Prognostic Impact of MRD Positivity at Ultra-sensitive ctDNA Levels Using a WGS-based Personalized Assay: A Pan-Cancer Analysis from MONSTAR-SCREEN-3

Tadayoshi Hashimoto[1,2], Shin Kobayashi[3], Eiji Oki[4], Hiroji Iwata[5], Hidemichi Watari[6], Takahiro Kinoshita[7], Norio Nonomura[8], Naoto Gotohda[3], Kazuto Matsuura[9], Takeo Fujita[10], Shintaro Iwata[11], Kenjiro Namikawa[12], Shingo Sakashita[13], Takao Fujisawa[1,14], Yoshiaki Nakamura[1], Hideaki Bando[1,2], Jeff Jasper[15], Katherine Johansen Taber[15], Dale Muzzey[15], and Takayuki Yoshino[2]

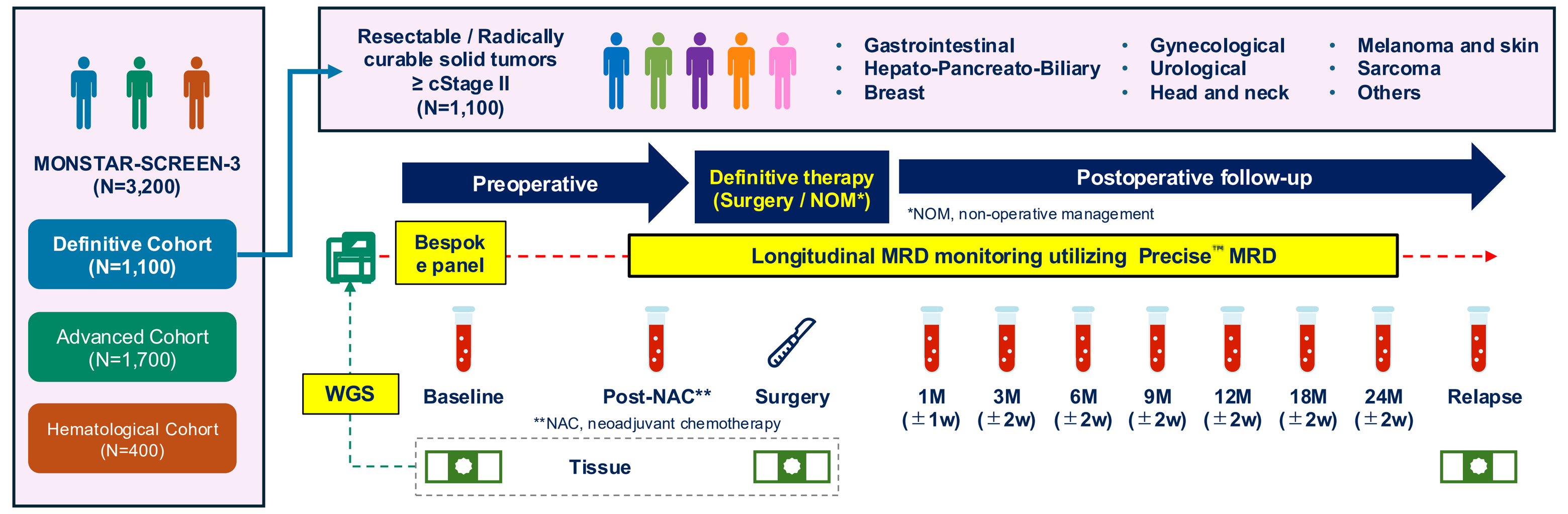
11. Translational Research Support Office, National Cancer Center Hospital East, Japan; 2. Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Japan; 3. Department of Hepatobiliary and Pancreatic Surgery, National Cancer Center Hospital East, Japan; 4. Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Japan; 5. Department of Advanced Clinical Research and Development, Nagoya City University, Graduate School of Medical Sciences, Japan; 6. Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine, Japan; 7. Department of Gastric Surgery, National Cancer Center Hospital East, Japan; 8. Department of Urology, Osaka University Graduate School of Medicine, Japan; 9. Department of Head and Neck Surgery, National Cancer Center Hospital East, Japan; 10. Division of Esophageal Surgery, National Cancer Center Hospital East, Japan; 11. Department of Musculoskeletal Oncology and Rehabilitation Medicine, National Cancer Center Hospital, Japan 12. Department of Dermatologic Oncology, National Cancer Center Hospital, Japan; 13. Division of Pathology, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center, Japan; 14. Department of Head and Neck Medical Oncology, National Cancer Center Hospital East, Japan; 15. Myriad Genetics, Inc., Salt Lake City, UT

