Granulocyte colony-stimulating factor (G-CSF) treatment of childhood acute myeloid leukemias that overexpress the differentiation-defective G-CSF receptor isoform IV is associated with a higher incidence of relapse.

Abstract:
PURPOSE: This prospective, multicenter Acute Myeloid Leukemia Berlin-Frankfurt-Muenster (AML-BFM) 98 study randomly tested the ability of granulocyte colony-stimulating factor (G-CSF) to reduce infectious complications and to improve outcomes in children and adolescents with acute myeloid leukemia (AML). However, a trend toward an increased incidence of relapses in the standard-risk (SR) group after G-CSF treatment was observed. PATIENTS AND METHODS: Of 154 SR patients in the AML-BFM 98 cohort, 50 patients were tested for G-CSF receptor (G-CSFR) RNA isoform I and IV expression, G-CSFR cell surface expression, and acquired mutations in the G-CSFR gene. RESULTS: In patients randomly assigned to receive G-CSF after induction, 16 patients overexpressing the G-CSFR isoform IV showed an increased 5-year cumulative incidence of relapse (50 % ± 13 %) compared with 14 patients with low-level isoform IV expression (14 % ± 10 %; log-rank P = .04). The level of G-CSFR isoform IV had no significant effect in patients not receiving G-CSF (P = .19).
Multivariate analyses of the G-CSF-treated subgroup, including the parameters G-CSFR isoform IV overexpression, sex, and favorable cytogenetics as covariables, revealed the prognostic relevance of G-CSFR isoform IV overexpression for 5-year event-free survival ($P = .031$) and the 5-year cumulative incidence of relapse ($P = .049$). CONCLUSION: Our results demonstrate that children and adolescents with AMLs that overexpress the differentiation-defective G-CSFR isoform IV respond to G-CSF administration after induction, but with a significantly higher incidence of relapse.

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