MEDICARE COVERAGE

AFTER DEFINITIVE THERAPY IN CRC

Signatera™ looks deeper

- 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

natera™ | Signatera™
Residual disease test (MRD)

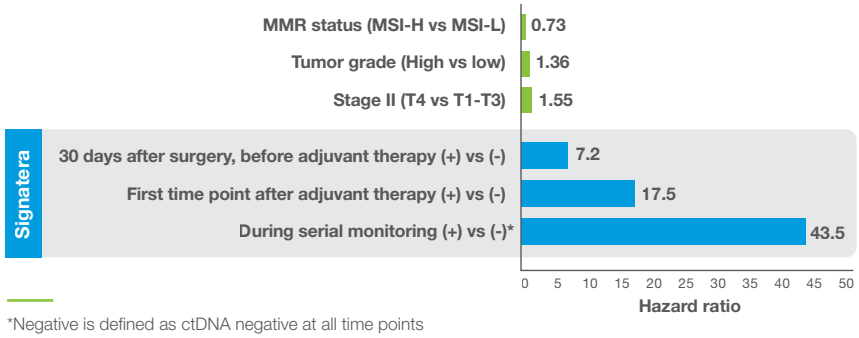
When to use Signatera

In the adjuvant setting

Use Signatera after surgery to evaluate the need for adjuvant chemotherapy and potentially avoid unnecessary treatment

Signatera accurately identifies patients at high risk of recurrence

Signatera MRD status outperforms know clinicopathologic risk factors in predicting relapse[1-4]



*Negative is defined as ctDNA negative at all time points

- 97% of patients with a positive Signatera result will relapse without additional treatment[1]
- Serial testing with Signatera improves sensitivity and negative predictive value of test results

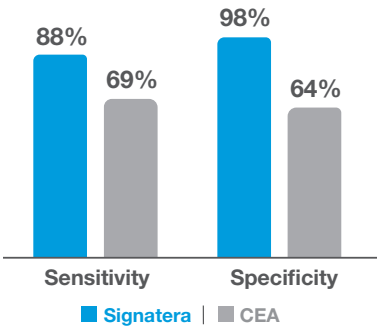
In the surveillance setting

Use Signatera along with CEA testing to detect recurrence earlier, while the tumor may still be resectable

Signatera detects 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

Accuracy in detecting relapse



Average lead time of ctDNA detection before CT scan

8.7

MONTHS

Maximum lead of 16.5 months

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

Decisions informed by the tumor for reliable MRD detection

Clinical utility of a Signatera ctDNA result

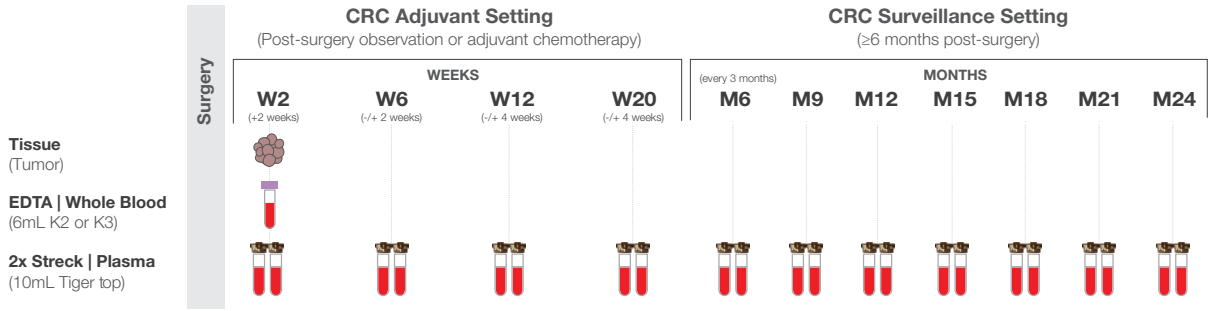
Adjuvant setting

	ctDNA high risk (+)	ctDNA low risk (−)
Stage II colon Stage IIA rectal	Manage as high risk	Risk similar to stage I, consider repeat testing and observation
Stage III colon	Manage as high risk	Consider repeat testing and de-escalation

