

NCCN Non-Hodgkin's Lymphomas Guidelines V.1.2012– Update Meeting – 07/14/11 and 07/15/11

Guidelines Page and Request	Panel Discussion	References	Vote		
			Yes	No	Abstain
Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma					
<p>CSLL-D External request: Submitted by Genentech to consider the recently presented data on rituximab plus chlorambucil for the treatment of CLL.</p>	<p>Based on the noted references, the panel consensus was to add rituximab to chlorambucil as an option for:</p> <p>CLL without del (11q) or del (17p)</p> <ul style="list-style-type: none"> • Frail patients with significant co-morbidities • First-line therapy, age ≥ 70 y or younger patients with co-morbidities • Relapsed/refractory therapy, short response < 2 y for age ≥ 70 y. <p>CLL with del (11q)</p> <ul style="list-style-type: none"> • First-line therapy, age ≥ 70 y or younger patients with co-morbidities 	<p>Hillmen P, Gribben JG, Follows GA, et al. Rituximab plus chlorambucil (R-chlorambucil) as first-line treatment for chronic lymphocytic leukaemia (CLL): final analysis of an open-label phase II study. <i>Ann Oncol</i> 2011;22(suppl 4):iv123-iv124. ICML Abstract #016</p> <p>Mauro FR, Ciolli S, Di Raimondo F, et al. A phase II study of chlorambucil plus rituximab followed by maintenance versus observation in elderly patients with previously untreated chronic lymphocytic leukemia: results of the induction phase. <i>J Clin Oncol</i> 2011;29(suppl):abstract 6629.</p>	26	0	0
<p>CSLL-D: CLL with del(17p) Internal request: Institutional review comment to change high-dose dexamethasone to high-dose methylprednisolone (HDMP) for relapsed or refractory disease.</p> <p>Internal request: Panel discussion comment to remove bendamustine + rituximab for both first-line therapy and for relapsed or refractory therapy in del(17p) cases.</p>	<p>The panel discussion and consensus was to change the recommendation for high-dose dexamethasone to HDMP for patients with relapsed/refractory disease.</p> <p>Based on the noted reference, the panel discussion and consensus was to remove bendamustine + rituximab as a treatment option in del(17p) cases for both first-line therapy and relapsed or refractory therapy due to a low response rate.</p>	<p>Fischer K, Cramer P, Busch R, et al. Bendamustine combined with rituximab in patients with relapsed and/or refractory chronic lymphocytic leukemia multicenter phase 2 trial of the German Chronic Lymphocytic Leukemia Study Group. <i>J Clin Oncol.</i> 2011; 29(26):3559-3566.</p> <p>Fischer K, Cramer P, Stilgenbauer S, et al. Bendamustine combined with rituximab (BR) in first-line therapy of advanced CLL: a multicenter phase II trial of the German CLL Study Group</p>	26	0	0
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		(GCLLSG) [abstract]. Blood 2009;114:Abstract 205.			
Follicular Lymphoma					
<p>FOLL-B: Internal request: Panel discussion comment to change bendamustine plus rituximab from a category 1 to a category 2A recommendation for first-line therapy.</p> <p>Internal request: Institutional review comment to remove fludarabine-based regimens as initial therapy for follicular lymphoma and add to second-line or subsequent therapy</p> <p>Internal request: Panel discussion comment to change RFND (rituximab, fludarabine, mitoxantrone, dexamethasone) from a category 2A to a category 2B recommendation for first-line therapy.</p> <p>Internal request: Panel discussion comment to change radioimmunotherapy from a category 2B to a category 3 recommendation for first-line therapy.</p>	<p>The panel discussion and consensus was to change bendamustine plus rituximab from a category 1 to a category 2A recommendation because the data have not been fully published in a peer-reviewed journal. Further details regarding censored events are required in a full publication of the data.</p> <p>The panel discussion and consensus was to remove only fludarabine + rituximab from first-line therapy due to associated toxicities and include fludarabine + rituximab as a second-line or subsequent therapy.</p> <p>The panel discussion and consensus was to change RFND from a category 2A to a category 2B recommendation due to associated toxicity.</p> <p>The panel discussion and consensus was to change radioimmunotherapy from a category 2B to a category 3 recommendation for first-line therapy due to lack of phase III randomized data with RIT in this setting, and availability of other first-line therapy options.</p>	<p>Rummel MJ, Niederle N, Maschmeyer G, et al. Bendamustine plus rituximab is superior in respect of progression free survival and CR rate when compared to CHOP plus rituximab as first-line treatment of patients with advanced follicular, indolent, and mantle cell lymphomas: final results of a randomized phase III study of the StiL (Study Group Indolent Lymphomas, Germany) [abstract]. Blood 2009;114:Abstract 405</p>	20	6	0
			26	0	0
			9	9	8
			9	4	13

