DATA AND PERSPECTIVES

Clinical Investigators Review Key Publications and Current Cases in Multiple Myeloma and Non-Hodgkin Lymphoma

CME Information

TARGET AUDIENCE

This activity is intended for hematologists, medical oncologists and other allied healthcare professionals involved in the treatment of hematologic cancers.

OVERVIEW OF ACTIVITY

One would be hard pressed to find another area of medical oncology in which the research database is evolving as rapidly as it is in multiple myeloma (MM) and non-Hodgkin lymphoma (NHL). Taken together, it is estimated that approximately 156,420 new lymphoid and myeloid cancer cases will be identified in the United States in the year 2014, and 55,350 individuals will die from these diseases. Recent advances have led to an explosion of genetic and biologic knowledge among scientists and clinicians working in this area, culminating in more than 60 drug products labeled for use in the management of hematologic cancers with more than 70 distinct FDA-approved indications.

By providing access to the latest research developments and expert perspectives, these proceedings from a case-based CME symposium held at the 2014 ASCO Annual Meeting aim to assist hematologists, medical oncologists and other healthcare providers who must maintain up-to-date knowledge of appropriate clinical management strategies and ongoing research in these 2 distinct yet related diseases.

LEARNING OBJECTIVES

- Compare and contrast completed and ongoing clinical trials evaluating novel investigational approaches for B-cell lymphomas and chronic lymphocytic leukemia (CLL), and prioritize clinical trial opportunities or expanded-access programs available to patients based on this information.
- Appreciate the recent FDA approvals of ibrutinib and obinutuzumab, and discern how these agents can be appropriately integrated into clinical practice for patients with CLL.
- Customize the selection of systemic therapy for patients with progressive mantle-cell lymphoma, recognizing the recent addition of new FDA-endorsed options for these patients.

- Recognize the role of novel agents in the management of peripheral T-cell lymphoma and/or advanced-stage T-cell lymphomas, and ensure appropriate supportive care measures to minimize side effects.
- Compare and contrast the benefits and risks of available immunomodulatory agents, proteasome inhibitors or both as systemic treatment for newly diagnosed active MM.
- Customize the use of maintenance therapeutic approaches in the post-transplant and nontransplant settings based on patient- and disease-related factors, including cytogenetic profile.
- Consider available data on the selection, sequencing and/ or combination of carfilzomib and pomalidomide in the management of relapsed/refractory MM.
- Assess the ongoing clinical trials evaluating innovative investigational approaches for NHL and MM, and refer appropriate patients for study participation.

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Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Byrd JC et al. Targeting BTK with ibrutinib in relapsed chronic lymphocytic leukemia. N Engl J Med 2013;369(1):32-42.

Döhner H et al. Genomic aberrations and survival in chronic lymphocytic leukemia. N Engl J Med 2000;343(26):1910-6.

Farooqui M et al. Single agent ibrutinib (PCI-32765) achieves equally good and durable responses in chronic lymphocytic leukemia (CLL) patients with and without deletion 17p. *Proc ASH* 2013; Abstract 673.

Furman RR et al. Idelalisib and rituximab in relapsed chronic lymphocytic leukemia. N Engl J Med 2014;370(11):997-1007.

Goede V et al. **Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions.** *N Engl J Med* 2014;370(12):1101-10.

Porter DL et al. Randomized, Phase II dose optimization study of chimeric antigen receptor modified T cells directed against CD19 (CTL019) in patients with relapsed, refractory CLL. *Proc ASH* 2013; Abstract 873.

Seymour JF et al. Bcl-2 inhibitor ABT-199 (GDC-0199) monotherapy shows anti-tumor activity including complete remissions in high-risk relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). *Proc ASH* 2013; Abstract 872.

Urba WJ, Longo DL. Redirecting T cells. N Engl J Med 2011;365(8):754-7.

Sagar Lonial, MD

Boccadoro M et al. Melphalan/prednisone/lenalidomide (MPR) versus high-dose melphalan and autologous transplantation (MEL200) plus lenalidomide maintenance or no maintenance in newly diagnosed multiple myeloma (MM) patients. *Proc ASCO* 2013:Abstract 8509.

