Ultra-Sensitive Whole-Genome Sequencing-Based Molecular Residual Disease Detection in Resectable Sarcoma in MONSTAR-SCREEN-3

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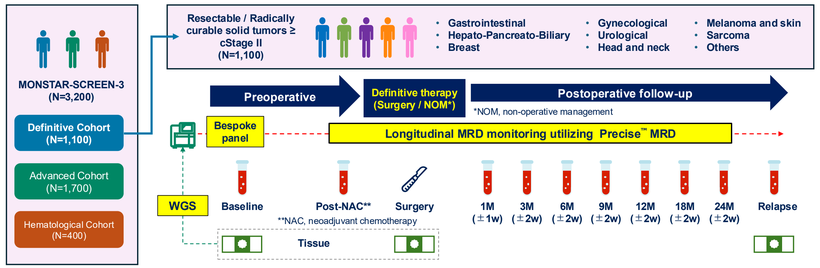
Background

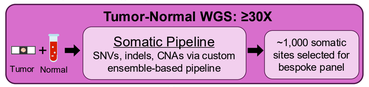
- Circulating tumor DNA (ctDNA)–based molecular residual disease (MRD) detection has shown strong prognostic value in multiple epithelial cancers, but its utility in sarcoma remains poorly defined.
- Sarcomas are highly heterogeneous and often represent low-shedding tumors, limiting the sensitivity of tumor-naive targeted assays. Tumor-informed approaches based on whole-genome sequencing (WGS) can capture patient-specific structural variants and copy-number alterations that are common in sarcoma, potentially enabling more sensitive MRD detection.
- However, systematic and longitudinal evaluation of WGS-based ctDNA MRD in sarcoma patients treated with curative intent is still lacking.
- 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 sarcoma.

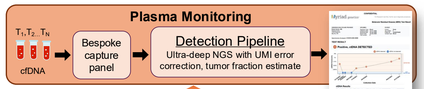
Methods

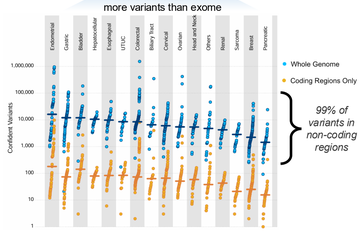
- MONSTAR-SCREEN-3 is a prospective, multicenter study enrolling 1,100 patients receiving curative-intent therapy in the definitive cohort. Serial plasma samples were collected at baseline, after neoadjuvant chemotherapy (if applicable), 1 month post-surgery, quarterly during the first year, and biannually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

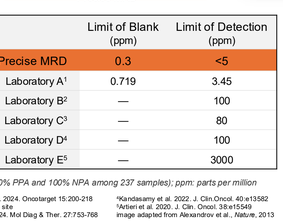


- Personalized ctDNA panels were generated using a WGS-based tumor-informed platform incorporating up to 1,000 tumor-specific alterations.









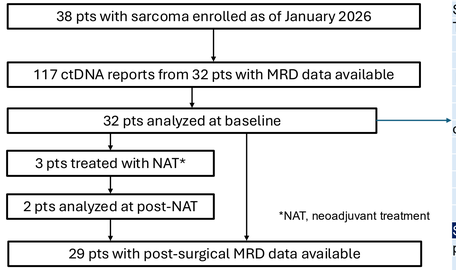
	Limit of Blank (ppm)	Limit of Detection (ppm)
Myriad Precise MRD	0.3	<5
Laboratory A[1]	0.719	3.45
Laboratory B[2]	—	100
Laboratory C[3]	—	80
Laboratory D[4]	—	100
Laboratory E[5]	—	3000

(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



Variables	N=32
Age, years, median [range]	66 [36-87]
Sex, n (%), F / M	19 / 13 (59% / 41%)
Treatment strategy, n (%)	
Upfront-surgery	29 (91%)
Neoadjuvant treatment (NAT)	3 (9%)
Disease status	
Primary	22 (69%)
Recurrent	9 (31%)
cStage, n (%)	
Stage I	7 (22%)
Stage II	4 (13%)
Stage III	18 (56%)
Stage IV	2 (6%)
NA	1 (3%)
Surgery performed	**N=30**
pStage, n (%)	
≤ Stage II	5 (17%)
≥ Stage III	25 (83%)

