



Know Cancer's Next Move

- > Does my patient need adjuvant chemotherapy?
- > Is the treatment working?
- > Is the cancer recurring?

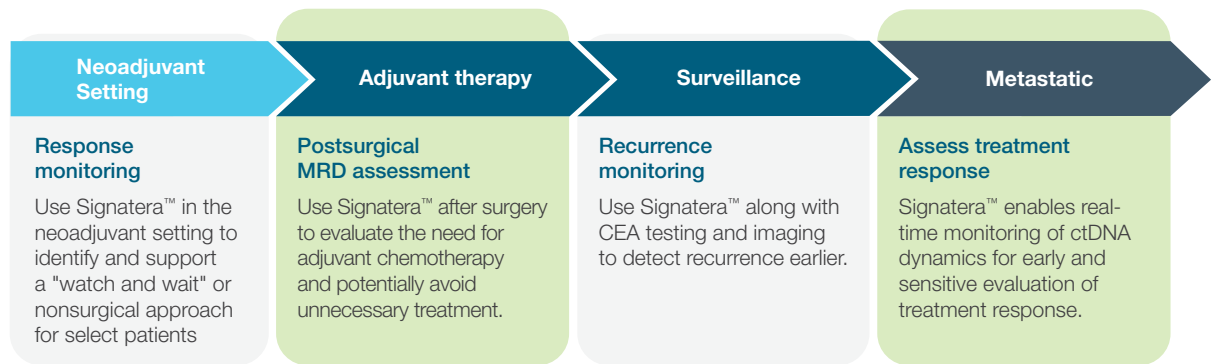
**A personalized,
tumor-informed
approach for
molecular
residual disease
(MRD) detection**



MEDICARE
COVERAGE



When to use Signatera™ MRD test



In the neoadjuvant setting

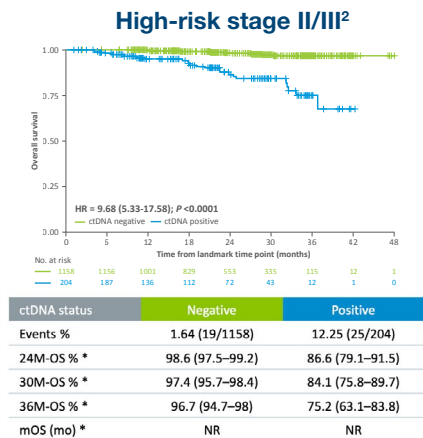
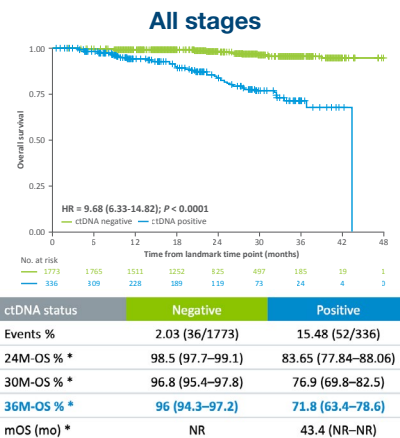
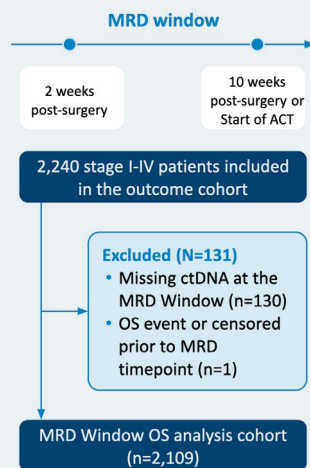
Tailor treatment or surgical strategies based on MRD status using primary tumor biopsy

In the adjuvant setting

The GALAXY study demonstrated Signatera's ability to predict adjuvant chemotherapy (ACT) benefit in resectable colorectal cancer¹

ctDNA-positivity at the MRD time point was predictive of inferior overall survival (OS)

