EPH111

Real-world patterns of ctDNA testing, molecular residual disease, and treatment after radical cystectomy for muscle-invasive bladder cancer

Jennifer Stuart[1] , Tyler Stewart[2], Xinyue Liu[1], Patrick Squires[1], Ching-Yu Wang[1], Vasily Aushev[3], Haojie Li[1], Chethan Ramamurthy[1], Blanca Homet Moreno[1], Ronac Mamtani[4], Mehmet Burcu[1]

[1] Merck & Co., Inc., Rahway, NJ; [2] University of California San Diego, La Jolla, CA; [3] Natera, Inc., Austin, TX; [4] University of Pennsylvania, Philadelphia, PA.

Background & Objectives

Background

- Patients with muscle-invasive bladder cancer (MIBC) remain at substantial risk for recurrence despite curative intent surgery with radical cystectomy (RC).
- Circulating tumor DNA (ctDNA) testing is increasingly used for early detection of molecular residual disease (MRD).
- However, real-world testing patterns and the extent to which MRD may inform subsequent treatment are unknown.

Objective

➢ To describe the use of ctDNA testing (e.g., timing, frequency, and status) in the real world and to examine treatment patterns following ctDNA testing in patients with MIBC treated with RC.

Methods

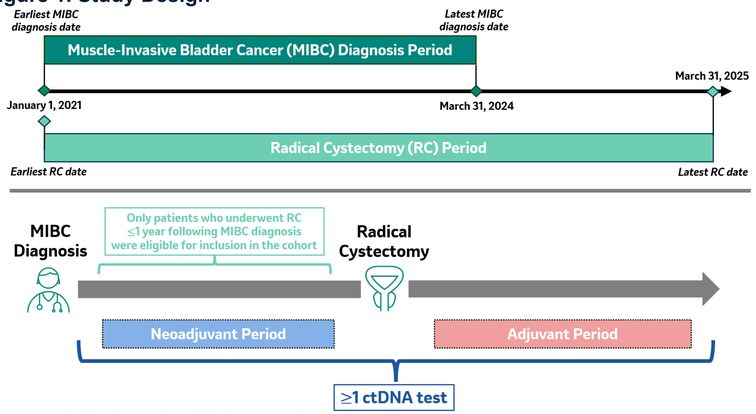
Patient Selection

- Adult US patients diagnosed with MIBC (cT2-T4aN0 or cT1-T4aN1 [Stages II-IIIA]) on or after 01Jan2021, with available electronic health records from Natera's Real-World Database who underwent RC (≤1y post-diagnosis) and received ≥1 commercial tumor-informed ctDNA test result (Signatera™ Exome; Natera, Austin, TX, USA) by 31Mar2025 were eligible **(Figure 1).**
  - Of 1,479 eligible patients, 500 were randomly selected for inclusion in the analytic cohort.

Analytic Approach

- We conducted a retrospective analysis of real-world data derived from ctDNA testing performed as part of routine clinical practice in a cohort of patients with MIBC treated with RC.
- Descriptive analyses of patient characteristics (at diagnosis) and testing and treatment patterns (at diagnosis and pre- and post-RC) were conducted. To assess testing and MRD status after RC but prior to adjuvant treatment, we examined testing within the first 90 days post-RC.
- Patients were considered **high-risk for recurrence** if they:
  a) received cisplatin-based neoadjuvant therapy (NAT) and had ypT2-T4 or pN+; or
  b) did not receive cisplatin-based NAT and had pT3-4 or pN+.
- **Pathologic complete response** (pCR) was defined as ypT0N0 (among those with NAT).
- **ctDNA positivity** (ctDNA+) was defined as ≥1 positive ctDNA test (within the time of interest).

