IMPROVING HEMATOLOGIST/ONCOLOGIST KNOWLEDGE AND COMPETENCE IN MANAGING LYMPHOMA THROUGH EDUCATIONAL INTERVENTIONS

Emily S. Van Laar, MS, Medscape Education, New York, New York, USA; Charlotte Warren, Medscape Education, New York, New York, USA; Myron S. Czuczman, MD, Roswell Park Cancer Institute, Buffalo, New York, USA

INTRODUCTION

Lymphoma, a malignant transformation of B or T cells or their subtypes, is the most common type of hematologic malignancy in the United States. In 2013, non-Hodgkin lymphoma (NHL), the major subtype, was expected to account for about 1200 deaths.[Siegel 2013] Survival rates for NHL also vary widely, depending on the lymphoma type, stage, age of the patient, and other variables. Although the survival of patients with lymphoma improved dramatically in the 1970s and 1980s because of advances in chemotherapy, radiation therapy, and stem cell transplantation, survival has since leveled off; the current 5-year survival rates are 80% for HL and 50% to 60% for NHL. [Oerlemans 2011] Discovery of new treatments for lymphoma that prolong survival and are less toxic than currently available agents represent an urgent unmet need.[Johnston 2010]

Beyond the need for improved therapy, surveys indicate that hematologists and oncologists find the treatment of patients with lymphoma complex and challenging and are not highly confident in their ability to deliver optimal care for their patients. [Medscape Oncology Survey 2012; 2013a; 2013b] In these surveys, hematologists and oncologists clearly state their need for continuing medical education (CME) related to the most prevalent lymphoma subtypes, on topics that range from risk stratification and staging of disease to treatment selection and toxicity management. Lymphoma expert guidance allowed further refinement of education needs for clinicians.

Based on these clinical gaps, a series of 6 online video lecture education programs were developed and launched in 2013. A study was conducted to determine if the educational interventions on lymphoma could improve knowledge and competence of hematologists/oncologists as well as identify areas of future education focus.

METHODS

CME Video Lecture Series

An expert panel was convened to identify education gaps within the areas of diagnosis, risk stratification, and tailored treatment for patients with lymphoma. Based on this guidance and data from hematologist/oncologist surveys on lymphoma education needs, a CME series of 6 video lectures, on topics including aggressive B-cell lymphoma (diffuse large B-cell lymphoma [DLBCL] and mantle cell lymphoma [MCL]), chronic lymphocytic leukemia, follicular lymphoma [FL], Hodgkin lymphoma [HL], T-cell lymphoma, as well as supportive care concerns in lymphoma, were developed by expert faculty and posted online (http://www.medscape.org/viewcollection/32917). Each CME activity was developed as a video-based lecture presentation for hematologists/oncologists who diagnose and treat patients with lymphoma.

Outcome Assessment

The effects of education were assessed using a pre-assessment/post-assessment study design. This study design compares participants' responses to questions before exposure to educational content (pre-assessment measurement) with the same participants' responses to the same questions placed after the educational content (post-assessment measurement). A paired 2-tailed t-test was used to assess whether the mean pre-assessment score was different from the mean post-assessment score. A Pearson's $\chi 2$ statistic was used to measure changes in responses to individual questions. Probability values (*P* values) were also calculated for both t-test and $\chi 2$ statistic to determine significance level (α). A *P* value of less than .05 was considered as meeting statistical significance, demonstrating that a change occurred from the pre-assessment to the post-assessment. The calculated effect size of the educational intervention also is reported. Effect sizes greater than 0.8 are large, between 0.8 and 0.4 are medium, and less than 0.4 are small.

The relative percentage change was calculated for each question. Analysis was performed to identify questions with the largest relative percentage increase to assess educational impact. To assess topics of further education needs, questions with the lowest percentage of correct answers were identified.

RESULTS

A total of 507 hematologist/oncologist participants were included in the outcomes assessment across all 6 interventions (Table 1). A statistically significant impact on knowledge and competence was demonstrated as a result of participation in each of the 6 interventions (*P* < .05). The effect sizes ranged from 0.538 to 1.108, with an average of 0.899 (> 0.8 is considered a large effect size, 0.4 - 0.8 is considered a medium effect size). The educational impact of the activities are identified in each figure (Figures 1-6).

