Investigator Perspectives on the Prevalence and Clinical Implications of Inaccurate or Misclassified Lymphoma Diagnoses in Community Oncology Practice

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ABIM CME MOC ACCREDITED

CME Certified

Lymphoma and Chronic Lymphocytic Leukemia™

UPDATE

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Investigator Perspectives on the Prevalence and Clinical Implications of Inaccurate or Misclassified Lymphoma Diagnoses in Community Oncology Practice — A Continuing Medical Education Audio Activity

OVERVIEW OF ACTIVITY

The misclassification of lymphoma is a common clinical reality that can impede effective therapeutic decision-making and compromise outcomes for patients. A number of factors can lead to misdiagnosis in these cases. However, many may be mitigated through multidisciplinary collaboration and awareness. To this end, this CME activity encourages exchange between medical oncologists and hematopathologists, reviews available information and helps better define strategies to improve diagnostic accuracy.

LEARNING OBJECTIVES

- Recognize common practical impediments (eg, inadequate sample size) to the accurate diagnostic assessment of lymphoid tissue, and use this information to improve internal and external processes and procedures.
- Empower oncologists to more actively assess pathologic reporting to identify factors that could lead to misinterpretation.
- Promote interdisciplinary collaboration between oncologists and pathologists to improve the accuracy of lymphoma subclassification.
- Highlight the importance of immunohistochemistry (IHC) for lymphoma classification, and alert oncologists to the challenges associated with its interpretation.
- Appreciate the specific IHC markers that should be included in a standard lymphoma panel, and discern how the selection and use of these markers differ in lymphoma subclassification.
- Increase awareness of the incidence and relevance of CD30 overexpression in patients with T-cell lymphoma, Hodgkin lymphoma and diffuse large B-cell lymphoma, and develop strategies to appropriately determine CD30 positivity.
- Formulate an evidence-based approach to biomarker analysis (cytogenetics, mutation status, et cetera) for patients with newly diagnosed and relapsed/refractory chronic lymphocytic leukemia, and appreciate the therapeutic implications of relevant findings.

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This activity is supported by educational grants from AbbVie Inc and Seattle Genetics.

Release date: February 2018; Expiration date: February 2019

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FACULTY — **Dr Gascoyne** has no relevant conflicts of interest to disclose. The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Smith** — Advisory Committee: Genentech BioOncology, Seattle Genetics; Contracted Research: Celgene Corporation, Takeda Oncology; Educational Presentation: AstraZeneca Pharmaceuticals LP. **Dr Cabanillas** — Advisory Committee: Lilly, Merck, Pfizer Inc; Consulting Agreement: Bristol-Myers Squibb Company; Contracted Research: Abbott Laboratories, Celgene Corporation.

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Interview with Mitchell R Smith, MD, PhD

Tracks 1-21

Track 1	Key components of correctly identifying and grading follicular lymphoma (FL)
Track 2	Diagnostic algorithm for mantle cell lymphoma (MCL)
Track 3	Stepwise process in the diagnosis of diffuse large B-cell lymphoma (DLBCL) and its subtypes
Track 4	Key pathologic features in identifying Hodgkin lymphoma (HL) and incidence of intraobserver variation
Track 5	FISH testing for cytogenetic abnormalities in chronic lymphocytic leukemia (CLL)
Track 6	Incidence of 17p deletion at diagnosis of CLL and after relapse
Track 7	Blood versus bone marrow samples for cytogenetic testing for CLL
Track 8	Minimal residual disease (MRD) assessment in CLL and lymphomas and its application in clinical practice
Track 9	Rates of MRD negativity in patients with CLL treated with venetoclax and/or ibrutinib
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Track 16	**Case:** A 62-year-old man with ibrutinib-refractory del(17p) CLL achieves a near-complete response with venetoclax
Track 17	Approach for patients at intermediate to high risk for tumor lysis syndrome (TLS) who are initiating venetoclax treatment
Track 18	Complementary activity of venetoclax and ibrutinib in CLL and investigational strategies evaluating the combination
Track 19	**Case:** A 70-year-old man who initially underwent treatment for marginal zone lymphoma is diagnosed with Waldenström macroglobulinemia
Track 20	**Case:** A 68-year-old man who initially underwent treatment for DLBCL for whom repeat pathology now indicates nodular lymphocyte-predominant HL
Track 21	**Case:** A 35-year-old man about to undergo intensive chemotherapy for Grade IIIb DLBCL for whom a pathologic review reclassifies his disease as an indolent pediatric-type FL

Interview with Fernando Cabanillas, MD

Tracks 1-15

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Track 2	Changes in WHO diagnostic criteria for lymphomas
Track 3	**Case:** A 63-year-old man with newly diagnosed CLL who initially underwent treatment with FCR (fludarabine/cyclophosphamide/rituximab) develops a 17p deletion
Track 4	Incidence of 17p deletion at diagnosis versus relapse
Track 5	Detection of 17p deletion
Track 6	Management of venetoclax-associated TLS
Track 7	**Case:** A 76-year-old woman with differential diagnoses of CLL with Richter's transformation versus DLBCL
Track 8	**Case:** A 33-year-old woman initially diagnosed with CD30-positive DLBCL, which is revised to HL with nodular sclerosis

