VOL 1 | ISSUE 1

Hodgkin Lymphoma™ UPDATE

Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

David J Straus, MD

Radhakrishnan Ramchandren, MD

EDITOR

Neil Love, MD

ABIM CME MOC ACCREDITED

CME Certified

Hodgkin Lymphoma™ UPDATE

Contact Information	Neil Love, MD Research To Practice One Biscayne Tower 2 South Biscayne Boulevard, Suite 3600 Miami, FL 33131 Fax: (305) 377-9998 Email: DrNeilLove@ResearchToPractice.com
For CME/CNE Information	Email: CE@ResearchToPractice.com

OVERVIEW OF ACTIVITY

In contrast to the more prevalent non-Hodgkin lymphomas, Hodgkin lymphoma (HL) is a rare cancer that is relatively chemosensitive and often curable when treated appropriately. However, a proportion of affected patients either receive diagnosis at an advanced stage of disease or harbor unfavorable risk factors that are associated with a suboptimal response to primary combined-modality treatment (chemotherapy/involved-field radiation therapy) and/or a high probability of early relapse. Historically the therapeutic challenge posed by this HL population was significant as no new systemic agent had been approved in this setting for more than 3 decades. The introduction of brentuximab vedotin (BV) and the anti-PD-1 antibodies nivolumab and pembrolizumab has improved outcomes but has also added considerable complexity to current treatment decision-making. Similarly, extensive published and ongoing research attempting to better define and expand the role of these agents and other compounds leveraging diverse mechanisms of action further add to the realm of educational priorities related to this challenging disease.

In order to offer optimal patient care — including the option of clinical trial participation — the practicing clinician must be well informed of these advances. Featuring information on the latest research developments along with the perspectives of leading clinical investigators, this CME program is designed to assist medical oncologists with the formulation of up-to-date clinical management strategies for the care of patients with HL.

LEARNING OBJECTIVES

- Appraise the FDA approval of BV as a component of first-line therapy for patients with newly diagnosed classical HL, and assess the current and future impact on routine clinical practice.
- Appreciate available Phase III data documenting the efficacy of BV as consolidation therapy after autologous stem cell transplant, and use this knowledge to identify patients appropriate for this therapeutic approach.
- Develop a long-term care plan for individuals with relapsed/refractory HL, considering prior exposure to systemic therapy, eligibility for transplant, symptomatology, performance status and personal goals for treatment.
- Compare and contrast the efficacy and safety of various approved immunotherapeutic approaches for HL to determine the current utility of each in clinical practice.
- Recall the design of ongoing clinical trials evaluating approved therapies and novel investigational agents for the treatment of HL, and counsel appropriately selected patients about availability and participation.

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CME INFORMATION

FACULTY AFFILIATIONS

David J Straus, MD
Attending Physician
Lymphoma Service
Department of Medicine
Memorial Sloan Kettering
Cancer Center
New York, New York

Radhakrishnan Ramchandren, MD
Professor, Hematology Oncology
Division Chief
University of Tennessee
Knoxville, Tennessee

EDITOR

Neil Love, MD
Research To Practice
Miami, Florida

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Interview with David J Straus, MD

Tracks 1-18

Track 1	**Case:** A 25-year-old woman with Stage IIA nodular sclerosing classical Hodgkin lymphoma (HL) receives risk-adapted doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD) therapy on the Phase II CALGB-50604 trial
Track 2	Use of chemotherapy versus combined-modality treatment for early-stage HL
Track 3	Risks and benefits of involved-field radiation therapy for patients with early-stage HL
Track 4	**Case:** A 19-year-old woman with bulky Stage IIA HL receives 6 cycles of ABVD
Track 5	Ongoing investigations of ABVD or brentuximab vedotin (BV) with doxorubicin/vinblastine/dacarbazine (AVD) with or without radiation therapy for newly diagnosed early-stage HL
Track 6	Perspective on potentially safer radiation therapy administration methods for early-stage HL
Track 7	**Case:** A 27-year-old man with nodular sclerosing Stage IVB classical HL receives front-line BV and AVD
Track 8	Design and major efficacy results from the Phase III ECHELON-1 trial evaluating BV with AVD versus ABVD as front-line therapy for advanced-stage classical HL
Track 9	ECHELON-1: Incidence and management of BV-associated neutropenia and peripheral neuropathy
Track 10	Pulmonary toxicity with bleomycin
Track 11	Estimating the risk of relapse after up-front therapy for advanced-stage HL
Track 12	Real-world analysis of cost, healthcare resource usage and supportive care for patients with HL who experience front-line therapy failure
Track 13	**Case:** A 40-year-old man with heavily pretreated HL experiences a prolonged response to nivolumab on a clinical trial
Track 14	Salvage therapy options
Track 15	Results of the Phase III AETHERA trial of BV as consolidation therapy after autologous stem cell transplant (ASCT) for patients with HL at risk of relapse or progression
Track 16	Efficacy of BV in combination with an anti-PD-1 immune checkpoint inhibitor for relapsed/refractory HL
Track 17	Activity of chimeric antigen receptor T-cell therapy in patients with HL
Track 18	Forecast of the future treatment of HL

