Blood-based Proteomic Profiling Identifies OSMR as a Novel Biomarker

HA Abbas[1], B Wang[1], J Marvin-Peek[1], B Yuan[1], A Garza[1], J Root[1], A Arruda[2], Y Liu[1], CD DiNardo[1], TM Kadia[1], NG Daver[1], PL Lorenzi[1], K Sasaki[1], S Kornblau[1], MD Minden[2], F Ravandi[1], HM Kantarjian[1], PK Reville[1]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA. [2]Princess Margaret Cancer Centre, Toronto, Ontario, Canada

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Background

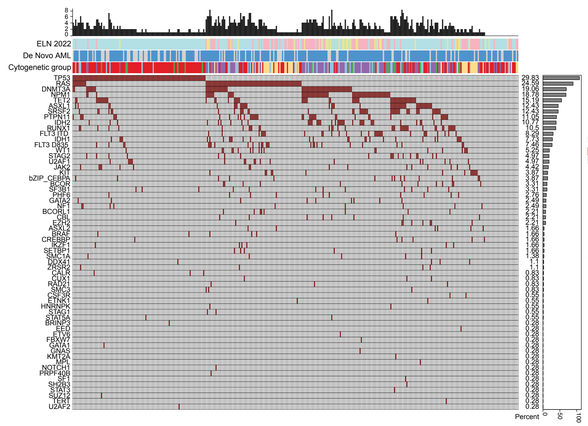
Risk stratification in acute myeloid leukemia (AML) is critical to tailor timely induction therapy. The most widely utilized risk stratification approach is the European LeukemiaNet (ELN) that usually requires bone marrow biopsy and genomic testing. Inflammation is increasingly recognized as a critical factor in AML. Novel biomarkers from robust blood-based tests are needed to accurately and efficiently risk stratify patients with newly diagnosed AML.

Methods

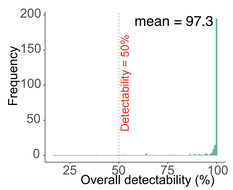
-- Inflammatory proteome was evaluated through blood-based proteomic profiling of 251 soluble inflammatory proteins using NUcleic acid Linked Immuno-Sandwich Assay (NULISA), a proximity-ligation assay based on NGS or PCR allowing attomolar (10^{-18}) detection in 543 newly diagnosed AML patients
-- Multivariable cox models with L1 regularization were used to test the independent prognostic ability. A seven-protein prognostic score (Leukemia Inflammatory Risk Score, LIRS) was developed
-- Model performance was assessed by cumulative concordance index (C-index) and time-dependent area under the curve (tdAUC).
-- Findings were validated in internal and external cohorts, including a prospective cohort of newly diagnosed AML patients.

Results

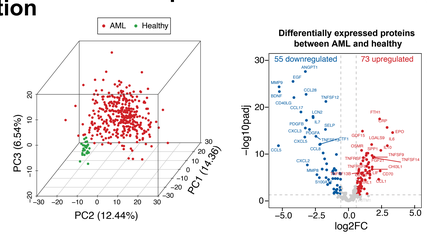
In-house cohort characteristics



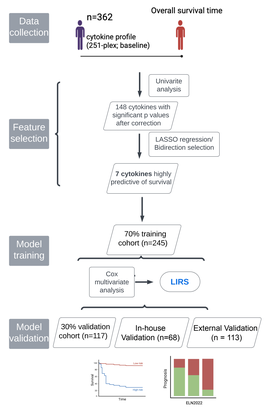
NULISA achieved high sentitivity in protein detection

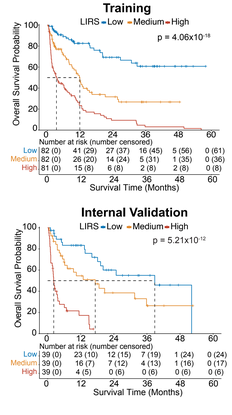


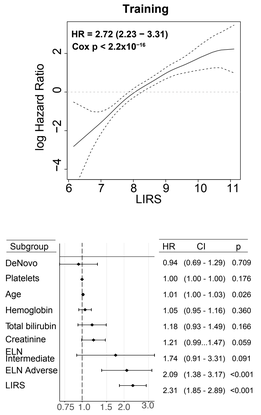
Proteomic profile of AML vs Healthy



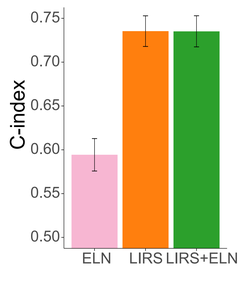
Defining Leukemia Inflammatory Risk Score (LIRS)

