Conversations in Oncology 2019

Final Live Outcomes Report

Clinical Advances: Individualizing Treatment for Chronic Lymphocytic Leukemia

Pharmacyclics LLC. • ME-2018-11247

January 30, 2020

RealCME

EINSTEIN Albert Einstein College of Medicine Montefiore NACE

Conversations in Oncology 2019

Clinical Advances: Individualizing Treatment for Chronic Lymphocytic Leukemia (CLL)

191 Participants

1 Activity

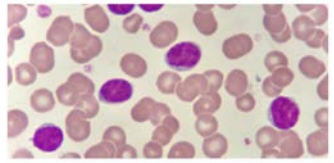
191 certificates issued to date

This education has the potential to impact 429,460 patients on an annual basis.

7,433–9,085 Patients Weekly

2019 Conversations Activity	Date	Participants
Conversations In Oncology 2019	5/18/19	191
Total		**191**

Clinical Advances: Individualizing Treatment for Chronic Lymphocytic Leukemia



Speakers

Noah Kornblum, MD
Assistant Professor, Department of Medicine (Oncology)
Bone Marrow Transplant/Heme Malignancy
Montefiore Einstein Center for Cancer Care
Bronx, NY

Brian Koffman, MDCM, DCFP, FCFP, DABFP, MSEd
Chief Medical Officer and Executive Vice President
CLL Society
Claremont, CA

COURSE SUMMARY

Cost: Free

Start Date: 06/15/2019

Expiration Date: 06/14/2020

Target Audience: Oncologists, Hematologists, and other clinicians that care for patients with CLL

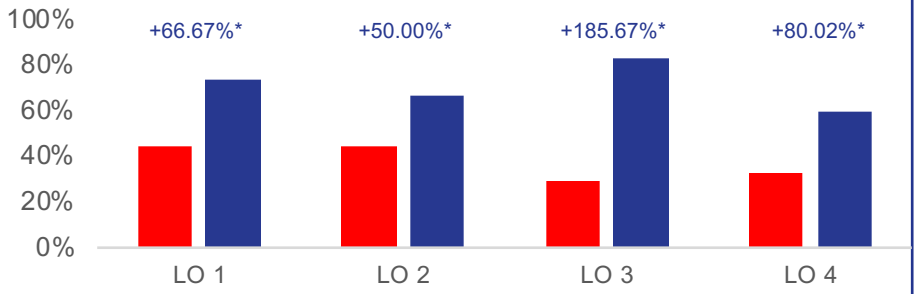
Format: Webcast

Estimated Time To Complete CME Activity: 1 hour

Credits:
1.0 *AMA PRA Category 1 Credit™*
1.0 AANP Contact hour including 0.75 pharmacology hours

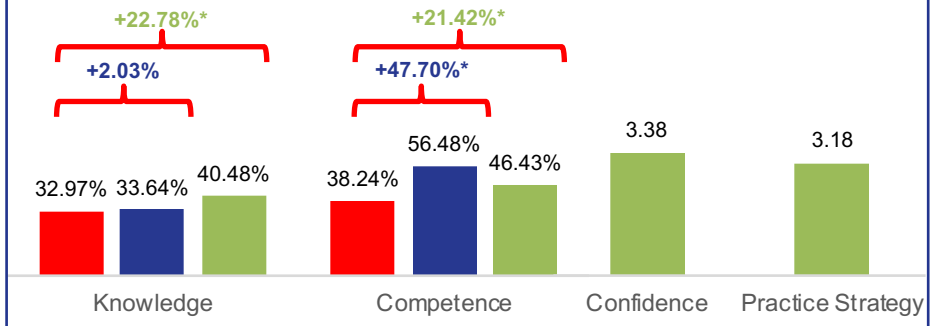
Hardware/Software Requirements: Any web browser