Background

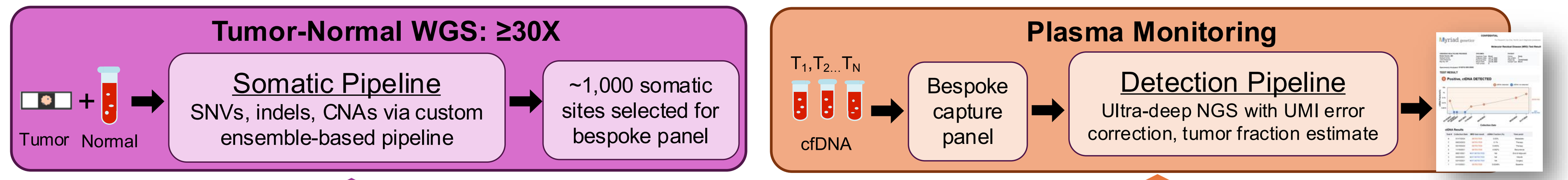
- While circulating tumor DNA (ctDNA) demonstrates promise as a molecular residual disease (MRD) biomarker, its clinical implementation has been primarily limited to tumors with favorable ctDNA shedding characteristics.
- The MONSTAR-SCREEN-3 evaluates a whole-genome sequencing (WGS)-based MRD assay to assess MRD positivity at ultra-sensitive level beyond conventional WES-based MRD, including traditionally low-shedding tumors.

