Editorial

Michael J. Mauro

I am delighted to announce that *Therapeutic Advances in Hematology* is now on PubMed Central (PMC) and all articles will be free to view or download in HTML or PDF format from PubMed/PMC. This is a clear step forward for the journal; many thanks to the editorial team for their tireless efforts to see this to fruition and congratulations to all the editors and contributors in light of this acknowledgement of efforts past and present.

We bring you a very full issue presently; our first piece, from K. Kolibaba of Compass Oncology in my neighboring city of Vancouver, WA, in collaboration with colleagues in industry and managed care, provides a retrospective chart review of bendamustine, a nitrogen mustard type of alkylating agent approved in the US in 2008, in patients over 70 with CLL. Their data demonstrate ‘real-world’ efficacy for bendamustine with or without rituximab in relapsed and previously untreated CLL in the elderly and safety data consistent with expectations from trials. Such confirmation of aggregate trial data in a specific cohort, such as older patients as in this study, are both reassuring and supportive of incorporation of this agent more into treatment algorithms. The second article, from A. Shustov from the University of Washington /Fred Hutchinson Cancer Research Center, Seattle, singlehandedly reviews the approach to peripheral T-cell lymphoma. Beginning with the challenge of proper diagnosis, the report then covers the key studies and approval of three agents recently approved for use in this diagnosis: pralatrexate, a novel antifolate with encouraging data in relapsed and refractory patients, including post transplant; romidepsin, a class I histone deacetylase inhibitor, also proven effective in relapsed and refractory patients including the pretransplant setting given minimal effect on stem cell collection and engraftment; and brentuximab vedotin, an immunoconjugate of the antitubulin agent MMAE and CD30, highly effective and suitable

for relapsed and refractory patients including those proceeding to transplant and with preliminary data in the front-line awaiting maturity. The paper also covers novel combination programs under development and the potential for other novel agents, leaving us well informed about options for this diagnosis.

Next, C. Lobetti-Bodoni of the University of Torino, Italy, and colleagues provide an excellent perspective on testing for and implications of minimal residual disease in follicular lymphoma. They begin with an overview of risk and response assessment, including PET imaging, followed by an in-depth review of MRD testing based mainly in tumor specific translocations and immunoglobulin heavy chain rearrangement status, with a very helpful list of clinical ‘pearls’ relative to MRD testing. They close with insight into studies utilizing MRD assessment for prognostics and the expanding array of tools forthcoming for best characterization of patients with this common cancer. This is followed by a precise overview by V. Tosello and A. Ferrando from Columbia University Medical Center in New York, of the notch-signaling pathway in T-cell leukemia and lymphoma. They describe in detail the importance of the signaling pathway and its centrality to regulated T-cell development as well as the discovery of NOTCH1 mutations in T-ALL and subsequent downstream events. They then turn to clinical implications, reviewing the somewhat favorable response characteristics, the potential and limitations for gamma secretase inhibitor therapy approaches under development, and the potential broader role this target may have in oncology.

Moving through this issue, we next find, from A. McCurdy and M. Lacy, both of the Mayo Clinic Rochester, a very handy update for the hematologist on the next-generation immunomodulatory drug (IMiD), pomalidomide. They review its mechanisms of action (notoriously elusive for the

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Correspondence to:

Michael J. Mauro, MD
Oregon Health & Science
University, 3181 SW Sam
Jackson Park Road,
UHN-73C, Portland, OR
972395, USA
maurom@ohsu.edu

IMiDs) including the E3 ligase cereblon. They then systematically review the development of pomalidomide starting with phase I studies, highlighting the heavily pretreated patients and the specifics of prior therapy resistance (including other IMiDs such as lenalidomide, steroid-resistant, as well as bortezomib-resistant subsets). They cover the details of comparisons of dose and schedule for pomalidomide, activity in cases of extramedullary disease and last the toxicity profile of this agent. This paper indeed serves as a primer for the development and use of pomalidomide and we are glad to have it in *Therapeutic Advances in Hematology*. The issue then closes with a very thoughtful perspective from A. Zabalza and colleagues from Complejo Hospitalario de Navarra, Pamplona, Spain, on the antifungal voriconazole with a focus on its proper use, balancing benefit and risk. They describe the problem—increasingly fragile patients with hematologic malignancies and stem cell transplant, in whom

fungal infections, increasingly with filamentous fungi such as *Aspergillus*, are prevalent—and the potential solutions. They review in-depth the stratification of risk in such patients for these infections, then the strategies of prophylaxis and data from studies with other agents such as fluconazole and posaconazole. This is followed by a review of the two large randomized trials of voriconazole, the BMT-CTN and IMPROVIT studies, and the conclusions drawn about risk and benefit of voriconazole. Lastly they cover voriconazole level testing, resistance, and breakthrough infections.

Again, as always, I hope you will find this issue as informative as I have; as mentioned earlier, look for the collective papers published previously, herein, and in the future on PubMed and once again thank you to all the contributors for this issue.

Enjoy!

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