patients got low doses of cytarabine shortly after diagnosis. All three of these patients remained well. Two additional patients received low-dose cytarabine for progressive symptoms and died 1 or 2 days later. On the strength of low-dose cytarabine for progressive symptoms after diagnosis. All three of these patients re-

It should be emphasized that the true incidence of transient leukemia is currently unknown, since blood counts are not routinely performed in Down syndrome patients. Conceivably, some of these leukemias resolve permanently without being diagnosed in the first place. Thus, an immediate challenge is to learn the exact prevalence and history of this disorder by prospectively studying all neonates with Down syndrome.

REFERENCES

How did we get here from there?

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In this issue of Blood, Milligan and colleagues report that survival was shorter (P = .05) in high-risk patients randomized to receive, generally as salvage therapy, the widely used combination of fludarabine and cytarabine (FLA) rather than standard cytotoxic arabinoside, daunorubicin, and etoposide (ADE). The relative effects of FLA and ADE were the same when used alone or when combined, in separate randomizations, with granulocyte colony-stimulating factor or all-trans retinoic acid.

Fludarabine and cytarabine (FLA) or FLA with granulocyte colony-stimulating factor (FLAG) may prove more effective in patients who have better prognoses. Nonetheless, a fundamental question is how enthusiasm for FLA/FLAG in high-risk patients has been sustained when Milligan and colleagues suggest that the enthusiasm was unjustified. Alternatively, why was the published literature on FLA, in retrospect, misleading? To understand how we got here from there, it may be useful to note that none of the studies of FLA or FLAG in acute myeloid leukemia (AML)/high-risk myelodysplastic syndrome (MDS) cited by Milligan et al made reference to a control group (ie, patients given other therapies). Although typical of published phase 2 studies and consistent with the accepted view that such studies are intended to determine efficacy with efforts at comparison reserved for phase 3, the lack of a control group seems inconsistent with accepted scientific practice. Together with the natural, laudatory desire of investigators to report “positive” results, the absence of controls, and the seeming failure to consider the prior probability of positive results, may result in pub-
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