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<p>Internal request: Institutional review comment for the inclusion of BVR (bendamustine, bortezomib, rituximab) as a treatment option for second-line and extended dosing.</p>	<p>Based on the noted reference and panel discussion, the panel consensus was to include BVR as a treatment option for second-line and extended dosing.</p>	<p>Friedberg J. W., Vose J. M., et al. The combination of bendamustine, bortezomib, and rituximab for patients with relapsed/refractory indolent and mantle cell non-Hodgkin lymphoma. Blood 2011;117:2807-2812.</p>	17	1	8
<p>External request: Submitted by Millennium to include bortezomib with rituximab, with or without additional chemotherapy, within the suggested treatment regimens for ‘Second-line and Subsequent Therapy’ of FL (grade 1–2) as a category 2A treatment option.</p>	<p>Based on the noted reference and panel discussion, the panel consensus was to not include bortezomib combined with rituximab as an option for follicular lymphoma at this time, as the supporting study (published as abstract only) showed potentially excessive toxicities.</p>	<p>Coiffier B, Osmanov E, Hong X, et al. A phase 3 trial comparing bortezomib plus rituximab with rituximab alone in patients with relapsed, rituximab-naive or -sensitive, follicular lymphoma. Presented at the 52nd Annual Meeting of the American Society of Hematology (ASH) in Orlando, FL; December 4–7, 2010. Oral presentation, abstract #857.</p>	0	26	0
<p>External request: Submitted by Genentech to consider data on rituximab plus lenalidomide for the treatment of NHL.</p>	<p>Based on the noted references and discussion, the panel consensus was to not include rituximab plus lenalidomide for the treatment of follicular lymphoma until additional published data, including with longer follow-up, become available.</p>	<p>Fowler N, Hagemester F, Mclaughlin P, et al. Lenalidomide plus rituximab is a highly effective and well-tolerated biologic therapy in untreated indolent B cell non-hodgkin’s lymphoma. Ann Oncol 2011;22(suppl 4):iv128-iv129. ICML Abstract #137. Wang M, Fayad L, Wagner-Bartak N, et al. Oral lenalidomide plus 4 doses of rituximab induced prolonged remissions in relapsed/refractory mantle cell lymphoma: a completed phase I/II clinical trial. Ann Oncol 2011;22(suppl 4):iv119-iv120. ICML Abstract #109. Nowakowski G, Reeder CB, Laplant B, et al. Combination of lenalidomide with R-CHOP (R2CHOP) is safe and effective as initial therapy for aggressive B-cell lymphomas – a phase I/II study. Ann Oncol 2011;22(suppl 4):iv119-iv120. ICML Abstract #110.</p>	0	26	0

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Mantle Cell Lymphoma					
<p>MANT-A: Internal request: Institutional review comment to consider inclusion of front- line consolidation with rituximab maintenance only for patients treated with R-CHOP as initial therapy. External request: Submitted by Genentech to consider data on rituximab maintenance for the treatment of mantle cell lymphoma.</p>	<p>Based on data in the noted reference, the panel consensus was to include rituximab maintenance 375 mg/m² every 8 wks until progression as a suggested treatment regimens for patients treated with RCHOP without intention for high-dose therapy with stem cell rescue consolidation.</p>	<p>Kluin-Nelemans JC, Hoster E, Hermine O, et al. R-CHOP versus R-FC followed by maintenance with rituximab or IFN: first results of a randomized trial for elderly patients mantle cell lymphoma. Ann Oncol 2011;22(suppl 4):iv86-iv89. ICML Abstract #016.</p>	26	0	0
Diffuse Large B-Cell Lymphoma					