Facon T et al. Initial Phase 3 results of the First (Frontline Investigation of Lenalidomide + Dexamethasone versus Standard Thalidomide) trial (MM-020/IFM 07 01) in newly diagnosed multiple myeloma (NDMM) patients (Pts) ineligible for stem cell transplantation (SCT). *Proc ASH* 2013; Abstract 2.

Facon T et al. Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99-06): A randomised trial. *Lancet* 2007;370(9594):1209-18.

Gay F et al. Complete response correlates with long-term progression-free and overall survival in elderly myeloma treated with novel agents: Analysis of 1175 patients. *Blood* 2011;117(11):3025-31.

Hulin C et al. Efficacy of melphalan and prednisone plus thalidomide in patients older than **75** years with newly diagnosed multiple myeloma: IFM **01/01** trial. *J Clin Oncol* 2009;27(22):3664-70.

Jasielec J et al. Predictors of treatment outcome with the combination of carfilzomib, lenalidomide, and low-dose dexamethasone (CRd) in newly diagnosed multiple myeloma (NDMM). *Proc ASH* 2013; Abstract 3220.

Korde N et al. Phase II clinical and correlative study of carfilzomib, lenalidomide, and dexamethasone followed by lenalidomide extended dosing (CRD-R) induces high rates of MRD negativity in newly diagnosed multiple myeloma (MM) patients. *Proc ASH* 2013; Abstract 538.

Kumar SK et al. Weekly MLN9708, an investigational oral proteasome inhibitor, in relapsed/refractory multiple myeloma: Results from a Phase I study after full enrollment. *Proc ASCO* 2013; Abstract 8514.

Richardson PG et al. Twice-weekly oral MLN9708 (ixazomib citrate), an investigational proteasome inhibitor, in combination with lenalidomide (Len) and dexamethasone (Dex) in patients (Pts) with newly diagnosed multiple myeloma (MM): Final Phase 1 results and Phase 2 data. *Proc ASH* 2013; Abstract 535.

Singh PP et al. Lenalidomide maintenance therapy in multiple myeloma: A meta-analysis of randomized trials. *Proc ASH* 2013:Abstract 407.

Sonneveld P et al. Bortezomib induction and maintenance treatment improves survival in patients with newly diagnosed multiple myeloma: Extended follow-up of the HOVON-65/GMMG-HD4 trial. *Proc ASH* 2013; Abstract 404.

Stewart AK et al. How I treat multiple myeloma in younger patients. Blood 2009;114(27):5436-43.

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Colombat P et al. Rituximab induction immunotherapy for first-line low-tumor-burden follicular lymphoma: Survival analyses with 7-year follow-up. *Ann Oncol* 2012;23(9):2380-5.

Dreyling MH et al. The t(11;14) disorders: How biology can drive therapy. ASCO Educational Book 2006.

Feuerlein K. First-line treatment of follicular lymphoma: A patient-oriented algorithm. Leuk Lymphoma 2009;50(3):325-34.

Fowler NH et al. Lenalidomide and rituximab for untreated indolent lymphoma: Final results of a Phase II study. *Proc ASH* 2012; Abstract 901.

Ghielmini M et al. ESMO guidelines consensus conference on malignant lymphoma 2011 part 1: Diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL). *Ann Oncol* 2013;24(3):561-76.

Gopal AK et al. **PI3Ko** inhibition by idelalisib in patients with relapsed indolent lymphoma. N Engl J Med 2014;370(11):1008-18.

Hiddemann W et al. Evaluation of myeloablative therapy followed by autologous stem cell transplantation in first remission in patients with advanced stage follicular lymphoma after initial immuno-chemotherapy (R-CHOP) or chemotherapy alone: Analysis of 940 patients treated in prospective randomized trials of the German Low Grade Lymphoma Study Group (GLSG). *Proc ASH* 2013; Abstract 419.

