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Letter to the Editor: FLAG (Fludarabine, High-Dose Cytarabine and G-CSF) for Refractory and High-Risk Relapsed Acute Leukemia in Children

We have read with interest the report about FLAG therapy in childhood acute leukemia by McCarthy et al. [1]. We want to add our experience with IDA-FLAG in poor-risk childhood leukemia. Between March 1997–July 1998, we treated 17 patients (3–18 yr) with IDA-FLAG (idarubicin, fludara, cytarabine, G-CSF) [2]. A total of 25 courses were administered. There were six patients with relapsed acute lymphoblastic leukemia (ALL), nine relapsed acute myeloblastic leukemia (AML), one chronic myelomonocytic leukemia (CMML), and one chronic myeloid leukemia (CML) in acute blast crisis. Five of the AML relapses were after bone marrow transplantation (BMT) and three patients were in the second relapse and one in the third. At the end of the first course, six patients were unresponsive, whereas five achieved complete remission (CR) and six died due to infections before marrow recovery. Only two of the nine AML patients and one of the six ALL patients completed two IDA-FLAG courses and achieved a complete response (CR). The median duration of neutropenia (ANC <500/ml) was 32 days (18–42 days) in the eight courses completed with CR. Our patients were previously heavily treated, but even so we conclude that the regimen is too toxic. Our patients experienced episodes of infection, mostly pulmonary, with every course, but we did not observe any acute cardiac toxicity.

In the study by Fleischhack et al. [3] of 23 poor-risk childhood AML who were refractory, relapsed, or secondary cases, IDA-FLAG courses were changed to FLAG courses for toxicity reasons. Only three patients had a second IDA-FLAG course. There were two therapy-related deaths. FLAG had a shorter duration of neutropenia than IDA-FLAG and less infectious complications. There were nine episodes of pulmonary involvement during 24 IDA-FLAG courses, whereas no pulmonary complication was observed with FLAG. Included in these cases was one of lethal Aspergillus sepsis and one of pulmonary tuberculosis following a second IDA-FLAG course. They reported cardiac toxicity in only three of 24 IDA-FLAG courses.

As a result, we emphasize that IDA-FLAG is a highly myelosuppressive therapy and the main regimen-related toxicity is infection, predominantly pulmonary. Cardiac toxicity is generally acceptable.

Our experience with IDA-FLAG was disappointing. The report by McCarthy et al. [1] by contrast suggested that FLAG is both effective in inducing remission in heavily pretreated children and has an acceptable toxicity. We are encouraged by that experience and hope that the FLAG regimen will give poor-risk patients another chance.

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