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<p>BCEL-3 External request: Submitted by Genentech to consider revising the number of rituximab treatment cycles to “up to eight cycles” for the treatment of DLBCL based on the recently presented data from the RICOVER-60 trial at the 2011 ASCO Annual Meeting and data from three pivotal, Phase III studies on the use of rituximab in combination with chemotherapy.</p>	<p>The panel consensus was to not include an additional 2 cycles of rituximab to RCHOP x 6 cycles based on the 6 cycles of RCHOP used in the large phase III study (MInT); in addition, 6 doses of rituximab given with 6 cycles of CHOP is more standard practice in the U.S.</p>	<p>Cunningham D, Smith P, Mouncey P, et al. R-CHOP14 versus R-CHOP21: Result of a randomized phase III trial for the treatment of patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma [abstract]. J Clin Oncol 2011;29: Abstract 8000.</p>	0	25	1
<p>BCEL-C Internal request: Institutional review comment to remove RCHOP-14 as a first-line therapy.</p>	<p>Based on panel discussion, the category was changed from a category 2B to category 3 due to potentially greater risk of toxicities associated with RCHOP-14 compared with RCHOP-21.</p>	<p>Delarue R, Tilly H, Salles G, et al. R-CHOP14 compared to R-CHOP 21 in elderly patients with diffuse large B-cell lymphoma: results of the interim analysis of the LNH03-6B GELA study [abstract]. Blood 2009;114:Abstract 406.</p>	14	7	5
<p>Internal request: Panel discussion comment to add bendamustine ± rituximab as an option for second-line therapy in non-candidates for transplant.</p>	<p>Based on the noted references, the panel consensus was to include bendamustine ± rituximab as an option for second-line therapy in non-candidates for transplant.</p>	<p>Ogura M, Ando K, Taniwaki M, et al. Feasibility and pharmacokinetic study of bendamustine hydrochloride in combination with rituximab in relapsed or refractory aggressive B cell non-Hodgkin's lymphoma. Cancer Sci 2011;102:1687-1692.</p>	26	0	0
<p>Internal request: Panel discussion comment to add GDP (gemcitabine, dexamethasone, carboplatin) ± rituximab for second-line therapy.</p>	<p>Based on the noted reference, the panel consensus was to include GDP (gemcitabine, dexamethasone, carboplatin) ± rituximab for second-line therapy.</p>	<p>Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma 2010;51:1523-1529.</p>	26	0	0
<p>Internal request: Panel discussion comment for the inclusion of treatment options for concurrent presentation with CNS disease.</p>	<p>Based on discussion and consensus, the panel added treatment options for both parenchymal (3 g/m² or more of systemic methotrexate at count recovery as an alternating regimen) and leptomeningeal (IT methotrexate/cytarabine, consider Ommaya reservoir placement and/or systemic methotrexate [3-3.5 g/m²]).</p>	<p>Abramson JS, Hellmann M, Barnes JA, et al. Intravenous methotrexate as central nervous system (CNS) prophylaxis is associated with a low risk of CNS recurrence in high-risk patients with diffuse large B-cell lymphoma. Cancer 2010;116:4283-4290.</p>	26	0	0