Interview with Radhakrishnan Ramchandren, MD

Tracks 1-16

Track 1	**Case:** A 29-year-old man with Stage IIIB HL receives up-front AVD and BV on a clinical trial
Track 2	Prognosis and risk of relapse with standard ABVD versus response-adapted ABVD versus BV with AVD for advanced-stage HL
Track 3	Incidence of pulmonary toxicity with bleomycin
Track 4	Quality and interpretation of PET scanning for patients receiving response-adapted therapy
Track 5	Risk of febrile neutropenia and peripheral neuropathy with BV in combination with AVD
Track 6	Clinical experience with and management of BV-associated peripheral neuropathy
Track 7	Fertility after chemotherapy for HL
Track 8	Consideration of bleomycin for older patients
Track 9	Evolution of treatment modalities in early- and advanced-stage HL

Interview with Dr Ramchandren (continued)

Track 10 **Case:** A 49-year-old man with relapsed HL receives consolidation BV after ASCT

Track 11 Design and results of the AETHERA trial of BV as consolidation therapy after ASCT for patients with HL at high risk of relapse or disease progression

Track 12 **Case:** A 45-year-old man with heavily pretreated HL achieves a complete response to 2 cycles of nivolumab before discontinuing therapy because of severe hepatitis

Track 13 Prevalence of PD-L1 amplification and response to immune checkpoint blockade in patients with HL

Track 14 Potential correlation between autoimmune toxicity and benefit from immune checkpoint inhibitors

Track 15 Management of autoimmune toxicities in patients receiving immune checkpoint inhibitors

Track 16 **Case:** A 21-year-old woman with Stage IIA nodular sclerosing classical HL and negative PET results after 2 cycles of ABVD

Video Program

View the corresponding video interviews with (from left) Drs Straus and Ramchandren by Dr Love at www.ResearchToPractice.com/HLUpdate119/Video

Have Questions or Cases You Would Like Us to Pose to the Faculty?

Submit them to us via Facebook or Twitter and we will do our best to get them answered for you

Facebook.com/ResearchToPractice or Twitter @DrNeilLove

SELECT PUBLICATIONS

A pilot study of brentuximab vedotin combined with AVD chemotherapy in patients with newly diagnosed early stage, unfavorable risk Hodgkin lymphoma. NCT01868451

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Ramchandren R et al. **Brentuximab vedotin (BV) plus chemotherapy in patients with newly diagnosed advanced stage Hodgkin lymphoma (HL): North American results.** *Proc ASCO* 2018;**Abstract 7541**.

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Patients with nonbulky early-stage HL on the Phase II CALGB-50604 trial received 2 cycles of ABVD and then underwent an interim PET scan, after which those with Deauville scores of 5 and 6 received _____.**
   a. Two more cycles of ABVD and involved-field radiation therapy (IFRT)
   b. Dose-escalated BEACOPP and IFRT
   c. Either a or b interchangeably

2. **Results of the ECHELON-1 trial demonstrated the combination of BV and AVD to be _____ to ABVD as front-line therapy for advanced-stage classical HL in regard to the primary endpoint of modified progression-free survival.**
   a. Equivalent
   b. Inferior
   c. Superior

3. **Use of primary prophylaxis with granulocyte colony-stimulating factor was mandated for all patients receiving treatment on the ECHELON-1 trial.**
   a. True
   b. False

4. **Results of the Phase III AETHERA trial of BV as consolidation therapy after ASCT for patients with classical HL at high risk of relapse or disease progression demonstrated a statistically significant improvement in _____ with BV compared to placebo.**
   a. Overall survival
   b. Progression-free survival
   c. Both a and b

