

NCCN Non-Hodgkin's Lymphomas Guidelines V.1.2013– Update Meeting – 06/14/12 and 06/15/12

Guidelines Page and Request	Panel Discussion	References	Vote		
			Yes	No	Abstain
Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (CLL/SLL)					
<p>CSLL-D Internal request: Panel discussion to include “lenalidomide” with or without rituximab as appropriate for the treatment of CLL.</p>	<p>Based on the noted references, the panel consensus was to add lenalidomide either with or without rituximab as an option for: CLL without del (11q) or del (17p) and CLL with del (11q)</p> <ul style="list-style-type: none"> • First-line therapy, age ≥ 70 y or younger patients with co-morbidities • Relapsed/refractory therapy, short response for both “age ≥70 y” and “for age <70 y or older patients without significant co-morbidities.” <p>CLL with del (11q)</p> <ul style="list-style-type: none"> • Relapsed/refractory therapy 	<ul style="list-style-type: none"> • Badoux XC, Keating MJ, Wen S, et al. Lenalidomide as initial therapy of elderly patients with chronic lymphocytic leukemia. <i>Blood</i> 2011;118:3489-3498. • Chen CI, Bergsagel PL, Paul H, et al. Single-agent lenalidomide in the treatment of previously untreated chronic lymphocytic leukemia. <i>J Clin Oncol</i> 2011;29:1175-1181. • Chanan-Khan A, Miller KC, Musial L, et al. Clinical efficacy of lenalidomide in patients with relapsed or refractory chronic lymphocytic leukemia: results of a phase II study. <i>J Clin Oncol</i> 2006;24:5343-5349. • Ferrajoli A, Lee BN, Schlette EJ, et al. Lenalidomide induces complete and partial remissions in patients with relapsed and refractory chronic lymphocytic leukemia. <i>Blood</i> 2008;111:5291-5297. • Badoux XC, Keating MJ, O'Brien SM, et al. Final analysis of a phase 2 study of lenalidomide and rituximab in patients with relapsed or refractory chronic lymphocytic leukemia (CLL) [abstract]. <i>Blood</i> 2011;118:Abstract 980. • Badoux XC, Keating MJ, Wen S, et al. Phase II Study of Lenalidomide and Rituximab As Salvage Therapy for Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia. <i>J Clin Oncol</i> 2012;31:584-591. 	26	1	0
<p>Internal request: Panel discussion comment to change “bendamustine with rituximab” to “bendamustine with or without rituximab.”</p>	<p>After panel discussion, the consensus was to change bendamustine with rituximab to bendamustine with or without rituximab as a treatment option for CLL without del (11q) or del (17p) and CLL with del (11q) cases for both first-line therapy and relapsed or refractory therapy to allow for the option of bendamustine monotherapy which reflects the available data.</p>		27	0	0

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Follicular Lymphoma					
<p>FOLL-B: Internal request: Panel discussion comment to remove “RFND (rituximab, fludarabine, mitoxantrone, dexamethasone)” as a first-line therapy option.</p> <p>Internal request: Panel discussion comment to remove “radioimmunotherapy” as a first-line therapy option.</p> <p>Internal request: Institutional review comment to remove “BVR (bendamustine, bortezomib, rituximab)” as a treatment option for second-line and subsequent therapy.</p> <p>Internal request: Panel discussion comment to add single agent “rituximab” as an option for second-line and subsequent therapy.</p> <p>External request: Submitted by Celgene Corporation to recommend the use of lenalidomide (with or without</p>	<p>The panel discussion and consensus was to remove RFND as a first-line therapy due to availability of other standard first-line treatment options, and potential concerns for stem cell toxicity with this regimen in patients who may undergo autologous transplant in the future.</p> <p>The panel discussion and consensus was to remove radioimmunotherapy as a first-line therapy due to the availability of other standard first-line treatment options. Radioimmunotherapy was retained as a first-line option for elderly patients.</p> <p>Based on the panel discussion, the consensus was to remove BVR regimen as a treatment option for second-line and extended dosing due to limited data to support its use in follicular lymphoma.</p> <p>Based on the noted references and panel discussion, the consensus was to add single agent rituximab as an option for second-line and subsequent therapy.</p> <p>Based on the noted references and panel discussion, the consensus was to add lenalidomide with or without rituximab as a treatment option for</p>	<ul style="list-style-type: none"> McLaughlin P, Grillo-Lopez AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. <i>J Clin Oncol</i> 1998;16:2825-2833. Ghielmini M, Schmitz SH, Cogliatti SB, et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly x 4 schedule. <i>Blood</i> 2004;103:4416-4423. Leonard JP, Jung S, Johnson J, et al. CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma [oral 	23	0	0
			18	4	1
			22	1	0
			23	0	0
			19	0	4

