The Cxbladder Bulletin

Dear Customers and Friends of Cxbladder,

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

Kaiser Permanente Test Volumes Build Following EMR Integration

Clinicians at Kaiser Permanente within Southern California are beginning to adopt Cxbladder Triage and Monitor on agreed patient types, having successfully integrated Cxbladder ordering with HealthConnect, the healthcare provider's electronic medical records (EMR) system.

The integration of Cxbladder tests into the EMR went live mid-November and with the Kaiser Permanente and Pacific Edge teams quickly addressing any operational issues that arose post-implementation. Clinicians across the urology medical centers of the Southern California Permanente Medical Group (Kaiser Permanente SoCal) are adopting the Cxbladder tests. The success of the integration is already visible in volumes ordered, with December, January and February all recording the volume records from the healthcare provider.

Kaiser Permanente is the largest integrated healthcare provider in the US, serving 12.6 million members, which equates to approximately 3.7% of the national population. Kaiser Permanente's Southern California region is the largest region by membership and manages the care for approximately 37% of all patients managed by the health plan. In aggregate Kaiser Permanente SoCal's urology team conducts ~25,000 cystoscopies each year across the relevant hematuria evaluation and bladder cancer surveillance clinical pathways. Kaiser Permanente and Pacific Edge are collectively working to further deliver the clinical value of Cxbladder testing more broadly to members in the remaining regions of the Kaiser system.

Enhancing the Clinician Experience

Faster Cxbladder turnaround times and the automation of our laboratory processes - these are among the range of performance excellence and Cxbladder simplification initiatives we are pursuing to enhance the customer experience and drive efficiencies in our operations.

The turnaround time project is focusing on processing and documentation bottlenecks in the sample receipt, accessioning and testing processes. The project is targeting a reduction in the average amount of time between a sample arriving at our laboratory door and the result being delivered to clinicians.

In tandem with reducing turnaround time, we are automating our RNA/DNA extraction process - the rate-limiting step in our laboratory workflow. Automation not only reduces the amount of time operators spend working with samples, it also enhances the repeatability and reproducibility of our tests. We are preparing for the technology transfer of this development to our commercial labs where we will document and publish the analytical validity (AV) of the new automated workflow, further enhancing the portfolio of evidence underpinning Cxbladder.

Chief Operating Officer Darrell Morgan says: "With reduced test turnaround times clinicians are more quickly able to use our tests to determine the appropriate management of patients, while quicker results can help to alleviate patient anxiety over their prognosis. Both outcomes enhance the attractiveness of Cxbladder to all involved in the bladder cancer patient care pathway."

AUA Registry Data Reinforces Value of Non-invasive Testing for NMIBC Surveillance

Recent AUA AQUA Registry data[1] suggests that the average length of follow-up for NMIBC surveillance patients is 1.8 years. This is significantly lower than the 5 year AUA guideline recommendation for low risk patients, suggesting compliance continues to be an issue, and reinforcing the value of genomic biomarker testing as a way to enhance the patient experience, while maintaining accuracy.

Cxbladder Monitor is a non-invasive alternative that can reduce the burden of repeated surveillance cystoscopies in non-muscle invasive bladder cancer patients with a low risk of recurrence.

- In suitable cases ≥9 months post the most recent confirmed UC diagnosis, Cxbladder Monitor

can alternate with cystoscopy to de-intensify surveillance, improving patient comfort and compliance.

- Cxbladder Monitor may be used to replace cystoscopy in patients with no recurrence long term after shared decision making with the patient.
- In-home sampling is available as a service to US patients, complementing the use of telemedicine, while reducing the need for patients to travel for in-clinic appointments.

Multiple clinical trials have shown Cxbladder Monitor to be a highly accurate test for ruling out tumors. A study with data from over 1,100 US patient samples found that Cxbladder Monitor significantly outperforms current FDA-approved urine-based monitoring tests, including cytology and UroVysion FISH[2]. Cxbladder Monitor has been clinically validated with a sensitivity of 93% and NPV of 97%[3].

