Is Complete Remission Rate Predictive of Median Overall Survival? A Model-Based Meta-Analysis in Patients with Acute Myeloid Leukemia

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Objectives: Overall survival (OS) is an important clinical endpoint for objectively assessing treatment outcomes in pivotal oncology studies. In acute myeloid leukemia (AML), treatment efficacy can be assessed acutely based on a patient’s response to induction therapy, e.g., achieving complete remission (CR). The objective of this analysis was to quantify the correlation between CR rate after induction (%CR) and median OS (mOS), based on summary data from published clinical studies in AML patients.

Methods: A literature search was undertaken to identify relevant sources that reported either %CR or mOS from studies with at least 100 AML patients who received induction therapies. Assessment of between-trial and within-trial correlation was performed via a linear mixed effect joint model1 with transformed endpoints: logit(%CR) and log(mOS). The R programming language (version 3.2.5) was used for all data manipulation and analysis.

Results: The analysis dataset consisted of summary-level data from 115 trials (205 arms, representing 41,333 patients). Including an adjustment for age (yes/no: maximum age < 61 years?), %CR was significantly correlated with mOS between trials (BT), as well as within trials (WT): \( \rho_{\text{BT,Young}} [90\% \text{ CI}] = 0.739 [0.321, 0.916], \rho_{\text{BT,NotYoung}} = 0.787 [0.607, 0.890], \rho_{\text{WT,All}} = 0.651 [0.477, 0.776]. \) Thus, both trials and treatment arms with higher %CR tended to have longer mOS. The relationship between relative treatment effects, odds-ratio (OR) for CR and hazard-ratio (HR) for OS, was also quantified (Figure 1).

Conclusions: These results suggest that it may be feasible to utilize an early clinical endpoint from AML trials to provide critical information for drug development decisions before direct clinical outcome has been assessed. This work adds to the body of knowledge encompassing surrogate endpoints in oncology, and could potentially lead to faster, more efficient drug development.