

# Lymphoma and Chronic Lymphocytic Leukemia™

U P D A T E

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

**FACULTY INTERVIEWS**

Stephen Maxted Ansell, MD, PhD

Ann S LaCasce, MD, MMSc

**EDITOR**

Neil Love, MD



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# Lymphoma and Chronic Lymphocytic Leukemia™

U P D A T E

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

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# *Lymphoma and Chronic Lymphocytic Leukemia Update*

## A Continuing Medical Education Audio Series

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### OVERVIEW OF ACTIVITY

The treatment of hematologic cancer remains a challenge for many healthcare professionals and patients despite recent gains in the management of this group of diseases. Determining which treatment approach is most appropriate requires careful consideration of patient characteristics, physician expertise and available health-system resources. To bridge the gap between research and patient care, this program features one-on-one discussions with leading hematology-oncology investigators. By providing information on the latest clinical developments in the context of expert perspectives, this activity assists medical oncologists, hematologists and hematology-oncology fellows with the formulation of evidence-based and current therapeutic strategies, which in turn facilitates optimal patient care.

### LEARNING OBJECTIVES

- Review emerging clinical trial data on the efficacy and safety of brentuximab vedotin for Hodgkin lymphoma and other CD30-positive lymphomas, and use this information to prioritize protocol and nonresearch options for patients.
- Compare and contrast the mechanisms of action, efficacy and safety of approved and investigational immunotherapeutic approaches (eg, checkpoint inhibitors, chimeric antigen receptor-directed T-cell therapy) for the treatment of Hodgkin and non-Hodgkin lymphoma and chronic lymphocytic leukemia (CLL) to determine the current and/or potential utility of each in clinical practice.
- Consider current and emerging clinical research data in the formulation of therapeutic recommendations for patients with newly diagnosed and relapsed/refractory follicular, mantle cell and diffuse large B-cell lymphomas.
- Appreciate the recent FDA approval of several novel therapies for newly diagnosed and relapsed/refractory CLL, and discern how these agents can be appropriately and safely integrated into routine clinical practice.
- Assess the benefits of ongoing clinical trials for patients with hematologic cancers, and inform appropriately selected patients about these options for treatment.

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## CME INFORMATION

### FACULTY AFFILIATIONS



**Stephen Maxted Ansell, MD, PhD**

Professor of Medicine  
Division of Hematology  
Mayo Clinic  
Rochester, Minnesota



**Ann S LaCasce, MD, MMSc**

Program Director, Fellowship in  
Hematology/Oncology  
Associate Professor of Medicine  
Harvard Medical School  
Lymphoma Program  
Dana-Farber Cancer Institute  
Boston, Massachusetts

### EDITOR



**Neil Love, MD**

Research To Practice  
Miami, Florida

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## Interview with Stephen Maxted Ansell, MD, PhD

### Tracks 1-18

- |                |   |                 |   |
|----------------|---|-----------------|---|
| <b>Track 1</b> | Biologic rationale for the high levels of activity of anti-PD-1/PD-L1 checkpoint inhibitors in Hodgkin lymphoma (HL)  | <b>Track 10</b> | Primary results of the Phase III GALLIUM study: Obinutuzumab-based induction and maintenance therapy prolongs progression-free survival (PFS) for patients with previously untreated FL |
| <b>Track 2</b> | <b>Case discussion:</b> A 26-year-old man with relapsed/refractory HL achieves a prolonged response with a checkpoint inhibitor   | <b>Track 11</b> | Investigation of anti-PD-1/PD-L1 antibodies for NHL   |
| <b>Track 3</b> | Durable objective responses to anti-PD-1 agents for advanced HL   | <b>Track 12</b> | <b>Case discussion:</b> A 55-year-old man with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) receives chimeric antigen receptor T-cell (CAR-T) therapy                      |
| <b>Track 4</b> | Tolerability of immune checkpoint inhibitors for advanced HL  | <b>Track 13</b> | Clinical experience with CAR-T therapy-associated toxicities  |
| <b>Track 5</b> | Phase II trial of brentuximab vedotin with nivolumab for patients with untreated HL who are older than age 60 or unable to receive doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD) | <b>Track 14</b> | <b>Case discussion:</b> A 61-year-old woman with relapsed/refractory peripheral T-cell lymphoma (PTCL) receives brentuximab vedotin   |
| <b>Track 6</b> | Five-year survival with brentuximab vedotin for relapsed/refractory HL  | <b>Track 15</b> | Relationship between CD30 expression and response to brentuximab vedotin in patients with lymphomas   |
| <b>Track 7</b> | <b>Case discussion:</b> A 47-year-old woman with relapsed/refractory follicular lymphoma (FL) achieves a durable partial response to idelalisib   | <b>Track 16</b> | Sequencing romidepsin, pralatrexate and belinostat for PTCL   |
| <b>Track 8</b> | Immune-related toxicities of FDA-approved (idelalisib) and investigational (copanlisib) PI3K inhibitors for indolent non-Hodgkin lymphoma (NHL)   | <b>Track 17</b> | Recent advances in the management of mantle cell lymphoma   |
| <b>Track 9</b> | Rituximab alone or in combination with chemotherapy for patients with FL  | <b>Track 18</b> | Clinical experience with ibrutinib for Waldenström macroglobulinemia  |

