natera™ | Signatera™ Residual disease test (MRD)

MEDICARE COVERAGE

BLADDER CANCER

# **IMvigor010:** Demonstrating the predictive value of ctDNA in the post-surgical setting

## Which patients will benefit from adjuvant immunotherapy?

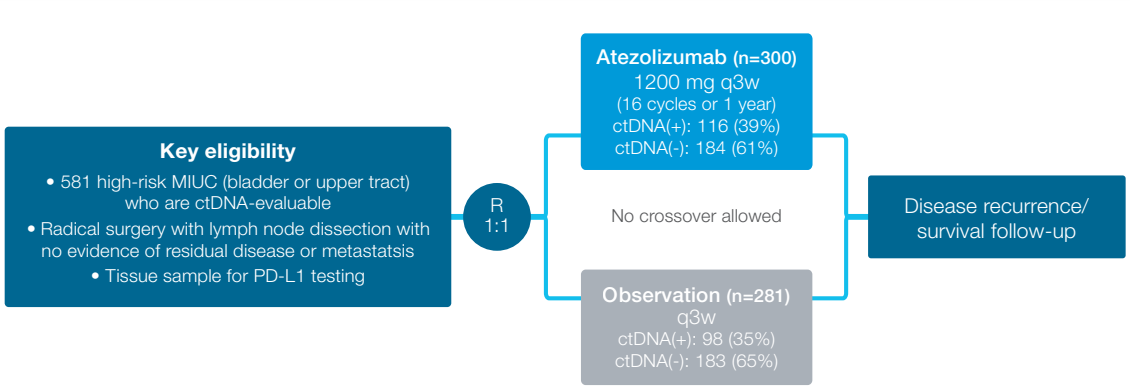
- Many patients who are cured by surgery are unnecessarily exposed to adjuvant therapy toxicities, while other patients don't receive potentially beneficial treatment until they have progressed on imaging[1]

## Nature 2021: ctDNA guiding adjuvant immunotherapy in urothelial carcinoma

### IMvigor010 Trial Design[1]

IMvigor010 is the first randomized, phase III, global registrational study, in high-risk, muscle-invasive bladder cancer (MIBC). Patients who received radical surgery were randomized 1:1 to atezolizumab or observation. The trial did not meet its primary endpoint of disease-free survival.

A prespecified ctDNA marker analysis was performed on the intent-to-treat (ITT) population with Signatera™ at the post-surgery and the 6-week on-treatment timepoints.




**Endpoints**

- Primary: DFS (ITT population)
- Key secondary: OS (ITT population)
- Other: Safety
- Exploratory: Predictive, prognostic and pharmacodynamic biomarkers in tumor tissue and blood, and their association with disease recurrence

## Post-cystectomy MRD assessment can help risk-stratify patients and identify those with residual disease who may benefit from adjuvant treatment

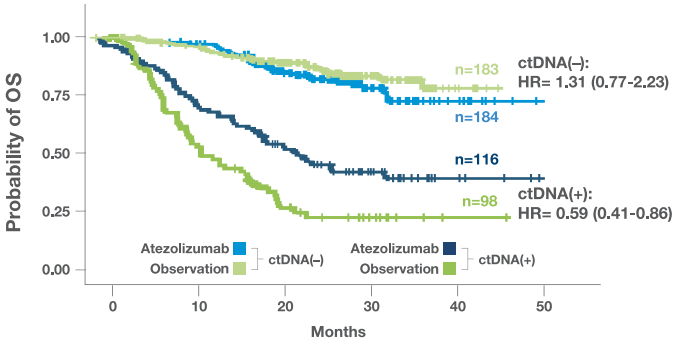
**42%** decreased risk of recurrence (DFS, HR 0.58, p=0.0024) and a 41% survival benefit in ctDNA-positive patients treated with atezolizumab (OS, HR 0.59).

# Key findings from IMvigor010

### Signatera™ ctDNA-positivity after surgery is predictive of adjuvant immunotherapy benefit[1]

- ctDNA-positive patients achieved improved OS when treated with adjuvant immunotherapy (OS HR=0.59)
- No treatment benefit was observed in ctDNA-negative patients treated with atezolizumab (OS, HR 1.31)
- Patients with serial negative ctDNA after cystectomy had 100% OS
- >75% of patients with detectable ctDNA post-surgery in the observation arm recurred by 20 month follow up

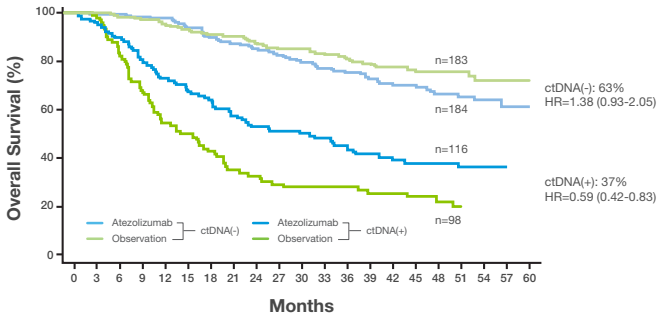
**OS by ctDNA status**




### Extended analysis from IMvigor010 confirmed predictive value of Signatera™ ctDNA status at 46.8-month median follow-up (OS, HR=0.59)[2]

- 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)
- >110% survival benefit observed in ctDNA-positive patients treated with atezolizumab (median OS: 29.8 mo vs 14.1 mo; HR 0.59)
- No treatment benefit was observed in ctDNA-negative patients treated with atezolizumab (OS, HR 1.38)

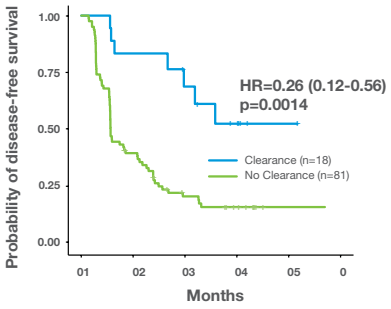
**OS by ctDNA status**



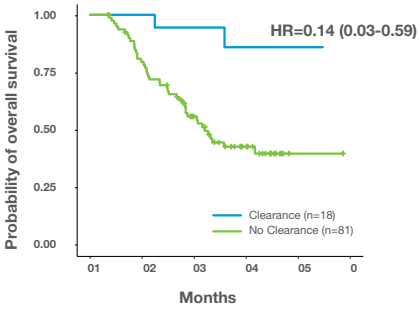

### Signatera™ ctDNA clearance was associated with improved outcomes in the treatment arm[1]

- ctDNA clearance at cycle 3 day 1 was associated with improved DFS and OS in the treatment arm

**DFS by ctDNA clearance**




**OS by ctDNA clearance**




**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 at natera.com/oncology**


References

**1.** Powles T, et al. *Nature*. 2021;595(7867):432-437. https://doi.org/10.1038/s41586-021-03642-9.

**2.** Powles T, et al. *European Urology*. 2023; https://doi.org/10.1016/j.eururo.2023.06.007



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





SGN_OS_IMvigor010_Publication_Summary_20231127_NAT-8021420


natera™