5. **BV-associated peripheral neuropathy can be successfully managed with _____.**
   a. Dose reduction
   b. Therapy hold until neuropathy improves
   c. Cessation of therapy
   d. All of the above
   e. Both a and b
   f. Both b and c

6. **Classical HL cells are characterized by a near universal chromosomal genetic alteration in 9p24.1, resulting in the constitutive expression of PD-1 ligands, making HL tumors particularly vulnerable to PD-1 blockade.**
   a. True
   b. False

7. **Results presented by Savage and colleagues from the British Columbia Cancer Agency demonstrated excellent outcomes for patients with advanced-stage classical HL and _____ who were PET-negative after ABVD without the need for additional consolidative radiation therapy.**
   a. Bulky disease
   b. Nonbulky disease
   c. Both a and b
   d. Neither a nor b

8. **_____ is an anti-PD-1 checkpoint inhibitor that is FDA approved for the treatment of relapsed/refractory HL.**
   a. Nivolumab
   b. Pembrolizumab
   c. Both a and b

9. **In the Phase III RAPID trial evaluating PET-directed therapy for favorable-risk early-stage HL, no statistically significant difference in progression-free survival was observed for patients with negative PET results after 3 cycles of ABVD who received no further treatment versus those who received IFRT after chemotherapy.**
   a. True
   b. False

10. **Which of the following subtypes of HL exhibits different clinical manifestation and patterns of relapse and thus should be treated differently from the other subtypes?**
    a. Nodular sclerosing
    b. Lymphocyte rich
    c. Mixed cellularity
    d. Nodular lymphocyte predominant

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Hodgkin Lymphoma Update — Volume 1, Issue 1

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — 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 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Key findings from the Phase III ECHELON-1 trial evaluating BV/AVD versus ABVD as front-line therapy for advanced-stage classical HL; implications of the recent FDA approval of BV with AVD	4 3 2 1	4 3 2 1
Frequency and severity of neutropenia and peripheral neuropathy with BV/AVD versus ABVD in the ECHELON-1 study	4 3 2 1	4 3 2 1
Incidence and management of pulmonary toxicity with bleomycin	4 3 2 1	4 3 2 1
Prevalence of PD-L1 amplification and response to immune checkpoint blockade in patients with HL	4 3 2 1	4 3 2 1
Management of autoimmune toxicities in patients receiving immune checkpoint inhibitors	4 3 2 1	4 3 2 1

Practice Setting:

⬭ Academic center/medical school ⬭ Community cancer center/hospital ⬭ Group practice

⬭ Solo practice ⬭ Government (eg, VA) ⬭ Other (please specify).....

Approximately how many new patients with Hodgkin lymphoma do you see per year? ..... patients

Was the activity evidence based, fair, balanced and free from commercial bias?

⬭ Yes ⬭ No If no, please explain: .....

Please identify how you will change your practice as a result of completing this activity (select all that apply).

⬭ This activity validated my current practice

⬭ 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 1 or more examples:

.....

.....

The content of this activity matched my current (or potential) scope of practice.

⬭ Yes ⬭ No If no, please explain: .....

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 applicable

As a result of this activity, I will be able to:

- Appraise the FDA approval of BV as a component of first-line therapy for patients with newly diagnosed classical HL, and assess the current and future impact on routine clinical practice. ..... 4 3 2 1 N/M N/A
- Appreciate available Phase III data documenting the efficacy of BV as consolidation therapy after autologous stem cell transplant, and use this knowledge to identify patients appropriate for this therapeutic approach. ..... 4 3 2 1 N/M N/A
- Develop a long-term care plan for individuals with relapsed/refractory HL, considering prior exposure to systemic therapy, eligibility for transplant, symptomatology, performance status and personal goals for treatment. ..... 4 3 2 1 N/M N/A

As a result of this activity, I will be able to:

- Compare and contrast the efficacy and safety of various approved immunotherapeutic approaches for HL to determine the current utility of each in clinical practice. . . . . 4 3 2 1 N/M N/A
- Recall the design of ongoing clinical trials evaluating approved therapies and novel investigational agents for the treatment of HL, and counsel appropriately selected patients about availability and participation. . . . . 4 3 2 1 N/M N/A

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: . . . . . .

PART 2 — Please tell us about the faculty and editor for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
David J Straus, MD	4 3 2 1	4 3 2 1
Radhakrishnan Ramchandren, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

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Neil Love, MD
Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

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