Figure 1. Study Design



Results

Patient Characteristics

- Patients were predominantly male (74.2%), White (87.4%), current/former smokers (61.4%), and treated in an academic setting (63.4%), with Stage II disease at diagnosis (59.8%), pure urothelial histology (70.4%), and an average age at MIBC diagnosis of 68.1 ± 9.5 years.
- Median follow-up post-RC was 15 months (IQR: 10-24).

Table 1. Characteristics of patients with MIBC undergoing RC and receiving ≥1 ctDNA test

Characteristic, n (%)	Overall N = 500	ctDNA Testing Window[a]		
		Pre-RC n = 163 (32.6%)	Post-RC n = 497 (99.4%)	≤3 months post-RC n = 362 (72.4%)
Demographics				
Male	371 (74.2)	126 (77.3)	368 (74.0)	271 (74.9)
White	437 (87.4)	144 (88.3)	434 (87.3)	322 (89.0)
Current/former smoker	307 (61.4)	88 (54.0)	306 (61.6)	213 (58.8)
Academic setting	317 (63.4)	111 (68.1)	316 (63.6)	241 (66.6)
Stage II disease at diagnosis	299 (59.8)	118 (72.4)	296 (59.6)	213 (58.8)
Pure urothelial histology	352 (70.4)	124 (76.1)	351 (70.6)	249 (68.8)
Age at MIBC diagnosis (years); mean (SD) | median (IQR)	68.1 (9.5) | 69 (63,75)	68.8 (9.0) | 69 (63,75)	68.0 (9.5) | 69 (63,75)	68.3 (9.5) | 69 (63,75)
ctDNA tests per patient; mean (SD) | median (IQR)	6.9 (4.1) | 6 (4,9)	7.3 (4.6) | 6 (4,9)	7.0 (4.1) | 6 (4,9)	7.3 (4.3) | 6 (4,9)
Post-RC follow-up (months); mean (SD) | median (IQR)	17.3 (9.8) | 15 (10,24)	11.8 (7.4) | 11 (6,16)	17.4 (9.7) | 15 (10,24)	15.3 (8.3) | 14 (9,21)
Treatment Received				
Neoadjuvant therapy (NAT)	326 (65.2)	132 (81.0)	323 (65.0)	229 (63.3)
Adjuvant therapy (AT)	246 (49.2)	65 (39.9)	246 (49.5)	179 (49.5)
NAT & AT	155 (31.0)	51 (31.3)	155 (31.2)	107 (29.6)

Values presented above are n (%) unless otherwise indicated. AT: adjuvant therapy; ctDNA: circulating tumor DNA; IQR: interquartile range; MIBC: muscle invasive bladder cancer; NAT: neoadjuvant therapy; RC: radical cystectomy; SD: standard deviation.
[a] Patients could have been tested multiple times following MIBC diagnosis, so a given patient may contribute data to more than one ctDNA testing window of interest (e.g., pre-RC and post-RC). "Pre-RC" refers to any time before undergoing RC and "post-RC" refers to any time after undergoing RC.

Testing Patterns

- 3,648 plasma samples from 500 patients were analyzed (90% of which were sampled post-RC, n=3,129), with a median of 6 ctDNA tests/patient (IQR: 4-9).
- Pre-RC ctDNA testing occurred in one-third of patients (n=163, 32.6%). The majority of ctDNA testing occurred post-RC, with 99% of patients receiving ≥1 ctDNA test following RC.
  - Post-RC, 88% of patients received ≥3 tests (n=441), with 72% receiving a test within 3-months (n=362).
- Compared to patients tested post-RC, those who received ≥1 ctDNA test before RC were slightly more likely to be male (77.3% vs. 74.0%), more likely to be seen in an academic setting (68.1% vs. 63.6%), have an earlier stage of disease (Stage II: 72.4% vs. 59.6%) and pure urothelial histology (76.1% vs. 70.6%), and less likely to be a smoker (54.0% vs. 61.6%).
- Among those tested ≤3-months post-RC, 83% received a second test by 6-months and, of those, 93% received a third by 12-months.
- The percentages of patients with ≥1 ctDNA test post-RC at 1-, 3-, 6-, 9-, and 12-months post-RC were 25%, 73%, 86%, 92%, and 94%, respectively **(Figure 2).**

