BJU Int 2024 doi:10.1111/bju.16389

BJUI
BJU International

Original Article

Improving detection of carcinoma *in situ* in bladder cancer: urinary cytology vs the Xpert® BC Monitor

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Objective

To investigate and compare the performance of urinary cytology and the Xpert BC Monitor test in the detection of bladder cancer in various clinically significant patient cohorts, including patients with carcinoma *in situ* (CIS), in a prospective multicentre setting, aiming to identify potential applications in clinical practice.

Patients and Methods

A total of 756 patients scheduled for transurethral resection of bladder tumour (TURBT) were prospectively screened between July 2018 and December 2020 at six German University Centres. Central urinary cytology and Xpert BC Monitor tests were performed prior to TURBT. The diagnostic performance of urinary cytology and the Xpert BC Monitor was evaluated according to sensitivity (SN), specificity (SC), negative predictive value (NPV) and positive predictive value (PPV). Statistical comparison of urinary cytology and the Xpert BC Monitor was conducted using the McNemar test.

Results

Of 756 screened patients, 733 (568 male [78%]; median [interquartile range] age 72 [62–79] years) were included. Bladder cancer was present in 482 patients (65.8%) with 258 (53.5%) high-grade tumours. Overall SN, SC, NPV and PPV were 39%, 93%, 44% and 92% for urinary cytology, and 75%, 69%, 59% and 82% for the Xpert BC Monitor. In patients with CIS (concomitant or solitary), SN, SC, NPV and PPV were 59%, 93%, 87% and 50% for urinary cytology, and 90%, 69%, 95% and 50% for the Xpert BC Monitor. The Xpert BC Monitor missed four tumours (NPV = 98%) in patients with solitary CIS, while potentially avoiding 63.3% of TURBTs in inconclusive or negative cystoscopy and a negative Xpert result.

Conclusion

Positive urinary cytology may indicate bladder cancer and should be taken seriously. The Xpert BC Monitor may represent a useful diagnostic tool for correctly identifying patients with solitary CIS and unsuspicious or inconclusive cystoscopy.

Keywords

bladder cancer, carcinoma *in situ*, cytology, NMIBC, urine marker, Xpert

Introduction

With an estimated 573 278 cases in 2020, bladder cancer is the 10th most common cancer worldwide, accounting for 3% of global cancer diagnoses [1,2].

Approximately 75% of patients initially present with a disease that is limited to the mucosa or submucosa and is therefore referred to as non-muscle-invasive bladder cancer (NMIBC) [3].

Transurethral resection of the bladder tumour (TURBT) represents the initial standard therapy for such patients [4]. However, NMIBC confers a particularly high risk for tumour recurrence, with 5-year recurrence rates of up to 70%. Progression to higher tumour stages is especially concerning in (very) high risk patients as per the 2021 European Association of Urology (EAU) NMIBC scoring model [4,5]. Guidelines therefore recommend standardised and risk-adapted follow-up protocols, including regular cystoscopies, urinary cytology and upper tract imaging [5,6].

Urinary cytology is well established as part of surveillance of high-grade tumours (including carcinoma *in situ* [CIS, pTis]) due to its high sensitivity (SN), as suggested by the EAU guidelines [5–7]. The SN in intermediate- and low-grade tumours, however, is relatively low [7].

The Xpert Bladder Cancer Monitor test (Cepheid, Sunnyvale, CA, USA; hereafter referred to as the Xpert BC Monitor), an mRNA-based urinary marker test, has shown a superior overall negative predictive value (NPV) compared to urinary cytology [8,9], along with an overall SN of 75% and a specificity (SC) of 89.6% [10–12].

CIS poses a significant diagnostic challenge, as it is a flat high-grade NMIBC, that can be misinterpreted as an inflammatory lesion or be missed during cystoscopy, if not biopsied. This is critical considering that up to 54% of patients with CIS eventually progress to muscle-invasive disease [13].

There is an urgent need for supplementary diagnostic tools to enhance the diagnostic performance of white-light cystoscopy (WLC) in order to correctly identify CIS, while minimising unnecessary TURBTs for inflammatory lesions.

The aims of this study therefore were to evaluate and compare the diagnostic performance of the Xpert BC Monitor and urinary cytology for different NMIBC subgroups in a large prospective multicentre cohort in order to identify potential applications in clinical practice, with a particular focus on patients with CIS (concomitant or solitary).