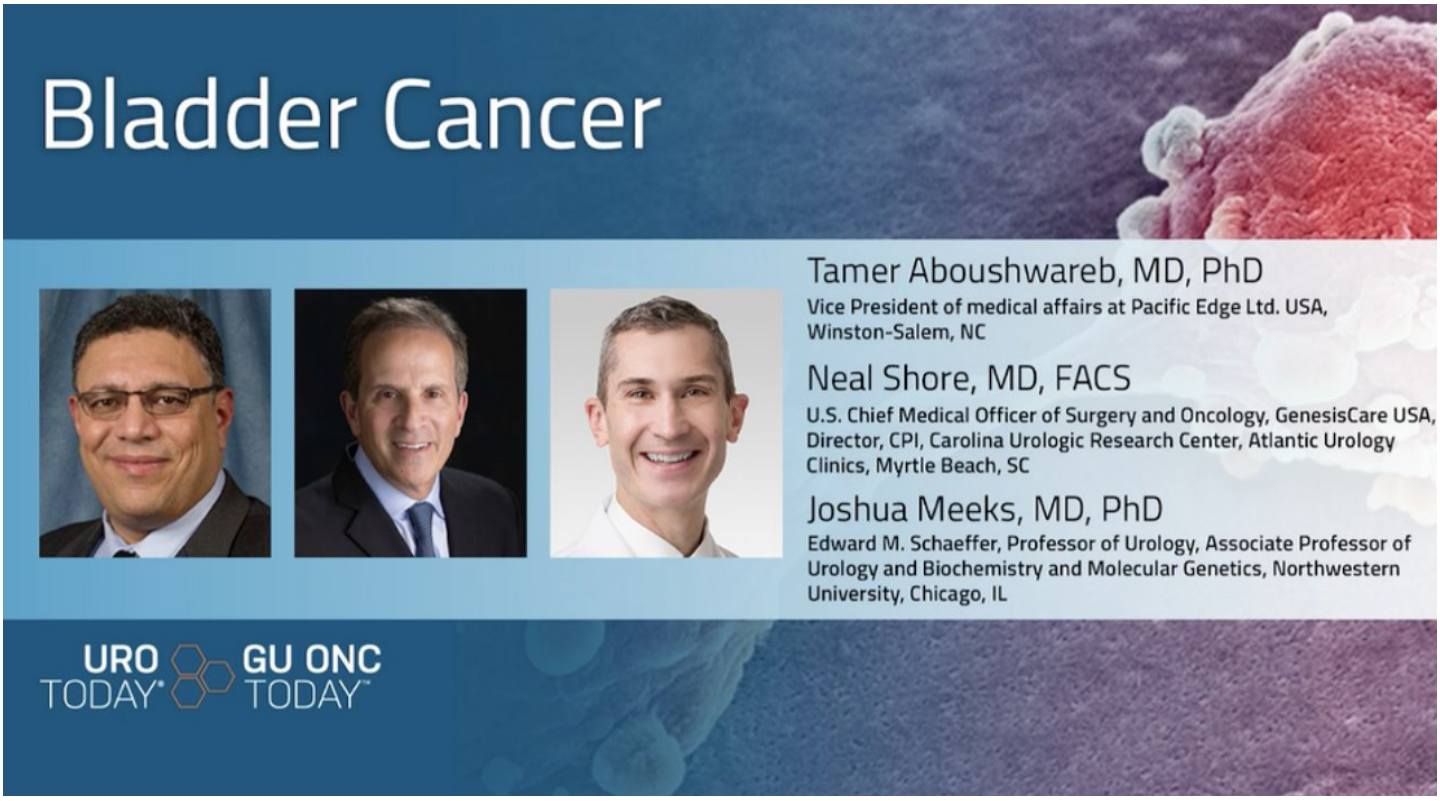
[1] AUA AQUA Registry Data, Nov 2023.

[2] Lotan Y, O'Sullivan P, Raman JD, Shariat SF, Kavalieris L, Frampton C, et al. Clinical comparison of non-invasive urine tests for ruling out recurrent urothelial carcinoma. Urologic Oncology: Seminars and Original Investigations. Elsevier; 2017;1–8.

[3] Kavalieris L, O'Sullivan PJ, Frampton C, et al. Performance Characteristics of a Multigene Urine Biomarker Test for Monitoring for Recurrent Urothelial Carcinoma in a Multicenter Study. J Urol 2017;197:6,1419-1426.

Video: Cxbladder Monitor for the Surveillance of Patients with Urothelial Cancer

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



Cxbladder Test Adoption Grows in Southeast Asia

Patients in Southeast Asia, notably the Philippines and Malaysia, are realizing the benefits of non-invasive genomic testing as we partner with established healthcare providers to offer our suite of non-invasive tests for the rule out and surveillance of urothelial cancer.

In all of these regions our focus is on populations that rely on the private healthcare systems and we select expert partners that have established relationships with clinical decision makers, government and private healthcare payers. In the Philippines, for example, we are partnering with Hi-Precision Diagnostics (HPD), a provider of pathology lab services that operates an extensive network of collection centers around the country. In Malaysia, where healthcare payment decisions are centralized around private hospitals and their own pathology laboratories, we have teamed up with a distributor, Wellspring Medical, which has a team that is already calling on decision makers.

