The Cxbladder Bulletin

Dear Customers and Friends of Cxbladder,

Welcome to the May 2024 edition of the Cxbladder Bulletin. In this issue:

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AUA 2024: STRATA and Cxbladder Triage Take Center Stage

AUA 2024 in San Antonio earlier this month was a great reminder of how bladder cancer is increasing its share of mind within urology. It was great to see and speak with all of you who attended.

Our scientific and medical program at the conference focused on the publication of clinical utility evidence for Cxbladder Triage from our randomized clinical trial: STRATA. Dr Yair Lotan, Professor of Urology at UT Southwestern, presented the study during a session covering advances in bladder cancer care. Linked to the podium presentation, the study was also published in the Journal of Urology and promoted in the lead up to, and during, the AUA conference as “practice changing research”.

STRATA is the first ever randomized controlled trial of a urine biomarker for hematuria evaluation, and demonstrates that Cxbladder Triage can help clinicians to safely and more effectively risk-stratify microhematuria patients when compared to AUA guidelines. Clinicians in the test arm of the STRATA study, who could use information generated by a Cxbladder Triage test to help determine the intensity of a patient workup, undertook 59% fewer cystoscopies than those in the control arm of the study who did not have access to this information.

This milestone paves the way for the consideration of Cxbladder Triage in AUA guidelines as a genomic approach to risk stratification that can be used in place of the existing guidelines which rely on clinical factors. This pathway, which helps to alleviate the burden of

unnecessary cystoscopies, results in less patient discomfort and morbidity, improved access to care, and reduced environment impacts associated with diagnostic testing. Authors of the paper led by Dr Lotan affirmed this point in an abstract to the study.

UroToday report on Dr Lotan's presentation: view the article

Review the STRATA study, published in the Journal of Urology: view the study

Dr Lotan presenting on the poduim at AUA 2024

Photos From Around AUA 2024

Our functions and our booth were a great way to connect with you all during AUA 2024. We had excellent foot traffic in the main hall and at the USAV session we sponsored. We also took the opportunity to schedule regular meetings with key clinical studies partners and research collaborators, and to throw celebratory customer dinners, particularly with those who participated in STRATA.

The meetings helped to bring us together, and this year, against the backdrop of the Alamo, we took the opportunity to immerse ourselves in San Antonio's steeped traditions and heritage, making plenty of memories at the restaurants along the River Walk, while enjoying some great vibes with the session musicians at Howl at the Moon.

A few photos from around the event:

Video: Cxbladder Detect for Patients with Hematuria

Click the video below or this link to launch it in a browser window.

Survey: Surveillance Patients Show Strong Interest in Non-Invasive Test Options

In December 2023, using the Bladder Cancer Advocacy Network's (BCAN's) Patient Survey Network, we surveyed 1,507 US patients being monitored for non-muscle invasive bladder cancer (NMIBC).

Those surveyed were a reflection of the typical NMIBC population - 66% of respondents were male and the average age was 65. Patient respondees shared their experience of cystoscopy – discomfort, embarrassment, anxiety and pain - and showed a strong preference for urine-based test alternatives. At the same time, many patients were unaware of leading test options having not discussed them with their physician. Following a brief introduction to Cxbladder Monitor, the majority of patients surveyed were either willing to use Cxbladder Monitor to reduce the frequency of surveillance cystoscopy or were interested to know more about the test.

The challenge for clinicians: non-compliance

American Urological Association (AUA) AQUA Registry Data suggests that the average length of follow-up monitoring among NMIBC patients is 1.8 years. To ensure early detection of any recurrence, the AUA surveillance guideline for low risk NMIBC patients is 5 years. It's recommended that higher risk patients continue regular scheduled cystoscopies indefinitely.

Reasons for this non-compliance will vary by individual, however the invasive nature of cystoscopy must be considered a factor. Survey participants were asked about their experience with cystoscopy:

- 42% of patients surveyed said they experienced moderate to extreme discomfort. This figure was 49% among men.
- 78% told us they had experienced some pain, with 25% saying it was moderate to "worst imaginable".
- 24% said they had experienced moderate to extreme embarrassment.
- 56% told us they had experienced moderate to extreme anxiety. This figure was 66% among 41 to 60 year olds.

Patient respondees were thankful to have a surveillance option available, however voiced their concerns around invasive testing through the pain, discomfort, embarrassment, and/ or anxiety they experienced before, during, and after the procedure.