Materials and Methods

Study Population

This observational study was conducted within the scope of the MoniTURB-trial, a prospective multicentre trial at six German university centres that was designed to assess whether the Xpert BC Monitor can predict the need for second TURBT [14].

The study included patients aged at least 18 years who underwent TURBT and were willing to give urine samples (voided, not bladder wash or via catheter). Patients were admitted for TURBT at the treating urologists' discretion. The indication for this was suspicion of a bladder tumour in WLC or in doubtful cases when malignancy could not be definitively ruled out (such as in cases of inflammatory redness) at initial diagnosis or during tumour surveillance.

All patients gave written informed consent. Findings, data acquisition, and processing complied with the latest Declaration of Helsinki ethical standards. The study was approved by the University of Regensburg local ethics committee (Ethics vote: 18-967-101) and registered in the German Register of Clinical Trials (DRKS-ID: DRKS00014974).

Study Procedures

Voided urine collection was performed at the pre-intervention consultation 1–10 days before the TURBT (several hours before the TURBT was also allowed). Xpert BC Monitor performance was established relative to histology (for disease-positive and -negative patients) and to urinary cytology, performed at a central pathology laboratory (Institute of Pathology, Friedrich-Alexander-University of Erlangen-Nuremberg).

The results from the Xpert BC Monitor were not used for patient management. To minimise bias in specimen analysis based on use of the Xpert BC Monitor, urinary cytology, WLC or TURBT, the operator(s) performing Xpert BC Monitor testing were blinded to patient status, cystoscopy, urinary cytology and central histology results and the person(s) performing the TURBT, cystoscopy and pathology analysis were blinded to the Xpert BC Monitor results.

Urinary Cytology

Urinary cytology was assessed according to The Paris System (TPS) for reporting urinary cytology by two blinded expert pathologists (A.H., M.E.). TPS is a well-established, standardised reporting system that was originally published in 2016 and has been validated in previous studies [15,16]. It redefined urinary cytology categories and was adapted to our study as follows: (1) no adequate diagnosis possible: 'no diagnosis'; (2) negative for urothelial carcinoma (UCA): 'negative'; (3) atypical urothelial cells: 'atypia'; and (4) high-grade (G3) UCA: 'malignant'.

For dichotomous analyses, only results that were allocated to the category 'malignant' were considered 'positive', all other results were considered 'negative'.

Xpert Bladder Cancer Monitor

The Xpert BC Monitor, performed on the Cepheid GeneXpert Instrument Systems, is a qualitative *in vitro* diagnostic test intended to monitor the recurrence of bladder cancer in patients previously diagnosed with bladder cancer. The test uses a voided urine specimen and measures the level of five

target mRNAs (ABL1, CRH, IGF2, UPK1B, ANXA10) by means of real-time reverse transcription-polymerase chain reaction (RT-PCR).

The Xpert BC Monitor provides positive or negative test results based on the results of a linear regression algorithm (linear discriminant analysis) that uses the cycle threshold results of the five mRNA targets. It is not necessary to detect all the mRNA targets for a positive test result. In patients for whom two Xpert BC Monitors did not reveal a valid result, the test results were classed as 'invalid'.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 29 (IBM, Armonk, NY, USA). Clinical test performance regarding the detection of tumours for various subgroups was assessed by calculating the SN, SC, positive predictive value (PPV) and NPV for Xpert BC Monitor and urinary cytology, respectively. Invalid Xpert BC Monitor results were excluded from the statistical analyses in order to avoid information bias. Comparison of the Xpert BC Monitor to urinary cytology was performed using the McNemar test. A *P* value below 0.05 indicated statistical significance and all analyses were two-tailed.

Results

Patient Cohort

Of the initial 756 patients who underwent TURBT between 1 July 2018 and 31 December 2020, 733 (97%) were included in the final analysis. Fourteen patients were excluded because either the Xpert BC Monitor result (seven patients), or urinary cytology result (seven patients) was missing. Nine patients showed histological evidence of malignancies other than UCA and were therefore also excluded.

