P1313 PREDICTING OUTCOMES IN AML PATIENTS CONSOLIDATED BY AN ALLOGENEIC STEM CELL TRANSPLANTATION USING THE KNOWLEDGE BANK APPROACH

Topic: Stem cell transplantation - Experimental

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Background:
Current risk stratification systems in acute myeloid leukemia (AML), e.g. by the European LeukemiaNet (ELN) 2017, help to inform treatment decisions, including those for an allogeneic stem cell transplantation (HSCT) in first remission. Recently Gerstung et al. (Nature Genetics, 2017) developed a knowledge bank (KB)-based algorithm to in order to more precisely predict individual outcomes based on demographic, clinical, and genetic data. Two studies validated the feasibility of the KB prediction in AML patients (pts) consolidated with chemotherapy. However, a validation in a HSCT-treated cohort - crucial with respect to informed decisions towards HSCT - is lacking.

Aims:
To validate the feasibility of KB outcome prediction in a HSCT-treated cohort.

Methods: We analyzed 545 AML pts (median age at diagnosis 62, range 21-77 years) consolidated by reduced-intensity (23%) or non-myeloablative (77%) allogeneic HSCT. 60% of pts were in first remission. All clinical variables included in the KB were available for this cohort, while our gene mutation panel did not cover 17/58 of genes included in the KB. KB predictions 3 years after diagnosis were retrospectively calculated by using the adapted transplant strategy and compared to the observed outcomes using receiver operating characteristics (ROC) curves. Additionally, the measurable residual disease (MRD) status at HSCT - based on NPM1 mutation and BAALC, MNI, and WT1expression - was evaluated by digital droplet PCR in pts with material available.

Results:
The area under the curve (AUC) to predict 3-year overall survival (OS) produced by the KB value was 0.69 (95% CI 0.62-0.72), not significantly different compared to the AUC based on ELN2017 risk groups (0.66 [95% CI 0.57-0.71], P= 0.23, Figure 1A), and worse compared to the published results in chemotherapy consolidated pts (AUCKB = 0.80, Bill et al, J Hematol Oncol 2021). Still, in a multivariate analysis the KB prediction for 3-year OS significantly impacted OS (OR 6.25, CI 2.9-13.2) after adjustment for the MRD-corrected remission status at HSCT. Aikake Information criterion comparison with a model including the ELN2017 risk groups and the MRD-corrected remission status at HSCT demonstrated the model containing the KB prediction as preferable. When introducing cut-offs according to the KB value for OS at 3 years similar to Fenwarth et al. (Blood 2021), we observed a clear separation of OS curves according to a KB value of <20, 20-39, and ≥ 40 with higher values indicating a higher likelihood for OS (P< 0.001, Figure 1B). Regarding additional endpoints, the KB algorithm had the highest probability to correctly predict death without previous achievement of a remission (AUCKB = 0.75, Figure 1C, black), restricted prediction for death in first remission (AUCKB = 0.61, Figure 1C, red) or after relapse (AUCKB = 0.63, Figure 1C, blue), but good prediction for being alive in first remission (AUCKB = 0.69, Figure 1D, red) or after relapse (AUCKB = 0.77, Figure 1D, blue).
Summary/Conclusion: For HSCT treated AML pts the KB-based outcome prediction was inferior compared to previous studies of pts receiving chemotherapy. The likely reason for this inferiority is the introduction of confounders (e.g. donor selection or conditioning regimens), that may impact treatment-related mortality, and are not integrated in and not predictable by the current KB algorithm. Future versions of the KB that also consider HSCT-associated factors might further improve outcome prediction by this promising clinical tool.