Molecular Residual Disease Detection Using Whole-genome Sequencing-based ctDNA assay for Resectable Colorectal Cancer in the MONSTAR-SCREEN-3 Project

AN: 187
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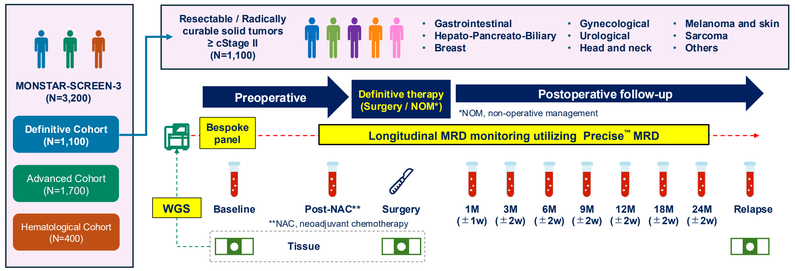
Background

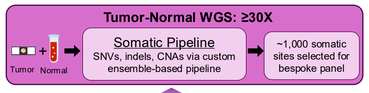
- Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for detecting molecular residual disease (MRD) and is increasingly integrated into both clinical practice and translational research in colorectal cancer.
- However, whole-exome sequencing (WES)-based approaches may lack sufficient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

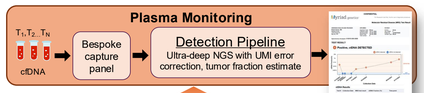
Methods

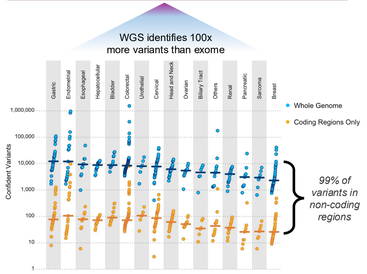
- MONSTAR-SCREEN-3 is a prospective, multicenter study enrolling 1,100 patients with solid tumors receiving curative-intent therapy in the definitive cohort.
- Serial plasma samples are collected at baseline, after neoadjuvant chemotherapy (if applicable), 1-month post-surgery, quarterly during the first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







Analytical performance of Precise MRD

	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: 03 Dec 2025

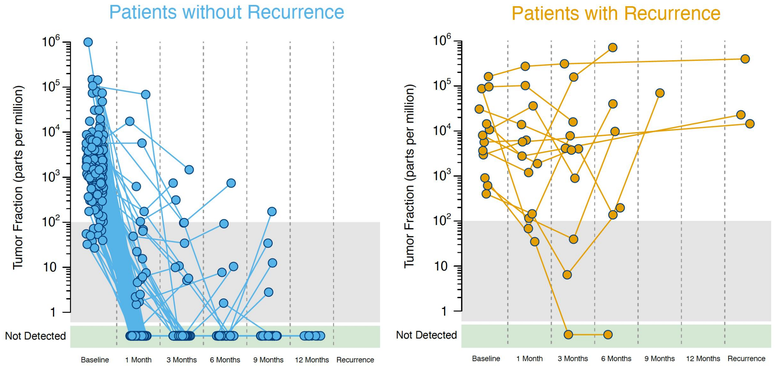
184 patients with CRC were enrolled in MONSTAR-SCREEN-3 "Definitive Cohort"
↓
178 patients received upfront surgery
↓
160 patients with Baseline ctDNA assessment*
↓
154 patients with Post-1M ctDNA assessment
↓
143 patients with Post-3M ctDNA assessment
↓
109 patients with ≥Post-6M ctDNA assessment

Baseline characteristics		n=160, n (%)
Age, median (range), years		64 (36－85)
Gender	Male	81 (51%)
	Female	79 (49%)
Primary tumor location	Cecum	13 (8%)
	Ascending	29 (18%)
	Transverse	12 (8%)
	Descending	7 (4%)
	Sigmoid	54 (34%)
	Rectosigmoid	24 (15%)
	Rectal	17 (11%)
	NE	4 (3%)
pT	T1	1 (1%)
	T2	16 (10%)
	T3	106 (66%)
	T4	37 (23%)
pN	N0	80 (50%)
	N1	53 (33%)
	N2	27 (17%)
pStage	I	14 (9%)
	II	67 (42%)
	III	76 (47%)
	IV	3 (2%)
Adjuvant chemotherapy	Performed	87 (54%)
	Not performed	62 (39%)
	NE	11 (7%)

NE, Not evaluated

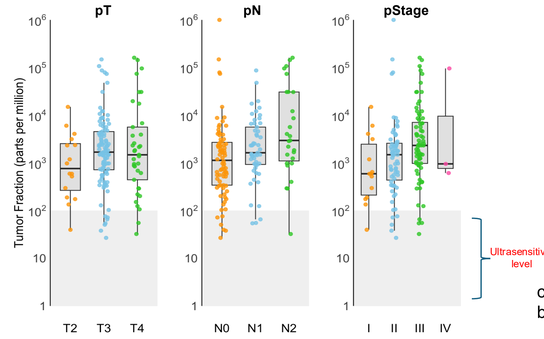
*Personalized ctDNA panels were successfully constructed for all patients except for one.

Figure 1. Dynamics of ctDNA from baseline time point



ctDNA positivity was 21% (32 / 154) at 1-month post-surgery, including 15 patients detected at ultra-sensitive levels. At 3 months, positivity was14 % (20 / 143), with 9 in the ultrasensitive range.

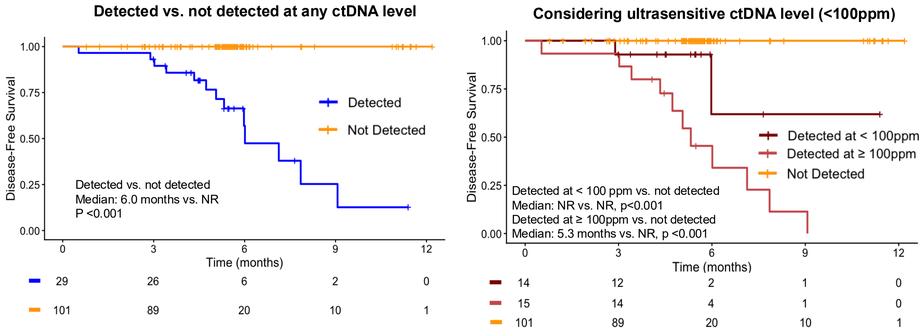
Figure 2. Baseline ctDNA levels across pathological stage



Factor		Ultrasensitive detection
pT	2	1 / 16 (6%)
	3	7 / 106 (7%)
	4	2 / 37 (5%)
pN	0	6 / 80 (8%)
	1	3 / 53 (6%)
	2	1 / 27 (4%)
pStage	I	1 / 14 (7%)
	II	5 / 67 (8%)
	III	4 / 76 (5%)
	IV	0 / 3 (0%)

ctDNA was detected in 100% of patients at baseline regardless of pathological stage.

Figure 3. Disease-free survival by ctDNA detection at post 1 month from surgery*



WGS-based MRD assay demonstrated outstanding sensitivity with perfect detection rates: 100% (13/13) at any ctDNA levels. Specificity was also remarkably high at 86% (101/117) at any ctDNA levels.
* Survival analysis was performed on patients with available surgical date and outcome information.

Conclusions

- A WGS-based MRD assay successfully identified patients at high risk of future recurrence.
- These findings support the potential clinical utility of this assay, though longer follow-up is needed to fully establish its role in colorectal cancer management.

Acknowledgements

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