Lopez-Guillermo A et al. A randomized Phase II study comparing consolidation with a single dose of ⁹⁰Y ibritumomab tiuxetan (Zevalin®) (Z) vs maintenance with rituximab (R) for two years in patients with newly diagnosed follicular lymphoma (FL) responding to R-CHOP. Preliminary results at 36 months from randomization. *Proc ASH* 2013; Abstract 369.

Taverna CJ et al. Rituximab maintenance treatment for a maximum of 5 years in follicular lymphoma: Results of the randomized Phase III trial SAKK 35/03. *Proc ASH* 2013; Abstract 508.

Michelle A Fanale, MD

Advani RH et al. Phase II study of cyclophosphamide, etoposide, vincristine and prednisone (CEOP) alternating with pralatrexate (P) as front line therapy for patients with peripheral T-cell Lymphoma (PTCL): Preliminary results from the T-cell consortium trial. *Proc ASH* 2013; Abstract 3044.

Coiffier B et al. Romidepsin for the treatment of relapsed/refractory peripheral T-cell lymphoma: Pivotal study update demonstrates durable responses. *J Hematol Oncol* 2014;7(1):11.

Coiffier B et al. Results from a pivotal, open-label, Phase II study of romidepsin in relapsed or refractory peripheral T-cell lymphoma after prior systemic therapy. *J Clin Oncol* 2012;30(6):631-6.

d'Amore F et al. **Up-front autologous stem-cell transplantation in peripheral T-cell lymphoma: NLG-T-01.** *J Clin Oncol* 2012;30(25):3093-9.

Friedberg JW et al. Phase II study of alisertib, a selective Aurora A kinase inhibitor, in relapsed and refractory aggressive **B-** and **T-cell non-Hodgkin lymphomas.** *J Clin Oncol* 2014;32(1):44-50.

O'Connor OA et al. Belinostat, a novel pan-histone deacetylase inhibitor (HDACi), in relapsed or refractory peripheral T-cell lymphoma (R/R PTCL): Results from the BELIEF trial. *Proc ASCO* 2013; Abstract 8507.

O'Connor OA et al. ECHELON-2: Phase 3 trial of brentuximab vedotin and CHP versus CHOP in the frontline treatment of patients (Pts) with CD30+ mature T-cell lymphomas (MTCL). Proc ICML 2013; Abstract 138.

O'Connor OA et al. Pralatrexate in patients with relapsed or refractory peripheral T-cell lymphoma: Results from the pivotal PROPEL study. *J Clin Oncol* 2011;29(9):1182-9.

Oki Y et al. A Phase I study of panobinostat in combination with ICE (ifosfamide, carboplatin and etoposide) in patients with relapsed or refractory classical Hodgkin lymphoma (cHL). *Proc ASH* 2013; Abstract 252.

Piekarz RL et al. Phase 2 trial of romidepsin in patients with peripheral T-cell lymphoma. Blood 2011;117(22):5827-34.

Pro B et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: Results of a Phase II study. *J Clin Oncol* 2012;30(18):2190-6.

Reimer P et al. Autologous stem-cell transplantation as first-line therapy in peripheral T-cell lymphomas: Results of a prospective multicenter study. *J Clin Oncol* 2009;27(1):106-13.

Savage KJ et al. MYC gene rearrangements are associated with a poor prognosis in diffuse large B-cell lymphoma patients treated with R-CHOP chemotherapy. *Blood* 2009;114(17):3533-7.

Savage KJ et al; International Peripheral T-Cell Lymphoma Project. ALK- anaplastic large-cell lymphoma is clinically and immunophenotypically different from both ALK+ ALCL and peripheral T-cell lymphoma, not otherwise specified: Report from the International Peripheral T-Cell Lymphoma Project. *Blood* 2008;111(12):5496-504.

Schmitz N 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(18):3418-25.

Shustov AR et al. Romidepsin is effective and well-tolerated in patients \geq 60 years old with relapsed or refractory peripheral T-cell lymphoma (PTCL): Analysis from Phase 2 trials. *Proc ASH* 2013; Abstract 4385.

