

The Lymphoma Medicine Cabinet

In the decade between 1996 and 2006, six new drugs were approved for lymphoma; in the subsequent 8 years, 12 new drugs were approved, and many others are in development. This edition of *CCR Focus* is aimed at the remarkable new developments in our understanding of lymphoma biology and the advent of a spate of new treatments, aptly labeled "stunning" by Guest Editors Owen O'Connor and Kensei Tobinai. Recently approved agents include a diversity of mechanisms of action—novel cytotoxic (bendamustine, pralatrexate, and a topical mustard), epigenetic (belinostat and romidepsin), targeted (ibrutinib and idelalisib), biologic (obinutuzumab, ofatumumab, and brentuximab vedotin), and immunomodulatory (lenalidomide). Add to that numerous agents in the pipeline, and the observation that some lymphomas can be treated with antibiotics when an infectious agent provides the antigenic stimulus driving the disease. Together, with rituximab and the classic B-cell lymphoma workhorses—cyclophosphamide, doxorubicin, vincristine, and prednisone—we now have what might seem to be an infinite number of potentially novel regimens for treating lymphoma. The questions of which patients should get what therapy and whether treatment intensity can be reduced must now be addressed. With that agenda, we also have to ask whether we need multiple agents of the same mechanism of action or aimed at the same target. The lesson from Bexxar, taken off the market by GlaxoSmithKline a decade after FDA approval, is that even a 74% complete response rate with 62% freedom from progression at 5 years does not guarantee a drug's acceptance and wide use when a myriad of alternatives exist (1, 2). According to the Surveillance Epidemiology and End Results database on cancer, a half-million individuals in the United States are living with lymphoma. Dividing these into the numerous subtypes that we now understand lymphoma to represent, each meets the rare disease definition. One can envision a future medicine cabinet for lymphoma, as seen in the figure, that includes drugs of broad applicability and others targeted to specific molecular aberrations. The experts contributing to this *CCR Focus* show us the future—therapy based on subsets of B-cell lymphoma identified by gene expression profile, proliferative index, or infectious etiology; "chemotherapy-free" regimens; and new treatment platforms for T-cell lymphomas. Stunning accomplishments, yes, but with great challenges for lymphoma drug development. As with every *CCR Focus* section, we strive to include articles that not only interest and inform the academic nonexpert but also challenge and encourage those already working in the field.

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See all articles in this *CCR Focus* section, "Paradigm Shifts in Lymphoma."

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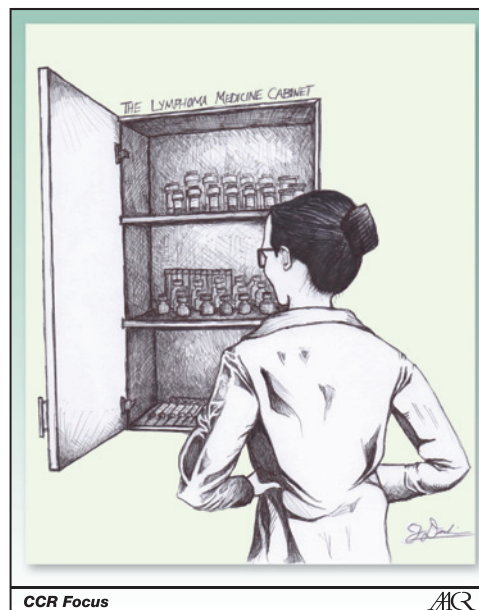


Figure 1. The lymphoma medicine cabinet. Image courtesy of Jacob Donkin.