# VIRTUAL CONSULT

## Current Cases and Emerging Research in the Management of Multiple Myeloma, Hodgkin and Non-Hodgkin Lymphomas and Chronic Lymphocytic Leukemia

## CME Information

### TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of hematologic cancers, including lymphoma and multiple myeloma (MM).

### OVERVIEW OF ACTIVITY

Hematologic cancers include the lymphomas, the leukemias, MM and other related disorders (eg, myelodysplastic syndromes, myeloproliferative diseases) stemming from lymphoid and myeloid progenitor cell lines. Taken together, it is estimated that approximately 171,550 new lymphoid, myeloid and leukemic cancer cases will be identified in the United States in the year 2016, and 58,320 individuals will die from these diseases. Of note, more than 60 drug products are currently labeled for use in the management of hematologic cancers with more than 70 distinct FDA-approved indications. Although this extensive list of available treatment options is reassuring for patients and oncology healthcare professionals, it poses a challenge to the practicing clinician who must maintain up-to-date knowledge of appropriate clinical management strategies across a vast spectrum of liquid and solid tumors. This is particularly true, however, within the realm of Hodgkin and non-Hodgkin lymphoma and MM, where the past several years have yielded a staggering number of important clinical and research advances.

These video proceedings from a CME symposium held during the 2016 ASCO Annual Meeting feature discussions with leading researchers with an expertise in hematologic cancers regarding actual patient cases and related clinical research findings. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to not only improve clinicians' knowledge of recent data related to the rapidly evolving hematologic oncology treatment landscape but also to provide them with practical perspectives to help them become better and more effective caregivers.

### LEARNING OBJECTIVES

- Customize the use of induction, consolidation and maintenance therapeutic approaches for patients with MM in the post-transplant and nontransplant settings, considering patient- and disease-related factors, including cytogenetic profile.
- Consider available research data and other clinical factors in the best-practice selection, sequencing or combining of carfilzomib and pomalidomide in the nonresearch care of patients with relapsed/refractory (R/R) MM.
- Recognize the recent FDA approvals of daratumumab, elotuzumab, ixazomib and panobinostat, and effectively identify where and how these novel agents should be integrated into the clinical management of R/R MM.
- Appreciate the FDA approvals of novel targeted agents — ibrutinib, idelalisib, obinutuzumab and venetoclax — for the treatment of newly diagnosed and R/R chronic lymphocytic leukemia, and discern how these therapies can be appropriately integrated into the clinical management of standard- and high-risk disease.
- Consider existing and emerging clinical research data in the formulation of therapeutic recommendations for patients with newly diagnosed and R/R follicular lymphoma.
- Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the additions of bortezomib, ibrutinib and lenalidomide as FDA-endorsed options.
- Utilize emerging research information on the use of novel prognostic and predictive clinical and molecular markers to aid in treatment decision-making for patients with newly diagnosed and R/R diffuse large B-cell lymphoma.
- Incorporate new therapeutic strategies into the best-practice management of newly diagnosed and R/R Hodgkin lymphoma.
- Communicate the benefits and risks of evidence-based systemic and targeted treatments to patients with advanced cutaneous or peripheral T-cell lymphoma.
- Assess the ongoing clinical trials evaluating novel investigational approaches for Hodgkin and non-Hodgkin lymphoma and MM, and obtain consent from appropriate patients for study participation.

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Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/ASCOHem16/CME**.

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**FACULTY** — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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**Consulting Agreements:** Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, FORMA Therapeutics, Janssen Biotech Inc, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology; **Contracted Research:** Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Spectrum Pharmaceuticals Inc, Takeda Oncology.

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No relevant conflicts of interest to disclose.

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No relevant conflicts of interest to disclose.

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**Speakers Bureau:** Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Genentech BioOncology.

**MODERATOR** — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Agendia Inc, Amgen Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

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**Hardware/Software Requirements:**
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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## Select Publications


### Robert Z Orlowski, MD, PhD

Attal M et al. **Autologous transplantation for multiple myeloma in the era of new drugs: A phase III study of the Intergroupe Francophone du Myélome (IFM/DFCI 2009 trial).** *Proc ASH* 2015;**Abstract 391**.

