

FACULTY INTERVIEWS

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Hematology Meeting in Orlando, Florida

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OVERVIEW OF ACTIVITY

Hematologic oncology is one of the most rapidly evolving fields in medicine. Results presented at major cancer conferences from a plethora of ongoing clinical trials lead to the continual emergence of new therapeutic agents and changes in the indications for existing treatments. In order to offer optimal patient care, the practicing hematologist-oncologist must be well informed of these advances. To bridge the gap between research and patient care, this issue of *Cancer Conference Update* uses one-on-one discussions with Drs Moskowitz, Orlowski, Leonard, Shah, Pinter-Brown and Garcia-Manero to apply clinical trial data presented at the 2010 American Society of Hematology Annual Meeting in Orlando, Florida to the management of various types of hematologic cancer. This CME activity is thus designed to assist hematologist-oncologists with the formulation of up-to-date therapeutic algorithms for patients with lymphoid and myeloid cancer.

LEARNING OBJECTIVES

- Apply emerging clinical trial data to the evidence-based selection of treatment for patients with hematologic cancer.
- Develop evidence-based treatment algorithms for frequently encountered adult chronic leukemias.
- Summarize emerging data with novel agents/combinations and radioimmunotherapy approaches for newly diagnosed or relapsed/refractory indolent or aggressive B-cell non-Hodgkin lymphomas.
- Tailor up-front/induction therapy based on individual and disease characteristics for patients with multiple myeloma (MM).
- Evaluate consolidation and maintenance therapy approaches for patients with MM.
- Describe the standard therapeutic approaches and investigational strategies for the treatment of acute promyelocytic leukemia (APL).
- Recall the efficacy and side effects of hypomethylating and immunomodulating agents in the treatment
 of myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).
- Describe therapeutic options for patients with peripheral and cutaneous T-cell lymphomas (PTCL and CTCL).

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AUDIO PROGRAM GUIDE



HODGKIN LYMPHOMA, DIFFUSE LARGE B-CELL LYMPHOMA Papers discussed by Craig Moskowitz, MD

Clinical Director, Division of Hematologic Oncology Member, Lymphoma Service Memorial Sloan-Kettering Cancer Center New York, New York

TRACKS

- Abstract 283: Results of a pivotal Phase II study of brentuximab vedotin (SGN-35) in relapsed or refractory Hodgkin lymphoma (HL)
- 2 Abstract 415: A Phase III trial of ABVD versus Stanford V with or without radiation therapy for locally extensive and advancedstage HL (Intergroup E2496)
- **3** Abstract 2828: Lenalidomide for relapsed or refractory HL
- 4 Abstract 764: Assessment of residual bulky tumor using FDG-PET in advanced-stage HL after completion of chemotherapy: Final report of GHSG HD15
- 5 Abstract 3879: Early interim

 18f-FDG PET in HL
- 6 Abstract 590: R-CHOP with iodine I 131 tositumomab consolidation (SWOG-S0433) for advancedstage diffuse large B-cell lymphoma (DLBCL)

- 7 Abstract 2871: REALO7 Phase I/II pilot study of lenalidomide and R-CHOP21 for elderly patients with untreated DLBCL
- 8 Abstract 2806: Bendamustine and rituximab for elderly patients with relapsed or refractory DLBCL
- 9 Abstract 420: Sequential dosedense R-CHOP followed by ICE consolidation without radiation therapy for primary mediastinal large B-cell lymphoma (MSKCC 01-142)
- 10 Abstract 320: Interim ¹⁸f-FDG PET SUVmax reduction is superior to visual analysis to predict early patient outcomes in DLBCL
- 11 Clinical approach to interim PET assessment in DLBCL



MULTIPLE MYELOMA Papers discussed by Robert Z Orlowski, MD, PhD

Director, Myeloma Section; Associate Professor, Departments of Lymphoma/ Myeloma and Experimental Therapeutics, Division of Cancer Medicine The University of Texas MD Anderson Cancer Center Houston, Texas

- 1 Abstract 619: Phase IIIb UPFRONT study of weekly bortezomib maintenance therapy after bortezomib-based induction regimens for elderly patients with newly diagnosed MM
- 2 Abstract 621: Randomized, Phase II EVOLUTION study of novel three- and four-drug combination regimens of bortezomib, dexamethasone, cyclophosphamide and lenalidomide for untreated MM

