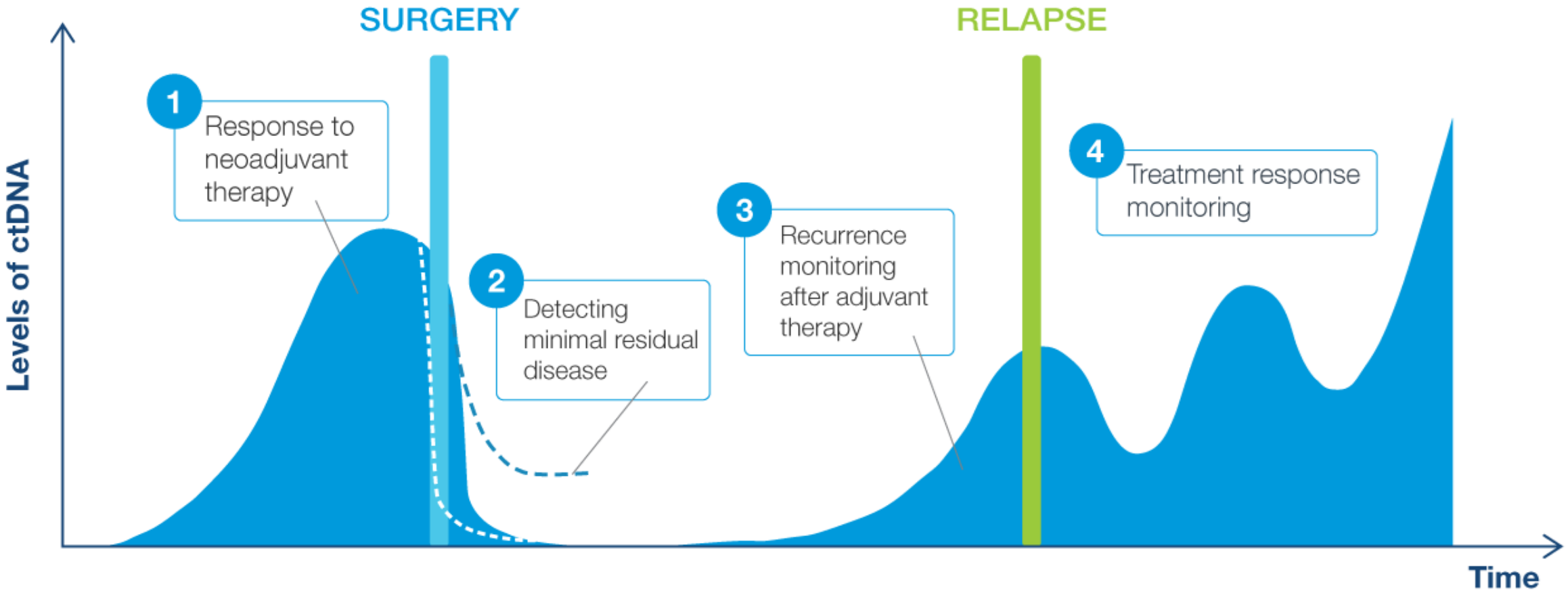
Assessment of MRD and treatment response with ctDNA

Clinical applications across the patient journey



natera™

Natera Overview

10M+
tests performed

10+
years of continued innovation

Reproductive health | **Oncology** | Organ transplant

Signatera™
Residual disease test (MRD)

- Molecular residual disease (MRD) status
- Surveillance for early recurrence detection
- Treatment response monitoring

Altera™
Tumor genomic profile

- Tumor profiling for therapy selection
- Whole Exome and Transcriptome Sequencing
- Introns and promoters, TMB, MSI and genes related to HRD

Empower™
Hereditary cancer test

- Inform treatment options following a cancer diagnosis
- Assess risk of developing cancer

