natera™ | Signatera™
Residual disease test (MRD)

Know
cancer's next move

Treat
with confidence

Signatera

Personalized, tumor-informed
molecular residual disease (MRD) detection

Signatera provides insight when current measures may be delaying answers to critical questions

Is there cancer left in the body?

Is additional treatment beneficial?

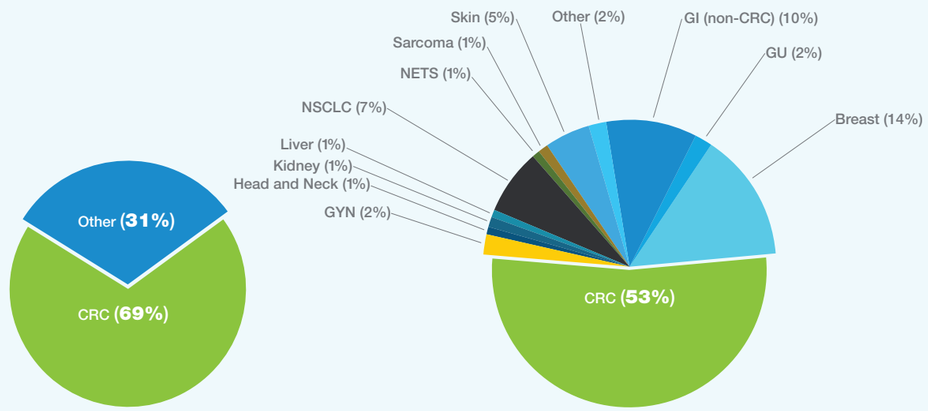
Is the treatment working?

Reliable results from a single test, deeper insights with serial sampling

	From a single test	With serial sampling
+	**Residual disease present** 97% of MRD-positive patients with early-stage CRC will relapse without further treatment[1,2]	**Actionable kinetics** Know if disease burden is increasing or shrinking with trackable MTM values[3]
−	**No evidence of residual disease** Only 12% of MRD-negative patients with early-stage CRC will relapse after surgery[1]	**Reduced recurrence risk** Only 3% of patients with serial ctDNA negative results relapsed[1]

Personalized approach, pan-cancer applicability

Broad clinical use[2]



Clinically validated

- >25K Signatera tests conducted in the United States since launch[2]*
- An additional 3000+ patient cases published or presented at major congresses[2]

Established Medicare coverage

- Medicare coverage for Stage II-III CRC, Stage IV oligometastatic CRC, and pan-cancer IO monitoring[2]

Breakthrough designation from the FDA

Signatera is a tumor-informed approach, clinically validated across multiple tumor types/settings[2]

*CLIA samples processed from 2H'19-1H'21.

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Signatera delivers deeper knowledge across the treatment journey

	Signatera clinical applications	Why tumor-informed MRD?
1	**Neoadjuvant response monitoring**	Tailor neoadjuvant treatment or surgical strategies to patient's specific needs (e.g., rectal cancer TNT)
2	**Postsurgical MRD assessment**	Identify patients who may or may not benefit from adjuvant therapy
3	**Recurrence monitoring**	Triage indeterminate nodules; rule in/rule out disease recurrence
4	**Assess treatment effectiveness**	Monitor ctDNA kinetics (increase or decrease in ctDNA levels) to quickly identify if there is any response to treatment

Add the Altera tumor genomic profiling test when you order Signatera to get clinically relevant biomarkers and MRD monitoring with no additional sample. Altera utilizes whole-exome and whole-transcriptome sequencing.