Avet-Loiseau H et al. **Evaluation of minimal residual disease (MRD) by next generation sequencing (NGS) is highly predictive of progression free survival in the IFM/DFCI 2009 trial.** *Proc ASH* 2015;**Abstract 191**.

Berenson J et al. **Weekly carfilzomib with dexamethasone for patients with relapsed or refractory multiple myeloma: Updated results from the phase 1/2 study CHAMPION-1 (NCT01677858).** *Proc ASH* 2015;**Abstract 373**.

Durie B et al. **Bortezomib, lenalidomide and dexamethasone vs lenalidomide and dexamethasone in patients (pts) with previously untreated multiple myeloma without an intent for immediate autologous stem cell transplant (ASCT): Results of the randomized phase III trial SWOG S0777.** *Proc ASH* 2015;**Abstract 25**.

**ENDURANCE: Randomized phase III trial of bortezomib, lenalidomide and dexamethasone (VRd) versus carfilzomib, lenalidomide, dexamethasone (CRd) followed by limited or indefinite lenalidomide maintenance in patients with newly diagnosed symptomatic multiple myeloma. NCT01863550**

Moreau P et al. **Prospective evaluation of MRI and PET-CT at diagnosis and before maintenance therapy in symptomatic patients with multiple myeloma included in the IFM/DFCI 2009 trial.** *Proc ASH* 2015;**Abstract 395**.

Stewart AK et al. **Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma.** *N Engl J Med* 2015;372(2):142-52.

### Sagar Lonial, MD

Badros AZ et al. **A phase II study of anti PD-1 antibody pembrolizumab, pomalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM).** *Proc ASH* 2015;**Abstract 506**.

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.

Dimopoulos MA et al. **An open-label, randomised phase 3 study of daratumumab, lenalidomide, and dexamethasone (DRD) versus lenalidomide and dexamethasone (RD) in relapsed or refractory multiple myeloma (RRMM): POLLUX.** *Proc EHA* 2016;**Abstract LB2238**.

Dimopoulos MA et al. **ELOQUENT-2 update: A phase 3, randomized, open-label study of elotuzumab in combination with lenalidomide/dexamethasone in patients with relapsed/refractory multiple myeloma — 3-year safety and efficacy follow-up.** *Proc ASH* 2015;**Abstract 28**.

Krejcik J et al. **Immunomodulatory effects and adaptive immune response to daratumumab in multiple myeloma.** *Proc ASH* 2015;**Abstract 3037**.

Lin P et al. **Flow cytometric immunophenotypic analysis of 306 cases of multiple myeloma.** *Am J Clin Pathol* 2004;121(4):482-8.

Lonial S et al. **Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): An open-label, randomised, phase 2 trial.** *Lancet* 2016;387(10027):1551-60.

Lonial S et al. **ELOQUENT-2: A phase III, randomized, open-label study of lenalidomide (Len)/dexamethasone (dex) with/without elotuzumab (Elo) in patients (pts) with relapsed/refractory multiple myeloma (RRMM).** *Proc ASCO* 2015;**Abstract 8508**.

Moreau P et al. **Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma.** *N Engl J Med* 2016;374(17):1621-34.

Overdijk MB et al. **Antibody-mediated phagocytosis contributes to the anti-tumor activity of the therapeutic antibody daratumumab in lymphoma and multiple myeloma.** *MAbs* 2015;7(2):311-21.

Palumbo A et al. **Phase III randomized controlled study of daratumumab, bortezomib, and dexamethasone (DVd) versus bortezomib and dexamethasone (Vd) in patients (pts) with relapsed or refractory multiple myeloma (RRMM): CASTOR study.** *Proc ASCO* 2016;**Abstract LBA4**.

San Miguel J et al. **Pembrolizumab in combination with lenalidomide and low-dose dexamethasone for relapsed/refractory multiple myeloma (RRMM): Keynote-023.** *Proc ASH* 2015;**Abstract 505**.

