It remains the case that in the US COG studies, National Cancer Institute (NCI) high-risk patients will get more intensive post-remission treatment based solely on NCI risk. In the UK, we can avoid this additional therapy in the 40% of patients who are deemed as low-risk by MRD yet NCI high risk.

Third, we did not to use marrow status at day 8 or 15 in patients aged 16 years or older because this group already receives a four-drug induction so that no immediate alteration of therapy is possible, and because we have data indicating that most patients older than 16 years with persisting disease at day 8 will have persisting disease at day 29.

Fourth, Rytting correctly observes that MRD could also be used to indicate patient groups who need less therapy, a point already alluded to above. The progress of ALL therapy over the past four decades has been one of intensification of therapy, with no sensitive method of identification of the group of patients—probably at least 50% overall—who could be treated effectively with minimal therapy. MRD provides such a method and any financial cost of the method is more than offset by the reduction in chemotherapy costs, days of hospital stay, and costs of supportive care. It is also self-evident that for a patient to be cured they must not have died of toxic effects; cure remains possible, though, after relapse. Now that 95% event-free survival is possible in the MRD low-risk group, even with reduced therapy, overtreatment is unacceptable.

Finally, it is important to note that even our high-risk group (ie, with persisting MRD) had an event-free survival of 89·6% in the augmented therapy group and 82·2% in the standard therapy group. These results emphasise the efficacy of the adopted chemotherapy regimen and, again, indicate that the need for bone marrow transplant, with its attendant toxic effects and costs, should be reserved only for the groups at the very highest risk, ideally within the context of clinical trials, so that its efficacy can be properly documented.

We declare no competing interests.

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Drug–drug interactions with tyrosine-kinase inhibitors

In their Review, Roelof van Leeuwen and colleagues[1] recommend various dose adjustments during concomitant use of tyrosine-kinase inhibitors and drugs that inhibit or induce cytochrome P450 3A4 (CYP3A4).[1] Most information is taken from the US Food and Drug Administration (FDA)'s drug label or the European Medicines Agency (EMA)'s Summary of Product Characteristics. However, we could not find support for their advice regarding concomitant use of pazopanib and strong CYP3A4 inducers such as carbamazepine. They suggested to gradually increase the pazopanib dose in 200 mg steps depending on patient's tolerance,[1] whereas both the FDA and EMA recommend that concomitant use should be avoided, and that the dose of pazopanib should not exceed 800 mg.[2,3] We are unaware of clinical evidence for safety and efficacy of dose enhancement. By contrast, concomitant use and enhancement might result in carbamazepine toxic effects, because pazopanib can also act as a CYP3A4 inhibitor,[2–4] whereas carbamazepine is not only a CYP3A4 inducer, but also a CYP3A4 substrate with a narrow therapeutic index. We wonder which evidence supports the dosing guidelines that have been recommended by the authors.[1]

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