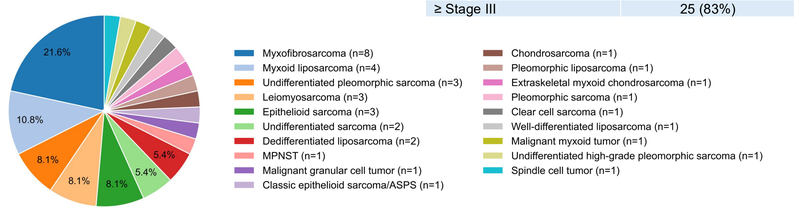
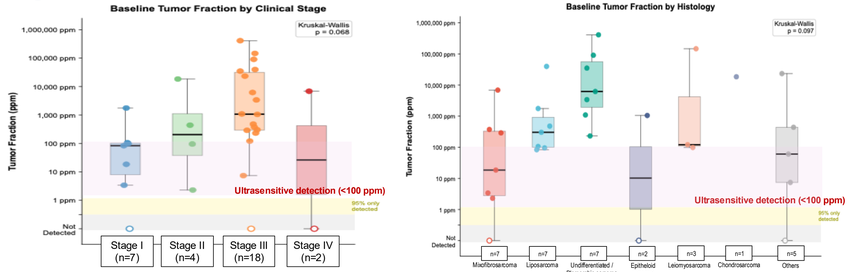
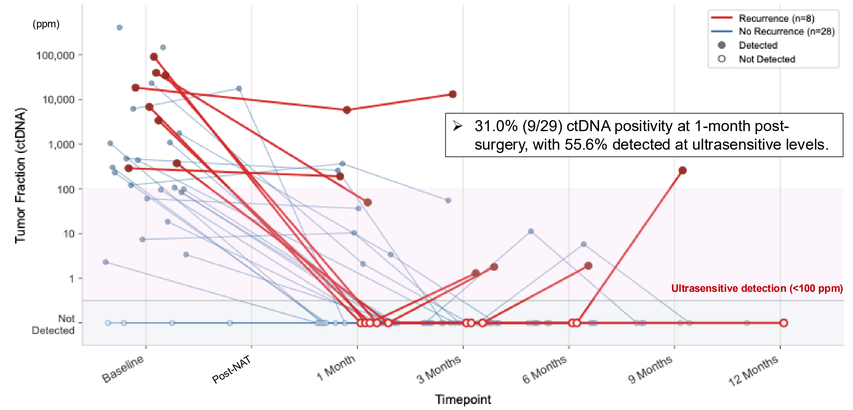


Figure 1. Baseline ctDNA tumor fraction



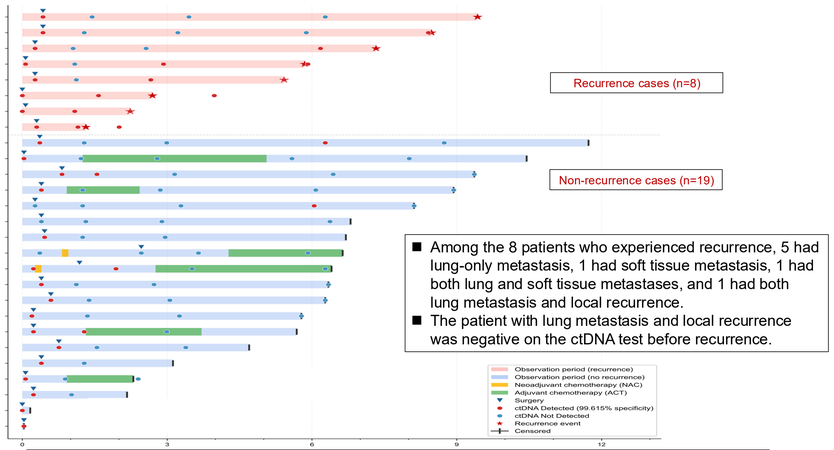
➢ The assay demonstrated 90.6% baseline ctDNA detection (29/32), with 31.0% detected at ultra-sensitive levels, across cStage and histology.

Figure 2. ctDNA dynamics



➢ 31.0% (9/29) ctDNA positivity at 1-month post-surgery, with 55.6% detected at ultrasensitive levels.

Figure 3. Swimmer plot (ctDNA monitoring in patients with resectable sarcoma)



- Among the 8 patients who experienced recurrence, 5 had lung-only metastasis, 1 had soft tissue metastasis, 1 had both lung and soft tissue metastases, and 1 had both lung metastasis and local recurrence.
- The patient with lung metastasis and local recurrence was negative on the ctDNA test before recurrence.

Among eight patients who developed radiographic recurrence, seven patients had MRD detection preceding imaging by median 1.1 months (0.1-3.0).

Conclusions

The WGS-based ctDNA assay demonstrated high technical feasibility in sarcoma, highlighting the potential utility of WGS-based tumor-informed MRD analysis for surveillance and risk stratification in sarcoma.

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