

DNA Methylation Markers for the Surveillance of Non-Muscle Invasive Bladder Cancer: Results from a Prospective Pilot Study

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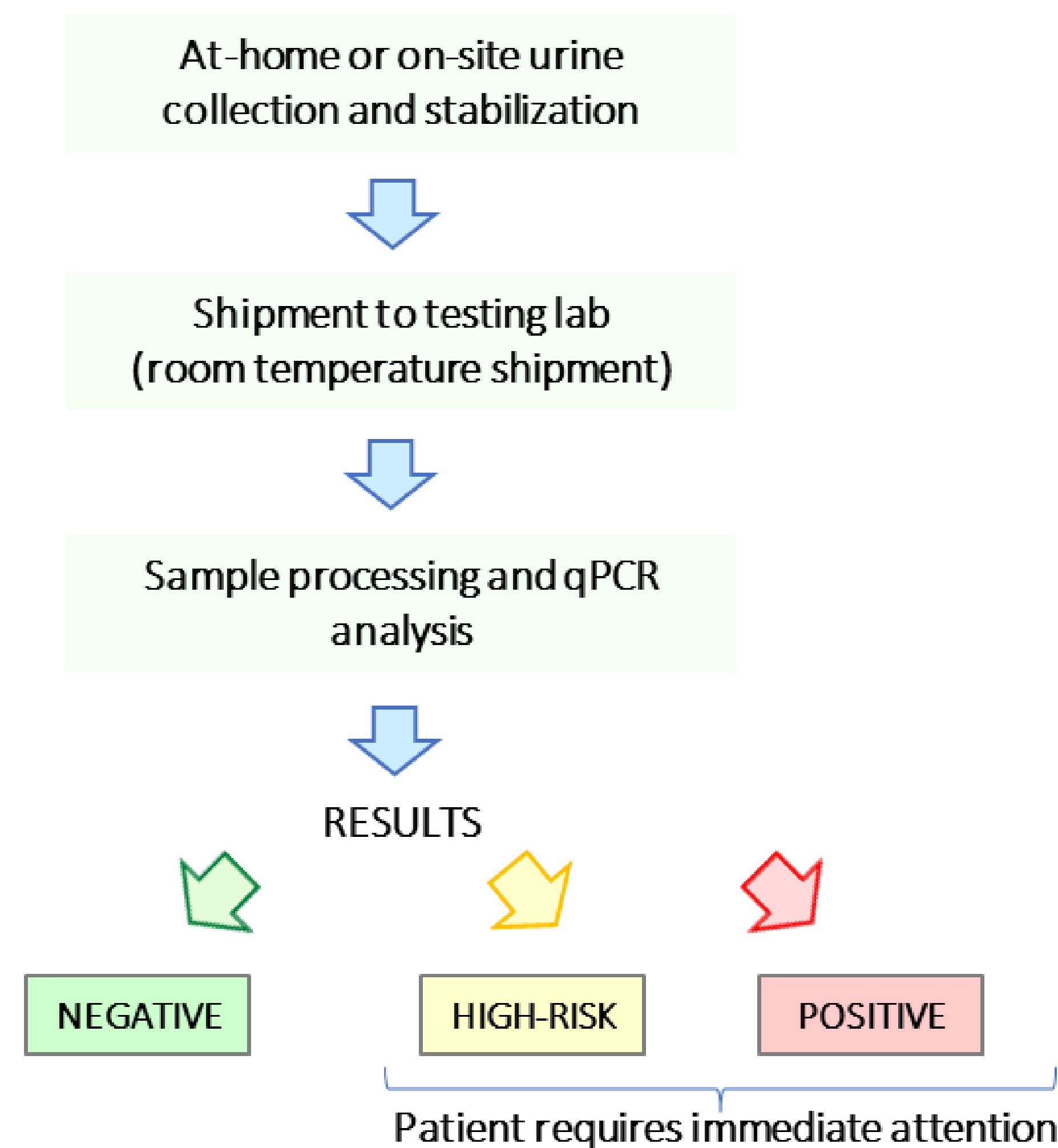
INTRODUCTION

- Cystoscopy and urine cytology are routinely employed during follow-up of patients with a history of non-muscle invasive bladder cancer (NMIBC) due to the high recurrence rate of this disease.
- Diagnostic accuracy of FDA approved urine-based tests is suboptimal.
- Herein, we compare the diagnostic value of urine cytology and a newly developed urine-based DNA methylation test (Bladder CARE™) for surveillance of NMIBC.

METHODS

- **Type of study:** Prospective cohort
- **Study group:** Under an IRB-approved protocol, urine samples were collected from patients with history of NMIBC during surveillance flexible blue-light cystoscopies between February 2019 and September 2021.
- **Diagnostic methods:**
 - 1) **Urine Cytology**
 - 2) **Bladder CARE™ test:** Bladder CARE™ is a urine-based qPCR cancer diagnostic test which detects the methylation level of urothelial-specific cancer biomarkers and internal control loci.
 - 3) **Cystoscopy**

Figure 1: Bladder CARE™ test workflow



Bladder CARE™ results are represented as Bladder CARE™ Index (BCI) which is proportional to the abundance of cancer DNA in the urine sample. Patients with a BCI < 2.5 are negative for the presence of urothelial cancer, while patients with a BCI > 2.5 and > 5 are classified high-risk and positive, respectively. Both, high-risk and positive results are considered abnormal, and follow-up is recommended.

