natera™ | Signatera™
Residual disease test (MRD)

BLADDER CANCER

Know cancer's next move

with personalized, tumor-informed molecular residual disease (MRD) detection for muscle invasive bladder cancer (MIBC)

Covered by Medicare

Inform critical decisions in MIBC

Many patients undergo unnecessary adjuvant therapy after surgery, while others miss out on beneficial treatments[1]

Existing tools can fall short at identifying risk of recurrence after cystectomy

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

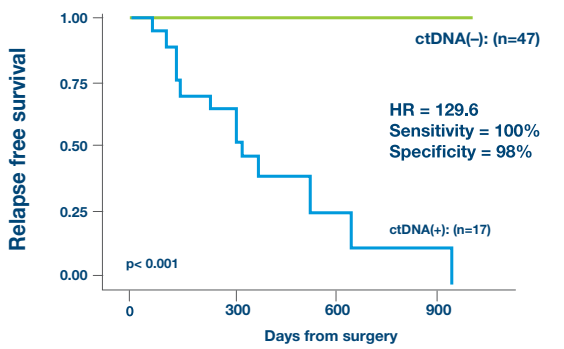
Identify patients at risk of relapse who may benefit from adjuvant therapy and monitor response to immunotherapy [1,3-5]

Neoadjuvant response monitoring	Postsurgical MRD assessment	Surveillance	Metastatic treatment response monitoring
Lack of ctDNA clearance during neoadjuvant treatment may predict recurrence better than pathologic response.[3]	MRD assessment after cystectomy helps identify which patients may benefit from adjuvant treatment[1,4]	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 in a pan-tumor trial[5]

Aarhus University Study: Signatera™ status at all assessed timepoints was highly prognostic of patient outcomes[3]

68 locally advanced MIBC patients with 656 plasma samples collected longitudinally with a median follow-up of 21 months

RFS in relation to ctDNA after cystectomy

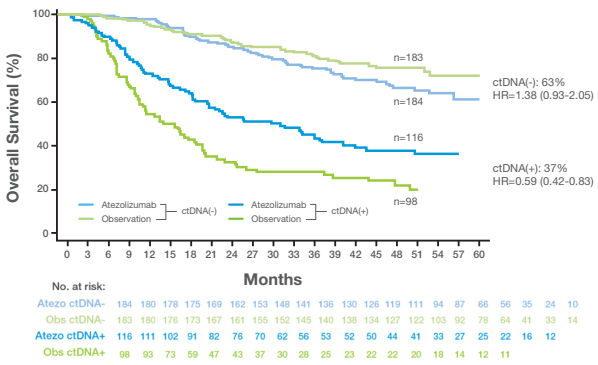


- Signatera™ ctDNA status before neoadjuvant chemo, before cystectomy, and after cystectomy was highly prognostic of patient outcomes[3]
- Signatera™ ctDNA status was a stronger predictive factor for recurrence than lymph node status or pathologic staging with a lead time to clinical recurrence of up to 245 days (median=96 days)[3]

IMvigor010: Signatera™ positivity after a single timepoint post-cystectomy may predict who will benefit from adjuvant immunotherapy treatment[1,4]

Phase III, randomized clinical trial of atezolizumab vs observation in high-risk adjuvant MIBC

OS by ctDNA status[4]

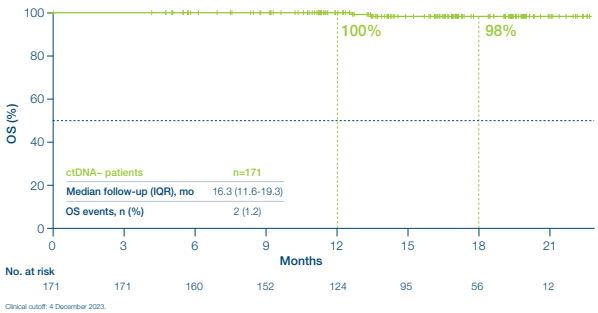


- ctDNA-positive patients had a significant survival benefit when treated with atezolizumab (OS, HR = 0.59).[4]
- No treatment benefit was observed in ctDNA-negative patients treated with atezolizumab (OS, HR = 1.38).[4]
- >75% of patients with detectable ctDNA post-surgery in the observation arm recurred by 20 month follow up.[1]

