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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

A Predictive Scoring System for Therapy Failure of Tyrosine-Kinase Inhibitors in Patients with Chronic-Phase Chronic Myeloid Leukemia

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Background In the latest version of WHO criteria (5th edition, 2022), accelerated-phase chronic myeloid leukemia (CML-AP) was re-defined as "high-risk" chronic-phase chronic myeloid leukemia (CML-CP). However, there is no robust predictive scoring system for therapy failure of tyrosine-kinase inhibitors (TKIs) in these newly-defined CML-CP patients.
Objectives To develop and validate a predictive scoring system for TKI-therapy failure in CML-CP patients.
Methods Data from 2,038 consecutive CML-CP patients according to the WHO 2022 criteria receiving initially TKI-therapy at one centre were interrogated as the training dataset to develop a predictive scoring system which was subsequently-validated in 4,640 patients from 76 other centres (validation dataset). TKI-therapy failure was defined by the 2020 European LeukemiaNet recommendation.
Results In the training dataset, 1,591 patients (78%) initially received imatinib; 326 (16%), nilotinib; 85 (4%), dasatinib; and 36 (2%), flumatinib (a novel 2G-TKI made in China). Median TKI-therapy duration was 58 months (IQR, 33-90 months). 515 patients (27%) experienced therapy failure at a median of 9 months (IQR 3-12 months) on TKI-therapy. Multi-variable analysis indicated that older age, male sex, lower hemoglobin concentration, higher proportion of blood blasts and basophils, larger spleen size below the costal margin and high-risk additional cytogenetic abnormalities (ACAs) in Ph $^{+}$ cells were significantly-associated with higher cumulative incidence of therapy failure. Based on the optimal Fine-Gray regression model, a formula to calculate

the therapy-failure risk score was established: " ***Initial TKI-therapy failure risk score = 1.9321 × (Age/100) + 0.2950 × Sex (male = 1, female = 0) - 0.8589 × (HGB/100)^2 + 0.0979 × Blood blasts + 0.023× Blood basophils + 0.0521 × Spleen size below the costal margin + 0.5075 × high-risk ACAs (existing = 1, no = 0)*** " which divided patients into low- (score ≤ 0.0545; n = 908; 47%), intermediate- (0.0545 < score < 1.1662; n = 791; 41%) and high-risk (score ≥ 1.1662; n = 216; 12%) cohorts with 7-year cumulative incidences of therapy failure of 8% (95%CI, 4, 12%), 39% (35, 43%) and 80% (76, 84%; p < 0.001; **Figure 1A**). Sub-distribution hazard ratios (sHRs) for therapy failure (low-risk cohort as reference) were 3.2 (2.6, 4.1, p < 0.001) and 9.5 (7.4, 12.2; p < 0.001) for the intermediate- and high-risk cohorts. In the validation dataset, 4,640 patients were classified into the low- (n = 2,168; 47%), intermediate- (n = 2,093; 45%) and high-risk (n = 379; 8%) cohorts using the scoring system. 7-year cumulative incidences of therapy-failure were 10% (7, 13%), 36% (33, 39%) and 70% (66, 74%; p < 0.001; **Figure 1B**). sHRs (low-risk cohort as reference) were 3.4 (3.0, 3.9; p < 0.001) and 8.8 (7.5, 10.3; p < 0.001) for the intermediate- and high-risk cohorts. Time-dependent AUROC values for therapy failure using the predictive scoring system were 0.84-0.92 and 0.79-0.86 in the training and validation datasets. Moreover, patients identified as intermediate- or high-risk cohorts by the predictive scoring system receiving initial 2G-TKI-therapy had significantly-lower therapy failure rate than those receiving imatinib-therapy (p-values = 0.002 and 0.017) both in the training and validation datasets.

Conclusions We developed and validated a robust predictive scoring system for TKI-therapy failure in newly-defined CML-CP patients according to the WHO criteria (5th edition, 2022), which might help physicians decide appropriate therapy strategy.

Disclosures No relevant conflicts of interest to declare.

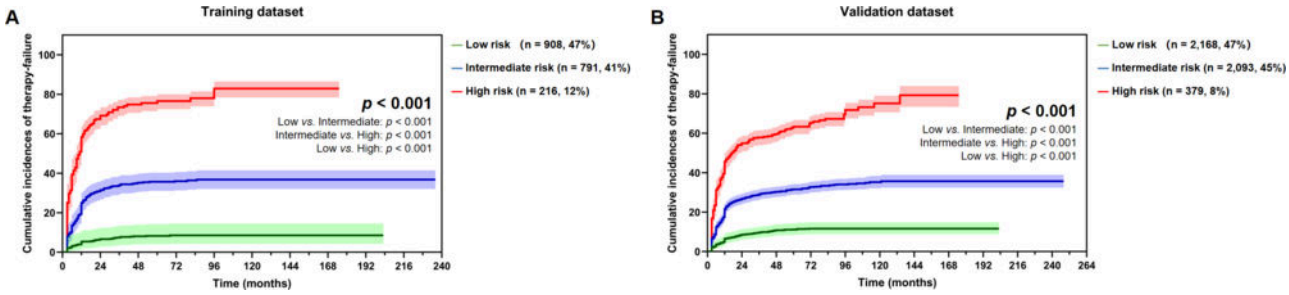

Figure 1

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