natera™ | Signatera™
Residual disease test (MRD)

COLORECTAL CANCER (CRC)

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

Neoadjuvant Setting	Adjuvant therapy	Surveillance	Metastatic
Response monitoring Use Signatera™ in the neoadjuvant setting to identify and support a "watch and wait" or nonsurgical approach for select patients	**Postsurgical MRD assessment** Use Signatera™ after surgery to evaluate the need for adjuvant chemotherapy and potentially avoid unnecessary treatment.	**Recurrence monitoring** Use Signatera™ along with CEA testing and imaging to detect recurrence earlier.	**Assess treatment response** Signatera™ enables real-time monitoring of ctDNA dynamics for early and sensitive evaluation of treatment response.

In the neoadjuvant setting

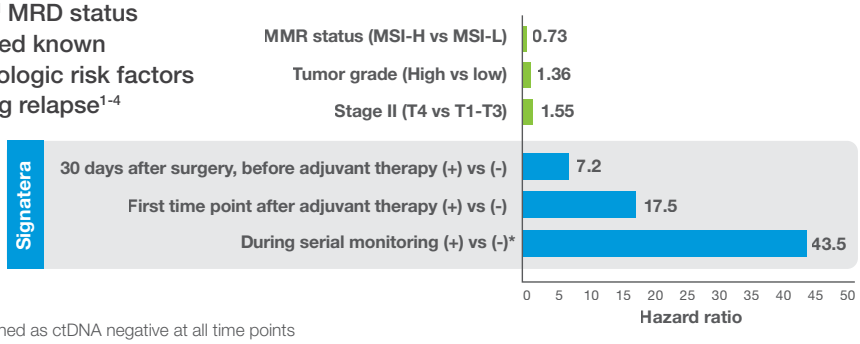
Tailor treatment or surgical strategies based on MRD status using primary tumor biopsy

In the adjuvant setting

Use after surgery to evaluate the benefit of adjuvant chemotherapy

Signatera™ more accurately identified patients at high risk of recurrence[1]

Signatera™ MRD status outperformed known clinicopathologic risk factors in predicting relapse[1-4]



*Negative is defined as ctDNA negative at all time points

- Serial testing improved sensitivity and negative predictive value of results
- Determined which ctDNA positive patients may benefit from adjuvant chemotherapy[5]

In the surveillance setting

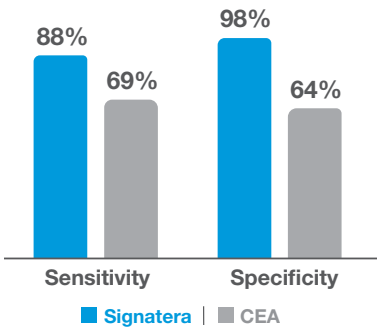
Use along with CEA testing and other surveillance tools to detect recurrence earlier, to inform surgical and / or other early intervention

Signatera™ was shown to detect relapse more accurately than CEA with clinically meaningful lead times over CT scans[1]

- Get clarity when evaluating patients with indeterminate CEA levels or CT scans
- Signatera™ facilitates shared decision-making and confident treatment planning

CEA = carcinoembryonic antigen
CT = computed tomography
ctDNA = circulating-tumor DNA