IMvigor011 (ongoing): Patients who remain serially Signatera™ negative post-cystectomy may be spared adjuvant therapy, underscoring the value of longitudinal monitoring[6]

Phase III, randomized double-blind study evaluating the efficacy of atezolizumab in patients with high-risk MIBC who are ctDNA-positive post-cystectomy

OS in the ctDNA– population



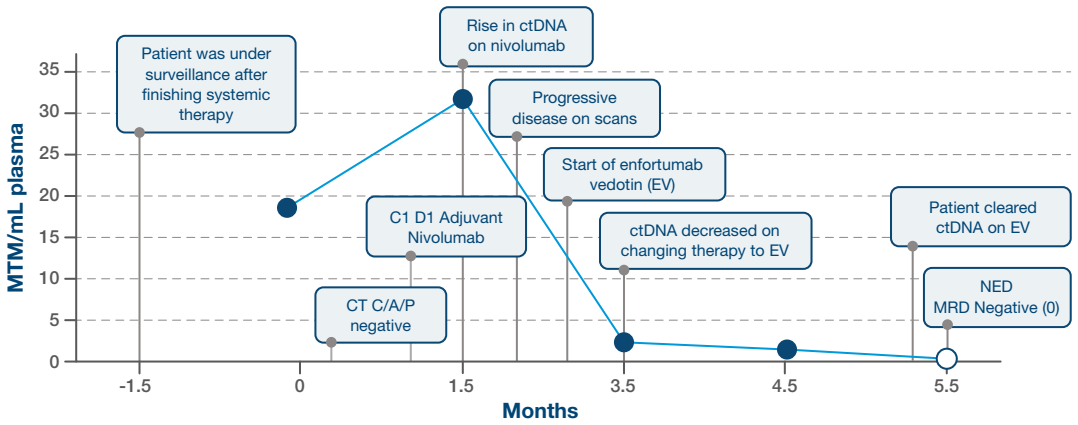
Signatera™ ctDNA-negative patients who were untreated had:

- OS rates of 100% at 12 months and 98% at 18 months.[6]
- DFS rates of 92% at 12 months and 88% at 18 months.[6]

Signatera™ is covered by Medicare and a growing number of commercial payers for monitoring patients with MIBC as well as any patient being treated with immunotherapy

Real world case study: 60 year old male with MIBC and persistently positive Signatera™ ctDNA

Historical results



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

The most comprehensively validated MRD assay

Extensively validated

Signatera™ has been validated in **>65** peer-reviewed publications studying **>6,500** patients across **>25** tumor types[7]

Deep experience

Signatera™ has been used to manage over **175,000** patients and has been ordered by **more than 1/3** of US oncologists[7]

Signatera™ can be run at any time point on the core biopsy or surgical resection and is covered by Medicare and a growing number of commercial payers for MIBC patients and any patient being treated with immunotherapy

Learn more about Natera's Oncology Portfolio:

Empower™ Hereditary cancer test

Empower™ for hereditary cancer testing which analyzes up to 81 genes across 12+ common hereditary cancers (panel can also be customizable, up to 190 genes) to help guide surgical and therapeutic decisions.)

Altera™ Tumor genomic profile

Add on Altera™ Genomic Profiling test which utilizes whole-exome and whole-transcriptome sequencing to identify clinically relevant biomarkers that may help guide treatment selection for advanced cancer patients– no additional sample needed.

References

1. Powles T, et al. *Nature*. 2021;595(7867):432-437. https://doi.org/10.1038/s41586-021-03642-9.
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. Powles T, et al. *European Urology*. 2023; https://doi.org/10.1016/j.eururo.2023.06.007.
5. Bratman SV, et al. *Nature Cancer*. 2020;1(9):873-881.
6. Powles T, et al Presented at EAU annual conference, 2024.
7. Natera Data on File as of May 1st, 2024.

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13011 McCallen Pass, Building A Suite 100 | Austin, TX 78753 | www.natera.com

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