Whole-Genome Sequencing-Based Ultra-sensitive ctDNA Molecular Residual Disease Assessment in Resectable Gastric Cancer: Results from MONSTAR-SCREEN-3

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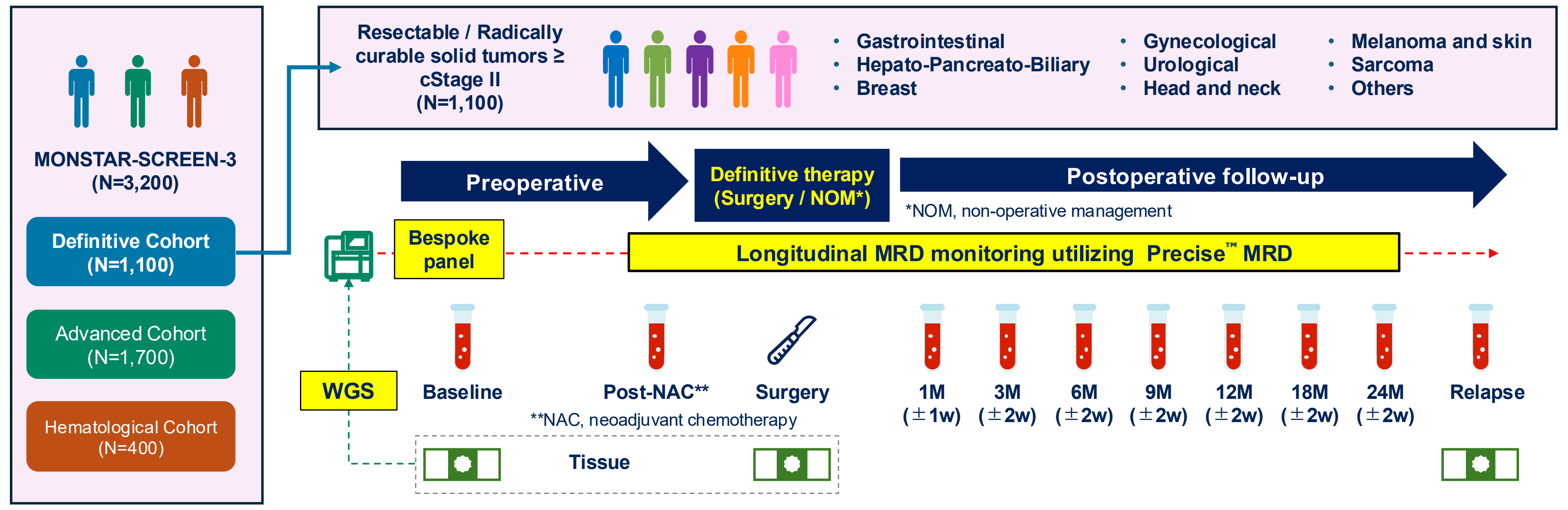
Background

- ☐ Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for post-surgical molecular residual disease (MRD) detection; however, its clinical utility in gastric cancer remains poorly defined.
- ☐ Gastric cancer is characterized by a high propensity for peritoneal recurrence, which may be associated with low levels of ctDNA shedding into the bloodstream. Therefore, highly sensitive ctDNA assays are likely required to enable reliable MRD detection in this disease setting.
- ☐ In gastroesophageal junction cancer, patients who achieve a clinical complete response after total neoadjuvant therapy may potentially be candidates for nonoperative management, an approach currently being evaluated in the EPOC2301 trial (Shitara K. ASCO-GI2026; TPS464).
- ☐ The MONSTAR-SCREEN-3 evaluates the clinical performance of a whole-genome sequencing (WGS)–based MRD assay in a pan-cancer cohort, including patients with gastric cancer.

Methods

- ☐ MONSTAR-SCREEN-3 is a prospective, multicenter study enrolling 1,100 patients receiving curative-intent therapy in the definitive cohort. Serial plasma samples were 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.