The median (interquartile range) age was 72 (62–79) years and 568 patients (77.5%) were male. UCA of the bladder was present in 482 patients (65.8%) with high-grade tumours in 258 patients (53.8%) and evidence of muscle invasion (≥pT2, MIBC) in 72 patients (14.9%). Stratification into the different EAU NMIBC risk groups was as follows: low risk: 95 patients (19.7%); intermediate risk: 121 patients (25.1%); high risk: 159 patients (33%); and very high risk: 35 patients (7.3%). Muscle was detected in 364 patients (75.5%; Table 1). In all, 262 patients (36%) had a history of recurrent bladder cancer and 160 patients (21.8%) had received intravesical instillation therapy prior to TURBT (Table S1).

Table 1 Histopathological characteristics at transurethral resection of bladder tumour.

Characteristic	*n* = 482 (65.8)*
T stage at TURBT	
PUNLMP	7 (1.5)
pTa	274 (56.8)
pTis	22 (4.6)
pT1	107 (22.2)
≥pT2	72 (14.9)
Focality	
Unifocal	231 (47.9)
Multifocal	245 (50.8)
n.a.	6 (1.2)
Tumour diameter (largest)	
<3 cm	285 (59.1)
≥3 cm	148 (30.7)
n.a.	49 (10.2)
Concomitant CIS	
No	390 (80.9)
Yes	64 (13.3)
n.a.	28 (5.8)
Grading 1973	
G1	98 (20.3)
G2	145 (30.1)
G3	181 (37.6)
n.a.	58 (12)
Grading 2016	
Low grade	224 (46.5)
High grade	258 (53.5)
Muscle available	
No	114 (23.7)
Yes	364 (75.5)
n.a.	4 (0.8)
EAU risk classification	
Low	95 (19.7)
Intermediate	121 (25.1)
High	159 (33)
Very high	35 (7.3)
MIBC	72 (14.9)

**Numbers reflect patients with histologically proven urothelial carcinoma of the bladder (percentages). CIS, carcinoma in situ; EAU, European Association of Urology; MIBC, muscle-invasive bladder cancer; n.a., information not available; NMIBC, non-muscle-invasive bladder cancer; PUNLMP, papillary urothelial neoplasm of low malignant potential; TURBT, transurethral resection of bladder tumour.*

Performance of Urinary Cytology and the Xpert BC Monitor

Urinary cytology was classified as malignant in 205 patients (28%), negative in 402 patients (54.8%), no diagnosis in 88 patients (12%), and atypical in 38 patients (5.2%). Hence, a positive result was seen in 205 patients (28%) and a negative result in 528 patients (72%). The Xpert BC Monitor revealed a positive result in 428 patients (58.4%). The test was determined to be invalid in 17 patients (2.3%). Details are provided in Table 2.

The overall SN for detecting any UCA was 75% with the Xpert BC Monitor and 39% with urinary cytology, with corresponding SCs of 69% (Xpert BC Monitor) and 93% (urinary cytology). NPVs were 59% (Xpert BC Monitor) and 44% (urinary cytology), PPVs were 82% (Xpert BC Monitor) and 92% (urinary cytology). The Xpert BC Monitor provided the correct diagnosis in 521 cases (71%), while urinary cytology did so in 422 cases (58%; $P < 0.001$).

Table 2 Results of the Xpert BC Monitor vs urinary cytology.

Result	*n* = 733 (100)*
Xpert BC Monitor	
Negative	288 (39.3)
Positive	428 (58.4)
Invalid	17 (2.3)
Median LDA value (IQR)	0.605 (0.324–0.951)
Urinary cytology	
TPS classification	
No adequate diagnosis possible	88 (12)
Negative for urothelial carcinoma	402 (54.8)
Atypical urothelial cells (atypia)	38 (5.2)
High-grade (G3) urothelial carcinoma	205 (28)
Binary result	
Negative	528 (72)
Positive	205 (28)

**Numbers reflect all patients included into the survey (percentages). IQR, interquartile range; LDA, linear discriminant analysis; TPS, The Paris System.*

In patients presenting with gross haematuria (n = 107), the Xpert BC Monitor demonstrated a SN of 88% and urinary cytology a SN of 49%, with SCs of 71% (Xpert BC Monitor) and 98% (urinary cytology), NPVs of 75% (Xpert BC Monitor) and 48% (urinary cytology), and PPVs of 86% (Xpert BC Monitor) and 98% (urinary cytology). The Xpert BC Monitor accurately diagnosed 122 patients (77%), while urinary cytology correctly diagnosed 102 patients (65%; P = 0.013).