The patient response to urine-based test options

Genomic urine tests like Cxbladder Monitor provide a non-invasive surveillance alternative that can reduce the burden of invasive testing. When asked for their views on urine-based testing for surveillance of NMIBC:

- 80% of patients surveyed rated having a urine-based testing option as moderately to extremely important.
- 82% were not aware of leading urine-based testing options.
- 80% had not discussed urine testing options with their physician.

Alongside the nature of cystoscopy, distance from clinic, the travel time required for in-person visits, is another factor that may be impacting compliance. When asked for their preference on urine-based sampling methods, 62% of patients surveyed said they preferred a test with the option of in-home sampling.

> **"80% of patients surveyed rated having a urine-based testing option as moderately to extremely important."**

Cxbladder Monitor comes with the option of in-home sampling for US patients and can reduce the frequency of cystoscopy required in those being monitored for recurrent NMIBC.

We presented patients with a slide on Cxbladder Monitor and asked patients if they would be willing to consider use of the test to reduce the frequency of surveillance cystoscopy based on this brief introduction - 38% said yes and 51% were interested, wanting to learn more. Only 11% were not interested.

Pacific Edge's Chief Medical Officer Tamer Aboushwareb said "The results of this survey suggest that the majority of patients currently under surveillance for recurrent disease are receptive to a new non-invasive standard of care. If applied to the right patient population, clinicians have an opportunity to dramaically reduce the burden of surveillance for recurrence

in their NMIBC patients through the use of Cxbladder Monitor, simultaneously maximizing patient comfort and improving compliance with long-term monitoring. Reducing the frequency of cystoscopy required and the travel burden linked to in-clinic visits also has a societal benefit that is often unrealized."

"As the leading bladder cancer advocacy organization in the United States, we know that patients are interested in having less invasive ways to diagnose and monitor NMIBC," said Andrea Maddox-Smith, CEO of the Bladder Cancer Advocacy Network. "Safe, reliable and effective non-invasive surveillance options are good news for patients."

"Stay on Track" for Bladder Cancer Awareness Month

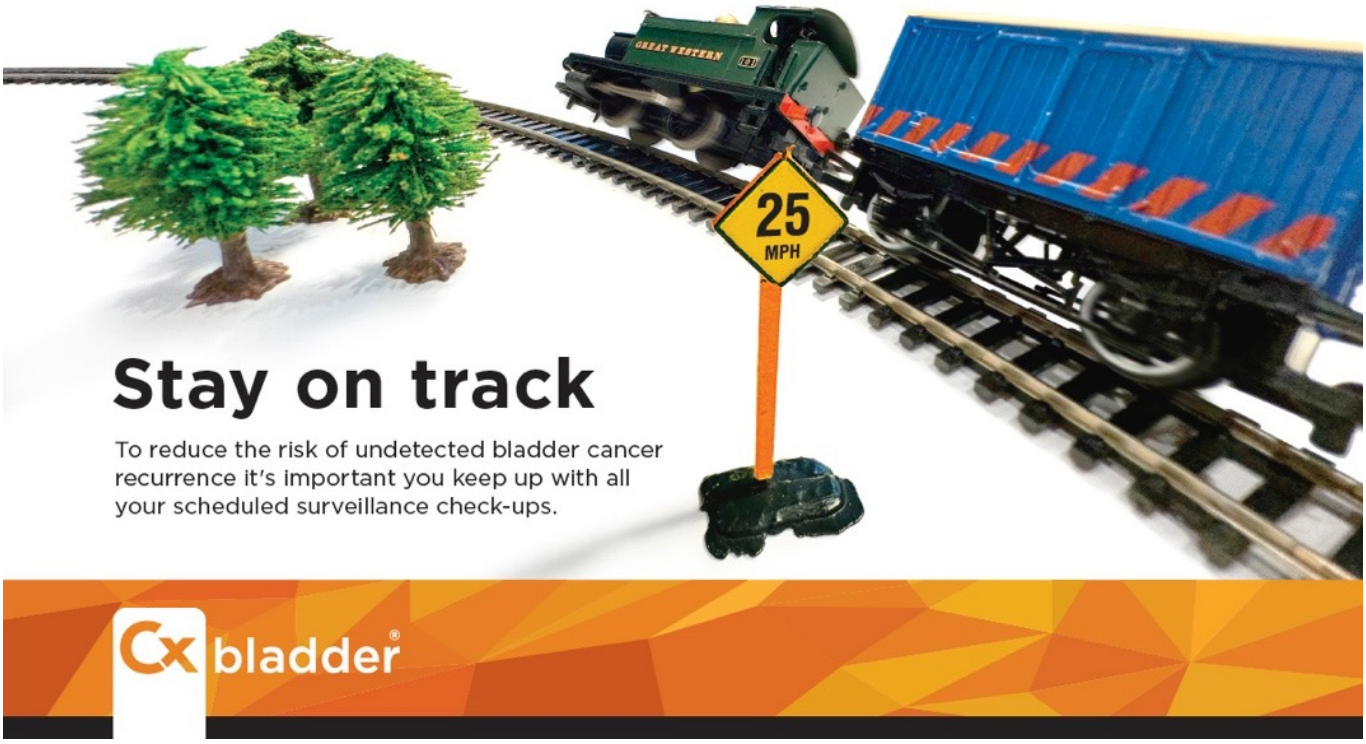
Every year, over 610,000 people are diagnosed with bladder cancer around the world, and more than 1.9 million people are living with and beyond bladder cancer. Bladder cancer is the 9th most commonly diagnosed cancer, and the 6th most common among men.