MONSTAR-SCREEN-3 (N=3,200)

- Definitive Cohort (N=1,100)
- Advanced Cohort (N=1,700)
- Hematological Cohort (N=400)

Resectable / Radically curable solid tumors ≥ cStage II (N=1,100)

- Gastrointestinal
- Hepato-Pancreato-Biliary
- Breast
- Gynecological
- Urological
- Head and neck
- Melanoma and skin
- Sarcoma
- Others

Preoperative → Definitive therapy (Surgery / NOM*) → Postoperative follow-up

*NOM, non-operative management

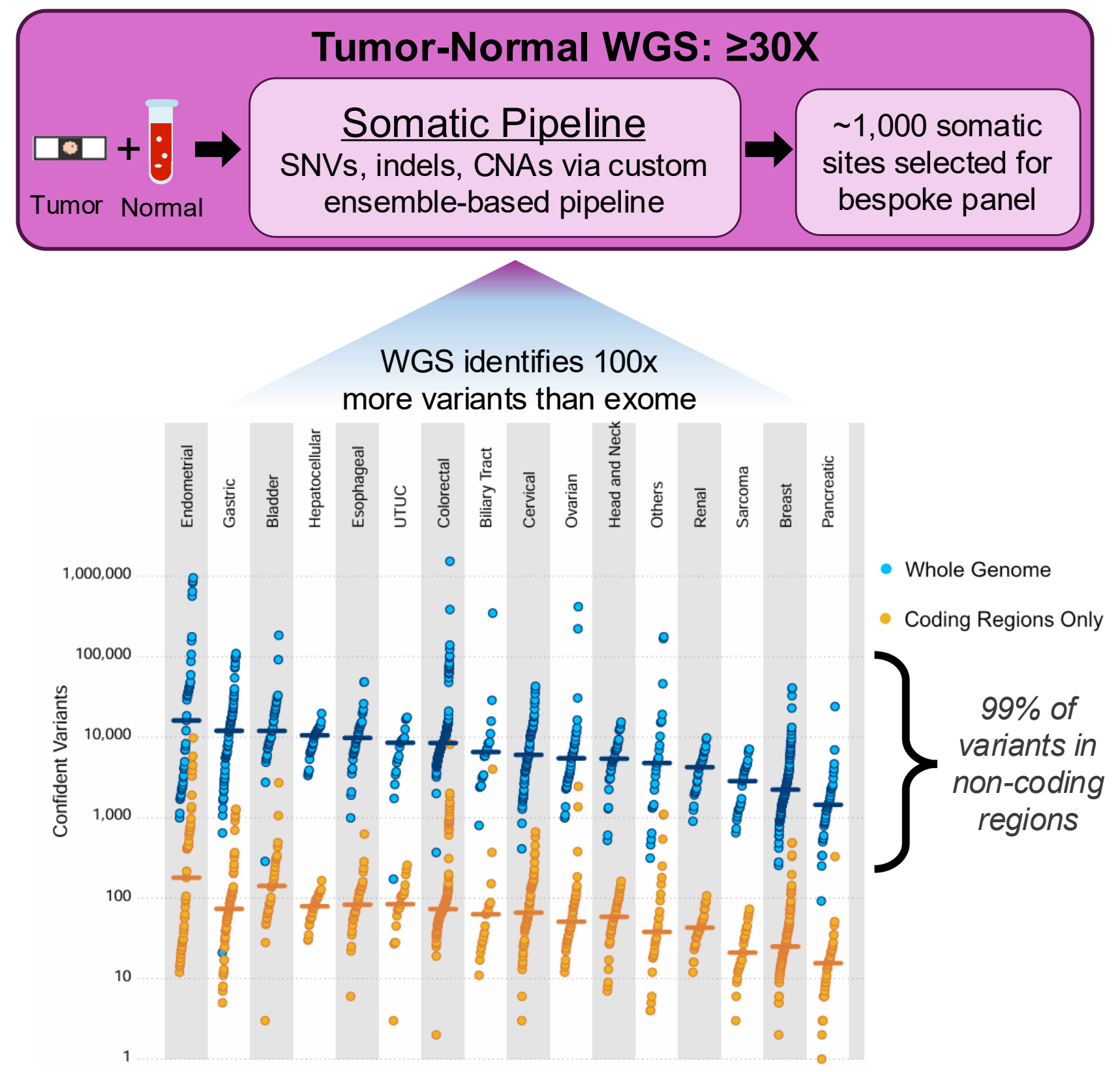
WGS → Bespoke panel → Longitudinal MRD monitoring utilizing Precise™ MRD

