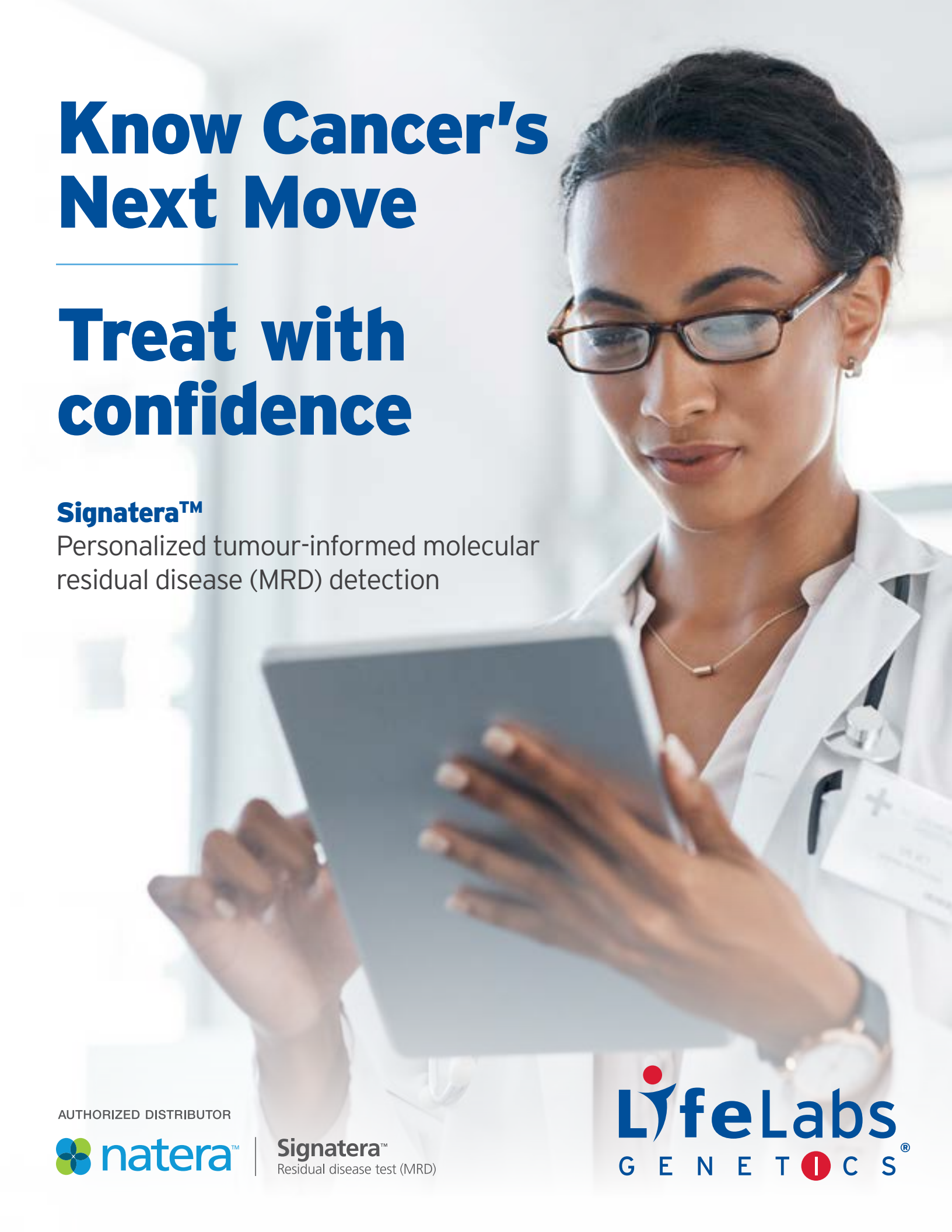

Know Cancer's Next Move

Treat with confidence

Signatera™
Personalized tumour-informed molecular residual disease (MRD) detection

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natera™ | Signatera™
Residual disease test (MRD)

LifeLabs GENETICS®

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

Who is this test for?

