

FURTHER COMPELLING CLINICAL EVIDENCE SUPPORTING CXBLADDER

DIAGNOSTIC OUTPERFORMANCE PUBLISHED IN LEADING CLINICAL JOURNAL

- Cxbladder providing enhanced diagnostic outcomes not currently available from existing technology.
- Enables physicians to remove the diagnostic dilemma faced, when existing gold standard tests and procedures are not able to determine a clear diagnostic outcome.
- Use of Cxbladder minimises the need for patients to have further unnecessary tests and procedures; resulted in 35% less invasive and expensive cystoscopy procedures.
- Paper published in number one ranked urology journal, European Urology.
- This real world outcome positions Cxbladder for consideration for inclusion in international guidelines.

Cxbladder's recent diagnostic outperformance has been published in the number one ranked urology journal, European Urology, adding to Cxbladder's comprehensive clinical evidence for physicians, reimbursers and healthcare providers alike. Titled "*Evaluation of Cxbladder and Adjudication of Atypical Cytology and Equivocal Cystoscopy*", the paper validated the performance of Cxbladder in correctly adjudicating all patients diagnosed with urothelial cancer¹ (UC) among those with atypical cytology and equivocal cystoscopy.

In simple terms, the paper provides compelling evidence further validating the performance of Cxbladder in evaluating patients who have inconclusive diagnosis for UC following cystoscopy and cytology². Cxbladder delivered 100% accuracy in adjudicating atypical and equivocal diagnostic results enabling physicians to resolve this diagnostic dilemma without the inconvenience and added cost of re-evaluating the patient. Cxbladder also significantly outperformed cytology for accurately identifying patients who do not have UC. This real world outcome positions Cxbladder for consideration for inclusion in international guidelines.

Approximately 7 million people present with haematuria³ every year in the US. While many of these will not have UC, clinical guidelines require investigation to be undertaken, with the existing gold standard procedures being cystoscopy and cytology.

A diagnostic dilemma occurs for physicians and patients when the evaluation of patients, using cystoscopy and cytology, does not give a conclusive diagnostic outcome. This provides a challenge for between 18% and 30% of patients evaluated and for patients returning to the clinic for follow up assessment for recurrence of UC. Currently physicians manage this dilemma by rescheduling and repeating some or all of the tests and procedures, with the consequential increases in costs, invasiveness and potentially poorer patient outcomes.

In the European Urology paper, the use of Cxbladder has been shown to enable physicians to resolve this diagnostic dilemma with 100% accuracy.

The international, real-world study recruited patients from mainstream urology in diverse physician practices in the USA, Australia and New Zealand and included 1,784 patients with haematuria or previously diagnosed with UC.

¹ Urothelial cancer includes bladder cancer and cancers of the upper urinary tract

² Cystoscopy is a procedure where a lighted tube with a camera is inserted via the urethra to view the inner wall of the bladder. Cytology is the examination of cells in a urine sample to look for abnormal cells which may be indicative of cancer.

³ Haematuria is the presence of blood in the urine and a key indicator of bladder cancer.

Key conclusions and outcomes from the study:

- (1) Cxbladder significantly outperformed urine cytology for identifying patients with UC;
- (2) Cxbladder correctly adjudicated atypical cytology and atypical cytology with equivocal cystoscopy in all cases;
- (3) Significant clinical utility can be gained from the inclusion of Cxbladder in the evaluation of patients for UC in both haematuria and monitoring settings, with the outperformance of Cxbladder compared with cytology;
- (4) The use of Cxbladder resulted in 35% of patients avoiding cystoscopies; and
- (5) Cxbladder, either as a reflex to cytology or as a replacement for cytology, would eliminate the diagnostic dilemma associated with atypical cytology results and/or equivocal cystoscopy.

David Darling, Chief Executive Officer of Pacific Edge states that: “The results from this pivotal international study show that the use of Cxbladder in this setting removes the need for cytology and the consequential challenges of atypical diagnostic outcomes, improving the clinical utility for both physicians and patients alike. The resultant outcome is a lowering of the number of invasive tests, procedures and overall healthcare costs.”

Canterbury (New Zealand) urologist Dr Stephen Mark, who is also the President of the Urological Society of Australia and New Zealand (USANZ), the governing body for Australian and New Zealand urologists, says: “The clinical evidence for Cxbladder is compelling, resulting in many of New Zealand’s public healthcare providers adopting Cxbladder into their standard of care. This most recent evidence adds significant extra clinical utility in the diagnostic performance of Cxbladder.

“The addition of Cxbladder into clinical pathways in Canterbury has led to a 30% reduction in patients attending outpatients for a bladder examination, improving the cost effectiveness of our service.”