RESULTS

- A total of 503 surveillance blue-light cystoscopies were performed on 159 patients.
- Urine samples for cytology and Bladder CARE™ tests were collected at each cystoscopy.

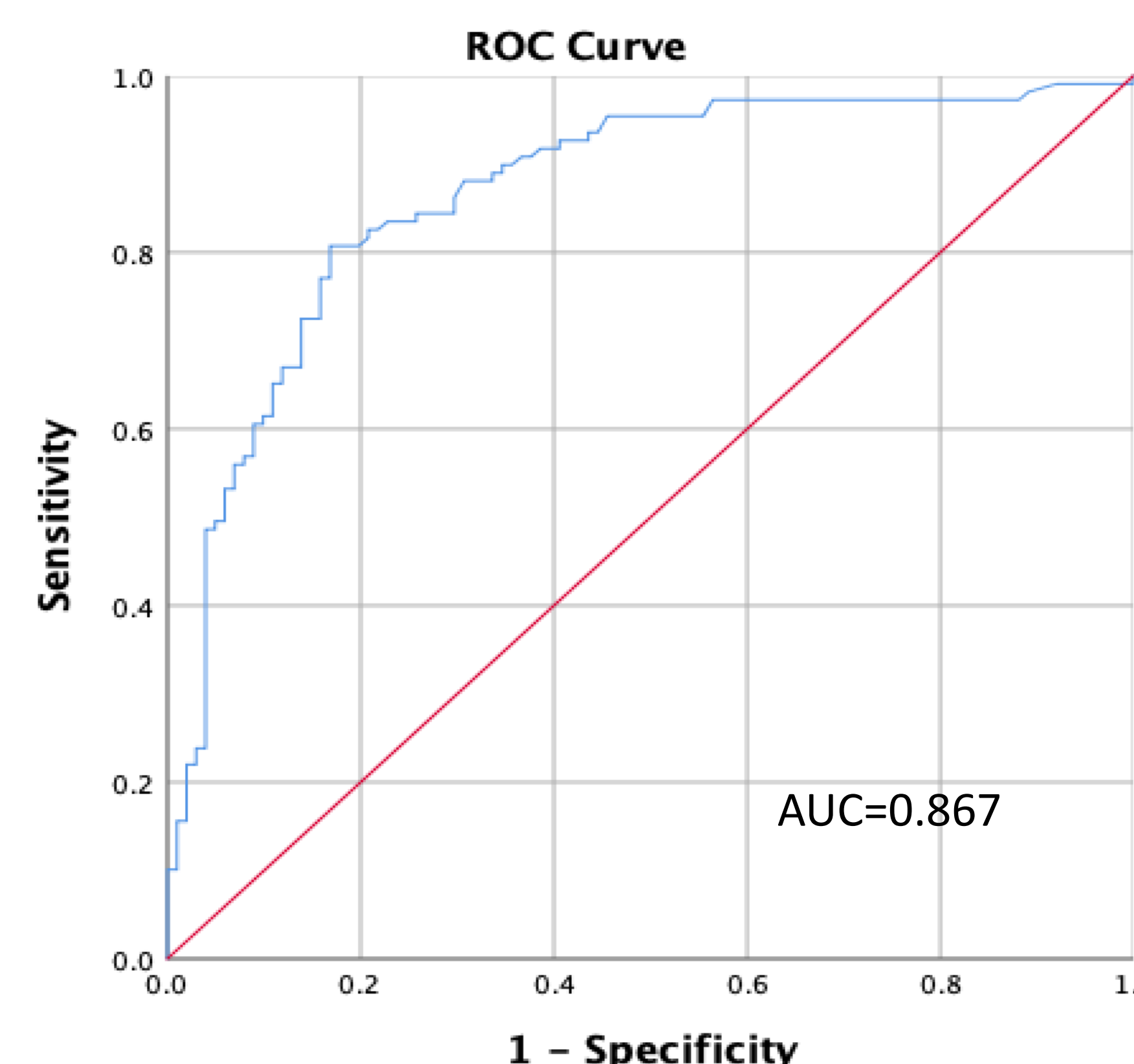
Table 1: Characteristics of the cohort included in the study (n=159)

Variables	Value
Total Number of Patients, n	159
Age, median, year	73
Sex, n (%)	
Male	122 (77)
Female	37 (23)
Total Number of Cystoscopies/Urine Samples Collected, n	503

Table 2: Performance of Bladder CARE™ and urine cytology compared to cystoscopy results (n=503)