Treatment Patterns

- Overall, 65.2% (n=326) of patients received NAT, 49.2% (n=246) received adjuvant therapy (AT), and 31.0% (n=155) received both.
- Compared to those tested post-RC, patients who received ≥1 ctDNA test before RC were more likely to receive NAT (81.0% vs. 65.0%) and slightly less likely to receive AT (39.9% vs. 49.5%)

Figure 2. ctDNA testing after RC

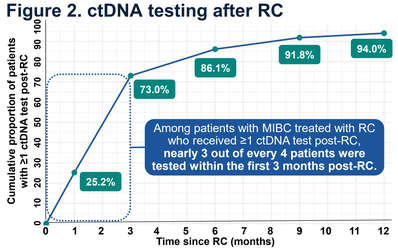


Table 2. ctDNA positivity by timing of testing and subgroups of interest

	ctDNA+
Overall (n=500)	212 (42.4)
Pre-RC (n=163)	89 (54.6)
Post-RC (n=497)	175 (35.2)
≤3 months post-RC (n=362)	80 (22.1)
Patients with pCR (n=38)	1 (2.6)
Patients without pCR (n=191)	48 (25.1)
High-risk for recurrence (n=233)	64 (27.5)
Not high-risk for recurrence (n=129)	16 (12.4)

Overall, **42.4% of patients received a positive ctDNA test** at some point following their MIBC diagnosis

ctDNA Positivity

- A little over half of those tested before RC (54.6%; n=89/163) had ≥1 ctDNA+ test compared to a little over one-third of those tested after RC (35.2%; n=175/497).
- Among those tested ≤3-months post-RC, ctDNA positivity was 22.1% overall (n=80/362) and 21.4% in NAT recipients (n=49/229).
- Among NAT recipients who were ctDNA-tested ≤3-months post-RC with available pathologic data (n=229), 16.6% (n=38) achieved pCR:
  - ctDNA positivity was higher among patients without pCR (25.1%) than among those with pCR (2.6%).
- Among those ctDNA-tested ≤3-months post-RC with available pathologic data (n=362), 64.3% (n=233) were at high risk for recurrence following RC.
  - ctDNA positivity was higher among high-risk patients (27.5%) than among those not at high-risk (12.4%)

ctDNA Positivity & Adjuvant Treatment

- Among patients at high risk for recurrence following RC, the proportion receiving AT was similar for ctDNA+ (70.3%; n=45/64) and ctDNA- patients (66.8%; n=113/169; p=0.62).

Strengths & Limitations

\+ Detailed clinical, testing, and treatment information for the population of interest

\- Lack of uniform plasma sample collection schedule

Conclusions

- ❖ In this real-world, RC-treated, ctDNA-tested MIBC cohort, ctDNA testing was primarily performed after RC, with frequent longitudinal monitoring. Patients with MIBC who received ctDNA testing were more likely to be seen in an academic facility, be at high risk for recurrence, and receive AT than the general MIBC patient population undergoing RC.
- ❖ Descriptively, ctDNA positivity was more common among patients without pCR and those at high risk. Among high-risk patients, AT use did not appear to vary by post-RC ctDNA status.

➢ ***Next Steps:*** Examining additional post-RC testing and treatment patterns utilizing extended cohort follow-up through March 31, 2026

Contact information
Jennifer Stuart (jennifer.stuart@merck.com)

Disclosures
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Abbreviations:
AT: adjuvant therapy; ctDNA: circulating tumor DNA; IQR: interquartile range; MIBC: muscle-invasive bladder cancer; NAT: neoadjuvant therapy; pCR: pathologic complete response; RC: radical cystectomy; SD: standard deviation.

https://bit.ly/4dfHvlF

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