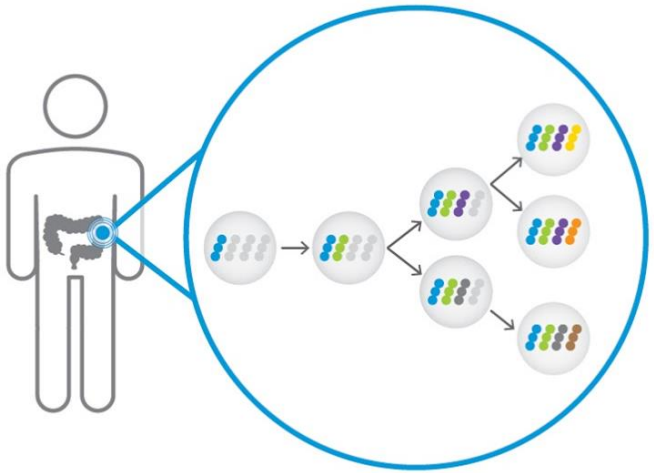
Signatera™ molecular residual disease (MRD) test

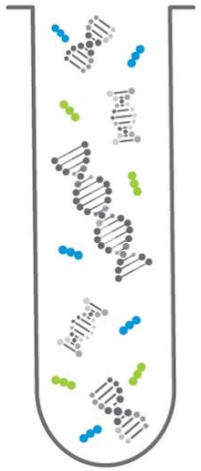
The personalized and tumor-informed approach

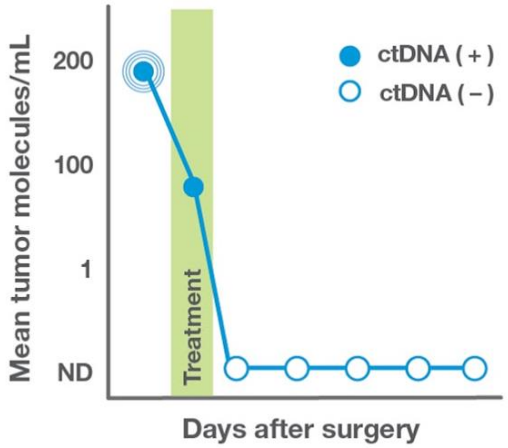
Sequence tumor tissue to identify unique signature of tumor mutations

Custom-design mPCR assay for each patient, targeting the top 16 clonal mutations found in tumor

Use personalized assay to test patient's blood for presence of circulating tumor DNA (ctDNA)







natera™

Optimize drug development with Signatera™

Know Sooner:	**Which patients are likely to relapse without additional treatment?**	**Is the treatment working?**
Drug Dev Implications:	**Focus drug development on high-risk patients most in need of additional therapy** ***>98%** relapse rate without further treatment, following a positive Signatera™ result*[1-4]	**Prioritize therapy programs based on early signals of therapy efficacy** *Predict immunotherapy response as early as **6 weeks***[5]

1. Reinert T, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. JAMA Oncol. 2019. 2. Coombes RC, et al. Personalized Detection of Circulating Tumor DNA Antedates Breast Cancer Metastatic Recurrence. Clin Cancer Res. 2019;25(14):4255-4263. 3. Abbosh C, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545(7655):446-451. 4. Christensen E, 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. 5. Bratman SV, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. Nature Cancer. 2020.1:873-881.

Signatera™ data published or presented across tumor types

>40 Peer reviewed publications **>100** Congress posters & presentations

4,000+
PATIENTS
ACROSS Signatera™
PUBLICATIONS[6]

JAMA Oncology
nature cancer
CLINICAL CANCER RESEARCH
nature
Journal of Clinical Oncology