Addendum:

Other findings from the study include:

- Cxbladder accurately rules out patients who do not have cancer and adjudicates those tests where the results are inconclusive, thereby minimising the need for patients to have further unnecessary tests and procedures;
- Cxbladder Detect (CxbD) provides two components of utility: (1) additional segregation of patients who have a low risk of having UC and (2) a complementary segregation of patients who have a high risk of having UC;
- When Cxbladder Triage (CxbT) and Cxbladder Detect (CxbD) are used concurrently in the evaluation of a patients’ haematuria, CxbT optimises the rule-out patients (73%) with a low risk of having UC and further clinical resolution for tumour positive patients when CxbD is used on samples that test positive on CxbT. This finding supports previous data that concurrent use of both CxbT and CxbD test modalities provided additional clinical utility relative to using CxbT alone in the diagnostic process for UC;
- Cxbladder correctly adjudicated all of the atypical cytology results that were subsequently diagnosed as UC;
- Cxbladder had an improved Negative Predictive Value (NPV) and a significantly higher sensitivity compared with urine cytology providing the power required for reliable rule-out of patients who do not have UC;

- The results from this study provide additional support for the previously published hypothesis that rule-out tests with high sensitivity combined with high NPV provide better clinical resolution for ruling out patients who have a low probability of disease;
- These findings support previous published results which have shown that all Cxbladder tests significantly outperformed urine cytology for identifying patients without UC;
- This study provides more evidence for using Cxbladder to evaluate haematuria in the diagnostic pathway for bladder cancer, sparing the need for cystoscopy or other imaging modalities, with the associated costs and discomfort;
- This study also demonstrates that no additional diagnostic resolution is provided by using cytology in an investigation of haematuria because of its low sensitivity and significant number of atypical results requiring adjudication;
- Cytology has been shown to miss more than 50% of UC-positive patients, including a substantial proportion with high-grade and/or muscle-invasive tumours;
- In this study, cytology missed 63% of the overall tumours and 55% in those with haematuria, but did not identify any UC cases that were not previously identified by Cxbladder;
- The results from this study provide a strong argument for using Cxbladder instead of cytology – thereby avoiding atypical cytology results and consequently minimising the number of cystoscopies performed during haematuria assessment.

Read the full European Urology paper here:

[https://www.europeanurology.com/article/S0302-2838\(19\)30351-3/pdf](https://www.europeanurology.com/article/S0302-2838(19)30351-3/pdf)

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For more information contact:

David Darling
Chief Executive Officer
Pacific Edge Ltd
P: +64 (3) 479 5800

OVERVIEW www.pacifedge.co.nz www.pacifedgedx.com

Pacific Edge Limited (NZX: PEB) is a New Zealand publicly listed, cancer diagnostic company specialising in the discovery and commercialisation of diagnostic and prognostic tests for better detection and management of cancer. Its non-invasive, simple to use and accurate Cxbladder tests enable the detection of bladder and other urinary tract cancers from a small volume of a patients' urine. Cxbladder provides actionable results and better detection and management of urothelial cancer. The company is developing and commercialising its range of Cxbladder tests globally and has two wholly owned accredited laboratories in New Zealand and the USA. The company's products have been tested and validated in multiple international clinical studies.

ABOUT Cxbladder Triage

Cxbladder Triage accurately identifies patients with haematuria who have a low probability of bladder cancer and may not require a more extensive urological evaluation. Cxbladder Triage is a tool for use by clinicians and physicians in primary evaluation of patients with haematuria and is intended to reduce the need for an expensive and invasive work-up in patients who have a low probability of having urothelial cancer.

ABOUT Cxbladder Detect

Cxbladder Detect provides clinicians with a quick, cost effective and accurate measure of the presence of the cancer as an effective adjunct to cystoscopy. Is often used in conjunction with Cxbladder Triage to provide greater rule-out and resolution of patients who have UC.

ABOUT Cxbladder Monitor

Cxbladder Monitor allows urologists to monitor bladder cancer patients for recurrence of the disease. Bladder cancer has a recurrence rate of 50-80% and requires life-long surveillance. Cxbladder Monitor accurately identifies patients with a prior history of urothelial cancer whose Cxbladder Monitor score shows that they have a low probability of recurrent urothelial cancer. Cxbladder Monitor is designed to be used as the preferred adjunct test to cystoscopy in the management of patients for ongoing evaluation of recurrent bladder cancer.

ABOUT Cxbladder Resolve

Cxbladder Resolve identifies those patients who are likely to have aggressive or more advanced bladder cancer. Cxbladder Resolve, when used as part of the primary evaluation of haematuria and/or in conjunction with other Cxbladder tests (Triage, Detect), is designed to assist clinicians by accurately identifying patients with a high probability of having high grade or late stage bladder cancer, for whom alternative or expedited treatment options may be warranted, or who can be prioritised for further investigation in high throughput settings.

Refer to www.cxbladder.com for more information.