Kenneth C Anderson, MD

de Weers M et al. Daratumumab, a novel therapeutic human CD38 monoclonal antibody, induces killing of multiple myeloma and other hematological tumors. *J Immunol* 2011;186(3):1840-8.

Demo SD et al. **Antitumor activity of PR-171**, a novel irreversible inhibitor of the proteasome. *Cancer Res* 2007;67(13):6383-91.

Dimopoulos MA et al. Final analysis, cytogenetics, long-term treatment, and long-term survival in MM-003, a Phase 3 study comparing pomalidomide + low-dose dexamethasone (POM + LoDEX) vs high-dose dexamethasone (HiDEX) in relapsed/refractory multiple myeloma (RRMM). *Proc ASH* 2013; Abstract 408.

Jagannath S et al. Pomalidomide (POM) with low-dose dexamethasone (LoDex) in patients (Pts) with relapsed and refractory multiple myeloma who have received prior therapy with lenalidomide (LEN) and bortezomib (BORT): Updated Phase 2 results and age subgroup analysis. *Proc ASH* 2012; Abstract 450.

Jakubowiak AJ et al. A Phase 1/2 study of carfilzomib in combination with lenalidomide and low-dose dexamethasone as a frontline treatment for multiple myeloma. *Blood* 2012;120(9):1801-9.

Kirk CJ et al. The selective proteasome inhibitor carfilzomib is well tolerated in experimental animals with dose intensive administration. *Proc ASH* 2008; Abstract 2765.

Laubach JP et al. Daratumumab granted breakthrough drug status. Expert Opin Investig Drugs 2014;23(4):445-52.

Leleu X et al. Pomalidomide plus low-dose dexamethasone is active and well tolerated in bortezomib and lenalidomide-refractory multiple myeloma: Intergroupe Francophone du Myélome 2009-02. *Blood* 2013;121(11):1968-75.

Lonial S et al. Prolonged survival and improved response rates with ARRY-520 in relapsed/refractory multiple myeloma (RRMM) patients with low α -1 acid glycoprotein (AAG) levels: Results from a Phase 2 study. *Proc ASH* 2013; Abstract 285.

Martin TG et al. SAR650984, a CD38 monoclonal antibody in patients with selected CD38+ hematological malignancies — Data from a dose-escalation Phase I study. *Proc ASH* 2013; Abstract 284.

National Comprehensive Cancer Network (NCCN®). NCCN clinical practice guidelines in oncology. Multiple myeloma — Version 2.2014. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

National Comprehensive Cancer Network (NCCN®). NCCN clinical practice guidelines in oncology. Non-Hodgkin's lymphomas — Version 2.2014. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

O'Donnell E, Raje NS. Targeting BRAF in multiple myeloma. Cancer Discov 2013;3(8):840-2.

Plesner T et al. Preliminary safety and efficacy data of daratumumab in combination with lenalidomide and dexamethasone in relapsed or refractory multiple myeloma. *Proc ASH* 2013; Abstract 1986.

Richardson PG et al. Panorama 1: A randomized, double-blind, Phase 3 study of panobinostat or placebo plus bortezomib and dexamethasone in relapsed or relapsed and refractory multiple myeloma. *Proc ASCO* 2014; Abstract 8510.

Richardson PG et al. Twice-weekly oral MLN9708 (ixazomib citrate), an investigational proteasome inhibitor, in combination with lenalidomide (Len) and dexamethasone (Dex) in patients (Pts) with newly diagnosed multiple myeloma (MM): Final Phase 1 results and Phase 2 data. *Proc ASH* 2013; Abstract 535.

Shah JJ et al. Phase I/II dose expansion of a multi-center trial of carfilzomib and pomalidomide with dexamethasone (Car-Pom-d) in patients with relapsed/refractory multiple myeloma. *Proc ASH* 2013; Abstract 690.