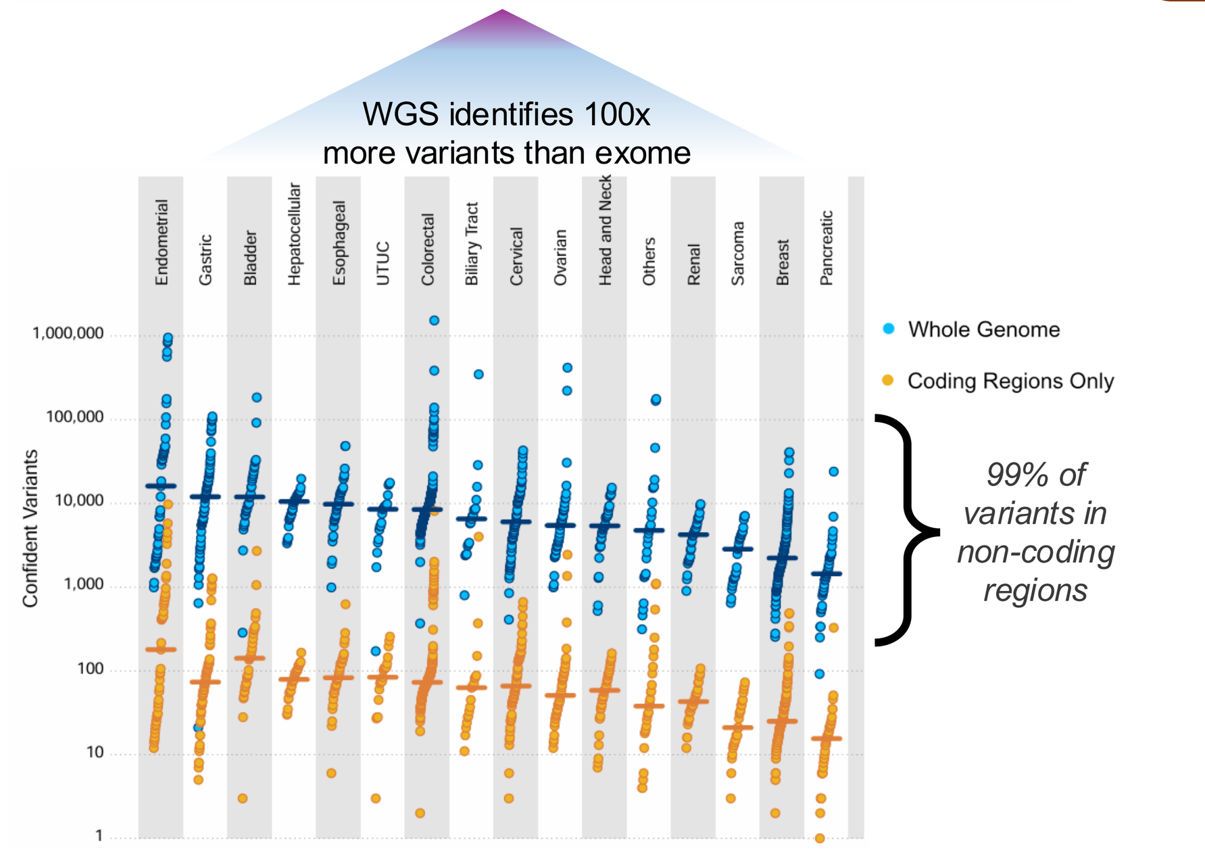
Methods

- MONSTAR-SCREEN-3 is a prospective multicenter study targeting over 1,100 patients with solid tumors undergoing curative-intent treatment. Serial plasma samples were collected at baseline, post-neoadjuvant treatment (NAT) (when applicable), 1-month (1M) post-surgery, every 3 months in year 1, and every 6 months thereafter up to 2 years. Assay performance was evaluated across multiple cancer types for ctDNA detection and recurrence monitoring.



- Personalized panels were constructed using Precise MRD (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

