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POSTER ABSTRACTS

803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Practical and Flexible Genome Profiling Study Using the Halo-Shape Annealing and Defer-Ligation Enrichment (HANDLE) System: HM-Screen-JAPAN02

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Background

Acute myeloid leukemia (AML) is known to have a relatively small number of genomic mutations compared to solid tumors. With the development and clinical application of drugs targeting genetic mutations involved in the pathogenesis of AML, the Japanese Society of Hematology has defined "fast-track mutations" as those that should be reported promptly due to clinical necessity. A multicenter genomic profiling study (HM-SCREEN-JAPAN01: HM01 study) was conducted to comprehensively sequence 406 DNA mutations and 265 RNA aberrations in 177 AML patients, suggesting its usefulness in clinical practice, but the turnaround time (TAT) until results are reported remains an issue (Hosono, *et al. Cancer Sci*, 2023).

Aims

We have launched the HM-SCREEN-JAPAN02 (HM02) study, a practice-oriented genome profiling study that improves on the previous HM01 study and uses a newly developed targeted sequencing method. The HM02 study adopted the novel Amoy Myeloid Panel® method, which uses the HANDLE (Halo-shape ANnealing and Defer-Ligation Enrichment) system to significantly shorten TAT and facilitate specimen submission, and was designed to be completed in 7 days from sequencing to reporting. The HM02 study allows mutation analysis at any treatment timing, such as at initial presentation, during treatment, or at relapse, as well as the capability to track clonal changes through repeat analysis; the HM02 study was designed to determine whether such flexible analysis is useful in determining treatment strategy.

Results

The study was conducted at 23 centers in Japan, enrolling a total of 154 cases from 2020 to 2022, with 191 samples analyzed to assess the usefulness of the study. Repetitive mutation analysis was performed in 21 cases, and clonal changes could be tracked. Among the mutations detected, we selected those that were determined to be pathogenic or likely pathogenic by ClinVar. Of the 154 cases analyzed, none of the pathogenic mutations were detected in 9 cases, and 6 were of the normal karyotype. The most frequently observed mutations were *TET2* (51%), *FLT3* (30%), *TP53* (18%), and *NPM1* (17%) (Figure 1). In multivariate analysis adjusted for age, gender, and stem cell transplantation status, *TP53* and *NRAS* mutations were associated with higher risk for death (HR=6.82 and 14.98, respectively).

Of the 19 cases in which pathological mutations were repeatedly investigated, 8 were useful in determining minimal/measurable residual disease (MRD) (2 cases of MRD loss and 6 cases of MRD retained), 6 cases showed the development of new clones and 5 cases showed clonal evolution, indicating that repeated mutation analysis can be used to evaluate detailed disease status. In terms of clinical utility, HM02 mutation analysis was useful in 62% of cases (98 of 158), particularly for risk assessment and determining the indication for stem cell transplantation (Figure 2).

Conclusion

Flexible analysis using the novel Amoy Myeloid Panel® method suggests that it can be used to assess the risk of relapse, evaluate the need for transplantation, and select optimal therapeutic agents. NGS-based mutation analysis provides useful information at any point in AML treatment and is expected to improve outcomes.

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Figure 2

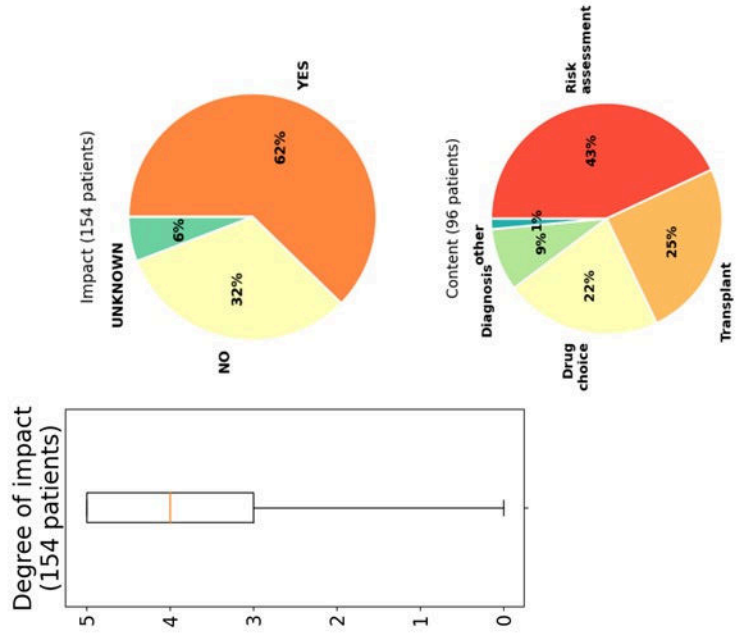

Figure 1

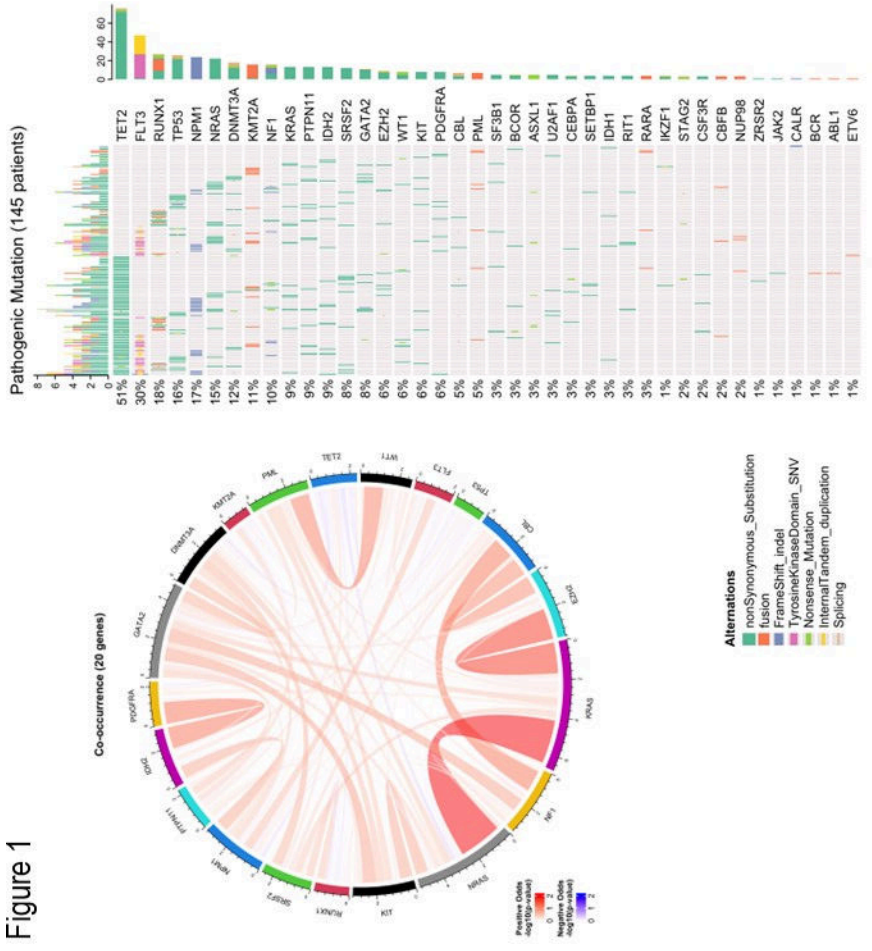

Figure 1