TABLE 1 Summary of Outcomes of Lymphoma Video Lecture Series

2013 Lymphoma Video Lecture Series	Outcomes Participants	Effect Size	*P* Value
Peripheral T-Cell Lymphoma in 2013 http://www.medscape.org/viewarticle/809373	60	0.8	< .05
Hot Topics in Lymphoma Supportive Care http://www.medscape.org/viewarticle/810653	93	1.108	< .05
Updates in Aggressive B-Cell Non-Hodgkin Lymphoma http://www.medscape.org/viewarticle/810790	56	0.893	< .05
Updates in Hodgkin Lymphoma http://www.medscape.net/viewarticle/810061	106	1.104	< .05
Updates in Follicular Lymphoma http://www.medscape.net/viewarticle/813243	127	0.953	< .05
Chronic Lymphocytic Leukemia in 2013 http://www.medscape.net/viewarticle/812257	65	0.538	< .05
Total/Average	**507**	**0.899**	

FIGURE 1 Peripheral T-Cell Lymphoma in 2013 Outcomes

Questions:

1. Which of the following subtypes of peripheral T-cell lymphoma (PTCL) confers the best prognosis?
2. Which of the following approaches have shown the most promise for improving the results of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) as first-line therapy?
3. Which of the following agents are approved for relapsed or refractory PTCL?
4. Brentuximab vedotin, which is approved for treatment of relapsed anaplastic large cell lymphoma (ALCL), is currently under study in other PTCLs that are CD30 positive. Which of the following best describes the relationship between CD30 expression and response to brentuximab in the data reported so far?

Education Impact:

Question 2: CHOP + etoposide and CHOP + autologous stem cell transplantation (ASCT) (46% relative increase, *P* < .05)
Question 4: Responses are seen in patients with both high and low expression of CD30 in patients treated with brentuximab vedotin (46% relative increase, *P* < .05)

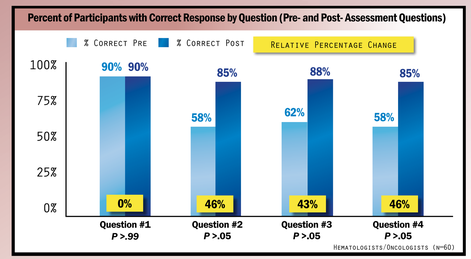


FIGURE 2 Hot Topics in Lymphoma Supportive Care Outcomes

Questions:

1. Skin reactions are most often associated with which of the following treatments?
2. Rituximab-associated hypogammaglobulinemia was most associated with which treatment approach in studies?
3. Neuroimaging results from a patient suspected of progressive multifocal leukoencephalopathy (PML) show multifocal areas of white matter demyelination that do not conform to cardiovascular territories. What other findings should be seen or not seen to confirm that it is PML?
4. Tumor lysis syndrome is caused by?

Education Impact:

Question 1: Skin reactions are most commonly associated with bendamustine (139% relative increase, *P* < .05)
Question 3: No mass effect, no contrast enhancement (95% relative increase, *P* < .05)

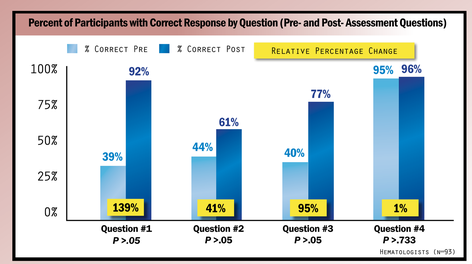


FIGURE 3 Updates in Aggressive B-Cell Non-Hodgkin Lymphoma Outcomes

Questions:

1. Which prognostic and clinical factors predict poor outcome in patients with DLBCL treated with dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R) regimen?
2. In patients with DLBCL, what are the typical responses associated with the sequential rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)/ifosfamide, carboplatin, and etoposide (ICE) (R-CHOP-14 for 4 cycles followed by 3 cycles of ICE) regimen?
3. Which statement is true regarding the activity of Bruton's tyrosine kinase (BTK) inhibitor, ibrutinib, in patients with relapsed/refractory DLBCL?
4. What is the target of ABT-199, an investigative agent currently being studied in patients with relapsed/refractory non-Hodgkin lymphoma?

