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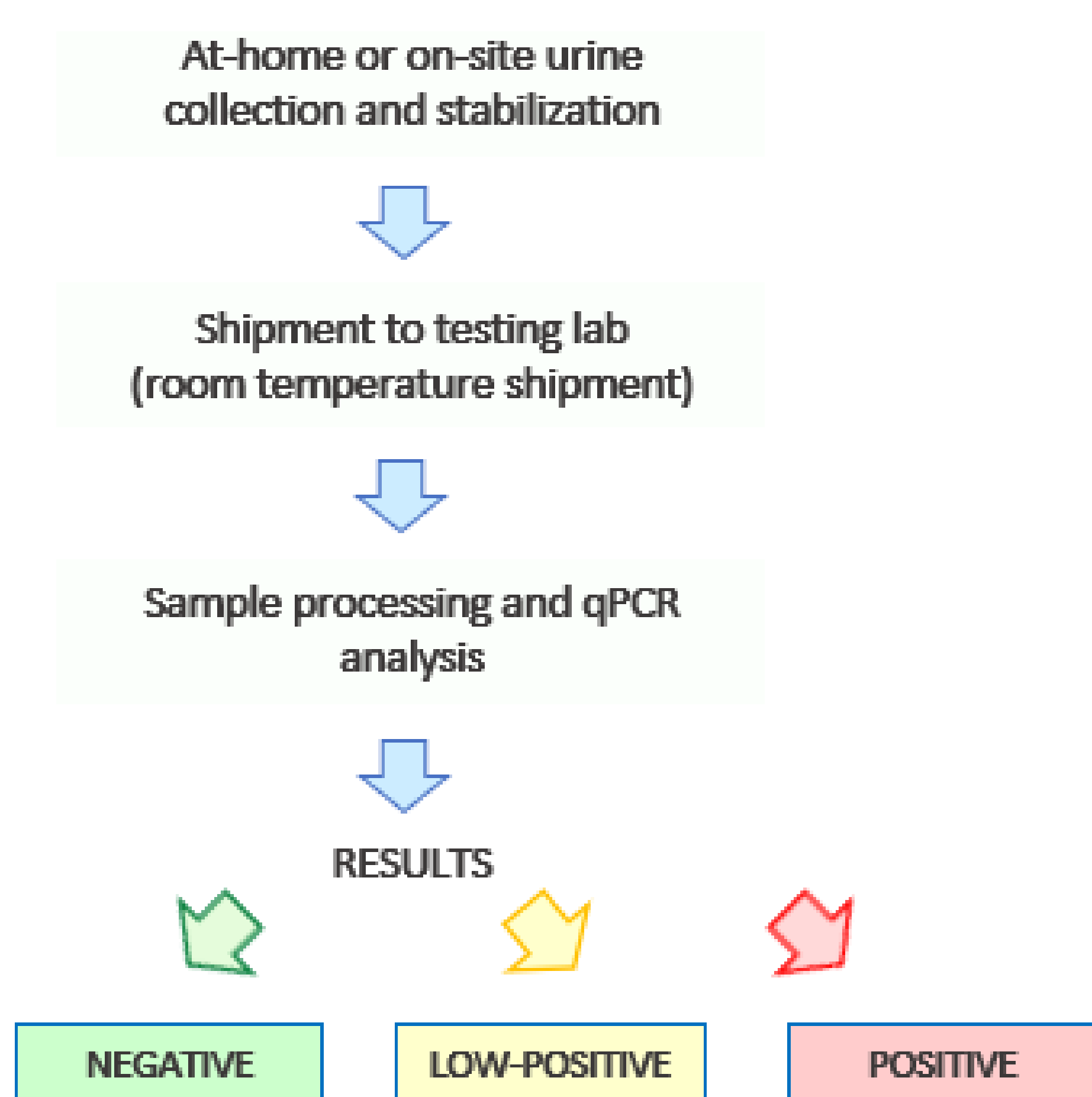
INTRODUCTION

- Cystoscopy and urine cytology are routinely employed for the detection and monitoring of bladder cancer.
- Diagnostic accuracy of FDA approved urine-based tests is suboptimal and provide no, or limited, prognostic value.
- Herein, we evaluate the diagnostic values of the Bladder CARE™ Assay, a urine-based DNA methylation test recently granted with FDA Breakthrough Device Designation, in:
 - 1) Detecting bladder cancer prior to current standard of care.
 - 2) Identifying response to anticancer therapies.
 - 3) Predicting tumor recurrence based on residual signal after TURBT.