Signatera is a simple solution

1. Simple to order

- Order Signatera at any time; only one tissue sample is needed
- Common initial time points are at diagnosis or before treatment
- Order Altera along with Signatera for genomic profiling to aid in treatment selection

2. Simple for MRD monitoring

Recurring order program
(cadence can be based on surgery date or customized to patient's needs)

3. Simple sampling

Resection or diagnostic biopsy obtained from pathology *(initial test only)*

Initial and follow-up tests use a single blood draw from the clinic or patient's home using mobile phlebotomy

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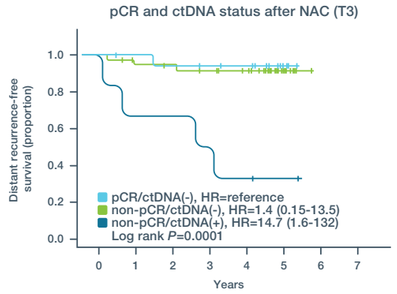
Residual disease test (MRD)

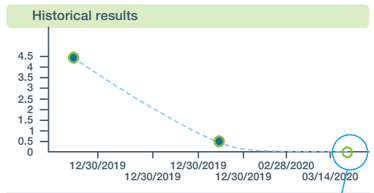
Signatera is proven across treatment phases and tumor types

1. Neoadjuvant response monitoring

Tailor neoadjuvant treatment or surgical strategies based on MRD status (e.g., rectal cancer TNT)



Breast cancer patients achieving ctDNA clearance but not pCR demonstrated similar risk of recurrence as those who achieved pCR.[4]

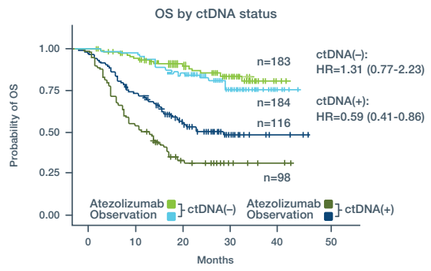


Date	MTM/mL
Dec 20, 2019	4.44
Feb 06, 2020	0.48
Mar 19, 2019	0.00

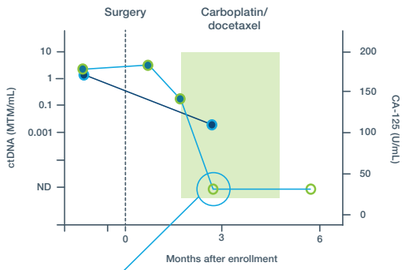
Case example: Rectal cancer patient who achieved ctDNA clearance during TNT elected for nonsurgical management[2]

2. Postsurgical MRD assessment

Evaluate the need for adjuvant therapy by identifying risk of postsurgical relapse



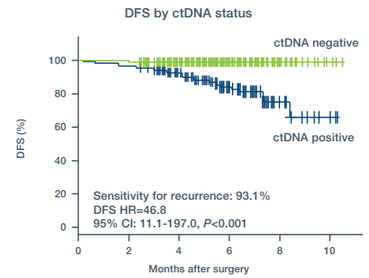
MIBC patients who were MRD-positive postsurgery derived treatment benefit with adjuvant therapy (OS HR=0.59). MRD-negative patients saw no improvement despite adjuvant treatment (OS HR=1.31).[5]



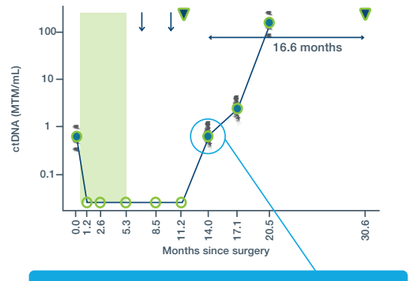
Case example: Ovarian cancer patient, who was MRD-positive after surgery, cleared ctDNA with carboplatin/docetaxel[6]

3. Recurrence monitoring

Triage indeterminate nodules; detect disease recurrence early while the tumor may still be resectable



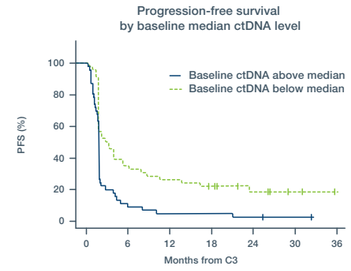
Signatera demonstrated 93% relapse sensitivity in a longitudinal analysis of more than 800 patients with colorectal cancer.[7]