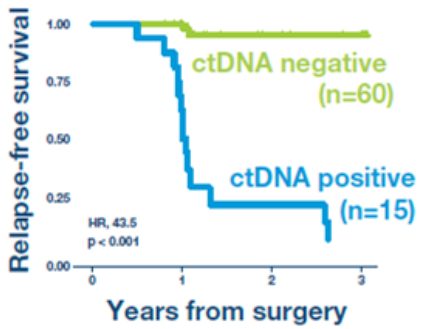
ASCO
ASCO GI
ESMO
ESMO GI
AACR

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. Bratman SV, Yang SYC, Iafolla MAJ, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. Nature Cancer. 2020;1(9):873-881. 3. Powles T, Assaf ZJ, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. Nature. 2021. 4. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545(7655):446-451. 5. 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. 6. Data on file, Natera

ctDNA as measured by Signatera™ is prognostic of disease recurrence across multiple tumor types

Colon[1,5]

JAMA Oncology



88%-93% sensitivity

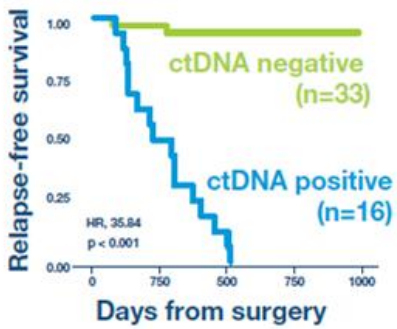
98% specificity

Avg lead time 8.7 mos

Medicare coverage

Breast[2]

Clinical Cancer Research



89% sensitivity

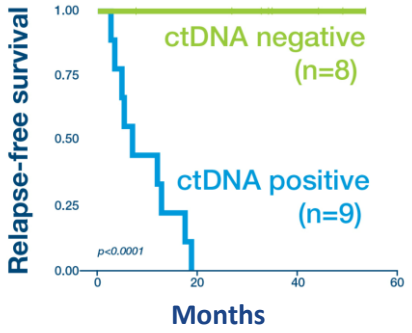
100% specificity

Avg lead time 9.5 mos

Medicare coverage

Lung[3]

Frontiers in Oncology



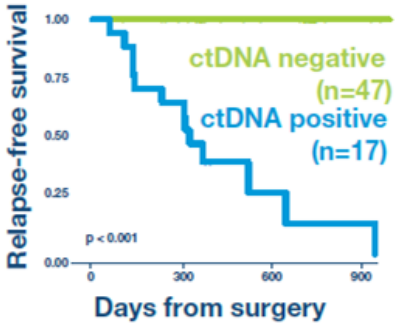
100%% sensitivity

100% specificity

Avg lead time 5.4 mos

Bladder[4,6]

Journal of Clinical Oncology



100% sensitivity

98% specificity

Avg lead time 2.8 mos

Medicare coverage

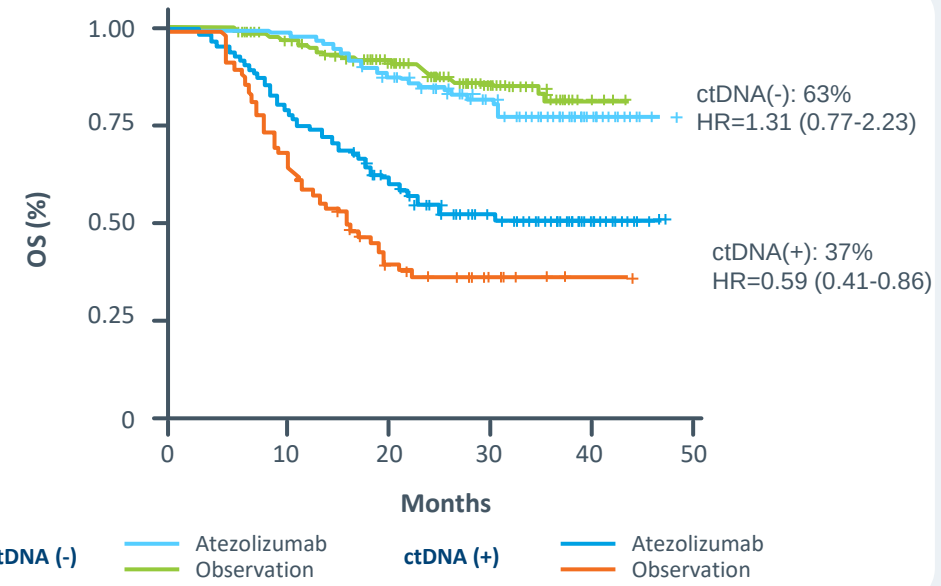
1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. JAMA Oncol. 2019. 2. Coombes RC, Page K, Salari R, et al. Personalized Detection of Circulating Tumor DNA Antedates Breast Cancer Metastatic Recurrence. Clin Cancer Res. 2019;25(14):4255-4263. 3. Lebow et al. ctDNA-based detection of molecular residual disease in stage I-III non-small cell lung cancer patients treated with definitive radiotherapy. Front. Oncol. Sec. Radiation Oncology Volume 13 – 2023 4. 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. 5.Kotaka et al. Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan. ASCO GI 2022 6 Data on file