## Interview with Ann S LaCasce, MD, MMSc

### Tracks 1-16

- |                |   |                |  |
|----------------|---|----------------|--|
| <b>Track 1</b> | Clinical and investigational strategies with brentuximab vedotin for advanced-stage HL  | <b>Track 5</b> | Similarities and differences between the Bruton tyrosine kinase inhibitors ibrutinib and acalabrutinib for CLL   |
| <b>Track 2</b> | Ongoing investigation of checkpoint inhibitors and/or brentuximab vedotin in earlier lines of therapy for HL  | <b>Track 6</b> | <b>Case discussion:</b> An 87-year-old man with previously treated trisomy 12-positive, non-del(17p) CLL and demonstrated intolerance to ibrutinib receives venetoclax |
| <b>Track 3</b> | <b>Case discussion:</b> A 49-year-old man with unmutated chronic lymphocytic leukemia (CLL) initially treated with FCR (fludarabine/cyclophosphamide/rituximab) experiences disease progression and receives ibrutinib/obinutuzumab on a clinical trial | <b>Track 7</b> | Investigating the potential role of a finite duration of ibrutinib treatment   |
| <b>Track 4</b> | Activity and tolerability of ibrutinib/obinutuzumab   | <b>Track 8</b> | Perspective on the current roles of idelalisib and CAR-T therapy in CLL  |

## Interview with Dr LaCasce (continued)

- Track 9** **Case discussion:** A 71-year-old woman with transformed FL achieves a near complete response to single-agent lenalidomide before allogeneic stem cell transplant
- Track 10** Improvement in PFS with the addition of maintenance lenalidomide compared to observation for patients with relapsed DLBCL not eligible for autologous stem cell transplant
- Track 11** Viewpoint on the use of maintenance therapy with an anti-CD20 antibody for indolent and aggressive lymphomas
- Track 12** Therapeutic options for patients with “double-hit” lymphomas
- Track 13** Activity of nivolumab for relapsed/refractory primary central nervous system lymphoma
- Track 14** **Case discussion:** A 66-year-old man with mantle cell lymphoma undergoes autologous stem cell transplant followed by maintenance rituximab
- Track 15** **Case discussion:** A 58-year-old man with relapsed/refractory DLBCL receives CD19 CAR-T therapy
- Track 16** **Second opinion:** Therapeutic approach for a 66-year-old patient with HL treated with ABVD who develops bleomycin-related pneumocystis pneumonia

## Video Program

View the corresponding video interviews with (from left) Drs Ansell and LaCasce by Dr Love at [www.ResearchToPractice.com/LymphomaCLLUpdate117/Video](http://www.ResearchToPractice.com/LymphomaCLLUpdate117/Video)



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

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## SELECT PUBLICATIONS

- Anderson MA et al. **Transformed lymphoma.** *Hematol Oncol Clin North Am* 2016;30(6):1317-32.
- Armand P et al. **Programmed death-1 blockade with pembrolizumab in patients with classical Hodgkin lymphoma after brentuximab vedotin failure.** *J Clin Oncol* 2016;[Epub ahead of print].
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- Dreyling M et al. **Phase II study of copanlisib, a PI3K inhibitor, in relapsed or refractory, indolent or aggressive lymphoma.** *Ann Oncol* 2017;[Epub ahead of print].
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- Nayak L et al. **Nivolumab (anti-PD1) therapy for relapsed/refractory primary central nervous system lymphoma and primary testicular lymphoma.** *Proc ASH* 2016;**Abstract 930.**
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- Rummel MJ et al. **Two years rituximab maintenance vs observation after first-line treatment with bendamustine plus rituximab (B-R) in patients with mantle cell lymphoma: First results of a prospective, randomized, multicenter phase II study (a subgroup study of the StiL NHL7-2008 MAINTAIN trial).** *Proc ASCO* 2016;**Abstract 7503.**
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- Timmerman J et al. **Checkmate 205 update with minimum 12-month follow up: A phase 2 study of nivolumab in patients with relapsed/refractory classical Hodgkin lymphoma.** *Proc ASH* 2016;**Abstract 1110.**
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- Wilson WH et al. **Phase III randomized study of R-CHOP versus DA-EPOCH-R and molecular analysis of untreated diffuse large B-cell lymphoma: CALGB/Alliance 50303.** *Proc ASH* 2016;**Abstract 469.**