- 3 Selection of induction therapy for patients with newly diagnosed MM who are eligible or ineligible for transplant
- 4 Abstract 624: IFM 2008 Phase II study of front-line therapy with bortezomib, lenalidomide and dexamethasone (VRD) induction followed by autologous stem cell transplant (ASCT), VRD consolidation and lenalidomide maintenance therapy for newly diagnosed MM
- 5 Perspective on the use of post-transplant maintenance lenalidomide in MM
- 6 Abstract 862: A Phase I/II MMRC study of carfilzomib, lenalidomide and dexamethasone in newly diagnosed MM

- 7 Viewpoint on carfilzomibversus bortezomib-associated neurotoxicity
- 8 Clinical strategies to reduce bortezomib-related neurotoxicity
- 9 Response to carfilzomib in patients with disease resistant to bortezomib-containing regimens
- 10 Abstract 1948: A Phase I study of lenalidomide, thalidomide and dexamethasone in relapsed or refractory MM
- 11 Abstracts 859, 863: Pomalidomide with low-dose dexamethasone in relapsed or refractory MM
- 12 Abstract 989: Safety and efficacy of bendamustine, lenalidomide and dexamethasone in a Phase I trial for relapsed or refractory MM



FOLLICULAR LYMPHOMA, MANTLE-CELL LYMPHOMA, CHRONIC LYMPHOCYTIC LEUKEMIA Papers discussed by John P Leonard, MD

Richard T Silver Distinguished Professor of Hematology and Medical Oncology Professor of Medicine, Weill Cornell Medical College; Associate Director for Clinical Research, Weill Cornell Cancer Center; Clinical Director, Center for Lymphoma and Myeloma; Attending Physician, NewYork-Presbyterian Hospital New York, New York

- Abstract 6: Preliminary analysis of an Intergroup randomized trial of rituximab versus watch and wait for Stage II to IV, asymptomatic, nonbulky follicular lymphoma (FL)
- 2 Abstract 1788: Updated results of the PRIMA trial confirming the benefit of two years of rituximab maintenance therapy for patients with FL responding to immunochemotherapy
- 3 Abstract 594: Updated 66-month First-line Indolent Trial (FIT) results with 90Y-ibritumomab tiuxetan consolidation of first remission in advanced-stage FL

- 4 Abstract 857: A Phase III trial of bortezomib/rituximab versus rituximab alone in relapsed, rituximab-naïve or rituximab-sensitive FL
- 5 Clinical investigation of bortezomib with R/chemotherapy in non-Hodgkin lymphoma
- 6 Abstract 856: Final results of the Phase III NHL 2-2003 study of bendamustine/rituximab versus fludarabine/rituximab in relapsed FL, indolent lymphoma and mantle-cell lymphoma (MCL)

- 7 Bendamustine/rituximab platform for future cooperative group investigations in MCL and FL
- 8 Abstract 1395: Lenalidomide/ rituximab induces complete and partial responses in relapsed or refractory chronic lymphocytic leukemia (CLL)
- 9 Abstract 1379: Lenalidomide consolidation therapy after firstline chemoimmunotherapy for previously untreated CLL

- **10** Activity of lenalidomide in indolent and aggressive lymphomas
- 11 Abstract 2449: Bendamustine induces higher remission rates and prolongs progression-free survival, time to next treatment and overall survival for patients in complete remission when compared to initial treatment with chlorambucil in CLL



CHRONIC MYELOID LEUKEMIA Papers discussed by Neil P Shah, MD, PhD

Co-Leader, Hematologic Malignancies Program, UCSF Helen Diller Comprehensive Cancer Center; Assistant Professor of Medicine Division of Hematology/Oncology, University of California, San Francisco San Francisco. California

- Abstract 206: Dasatinib versus imatinib in newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) in the DASISION trial
- 2 Selection of a BCR-ABL inhibitor for the initial treatment of CML
- 3 Abstract 3421: Safety and efficacy of dasatinib versus imatinib by baseline comorbidity in the DASISION study
- 4 Dasatinib-associated pleural effusion
- 5 Abstract LBA-6: A randomized Phase II study of dasatinib 100 mg versus imatinib 400 mg in newly diagnosed CML-CP (Intergroup S0325 trial)
- 6 Abstract 358: Lymphocytosis after first-line dasatinib for CML-CP is associated with improved responses: An evaluation of imatinib