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Burkitt Lymphoma					
<p>BURK-A Internal request: Panel discussion comment for the inclusion of RICE (rituximab, ifosfamide, carboplatin, etoposide) for second-line therapy.</p> <p>Internal request: Panel discussion comment to change the CALGB 9251 regimen to the CALGB 10002 regimen with the addition of “+ rituximab.”</p>	<p>Based on noted reference, the panel consensus was to include RICE as an option for second-line therapy for select patients with a reasonable remission.</p>	<p>Griffin TC, Weitzman S, Weinstein H, et al. A study of rituximab and ifosfamide, carboplatin, and etoposide chemotherapy in children with recurrent/refractory B-cell (CD20+) non-Hodgkin lymphoma and mature B-cell acute lymphoblastic leukemia: a report from the Children's Oncology Group. <i>Pediatr Blood Cancer</i> 2009;52:177-181.</p>	26	0	0
	<p>Based on noted reference, the panel consensus was to include the CALGB 10002 regimen with the addition of rituximab.</p>	<p>Rizzieri DA, Johnson JL, Byrd JC, et al. Efficacy and toxicity of rituximab and brief duration, high intensity chemotherapy with filgrastim support for Burkitt or Burkitt-like leukemia/lymphoma: Cancer and Leukemia Group B (CALGB) Study 10002 [abstract]. <i>Blood</i> 2010;116: Abstract 858.</p>	26	0	0
AIDS-Related B-cell Lymphomas					
<p>AIDS-2 Internal request: Panel discussion comment to add hyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) ± rituximab as a treatment option for Burkitt lymphoma.</p> <p>Internal request: Panel discussion comment to remove CHOP with high-dose methotrexate ± rituximab as a treatment option for Burkitt lymphoma.</p>	<p>Based on the noted reference and discussion, the panel consensus was to include hyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) ± rituximab as a treatment option for AIDS-related lymphoma.</p>	<p>Cortes J, Thomas D, Rios A, et al. Hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone and highly active antiretroviral therapy for patients with acquired immunodeficiency syndrome-related Burkitt lymphoma/leukemia. <i>Cancer</i> 2002;94:1492-1499.</p>	23	1	0
	<p>Based on discussion and consensus, the panel removed CHOP with high-dose methotrexate ± rituximab as a treatment option for Burkitt lymphoma.</p>			24	0

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Peripheral T-Cell Lymphoma					
<p>TCEL-B Internal request: Panel discussion comment for the inclusion of CHOEP-21 (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone) for ALCL, ALK+ histology as first-line therapy.</p>	<p>Based on data in the noted reference, the panel consensus was to include CHOEP-21 (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone) for ALCL, ALK+ histology as first-line therapy.</p>	<p>Schmitz N, Trumper L, Ziepert M, et al. Treatment and prognosis of mature T-cell and NK-cell lymphoma: an analysis of patients with T-cell lymphoma treated in studies of the German High-Grade Non-Hodgkin Lymphoma Study Group. Blood 2010;116:3418-3425.</p>	24	0	0
Extranodal NK/T-cell Lymphoma, nasal type					
<p>NKTL-B Internal request: Panel discussion comment for the inclusion of the combination chemotherapy regimen AspaMetDex (L-asparaginase, methotrexate, and dexamethasone) as a suggested treatment option.</p> <p>Internal request: Panel discussion comment for the inclusion of sequential chemoradiation regimens:</p> <ul style="list-style-type: none"> • SMILE (steroid [dexamethasone], methotrexate, ifosfamide, L-asparaginase, and etoposide) followed by RT 45-50.4 Gy • VIPD (etoposide, ifosfamide, cisplatin, and dexamethasone) followed by RT 45-0.4 Gy 	<p>Based on noted reference, the panel consensus was to include combination chemotherapy regimen AspaMetDex (L-asparaginase, methotrexate, and dexamethasone) as a suggested treatment option.</p> <p>Based on panel consensus, the sequential chemoradiation regimens SMILE followed by RT and VIPD followed by RT were added as suggested treatment regimens.</p>	<p>Jaccard A, Gachard N, Marin B, et al. Efficacy of L-asparaginase with methotrexate and dexamethasone (AspaMetDex regimen) in patients with refractory or relapsing extranodal NK/T-cell lymphoma, a phase 2 study. Blood 2011;117:1834-1839.</p>	24	0	0
			24	0	0