Surveillance setting

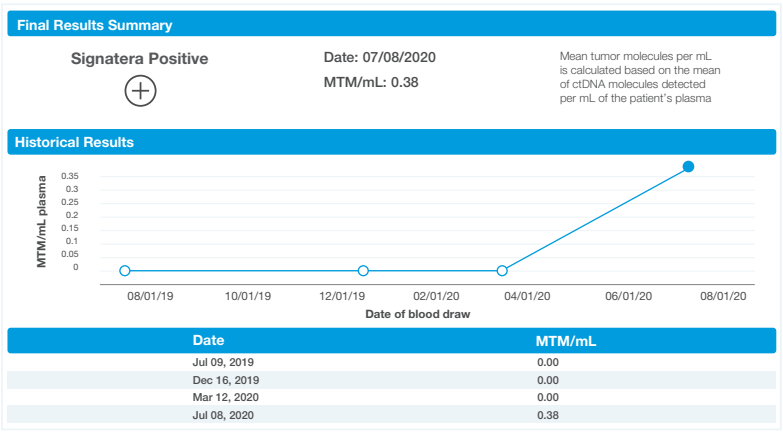
	ctDNA high risk (+)	ctDNA low risk (−)
Stage II and III colorectal	Consider more frequent CT scans or escalating to PET or MRI to locate disease while potentially resectable	Consider monitoring with reassurance

Recommended post-surgical draw schedules



- Medicare patients with stage II/III CRC are fully covered, for both serial and single time point use
- Turnaround times: Initial test design = 2-3 weeks; subsequent blood draws = 1 week

Quantitative ctDNA results enable longitudinal monitoring



- Signatera reports presence/absence of ctDNA and ctDNA quantity in terms of MTM/mL for longitudinal assessment
- Unlike other ctDNA assays, Signatera is designed to accurately detect MRD (i.e., not designed for early cancer screening nor for identifying actionable mutations for therapy selection)

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 by targeting the top clonal mutations

Optimized sensitivity and specificity for accurate MRD assessment

- By only tracking tumor-specific variants, sensitivity is maximized with a LOD down to 0.01% VAF[5]
- Filters out germline and CHIP mutations to reduce background noise and to minimize false positives

Reliable longitudinal monitoring for confident decision-making

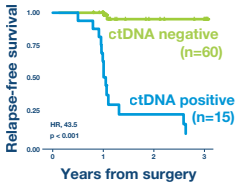
- By following clonal mutations that persist as the tumor evolves, full disease burden is reflected
- Quantification of MRD by MTM/mL enables longitudinal monitoring with a simple blood draw

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

Look deeper—so you can know sooner

Signatera is validated across multiple tumor types[1,5-7]

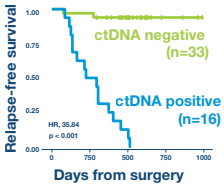
Colon[1]
JAMA Oncology



88%
sensitivity to relapse

Average lead time 8.7 mos

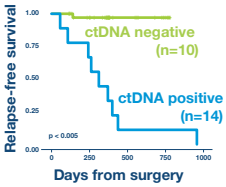
Breast[5]
Clinical Cancer Research



89%
sensitivity to relapse

Average lead time 9.5 mos

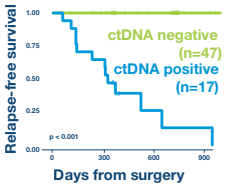
Lung[6]
NATURE



92%
sensitivity to relapse

Average lead time 4.0 mos

Bladder[7]
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. 3. 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. 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. 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. 6. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. *Nature.* 2017;545(7655):446-451. 7. 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.

Learn more about Signatera:

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