METHODS

- **Type of study:** Prospective cohort
- **Study group:** Following an IRB-approved protocol, voided urine samples were collected from USC patients with BC history under surveillance/anticancer treatment. Enrollment spanned from February 2019 to September 2021.
- **Diagnostic methods:**
 - 1) Urine Cytology
 - 2) Cystoscopy
 - 3) Bladder CARE™ Assay: Bladder CARE™ is a urine-based qPCR cancer diagnostic test which detects the methylation level of bladder cancer and UTUC biomarkers.

Figure 1: Bladder CARE™ Assay Workflow



Bladder CARE™ results are represented as a 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 low-positive and positive, respectively.

RESULTS

STUDY COHORT:

- A total of 110 previously diagnosed BC patients were enrolled in this study.
- Urine samples for cytology and Bladder CARE™ Assay were collected during follow-up visits.

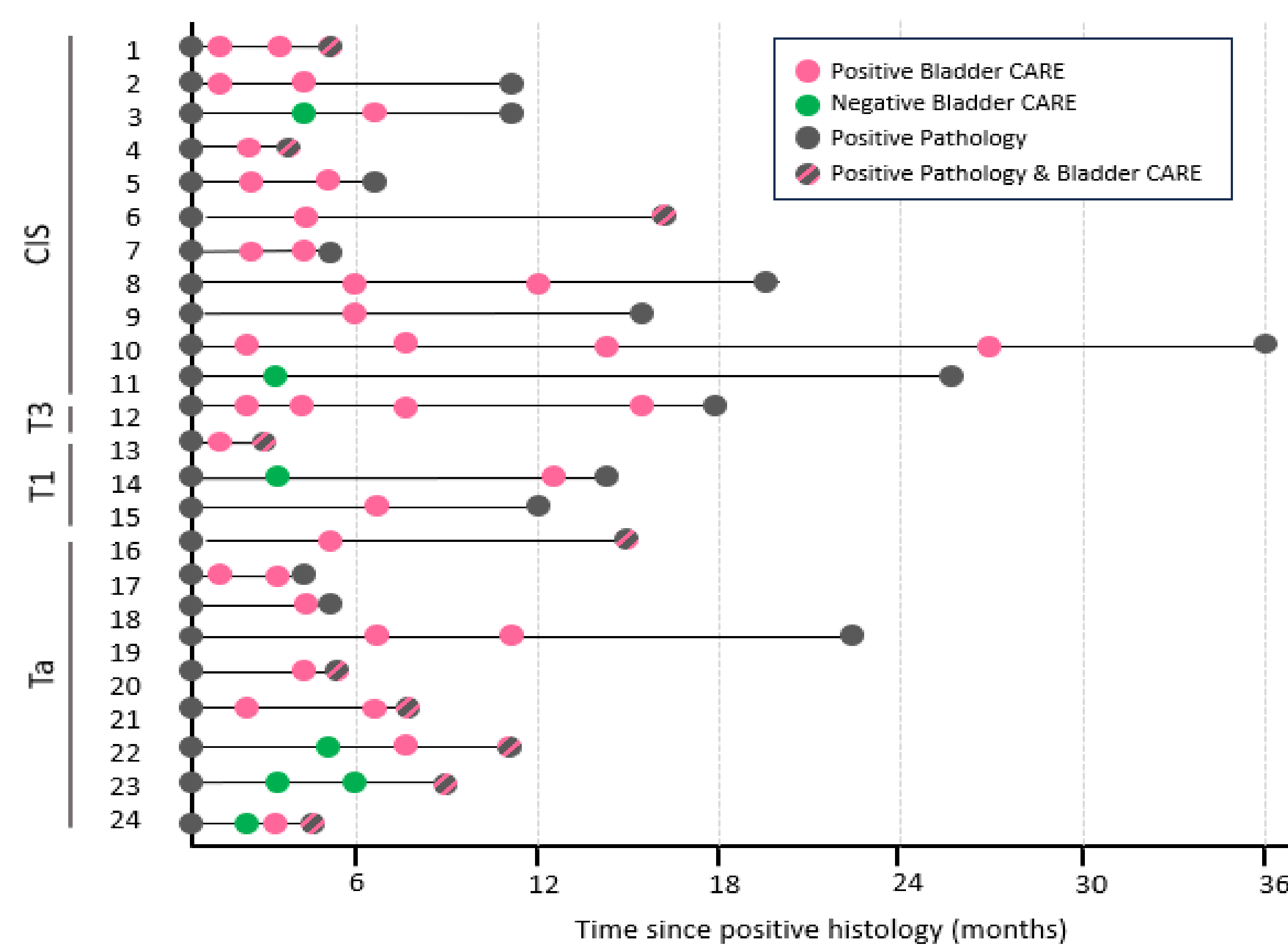
Table 1: Characteristics of the cohort included in the study (n=110)

Variables	Value
Total Number of Patients, n	110
Age, median, year	74
Sex, n (%)	
Male	95 (96)
Female	15 (14)

BLADDER CARE™ PROMISES TO DETECT CANCER EARLY:

- Within 36 months post-TURBT, 24 patients (21.8%) showed evidence of recurrence.
- Bladder CARE™ Assay detected all but one recurrences, averagely 7.35 months earlier than cystoscopy.