Individuals who have been diagnosed with solid tumours (e.g., CRC, breast, ovarian, lung, bladder, melanoma) and those diagnosed with cancer (solid tumours) being treated with immunotherapy, and are seeking answers to the following questions:

- **Is there cancer left in the body?**
- **Is additional treatment beneficial?**
- **Is the treatment working?**

Signatera™ is not currently recommended for leukemias, non-solid-mass lymphomas, and cancer behind the blood-brain barrier such as CNS tumours.

Signatera™ is a tumour-informed test that detects/ quantifies ctDNA in patients diagnosed with a solid tumour

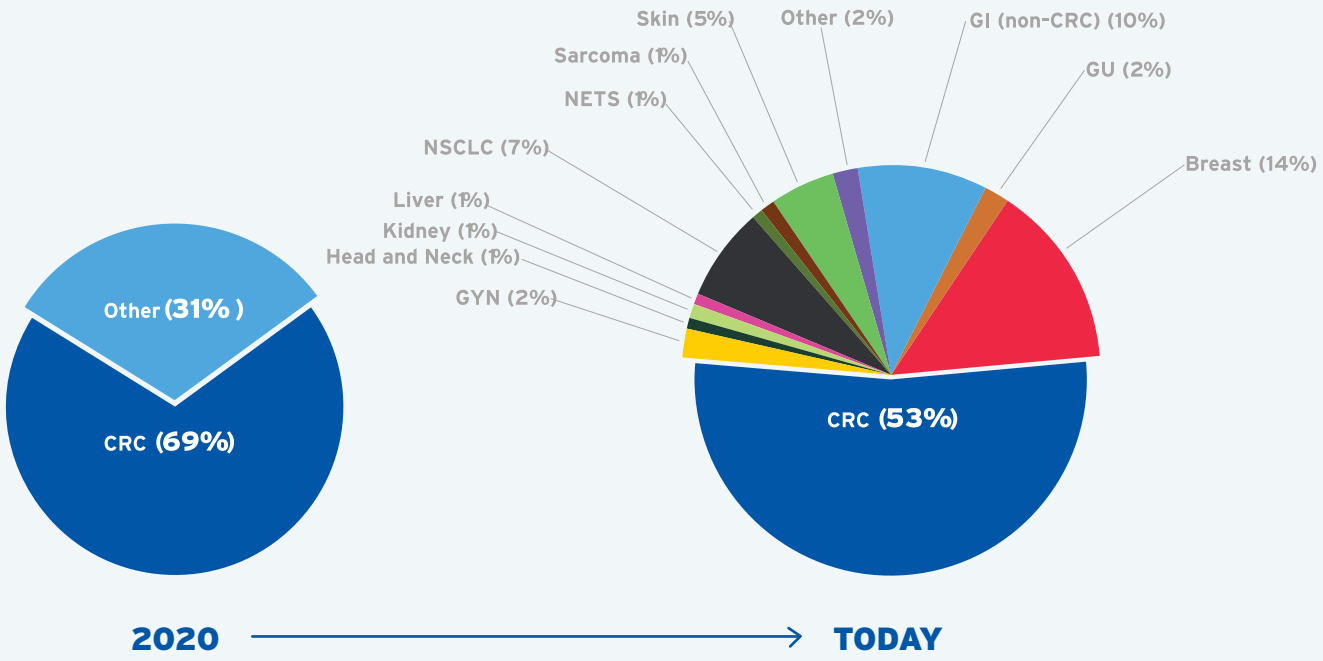
Reliable results from a single test, deeper insights with serial sampling

	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]

MTM = mean tumour molecules (per mL of plasma); **CRC** = Colorectal Cancer

Personalized approach, pan-cancer applicability

Broad Clinical Use[2]



Clinically validated

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

Breakthrough designation from the FDA

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

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

Signatera delivers deeper knowledge across the treatment journey

	SIGNATERA CLINICAL APPLICATIONS	WHY TUMOUR-INFORMED MRD?
1	**Neoadjuvant response monitoring**	Tailor neoadjuvant treatment or 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

MTM = mean tumour molecules (per mL of plasma)

Signatera is a simple solution

1. Simple to order

Neoadjuvant | Adjuvant | Surveillance | Advanced / Metastatic

- Only the one-time initial test requires a tissue sample; subsequent tests require only a blood draw.
- Common initial points for ordering are at diagnosis or before treatment

2. Simple for MRD monitoring (Subsequent Test)

- Testing frequency may be based on timing of interventions (e.g., surgery, chemotherapy) and customized to patient needs.