Baseline · Post-NAC** · Surgery · 1M (±1w) · 3M (±2w) · 6M (±2w) · 9M (±2w) · 12M (±2w) · 18M (±2w) · 24M (±2w) · Relapse

**NAC, neoadjuvant chemotherapy

Tissue

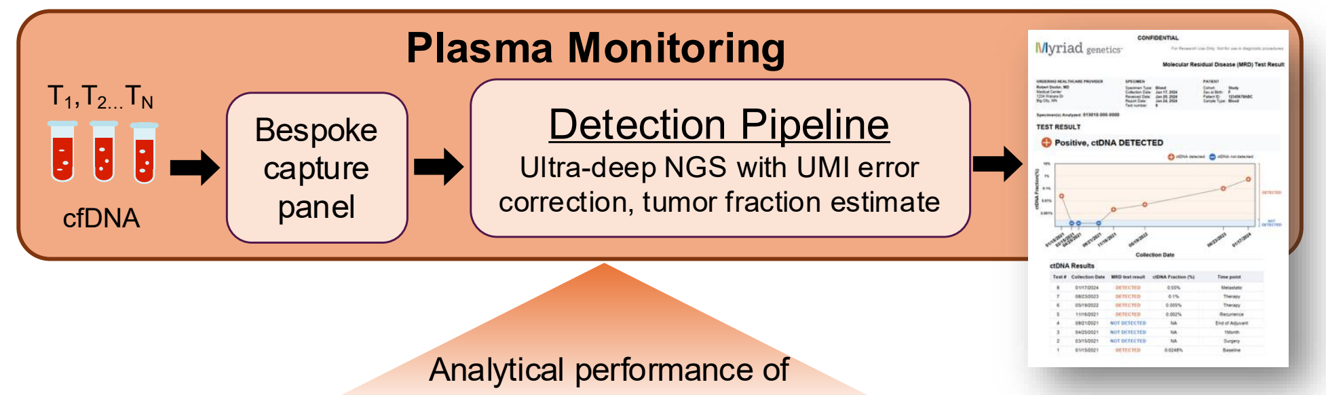
- ☐ Personalized ctDNA panels were generated using a WGS-based tumor-informed platform incorporating up to 1,000 tumor-specific alterations.



Tumor-Normal WGS: ≥30X

Tumor + Normal → **Somatic Pipeline**: SNVs, indels, CNAs via custom ensemble-based pipeline → ~1,000 somatic sites selected for bespoke panel

WGS identifies 100x more variants than exome



Plasma Monitoring

$T_1, T_2 \ldots T_N$ cfDNA → Bespoke capture panel → **Detection Pipeline**: Ultra-deep NGS with UMI error correction, tumor fraction estimate →

