worsened during first-line panitumumab treatment either recovered (i.e., median baseline value was restored) or did not show any further deterioration throughout further course of treatment. QLQ-C30 functional scales are exemplarily shown for social and physical functioning (**Figure 3**). QLQ-C30 symptoms scales are exemplarily shown for diarrhea, fatigue, pain and nausea and vomiting (**Figure 4**). QLQ-CR29 scales are exemplarily shown for sore skin, dry mouth, trouble with taste and weight (**Figure 5**).

Figure 1

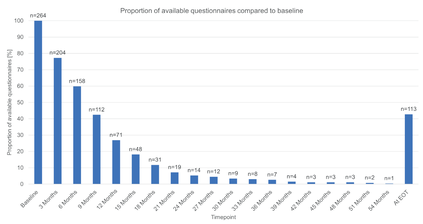

Figure 1: Proportion of available questionnaires compared to baseline.

The EOT questionnaire was handed out at the patients' individual end of treatment and cannot be placed chronologically within the other questionnaire timepoints.

Table 1

	Total (N = 316)
Patient characteristics	
Age at date of informed consent [years]	
Median	66.1
Gender	
Male	223 (70.6%)
ECOG Performance Status at baseline	
0 / 1	276 (87.3%)
≥ 2	14 (4.4%)
Unknown	26 (8.2%)
General patient condition at baseline (as documented)*	
Fit	294 (93.0%)
Unfit	22 (7.0%)
Disease characteristics	
Localization of tumor	
Colon	189 (59.8%)
Rectum	127 (40.2%)
Sidedness of tumor (left vs. right vs. colon unspecified)	
Left	272 (86.1%)
Right	42 (13.3%)
Colon (unspecified)	2 (0.6%)
Resection of primary tumor	
Yes	256 (81.0%)
No	60 (19.0%)
Tumor stage at primary diagnosis	
Stage I-III	102 (32.3%)
Stage IV	195 (61.7%)
Unknown	19 (6.0%)
Number of metastatic sites at inclusion	
1	193 (61.1%)
2	94 (29.7%)
3-4	29 (9.2%)

*as documented according to physician's judgement

Table 1: Patient and disease characteristics

Limitiation:

When interpreting quality of life results it must be kept in mind that patients who benefited most from therapy are overrepresented and only patients alive at the respective time point were able to be analyzed (Survivor bias).

CONCLUSION

The global health status remained stable over time without any clinically relevant deterioration during first-line treatment with panitumumab + FOLFIRI or FOLFOX. Symptom scales reflecting commonly reported side effects of panitumumab (e.g., skin reactions, diarrhea, nausea) also did not show any clinically relevant deteriorations during treatment, which is of greatest importance for patients diagnosed with advanced or metastatic disease.

Figure 2

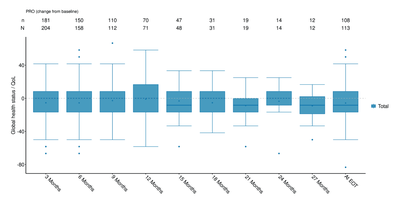

Figure 2: EORTC QLQ-C30 - Change from baseline in global health status over time

Positive values indicate an improvement; negative values indicate a worsening in quality of life.

Figure 3

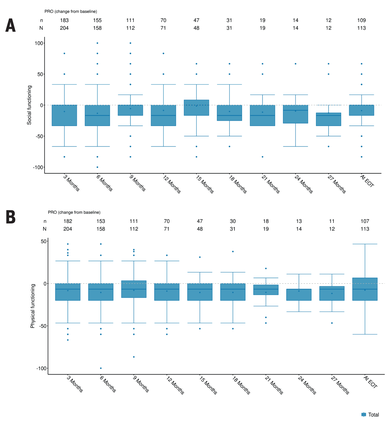

Figure 3: Change from baseline in selected EORTC QLQ-C30 functional scale scores over time. Change from baseline in (A) social and (B) physical functional scale score over time.