Among patients with CIS (solitary or concomitant, n = 86), the Xpert BC Monitor exhibited a SN of 90% and urinary cytology a SN of 59%, with SCs of 69% (Xpert BC Monitor) and 93% (urinary cytology), NPVs of 95% (Xpert BC Monitor) and 87% (urinary cytology), and PPVs of 50% (Xpert BC Monitor) and 75% (urinary cytology). The Xpert BC Monitor provided accurate diagnosis for 246 patients (73%) compared to 285 patients (85%) diagnosed correctly with urinary cytology (P < 0.001).

Specifically in patients with solitary CIS (n = 22), the Xpert BC Monitor showed a SN of 82% compared to a SN of 46% for urinary cytology, with SCs of 69% (Xpert BC Monitor) and 93% (urinary cytology), NPVs of 98% (Xpert BC Monitor) and 95% (urinary cytology), and PPVs of 19% (Xpert BC Monitor) and 37% (urinary cytology). The Xpert BC Monitor correctly diagnosed 187 patients (69%) and urinary cytology 244 patients (89%; P < 0.001).

Across various EAU risk groups, urinary cytology exhibited higher SC and PPV, whereas the Xpert BC Monitor demonstrated higher SN and NPV but lower SC and PPV compared to urinary cytology. These results were reproducible when considering subgroups of patients with a history of recurrent bladder cancer or those with first diagnosis. Further details can be found in Table 3a,b and Table S1.

Discussion

Bladder cancer confers a high risk for tumour recurrence and progression, especially in (very) high risk patients as per the 2021 EAU NMIBC scoring model [4,5]. This study aimed to assess the diagnostic performance of the Xpert BC Monitor and urinary cytology for different subgroups and to evaluate if those tests could reduce unnecessary TURBTs during tumour monitoring.

The EAU guidelines provided an updated and widely accepted risk classification for tumour progression in NMIBC patients in 2021 [5], based on a large retrospective survey including 3401 patients, which stratified patients into four risk groups (low, intermediate, high, and very high risk) for tumour progression according to tumour stage, grading, concomitant CIS, number of tumours, tumour size, and age [5]. Another 1528 patients received adjuvant intravesical BCG and were excluded from the analysis, because BCG may reduce the risk of disease progression [4]. Very high risk patients are a particularly interesting subgroup, since the probability of progression increased from 12% in high risk patients to 44% in very high risk patients. Although those patients represented only a small proportion of the included cohort (2%–3%), they made up 15% (WHO 1973) and 18% (WHO 2004/2016) of the 1528 excluded BCG-treated patients [4]. It is therefore of great importance to recognise this subgroup and detect (very) high risk tumours as early as possible, which necessitates non-invasive screening tools to enhance the diagnostic accuracy of WLC.

This study, to the best of our knowledge, is the first to evaluate the diagnostic performance of urinary cytology and the Xpert BC Monitor across various EAU risk groups. Furthermore, it provides a large prospective patient cohort including 733 patients for validation of these tests.

Previous research investigated the diagnostic performance of the Xpert BC Monitor and urinary cytology and found higher SN and NPV for the Xpert BC Monitor, while urinary cytology showed a higher SC of up to 95% in high-grade tumours [9–12,17]. Urinary cytology demonstrated high SN in high-grade tumours (84%), while SN in low-grade tumours was relatively low (19%–53%) [7,12,15,18,19].

Accordingly, we also found a high SC for urinary cytology across different EAU risk groups (≥93%, even for intermediate-risk tumours), which was particularly true for patients with gross haematuria. The SC and PPV in those patients were each 98%. This means that nearly all patients with gross haematuria and positive urinary cytology (50/51patients) in fact had UCA. The SN, however, was relatively low (49%). The rather low SN also applied to the other analysed subgroups, in which it varied from 39% to 65%. With that said, positive urinary cytology may indicate UCA anywhere in the urinary tract and should be treated

Table 3 (a) Performance of urinary cytology and the Xpert BC Monitor with regard to different patient groups. (b) Performance of urinary cytology and the Xpert BC Monitor with regard to different EAU risk groups.

