Improved Early Mortality Prediction for AML Patients Receiving Intensive Chemotherapy

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Acute myeloid leukemia (AML) is characterized by rapid growth of abnormal immature white blood cells of the myeloid line, which accumulate in the bone marrow and interfere with the development of normal blood cells. AML is the most common adult leukemia, and while its incidence increases with age, patient survival greatly decreases with age. Five-year survival for patients younger than 15 is approximately 60%, however 5-year survival decreases to 5% or less for patients greater than 65 years old. Although biological differences between AMLs in young and old individuals partially account for this observation, older patients more frequently have underlying health issues. This impacts their response to treatments and increases their risk for treatment-related mortality (TRM) from curative-intent high-dose treatment regimens. As a result, distinct AML treatment protocols have been developed for young and older adults, with the age of 55-60 as the cut-off between these categories.

The use of age for selection of treatment protocols has been used as a surrogate for other factors that have been suggested to influence the health status of patients and likelihood of death after intensive chemotherapy, including neutrophil count and levels of bilirubin, albumin, hemoglobin and fibrinogen. To determine if a more accurate prediction of early death could be obtained by the inclusion of specific health-related factors, Drs. Walter and Estey and colleagues from the Clinical Research Division as well as the M.D. Anderson Cancer Center examined the correlation of early death with 17 different health factors among AML patients, and created predictive models using a subset of these factors.

Analysis of 3,365 newly diagnosed AML patients receiving intensive chemotherapy demonstrated the highest risk of early death among all age groups occurred within the first 28 days of treatment, which was used to empirically define TRM. The authors then modeled the effects of individual and combined health parameters on death within this period, wherein a value of 1.0 denotes a perfect prediction and a value of 0.5 is the rate of chance. Performance status (PS), a measure of patients' general well-being and activity level, was the single most successful parameter to predict TRM, with a modeled value of 0.75. Some factors such as age, platelet and white blood cell counts (WBC), and

albumin levels were individually less predictive, while several other factors had minimal ability to predict TRM. A simplified model that combined eight factors was highly able to predict TRM with a modeled value of 0.82. Factors included performance status, age, platelet count, serum albumin and creatine level, if the event was a secondary AML, WBC count and peripheral blast percentage. A simplified three-factor model was further developed for clinical use, consisting of age, PS and platelet count; however, this minimal model was much less accurate in predicting early death, emphasizing the need to integrate information from several factors for best results. Together these results demonstrate the superiority of using multiple health-related factors for accurate prediction of TRM risk.

RB Walter, M Othus, G Borthakur, F Ravandi, JE Cortes, SA Pierce, FR Appelbaum, HA Kantarjian, EH Estey. 2011. Prediction of early death after induction therapy for newly diagnosed acute myeloid leukemia with pretreatment risk scores: a novel paradigm for treatment assignment. *Journal of Clinical Oncology.* 29(33): 4417-4423.

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