## QUESTIONS (PLEASE CIRCLE ANSWER):

1. HL tumor cells produce an abundance of PD-L1 and PD-L2 ligands in comparison to other tumor types, making HL tumors particularly vulnerable to PD-1 blockade.
  - a. True
  - b. False
2. Which of the following categories reflects the mechanism of action of copanlisib?
  - a. Anti-PD-1/PD-L1 antibody
  - b. Bruton tyrosine kinase inhibitor
  - c. CAR-T agent
  - d. PI3K inhibitor
3. Updated results presented at the 2016 ASH meeting from Phase II trials of both nivolumab and pembrolizumab continue to demonstrate durable response rates of approximately 65% for patients with relapsed/refractory classical HL.
  - a. True
  - b. False
4. A publication by Ansell and colleagues in *Blood* demonstrated that approximately \_\_\_\_\_ of patients with relapsed/refractory HL were sustaining disease remission 5 years or more beyond initial treatment with brentuximab vedotin.
  - a. 5%
  - b. 20%
  - c. 50%
5. An ongoing Phase II study is evaluating the combination of brentuximab vedotin and nivolumab for patients with untreated classical HL who are older than 60 years or unable to receive ABVD chemotherapy.
  - a. True
  - b. False
6. Which of the following agents is approved for the treatment of relapsed/refractory PTCL?
  - a. Belinostat
  - b. Pralatrexate
  - c. Romidepsin
  - d. All of the above
  - e. Both a and b
  - f. Both a and c
7. Acalabrutinib is a(n) \_\_\_\_\_.
  - a. Anti-PD-1/PD-L1 antibody
  - b. Bruton tyrosine kinase inhibitor
  - c. Immunomodulatory drug
8. Venetoclax is active in patients with \_\_\_\_\_.
  - a. CLL with 17p deletion
  - b. CLL without 17p deletion
  - c. Both a and b
  - d. Neither a nor b
9. A StIL NHL7-2008 MAINTAIN subgroup study presented by Dr Mathias Rummel at ASCO 2017 demonstrated no advantage to maintenance therapy with \_\_\_\_\_ after treatment with the combination of bendamustine and rituximab for older patients with mantle cell lymphoma.
  - a. Lenalidomide
  - b. Rituximab
  - c. Obinutuzumab
10. Which of the following observations was made in the Phase III GALLIUM study evaluating obinutuzumab- versus rituximab-based induction and maintenance therapy for previously untreated FL?
  - a. No difference in PFS
  - b. PFS favoring rituximab
  - c. PFS favoring obinutuzumab

**EDUCATIONAL ASSESSMENT AND CREDIT FORM**

*Lymphoma and Chronic Lymphocytic Leukemia 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	
Phase II trial of brentuximab vedotin with nivolumab for patients with untreated HL who are older than age 60 or unable to receive ABVD	4	3	2	1
PFS improvement with the addition of lenalidomide maintenance therapy versus observation for patients with relapsed DLBCL not eligible for autologous stem cell transplant	4	3	2	1
Risk-benefit ratio for patients with aggressive lymphomas treated with CAR-T therapy	4	3	2	1
Activity and immune-related toxicities of FDA-approved (idelalisib) and investigational (copanlisib) PI3K inhibitors for indolent NHL	4	3	2	1
Tolerability and side-effect differences among Bruton tyrosine kinase inhibitors, particularly lower risk of atrial fibrillation and bleeding with acalabrutinib compared to ibrutinib	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 the following do you see per year?**

CLL ..... HL ..... FL .....  
 Mantle cell lymphoma ..... DLBCL ..... T-cell lymphoma .....

**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  
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 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:**

- Review emerging clinical trial data on the efficacy and safety of brentuximab vedotin for Hodgkin lymphoma and other CD30-positive lymphomas, and use this information to prioritize protocol and nonresearch options for patients. .... 4 3 2 1 N/M N/A
- Compare and contrast the mechanisms of action, efficacy and safety of approved and investigational immunotherapeutic approaches (eg, checkpoint inhibitors, chimeric antigen receptor-directed T-cell therapy) for the treatment of Hodgkin and non-Hodgkin lymphoma and chronic lymphocytic leukemia (CLL) to determine the current and/or potential utility of each in clinical practice. .... 4 3 2 1 N/M N/A

**EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)**

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

- Consider current and emerging clinical research data in the formulation of therapeutic recommendations for patients with newly diagnosed and relapsed/refractory follicular, mantle cell and diffuse large B-cell lymphomas. . . . . 4 3 2 1 N/M N/A
- Appreciate the recent FDA approval of several novel therapies for newly diagnosed and relapsed/refractory CLL, and discern how these agents can be appropriately and safely integrated into routine clinical practice. . . . . 4 3 2 1 N/M N/A
- Assess the benefits of ongoing clinical trials for patients with hematologic cancers, and inform appropriately selected patients about these options for treatment. . . . . 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: .....

**Additional comments about this activity:**

.....

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Ann S LaCasce, MD, MMSc		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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