Improved outcome in pediatric relapsed acute myeloid leukemia: results of a randomized trial on liposomal daunorubicin by the International BFM Study Group.

Abstract

PURPOSE: In pediatric relapsed acute myeloid leukemia (AML), optimal reinduction therapy is unknown. Studies suggest that liposomal daunorubicin (DNX; DaunoXome; Galen, Craigavon, United Kingdom) is effective and less cardiotoxic, which is important in this setting. These considerations led to a randomized phase III study by the International Berlin-Frankfurt-Münster Study Group. PATIENTS AND METHODS: Patients with relapsed or primary refractory non-French-American-British type M3 AML who were younger than 21 years of age were eligible. Patients were randomly assigned to fludarabine, cytarabine, and granulocyte colony-stimulating factor (FLAG) or to FLAG plus DNX in the first reinduction course. The primary end point was status of the bone marrow (BM) sampled shortly before the second course of chemotherapy (the day 28 BM). Data are presented according to intention-to-treat for all 394 randomly assigned patients (median follow-up, 4.0 years). RESULTS: The complete remission (CR) rate was 64%, and the 4-year probability of survival (pOS) was 38% (SE, 3%). The day 28 BM status (available in 359 patients) was good (≤ 20% leukemic blasts) in 80% of patients randomly assigned to FLAG/DNX and 70% for patients randomly assigned to FLAG (P = .04). Concerning secondary end points, the CR rate was 69% with FLAG/DNX and 59% with FLAG (P = .07), but overall survival was similar. However, core-binding factor (CBF) AML treated with FLAG/DNX resulted in pOS of 82% versus 58% with FLAG (P = .04). Grade 3 to 4 toxicity was essentially similar in both groups. CONCLUSION: DNX added to FLAG improves early treatment response in pediatric relapsed AML. Overall long-term survival was similar, but CBF-AML showed an improved survival with FLAG/DNX. International collaboration proved feasible and resulted in the best outcome for pediatric relapsed AML reported thus far.

-Michaela Kotrová-

Published: 3. 2. 2014 / Responsible person: Mgr. Ing. Tereza Kostková