Our agreements with HPD and Wellspring build on similar agreements signed in Vietnam, Israel, and Latin America. In all markets the relationships the distributor/partner has with clinicians is crucial, which reflects our priorities when selecting distribution partners. With the support of Pacific Edge and our Medical Affairs team, our partners engage with clinicians the same way the Medical Affairs Team engages with US clinicians - through conferences, symposia and face-to-face meetings.

Medical Affairs: An Increasingly Global Role

Working closely with clinicians while supporting our clinical studies program, the Pacific Edge Medical Affairs Team is playing an increasingly global role as we continue our expansion into emerging markets.

In all regions the Medical Affairs Team is led by Dr Daniel Shoskes, who has recently been promoted to VP Global Medical Affairs. In his new position, Danny is helping to scale the service traditionally focused towards US clinicians. In support of this we've just appointed our first Medical Science Liaison (MSL) dedicated to the Asia Pacific Region.

Alongside day-to-day activities working closely with clinicians at events and face-to-face meetings, the Medical Affairs Team plays an important role in our clinical evidence generation program. This includes guiding the development of new studies, while medically monitoring existing studies, and helping to translate results into published peer reviewed papers in leading urological journals. Two notable studies have recently completed enrolment.

Our STRATA study, which included a prospective two-armed randomized design to demonstrate the clinical utility of Cxbladder Triage in risk stratifying hematuria patients to rule out from cystoscopy, is the first randomly controlled trial (RCT) of a urine biomarker in a clinical pathway for bladder cancer. Trial data has now been successfully cleaned and monitored for statistical analysis, and subsequently compiled into a manuscript to be published as soon as possible and presented at AUA 2024.

Results from STRATA will play an important role generating clinical utility evidence to support the upcoming launch of Detect+, a second generation Cxbladder test that combines an analysis of five core mRNA biomarkers with DNA markers to enhance performance. The results of STRATA provide the strongest evidence to date for the inclusion of Cxbladder in the AUA microhematuria guidelines[1].

Our DRIVE trial, a single arm observational study, was designed to demonstrate the clinical validity of Cxbladder Detect+ in risk stratifying Veterans presenting with micro and gross hematuria. With patient enrolment now complete, it's our intention to submit DRIVE results for publication in Q1 2025. As our Medical Affairs Team support Pacific Edge led studies, they also help to guide investigator initiated trials (IITs). IITs, studies proposed by investigators and supported by Pacific Edge, help to generate clinical evidence, while giving clinicians firsthand experience with our suite of tests. We're pleased to be initiating IITs with several reputable organizations, including the Mayo Clinic, UT Southwestern, University of Miami, and the Cleveland Clinic. We'll also be supporting the launch of a multi-center trial in Israel.

[1] Hematuria evaluation is outside the scope of NCCN, which for bladder cancer is focused on post-diagnosis patient management.

Medicare Coverage Update

Cxbladder remains a covered test as we continue to wait for a decision.

Leading US Urological Societies called for a revision of LCD (DL39365) as the comment period concluded in early September. Our representations to Novitas were strongly supported by the leading professional societies in urology - the American Urological Association (AUA), the Large Urology Group Practice Association (LUGPA) and the American Association of Clinical Urologists (AACU) – and by our industry partners, the Coalition for 21st Century Medicine (C21), the American Clinical Laboratory Association (ACLA) and by many other key urologic opinion leaders.

The presentations given at the open meetings and details of written submissions are available on our website: https://www.pacificedgedx.com/investors/presentations

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.

Our continued view is that Novitas should recognize the merit of the evidence Pacific Edge has submitted during the 'Open Comment' period that ended on September 9, 2023, and the series of highly supportive representations from peers, industry and the professional urology community for Cxbladder products to retain the 'claim-by- claim' coverage, subject to medical necessity, we have been afforded for the last three and a half years.

We are meanwhile pleased to have had the opportunity to meet in November with the Centers for Medicare & Medicaid Services (CMS), the body to whom Novitas is ultimately accountable on coverage decisions. 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.

Ensuring Sample Quality: In-Clinic Sampling Guidelines

Cxbladder is an advanced genomic test that analyzes biomarker genes to help rule out urothelial cancer. To help ensure a high-quality sample reaches our laboratory it's important to keep the following points in mind during sample collection.

- 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

To learn more, we invite you to watch this video which demonstrates the in-clinic sampling process.

Upcoming Events

Date	Event Name	Location
Apr 11-13	Arkansas Urologic Society (AUS)	Bentonville, AR
May 3-6	AUA 2024	San Antonio, TX

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