Accuracy in detecting relapse



Average lead time of ctDNA detection before CT scan

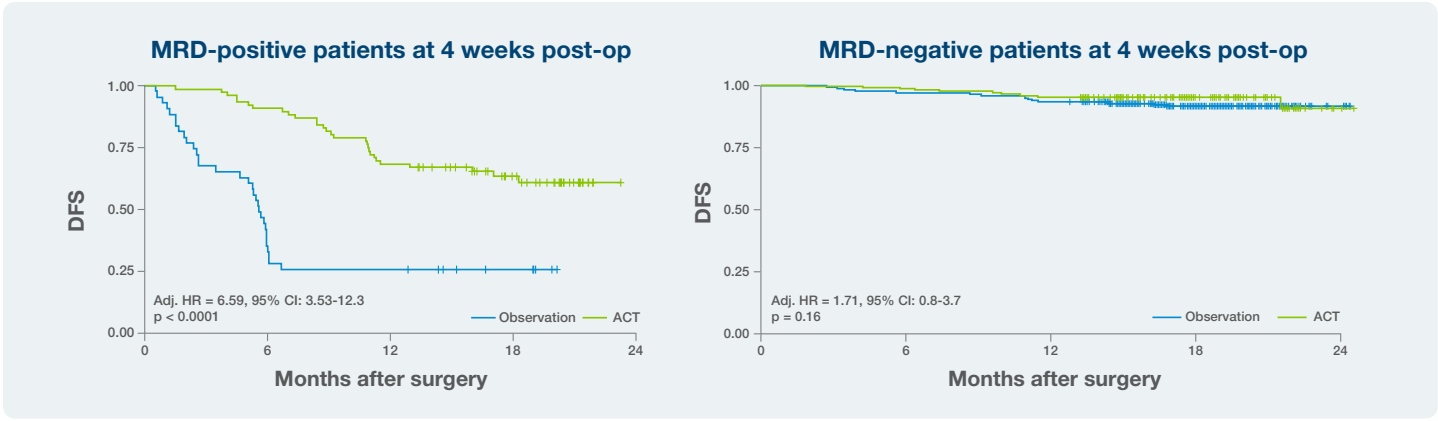
8.7

MONTHS

Maximum lead of 16.5 months

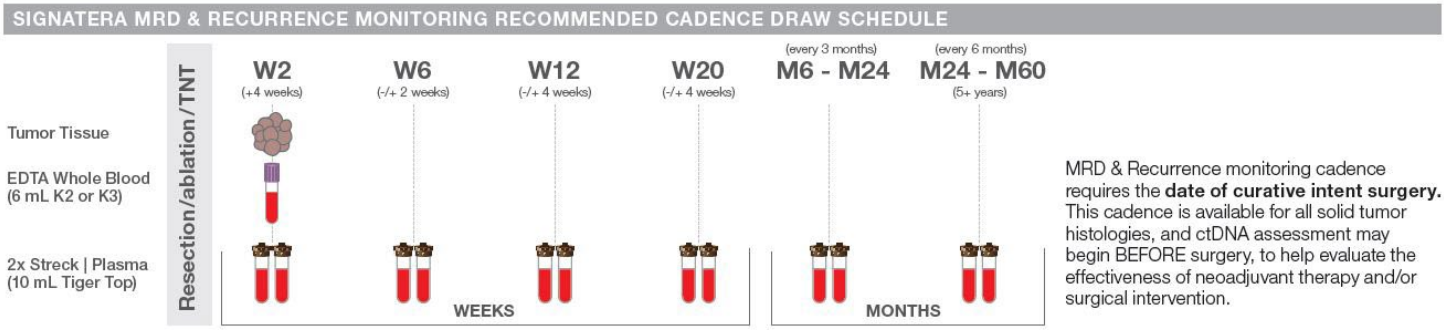
A large-scale prospective, MRD-guided study evaluated the clinical utility of ctDNA analysis in colorectal cancer (CRC)

MRD-positive CRC patients at 4 weeks post-op benefited significantly from chemotherapy while MRD-negative patients at 4 weeks post-op *did not* demonstrate any significant trend in treatment benefit



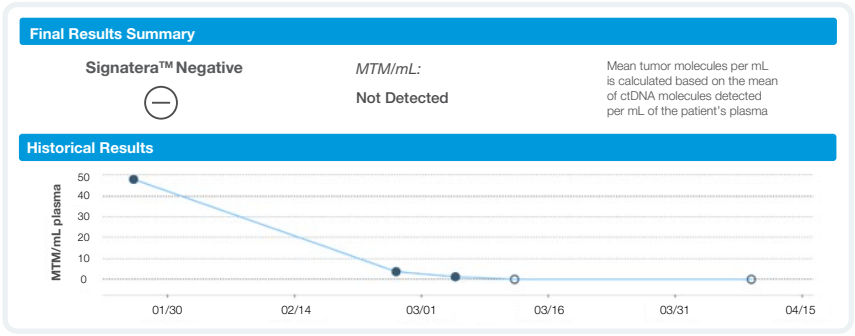
Ordering Signatera™ for patients with colorectal cancer

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



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

Just like no two tumors are alike—Signatera™ is personalized for each patient

Tumor-informed MRD assay for individualized care

- Customized for each patient's unique tumor signature using WES to target the top clonal mutations

High sensitivity and specificity for accurate MRD assessment

- By only tracking tumor-specific variants, sensitivity is optimized with a LOD down to 0.01% VAF[6]
- Filters out germline and CHIP mutations to reduce background noise and to minimize false positives

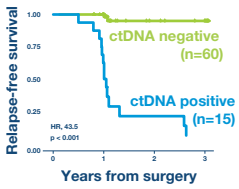
Reliable longitudinal monitoring for confident decision-making

- Tracks ctDNA dynamics by MTM/mL to enable longitudinal monitoring with a simple blood draw
- Follows clonal mutations that should persist as the tumor evolves

LOD = limit of detection; **CHIP** = clonal hematopoiesis of indeterminate potential; **VAF** = Varient allele frequency; **WES** = whole exome sequencing

Signatera™ is validated across multiple tumor types[1,6-8]

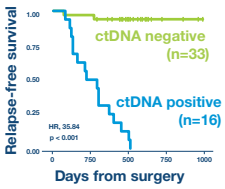
Colon[1]
JAMA Oncology



88%
sensitivity to relapse

Average lead time 8.7 mos

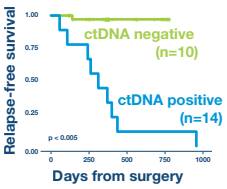
Breast[6]
Clinical Cancer Research



89%
sensitivity to relapse

Average lead time 9.5 mos

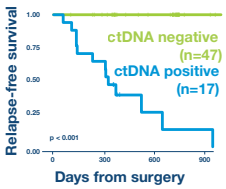
Lung[7]
NATURE



92%
sensitivity to relapse

Average lead time 4.0 mos

Bladder[8,9]
Journal of Clinical Oncology



100%
sensitivity to relapse

Average lead time 2.8 mos

References

1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. *JAMA Oncol*. 2019.
2. 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.
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4. Yothers G, O'Connell MJ, Lopatin M, et al. Validation of the 12-gene colon cancer recurrence score in NSABP C-07 as a predictor of recurrence in patients with stage II and III colon cancer treated with fluorouracil and leucovorin (FU/LV) and FU/LV plus oxaliplatin. *J Clin Oncol.* 2013;31(36):4512-4519.
5. Kotani D. et al., Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer, *Nature Medicine* v29 Issue 1 Jan 2023
6. 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.
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8. 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.
9. Data on file

Learn more about Signatera™:

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