

SCRUM-Japan MONSTAR-SCREEN-3: Comprehensive tumor microenvironment analysis via multi-omics in a large-scale prospective study.

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Background: SCRUM-Japan is a multi-institutional, industry-academia collaborative cancer genome screening project launched in 2015, consisting of LC-SCRUM-Asia for lung cancer and SCRUM-MONSTAR for other malignancies. The project has successfully implemented organ-agnostic liquid biopsy-based precision oncology and molecular residual disease (MRD)-guided therapeutic development, resulting in multiple regulatory approvals of therapeutic agents and diagnostics. In 2024, MONSTAR-SCREEN-3 was launched to expand the scope of multi-omics analysis beyond advanced solid tumors to include resectable solid tumors and hematologic malignancies, aiming for a comprehensive understanding of tumor microenvironment (TME) dynamics. The project integrates a multi-omics platform, including spatial transcriptomics, ctDNA analysis, and proteomics, to advance personalized medicine and accelerate drug development. **Methods:** MONSTAR-SCREEN-3 (UMIN000053975) is a large-scale, multi-institutional prospective study involving 55 centers across Japan, aiming to enroll 3,200 patients across three cohorts: Cohort A: Advanced solid tumors undergoing systemic therapy (n=1,700); Cohort B: Resectable solid tumors receiving perioperative treatment (n=1,100); Cohort C: Hematologic malignancies (n=400). Our analysis platform combines spatial transcriptomics with circulating tumor DNA/RNA sequencing, bulk tissue whole exome/transcriptome sequencing, plasma proteomics, and microbiome analyses. For resectable cases, standardized longitudinal monitoring with whole genome sequencing-based MRD analysis is implemented, while disease-specific MRD approaches are applied to hematologic malignancies. Following SCRUM-Japan's quality assurance system, standardized monitoring collects regulatory-grade clinical data, including key indicators such as response rate, progression-free survival, and overall survival. MONSTAR-SCREEN-3 applies standardized protocols for tissue preservation and data acquisition across all centers, ensuring high-quality data. The project leverages the VAPOR CONE supercomputing infrastructure for real-time data integration and AI-driven analysis to identify biomarkers, elucidate resistance mechanisms, and deepen the understanding of tumor-immune interactions. The study aims to establish a framework for next-generation precision oncology. The latest enrollment status and initial operational results will be reported at the ASCO meeting. MONSTAR-SCREEN-3 is expected to contribute to new therapies, cross-cancer MRD assays, and the resolution of drug lags in hematologic malignancies, driving advancements in personalized cancer treatment. Clinical trial information: UMIN000053975. Research Sponsor: None.