Quality assurance for systemic therapy in metastatic colorectal carcinoma(QS-mCRC)

SYNOPSIS

Principal Investigator	Prof. Dr. med Sebastian Stintzing (Berlin) Spokesman of the Colon/Rectum/Small Intestine Tumor Working Group in the Association of Internal Oncology (AIO)
Scientific Committee	N.N. Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselerkrankungen (DGVS) N.N. Bundesverband der Niedergel. Hämatologen und Onkologen (BNHO) N.N. Berufsverband Niedergelassene Gastroenterologen (BNG) N.N. Arbeitsgemeinschaft Deutscher Darmkrebszentren (addz) N.N. Patient representative (ILCO)
Title of the study	Quality assurance for systemic therapy in metastatic colorectal carcinoma
Acronym	QS-mCRC
Version	2.1 (25.01.2024)
Background	With around 60,000 new cases, colorectal cancer is the second most common cancer in women and the third most common in men in Germany. Thanks to modern screening and innovative therapies, mortality has been decreasing since 2012, but it is still the second most common cause of cancer-related deaths in Europe. The ESMO guideline updated in 2022 [1] recommends a biomarker-driven treatment decision in the metastatic setting if the metastases are not primarily resectable and has developed a differentiated treatment algorithm for this, broken down by treatment line. The core recommendations of this algorithm are identical to those of the DGHO's Onkopedia guideline[2], which will also be updated in 2022, and also correspond to the recommendations of the German S3 guideline "Colorectal carcinoma", which is currently being updated [3].
Primary objective	Aim of the study is to examine the quality of diagnosis and therapy in the first and second-line treatment of metastatic colorectal carcinoma on a representative and nationwide basis. The implementation of the diagnostic and therapeutic recommendations of national and international guidelines (S3-LL; ESMO-GL and Onkopedia) in routine clinical treatment will be examined. The focus is on the implementation of therapy-relevant biomarker testing (dMMR/MSI; RAS mutations (KRAS and NRAS); BRAF;

	possibly HER2, NTRK) with the corresponding methodology (NGS, IHC, FISH), the first-line therapy then initiated as well as therapy sequences and therapy decisions depending on molecular alterations, including the timing of testing (and possibly re-testing) in second-line therapy. In addition, the establishment of "liquid biopsy" will be investigated in more detail.
Hypothesis	The core hypothesis is that the recommendations of the guidelines are insufficiently implemented in Germany, both regarding biomarker testing and its timing as well as the resulting treatment strategies with immune checkpoint, VEGF and EGFR inhibitors.
Intervention(s)	None. Recording of clinical routine
Target criteria	The target criterion is the degree to which the guideline recommendations are implemented in routine clinical practice. For the implementation of the diagnostic and therapeutic recommendations, standards are developed together with the scientific director on the basis of guideline recommendations, against which the implementation or the degree of deviation from the guideline recommendations can be measured.
Study design	Explorative retrospective register study with non-interventional study design. As part of the center survey (phase 1), all institutions in Germany that diagnose and treat colorectal carcinomas in Germany (gastroenterological and oncological hospital departments, as well as oncologists in private practice and gastroenterologists with an oncological focus) are contacted with the help of a pen-to-paper questionnaire. In order to adequately reflect the distribution of patients among the specialist groups and the care facilities (clinics of the various care centers and practices) as well as the corresponding proportions of patients treated there, the main survey (phase 2) is controlled exactly according to the distribution ratios surveyed in phase 1. To prevent a selection bias, all patients who meet the inclusion criteria are documented chronologically backwards in the participating facilities from a specified cut-off date until the allocated number of cases is reached (random selection). The data is collected individually, retrospectively and anonymously in a multi-page online questionnaire (eCRF) directly from the patient file, so that valid and reliable data is obtained from routine treatment in Germany (real-life data). Documentation is carried out via the eCRF system, which complies with the "Standard requirements for GCP-compliant data management in multinational clinical trials". Where possible, completeness checks and plausibility checks are programmed so that quality controls are carried out as soon as data is entered and participants can be interactively prompted to check and complete their entries. Once the survey has been completed, the data is subjected to comprehensive plausibility checks and any remaining contradictions or questions are clarified by the internal query management system and corrected in the database.

	During the entire field phase, participants will receive intensive telephone and e-mail support from employees with many years of expertise in the field of oncology for all content-related and technical questions.
Population	Inclusion criteria:: ▪ Age ≥ 18 years ▪ For 1st line patients: Diagnosis of mCRC with primary non-resectable metastases in QIII/23 and QIV/23; 1st line systemic therapy in the metastatic setting ▪ For 2nd line patients: therapy decision about 2nd line systemic therapy in QIII/23 and QIV/23
Statistics	Descriptive statistics include absolute and relative frequencies for qualitative characteristics. For continuous characteristics such as age, for example, measures of length are calculated with associated measures of dispersion (mean value with standard deviation, median with interquartile range as well as minimum and maximum). With the help of multivariable logistic regression models, the factors for the implementation of the guideline recommendation or the deviation from the recommendations are examined both with regard to patient characteristics and various care parameters (e.g. certification, patient volume, level of care, regional distribution).
Sample size	≈ 2100 patients with a diagnosis of mCRC and 1st or 2nd line system therapy (approx. 1400 patients in the 1st line and 700 patients in the 2nd line) The sample is selected on the basis of the care structure analysis collected in phase 1 in order to generate representative, valid, reliable and up-to-date data (see Study Design).
Duration of study	2024/25
Number of sites	≈ 400-500 centers for phase 1; ≈ 200-250 centers for phase 2

STUDY MANAGEMENT

Institution	*Function*	*Contact*
AIO AG Kolon-/Rektum-/Dünndarmtumoren	Principal Investigator	**Prof. Dr. Sebastian Stintzing**
Institute MMF	Logistic, data collections, programming, data management, analysis, and statistics	**Markus Kerkmann** **Patrik Lindenmaier** **Andreas Jaeger**

Literatur

1. Cervantes, A., et al., *Metastatic colorectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up.* Annals of Oncology, 2023. **34**(1): p. 10-32.

2. Hofheinz, R.-D., et al. *Onkopedia-Leitlinie Kolonkarzinom*. 2022; Available from: https://www.onkopedia.com/de/onkopedia/guidelines/kolonkarzinom/@@guideline/html/index.html.
3. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, D.K., AWMF). *S3-Leitlinie Kolorektales Karzinom*. AWMF Registernummer: 021/007OL 2019; Langversion 2.1, 2019]. Available from: https://www.leitlinienprogramm-onkologie.de/leitlinien/kolorektales-karzinom.