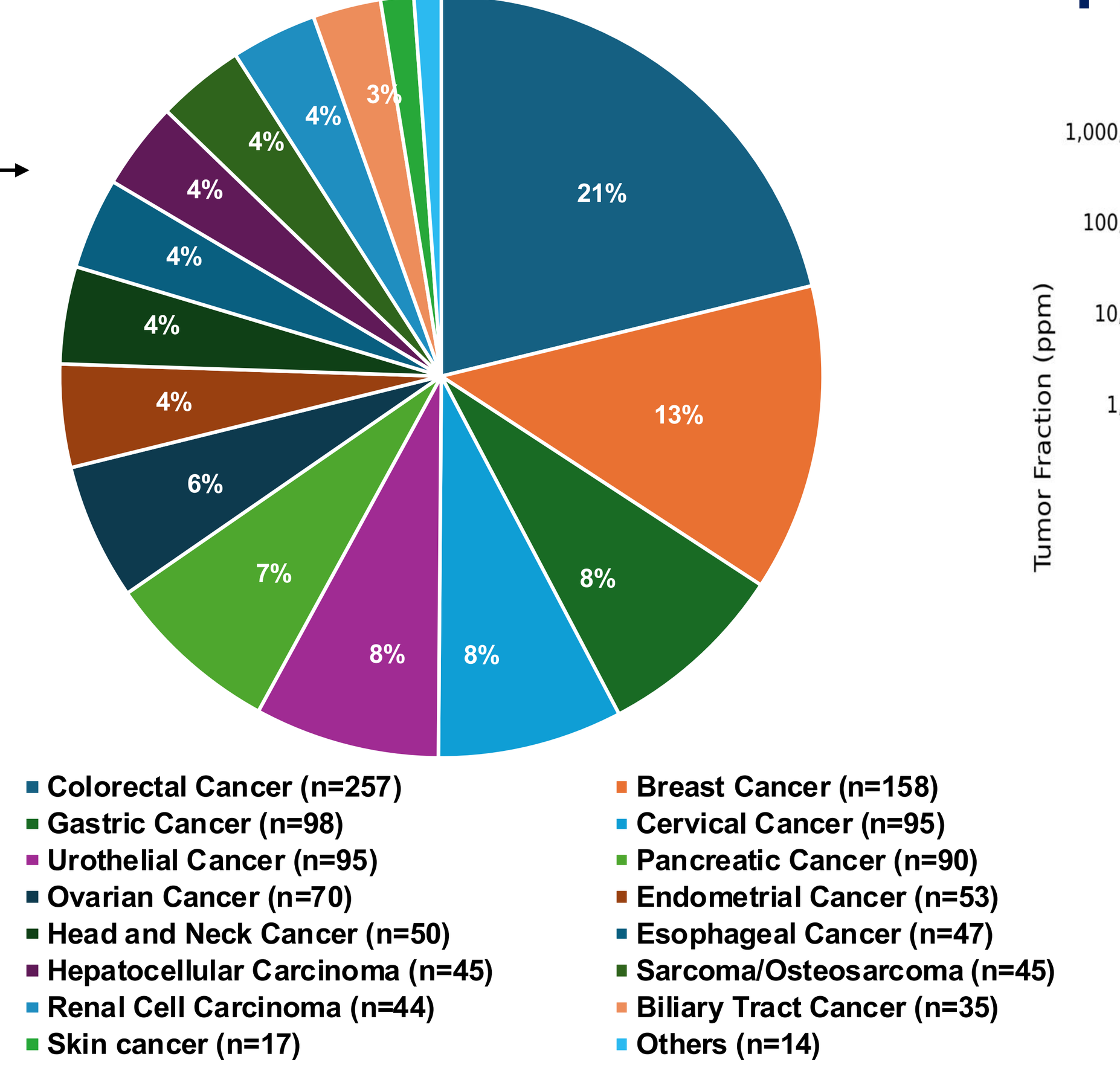
Fig 1. Consort Diagram

1,213 pts enrolled as of March 2026

→ 3,812 MRD results from 938 pts were reported as of March 2026

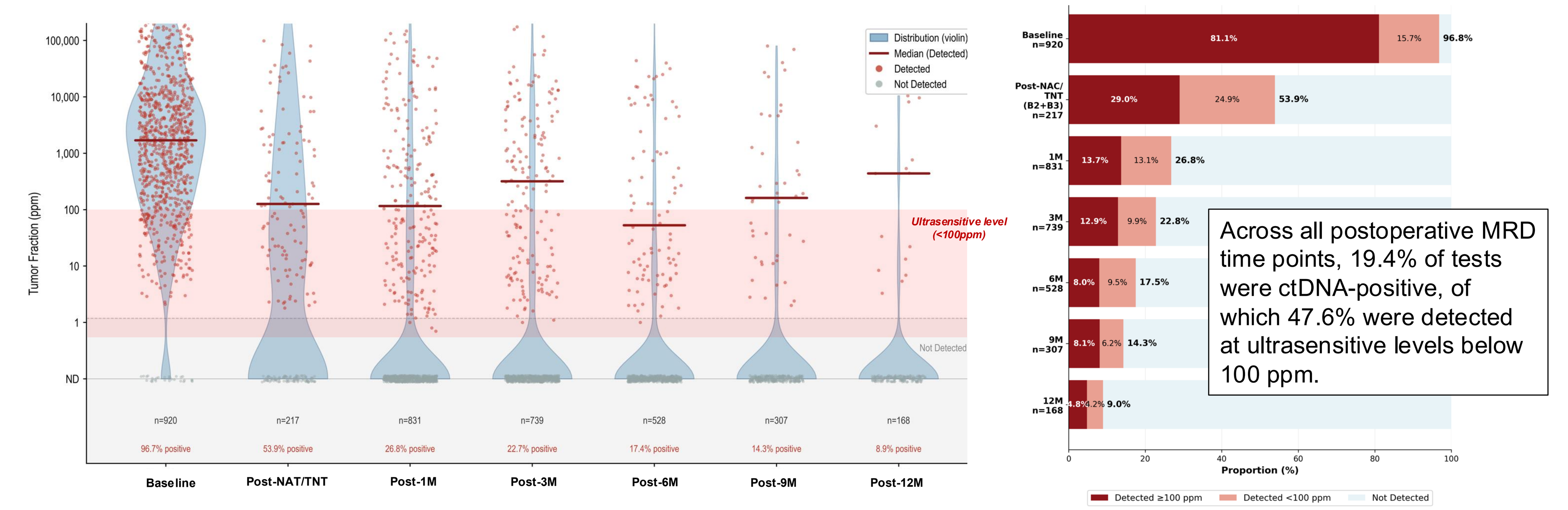
→ 2,789 MRD reports from B1 cohort* | 1,023 MRD reports from B2/B3 cohort**

→ DFS analysis in 659 patients enrolled as of September 2025 with survival data available



*B1: Upfront-surgery, **B2: Neoadjuvant-treatment (NAT), B3: Total-neoadjuvant treatment (TNT) for non-operative management

Fig 2. ctDNA positivity and tumor fraction levels across timepoints



Across all postoperative MRD time points, 19.4% of tests were ctDNA-positive, of which 47.6% were detected at ultrasensitive levels below 100 ppm.

- 96.7% (890/920) ctDNA positivity at baseline, with 16.2% (144/890) detected at ultrasensitive levels.