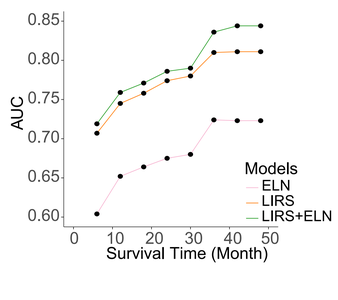


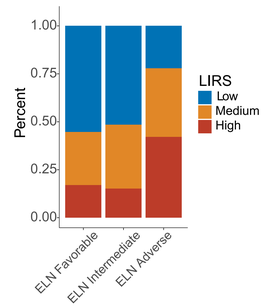




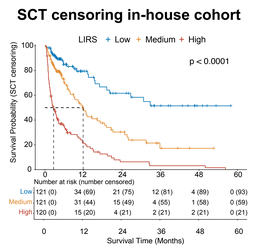
LIRS further refines ELN2022

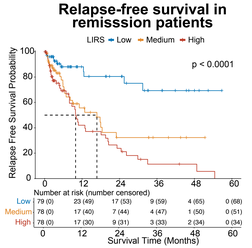


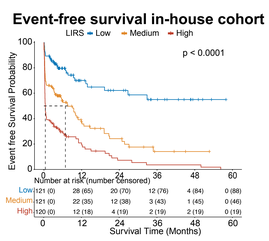


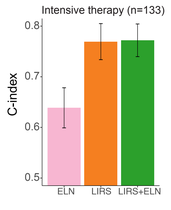


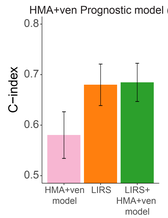
LIRS holds prognostic value in various clinical settings

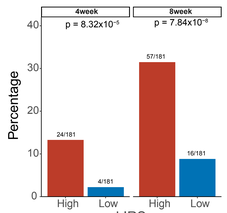




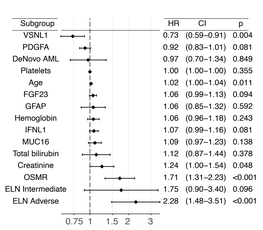


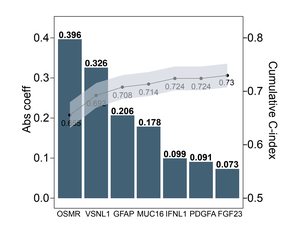


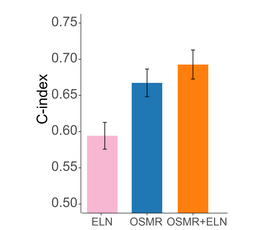




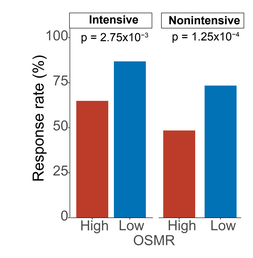
OSMR is a novel prognostic feature in newly diagnosed AML

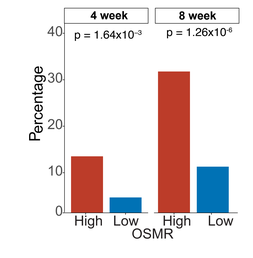


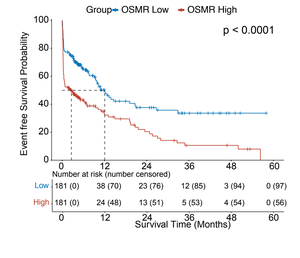




OSMR predicts relevant clinical endpoints

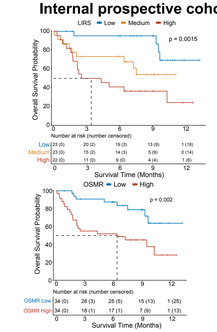




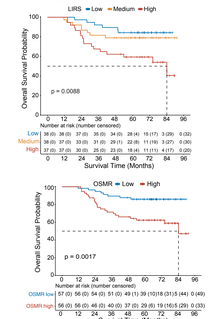


Validation of LIRS and OSMR

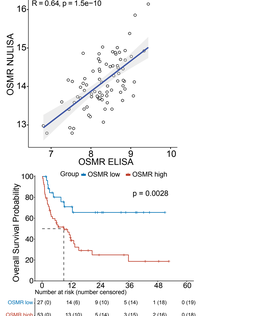
Internal prospective cohort



External cohort



ELISA testing



Conclusions

Through high-throughput blood-based proteomic profiling, we identified a novel prognostic signature of survival, early mortality and treatment response termed LIRS. OSMR emerged as the best single biomarker that may improve on current risk stratification guidelines for early and long-term risk of death in newly diagnosed AML patients (Patent Pending 63/573,150). This work adds important information for clinical translation to better inform AML patient risk.

References

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Contact information

Hussein A. Abbas, MD, PhD. EMAIL: habbas@mdanderson.org

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618. Acute Myeloid Leukemias: Biomarkers and Molecular Markers in Diagnosis and Prognosis: Poster II

Hussein A. Abbas

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