36-month OS was 96% in ctDNA negative patients vs. 71.8% in ctDNA positive patients



MRD window: 2-10 weeks post surgery, prior to start of any adjuvant therapy – Landmark from MRD timepoint date

In the surveillance setting

ctDNA-positivity in the surveillance window was predictive of inferior disease-free survival (DFS)¹

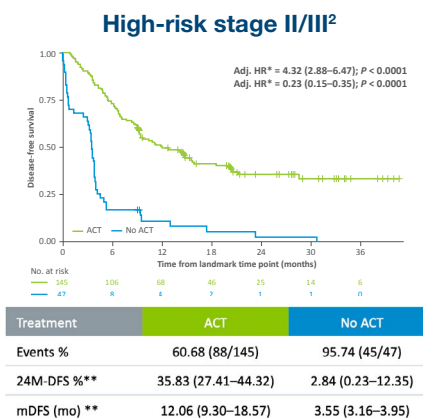
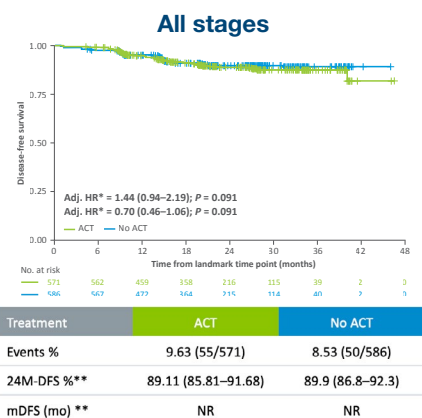
Evaluation of benefit of adjuvant chemotherapy (High risk stage II/III)

MRD-negative patients derived no significant benefit from adjuvant chemotherapy



Poor outcomes in MRD-positive patients could be improved with adjuvant therapy

*Adjusted for age, gender, Stage, ECOG.
**Estimates from landmark time point.



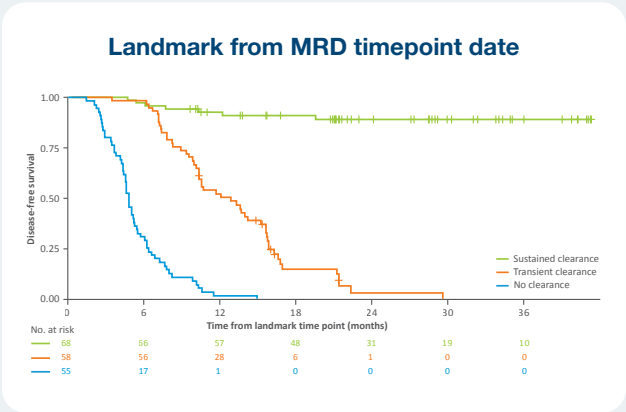
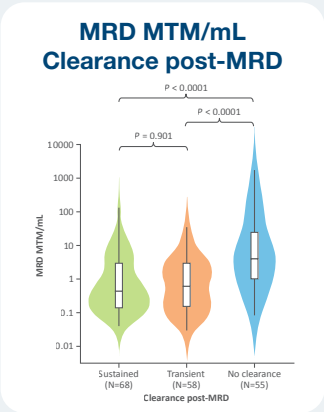
Can intervention with ACT in ctDNA positive patients impact survival?

DFS stratified by ctDNA clearance in patients with ctDNA positivity in the MRD window

Sustained ctDNA clearance in response to ACT was an indicator of favorable DFS, compared to transient clearance (24-month DFS: 89.0% vs 3.3%)

Superior DFS was achieved with sustained clearance compared to transient or no clearance

*P values from Wilcoxon rank-sum test.
**Estimates from landmark time point.