Siegel D et al. Integrated safety profile of single-agent carfilzomib: Experience from 526 patients enrolled in 4 phase II clinical studies. *Haematologica* 2013;98(11):1753-61.

Siegel DS et al. A Phase 2 study of single-agent carfilzomib (PX-171-003-A1) in patients with relapsed and refractory multiple myeloma. *Blood* 2012;120(14):2817-25.

Tai YT, Anderson KC. Antibody-based therapies in multiple myeloma. Bone Marrow Res 2011;2011:924058.

Tai YT et al. Anti-CS1 humanized monoclonal antibody HuLuc63 inhibits myeloma cell adhesion and induces antibody-dependent cellular cytotoxicity in the bone marrow milieu. *Blood* 2008;112(4):1329-37.

Terpos E et al. International Myeloma Working Group recommendations for the treatment of multiple myeloma-related bone disease. *J Clin Oncol* 2013;31(18):2347-57.

Wang M et al. Interim results from PX-171-006, a Phase II multicenter dose-expansion study of carfilzomib, lenalidomide, and low-dose dexamethasone in relapsed and/or refractory multiple myeloma. *Proc ASCO* 2011; Abstract 8025.

Yee A et al. ACY-1215, a selective histone deacetylase (HDAC) 6 inhibitor, in combination with lenalidomide and dexamethasone (dex), is well tolerated without dose limiting toxicity (DLT) in patients (Pts) with multiple myeloma (MM) at doses demonstrating biologic activity: Interim results of a Phase 1b trial. Proc ASH 2013; Abstract 3190.

Michael E Williams, MD, ScM

Cavalli F et al. Randomized Phase 3 study of rituximab, cyclophosphamide, doxorubicin, and prednisone plus vincristine (R-CHOP) or bortezomib (VR-CAP) in newly diagnosed mantle cell lymphoma (MCL) patients (pts) ineligible for bone marrow transplantation (BMT). *Proc ASCO* 2014;Abstract 8500.

Cheson BD et al. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. *J Clin Oncol* 1999:17(4):1244-53.

Fisher RI et al. Multicenter phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. *J Clin Oncol* 2006;24(30):4867-74.

Gandhi M et al. Impact of induction regimen and consolidative stem cell transplantation in patients with double hit lymphoma (DHL): A large multicenter retrospective analysis. *Proc ASH* 2013; Abstract 640.

Goy A et al. Single-agent lenalidomide in patients with mantle-cell lymphoma who relapsed or progressed after or were refractory to bortezomib: Phase II MCL-001 (EMERGE) study. *J Clin Oncol* 2013;31(29):3688-95.

Goy A et al. Phase II multicenter study of single-agent lenalidomide in subjects with mantle cell lymphoma who relapsed or progressed after or were refractory to bortezomib: The MCL-001 "EMERGE" study. *Proc ASH* 2012; Abstract 905.

Kane RC et al. Bortezomib for the treatment of mantle cell lymphoma. Clin Cancer Res 2007;13(18 Pt 1):5291-4.

Ramsay AG et al. Follicular lymphoma cells induce T-cell immunologic synapse dysfunction that can be repaired with lenalidomide: Implications for the tumor microenvironment and immunotherapy. *Blood* 2009;114(21):4713-20.

Ruan J et al. Combination biologic therapy without chemotherapy as initial treatment for mantle cell lymphoma: Multi-center Phase II study of lenalidomide plus rituximab. *Proc ASH* 2013; Abstract 247.

Vaidya R, Witzig TE. **Prognostic factors for diffuse large B-cell lymphoma in the R(X)CHOP era.** Ann Oncol 2014;[Epub ahead of print].

Wang ML et al. **Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma.** *N Engl J Med* 2013;369(6):507-16.

Witzig TE et al. Lenalidomide oral monotherapy produces durable responses in relapsed or refractory indolent non-Hodgkin's Lymphoma. *J Clin Oncol* 2009;27(32):5404-9.

Zhou Z et al. An enhanced International Prognostic Index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era. *Blood* 2014;123(6):837-42.