Learning Gains Across Objectives



- **LO 1:** Use patient's age, prognostic markers, comorbidities and patient's preferences when individualizing CLL management
- **LO 2:** Utilize new and emerging therapies as well as chemo-immunotherapy for the appropriate patients with CLL
- **LO 3:** Understand the importance of degree of response to therapy, including U-MRD (undetectable Minimal Residual Disease), in managing care
- **LO 4:** Recognize and manage the common complications related to the medications used to treat CLL

Learning Domain Analysis



- Substantial and significant improvements were measured from Pre- to Post-Test in both Knowledge and Competence
- Post-Test scores in both Knowledge and Competence varied from low to moderate, but uniformly represented strong increases from low Pre-Test scores
- Confidence and practice strategy ratings, collected only at follow-up, were moderate

Persistent Learning Gaps/Needs

Managing risk of tumor lysis syndrome in treatment resistant CLL patients

On a Competence question presenting the case of a patient who becomes symptomatic after two years of ibrutinib treatment, learners struggled at Post-Test to identify the correct treatment action to reduce risk for tumor lysis syndrome.

A 65 y/o woman with del17p CLL becomes symptomatic after 2 years of treatment with ibrutinib. ECOG performance status is 1. Her clinician recommends venotoclax for second-line therapy. Which of the following may help reduce risk for tumor lysis syndrome in this patient?
At Post-Test, 46% of learners correctly answered: "Gradually increase dose of venotoclax and add allopurinol"

Factors associated with poor outcomes in CLL patients

On a Knowledge item asking learners to identify a prognostic factor associated with poor outcomes in patients with CLL, low scores were measured at Post-Test.

Which of the following is a prognostic factor associated with poorer outcome in CLL?
At Post-Test, 70% of learners correctly answered: "Del17p/TP53 mutations"

First-line therapy for CLL

On a Knowledge item asking learners struggled at Post-Test to identify the correct first-line therapy for CLL.

Which of the following agents/combinations is indicated for first-line therapy of CLL?
At Post-Test, 53% of learners correctly answered: "Ibrutinib + obinutuzumab"

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Course Director and Moderator

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Conversations in Oncology 2019

The Conversations in Oncology: 2019 series of CME activities were supported through educational grants or donations from the following companies:

- Pharmacyclics LLC
- Boehringer Ingelheim Pharmaceuticals, Inc.

Overview

Learning Objectives

- Use patient's age, prognostic markers, comorbidities and patient's preferences when individualizing CLL management
- Utilize new and emerging therapies as well as chemo-immunotherapy for the appropriate patients with CLL
- Understand the importance of degree of response to therapy, including U-MRD (undetectable Minimal Residual Disease), in managing care
- Recognize and manage the common complications related to the medications used to treat CLL

Conversations in Oncology 2019

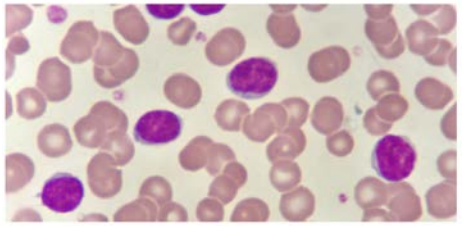
Curriculum Overview

One Live Virtual CME Symposium



Enduring CME Symposium Webcast


Clinical Advances: Individualizing Treatment for Chronic Lymphocytic Leukemia



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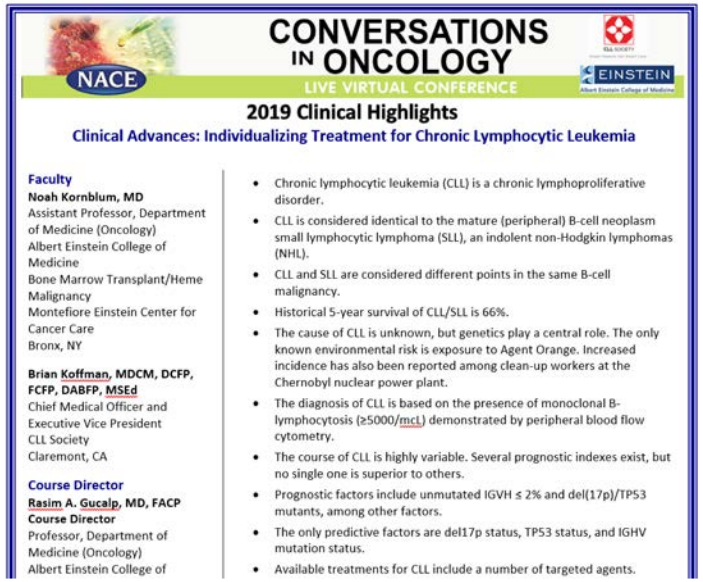
Clinical Highlights eMonograph

