treatment plan, romiplostim administered in 12 weekly doses was successful for achieving a platelet count of more than $5 \times 10^9/L$ for 2 consecutive weeks, at a median dose of 5 μg/kg/day, in 15 of 17 children (88%) compared with 0 of 5 (0%) who received placebo ($P = .0008$).1

In addition, important short-term safety data are provided, with no treatment-related serious adverse events noted, and only headache and epistaxis observed more commonly among children receiving romiplostim. Although almost all subjects (94%) had at least 1 adverse event, most were mild and none led to withdrawal or removal from the study. Drug pharmacokinetics in those children who had favorable responses were also obtained. Considering the fact that these patients were severely affected and often refractory to other therapies, the superiority of romiplostim over placebo suggests that this will become a valuable treatment option for patients who have failed standard frontline therapies. These results are important for practicing hematologists caring for children with severe and refractory ITP, as well as researchers seeking to better understand the role of this class of drugs in the treatment of immune-mediated thrombocytopenia.

Despite these exciting and encouraging data, there are long-term risks that must be addressed in future studies. First is the issue of antibody production against endogenous TPO (eTPO), which led to the discontinuation of first-generation TPO-R agonists. The second-generation agonist romiplostim has no sequence homology with eTPO, resulting in a significantly decreased incidence of anti-eTPO antibody development. The development of anti-romiplostim antibodies has also been reported, but there have been no reports of neutralizing eTPO activity. Although the current study contains a relatively small sample size (22 patients) and only short-term data, the lack of antibody production is promising. The second issue is marrow reticulin formation and potential marrow fibrosis; studies in rats suggest romiplostim does alter marrow fiber content,1 although careful serial measurements in humans have not been conducted. Especially in young patients for whom long-term therapy would be considered based on adult ITP data,2 this safety concern must be addressed prospectively in future clinical trials. It will be especially important to gather long-term safety data in children, who could potentially receive this therapy for many years. However, these pediatric data are consistent with a growing amount of data in adults, and suggest that this treatment may be a safe, well-tolerated, and efficacious option for the most severely affected children with refractory ITP.


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PET scans: when and how?

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PET scans are almost always abnormal at diagnosis in the most common B-cell lymphomas (diffuse large B-cell lymphoma, follicular lymphoma, and Hodgkin lymphoma), and normalization after therapy is highly predictive of a good outcome. But how to apply PET scans to the management of these patients remains problematic. The major controversies include when (ie, for staging, after 2-4 cycles of therapy, after completion of therapy, surveillance in remission) and how (ie, we know they should always be combined with CT scanning, but the relative merits of visual interpretation and SUV [standard uptake value] calculation are debated).

Pretreatment PET/CT

Posttreatment PET/CT

Pretreatment and posttreatment PET/CT scans.

The concept of interim (early) PET/CT scans to predict the eventual result of treatment is relatively new. In most but not all studies, patients with a positive scan after 2-3 cycles of treatment have a poorer outcome than those whose scans are negative.3,4 One hope of proponents of this approach is that patients with a positive interim scan might...
have their treatment changed and their chances for long survival increased. However, those patients whose interim scans are positive but turn negative by the end of treatment seem to do about as well as those with negative scans at both times.\textsuperscript{1,2,5-7} In fact, it appears that a negative scan at the end of therapy is the most powerful predictor of a long remission in the 3 common B-cell lymphomas.\textsuperscript{8-10} Thus the value of changing treatment on the basis of a positive interim scan depends on the new treatment still curing those patients destined to do well with the initial regimen, and curing some of the patients destined to do poorly. Of course, the results could vary from one disease to another and with different initial treatment regimens. These are questions for randomized trials, not standard therapy, and several such trials are in progress.

For studies such as PET/CT scans to be helpful in the clinic, they need to be reproducible (minimal intra- and interobserver variability) and need to be shown to correlate to the desired clinical end point. The report by Casasnovas et al in this issue of Blood addresses these issues for patients with diffuse large B-cell lymphoma.\textsuperscript{11} They identified cutoff points of reduction of the SUV\textsubscript{MAX} from pretreatment to scans after 2 and 4 cycles of therapy that provided the best discrimination between no relapse versus relapse and death versus survival. However, it seems likely that resolution of the SUV\textsubscript{MAX} to background at the end of therapy might provide the optimum chance for a good outcome. The percent reduction SUV\textsubscript{MAX} Casasnovas et al found optimal might not be the most advantageous in all situations (eg, interim versus end-of-therapy scanning, different treatment regimens) and with all types of lymphoma.

PET/CT scans provide a powerful tool to improve the care of our patients. Clinical trials aimed at defining the optimal use of these studies must be completed if we are ever to give our patients the maximum benefit the tests can provide. In the meantime, they represent a valuable staging study and a complete remission defined by PET/CT is the most powerful predictor of a durable remission (see figure).

Conflict-of-interest disclosure: The author declares no competing financial interests.

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2. Straus DJ, Portlock CS, Qin J, Myers J, Zelenetz AD, Moskowitz C, et al. Results of a prospective randomized clinical trial of doxorubicin, bleomycin, vincristine, prednisone, and rituximab and were then transplanted if the scan normalized after 4 cycles.

So where do we stand today in using PET/CT scans to benefit our patients? They seem to provide a useful staging study and can both upstage and downstage patients in comparison to CT scanning alone. The PET/CT scan at the end of treatment is the most powerful predictor of outcome. Currently both interim scanning and surveillance scanning in remission are topics for research, have not been shown to improve survival, and their use should be restricted to clinical trials. The study by Casasnovas et al makes a strong argument that interpretation using calculated SUV\textsubscript{MAX} is better than using visual interpretation.\textsuperscript{11} They identified cutoff points of reduction of the SUV\textsubscript{MAX} from pretreatment to scans after 2 and 4 cycles of therapy that provided the best discrimination between no relapse versus relapse and death versus survival.

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