Positive values indicate an improvement; negative values indicate a worsening in quality of life and a lower level of functioning.

The EOT questionnaire was handed out at the patients' individual end of treatment and cannot be placed chronologically within the other questionnaire timepoints. Only timepoints with n≥10 are shown.

N: number of available questionnaires, n: number of evaluable questionnaires, StD: standard deviation, Box: lower to upper quartile, horizontal line inside box: median, diamond inside box: mean, whisker: minimum/maximum value within lower quartile minus 1.5x IQR / upper quartile plus 1.5x IQR, respectively, circles: outlier outside of lower quartile minus 1.5x IQR / upper quartile plus 1.5x IQR, respectively (IQR = interquartile range).

Figure 4

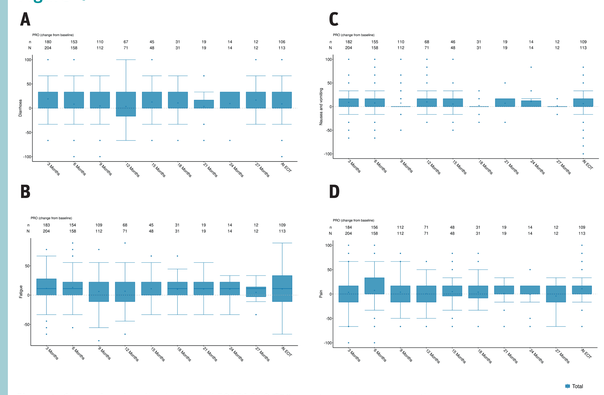

Figure 4: Change from baseline in selected EORTC QLQ-C30 symptom scale scores over time.

Change from baseline in (A) diarrhoea, (B) fatigue, (C) nausea and vomiting and (D) pain scale scores over time. Negative values indicate an improvement; positive values indicate a worsening in burden on daily life/symptoms.

Figure 5

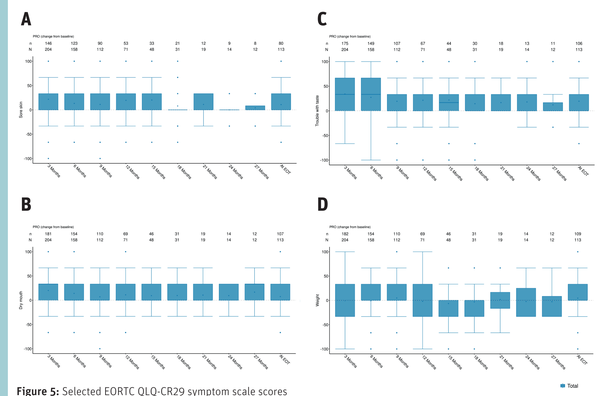

Figure 5: Selected EORTC QLQ-CR29 symptom scale scores

Change from baseline in (A) sore skin, (B) dry mouth, (C) trouble with taste and (D) weight scale scores over time. Negative values indicate an improvement; positive values indicate a worsening in burden on daily life/symptoms.

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Conflicts of Interest:

Marscher N: CEO of iOMEDICO; Shareholder of iOMEDICO; Consultancy for AstraZeneca, Bayer, Beigene, BMS, Clovis, Daiichi-Sankyo, Deloitte, Eusapharm, EISAI, GSK, IPSEN, J&J, Lilly, MSD, Mylan, Novartis, Oncopeptides, Onkovis, Pfizer, Pierre Fabre, Roche, Sanofi, Seagen, Servier; Financial support of research by Abbvie, Amgen, AstraZeneca, Bayer, Beigene, BMS, Clovis, Daiichi-Sankyo, Deloitte, Eusapharm, EISAI, Gilead, GSK, IPSEN, J&J, Lilly, Morphosys, MSD, Mylan, Novartis, Oncopeptides, Onkovis, Pfizer, Pierre Fabre, Roche, Sanofi, Seagen, Servier.

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Schuch A, Siebenbach HU, de Buhr R, Serrer L, Potthoff K: Employee of iOMEDICO.

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