Analytical performance of Precise MRD

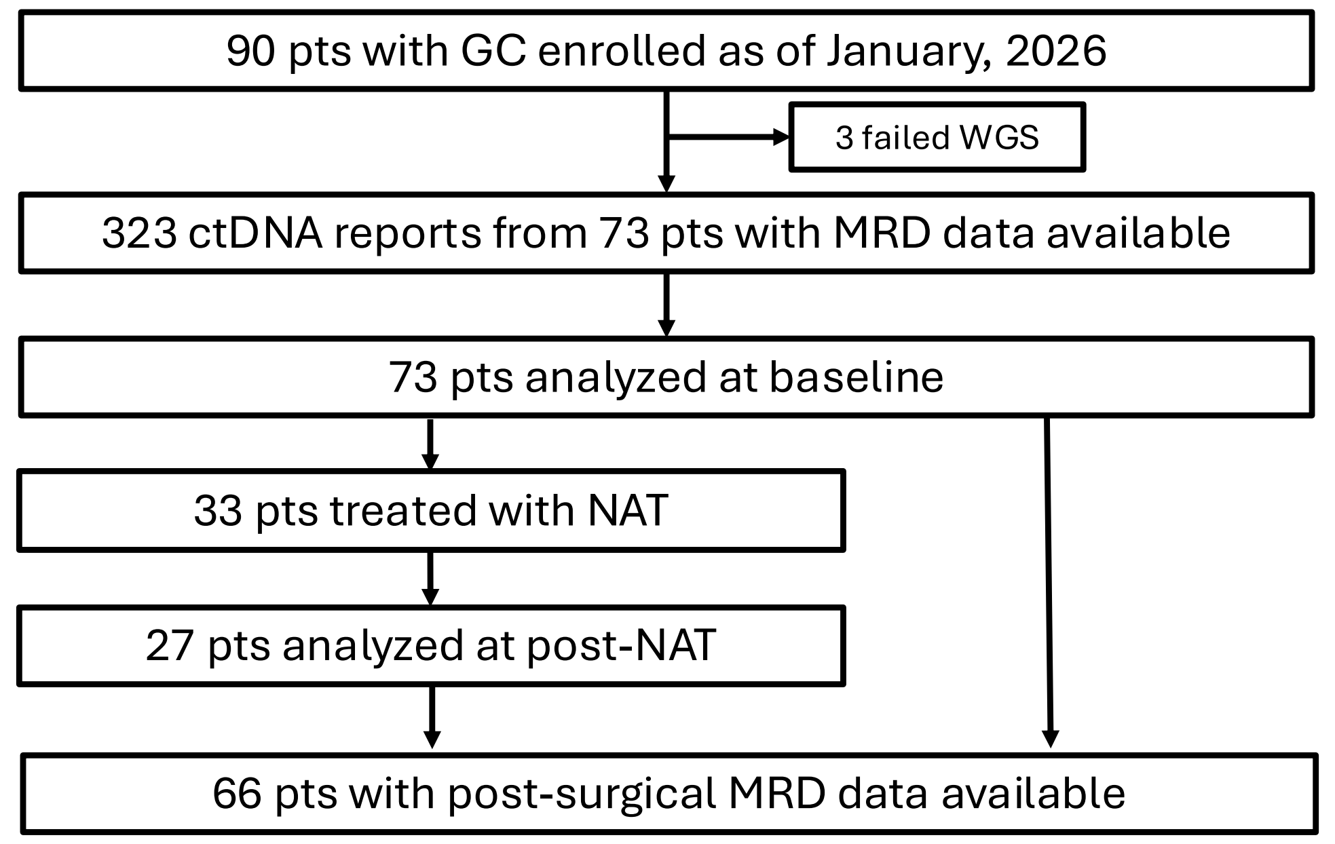
	Limit of Blank (ppm)	Limit of Detection (ppm)
Myriad Precise MRD	0.3	<5
Laboratory A[1]	0.719	3.45
Laboratory B[2]	—	100
Laboratory C[3]	—	80
Laboratory D[4]	—	100
Laboratory E[5]	—	3000