		Urinary cytology, *n* (%; 95% CI)	Xpert BC Monitor, *n* (%; 95% CI)
(a)			
Total cohort	Sensitivity	188/482 (39; 36–44)	352/471 (75; 71–79)
n = 482 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 71–81)
n = 471 (Xpert BC Monitor)†	NPV	234/528 (44; 42–46)	169/288 (59; 64–71)
	PPV	188/205 (92; 87–95)	352/428 (82; 79–85)
All CIS	Sensitivity	51/86 (59; 48–70)	77/86 (90; 81–95)
n = 86 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 63–75)
n = 86 (Xpert BC Monitor)†	NPV	234/269 (87; 84–90)	169/178 (95; 91–97)
	PPV	51/68 (75; 65–83)	77/153 (50; 45–55)
Primary/solitary CIS	Sensitivity	10/22 (46; 24–68)	18/22 (82; 60–95)
n = 22 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 63–75)
n = 22 (Xpert BC Monitor)†	NPV	234/246 (95; 93–96)	169/173 (98; 95–99)
	PPV	10/27 (37; 24–53)	18/94 (19; 15–23)
MIBC	Sensitivity	45/72 (63; 50–74)	61/68 (90; 80–96)
n = 72 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 63–75)
n = 68 (Xpert BC Monitor)†	NPV	234/261 (90; 87–92)	169/176 (96; 92–98)
	PPV	45/62 (73; 62–81)	61/137 (45; 40–50)
Gross haematuria	Sensitivity	52/107 (49%; 39–58)	87/107 (88; 80–94)
n = 107 (urinary cytology)	Specificity	50/51 (98; 90–100)	35/51 (71; 57–84)
n = 107 (Xpert BC Monitor)†	NPV	50/105 (48; 43–52)	35/47 (75; 63–84)
	PPV	52/53 (98; 88–100)	87/101 (86; 80–91)
(b)			
Intermediate risk*	Sensitivity	176/386 (46; 41–51)	309/376 (82; 79–86)
n = 386 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 63–75)
n = 376 (Xpert BC Monitor)†	NPV	234/444 (53; 50–55)	169/236 (72; 67–76)
	PPV	176/193 (91; 87–94)	309/385 (80; 77–83)
High risk*	Sensitivity	144/265 (54; 48–60)	229/257 (89; 85–93)
n = 265 (urinary cytology)	Specificity	234/251 (93; 89–96)	169/245 (69; 63–75)
n = 257 (Xpert BC Monitor)†	NPV	234/355 (66; 63–69)	169/197 (86; 81–90)
	PPV	144/161 (89; 84–93)	229/305 (75; 71–78)
Very high risk*	Sensitivity	70/107 (65; 55–74)	95/103 (92; 85–97)
n = 107 (urinary cytology)	Specificity	234/271 (93; 89–96)	169/245 (69; 63–75)
n = 103 (Xpert BC Monitor)†	NPV	234/271 (86; 83–89)	169/177 (96; 92–98)
	PPV	70/87 (81; 72–87)	95/171 (56; 51–60)

**Patients attributed to the respective EAU risk group or higher. †Number of patients may diverge because patients with Xpert result 'INVALID' were excluded from statistical analysis. CI, confidence interval, EAU, European Association of Urology; MIBC, muscle-invasive bladder cancer; NPV, negative predictive value; PPV, positive predictive value.*

with utmost seriousness. Negative urinary cytology, on the other hand, does not exclude its presence.

The reported SN of urinary cytology in patients with CIS varies widely, from 28% to 100%, although TPS for reporting urinary cytology, a standardised reporting system, that has been validated in several studies, is well recognised and generally used nowadays [16,20]. Urinary cytology has some further disadvantages. It requires review by a pathologist, may be subject to inter- and intra-observer variability, and may be prone to error and inaccuracies due to a low cellular yield, stones, intravesical instillation therapy, and UTIs [17].

The Xpert BC Monitor is an assay that measures the expression of five target mRNAs that are frequently overexpressed in bladder cancer and can be detected in urine. Its advantages are its automation, the easy use in self-contained cartridges, a hands-on time of <2 min, and a turnaround time of 90 min. It was shown to be robust in reproducibility and even showed comparable SN, SC and NPV values in a subset of patients who had been treated with BCG <3 months prior to enrolment [8,12].