Santonocito AM et al. **Flow cytometric detection of aneuploid CD38(++) plasma cells and CD19(+) B-lymphocytes in bone marrow, peripheral blood and PBSC harvest in multiple myeloma patients.** *Leuk Res* 2004;28(5):469-77.

## Select Publications


### Brad S Kahl, MD

**A randomized phase III study of bendamustine plus rituximab versus ibrutinib plus rituximab versus ibrutinib alone in untreated older patients (≥ 65 years of age) with chronic lymphocytic leukemia (CLL). NCT01886872**

**A randomized phase III study of ibrutinib (PCI-32765)-based therapy vs standard fludarabine, cyclophosphamide, and rituximab (FCR) chemoimmunotherapy in untreated younger patients with chronic lymphocytic leukemia (CLL). NCT02048813**

Burger JA et al. **Ibrutinib as initial therapy for patients with chronic lymphocytic leukemia.** *N Engl J Med* 2015;373(25):2425-37.

Byrd J et al. **Acalabrutinib (ACP-196) in relapsed chronic lymphocytic leukemia.** *N Engl J Med* 2016;374(4):323-32.

Byrd JC et al. **Three-year follow-up of treatment-naïve and previously treated patients with CLL and SLL receiving single-agent ibrutinib.** *Blood* 2015;125(16):2497-506.

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

Roberts AW et al. **Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia.** *N Engl J Med* 2016;374(4):311-22.

Rossi D et al. **Molecular prediction of durable remission after first-line fludarabine-cyclophosphamide-rituximab in chronic lymphocytic leukemia.** *Blood* 2015;126(16):1921-4.

Stilgenbauer S et al. **Venetoclax (ABT-199/GDC-0199) monotherapy induces deep remissions, including complete remission and undetectable MRD, in ultra-high risk relapsed/refractory chronic lymphocytic leukemia with 17p deletion: Results of the pivotal international phase 2 study.** *Proc ASH* 2015;**Abstract LBA-6**.

### Ranjana Advani, MD

Advani RH et al. **Randomized phase III trial comparing ABVD plus radiotherapy with the Stanford V regimen in patients with stages I or II locally extensive, bulky mediastinal Hodgkin lymphoma: A subset analysis of the North American Intergroup E2496 trial.** *J Clin Oncol* 2015;33(17):1936-42.

Armand P et al. **A phase 2 study of a nivolumab (nivo)-containing regimen in patients (pts) with newly diagnosed classical Hodgkin lymphoma (cHL): Study 205 cohort D.** *Proc ASCO* 2016;**Abstract TPS7573**.

Ansell SM et al. **PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma.** *N Engl J Med* 2015;372(4):311-9.

Bonadonna G et al. **ABVD plus subtotal nodal versus involved-field radiotherapy in early-stage Hodgkin's disease: Long-term results.** *J Clin Oncol* 2004;22(14):2835-41.

Cassady KM et al. **PD-L1/CD80 and PD-L1/PD-1 signaling reciprocally regulate alloreactive CD8+ T cell glycolysis, proliferation, apoptosis and GVHD-inducing capacity.** *Proc ASH* 2015;**Abstract 4282**.

Chen R et al. **Results of a multicenter phase II trial of brentuximab vedotin as second-line therapy before autologous transplantation in relapsed/refractory Hodgkin lymphoma.** *Biol Blood Marrow Transplant* 2015;21(12):2136-40.

Garcia-Sanz R et al. **Evaluation of the regimen brentuximab vedotin plus ESHAP (BRESHAP) in refractory or relapsed Hodgkin lymphoma patients: Preliminary results of a phase I-II trial from the Spanish group of lymphoma and bone marrow transplantation (GELTAMO).** *Proc ASH* 2015;**Abstract 582**.

LaCasce AS et al. **Brentuximab vedotin in combination with bendamustine for patients with Hodgkin lymphoma who are relapsed or refractory after frontline therapy.** *Proc ASH* 2015;**Abstract 293**.

LaCasce AS et al. **Brentuximab vedotin plus bendamustine: A highly active salvage treatment regimen for patients with relapsed or refractory Hodgkin lymphoma.** *Proc ASH* 2015;**Abstract 3982**.

