HIV infection are unclear; however, previous studies have indicated an increased risk of plasma cell neoplasms in patients with HIV infection. In this context, future studies should aim at understanding the mechanisms of B-cell dysregulation in patients with persistent HIV and EBV infection and the risk of plasma cell dyscrasias in these patients.

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Comment on Malcovati et al 2943

Flying without a net in MDS

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In this issue of *Blood*, Malcovati et al discuss the findings of an expert panel of the European LeukemiaNet (ELN) and their recommendations for treating myelodysplastic syndromes (MDS). Guidance from expert panels on how to treat medical conditions abound, and it is easy to be jaded into thinking they represent no more than a “World According To Us” view of managing disease. But the ELN Expert Panel stepped up to the task of making rigorous recommendations. How did they do it? They started by identifying experts on the basis of established criteria, such as those of the National Institutes of Health Consensus Development Program and not on the basis of proximity to their offices. Check. They then systematically reviewed the literature for all articles guiding practice, both full manuscripts and abstracts at major conferences. Check minus, because the ELN used only English-language articles, and it did not disclose how many were.
Identified or how many ultimately contributed to recommendations. Articles should be rated according to level of evidence, so case report findings and results from advanced phase studies are not given equal weight. Check—though note that meta-analyses garner the same score as randomized control trials. Finally, panelists are locked in a room and forced to listen to Barbara Streisand music until they come to a consensus on recommendations, which are graded according to level of evidence, consistency of results across studies, and applicability to the patient population—in this case, people with MDS. Check. And this took three consensus conferences (I suspect with music being unnecessary).

The ELN authors then took on the broad task of addressing all aspects of MDS, starting with making the diagnosis. They included standard procedures, such as the necessity for a bone marrow biopsy and cytogenetics (although including such obvious procedures in panel recommendations may seem superfluous, neither one is routinely performed, even in the United States) and more sophisticated approaches such as single nucleotide polymorphism arrays to detect cryptic chromosomal defects. They reaffirmed the utility of the World Health Organization classification of myeloid neoplasms and covered the broad collection of risk assessment tools available. Interestingly, while they acknowledged the shortcomings of the International Prognostic Scoring System (IPSS), they recommended its use to stratify risk for all MDS patients, given the large body of data supporting its applicability in therapeutic decisions and the relative paucity of data supporting its applicability in this subtype of MDS, what drug should I use?

Impressively though, the ELN panel confirms minimum criteria for diagnosing and classifying MDS, which is more challenging than is widely appreciated. They also make clear statements regarding recommendations on controversial topics, such as remission induction therapy preceding stem cell transplantation or the use of iron chelation therapy, along with a recommendation grade. Although I may not agree with all of these recommendations, I can appreciate how they can guide physicians who do not have the time or interest to immerse themselves in the nuances of MDS literature and can keep them from falling to the floor of the Big Top.

Conflict-of-interest disclosure: Dr Sekeres serves on advisory boards for Celgene and Amgen.

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Comment on Walker et al, page 3034

Redirecting traffic using the XP01 police

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In this issue of Blood, Walker et al investigate the preclinical potential of KPT-330, an exportin-1 (XP01, also known as chromosome maintenance protein 1 [CRM1]) inhibitor, against both accelerated phase (AP) and blast crisis chronic myeloid leukemia (CML-BC) and against Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL), all of which are diseases of significant unmet clinical need. The authors provide encouraging data from both a leukemic mouse model and a single CML-AP patient, corroborating mechanistic studies suggesting that KPT-330 efficacy relies on targeting abundantly expressed XPO1, followed by the reactivation of protein phosphatase 2A (PP2A).

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