UKE Paper of the Month April 2019

Comprehensive clinical-molecular transplant scoring system for myelofibrosis undergoing stem cell transplantation

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Blood. 2019 Feb 13

ABSTRACT: Allogeneic hematopoietic stem cell transplantation is curative in myelofibrosis and current prognostic scoring systems aim to select patients for transplantation. Here, we aimed to develop a prognostic score to determine prognosis after transplantation itself using clinical, molecular and transplant-specific information of a total of 361 myelofibrosis patients. Of these, 205 patients were used as a training cohort to create a clinical-molecular myelofibrosis transplant scoring system (MTSS), which was then externally validated in a cohort of 156 patients. Multivariable analysis on survival identified age ≥ 57 years, Karnofsky performance status < 90%, platelet count < 150 x 109/L and leukocyte count > 25 x 10^9/L prior to transplantation, HLA-mismatched unrelated donor, ASXL1 mutation and non-CALR/MPL driver mutation genotype being independent predictors of outcome. The uncorrected concordance index for the final survival model was 0.723, and bias-corrected indices were similar. Risk factors were incorporated into a 4-level MTSS: low (score of 0-2), intermediate (score of 3-4), high (score of 5), and very high (score of > 5). The 5-year survival according to risk groups in the validation cohort was 83% (95% CI, 71-95%), 64% (95% CI, 53-75%), 37% (95% CI, 17-57%), and 22% (95% CI, 4-39%), respectively (p < 0.001). Increasing score was predictive of non-relapse mortality (p < 0.001) and remained applicable to primary (0.718) and post-ET/PV myelofibrosis (0.701) improving prognostic ability in comparison to all currently available disease-specific systems. In conclusion, this myelofibrosis transplant score (MTSS) predicts outcome of primary and post-ET/PV myelofibrosis patients undergoing allogeneic stem cell transplantation.

STATEMENT: *This work shows for the first time that by including disease-, patient-, and transplant-specific risk factors, this new risk score can predict outcome after curative allogeneic stem cell transplantation better than all other risk scores. The work resulted in "practice changing" worldwide for selecting and considering patients with myelofibrosis for allogeneic stem cell transplantation.*

BACKGROUND: This work was performed in the Department of Stem Cell Transplantation in close collaboration with the hematological department of hospital St Louis/Paris, Medical School Hannover and Westdeutsches Tumorzentrum/Essen. Next Generation Sequencing was performed in the laboratory of the Dept of Stem Cell Transplantation. Major work was performed by Nico Gagelmann (medical student at UKE) under the mentorship of Prof Kröger. One of the scientific research activity at the Department of Stem Cell Transplantation at UKE is the stem cell biology in Myeloproliferative Neoplasm and optimizing allogeneic stem cell transplantation as curative treatment option in this rare disease. The Department of

Stem Cell Transplantation has developed several international studies and is known as the largest center for stem cell transplantation for MPN in Europe.