TPS4617 Poster Session

Clinical effectiveness of urine DNA for minimal residual disease (MRD) monitoring of urothelial carcinoma in urine: A multicenter, prospective, observational study.

Xuanjun Guo, Lei He, Kaiwei Yang, Han Hao, Wei Yu, Yanqing Gong, Zhisong He, Cuijian Zhang; Peking University First Hospital, Beijing, China; Department of Urology, Peking University First Hospital, Beijing, China

Background: Limited methods and poor compliance are major issues in urothelial carcinoma (UC) surveillance. Non-invasive monitoring of minimal residual disease (MRD) using urine tumor DNA (utDNA) represents a significant advancement, potentially reducing reliance on invasive cystoscopy and low-sensitivity imaging. Preclinical studies have demonstrated the utDNA multidimensional bioinformatic algorithm's high sensitivity (92.8%) and specificity (96.0%) by integrating copy-number variations (CNVs) and genetic mutations, showcasing its potential to improve cancer detection accuracy. However, large prospective clinical trials validating its clinical utility in postoperative recurrence and treatment efficacy monitoring remain scarce. Clinically, UC patients with similar manifestations and pathology often show divergent outcomes. Accurately assessing recurrence risk, metastasis, and treatment efficacy is an urgent need. This study aims to validate the clinical utility for recurrence monitoring and efficacy assessment in larger cohorts. **Methods:** This multicenter, prospective, observational trial evaluates the algorithm's efficacy in MRD detection among UC patients. The trial design incorporates stratification by clinical stage, including non-muscle-invasive bladder cancer (NMIBC), muscle-invasive bladder cancer (MIBC), and upper tract UC (UTUC). We divided the study population into four cohorts: Cohort 1 includes patients with high-risk UTUC (pT3-4 or N+) who have undergone surgery; Cohort 2 consists of NMIBC patients after transurethral resection of bladder tumor (TURBT); Cohort 3 comprises MIBC patients scheduled for neo-adjuvant therapy; Cohort 4 includes patients assessed as complete response (CR) after standard trimodality treatment (TMT). In each Cohort, the accuracy for recurrence monitoring is evaluated using cystoscopy ± biopsy/surgical pathology, combined with imaging (CT/MRI) as the gold standard. Morning urine samples were collected from patients who had met the eligibility criteria and volunteered to participate in the study. Next-generation sequencing (NGS) was carried out on cell-free urinary DNA (ucfDNA) and urinary exosomal DNA (uexDNA). The minimal residual disease (MRD) score was computed by the algorithm, developed based on a feature matrix incorporating genetic alterations and copy number variations (CNVs). A classification threshold of 60 was established for clinical decision-making in the context of this study. We planed to enroll a total of 400 patients in this study. The sample sizes for the four cohorts were as follows: 100 for cohort 1, 200 for cohort 2, 50 for cohort 3, and 50 for cohort 4. As of January 2025, enrollment is ongoing, with cohorts actively monitored. The study was registered under ChiCTR2400081246. Reference: DOI: 10.1186/s12943-023-01729-7. Clinical trial information: ChiCTR2400081246. Research Sponsor: Peking University First Hospital High Quality Clinical Research Specialization.