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rituximab) as a suggested treatment regimen in the guidelines for follicular lymphoma (grade 1-2) as second line and subsequent therapy with a Category 2A recommendation.	second-line and subsequent therapy.	<p>presentation]. Proceedings of the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2012; June 1-5; Chicago, IL; USA.</p> <ul style="list-style-type: none"> Dutia M, DeRoock I, Reed-Pease C, et al. Lenalidomide plus rituximab leads to a high rate of durable responses in patients with relapsed/refractory indolent non-Hodgkin's lymphoma [poster]. Poster presented at: 11th International Conference on Malignant Lymphoma (ICML) 2011; June 15-18; Lugano, Switzerland. 			
Mantle Cell Lymphoma					
<p>MANT-A: Internal request: Add all treatment steps to the CALGB 59909 regimen which includes: Treatment 3: etoposide, cytarabine, rituximab; Treatment 4: carmustine, etoposide, cyclophosphamide/ autologous stem cell rescue; Treatment 5: rituximab maintenance.</p> <p>Internal request: Clarify rituximab maintenance as a category 1 recommendation for the following treatment option, "CHOP + rituximab followed by consolidation <i>with rituximab maintenance</i> (375 mg/m2 every 8 wks until progression)."</p> <p>External request: Submitted by Genentech, Inc to consider the recently presented data on rituximab plus FC for the treatment MCL.</p>	<p>The panel discussion and consensus was to add the complete CALGB 59909 regimen to include treatments 3 through 5.</p> <p>The panel consensus was to clarify rituximab maintenance as a category 1 recommendation for patients treated with CHOP + rituximab followed by consolidation with rituximab maintenance.</p> <p>The panel consensus was that FC + rituximab is already included in the NHL Guidelines for the appropriate indications.</p>	<p>Damon LE, Johnson JL, Niedzwiecki D, et al. Immunochemotherapy and autologous stem-cell transplantation for untreated patients with mantle-cell lymphoma: CALGB 59909. J Clin Oncol 2009;27:6101-6108.</p> <p>Kluin-Nelemans HC, Hoster E, Hermine O, et al. Treatment of older patients with mantle-cell lymphoma. N Eng J Med 2012;367:520-531.</p>	23	0	0
			19	0	4

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Lymphoblastic Lymphoma					
<p>BLAST Due to the creation of the NCCN Guidelines for Acute Lymphoblastic Leukemia (ALL), all regimens were removed from the Lymphoblastic Lymphoma section. The LL Guidelines are now directed to the ALL Guidelines.</p>					
AIDS-Related B-cell Lymphomas					
<p>AIDS-2 Internal request: Panel discussion comment to remove “CDOP (cyclophosphamide, liposomal doxorubicin, vincristine, prednisone) + rituximab” as a treatment option for AIDS-related diffuse large B-cell lymphoma, lymphoma associated with Castleman’s disease, and primary effusion lymphoma.</p>	<p>Based on panel discussion and results of the AMC 047 trial that suggested that this regimen may be inferior to EPOCH-containing therapy in patients with AIDS-related NHL, the consensus was to remove CDOP-R as a treatment option for AIDS-related diffuse large B-cell lymphoma, lymphoma associated with Castleman’s disease, and primary effusion lymphoma.</p>	<p>Levine AM. A phase II trial of pegylated doxorubicin, rituximab, cyclophosphamide, vincristine, and prednisone (DR-COP) in patients with newly diagnosed AIDS-associated B-cell non-Hodgkin's lymphoma (ARL): An AIDS Malignancy Consortium trial (AMC 047) [abstract]. J Clin Oncol 2010;28:Abstract 8034.</p>	25	0	0
Peripheral T-Cell Lymphoma					
<p>TCEL-B Internal request: Panel discussion comment to add “dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)” as a treatment option for first-line and second-line therapy.</p>	<p>Based on data in the noted references and panel discussion, the consensus was to add dose-adjusted EPOCH as a treatment option for first-line and second-line therapy.</p>	<ul style="list-style-type: none"> Dunleavy K, Shovlin M, Pittaluga S, et al. DA-EPOCH Chemotherapy is highly effective in ALK-positive and ALK-negative ALCL: Results of a prospective study of PTCL subtypes in adults [abstract]. Blood 2011;118:Abstract 1618. Wilson WH, Bryant G, Bates S, et al. EPOCH chemotherapy: toxicity and efficacy in relapsed and refractory non-Hodgkin's lymphoma. J Clin Oncol 1993;11:1573-582. Peng YL, Huang HQ, Lin XB, et al. [Clinical outcomes of patients with peripheral T-cell lymphoma (PTCL) treated by EPOCH regimen]. 	26	1	0