Moskowitz AJ et al. **PET-adapted sequential salvage therapy with brentuximab vedotin followed by augmented ifosfamide, carboplatin, and etoposide for patients with relapsed and refractory Hodgkin's lymphoma: A non-randomised, open-label, single-centre, phase 2 study.** *Lancet Oncol* 2015;16(3):284-92.

Moskowitz CH et al. **Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2015;385(9980):1853-62.

Moskowitz CH et al. **PD-1 blockade with the monoclonal antibody pembrolizumab (MK-3475) in patients with classical Hodgkin lymphoma after brentuximab vedotin failure: Preliminary results from a phase 1b study (KEYNOTE-013).** *Proc ASH* 2014;**Abstract 290**.

## Select Publications


Radford J et al. **Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma.** *N Engl J Med* 2015;372(17):1598-607.

Raemaekers JM et al. **Early FDG-PET adapted treatment improves the outcome of early FDG-PET-positive patients with stages I/II Hodgkin lymphoma (HL): Final results of the randomized Intergroup EORTC/LYSA/FIL H10 trial.** *Proc ICML* 2015;**Abstract 20051**.

Raemaekers JM et al. **Omitting radiotherapy in early positron emission tomography-negative stage I/II Hodgkin lymphoma is associated with an increased risk of early relapse: Clinical results of the preplanned interim analysis of the randomized EORTC/LYSA/FIL H10 trial.** *J Clin Oncol* 2014;32(12):1188-94.

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Stathis A, Younes A. **The new therapeutical scenario of Hodgkin lymphoma.** *Ann Oncol* 2015;26(10):2026-33.


### Stephen M Ansell, MD, PhD


Ardeshna KM et al. **Rituximab versus a watch-and-wait approach in patients with advanced-stage, asymptomatic, non-bulky follicular lymphoma: An open-label randomised phase 3 trial.** *Lancet Oncol* 2014;15(4):424-35.

Coutré SE et al. **Management of adverse events associated with idelalisib treatment: Expert panel opinion.** *Leuk Lymphoma* 2015;56(10):2779-86.

Dreyling M et al. **Ibrutinib versus temsirolimus in patients with relapsed or refractory mantle-cell lymphoma: An international, randomised, open-label, phase 3 study.** *Lancet* 2016;387(10020):770-8.

Fowler NH et al. **Safety and activity of lenalidomide and rituximab in untreated indolent lymphoma: An open-label, phase 2 trial.** *Lancet Oncol* 2014;15(12):1311-8.

Gopal AK et al. **PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma.** *N Engl J Med* 2014;370(11):1008-18.

Humala K, Younes A. **Current and emerging new treatment strategies for mantle cell lymphoma.** *Leuk Lymphoma* 2013;54(5):912-21.

Kahl BS et al. **Rituximab extended schedule or re-treatment trial for low-tumor burden follicular lymphoma: Eastern Cooperative Oncology Group protocol E4402.** *J Clin Oncol* 2014;32(28):3096-102.

Martin P et al. **Outcome of deferred initial therapy in mantle-cell lymphoma.** *J Clin Oncol* 2009;27(8):1209-13.

Robak T et al. **Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma.** *N Engl J Med* 2015;372(10):944-53.

Ruan J et al. **Lenalidomide plus rituximab as initial treatment for mantle-cell lymphoma.** *N Engl J Med* 2015;373(19):1835-44.

Rummel MJ et al. **Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: An open-label, multicentre, randomised, phase 3 non-inferiority trial.** *Lancet* 2013;381(9873):1203-10.

Sehn LH et al. **GADOLIN: Primary results from a phase III study of obinutuzumab plus bendamustine compared with bendamustine alone in patients with rituximab-refractory indolent non-Hodgkin lymphoma.** *Proc ASH* 2015;**Abstract LBA8502**.

Sehn LH et al. **Randomized phase II trial comparing obinutuzumab (GA101) with rituximab in patients with relapsed CD20+ indolent B-cell non-Hodgkin lymphoma: Final analysis of the GAUSS study.** *J Clin Oncol* 2015;33(30):3467-74.

