Ultra-sensitive Molecular Residual Disease Detection in Breast Cancer Using Whole-Genome Sequencing-Based Personalized ctDNA Panels: Preliminary Results from the MONSTAR-SCREEN-3 Project

AN: 3026
PN: PS2-09-07

Y. Naito[1], M. Nishimura[2], Y. Hisamatsu[3], M. Futamura[4], T. Toyama[5], T. Yamanaka[6], M. Tsukabe[7], S. Hashimoto[8], E.Tokunaga[9], M. Ishihara[10], R. Nakamura[11], H. Yasojima[12], T. Hashimoto[1], T. Shibuki[1], M. Imai[1], T. Fujisawa[1], H. Bando[1], S. Kobayashi[1], S.Sakashita[1], T. Kuwata[1], A. Blackler[13], G. Hogan[13], K. Johansen Taber[13], J. Jasper[13], D. Muzzey[13], E. Oki[3], T. Yoshino[1], H. Iwata[5]

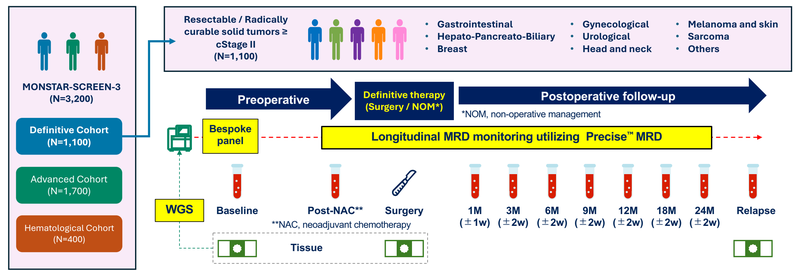
1. National Cancer Center Hospital East, Kashiwa, JAPAN, 2. Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, JAPAN,3. Kyushu University, Fukuoka, JAPAN, 4. Gifu University Hospital, Gifu, JAPAN, 5. Nagoya City University, Nagoya, JAPAN, 6. Kanagawa Cancer Center, Kanagawa, JAPAN, 7. The University of Osaka, Suita, JAPAN, 8. University of Tsukuba, Ibaraki, JAPAN, 9. NHO Kyushu Cancer Center, Fukuoka, JAPAN, 10. Osaka International Cancer Institute, Osaka, JAPAN, 11. Chiba Cancer Center, Chiba, JAPAN, 12. NHO Osaka National Hospital, Osaka, JAPAN, 13. Myriad Genetics, Inc., Salt Lake City, UT.

Background

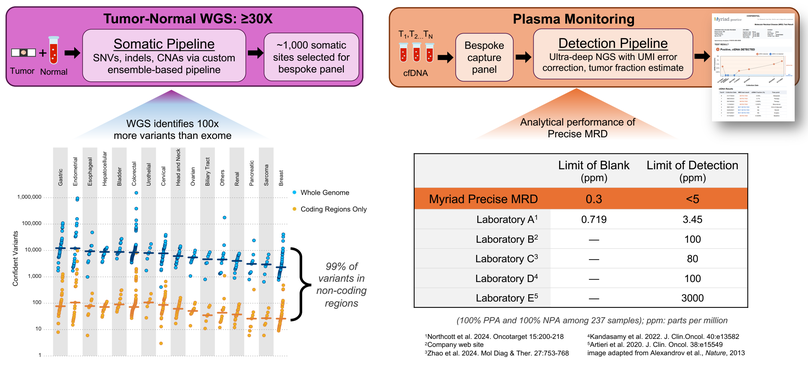
- Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for detecting molecular residual disease (MRD) and is increasingly integrated into both clinical practice and translational research in breast cancer.
- However, whole-exome sequencing (WES)-based approaches often lack sufficient sensitivity for MRD detection, particularly in low-shedding tumors such as luminal breast cancer.
- To address this limitation, the MONSTAR-SCREEN-3 study is evaluating an ultra-sensitive MRD assay based on whole-genome sequencing (WGS).

Methods

- MONSTAR-SCREEN-3 is a prospective, multicenter study enrolling 1,100 patients with solid tumors receiving curative-intent therapy in the definitive cohort.
- Serial plasma samples are collected at baseline, after neoadjuvant chemotherapy (if applicable), 1-month post-surgery, quarterly during the first year, and biannually thereafter for up to two years.



- Personalized ctDNA panels are generated using the Precise MRD assay (Myriad Genetics), incorporating up to 1,000 tumor-specific alterations identified through WGS of matched tumor tissue.



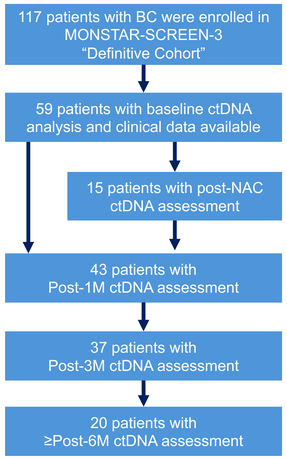
	Limit of Blank (ppm)	Limit of Detection (ppm)
Myriad Precise MRD	0.3	<5
Laboratory A[1]	0.719	3.45
Laboratory B[2]	—	100
Laboratory C[3]	—	80
Laboratory D[4]	—	100
Laboratory E[5]	—	3000

(100% PPA and 100% NPA among 237 samples); ppm: parts per million

[1]Northcott et al. 2024. Oncotarget 15:200-218
[2]Company web site.
[3]Zhao et al. 2024. Mol Diag & Ther. 27:753-768
[4]Kandasamy et al. 2022. J. Clin.Oncol. 40:e13582
[5]Artieri et al. 2020. J. Clin. Oncol. 38:e15549
image adapted from Alexandrov et al., *Nature*, 2013