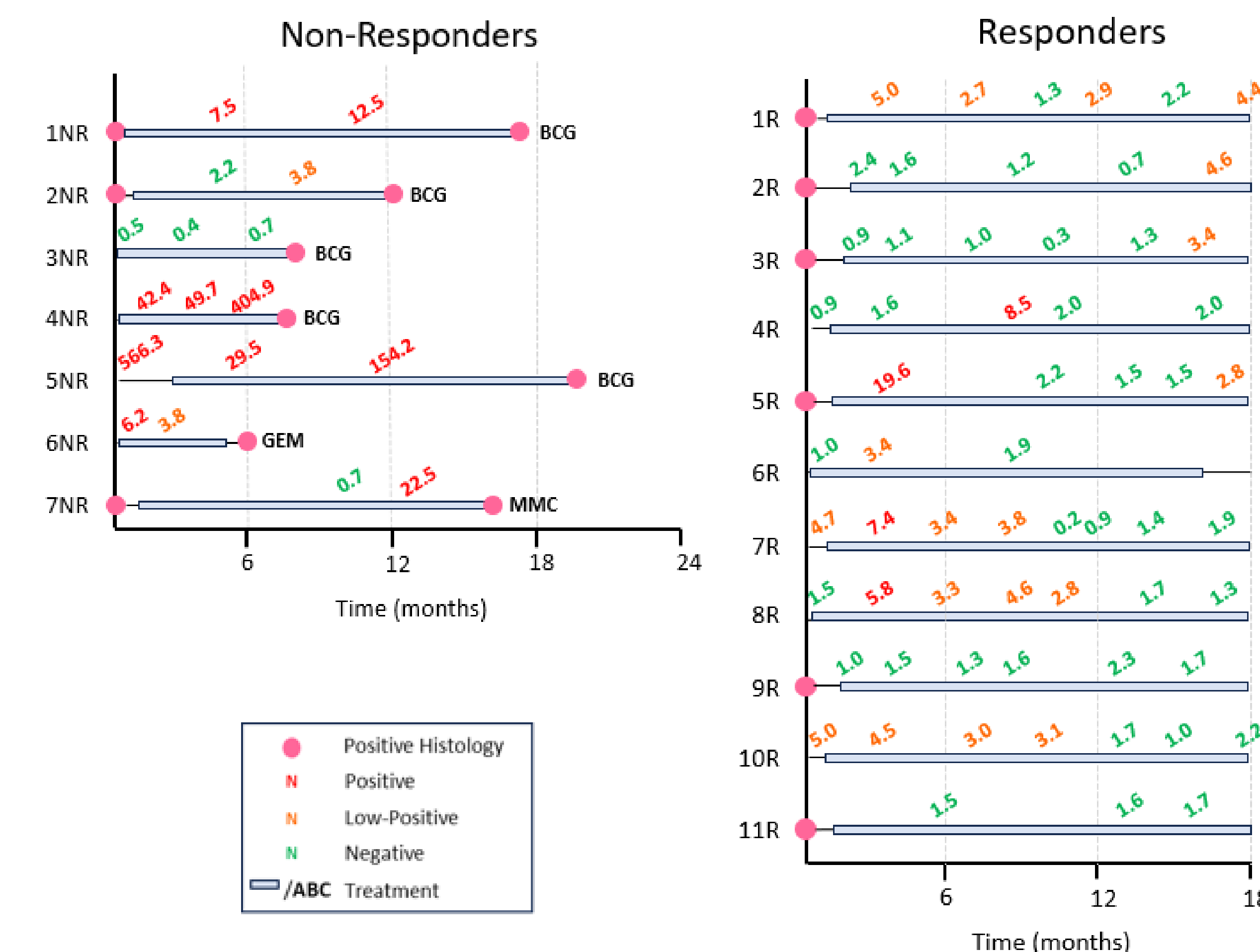
Figure 2: Time-Course Representation of Bladder Cancer Recurrence from Initial Diagnosis



BCI TREND INFORMS ABOUT RESPONSE TO ANTICANCER TREATMENTS:

- Of 55 patients (50%) undergoing anticancer therapies, 7 (12.7%) recur (non-responders) and 11 (20%) did not show evidence of recurrence by 18 months post-TURBT (responders).
- 18-month post-operative data was unavailable for 37 patients (67.3%).
- Bladder CARE™ detected 85.7% of non-responders, with BCI increasing prior to positive histology (avg. BCI: 86.1). In responders, BCI remained stable in negative/low-positive range post-TURBT (avg. BCI: 2.5).