(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

Table 1. Patient characteristics

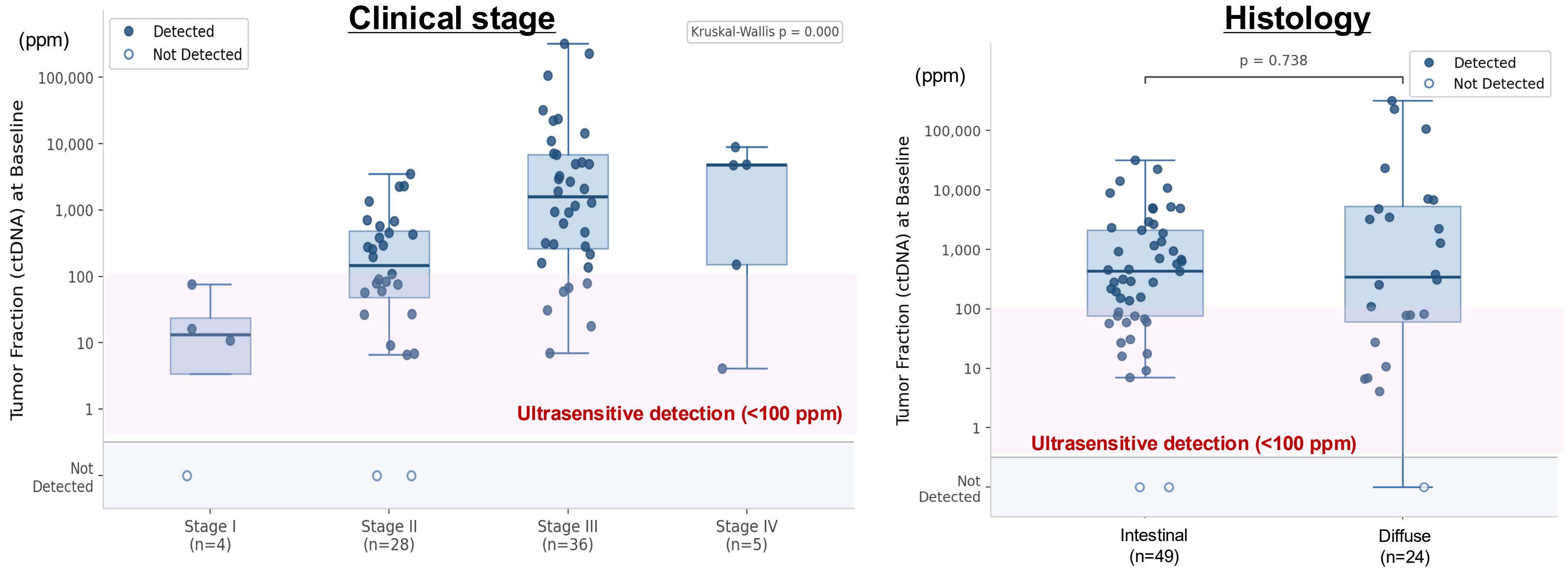


90 pts with GC enrolled as of January, 2026
→ 3 failed WGS
323 ctDNA reports from 73 pts with MRD data available
73 pts analyzed at baseline
33 pts treated with NAT
27 pts analyzed at post-NAT
66 pts with post-surgical MRD data available

Variables	N=73
Age, years, median [range]	70 [30-88]
Sex, n (%), F / M	21 / 52 (29%/71%)
Histology	
Intestinal	49 (67%)
Diffuse	24 (33%)
cStage, n (%)	
Stage I	4 (5%)
Stage II	28 (38%)
Stage III	36 (49%)
Stage IV	5 (7%)
Treatment strategy, n (%)	
Upfront-surgery	40 (55%)
Neoadjuvant treatment (NAT)	33 (45%)
On treatment	6
Surgery performed	24
Non-operative management	3
pStage, n (%)	
≤ Stage II	43 (59%)
≥ Stage III	21 (41%)

Figure 1. Baseline ctDNA tumor fraction

*ppm, parts per million



- ■ 95.9% (70/73) ctDNA positivity at baseline, with 34.3% (24/70) detected at ultrasensitive levels.

Conclusions

- ➢ WGS-based personalized ctDNA assay demonstrated high technical feasibility and baseline detection sensitivity in gastric cancer, with notable ultra-sensitive detection capability.
- ➢ Post-NAT MRD status demonstrated potential as a predictor of NAT treatment response.