Prognostic and predictive of treatment benefit

Does additional therapy benefit my patient?

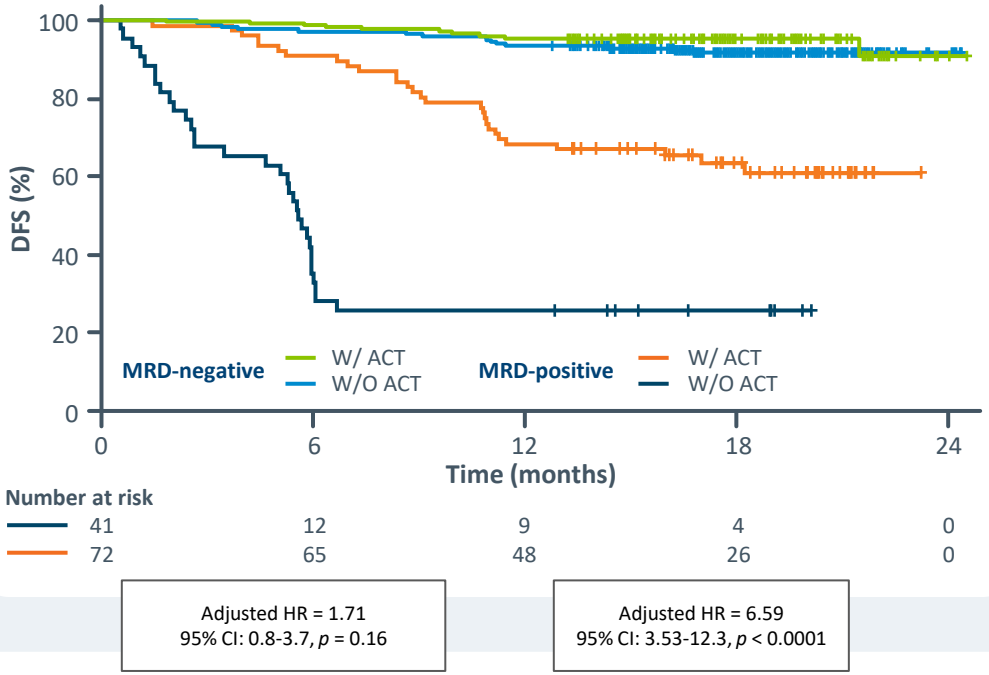
Bladder Cancer[1]

Overall Survival by ctDNA status in MIBC patients treated vs observation



Colorectal Cancer[2,3]

ctDNA status in high risk stage II/III patients – treated vs not treated



Signatera™ can help identify high risk patients who are likely to benefit from additional therapy[2]

