LifeLabs® EMPOWERING HEALTHIER CANADIANS FOR OVER 60 YEARS

Bladder Cancer

Identify MIBC patients who may benefit from adjuvant therapy after cystectomy

How do you determine which patients are likely to recur after cystectomy without adjuvant treatment?

Many patients are cured by surgery alone but receive potentially unnecessary adjuvant therapy toxicity, while other patients don't receive potentially beneficial treatment until they have progressed clinically[1]

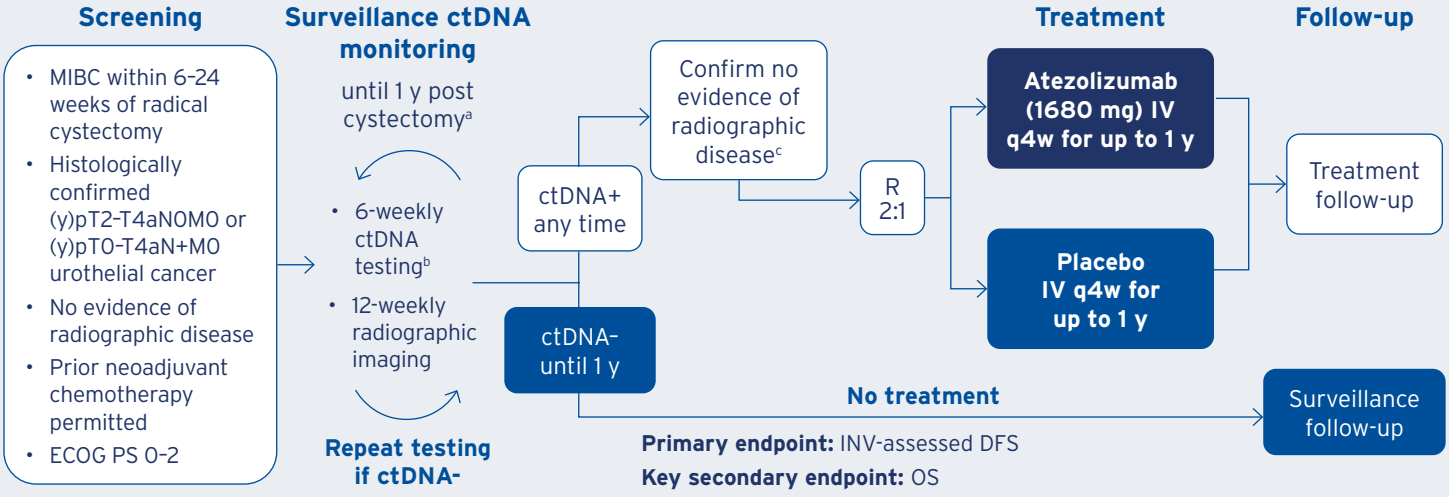
Existing tools fall short at identifying remaining residual disease and recurrence early before patients become symptomatic

Up to 50% of patients will develop metastases following cystectomy for localized disease and it can be difficult to determine response to immunotherapy treatment quickly[2]

Signatera™ testing may help inform which patients will benefit from adjuvant therapy, if they are responding to immunotherapy, or if they are relapsing – before standard of care tools[1,3,4]

Neoadjuvant response monitoring	Postsurgical MRD assessment	Surveillance	Metastatic treatment response monitoring
Lack of ctDNA clearance during neoadjuvant treatment may be a better predictor of recurrence than pathologic response.[3]	Post cystectomy MRD assessment can identify which patients may benefit from adjuvant treatment[1,5]	ctDNA can detect recurrence up to 245 days before clinical progression (median 96 days)[3]	98% of patients with an increase in ctDNA after 2 cycles of immunotherapy did not derive an objective response[4]

IMvigor011: First randomized Phase 3 trial to use a Signatera™-guided adjuvant design



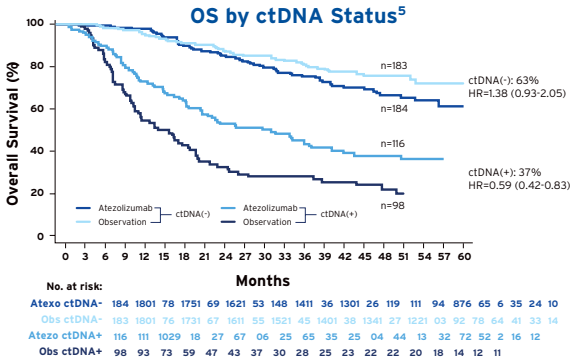
The global, randomized, Phase III IMvigor011 trial was designed to evaluate ctDNA-guided adjuvant atezolizumab vs placebo in patients with MIBC