Bladder Cancer Awareness Month in May is a time for those affected by bladder cancer to stand together and raise awareness of the disease while working to better support its care.

Recurrence rates in patients treated for NMIBC can be as high as 70-80%, leading to intense monitoring protocols that protect against the threat of recurrence. After assessing a patient's risk profile, doctors will recommend a regular ongoing schedule of cystoscopies to examine the inside of the bladder and urethra that for high-risk patients may be as frequent as every three months

This May, to reduce the risk of an undetected spread of disease, we've urged NMIBC surveillance patients being monitored for recurrent disease to "stay on track" and keep up with scheduled check-ups using Cxbladder Monitor, a genomic urine test that can help reduce the frequency of cystoscopy required in suitable patients, or replace it in patients with no recurrence long term.

Learn more Bladder Cancer Awareness Month and our Stay on Track campaign.



Medicare Coverage Update

Cxbladder remains a covered test as we wait for Novitas to finalize its draft following the conclusion of the comment period in September. Our representations to Novitas were strongly supported by leading US Urological Societies - the AUA, LUGPA, and AACU; alongside our industry partners, the Coalition for 21st Century Medicine (C21); and by the American Clinical Laboratory Association (ACLA). A number of key urologic opinion leaders also voiced their support through formal submissions.

Novitas must now consider and respond publicly to all of the comments presented during the notice and comment period. The MAC has given no indication on when it is likely to finalize the LCD, but it is statutorily required to do so (or withdraw the LCD) within 365 days of the original publication date, which is July 26, 2024 (US Time). An LCD becomes effective 45 days after it is finalized.

In the meantime we are pleased to have had the opportunity to meet in November with the Centers for Medicare & Medicaid Services (CMS). This meeting precipitated a further meeting with Novitas in January, in which CMS representatives also participated. We view the involvement of CMS as a positive engagement in response to the seriousness of the issues we and others have raised, but not definitive of any particular outcome.

In April we have strengthened our case to Novitas and CMS further with the submission of the STRATA study, now published in the Journal of Urology. In May we met with members of the AUA Public Policy Team at the AUA Meeting to discuss ways in which they can support our ongoing efforts with Medicare and Novitas.

Automation Provides Opportunity For New Validation Data

Pacific Edge, as part of our commitment to continuous improvement, is automating the extraction and processing of DNA and RNA in patient samples, a key step in the Cxbladder testing process.

The new approach enhances our ability to scale as demand for our tests grow while reducing the use of various chemicals in the extraction procedure.

Importantly, this gives the opportunity for Pacific Edge to publish new Analytical Validation data. This data, once published, will allow healthcare payers, including Novitas to more easily assess the analytical validity of our tests. It will also give Pacific Edge an opportunity to apply for coverage reconsideration should Novitas make a Medicare non-coverage determination.

We expect the required analytical validation to be completed in the next few weeks and are targveting the publication of the data in the second or third quarter of this calendar year.

Ensuring Sample Quality to Support a Reliable Result: In-Clinic Sampling Guidelines

Cxbladder is an advanced genomic test that delivers exceptional performance in the rule out of urothelial cancer. To ensure a reliable result it's important you consider the following sample collection guidelines. These will ensure a high-quality sample reaches our laboratory, minimizing factors that can lead to a 'no result' or undermine the reliability of a result.

Sample collection guidelines: View a video demonstration.

- Voided urine only (2nd void or later preferred)
- The sample must be from a natural bladder
- You must collect urine in the Cxbladder cup
- Please transfer to Cxbladder tube as soon as possible, preferably within 15 minutes
- Please ensure there's no visible blood in the urine sample
- No dip sticks or fixative in the Cxbladder urine sample please

Upcoming Events

Come and see us at any upcoming event:

Date	Event Name	Location
Jun 6-7	Texas Urological Society	Houston, TX

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