- 7 Abstract 207: Continued superiority of nilotinib versus imatinib in newly diagnosed CML-CP (ENESTnd trial update)
- 8 Abstract 2291: Cardiac safety profile of imatinib and nilotinib in newly diagnosed CML-CP (ENESTnd trial)
- 9 Abstract 2301: Patients with Philadelphia-positive CML-CP with a suboptimal molecular response to imatinib can achieve deeper responses when switched to nilotinib
- 10 Abstract 208: A Phase III study of bosutinib (SKI-606) versus imatinib in newly diagnosed CML-CP
- 11 Abstract 210: Emerging safety and clinical response findings in a Phase I trial of oral ponatinib (AP24534) in refractory CML and other hematologic cancer types
- 12 Novel agents targeting CML stem cell eradication



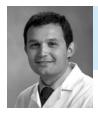
MANTLE-CELL LYMPHOMA, T-CELL LYMPHOMAS Papers discussed by Lauren C Pinter-Brown, MD

Director, UCLA Lymphoma Program Clinical Professor of Medicine Geffen School of Medicine at UCLA Los Angeles, California

TRACKS

- 1 Abstract 110: Alternating 3 x CHOP and 3 x DHAP with rituximab followed by a high-dose Ara-C-containing myeloablative regimen and ASCT is superior to 6 x R-CHOP followed by myeloablative radiochemotherapy and ASCT in MCL
- 2 Initial treatment approach for younger versus older patients with MCL
- 3 Abstract 966: Salvage lenalidomide/dexamethasone for relapsed or refractory MCL
- 4 Abstract 961: Complete remissions with brentuximab vedotin (SGN-35) in relapsed or refractory systemic anaplastic large-cell lymphoma

- Mechanism of action and future clinical development of brentuximab vedotin in T-cell lymphomas
- 6 Abstract 114: Final results from a pivotal Phase II study of romidepsin in progressive or relapsed PTCL after systemic therapy
- 7 Abstract 1753: Pralatrexate in relapsed or refractory PTCL after ICE-based regimens
- 8 Integration of romidepsin and pralatrexate in the treatment of CTCL and PTCL
- 9 Abstract 2360: A single institution's 12-year experience with allogeneic hematopoietic stem cell transplantation for PTCL



ACUTE PROMYELOCYTIC LEUKEMIA, ACUTE MYELOID LEUKEMIA, MYELODYSPLASTIC SYNDROMES Papers discussed by Guillermo Garcia-Manero, MD

Associate Professor of Medicine Chief, Section of Myelodysplastic Syndromes, Department of Leukemia The University of Texas MD Anderson Cancer Center Houston, Texas

- Abstract 1080: A Phase II study of front-line all-trans retinoic acid and arsenic trioxide, with or without gemtuzumab ozogamicin for APL
- 2 Initial management of APL
- 3 Abstract 13: Requirement for Ara-C in the treatment of standardrisk APL (APL 2000)
- 4 Abstract 2183: Prolonged survival without complete remission in patients with AML treated with azacitidine
- 5 Abstract 332: A Phase II study of lenalidomide for patients with previously untreated deletion 5q AML who are age 60 or older and are not candidates for remission induction chemotherapy (SWOGS0605)

- 6 Abstract 655: A Phase IIb randomized study of CPX-351 versus cytarabine and daunorubicin (7 + 3 regimen) for patients age 60 to 75 with newly diagnosed AML
- 7 Abstract 508: GFM Phase I/II study of lenalidomide and intensive chemotherapy in AML and higher-risk MDS with deletion 5q
- 8 Abstract 976: Risk of AML evolution in lower-risk MDS with deletion 5q treated with or without lenalidomide

- 9 Abstract 439: Presence of TET2 mutation predicts a higher response rate to azacitidine in MDS and post-MDS AML
- 10 Abstract 603: A Phase I study of oral azacitidine using extended treatment schedules
- 11 Abstract 4032: Efficacy and safety of decitabine in chronic myelomonocytic leukemia
- 12 Abstract 2936: Efficacy of decitabine in MDS after failure on prior intensive therapy
- 13 Focus on molecular genetics in MDS/AML at ASH 2010