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<p>Internal request: Panel discussion comment to review the NCCN category for pralatrexate for second-line therapy for candidates for transplant.</p> <p>Other: “Denileukin diftitox” was removed as a second-line therapy option as it is no longer commercially available.</p>	<p>Based on discussion, the panel consensus resulted in a change from a category 2B to a category 2A recommendation for pralatrexate for second-line therapy for candidates for transplant.</p>	<p>Ai Zheng 2004;23:943-946.</p>	<p>27</p>	<p>0</p>	<p>0</p>
<p>Mycosis Fungoides/Sezary Syndrome</p>					
<p>MFSS-A Other: “Denileukin diftitox” was removed as a systemic therapy option as it is no longer commercially available.</p>					
<p>Adult T-cell Leukemia/Lymphoma</p>					
<p>ATLL-C Internal request: Panel discussion comment to add “CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone)” as a suggested chemotherapy option.</p>	<p>Based on panel discussion, the consensus was to add CHOEP as an option for chemotherapy.</p>		<p>21</p>	<p>5</p>	<p>0</p>
<p>Extranodal NK/T-cell Lymphoma, nasal type</p>					
<p>NKTL-B Other: “Asparaginase” was replaced with “pegaspargase” in all associated regimens as “asparaginase” is no longer</p>					

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commercially available.					
Posttransplant Lymphoproliferative Disorder					
PTLD-A Internal request: Panel discussion comment for frail patients who cannot tolerate anthracycline to add: “RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine)” and “RCEOP (rituximab, cyclophosphamide, etoposide, vincristine, prednisone)”.	Based on panel discussion, the consensus was to add both “RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine)” and “RCEOP (rituximab, cyclophosphamide, etoposide, vincristine, prednisone)” for frail patients who cannot tolerate anthracycline.		27	0	0
Other					
External request: Submitted by BTG International Inc. to review the data for inclusion of (glucarpidase) for the treatment of toxic plasma methotrexate (MTX) concentrations in NHL patients receiving high-dose methotrexate therapy and who have delayed methotrexate clearance due to impaired renal function.	The panel discussion resulted in a statement being added to the Supportive Care for NHL page: “Consider use of glucarpidase if significant renal dysfunction and methotrexate levels are >10 microM beyond 42-48 h. Leucovorin remains a component in treatment of methotrexate toxicity and should be continued for at least 2 days following glucarpidase administration. However, be aware that leucovorin is a substrate for glucarpidase, and therefore should not be administered within two hours prior to or following glucarpidase.”		27	0	0
External request: Submitted by Genentech, Inc to consider updating the NCCN Guidelines with results from the recently presented Phase III RATE Trial, which evaluated the safety of accelerated infusions of Rituxan in patients with previously untreated diffuse large B-cell lymphoma (DLBCL) and follicular NHL.	After discussion, the panel consensus was not to make a change to the guidelines regarding accelerated rituximab infusion.		0	27	0

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External request: Submitted by Genentech, Inc to consider the recently presented data on the use of rituximab plus bendamustine for the treatment of indolent NHL for updating purposes.	The panel consensus was that bendamustine + rituximab is already included in the NHL Guidelines for the appropriate indications.				
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