Quality Assurance Initiative on the Therapy of Bladder Cancer 2023 (QS-Harnblase)

SYNOPSIS	
Titel	Quality Assurance Initiative on the Therapy of Bladder Cancer 2023
Topic	Bladder cancer has an annual incidence of almost 18,000 new patients in Germany[1]; men are affected about three times more frequently than women. This makes it the fourth most common malignancy in men and the fourteenth most common in women.[2] Patients with non-muscle-invasive bladder cancer (NMIBC) are treated with TURB followed by instillation with Mitomycin C or BCG. Muscle-invasive bladder cancer (MIBC) is usually treated with a radical cystectomy. In addition, peri-operative platinum-based chemotherapy is conducted (adjuvant/neoadjuvant). In patients with advanced or metastatic disease, maintenance therapy with avelumab should be considered. Furthermore, checkpoint-inhibitor therapy is recommended for patients who are not platinum-eligible (depending on PD-L1 expression) or after failure of platinum-containing therapy.[3]
Objective	The planned project is intended to provide representative Real World Data on day-to-day diagnostic and therapeutic practice in the treatment of NMIBC, MIBC and metastatic urothelial cancer (mUC) throughout Germany. One focus is on changes in treatment patterns and pathways to the first survey in 2020.[4] Furthermore, demographic and clinical characteristics of patients without systemic treatment will be analyzed. These data will be used to gain insights into the quality of treatment - e.g. the degree of implementation of the therapy recommendations of the guidelines - from which measures for improving the quality of therapy can be derived. In a first step, the care structure will be analyzed, i.e. all urological and oncological institutions (clinics and office based urologists/oncologists) that potentially diagnose and/or treat bladder cancer will be asked about their number of patients (according to stage and therapy setting). In the second step, the diagnostic measures (including marker analyses, e.g. PD-L1 testing) and operative and systemic therapies (chemotherapy, immunotherapy and targeted therapies) are documented and analyzed (ad hoc) in a predefined period (Q4/2022-Q1/2023) on the basis of patient files. The sample is representative and adjusted according to the previously raised care structure.
Target criteria	The diagnosis and therapy reality will be exploratively examined, the target criterion here being the stage-adapted, guideline-adherent therapy. To be analyzed: Diagnostic parameters: type of cystoscopy (FLC, WLC); mutation status (e.g. FGFR3) and performed expression analyses (e.g. PD-L1). Surgerical parameters: type of surgery (TURB, radical cystectomy or bladder-preservation, formation of neobladder/conduit), success of surgery (residual tumor/R classification), Medical treatment parameters: instillation therapy, perioperative chemotherapy; radiochemotherapy, checkpoint inhibitors and targeted therapies. One focus is on the definition of cisplatin eligibility, as well as, in advanced therapy lines, the therapy sequences over different lines. The demographic and clinical characteristics of patients without cancer-specific treatment (best supportive care).

Hypothesis	The therapy habits and the implementation of therapy recommendations of the guidelines are subject to great heterogeneity throughout Germany, which is reflected in both regional differences and along the care structure.
Intervention(s)	None. In the patient documentation, only such health data are collected and evaluated that are routinely generated.
Study design	This a non-interventional observational study with explorative character. *Phase I - Analysis of care structure and recruitment:* For the analysis of the care structure, all urological hospital departments and all resident urologists are contacted in order to obtain data on the care facilities (e.g. care level, certification) and on the corresponding patient numbers (number of primary diagnoses, number of patients in treatment, differentiated according to stages, number of IV treatment places) as well as the willingness to participate in the main survey (phase II) of the QS bladder cancer (pen-to-paper questionnaire). *Phase II - Patient documentation:* To obtain a reliable, representative sample of patients treated in Germany, the patients to be documented will be selected in a representative way based on the previously performed health care structure analysis data and distribution ratios from phase 1. The participating centers will be assigned to the following four clusters (each subdivided by stage and hospital/practice) according to the number of patients to be documented: Centers with very high, high, medium, and low patient volume (PV). Cut-offs for the distribution will be determined using the 75%, 50%, and 25% quartiles of PV. This sample is modulated according to the previous care structure analysis. Thus, the real care situation is proportionally and representatively reflected in the sample. In order to avoid a selection bias, the centers are asked to document the number of assigned patients chronologically from a defined cut-off date (10/01/2022) until the assigned number of cases is reached. The documentation will be based on the patient file retrospectively and online via a specially created and SSL-encrypted eCRF protected by individual access data, which complies with the "Standard requirements for GCP-compliant data management in multinational clinical trials".[5] *Repeated surveys:* The data collection should be repeated at regular intervals in order to observe the changes in the therapy landscape and to continuously monitor therapy quality.
Population	Patients with the indication non-muscle-invasive bladder cancer (NMIBC) muscle-invasive bladder cancer (MIBC) or metastatic urothelial cancer (mUC). Inclusion criteria: • Age at least 18 years • Diagnosis in Q4/2022-Q1 2023 (diagnosis of NMIBC or MIBC, newly diagnosed mUC or relapsed/progressive metastatic disease)
Statistical analysis	The data is evaluated after complete documentation according to the intention-to-treat principle. The statistical data analysis is performed with the program SPSS 27 (IBM Corp. Released 2020) or higher and R version 4.2.2. Since this is an explorative study, the evaluation of all variables is primarily descriptive. The p-values are also descriptive. The significance level ($p < 0.05$, two-sided) is not adjusted. The descriptive statistics include absolute and relative frequencies for qualitative characteristics. For continuous characteristics position measures with corresponding scattering measures are calculated (mean value with standard deviation, median with interquartile distance as well as minimum and maximum). Regression coefficients and two-sided 95% confidence intervals are reported for the effect estimators.

Sample size	The main survey (Phase II) is planned as a representative sample. Depending on the willingness of the centers to participate, a sample of 1700 patients (600 NMIBC, 600 MIBC, 500 mUC) is targeted. An expense allowance will be paid for the documentation of the patients (approx. 70 Euro per patient). As an additional incentive, the centers participation in the quality assurance initiative can be recognized with a participation certificate.
Duration of study	September 2023 - March 2024 (start of the survey until the final report after full evaluation)
Participating centres	For Phase I, all urological clinic departments (approx. 600) and office-based urologists (approx. 3500), as well as office-based oncologists (approx. 450) will be contacted (target size responses: 500 centers). Phase II will involve all centers that treat bladder cancers and have agreed to participate (target size approx. 200 centers).

STUDYMANAGEMENT		
Organisation	***Assignment***	***Contact***
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