Ultra-sensitive molecular residual disease detection via tumor-informed whole-genome sequencing-based ctDNA assay in resectable urothelial cancer in the MONSTAR-SCREEN-3 project

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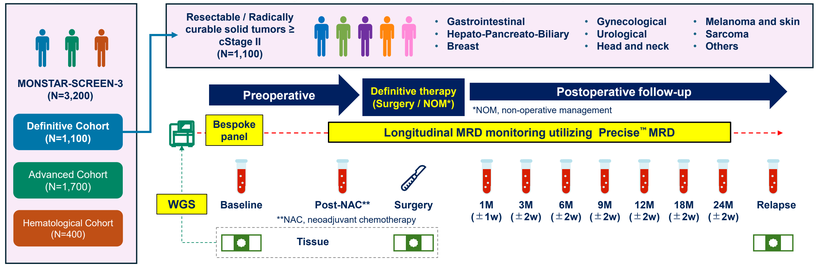
Background

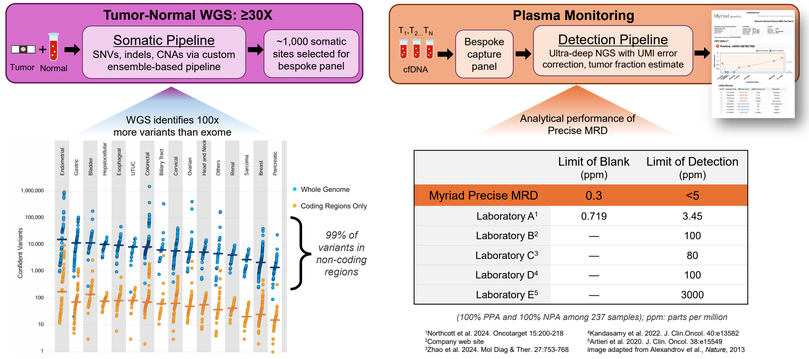
- Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for detecting molecular residual disease (MRD) and is increasingly integrated into both clinical practice and translational research in urothelial cancer.
- However, Conventional methods often lack sensitivity for MRD, particularly in low-shedding tumors, minimal disease burden or dynamics related to tumor location and stage.
- To overcome this limitation, the MONSTAR-SCREEN-3 study is evaluating the utility of a tumor-informed whole-genome sequencing (WGS)-based MRD assay across cancer types.
- Preliminary results from the urothelial cancer cohort, including upper tract urothelial cancer (UTUC) and bladder cancer (BC), were reported.

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.



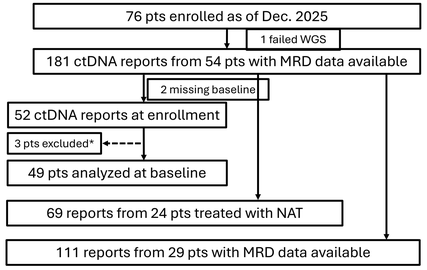
	Limit of Blank (ppm)	Limit of Detection (ppm)
Myriad Precise MRD	0.3	<5
Laboratory A[1]	0.719	3.45
Laboratory B[2]	—	100
Laboratory C[3]	—	80
Laboratory D[4]	—	100
Laboratory E[5]	—	3000