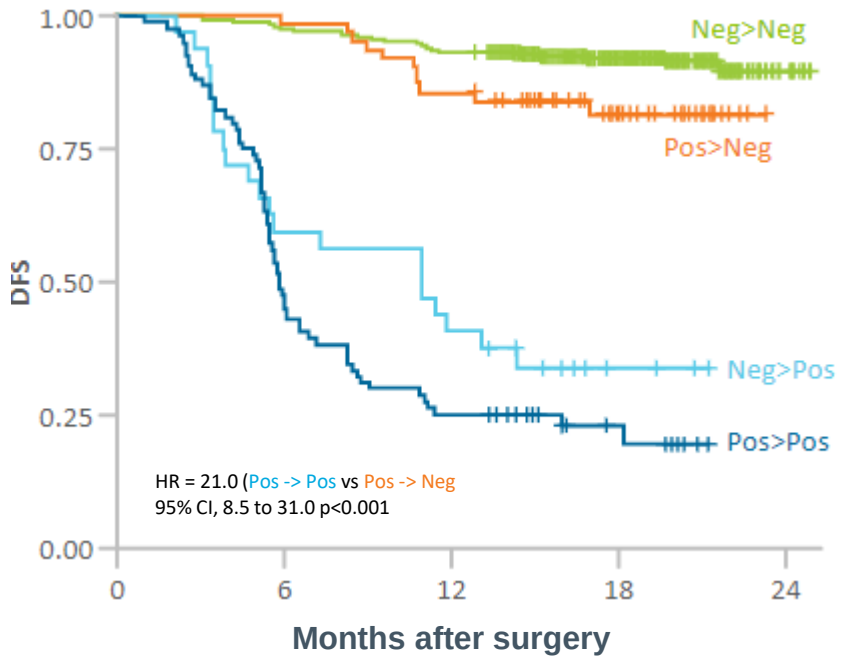
1.Powles T, Assaf ZJ, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. Nature. 2021 2. Kotani D. et al., Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer, Nature Medicine v29 Issue 1 Jan 2023
3. Hazard ratio (HR) for 4 week post-op ctDNA-positive patients calculated for pStage III patients, HR for 4 week post-op ctDNA-negative patients calculated for pStage II and III patients

ctDNA dynamics prognostic of survival outcomes

Is the treatment working?

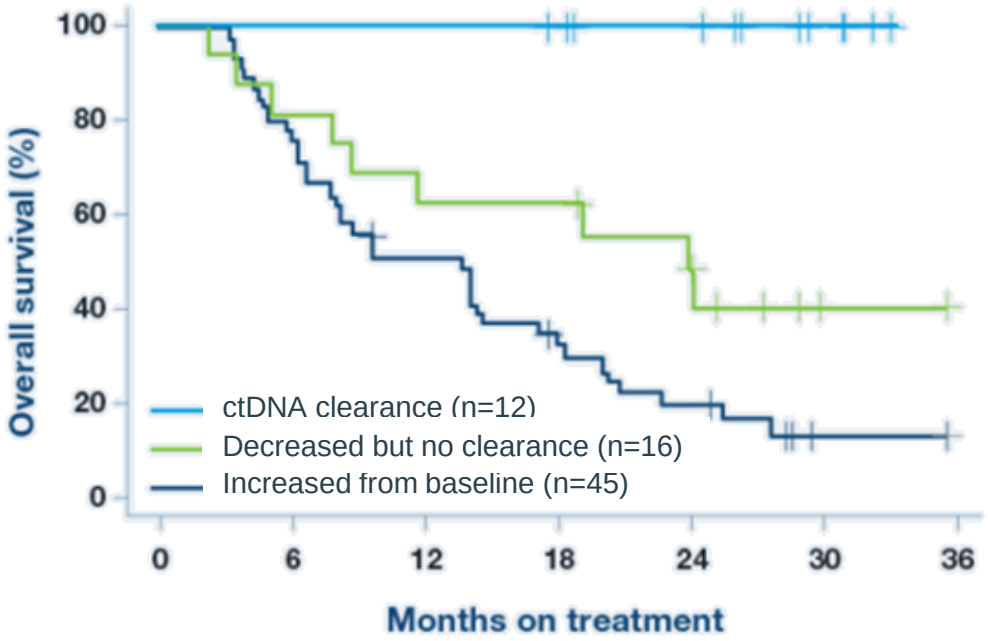
Colorectal Cancer [1]

