marked cardiac dysfunction measured by elevations in the serum biomarkers NT-proBNP and troponin. Grade 3 or 4 toxicity was observed in 54%, which was similar in nature to that observed in other IMiD trials in AL and included fluid retention, infection, atrial fibrillation, and venous thromboembolism. Nevertheless, analogous to the recent trend noted previously by Muchtar et al, no deaths occurred within the initial 100 days of pomalidomide therapy. However, these side effects and the rates of pomalidomide dose reduction (32%) and discontinuation (29%) resulting from adverse events emphasize the challenges in optimizing the treatment of AL and support future trials to explore dose and schedule modifications to improve tolerance. Such efforts might include dose reduction of pomalidomide, as suggested by the authors, dose reduction of dexamethasone, or administration of pomalidomide on days 1 through 21 of a 28-day schedule (as approved for myeloma) rather than continuously; pomalidomide combinations as initial therapy for AL would also be of interest.

Exciting laboratory research also portends well for identifying better prognostic factors and treatment strategies in AL. Fluorescence in situ hybridization cyogenetics, preferential organ tissue tropism according to AL variable region gene selection, relevance of marrow minimal residual disease, and chemical characteristics of specific ALs that predict their predisposition for self-aggregation are subjects of active investigation, and the results may be leveraged in the future to improve management strategies. We look forward to the next analysis of the Mayo Clinic or other large AL database to demonstrate that further improvements in outcomes for AL patients have been achieved in the real-world setting.

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HSC niche: ample room for every guest stem cell

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It has long been thought that nearly all bone marrow niches are occupied by hematopoietic stem cells (HSCs). In this issue of Blood, Shimoto et al show that the bone marrow contains more habitable niches for HSCs. Other studies have shown that transplanting large numbers of unfractionated bone marrow cells led to high levels of engraftment in unconditioned mice. These data suggest that chimerism levels after transplantation are determined by the ratio of exogenous to endogenous stem cells, suggesting a model in which exogenous HSCs can compete with endogenous HSCs to engraft bone marrow without the niches being empty. Certain accessory cells in the bone marrow transplant have been suggested to account for the experimental differences between purified HSCs and bone marrow cell transplantation. Regardless of the model of how exogenous HSCs engraft, it is thought that essentially all niches or spaces within bone marrow are occupied by endogenous HSCs in unconditioned mice.

Now, Shimoto et al challenge this view by showing that donor HSCs can significantly engraft in the bone marrow and occupy distinct perivascular niches of unconditioned mice without competing out endogenous HSCs (see
stromal cells are a key component. These cells

HSCs. Surprisingly, they found that these

cells (endogenous HSCs) into unconditioned mice, 

a very large number of HSCs (up to 390% of

100 to 200 donor mice. By transplanting 

effort by sorting a large number of HSCs from

the bone marrow has made it technically

needed. However, the rarity of HSCs in

Bone marrow has made it technically

required to achieve engraftment

conditioning is required to achieve engraftment 

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