3. Simple sampling

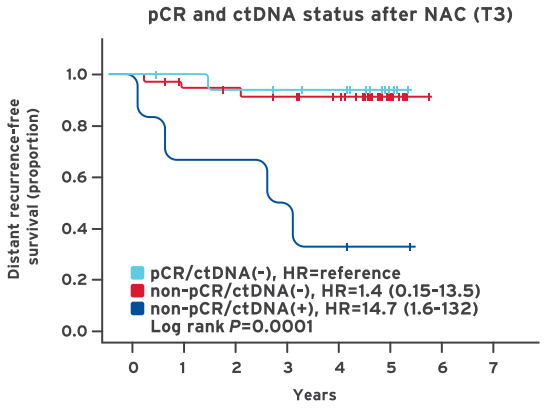
Resection or diagnostic biopsy obtained from pathology (Initial Test only)

Initial Test and Subsequent Tests use a single blood draw from the clinic or a Lifelabs community location (ON/BC/SK)

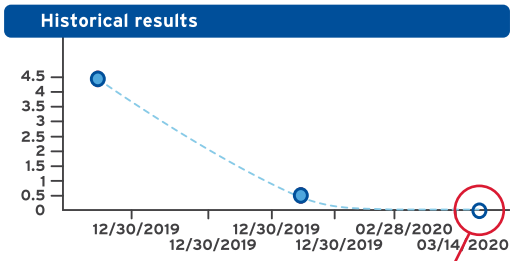
Signatera is proven across treatment phases and tumour types

1. Neoadjuvant Response Monitoring

Tailor neoadjuvant treatment 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]

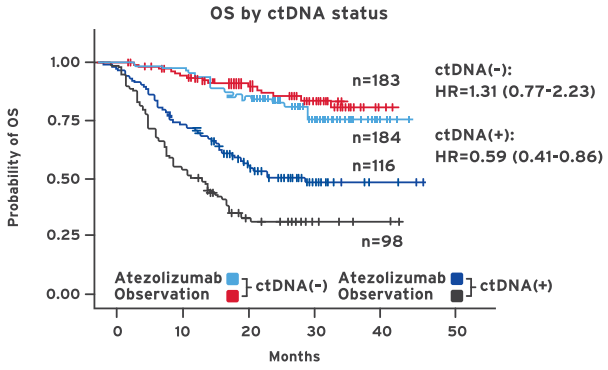


Date	MTM/mL
Dec 20, 2019	4.44
Feb 06, 2020	0.48
Mar 19, 2019	0.00

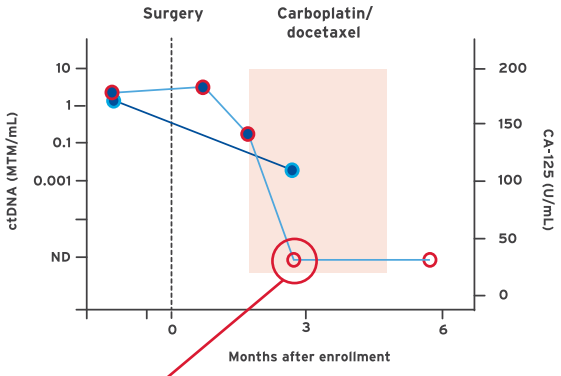
Case example: Rectal cancer patient who achieved ctDNA clearance during TNT elected for nonsurgical management[2]

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]

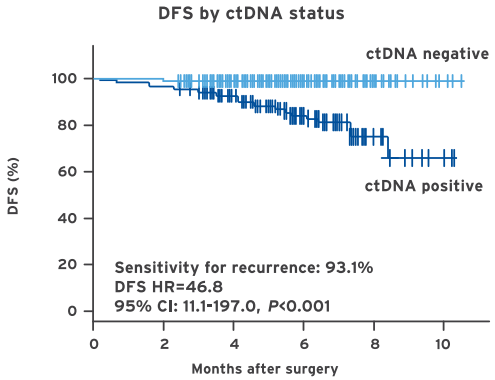


Case example: Ovarian cancer patient, who was MRD-positive after surgery, cleared ctDNA with carboplatin/docetaxel[6]

