To the editor:

Platelet transfusion in neonatal alloimmune thrombocytopenia

We read with interest the article “Antigen-positive platelet transfusion in neonatal alloimmune thrombocytopenia (NAIT)” by Kiefel et al.1 The authors describe the outcome of 27 neonates with anti–HPA-1a–mediated NAIT treated with random donor platelet transfusions. They found that 24 of these neonates achieved platelet counts higher than 40×10^9/L compared with an average of 8701 nM/mL per hour for the patients without bone lesions. Hollak et al again cite their earlier work with Maas et al4 that the fat fraction is a good surrogate for severity of bone disease. We reproduced Figure 3 from this paper in our commentary1 to show how weak the correlation was. Their study shows that 7 of 9 patients with mild or severe bone complications had fat fractions of less than 0.23, an arbitrary cutoff based on the data. But it also shows that 11 of 21 patients without bone complications had fat fractions below this arbitrary cutoff.4

Finally, while we agree that more work needs to be done to establish a role of surrogates in the treatment of Gaucher disease, the results with the parameters that gave “superior results” with high-dose therapy are not promising. These are slender reeds, indeed, upon which to make a $300 000-a-year treatment decision.

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Figure 1. Mean platelet increments in neonates with NAIT following HPA-1a/5b–negative platelet transfusions or random donor platelet transfusions. The mean platelet increments in neonates with anti–HPA-1a/5b–mediated NAIT following HPA-1a/5b–negative platelet transfusions (n = 29) (open circles) or random donor platelet transfusions (n = 9) (closed squares) are shown. The error bars represent the standard deviation of the measurements. The dotted curves represent the fitted exponential decay curves to the data. The individual patient data are given in Figure 2.
To the editor:

A recurrent in-frame insertion in a CEBPA transactivation domain is a polymorphism rather than a mutation that does not affect gene expression profiling–based clustering of AML

Mutations in CEBPA, the gene encoding the transcription factor CCAAT/enhancer binding protein alpha (C/EBPα), have been reported in multiple studies, and are found in approximately 8% of patients with acute myeloid leukemia (AML).1,2 Specific regions of the gene tend to be most commonly mutated: (1) in-frame insertions in the basic/leucine zipper (bZIP) region and (2) truncating out-of-frame insertions or deletions in the N-terminus.1,2 Although mutations are most frequently found in these 2 regions, other abnormalities have been described as well.3 Frohling et al reported in 6 of 236 AML cases the existence of an in-frame insertion mutation of 6 nucleotides.3 This insertion is predicted to result in a histidine-proline duplication (HP196-197ins) in a transactivation domain of C/EBPα. In vitro studies have suggested that this proline-histidine–rich region may play a role in antiproliferative control, although this notion has not been supported by in vivo experiments.4,5 Remarkably, in none of the other initial CEBPA mutation studies was the insertion reported as either a mutation or a polymorphism, notwithstanding the fact that investigators frequently applied single-strand conformation polymorphism (SSCP) analysis or nucleotide-sequenced the complete CEBPA cDNA (see Leroy et al2 for references). More recently, one other group described the HP duplication in 20 (20%) of 100 AML cases with the HP duplication in 20 (20%) of 100 AML cases.

The range of day-1 increments varied widely, both with R-Tx (range: 10-217 × 10^9/L) and AC-Tx (range: 62-216 × 10^9/L). Unexpectedly large increments may occur with R-Tx when a proportion of the platelets is coincidentally HPA-1a/5b negative (estimated likelihood, 1 in 13 where the platelet pool is from 4 “random” donors);6 unexpectedly low increments may be seen with AC-Tx due to the presence in the fetal circulation of maternal HLA class I antibodies7 or when platelet transfusions are inappropriately administered. Babies with NAIT should therefore have their platelet counts monitored regularly whatever treatment is used and appropriate changes to treatment instigated when necessary.

In conclusion, we agree with Kiefel et al that R-Tx is an acceptable initial treatment for NAIT where HPA-1a/5b–negative platelets are not immediately available. However, our data show that HPA-1a/5b–negative platelets give larger increments, have a longer half-life, and only occasionally fail to provide therapeutically significant platelet increments. We therefore encourage blood services in other countries to establish panels of HPA-1a/5b–negative donors to provide HPA-1a/5b–negative platelets for immediate use in cases of suspected NAIT and for intrauterine or neonatal therapy of cases of known NAIT.8

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