Fig 3. ctDNA dynamics stratified by recurrence status

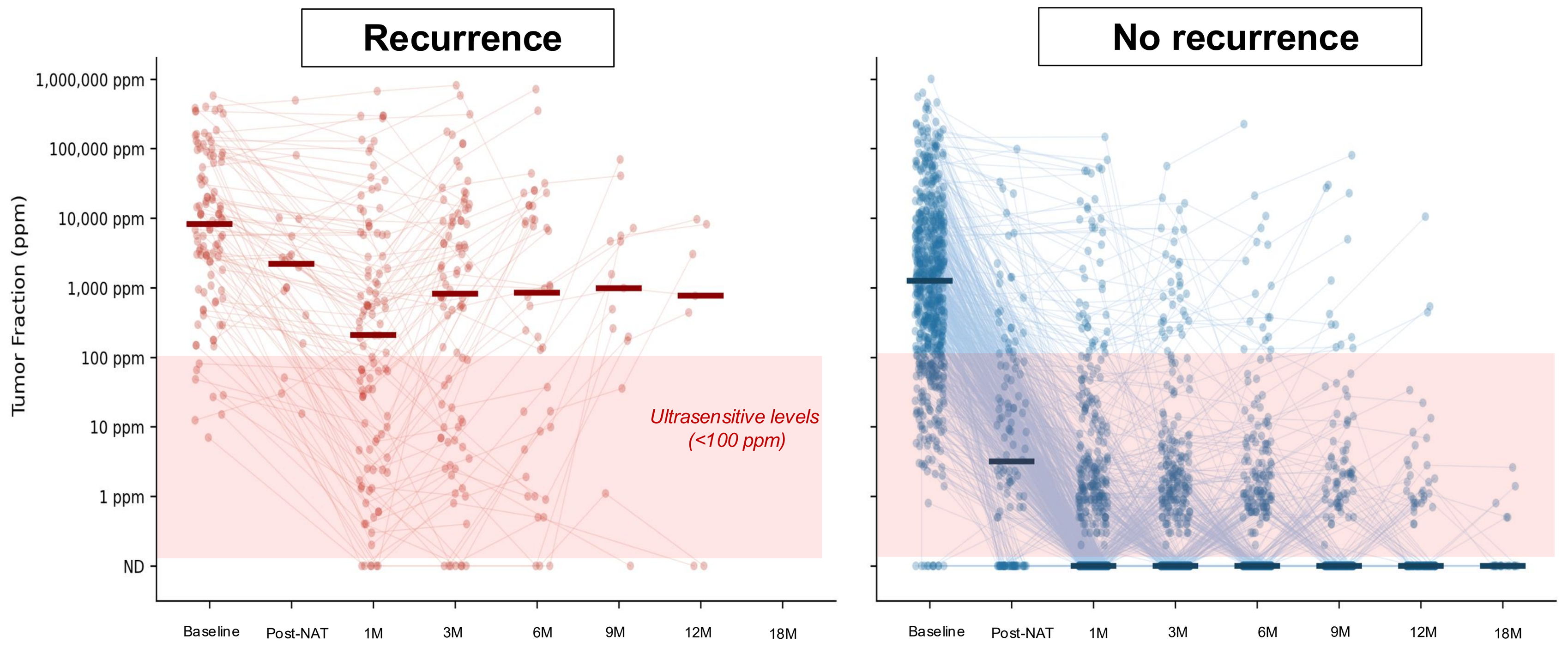
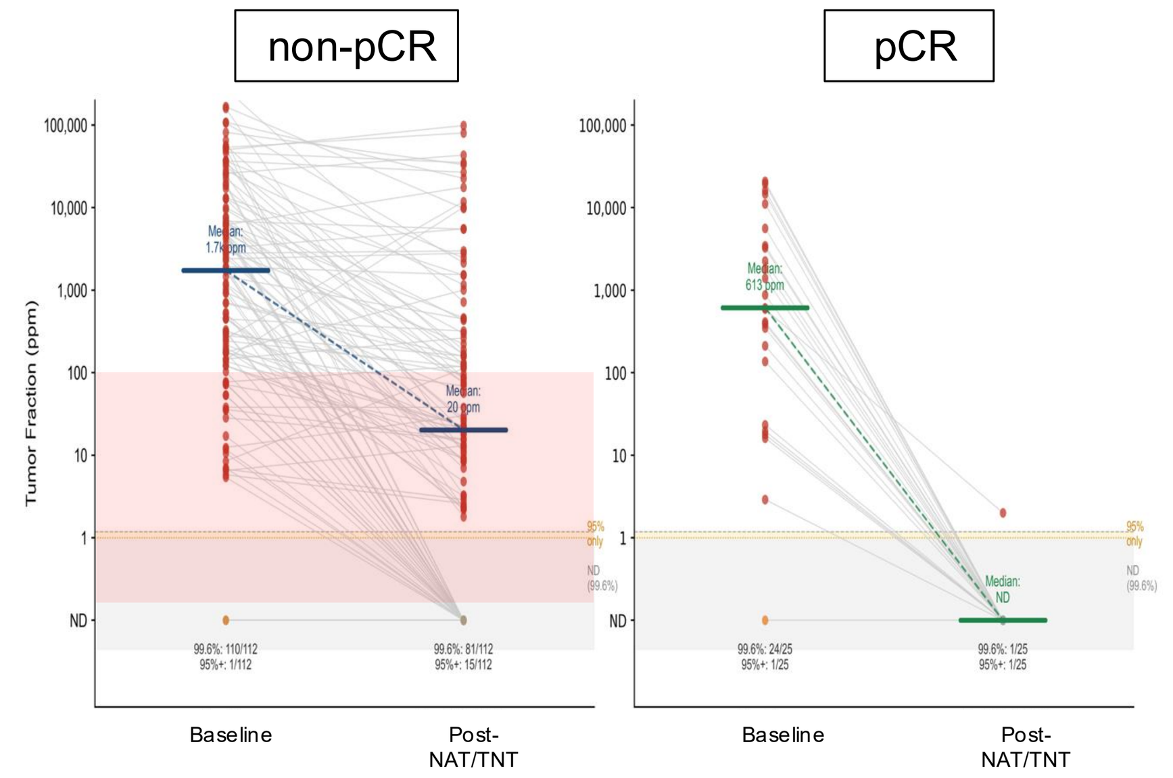