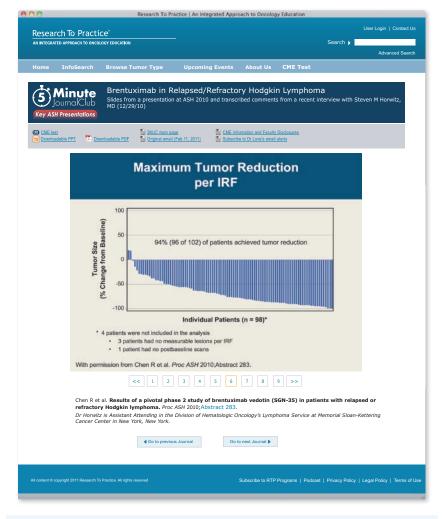
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Cancer Conference Update — Issue 1, 2011

QUESTIONS (PLEASE CIRCLE ANSWER):

1.	Brentuximab vedotin (SGN-35) is an
	antibody-drug conjugate targeted to
	CD30 and linked to

- a. Daunorubicin
- b. Nanoparticle albumin-bound paclitaxel
- c. Monomethyl auristatin E
- In a Phase II study for patients with heavily pretreated relapsed or refractory HL, approximately one third of patients experienced a complete response with brentuximab vedotin.
 - a. True
 - b. False
- 3. Bendamustine/rituximab has demonstrated activity in elderly patients with relapsed or refractory DLBCL.
 - a. True
 - b. False
- 4. The UPFRONT study evaluated maintenance therapy after bortezomib-based induction therapy for elderly patients with newly diagnosed MM.
 - a. Lenalidomide
 - b. Thalidomide
 - c. Weekly bortezomib
 - d. Bortezomib every three weeks
- 5. What regimen was used as the backbone in the EVOLUTION study evaluating three- and four-drug regimens for untreated MM?
 - a. Melphalan/prednisone
 - b. Lenalidomide/dexamethasone
 - c. Bortezomib/dexamethasone
- 6. In the IFM 2008 study, maintenance resulted in a significant prolongation in progression-free survival among patients who received induction bortezomib/lenalidomide/dexamethasone (VRD) followed by ASCT and VRD consolidation therapy.
 - a. Bortezomib
 - b. Lenalidomide
 - c. Thalidomide

- 7. Which of the following is a secondgeneration, irreversible proteasome inhibitor being evaluated in MM?
 - a. Bortezomib
 - b. Dendramusib
 - c. Carfilzomib
- 8. A number of studies have demonstrated that once-weekly and twice-weekly bortezomib result in comparable efficacy, but the once-weekly schedule is associated with a substantial decrease in the rate of peripheral neuropathy.
 - a. True
 - b. False
- 9. Pomalidomide is a third-generation immunomodulatory drug that has been demonstrated to be active in patients with MM that is ______.
 - a. Bortezomib refractory
 - b. Lenalidomide refractory
 - c. Bortezomib and lenalidomide refractory
 - d. All of the above
- 10. An Intergroup randomized trial of rituximab versus watch and wait for patients with Stage II to Stage IV asymptomatic, nonbulky FL demonstrated
 - a. No difference in time to initiation of new therapy
 - b. An improvement in time to initiation of new therapy with rituximab compared to watch and wait
- 11. The First-line Indolent Trial (FIT) demonstrated a progression-free survival with 90Y-ibritumomab tiuxetan consolidation therapy of first remission in advanced-stage FL of approximately

_____ compared to one year with observation.

- a. Eight years
- b. Four years
- c. One year

Cancer Conference Update — Issue 1, 2011

QUESTIONS (PLEASE CIRCLE ANSWER):

- Which regimen resulted in a significantly better response rate and progression-free survival in the Phase III NHL 2-2003 study among patients with relapsed FL, indolent and mantle-cell lymphomas?
 - a. Fludarabine/rituximab
 - b. Bendamustine/rituximab
 - c. Neither; both regimens were equally efficacious
- 13. Which of the following were improved with bendamustine compared to chlorambucil as the initial treatment for CLL?
 - a. Overall response rate
 - b. Progression-free survival
 - c. Overall survival
 - d. All of the above
 - e. None of the above
- 14. In the DASISION trial, the confirmed complete cytogenetic response rate by 12 months was significantly better with imatinib compared to dasatinib in patients with newly diagnosed CML-CP.
 - a. True
 - b. False
- 15. In the ENESTnd study, the major molecular response rate at 12 months was significantly better with nilotinib compared to imatinib in patients with newly diagnosed CML-CP.
 - a. True
 - b. False
- Brentuximab vedotin was highly active in patients with heavily treated relapsed or refractory systemic anaplastic largecell lymphoma.
 - a. True
 - b. False