We found higher SN and NPV for the Xpert BC Monitor, especially in high risk (89% and 86% vs 54% and 66%) and very high risk patients (92% and 96% vs 65% and 86%). Patients with CIS occupy a special position and tumour monitoring is particularly challenging, since it often presents as a velvet-like, reddish area, or may not be visible at all. WLC can therefore only be interpreted with difficulty and may result in false-negative results (low SN) on the one hand, or cause unnecessary TURBTs with sample extraction to exclude malignancy in unclear cases on the other hand.

Although considered a minor surgery, TURBT is associated with an overall complication rate of up to 20%, potentially causing a decrease in quality of life, with substantial voiding problems, reduced sexual function, anxiety, and even depression in a significant proportion of patients [21–25]. We

found a superior SN and NPV of 90% and 95% for the Xpert BC Monitor vs 59% and 87% for urinary cytology in patients with CIS (concomitant or solitary). The NPV of the Xpert BC Monitor in patients with solitary CIS was even higher (98%). In other words, 98% of negative test results were truly negative, which allows us to hypothesise that malignancy can reliably be excluded. In absolute numbers, this means that four tumours would have been missed, while 169 of 245 TURBTs (69%) could have been spared in cases of inconclusive or negative cystoscopy and a negative Xpert BC Monitor result. Avoiding this 69% of potentially unnecessary invasive TURBTs would affect a massive proportion of patients. In line with this, prior studies have identified the Xpert BC Monitor as a valuable diagnostic tool that could considerably reduce the number of unnecessary TURBTs throughout the tumour monitoring of patients with low-grade NMIBC under active surveillance [26,27].

We observed comparable results when considering certain subgroups, such as patients with a history of recurrent bladder cancer, patients with initial diagnosis, and those with a history of instillation therapy (NPVs 91%, 97% and 90%, respectively, for patients with concomitant CIS and 94%, 99% and 93%, respectively, for patients with solitary CIS). However, the smaller sample sizes, especially in the subgroup of patients with initial diagnosis of solitary CIS, need to be taken into consideration when interpreting these numbers.

In conclusion, the Xpert BC Monitor could improve the diagnosis and tumour monitoring in patients with CIS (solitary or concomitant) by enhancing the interpretation of WLC across various clinical scenarios. This includes patients with a history of recurrent bladder cancer and those with a history of instillation therapy. It may therefore help to identify those patients for whom TURBT is necessary, while reducing the number of invasive procedures during tumour monitoring, benefiting patients, reducing costs, and enhancing healthcare efficiency [28,29].

Although this study provides a large prospective multicentre cohort including 733 consecutive patients who underwent TURBT due to clinical suspicion of bladder cancer, patients with CIS only represented a small proportion. To evaluate the value of the Xpert BC Monitor in the course of tumour monitoring in those patients, longitudinal observational studies are needed. In addition, the multicentre design could have potentially influenced test conduct and analysis. However, we tried to minimise this risk by establishing binding specifications on test conduction that were mandatory for all participating centres. Probe analysis for all centres was carried out exclusively by two blinded expert pathologists in a central laboratory.

In conclusion, because of its high SC, positive urinary cytology may indicate UCA anywhere in the urinary tract and should be taken very seriously. The Xpert BC Monitor showed promising results regarding SN and NPV, especially in patients with solitary CIS. It may therefore represent a useful supplemental tool in the diagnosis and monitoring of these patients that may help to correctly identify those patients who do in fact require TURBT, while preventing or deferring potentially unnecessary TURBTs in the course of tumour monitoring when there is no evidence of tumour in WLC.

Funding

This study was funded by Cepheid. The sponsor was involved in: the design and conduct of the study; analysis and interpretation of the data; review; approval of the manuscript; and decision to submit the manuscript for publication.

Acknowledgements

Priya Balakrishnan, Clinical Research, Cepheid (data management); Marine Gergondey, Medical and Scientific Affairs, Oncology, Cepheid (clinical study coordination). English language editing was provided by American Journal Experts. Open Access funding enabled and organized by Projekt DEAL.

