Approvals and presentations flag notable advances in the hem-onc space

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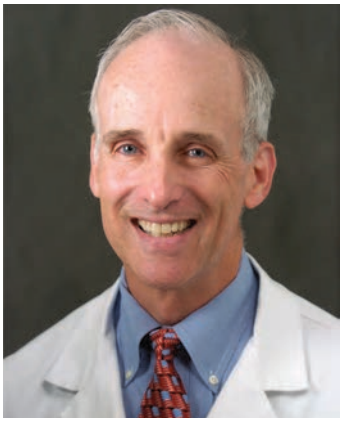
Scientific advances and their translation from bench to bedside were front and foremost in the hematology-oncology sphere during 2015 and were bolstered by a record number of therapy approvals by the US Food and Drug Administration (FDA).[1] The most recent of those approvals included elotuzumab and ixazomib (both with lenalidomide plus dexamethasone) for previously treated patients with multiple myeloma; and daratumumab as a single agent, also for previously treated multiple myeloma. In January, ofatumumab was approved for the extended treatment of patients in complete or partial response after treatment for recurrent or progressive chronic lymphocytic leukemia. It was quite a notable annual line-up of approvals for a single area of specialty.



Likewise, the presentations at the 2015 American Society of Hematology meeting in Orlando were outstanding. Investigators reported on sound, practice-changing scientific findings that could likely have a bearing on disease burden, patient outcomes, and patient quality of life (see p. 132). There were a number of standout reports, some of which I'll discuss here.

As the average age and life expectancy increase in the United States, there is a corresponding uptick in the incidence of myelodysplastic syndrome (MDS), which continues to present a therapeutic challenge among elderly patients. For anemia, we have always used the erythropoietin-stimulating agents (ESAs) first, with a fall-back to transfusion, but new science around a transforming growth factor-beta (TGF-beta)-block was presented at the meeting, with 2 exciting fusion proteins accomplishing this feat and demonstrating significant response rates for decreasing and occasionally eliminating the need for transfusion. ACE-536 (luspatercept) as a single agent was found to increase hemaglobin and reduce the transfusion burden in patients with MDS,[2] and for patients with multiple myeloma, preliminary data suggest that ACE-011 (sotatercept) in combination with lenalidomide and dexamethasone may yield early increases in hemoglobin and bone mineral density.[3] Also in MDS, eltrombopag, one of the drugs that received FDA approval last year, continues to impress both with its ability to increase platelet count and its broader stem-cell stimulation effect, which also decreases the transfusion burden.[4]

The former novel oral anticoagulants, or NOACs, have at last been renamed, since they are no longer considered novel, and are now referred to as DOACs, or direct-acting oral anticoagulants. The most widely used of the DOACs are rivaroxaban, a factor Xa inhibitor, and dabigatran, a direct thrombin inhibitor. Idazumumab is a new antibody (approved last year) that can instantly neutralize dabigatran, making it the first antidote to the anticoagulant's effect.[1] In addition, Lu and colleagues reported at the ASH meeting that factor Xa inhibition with anticoagulants such as apixaban or rivaroxaban can be reversed with andexanet alfa in a clinical trial setting.[5] I hope we will see it approved soon. That said, during an education program session at the meeting, participants reviewed data demonstrating that in a patient cohort of some 27,000 patients, the incidence of life-threatening bleeding was slightly lower in patients who received the DOACs than in those receiving the vitamin K antagonist.[6]

Finally, also reported at the meeting were the incredibly exciting developments in therapies for multiple myeloma. In particular, ixazomib, which was recently approved by the FDA, is an oral proteasome inhibitor taken once a week in combination with lenalidomide, an immunomodulatory drug, and dexamethasone by patients who have failed at least 1 regimen. Moreau and colleagues reported findings at the meeting showing that in patients with elapsed and/or refractory multiple myeloma, the addition of ixazomib to the lenalidomide-dexamethasone combination increased median progression-free survival to 20.6 months from 14.7 months, without a substantial increase in overall toxicity.[7]

As already noted, 2 antibodies – elotuzumab, an anti-SLAMF7 antibody, and daratumumab, an anti-CD 38 antibody – have been approved by the FDA. Elotuzumab has no single-agent activity, but has shown efficacy in combination with lenalidomide and dexamethasone.[8] It also has the curious side effect of causing patients to develop an abnormal (positive) indirect Coombs test, perhaps confus-

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ing our blood bank unless we inform them ahead of time that the patient is receiving this drug. Daratumumab does have single-agent activity.[9] It is an immunoglobulin G antibody, so it may confuse the serum protein electrophoresis test results in myeloma evaluation. The debate continues over whether or not to use autologous stem-cell transplant (ASCT) in first-line after early remission in multiple myeloma, but findings by French investigators have moved the debate in the direction of ASCT.[10] An American trial on the same topic is ongoing and its findings will be reported later this year.

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