Fig 4. Post-NAT ctDNA status and treatment response (n=137)

pCR, pathological complete response



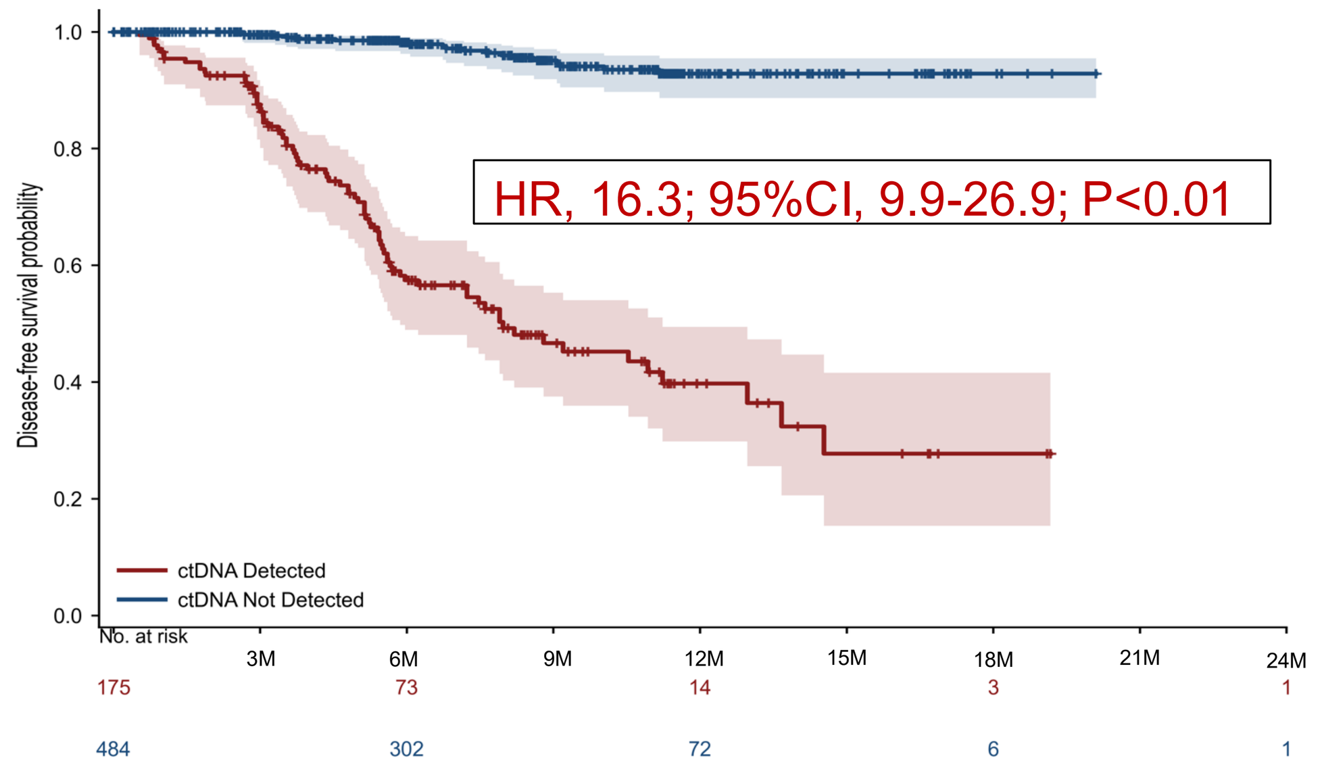
Threshold	Post-NAT/TNT ctDNA	pCR	non-pCR	Total
99.615% specificity	Positive	1	81	82
	Negative	24	31	55
95% specificity	Positive	1	96	97
	Negative	24	16	40
	Total	25	112	137

Using the 99.615% specificity threshold, post-NAT MRD status demonstrated a sensitivity of 72.3% (81/112) and a specificity of 96.0% (24/25) for predicting pCR (P<0.01).