(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

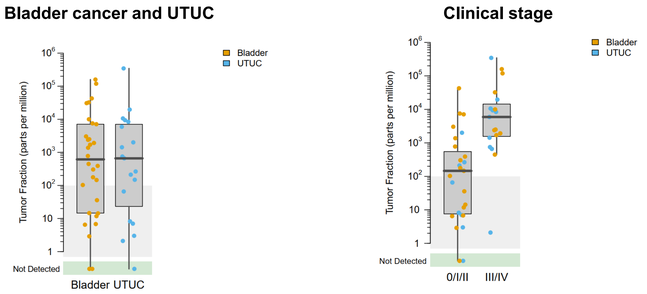
Table 1. Patient characteristics



*Two received TUR-BT; one received TUR-BCG

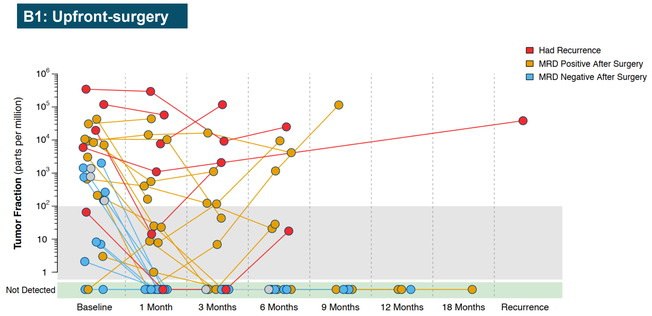
Variables	Bladder cancer N=50	UTUC N=26
Age, years, median [range]	74 [49-90]	78 [57-87]
Sex, n (%)		
Male	36 (72%)	18 (69%)
Female	14 (28%)	8 (31%)
Cohort, n (%)		
B1: Upfront-surgery	15 (30%)	25 (96%)
B2: NAT	35 (70%)	1 (4%)
cStage, n (%)		
≤ Stage II	29 (58%)	13 (50%)
≥ Stage III	15 (30%)	12 (46%)
NA	6 (12%)	1 (4%)
Surgery performed	**N=34**	**N=23**
pStage, n (%)		
≤ Stage II	20 (59%)	12 (52%)
≥ Stage III	12 (35%)	11 (48%)
NA	2 (6%)	0

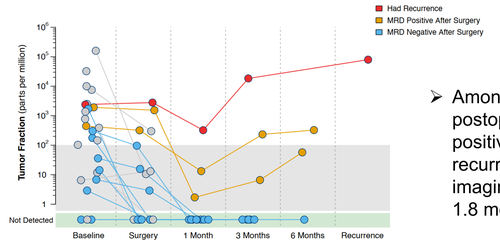
Figure 1. Baseline ctDNA detection



- 93.9% (46/49) ctDNA positivity at baseline, with 26.1% detected at ultrasensitive levels.
- 92.6% (25/27) ctDNA positivity in cStage ≤ II, with 40.0% detected at ultrasensitive levels.

Figure 2. ctDNA dynamics in cohort B1 and B2

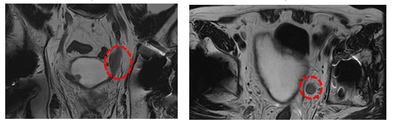




- Among the six patients who developed postoperative recurrence, MRD was positive in all cases and detected recurrence earlier than radiographic imaging, with a median lead time of 1.8 months (range, 0–4.4).

Figure 3. A case report of ureteral cancer patient

- Aged 85 years old, left ureteral tumor
- Clinical diagnosis: cT3N0M0, cStage III

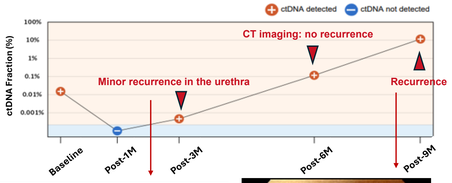


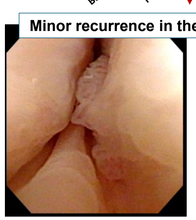
Treated with up-front radical surgery

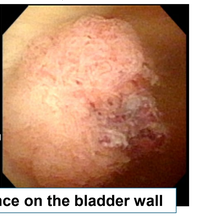
- pT3N0M0, pStage III
- No adjuvant therapy performed

- Post-3M, minor recurrence in the urethra
- Endoscopic R0 resection

- Post-9M, recurrence on the bladder wall







Conclusions

The WGS-based personalized ctDNA assay demonstrated technical feasibility in urothelial cancer, highlighting the critical importance of ultra-sensitive platforms for low-shedding tumors.

Acknowledgements

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