Adjuvant chemotherapy response monitoring



Pan Cancer (25 tumor types)[2]

Immunotherapy response monitoring



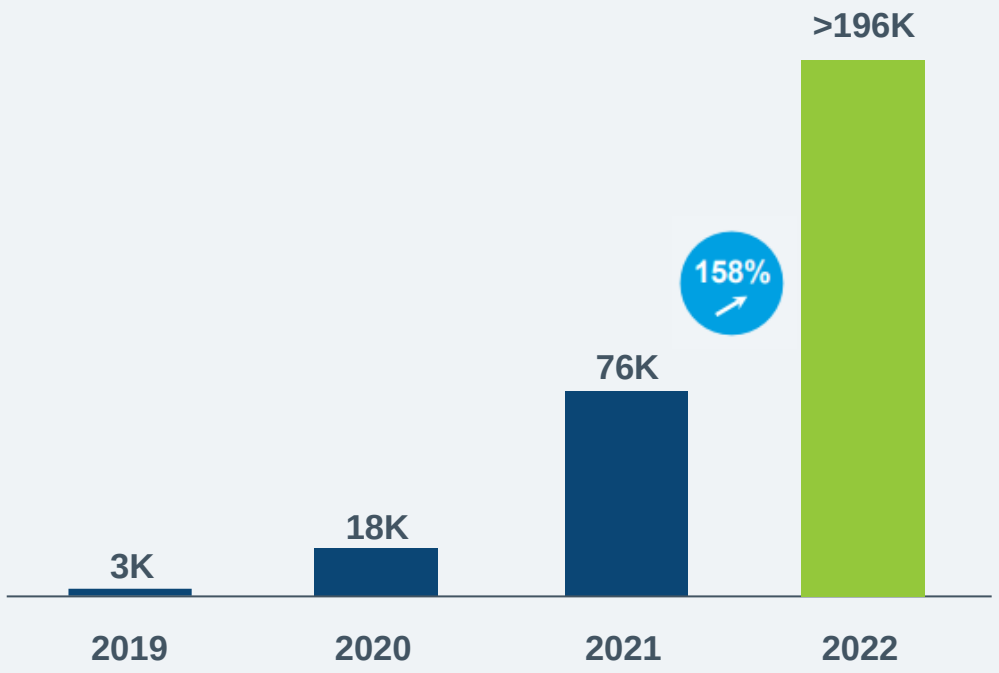
Patients who remained ctDNA negative had better outcomes than patients who started or became ctDNA positive [2]

1 Kotani D. et al., Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer, Nature Medicine v29 Issue 1 Jan 2023 2. 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..

Rapid growth in commercial adoption, with significant runway driven by Medicare and Commercial payor coverage

Signatera™ and Altera™

Total Oncology Unit Volumes



Medicare Local Coverage Determination

- Serial use of Signatera™ in stage II, III and IV oligometastatic **colorectal cancer**
- Immunotherapy response monitoring in **solid tumors**
- Neoadjuvant, adjuvant, and recurrence monitoring for muscle-invasive **bladder cancer**
- Adjuvant and surveillance monitoring for locally and regionally advanced **breast cancer**

Commercial Payor Coverage

- BS California - **pan-cancer coverage** for adjuvant, recurrence monitoring, and treatment monitoring
- BCBS Louisiana - serial testing for **colorectal cancer**, **muscle invasive bladder cancer**, and **pan-cancer immunotherapy monitoring**

As reported in 2022 Q4 / FY earnings call

Learn more at http://www.natera.com/clinical-trials/