Trněný M et al. **Lenalidomide versus investigator's choice in relapsed or refractory mantle cell lymphoma (MCL-002; SPRINT): A phase 2, randomised, multicentre trial.** *Lancet Oncol* 2016;17(3):319-31.


### Christopher Flowers, MD, MS


Bossard C et al. **Immunohistochemistry as a valuable tool to assess CD30 expression in peripheral T-cell lymphomas: High correlation with mRNA levels.** *Blood* 2014;124(19):2983-6.

Foss F et al. **Romidepsin for the treatment of relapsed/refractory peripheral T cell lymphoma: Prolonged stable disease provides clinical benefits for patients in the pivotal trial.** *J Hematol Oncol* 2016;9:22.

**GOYA: A phase III, multicenter, open-label randomized trial comparing the efficacy of GA101 (RO5072759) in combination with CHOP (G-CHOP) versus rituximab and CHOP (R-CHOP) in previously untreated patients with CD20-positive diffuse large B-cell lymphoma (DLBCL). NCT01287741**

## Select Publications


Hernandez-Ilizaliturri FJ et al. **Higher response to lenalidomide in relapsed/refractory diffuse large B-cell lymphoma in nongerminal center B-cell-like than in germinal center B-cell-like phenotype.** *Cancer* 2011;117(22):5058-66.

Horwitz SM et al. **Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin.** *Blood* 2014;123(20):3095-100.

Jacobsen ED et al. **Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression.** *Blood* 2015;125(9):1394-402.

Lamarque M et al. **Brentuximab vedotin in refractory or relapsed peripheral T-cell lymphomas: The French named patient program experience in 56 patients.** *Haematologica* 2016;101(3):e103-6.

Lugtenburg PJ et al. **Randomized phase III study on the effect of early intensification of rituximab in combination with 2-weekly CHOP chemotherapy followed by rituximab or no maintenance in patients with diffuse large B-cell lymphoma: Results from a HOVON-Nordic Lymphoma Group study.** *Proc ASCO* 2016;**Abstract 7504**.

Nowakowski GS et al. **Lenalidomide combined with R-CHOP overcomes negative prognostic impact of non-germinal center B-cell phenotype in newly diagnosed diffuse large B-cell lymphoma: A phase II study.** *J Clin Oncol* 2015;33(3):251-7.

O'Connor OA et al. **Belinostat in patients with relapsed or refractory peripheral T-cell lymphoma: Results of the pivotal phase II BELIEF (CLN-19) study.** *J Clin Oncol* 2015;33(23):2492-9.

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.

Pilorge S et al. **Primary bone diffuse large B-cell lymphoma: A retrospective evaluation on 76 cases from French institutional and LYSA studies.** *Leuk Lymphoma* 2016:1-7.

**PYRAMID: An open-label, randomized, phase 2 study to assess the effectiveness of RCHOP with or without Velcade in previously untreated non-germinal center B-cell-like diffuse large B-cell lymphoma patients. NCT00931918**

**Randomized phase II open label study of lenalidomide R-CHOP (R2CHOP) vs RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) in patients with newly diagnosed diffuse large B-cell lymphoma. NCT01856192**

**REMoDL-B: A randomised evaluation of molecular guided therapy for diffuse large B-cell lymphoma with bortezomib. NCT01324596**

Slack GW et al. **CD30 expression in de novo diffuse large B-cell lymphoma: A population-based study from British Columbia.** *Br J Haematol* 2014;167(5):608-17.

Witzig TE et al. **PILLAR-2: A randomized, double-blind, placebo-controlled, phase III study of adjuvant everolimus (EVE) in patients (pts) with poor-risk diffuse large B-cell lymphoma (DLBCL).** *Proc ASCO* 2016;**Abstract 7506**.

Zinzani et al. **Romidepsin in relapsed/refractory T-cell lymphomas: Italian experience and results of a named patient program.** *Leuk Lymphoma* 2016;57(10):2370-4.