

CD20-positive CLL. The study also included a rituximab in combination with chlorambucil arm [102].

Lymphoma Panel Recommendations:

- The panel had no specific recommendation for obinutuzumab for lymphoma as the results in this disease, as opposed to CLL, were not viewed as providing any significant clinical advantages over rituximab.

Alemtuzumab

Alemtuzumab is a recombinant DNA-derived humanized IgG1 kappa anti-CD52 monoclonal antibody indicated as a single agent for the treatment of B cell CLL. Alemtuzumab was initially FDA-approved in 2001 under accelerated approval and subsequently to regular approval based on an international, multicenter trial in 297 previously untreated CLL patients randomized to either alemtuzumab or chlorambucil [103]. The PFS was significantly longer in the alemtuzumab arm; no differences in survival were observed.

Lymphoma Panel Recommendations:

- Alemtuzumab significantly impairs most important immunologic effectors and potentially impairs the utility of other immunotherapeutics.
- CD52 is expressed by approximately half of all peripheral T cell lymphomas, and alemtuzumab has been used alone and in combination with conventional chemotherapy in their treatment. However, as with CLL, there is significant concern over toxicity and immunosuppression.

Other lymphoma immunotherapies

Lenalidomide

Lenalidomide, a thalidomide analogue, is an immunomodulatory agent with antiangiogenic and antineoplastic properties. Lenalidomide is FDA-approved for the treatment of mantle cell lymphoma (MCL) that has relapsed or progressed after two prior therapies, one of which included bortezomib. The approval of lenalidomide for MCL was based on a multicenter, single-arm, open-label trial of single-agent lenalidomide in 134 patients whose MCL had relapsed after or were refractory to bortezomib or a bortezomib-containing regimen [104]. Treatment with lenalidomide resulted in an ORR of 26%; the median duration of response was 16.6 months. The combination of lenalidomide plus rituximab (LR) has been investigated as initial therapy in MCL [105]. In a single-group, multicenter, phase 2 study, 38 patients with untreated MCL received lenalidomide (20 mg/day x 21 days of a 28-day cycle) as induction therapy for 12 cycles. Rituximab was administered once weekly for the first 4 weeks and then once every other cycle until

disease progression. The most common grade 3 or 4 adverse events were neutropenia (50%), rash (29%), thrombocytopenia (13%), an inflammatory syndrome (11%), anemia (in 11%), serum sickness (in 8%), and fatigue (in 8%). At the median follow-up of 30 months, the overall response rate in evaluable patients was 92%, and the CR rate was 64%. Median PFS had not been reached at the time of this report. The 2-year PFS and OS were estimated to be 85% and 97%, respectively. A response to treatment was associated with improvement in quality of life [105].

In a multicenter phase II/III study, DLBCL patients were stratified by germinal center B cell-like (GCB) versus non-GCB subtype, then randomized 1:1 to receive lenalidomide or investigator's choice (IC) chemotherapy until progressive disease, unacceptable toxicity, or voluntary withdrawal [106]. Patients with GCB or non-GCB DLBCL treated with lenalidomide had similar ORR, but the data suggested greater improvements in PFS and OS with lenalidomide versus IC in the non-GCB patients, particularly the ABC subtype. In the Alliance phase II trial, patients with relapsed follicular lymphoma (FL) were randomized to rituximab alone or lenalidomide alone or LR [107]. The rituximab-alone arm was discontinued as a result of poor accrual. The ORR was 53% (CR = 20%) and 76% (CR = 39%) for lenalidomide alone and LR, respectively ($P = 0.029$). Patients were treated until time of progression. At the median follow-up of 2.5 years, median time to progression was 1.1 years for lenalidomide alone and 2 years for LR ($P = 0.0023$).

Lymphoma Panel Recommendations:

- It was the consensus opinion that lenalidomide as a single agent has clinical activity in relapsed MCL and that LR was an option as initial therapy in untreated MCL based on level B evidence.
- It was the consensus opinion that lenalidomide has clinical activity in DLBCL based on level B evidence.
- The lenalidomide dose of 25 mg used in DLBCL is higher than clinicians are accustomed to using in CLL; however, the risk of toxicity and clots/thrombosis is decreased for lymphoma patients. For patients without standard risk factors for deep vein thrombosis, the panel suggested giving low-dose aspirin.
- The panel felt that clinical endpoints were needed to better define the duration of therapy for LR in FL.

Interferon (IFN)- α -2b

IFN- α -2b belongs to family of interferons, which are naturally occurring small proteins and glycoproteins produced and secreted by cells in response to viral infections and to synthetic or biological inducers. Interferons exert their effects through a complex sequence of