#523

Clinical Validation of Ultra-Sensitive WGS-based MRD Detection in Head and Neck Squamous Cell Carcinoma: Results from MONSTAR-SCREEN-3

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Background

- Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for detecting molecular residual disease (MRD) in solid tumors.
- Our research has demonstrated that the presence or absence of MRD (ctDNA) significantly impacts prognosis in colorectal cancer.
- However, its utility in HPV-negative head and neck squamous cell carcinoma (HNSCC) remains underexplored due to typically low ctDNA levels.
- This study is underway to evaluate the utility of ctDNA created using a WGS-based tumor-informed platform (Myriad Genetics).

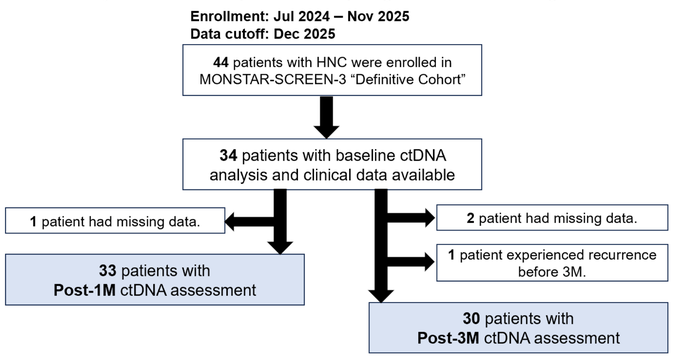
✓ Our ultra-sensitive WGS-based personalized ctDNA assay demonstrated 100% technical success and reliably detected tumor-specific variants in all patients.

✓ Post-operative MRD positivity, particularly at 1 month, was strongly associated with early recurrence and significantly worse disease-free survival (HR 18.9).

✓ These findings highlight the potential of ctDNA-based MRD assessment as a powerful tool for recurrence surveillance in resectable HNSCC.

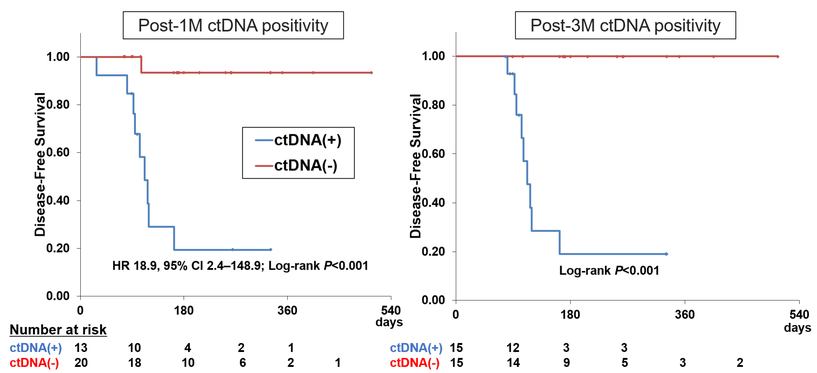
Methods

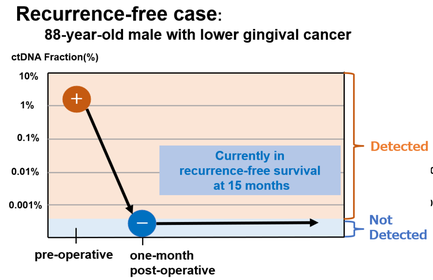
- Registered facilities: 5 of the 63 institutions participating in SCRUM-Japan MONSTAR-SCREEN-3.
- Subjects: Patients with cT3 or higher oral cancer who have undergone surgery. Non-recurrent cases.
- Methodology: Whole genome sequencing (WGS) is performed on tumor tissue from surgical specimens.
- Evaluation: MRD was evaluated by personalized ctDNA analysis using the Precise MRD assay (Myriad Genetics). Blood samples were collected at multiple time points.
- Up to 1,000 tumor-specific variants were selected for each patient. Plasma samples were collected at baseline, at **1 month** after surgery, every **3 months** during the first year, and every 6 months during the second year. In total, 34 patients were enrolled, and 139 plasma samples were analyzed.
- In this analysis, we compared the prognosis according to MRD

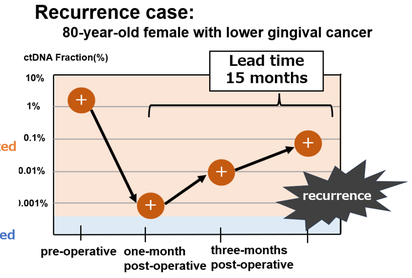


Results/Graphs/Data

- Among 44 enrolled patients, 34 had evaluable ctDNA and clinical data.
- The median age was 65 years, and 65.7% were male; most had Stage IVA.
- Personalized WGS-based ctDNA panel creation succeeded in 100% of patients, identifying a median of 6,119 tumor-specific variants and enabling baseline ctDNA detection in all cases including 5.9% at ultra-sensitive levels (<100 ppm).
- Post-operative MRD positivity was observed in 41.2% at 1 month, 50% at 3 months, and 33.3% at 6 months.
- During follow-up, 10 patients developed radiologic recurrence, with a median lead time of 2.7 months from MRD positivity.
- One-month MRD positivity was strongly associated with inferior disease-free survival (HR 18.9, 95% CI 2.4–148.9; P<0.0001). Recurrence occurred in 9 of 12 MRD-positive patients versus 1 of 20 MRD-negative patients.







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Future Directions for Research

Further enrollment toward the target n=1,100 and extended follow-up will refine MRD-guided risk stratification. Integration of ctDNA-based MRD into postoperative management and the development of interventional trials for MRD-positive patients represent key next steps.

Acknowledgements

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