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# REFINEMENT OF MYELODYSPLASIA-RELATED GENE MUTATIONS IN ELN-2022 ENHANCES PROGNOSTIC STRATIFICATION IN ACUTE MYELOID LEUKEMIA

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## INTRODUCTION

It remains to be elucidated whether all nine myelodysplasia-related (MR) mutations listed in ELN-2022 contribute similarly to prognostic outcomes in acute myeloid leukemia (AML).

## AIM

This study aimed to explore the prognostic relevance of the components within the ELN2022 MR mutation group and evaluate the potential for simplifying this group. These findings were subsequently validated using international validation cohorts.

## METHOD

- 4,672 adult patients with newly diagnosed non-M3 AML were included.
- Comprising data from National Taiwan University Hospital (NTUH, n=1,103, training cohort), National Cancer Research Institute (NCRI; n=2,095, validation cohort), and Acute Myeloid Leukemia Study Group (AMLSG; n=1,474, validation cohort).
- From April 1994 to January 2024, adult patients, eligible for receiving intensive chemotherapy, with de novo AML at the NTUH were consecutively enrolled.
- Exclusions included patients with antecedent hematological diseases, a history of cytopenia, a family history of myeloid neoplasms, or prior exposure to leukemogenic therapy.
- Survival analyses were performed using time-dependent areas under the receiver operating characteristic curve with the Kaplan-Meier model.

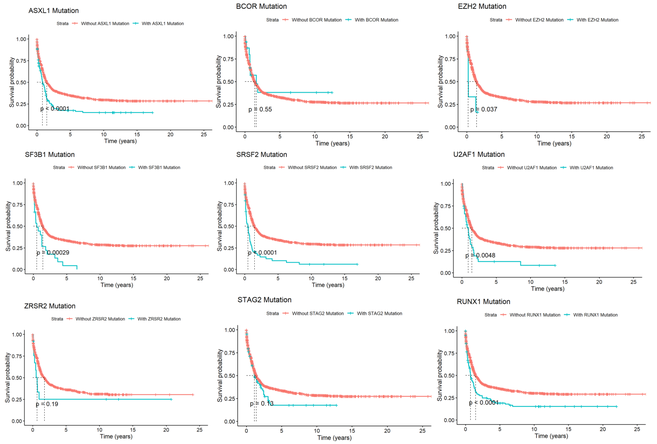
## RESULTS

- Survival analysis led to the proposal of a revised MR mutation group composed of *ASXL1*, *EZH2*, *SF3B1*, *SRSF2*, *U2AF1*, and *RUNX1*.
- In the multivariate Cox proportional hazards regression model for overall survival, incorporating age and white blood cell counts at diagnosis, and either ELN-2022 or ELN-2022 with the revised MR mutation group, the model using the revised group provided comparable Concordance Index (CI=0.686) and time-dependent area under curve to the original ELN-2022 (CI=0.687) in the training and the two validation cohorts.
- ELN-2022-defined favorable-risk AML patients with revised MR mutations still exhibited better outcome compared with intermediate-risk or adverse-risk patients with revised MR mutations (mOS NR vs.1.43, $p<0.001$; mOS NR vs. 1.13, $p<0.001$).

Table 1. Patient characteristics

| Characteristic | NTUH n = 1103 | UK NCRI n = 2095 | AMLSG n = 1474 |
|---|---|---|---|
| Age | 48.8 | 59.3 | 48.6 |
| WBC | 42.9 | 40.5 | 37.2 |
| Hemoglobin | 8.3 | 9.3 | 9.1 |
| Platelets | 71.2 | 80.7 | 83.5 |
| BM blast, % | 58.3% | 58.6% | 67.6% |
| *RUNX1* | 112 (10.2%) | 311 (14.9%) | 133 (9.0%) |
| *ASXL1* | 96 (8.7%) | 165 (7.9%) | 69 (4.7%) |
| *SF3B1* | 26 (2.4%) | 63 (3.0%) | 38 (2.6%) |
| *U2AF1* | 36 (3.3%) | 101 (4.8%) | 37 (2.5%) |
| *SRSF2* | 42 (3.8%) | 300 (14.3%) | 88 (6.0%) |
| *ZRSR2* | 12 (1.1%) | 21 (1.0%) | 13 (0.9%) |
| *STAG2* | 35 (3.2%) | 129 (6.2%) | 66 (4.5%) |
| *EZH2* | 14 (1.3%) | 82 (3.9%) | 45 (3.1%) |
| *BCOR* | 27 (2.5%) | 96 (4.6%) | 35 (2.4%) |

Figure 1. Survival Analyses of NTUH AML Cohort with/without MR Mutations




## RESULTS

Figure 2. Time-dependent ROC Analyses of ELN-2022 Model & ELN-2022 with the Revised MR Mutation Group Model, and Concordance Index Comparison

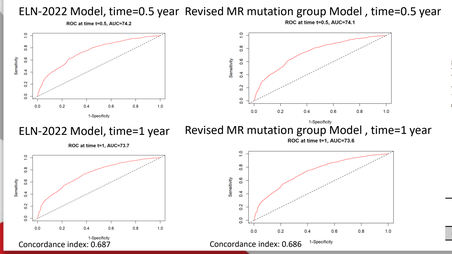
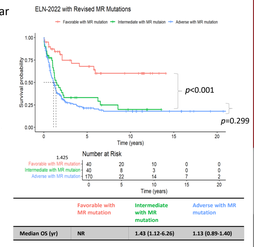



Figure 3. Survival Analysis of Modified ELN-2022 with revised MR mutations




## CONCLUSIONS

The proposed revised MR mutation group, with *ASXL1*, *EZH2*, *SF3B1*, *SRSF2*, *U2AF1*, and *RUNX1* mutations, may enhance ELN-2022 risk stratification among AML patients.

Further prospective validation of this refinement is required.

## ACKNOWLEDGEMENTS

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## CONTACT INFORMATION

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