Results

Enrollment: May 2024 ~ Aug 2025
Data cutoff: 11 Nov 2025



NAC, neoadjuvant chemotherapy

Baseline characteristics		n=59, n (%)
Age, median (range), years		50 (29—87)
Subtype	HR(+)/HER2(-)	32 (54%)
	HER2(+)	21 (36%)
	Triple negative	6 (10%)
Cohort	Neoadjuvant	24 (41%)
	Up-front Surgery	35 (59%)
Side	Left	30 (51%)
	Right	28 (47%)
	Occult	1 (2%)
Histology	IDC	50 (85%)
	ILC	4 (7%)
	Others	5 (8%)
cStage	IA	1 (2%)
	IIA	34 (58%)
	IIB	13 (22%)
	IIIA	5 (8%)
	IIIB	3 (5%)
	IIIC	3 (5%)
Surgery	Done	54 (92%)
	Not yet	5 (8%)
Adjuvant chemotherapy	Performed	20 (34%)
	Not performed	34 (58%)
	NA	5 (8%)

HR, hormone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma

Figure 1. Number of variants identified in WGS according to subtypes

100x more variants were identified with the use of WGS compared to analysis with coding regions

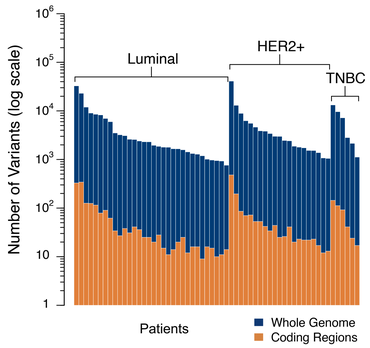
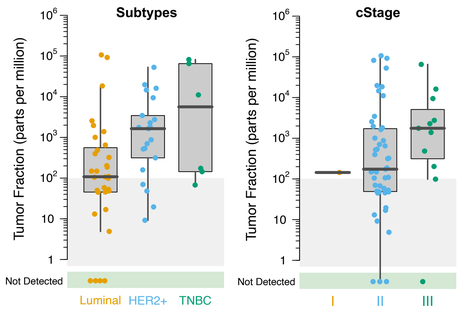


Table 1. Panel sizes by subtype

Panel Size	All	Luminal	HER2+	TNBC
1000	37	18	14	5
450-999	22	14	7	1

Figure 2. Baseline ctDNA levels across subtypes and clinical stage

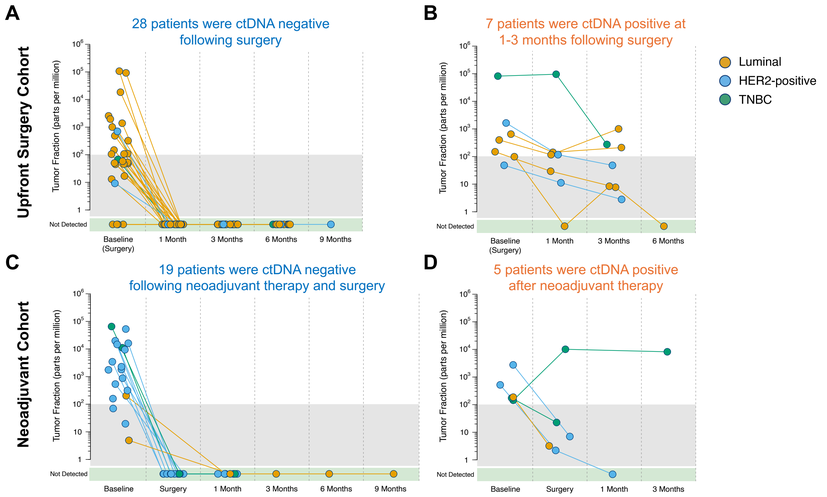


The assay showed 93.2% baseline sensitivity (55/59), with 25.4% (15/59) detected at an ultra-sensitive level below 100 parts per million.

Sensitivity by subtype was luminal 87.5% (28/32), HER2-positive 100% (21/21), and TNBC 100% (6/6), with ultra-sensitive detection in 35.7% (10/28), 19.0% (4/21), and 16.7% (1/6), respectively.

Figure 3. MRD results following treatment identify a set of patients at higher risk

A) ctDNA levels in patients who underwent up-front surgery and were ctDNA-negative at follow-up. B) ctDNA levels in patients who underwent up-front surgery and were ctDNA-positive at 1- or 3-Months following surgery. C) ctDNA levels in patients who received neoadjuvant chemotherapy and became ctDNA-negative as a result. D) ctDNA levels in patients who remained ctDNA-positive following NAC.



ctDNA positivity was 13.9% (6/43) at 1-month post-surgery, including 2 cases detected at ultra-sensitive levels. At 3 months, positivity increased to 21.6% (8/37), with 4 in the ultrasensitive range.

Post-NAC ctDNA results were available for 15 patients; 13 achieved pCR. All 10 ctDNA-negative patients reached pCR, and 3 patients with low-level positivity also achieved pCR. The 2 patients with residual disease were ctDNA-positive. All 6 ctDNA-positive cases at 1-Month remained positive at 3-Months.

Conclusions

- The WGS-based personalized ctDNA assay achieved ultra-sensitive ctDNA detection (<100 parts per million) across breast cancer subtypes.
- Additional validation with extended follow-up and an expanded cohort is necessary to confirm these promising initial findings.

Acknowledgements

- We would like to thank all the patients and their families/caregivers for their participation as well as all the investigators, research coordinators, and site staff for their contribution.
- This study was sponsored by SCRUM-Japan and carried out in collaboration with Myriad Genetics.