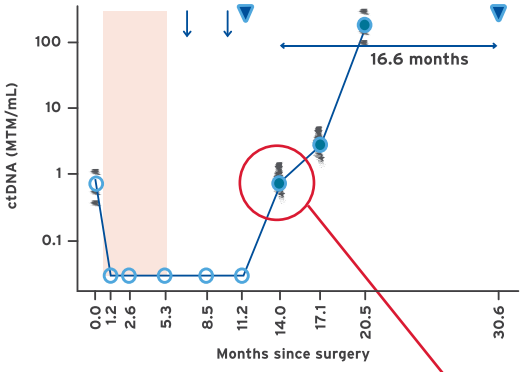
OS = overall survival

3. Recurrence Monitoring

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



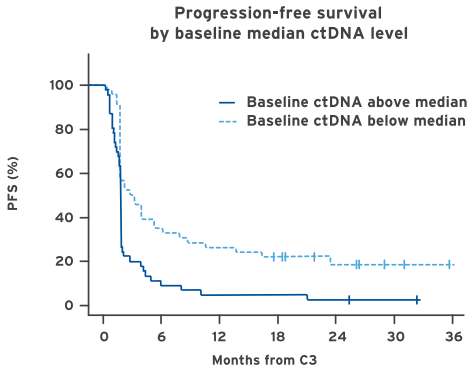
Signatera demonstrated 93% relapse sensitivity in a longitudinal analysis of more than 800 patients with colorectal cancer[7]



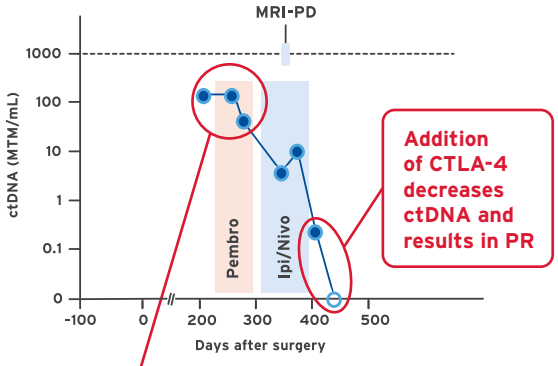
Case example: Colon cancer patient with ctDNA detected 16.6 months ahead of radiographic recurrence[1]

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]



Addition of CTLA-4 decreases ctDNA and results in PR

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

DFS = disease-free survival

Track ctDNA dynamics to enable longitudinal monitoring

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

Final Results Summary

Signatera™ Negative ⊖	MTM/mL **Not Detected**	Mean tumour molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma

Historical Results

MTM = mean tumour molecules

Knowledge at every step to support optimal patient care

Signatera™

Validated in >3000 patients
Pan-cancer
Able to track ctDNA kinetics
Personalized
Tumour informed
Breakthrough designated by FDA

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CLIA=Clinical Laboratory Improvement Amendments; CRC=colorectal cancer; ctDNA=circulating tumour 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 tumour molecules; NAC=neoadjuvant chemotherapy; NETS=neuroendocrine tumours; 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 tumour 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. 2021. doi:10. 1158/1078-0432.CCR-21-2404 4. Magbanua MJM, Swigart LB, Wu HT, et al. Circulating tumour DNA in neoadjuvant-treated breast cancer reflects response and survival. Ann Oncol. 2021;32(2):229-239. 5. Powles T, Assaf Z J, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. Nature. 2021;595:432-437. 6. Chapman J, Pierson W, Smith McCune K, et al. Circulating tumour 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 tumour 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 tumour DNA analysis as a predictive biomarker in solid tumour patients treated with pembrolizumab. Nat Cancer. 2020;1:873-881. 9. Kasi P, Krainock M, Budde G, et al. Circulating tumour 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 ancer 35th Annual Meeting; November 9-14, 2020; Virtual.

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