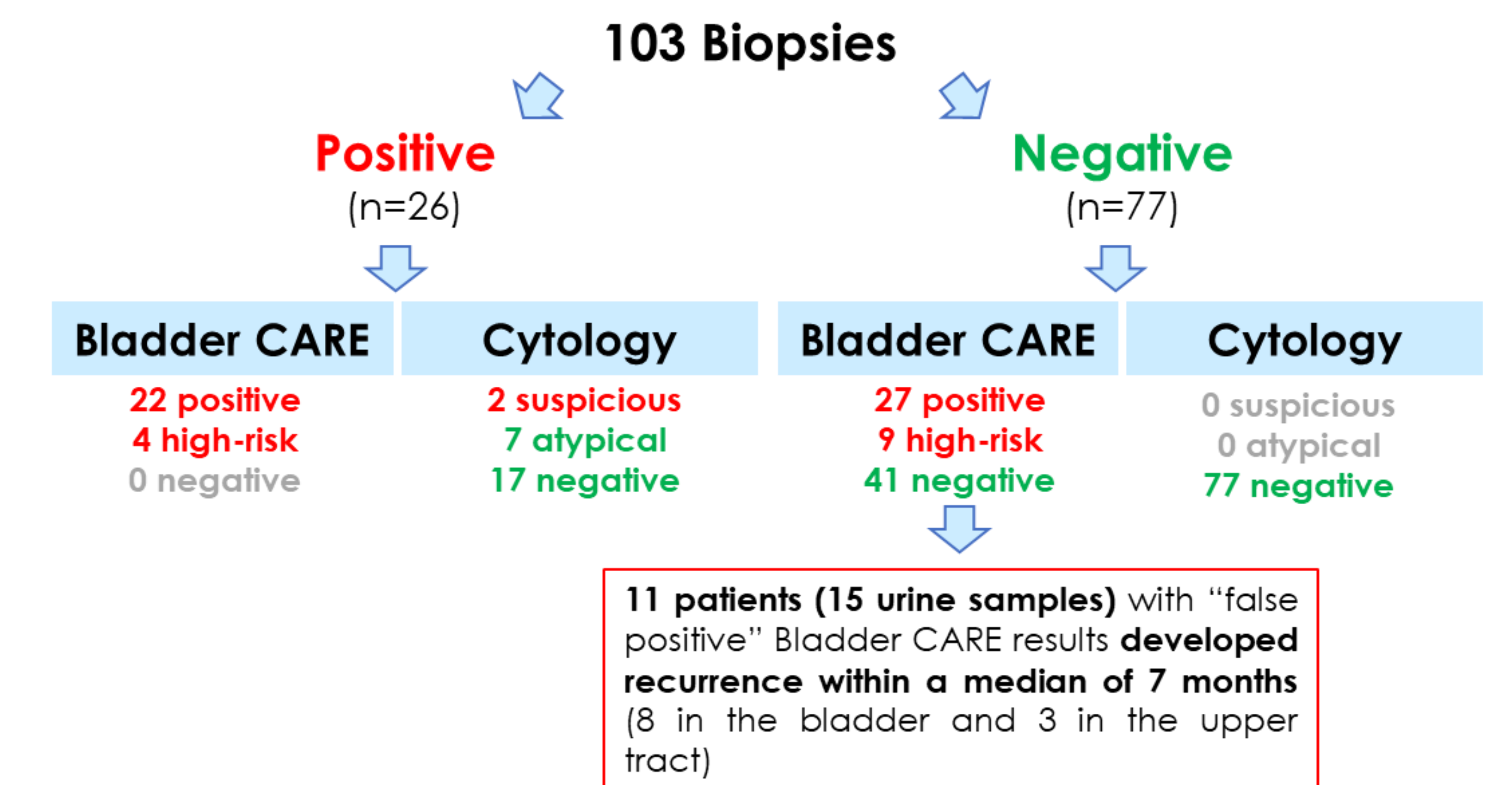
	Bladder CARE™	Urine Cytology
Sensitivity	93%	45%
Specificity	65%	92%
PPV	74%	60%
NPV	90%	86%

Figure 2: Receiver Operating Characteristic (ROC) curve for Bladder CARE™



- Among the 503-surveillance blue-light cystoscopies performed, 103 required biopsy.
- 26 (25%) out of 103 biopsies showed evidence of recurrence.
- 15 out of 36 (42%) of the negative biopsies classified as positive or high-risk by Bladder CARE™ were collected from patients (n=11) that developed recurrence later (8 in the bladder and 3 in the upper tract).

Figure 3: Bladder CARE™ may detect recurrences within a median of 7 months prior cystoscopy



CONCLUSIONS

- Urine cytology had low sensitivity and positive predictive value for urothelial carcinoma in this cohort
- These findings demonstrates the necessity of using more accurate urine biomarkers in the surveillance of NMIBC patients.
- Our preliminary results showed that Bladder CARE™ has high sensitivity and may detect cancer recurrence within a median of 7 months prior to cystoscopy.
- We are collecting additional data to confirm these preliminary results.

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