Suggested ordering cadence for patients with colorectal cancer

Signatera™ is custom-designed for each patient using their own tumor tissue

Tumor Tissue

**EDTA Whole Blood
(6 mL K2 or K3)**

**2x Streck | Plasma
(10 mL Tiger Top)**

Biopsy & surgical resection

Weeks

W2
(+/- 2 weeks)

W6
(+/- 2 weeks)

W12
(+/- 4 weeks)

W20
(+/- 4 weeks)

Months

M6–M24
(every 3 months)

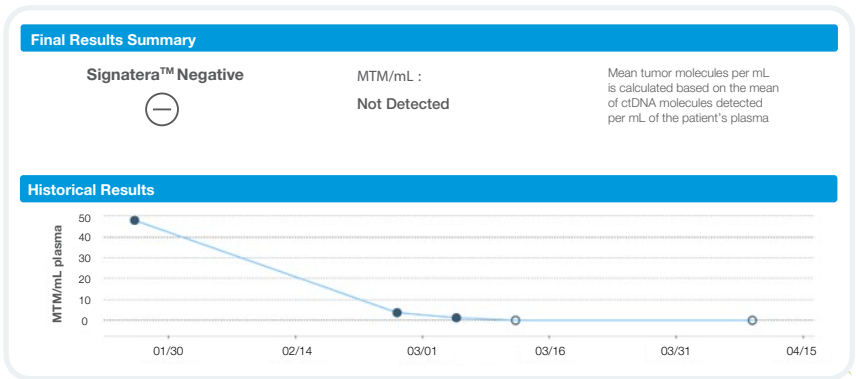
M24–M60
(every 6 months up to 5 years)

Note: Signatera™ test can also be designed using core biopsy tissue. Contact oncologyce@natera.com to learn more.

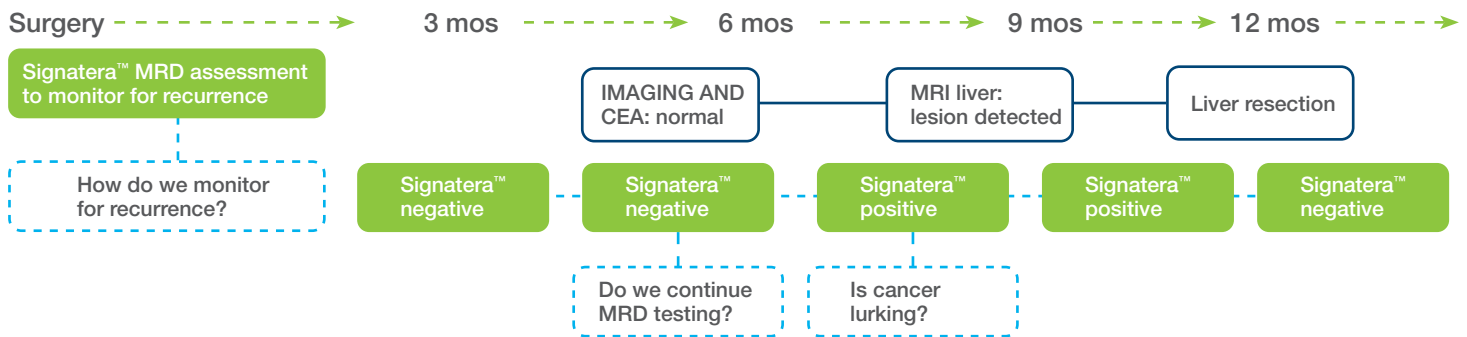
Track ctDNA dynamics to enable longitudinal monitoring

- Signatera™ reports presence/absence of ctDNA and ctDNA quantity in terms of MTM/mL for longitudinal assessment