Acknowledgements

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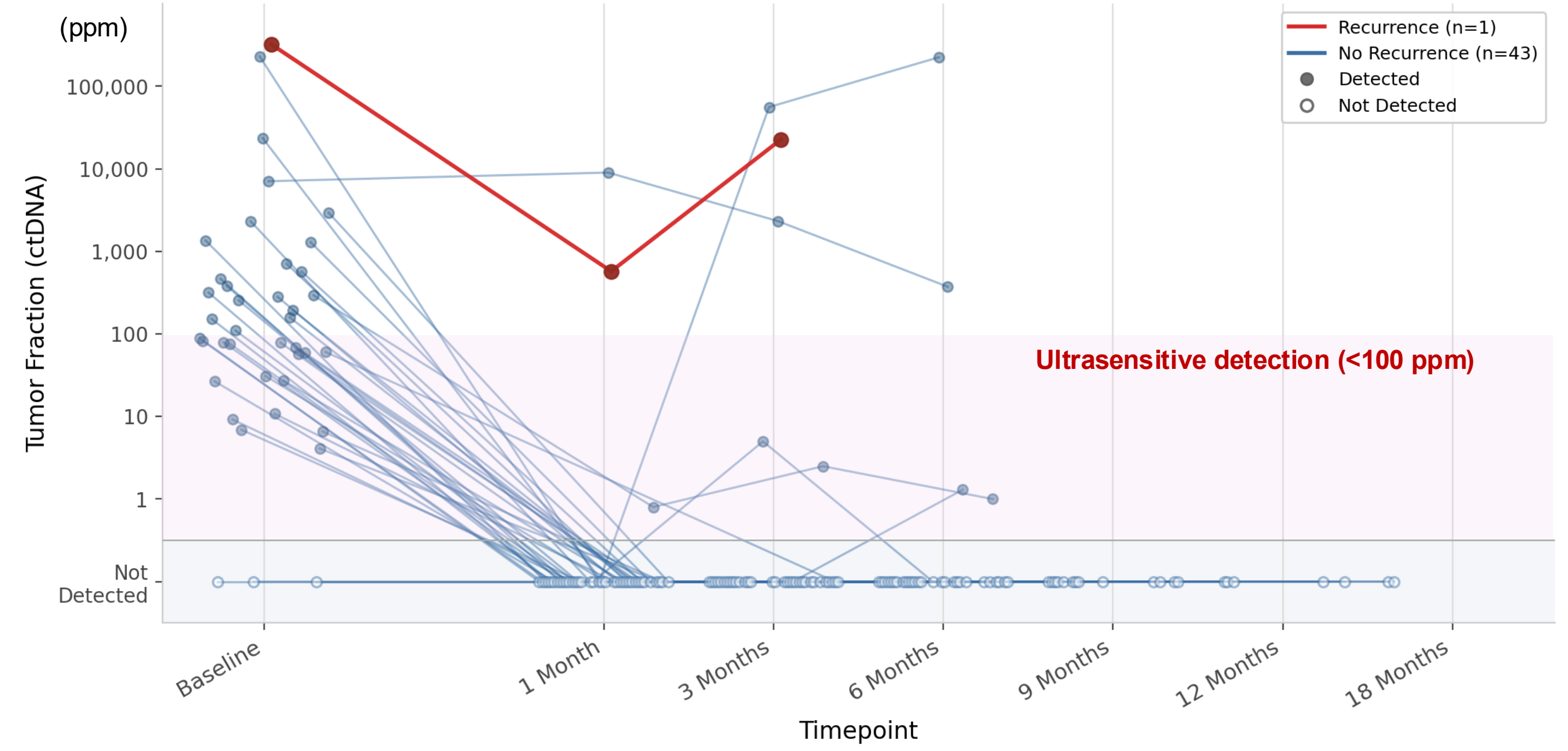
Figure 2. ctDNA dynamics in cohort B1 and B2