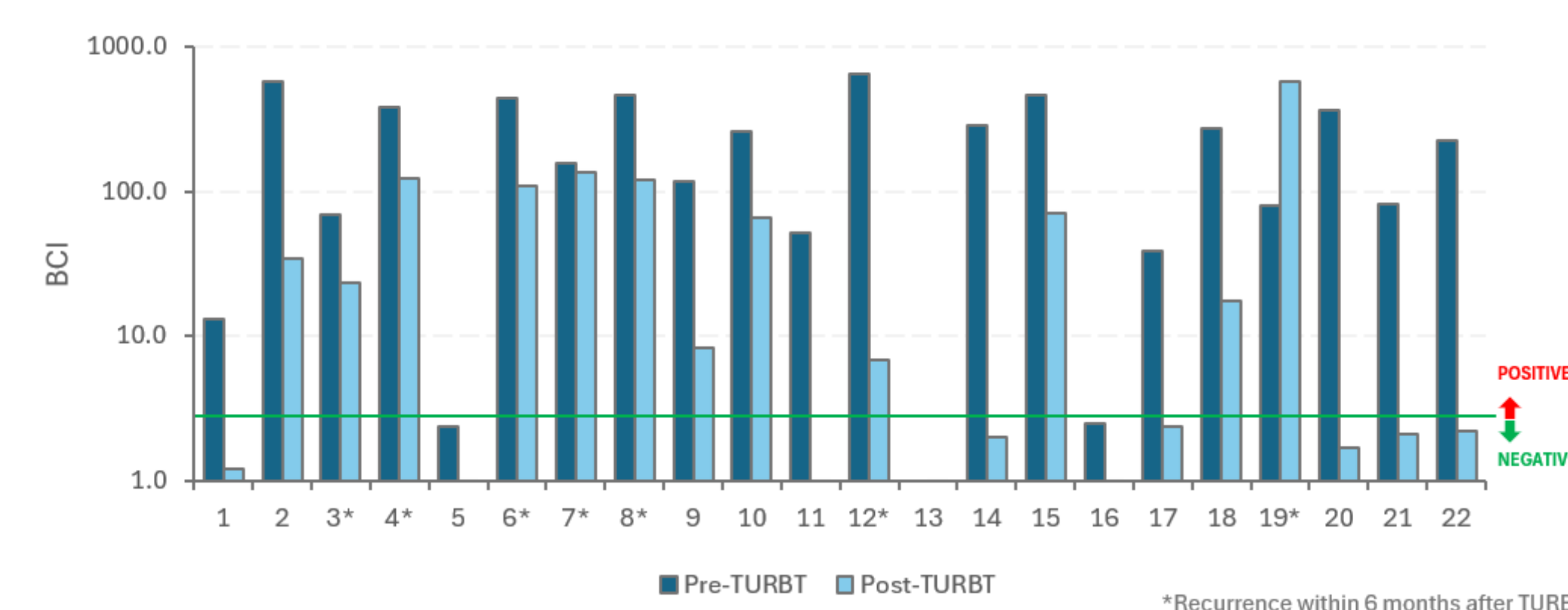
Figure 3: Time-Course Representation of BCI During Anticancer Treatments



POST-TURBT BCI VALUES MAY INFORM ABOUT INCOMPLETE RESECTION:

- Data from pre- and post-TURBT assessments were available for 22 of the 110 enrolled patients.
- The Bladder CARE™ Assay demonstrated a decrease in BCI post-TURBT in 21 of these 22 patients (95%).
- All the patients with BCI > 100 after TURBT recur within 6 months.

Figure 4: BCI Before and After TURBT



CONCLUSIONS

- Our data show that the Bladder CARE™ Assay detects cancer signal up to 7.35 months prior to cystoscopy.
- Bladder CARE™ Index trend informs about response to anticancer treatments.
- Our preliminary data shows that Bladder CARE™ Index after TURBT may provide information about the completeness of tumor resection and may hold prognostic values.

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