- 17. What is the overall response rate with romidepsin in patients with progressive or relapsed PTCL?
 - a. 10 percent
 - b. 30 percent
 - c. 70 percent
- 18. In the Phase II study of front-line alltrans retinoic acid and arsenic trioxide with or without gemtuzumab ozogamicin for APL, what percent of patients achieved a complete remission?
 - a. 27 percent
 - b. 53 percent
 - c. More than 95 percent
- 19. In an analysis of the AZA-001 trial and the French AZA compassionate program (ATU), patients with AML who did not achieve a complete remission or partial remission with azacitidine appeared to have a significantly poorer survival than similar patients with azacitidine-treated MDS.
 - a. True
 - b. False
- In an analysis of patients with lower-risk MDS without deletion 5q, treatment with lenalidomide was associated with an increased incidence of progression to AML.
 - a. True
 - b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Cancer Conference Update — Issue 1, 2011

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PART ONE — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics? 4 = Excellent 3 = Good1 = Suboptimal 2 = Adequate **BEFORE AFTER** Brentuximab vedotin (SGN-35) in relapsed/refractory HL and 4 3 2 1 4 3 2 1 anaplastic large-cell lymphoma Bendamustine and rituximab for elderly patients with relapsed 4 3 2 1 4 3 2 1 or refractory DLBCL Activity of carfilzomib in patients with MM who have previously 4 3 2 1 4 3 2 1 received bortezomib Clinical strategies to reduce proteasome inhibitor-associated 4 3 2 1 4 3 2 1 peripheral neuropathy New findings from a randomized trial of rituximab versus watch 4 3 2 1 4 3 2 1 and wait in asymptomatic, nonbulky FL Updated results from studies of dasatinib (DASISION) or nilotinib 4 3 2 1 4 3 2 1 (ENESTnd) versus imatinib in newly diagnosed CML-CP Romidepsin in progressive or relapsed PTCL 4 3 2 1 4 3 2 1 Role of arsenic trioxide in the front-line management of APL 4321 4 3 2 1 Prolonged survival without complete remission in patients with 4 3 2 1 4 3 2 1 AML treated with azacitidine

Presence of TET2 mutation and effect on azacitidine efficacy in 4 3 2 1 4 3 2 1 MDS and post-MDS AML Was the activity evidence based, fair, balanced and free from commercial bias? If no, please explain: Please identify how you will change your practice as a result of attending this activity (select all that apply). This activity validated my current practice; no changes will be made Create/revise protocols, policies and/or procedures Change the management and/or treatment of my patients Other (please explain): If you intend to implement any changes in your practice, please provide one or more examples: The content of this activity matched my current (or potential) scope of practice. Yes No, please explain:

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicableAs a result of this activity, I will be able to: Apply emerging clinical trial data to the evidence-based selection of • Develop evidence-based treatment algorithms for frequently encountered • Summarize emerging data with novel agents/combinations and radioimmunotherapy approaches for newly diagnosed or relapsed/ refractory indolent or aggressive B-cell non-Hodgkin lymphomas. 4 3 2 1 N/M N/A • Tailor up-front/induction therapy based on individual and disease characteristics for patients with multiple myeloma (MM). 4 3 2 1 N/M N/A • Evaluate consolidation and maintenance therapy approaches for • Describe the standard therapeutic approaches and investigational strategies for the treatment of acute promyelocytic leukemia (APL). 4 3 2 1 N/M N/A · Recall the efficacy and side effects of hypomethylating and immunomodulating agents in the treatment of myelodysplastic • Describe therapeutic options for patients with peripheral and Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities: Would you recommend this activity to a colleague? ☐ Yes
 ☐ □ No If no, please explain:

Additional comments about this act	ivity:	

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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PART TWO — Please tell us about the faculty and editor for this educational activity

☐ Yes, I am willing to participate in a follow-up survey.

☐ No, I am not willing to participate in a follow-up survey.

4 = Excellent	3 = Good	2 =	Adeq	uate 1 =	= Suboptima	al		
Faculty	Knowled	ge of	subje	ct matter	Effective	ness	as an	educator
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Robert Z Orlowski, MD, PhD	4	3	2	1	4	3	2	1

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Please recommend additional facult						
Other comments about the faculty a	and editor fo	r this activ	ity:			
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