Disclosure of Interests

Maximilian Haas declares speaker honoraria from Pfizer and Merck. Maximilian Kriegmair declares an advisory role for BMS, Esai, Cepheid and Photocure, and speaker honoraria from BMS, Pfizer, Merck, Astellas and Medac. Johannes Breyer declares an advisory role for Pfizer, personal fees and travel costs from Apogepha, Ipsen, Janssen, Pfizer and Photocure, research support from Cepheid and Janssen, and speaker honoraria from Ipsen, Pfizer, BMS, AstraZeneca, Merck and Roche. Danijel Sikic declares no conflict of interest. Felix Wezel declares advisory roles for Bayer and AstraZeneca, speaker honoraria and travel expenses from Medac, and travel costs from Pfizer. Florian Roghmann declares speaker honoraria and travel expenses from Janssen, Roche, Merck, MSD, Pfizer, AstraZeneca and QED, advisory roles for Janssen, Roche, Merck and QED, and research funding from Janssen. Mirco Brehmer declares no conflict of interest. Ralph M. Wirtz is founder and employee of STRATIFYER Molecular Pathology GmbH. Jonas Jarczyk declares speaker honoraria from Medac GmbH. Philipp Erben declares research support from Janssen, Cepheid and STRATIFYER. Veronika Bahlinger declares personal fees from MSD, research support from Gilead, and speaker honoraria from MSD. Franziska Goldschmidt declares no conflict of interest. Guido Fechner declares no conflict of interest. Jack Chen is an employee of Cepheid. Ellen Paxinos is an employee of Cepheid. Michael Bates is an employee of Cepheid. Friedemann Zengerling declares honoraria from Astellas, Bayer Health, Bristol-Myers Squibb, Ipsen, Novartis,

Roche, Sanofi/Aventis, Pfizer and Merck Healthcare, consulting fees from Apogepha, Bristol-Myers Squibb, Ipsen, Janssen-Cilag, Novartis, Roche, Sanofi/Aventis, Pfizer, Merck Healthcare and MSD, and travel support from Bayer Health, Ipsen, Janssen-Cilag and Pfizer. Christian Bolenz declares honoraria from AstraZeneca GmbH, Janssen-Cilag GmbH, Medac GmbH, Takeda Pharma GmbH and Roche Pharma AG, and research support from AstraZeneca GmbH and ERBE Elektromedizin GmbH. Maximilian Burger declares honoraria from Bayer, BMS, Janssen, Medac, MSD and Pfizer, and consulting honoraria from Photocure. Arndt Hartmann declares honoraria from Agilent, AstraZeneca, BMS, CEA, Cepheid, Diaceutics, Ipsen, Janssen, Lilly, MSD, Phäon, QIAGEN and Roche, consulting fees from Abbvie, Agilent, AstraZeneca, BMS, Cepheid, Diaceutics, Illumina, Ipsen, Janssen, Lilly, Nanostring, Phäon and QIAGEN, travel support from Agilent, AstraZeneca, BMS, Cepheid, Diaceutics, Ipsen, Janssen, Lilly, MSD, Phäon, QIAGEN and Roche, participation on data safety monitoring boards or advisory boards for Agilent, AstraZeneca, BMS, Cepheid, Diaceutics, Ipsen, Janssen, Lilly, MSD, Phäon, QIAGEN and Roche, and has a leadership role as president of the German IAP. Markus Eckstein declares advisory roles for Janssen, AstraZeneca, MSD, Cepheid, Diaceutics and GenomicHealth, personal fees and travel costs from Janssen, AstraZeneca, MSD, Cepheid, Diaceutics, GenomicHealth, research support from Janssen, AstraZeneca, Cepeheid and STRATIFYER; speaker honoraria from Janssen, AstraZeneca, MSD, Diaceutics, Roche, Astellas, and part-time employment at Diaceutics.

Data Availability Statement

Data are available for bona fide researchers who request it from the authors.

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Abbreviations: BCa, bladder cancer; CIS, carcinoma *in situ*; EAU, European Association of Urology; NMIBC, non-muscle-invasive bladder cancer; NPV, negative predictive value; PPV, positive predictive value; SC, specificity; SN, sensitivity; TPS, The Paris System; TURBT, transurethral resection of bladder tumour; UCA, urothelial carcinoma; WLC, white-light cystoscopy.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Performance of urinary cytology and Xpert BC Monitor in patients with (1) a history of recurrent bladder cancer, (2) first diagnois, and (3) with a history of intravesical instillation therapy across different clinical patient cohorts.