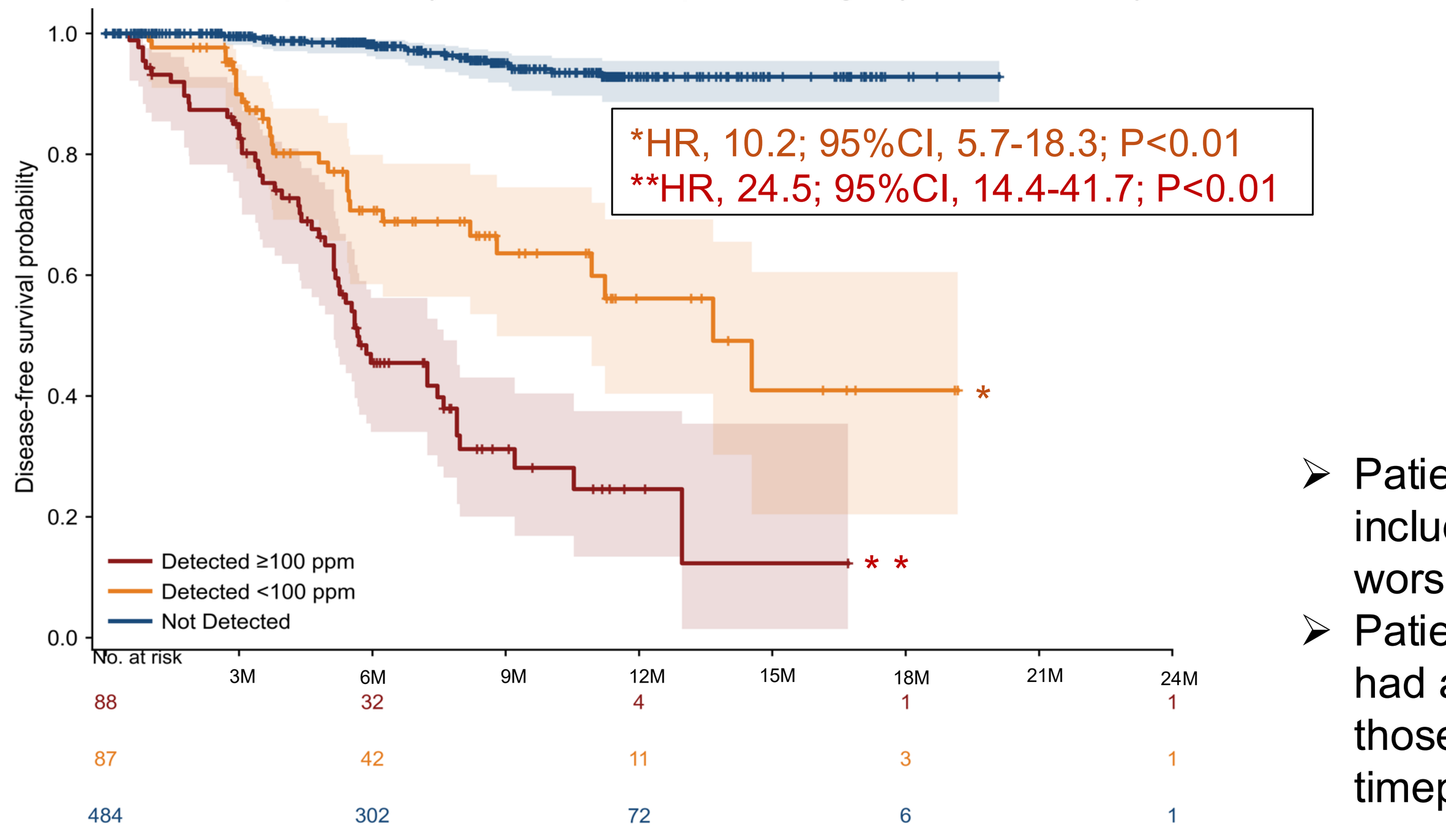
*95% specificity: 85.7% (96/112) sensitivity for predicting pCR

