Background and Objectives

The current standard for treating newly-diagnosed metastatic colorectal cancer (mCRC) consists of a doublet backbone chemotherapy plus cetuximab or bevacizumab. However, uncertainty exists concerning the comparative risk-benefit assessment of these interventions in mCRC, particularly due to the absence of clinical data studying their impact in patients’ Health-Related Quality of Life (HRQoL). Patient-Reported Outcomes (PROs), which provide direct measurements of cancer patients’ experiences through validated scales, offer a unique angle on treatment toxicity assessments, often showing clinically meaningful differences when compared to standardised clinician assessed tools, as the universally used Common Terminology Criteria for Adverse Events (CTCAE). Moreover, as the cornerstone of a Value-Based Health Care (VBHC) concept, a patient-centred approach requires that patient-driven health information completes the objective clinical data traditionally demanded by regulatory agencies upon drug approval. Patients with mCRC commonly present a considerable burden of symptoms that can, adding to treatment toxicities, have a substantial negative effect on HRQoL and functioning. Therefore, the repercussion of existing treatments on symptom control and HRQoL needs to be considered alongside survival, when comparing the clinical effectiveness of competing therapies. Nevertheless, although two head-to-head clinical trials tested the efficacy and safety of cetuximab versus bevacizumab, none of the studies included PROs as endpoints, and only “equivalent” CTCAE assessed toxicities were reported. We aimed to bridge this gap by conducting a prospective cohort study in mCRC, in order to measure and compare HRQoL outcomes reported by patients treated with cetuximab or bevacizumab.

Methods and Results

PROs were measured through two disease-specific instruments, widely used and thoroughly validated: EORTC QLQ-C30 and QLQ-CR29 questionnaires, which were answered at three sequential time points during treatment, including baseline. Global Health Status (GHS), functional and symptom scales, and Overall Treatment Utility (OTU), a survival endpoint derived from clinical and patient-reported outcomes) were compared for the two treatments. Methods and followed up with STROBE guidelines for observational studies and SISAQOL / SPIRIT-PRO recommendations for HRQoL data.

Between January 2017 and April 2018, 44 patients were allocated to cetuximab (n=19) or bevacizumab (n=25). Except for RAS mutation status, patient baseline characteristics were generally well balanced across treatment groups. A higher proportion of patients experienced a clinically meaningful (≥10) deterioration in GHS in cetuximab arm – 53.8% (95% CI: 25.1% to 80.8%) at 6 weeks and 66.7% (95% CI: 29.9% to 92.5%) at 12 weeks – compared to bevacizumab cohort: 18.2% (95% CI: 5.2% to 40.3%) at 6 weeks and 12.5% (95% CI: 1.6% to 38.3%) at 12 weeks (Table 1, Figure 1).

Conclusions and Relevance

This head-to-head prospective cohort study provides evidence suggesting that, in mCRC patients, cetuximab-containing regimens lead to a progressive negative impact on PROs and HRQoL, when compared to baseline and bevacizumab. Future research is needed to confirm these results. Our findings demonstrate the value of PROs when assessing comparative effectiveness of different treatment regimens.