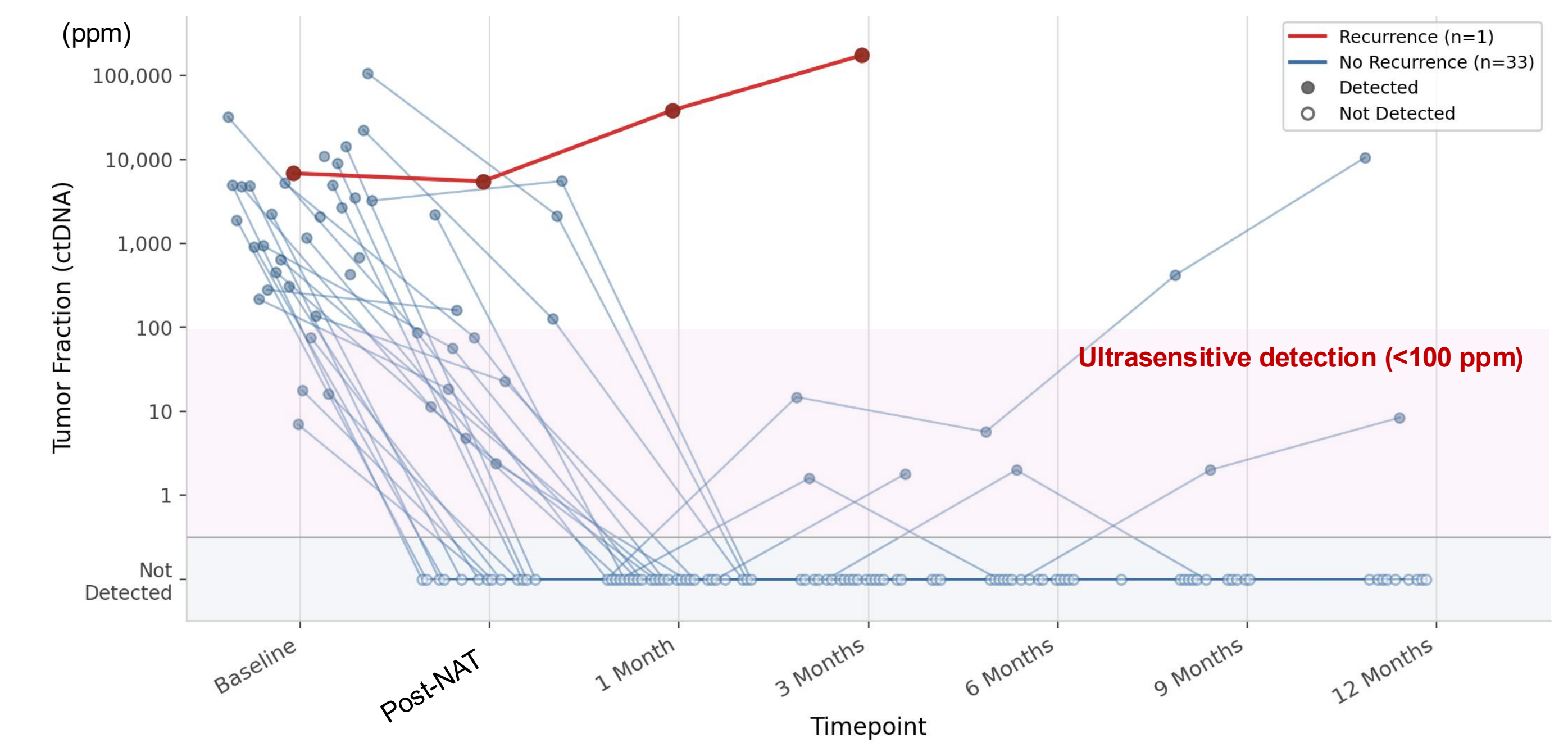
B1: Upfront-surgery



- ➢ 7.7% (3/39) ctDNA positivity at 1-month post-surgery, with 1 detected at ultrasensitive levels.
- ➢ In a patient who developed postoperative LN recurrence, MRD was detected earlier than radiographic imaging, with a lead time of 4.1 months.