MTM = mean tumor molecules



Clinical application: Value of serial testing in surveillance setting



Standard of care

Signatera™'s value

Discussion question

GALAXY 36M-Analysis

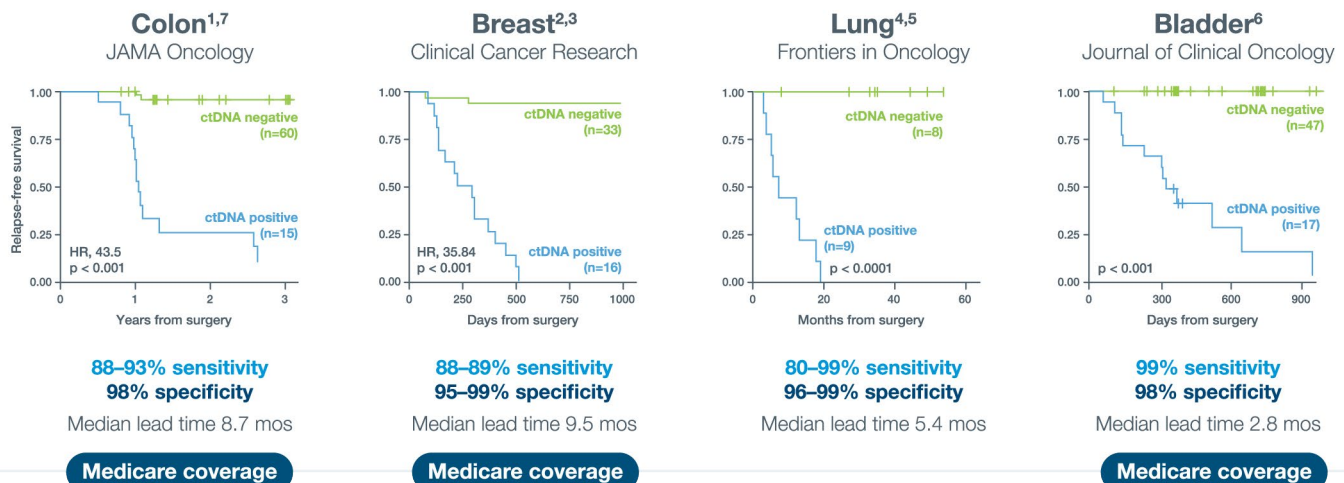
- 2,100 patients with stage II-IV CRC
- Patients who were ctDNA positive post-operatively were shown to have significantly lower DFS at 24 months than patients who were ctDNA negative
- ctDNA status during surveillance was significantly associated with DFS
- Sustained ctDNA clearance after ACT was significantly associated with >90% DFS



Signatera™ is covered by Medicare for monitoring disease progression, disease recurrence, or relapse for patients with:

Stage II-IV and oligometastatic colorectal cancer (CRC) in the adjuvant and recurrence monitoring settings

Signatera™ is validated across multiple tumor types^{1,6-8}



References

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3. Reinhart T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultra-deep Sequencing in Patients With Stages I to III Colorectal Cancer. *JAMA Oncol*. 2019.
4. Sinicrope FA, Foster NR, Thibodeau SN, et al. DNA Mismatch Repair Status and Colon Cancer Recurrence and Survival in Clinical Trials of 5-Fluorouracil-Based Adjuvant Therapy. *J Natl Cancer Inst*. 2011;103(11):863-875.
5. Aoyama, Oba K, Honda M, et al. Impact of postoperative complications on the colorectal cancer survival and recurrence: analyses of pooled individual patients' data from three large phase III randomized trials. *Cancer Med*. 2017;6(7):1573-1580.
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7. Kotani D, et al. Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer. *Nature Medicine* v29 Issue 1 Jan 2023
8. Coombes RC, Page K, Salari R, et al. Personalized Detection of Circulating Tumor DNA Antedates Breast Cancer Metastatic Recurrence. *Clin Cancer Res*. 2019;25(14):4255-4263.
9. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. *Nature*. 2017;545(7655):446-451.
10. Christensen E, Birkenkamp-Demtroder K, Sethi H, et al. Early Detection of Metastatic Relapse and Monitoring of Therapeutic Efficacy by Ultra-Deep Sequencing of Plasma Cell-Free DNA in Patients With Urothelial Bladder Carcinoma. *J Clin Oncol*. 2019;37(18):1547-1557.
11. Data on file

Learn more about Signatera™

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Scan to learn more



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Signatera™ has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified.
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