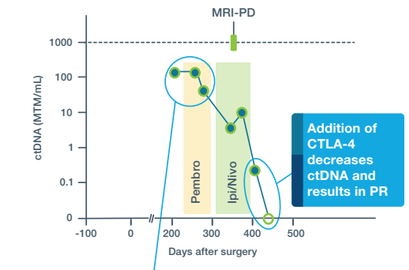
Case example: Colon cancer patient with ctDNA detected 16.6 months ahead of radiographic recurrence[1]

4. Assess treatment effectiveness

Identify patients who may not be responding to therapy, as well as exceptional responders who clear ctDNA



Signatera assessment of ctDNA kinetics at 6 weeks in conjunction with imaging was 100% predictive of treatment nonresponse to immunotherapy.[8]



Case example: CRC patient with elevated ctDNA, despite pembrolizumab monotherapy, experiences radiographic recurrence[9]

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Knowledge at every step to support optimal patient care

Is your cancer MRD test

Validated in >3000 patients

Pan-cancer

Able to track ctDNA kinetics

Personalized

Tumor informed

Breakthrough designated by FDA

Signatera™

CLIA=Clinical Laboratory Improvement Amendments; CRC=colorectal cancer; ctDNA=circulating tumor DNA; CTLA-4=cytotoxic T-lymphocyte antigen 4; DFS=disease-free survival; GI=gastrointestinal; GU=genitourinary; GYN=gynecological; IO=immuno-oncology; MIBC=muscle-invasive bladder cancer; MRD=molecular residual disease; MTM=mean number of tumor molecules; NAC=neoadjuvant chemotherapy; NETS=neuroendocrine tumors; NSCLC=non-small cell lung cancer; OS=overall survival; pCR=pathologic complete response; TNT=total neoadjuvant treatment.

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;5(8):1124-1131. doi:10.1001/jamaoncol.2019.0528 **2.** Natera. Data on file. **3.** Henriksen TV, Tarazona N, Frydendahl A, et al. Circulating tumor DNA in stage III colorectal cancer, beyond minimal residual disease detection, towards assessment of adjuvant therapy efficacy and clinical behavior of recurrences. *Clin Cancer Res.* Published online October 8, 2021. doi:10.1158/1078-0432.CCR-21-2404 **4.** Magbanua MJM, Swigart LB, Wu H-T, et al. Circulating tumor DNA in neoadjuvant-treated breast cancer reflects response and survival. *Ann Oncol.* 2021;32(2):229-239. doi:10.1016/j.annonc.2020.11.007 **5.** Powles T, Assaf ZJ, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. *Nature.* 2021;595(7867):432-437. doi:10.1038/s41586-021-03642-9 **6.** Chapman J, Pierson W, Smith McCune K, et al. Circulating tumor DNA predicts disease recurrence in ovarian cancer patients. Presented at: American Association of Cancer Research; April 9-14, 2021; Virtual. **7.** Shirasu H, Taniguchi H, Watanabe J, et al. Monitoring molecular residual disease by circulating tumor DNA in resectable colorectal cancer: molecular subgroup analyses of a prospective observational study GALAXY in CIRCULATE-Japan. Presented at: ESMO World Congress on Gastrointestinal Cancer; June 30-July 3, 2021; Lugano, Switzerland; Virtual. **8.** Bratman SV, Yang SYC, Iafolla MAJ, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. *Nat Cancer.* 2020;1:873-881. doi:10.1038/s43018-020-0096-5 **9.** Kasi P, Krainock M, Budde G, et al. Circulating tumor DNA (ctDNA) serial analysis during progression on PD-1 blockade and later CTLA-4 rescue in patients with mismatch repair-deficient metastatic colorectal cancer. Presented at: Society for Immunotherapy of Cancer 35th Annual Meeting; November 9-14, 2020; Virtual.

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