Education Impact:

Question 2: A proliferation index greater than 60%, high-risk International Prognostic Index (IPI), and non-Germinal center B-cell-like (GCB) phenotype are predictive of treatment response outcomes of sequential R-CHOP-14/ICE regimen in DLBCL (283% relative increase, *P* < .05)
Question 4: BCL-2 (95% relative increase, *P* < .05)

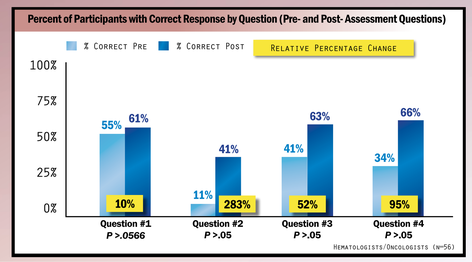


FIGURE 4 Updates in Hodgkin Lymphoma Outcomes

Questions:

1. How do the risk stratification schemas for unfavorable stages I and II HL of the German Hodgkin Study Group (GHSG) and European Organization for Research and Treatment of Cancer (EORTC) differ?
2. What is the current standard of treatment for patients with early-stage unfavorable classical Hodgkin lymphoma (cHL)?
3. What is the established dose of brentuximab vedotin monotherapy?
4. Which of the following statements regarding the clinical trial comparing brentuximab vedotin + doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) or AVD (ABVD minus bleomycin) is true?

Education Impact:

Question 2: 4 cycles of ABVD followed by involved-field radiotherapy (IFRT) 30 Gy (65% relative increase, *P* < .05)
Question 3: The established dose of brentuximab vedotin monotherapy for HL is 1.8 mg/kg (148% relative increase, *P* < .05)

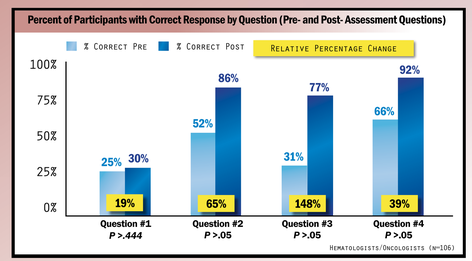


FIGURE 5 Updates in Follicular Lymphoma Outcomes

Questions:

1. What did the study led by Rummel and colleagues that looked at bendamustine-rituximab (BR) vs R-CHOP as frontline therapy for indolent lymphoma as well as MCL show?
2. What did the same study show with regard to the toxicity profile of BR vs R-CHOP?
3. Which statement is true regarding the RELEVANCE study?
4. What is the target of idelalisib, also known as CAL-101 and GS-1101?

Education Impact:

Question 3: It is enrolling patients with previously untreated FL and randomly assigning them to a variety of chemotherapy regimens plus rituximab vs lenalidomide plus rituximab (89% relative increase, *P* < .05)
Question 4: PI3K δ is the molecular target of emerging agent idelalisib in FL (165% relative increase, *P* < .05)

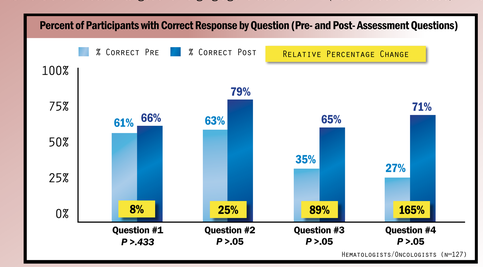


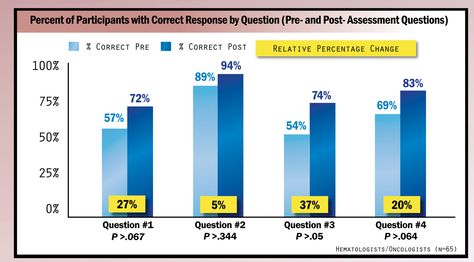
FIGURE 6 Chronic Lymphocytic Leukemia in 2013 Outcomes

Questions:

1. A 62-year-old man complaining of fatigue and night sweats was found to have palpable bilateral cervical lymph nodes and spleen and was referred for workup. His platelet count is in the normal range, but his hemoglobin is 9.8 g/dL. His beta-2-microglobulin level is elevated at 4.9 mg/L, and his absolute lymphocyte count is 5 x 109/L. His reticulocyte count was low and bilirubin was normal. Performance status was 1. A biopsy of the lymph nodes identified chronic lymphocytic leukemia (CLL). Flow cytometry of the peripheral blood indicated the presence of circulating clonal B-lymphocytes expressing CD5, CD19, CD20(dim), CD23, and an absence of FMC-7 staining. His disease was Rai stage III. He has had a coronary bypass graft. What is the best treatment approach for this patient?
2. In a patient diagnosed with early-stage CLL (Rai stage 0), which of the following procedures is appropriate?
3. The new IPI uses patient and CLL characteristics to define 4 risk groups for CLL. What are the characteristics used to predict outcome in this index?
4. In the phase 1b/phase 2 trial where ibrutinib was tested in patients with relapsed/refractory CLL, the progression-free survival rate at 2 years was about 80%. Which of the following is typical of patients treated with ibrutinib and also GS-1101?

Education Impact:

Question 3: Age, gender, Eastern Cooperative Oncology Group (ECOG) performance status, beta-2 microglobulin level, serum thymidine kinase levels, immunoglobulin variable (IgVH) mutation status, and fluorescence in-situ hybridization (FISH) evaluation of genetic defects (13q, 11q deletion [del], 17p del) are the charcteristics used in the new IPI for CLL (37% relative increase, *P* < .05)



CONCLUSIONS AND IMPLICATIONS

This study demonstrated the success of a comprehensive lymphoma educational intervention by improving the knowledge and competence of hematologists/oncologists in most facets of lymphoma care, ranging from diagnosis and risk stratification to disease management, increased understanding of new and emerging therapies, and strategies for managing adverse effects. It also identified avenues of future educational focus, including the following:

Peripheral T-Cell Lymphoma
- Appropriate risk stratification
- Treatment for newly diagnosed and relapsed or refractory disease

Supportive Care
- Prevention and management of treatment-related adverse effects, including hypogammaglobulinemia and progressive multifocal leukoencephalopathy

Aggressive Lymphoma
- Better understanding of the prognostic and clinical factors to be considered when selecting treatment for patients with aggressive B-cell NHL such as DLBCL or MCL
- Current treatment strategies for DLBCL and MCL
- Recent safety and efficacy data from clinical trials evaluating new treatment strategies in patients with DLBCL or MCL

Hodgkin Lymphoma
- Better understanding of prognostic and clinical factors that guide decision points
- Current management approaches in patients with HL

Follicular Lymphoma
- Current and emerging treatment options for patients with FL
- Personalized therapy on the basis of patient- and disease-related factors
- Better understanding of patient goals

Chronic Lymphocytic Leukemia
- Selecting appropriate therapy for CLL based on patient risk and prognosis

Additional lymphoma programs are required to address these gaps and allow hematologist/oncologist increase their knowledge and competence in managing patients with lymphoma.

Acknowledgements

The 2013 Video Lecture Series was funded, in part, through independent educational grants from Celgene, Genentech, Millennium, Lilly, Seattle Genetics, and Teva Oncology. Review and editorial help were provided by Nimish Mehta, PhD, MBA, and Ronald Viggiani, MD, both of Medscape Education.

For more information contact: Emily Van Laar, MS, Director, Educational Strategy, Medscape, LLC, evanlaar@medscape.net.

References

Johnston PB, Yuan R, Cavalli F, Witzig TE. Targeted therapy in lymphoma. *J Hematol Oncol.* 2010,3:45.

Medscape Education Survey. Pan Pacific Lymphoma Conference survey. July 2012. Data on file.

[a]Medscape Education Survey. Chronic lymphotic leukemia – treatment evolution. March 2013. Data on file.

[b]Medscape Education Survey. Hodgkin lymphoma education survey. April 2013. Data on file.

Oerlemans S, Mols F, Nijziel MR, et al. The impact of treatment, socio-demographic and clinical characteristics on health-related quality of life among Hodgkin's and non-Hodgkin's lymphoma survivors: a systematic review. *Ann Hematol.* 2011;90:993-1004.

Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013;63:11-30.