- Signatera-positive patients treated with atezolizumab experienced a >2x increase in median DFS compared to placebo (median of 9.9 vs 4.8 months) (HR: 0.64; P=0.005)
- Signatera-positive patients in the treatment arm had a meaningful improvement in OS (median of 32.8 vs. 21.1 months HR: 0.59; P=0.01)
- Signatera-negative patients had excellent outcomes without adjuvant immunotherapy. Patients who remained Signatera-negative during surveillance without adjuvant treatment had very low recurrence risk (DFS of 95.4% at 1 year and 88.4% at 2 years). OS outcomes were also incredibly strong, sparing patients from unnecessary treatment

Signatera™ ctDNA positivity after cystectomy may predict adjuvant immunotherapy treatment benefit[1,5]

Key results from extended follow-up published in European Urology:[5]

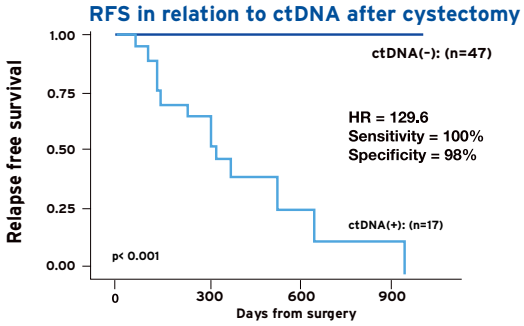
- >110% survival benefit observed in ctDNA-positive patients treated with atezolizumab (OS, HR 0.59).[5]
- No treatment benefit was observed in ctDNA-negative patients treated with atezolizumab (OS, HR 1.38)[5]
- 37% of patients were ctDNA-positive at C1D1 and ctDNA positivity predicted benefit from immunotherapy at 46.8-month median follow-up (OS, HR=0.59)[5]
- >75% of patients with detectable ctDNA post-surgery in the observation arm recurred by 20 month follow up[1]



Natera and Aarhus University Study: Longitudinal ctDNA status after cystectomy was predictive of relapse[3]

Key results:

- Signatera™ ctDNA status at all assessed timepoints (before neoadjuvant chemo, before cystectomy, and after cystectomy) was highly prognostic of outcomes
- ctDNA was a stronger predictive factor for recurrence than lymph node status or pathologic staging
- Lead time to clinical recurrence of up to 245 days (median=96 days)
- Patients with serial negative ctDNA after cystectomy had 100% OS

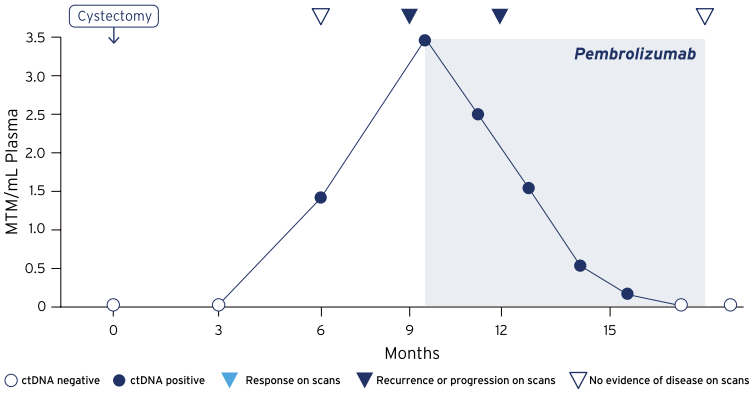


Metastatic bladder cancer case review*

Is the tumor truly progressing?

- **Age:** 71
- **Original diagnosis:** pT3N0M0 muscle-invasive bladder cancer
- **Treatment course:** Preexisting renal insufficiency precluded the use of neoadjuvant cisplatin-based chemotherapy. Patient underwent radical cystectomy
- **Monitoring:** Two postoperative ctDNA tests were negative

*Case features modified to protect patient confidentiality. No treatment recommendations are made or should be implied.



Signatera™ can be run at any time point on the core biopsy or surgical resection.

Learn more about LifeLabs Cancer Testing

Hereditary Cancer Panel: Understand your patients' genetic risk. Includes full sequencing and analysis of 84 of the most common genes linked to hereditary cancers, including breast, ovarian, colorectal, and more.

Tumor Markers: Monitor cancer progression, assess treatment response, and detect recurrence with comprehensive testing across multiple cancer types.

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References: 1. Powles T, Kann AG, Castellano D, et al. ctDNA guided Adjuvant Atezolizumab in Muscle Invasive Bladder Cancer (MIBC). N Engl J Med. 2025 Sep. **2.** Svatek RS, et al. Can Urol Assoc J. 2009. doi: 10.5489/cuaj.1203. **3.** Christensen E, et al. J Clin Oncol. 2019. doi: 10.1200/JCO.18.02052. **4.** Bratman SV, et al. Nature Cancer. 2020;1(9):873-881. **5.** Powles T, et al. European Urology. 2023; https://doi.org/10.1016/j.eururo.2023.06.007

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