Interview with Dr Cabanillas (continued)

Interview with Randy David Gascoyne, MD

Tracks 1-27

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POST-TEST

Investigator Perspectives on the Prevalence and Clinical Implications of Inaccurate or Misclassified Lymphoma Diagnoses in Community Oncology Practice

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The majority of patients with del(17p) CLL _____.**
   a. Present up front with the 17p deletion
   b. Acquire the 17p deletion over the course of their disease

2. **Which of the following categories reflects the mechanism of action of venetoclax?**
   a. Antibody-drug conjugate
   b. Anti-PD-1/PD-L1 antibody
   c. Bcl-2 inhibitor
   d. PI3K inhibitor

3. **Treatment with _____ for patients with CLL can result in high rates of MRD negativity, which typically correlates with longer progression-free survival, time to next treatment and longer durations of remission.**
   a. Ibrutinib
   b. Venetoclax
   c. Both a and b
   d. Neither a nor b

4. **The Phase III ECHELON-1 trial evaluating brentuximab vedotin with doxorubicin, vinblastine and dacarbazine versus bleomycin with doxorubicin, vinblastine and dacarbazine as front-line therapy for patients with previously untreated Stage III or IV HL demonstrated superior _____ for patients who received the brentuximab vedotin-based combination.**
   a. Progression-free survival
   b. Overall survival
   c. Both a and b
   d. Neither a nor b

5. **Hospitalization for the purpose of monitoring for TLS is required for all patients starting therapy with venetoclax.**
   a. True
   b. False

6. **A study published by Bartlett and colleagues evaluating brentuximab vedotin monotherapy in patients with DLBCL reported response rates of 30% to 40% for patients with CD30-undetectable disease.**
   a. True
   b. False

7. **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

8. **A publication by Zinzani and colleagues in *Blood* stated that pembrolizumab monotherapy demonstrated activity in patients with primary mediastinal large B-cell lymphoma.**
   a. True
   b. False

9. **Technical issues with core needle biopsies that can lead to inaccurate diagnosis include _____.**
   a. Crush artifact
   b. Edge effect
   c. Limited amount of tissue
   d. All of the above
   e. Both a and b
   f. Both a and c

10. **Which of the following lymphomas exhibits constant expression of the CD30 antigen?**
    a. Anaplastic large cell lymphoma
    b. DLBCL
    c. HL
    d. PTCL

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Investigator Perspectives on the Prevalence and Clinical Implications of Inaccurate or Misclassified Lymphoma Diagnoses in Community Oncology Practice

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
Changes in WHO diagnostic criteria for lymphomas	4 3 2 1	4 3 2 1
Results of the Phase III ECHELON-1 trial: Progression-free survival improvement with front-line brentuximab vedotin-based therapy for previously untreated Stage III and IV HL	4 3 2 1	4 3 2 1
MRD assessment in CLL and lymphomas and its application in clinical practice	4 3 2 1	4 3 2 1
Testing for cytogenetic abnormalities in CLL	4 3 2 1	4 3 2 1
CD30 testing and interpretation in lymphomas	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 the following do you see per year?

Anaplastic large cell lymphoma..... CLL..... DLBCL..... FL..... HL.....MCL ..... TCL/PTCL.....

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:

- Recognize common practical impediments (eg, inadequate sample size) to the accurate diagnostic assessment of lymphoid tissue, and use this information to improve internal and external processes and procedures..... 4 3 2 1 N/M N/A
- Empower oncologists to more actively assess pathologic reporting to identify factors that could lead to misinterpretation..... 4 3 2 1 N/M N/A
- Promote interdisciplinary collaboration between oncologists and pathologists to improve the accuracy of lymphoma subclassification..... 4 3 2 1 N/M N/A
- Highlight the importance of immunohistochemistry (IHC) for lymphoma classification, and alert oncologists to the challenges associated with its interpretation..... 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:

- Appreciate the specific IHC markers that should be included in a standard lymphoma panel, and discern how the selection and use of these markers differ in lymphoma subclassification. . . . . 4 3 2 1 N/M N/A
- Increase awareness of the incidence and relevance of CD30 overexpression in patients with T-cell lymphoma, Hodgkin lymphoma and diffuse large B-cell lymphoma, and develop strategies to appropriately determine CD30 positivity. . . . . 4 3 2 1 N/M N/A
- Formulate an evidence-based approach to biomarker analysis (cytogenetics, mutation status, et cetera) for patients with newly diagnosed and relapsed/refractory chronic lymphocytic leukemia, and appreciate the therapeutic implications of relevant findings. . . . . 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
Mitchell R Smith, MD, PhD	4 3 2 1	4 3 2 1
Fernando Cabanillas, MD	4 3 2 1	4 3 2 1
Randy David Gascoyne, 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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This activity is supported by educational grants from AbbVie Inc and Seattle Genetics.

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Release date: February 2018
Expiration date: February 2019
Estimated time to complete: 3.25 hours