B2: Neoadjuvant treatment

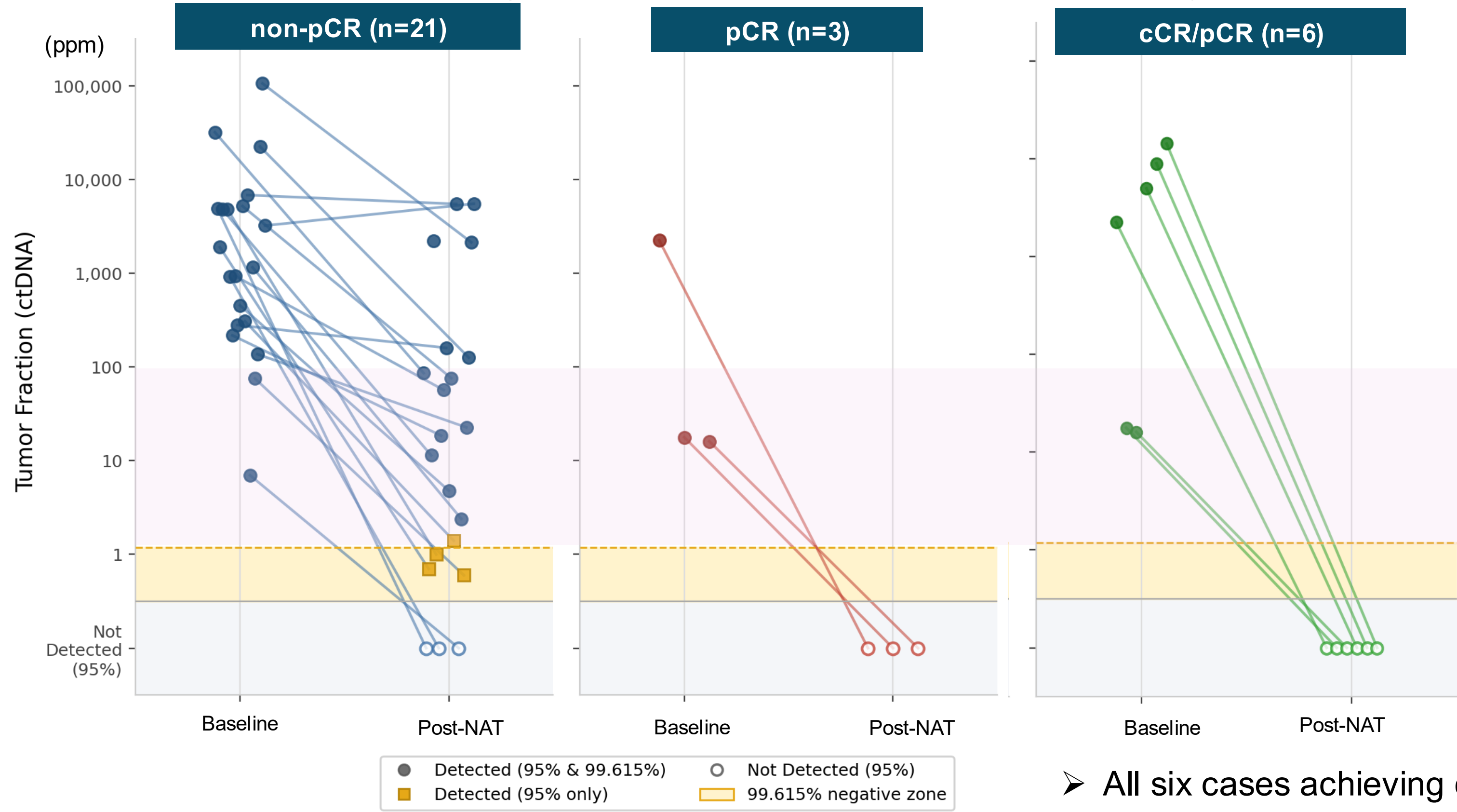
*For patients who underwent TNT and subsequently opted for NOM, the end date of treatment was used as a surgery date when calculating the post-surgery interval.



- ➢ 51.9% (14/27) ctDNA positivity at Post-NAT, with 57.1% detected at ultrasensitive levels.
- ➢ A patient who developed postoperative liver recurrence, MRD was detected earlier than radiographic imaging, with a lead time of 1.9 months.

Figure 3. Relationship between ctDNA dynamics and treatment response

ctDNA status was assessed using two thresholds: one calibrated to a specificity of 99.615% and the other to 95%.



- ➢ <u>99.615% specificity</u>
66.7% (14/21) in non-pCR vs. 0% in pCR;
57.1%(8/14) detected at ultrasensitive levels
- ➢ <u>95% specificity</u>
85.7% (18/21) in non-pCR vs. 0% in pCR;
66.7%(15/18) detected at ultrasensitive levels

- ➢ All six cases achieving cCR/pCR were ctDNA-negative post-NAT

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