Figure 5. Disease-free survival

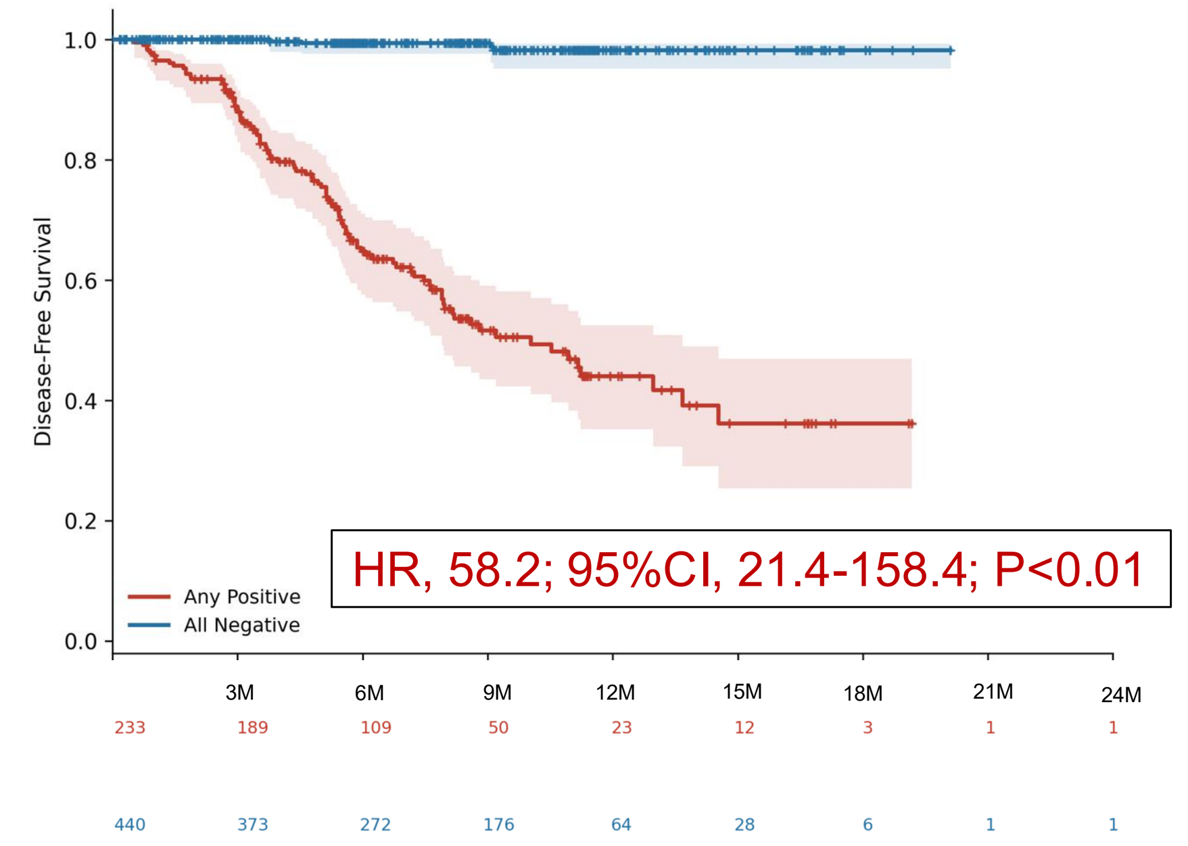
- MRD positivity at 1-month post surgery



- MRD positivity at 1-month post surgery stratified by tumor fraction



- MRD Positivity at any post-operative timepoint



- Patients who were ctDNA-positive at 1-month post-surgery, including at ultrasensitive levels, exhibited significantly worse DFS compared to ctDNA-negative.
- Patients with ctDNA positivity at any timepoint post-surgery had a significantly higher risk of recurrence compared to those who remained ctDNA-negative at all post-operative timepoints.

Conclusions

- The WGS-based MRD assay showed high baseline sensitivity and **robust ultrasensitive ctDNA detection** across multiple cancer types.
- Post-NAT/TNT ctDNA status may serve as a **useful predictor of pathological complete response.**
- MRD positivity at 1-month post surgery, including at ultrasensitive levels, is **highly prognostic for recurrence risk.**

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.

Presented at ASCO Annual Symposium (ASCO 2026). May 28th – June 3rd, 2026. E-mail: tadhashi@east.ncc.go.jp