eMonograph, containing key teaching points from the CME activity, was distributed 1 week after the meeting to all attendees.



CONVERSATIONS IN ONCOLOGY
LIVE VIRTUAL CONFERENCE
2019 Clinical Highlights
Clinical Advances: Individualizing Treatment for Chronic Lymphocytic Leukemia

Faculty
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Professor, Department of Medicine (Oncology)
Albert Einstein College of

- Chronic lymphocytic leukemia (CLL) is a chronic lymphoproliferative disorder.
- CLL is considered identical to the mature (peripheral) B-cell neoplasm small lymphocytic lymphoma (SLL), an indolent non-Hodgkin lymphomas (NHL).
- CLL and SLL are considered different points in the same B-cell malignancy.
- Historical 5-year survival of CLL/SLL is 66%.
- The cause of CLL is unknown, but genetics play a central role. The only known environmental risk is exposure to Agent Orange. Increased incidence has also been reported among clean-up workers at the Chernobyl nuclear power plant.
- The diagnosis of CLL is based on the presence of monoclonal B-lymphocytosis (≥5000/mcL) demonstrated by peripheral blood flow cytometry.
- The course of CLL is highly variable. Several prognostic indexes exist, but no single one is superior to others.
- Prognostic factors include unmutated IGVH ≤ 2% and del(17p)/TP53 mutants, among other factors.
- The only predictive factors are del17p status, TP53 status, and IGHV mutation status.
- Available treatments for CLL include a number of targeted agents.

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Outcomes Methodology

Learning outcomes were measured using matched Pre-Test and Post-Test scores for Knowledge, Performance, Confidence, and practice strategy and across all of the curriculum's Learning Objectives.

Outcomes Metric	Definition	Application
Percentage change	This is how the score changes resulting from the education are measured. The change is analyzed as a relative percentage difference by taking into account the magnitude of the Pre-Test average.	Differences between Pre-Test, Post-Test, and PCA score averages
P value (p)	This is the measure of the statistical significance of a difference in scores. It is calculated using dependent or independent samples t-tests to assess the difference between scores, taking into account sample size and score dispersion. Differences are considered significant for when $p \leq .05$.	Significance of differences between Pre-Test, Post-Test, and PCA scores and among cohorts
Effect size (d)	This is a measure of the strength/magnitude of the change in scores (irrespective of sample size). It is calculated using Cohen's d formula, with the most common ranges of d from 0-1: d < .2 is a small effect, d=.2-.8 is a medium effect, and d > .8 is a large effect.	Differences between Pre-Test and Post-Test score averages
Power	This is the probability (from 0 to 1) that the "null hypothesis" (no change) will be appropriately rejected. It is the probability of detecting a difference (not seeing a false negative) when there is an effect that is dependent on the significance (p), effect size (d), and sample size (N).	Differences between Pre-Test and Post-Test score averages
Percentage non-overlap	This is the percentage of data points at the end of an intervention that surpass the highest scores prior to the intervention. In this report, it will reflect the percentage of learners at Post-Test who exceed the highest Pre-Test scores.	Differences between Pre-Test and Post-Test score averages

Participation

2019 Conversations Activity	Date	Participants
Conversations In Oncology 2019	5/18/19	191
Total		**191**

Level 1
Participation
Demographics
Patient Reach

Participation

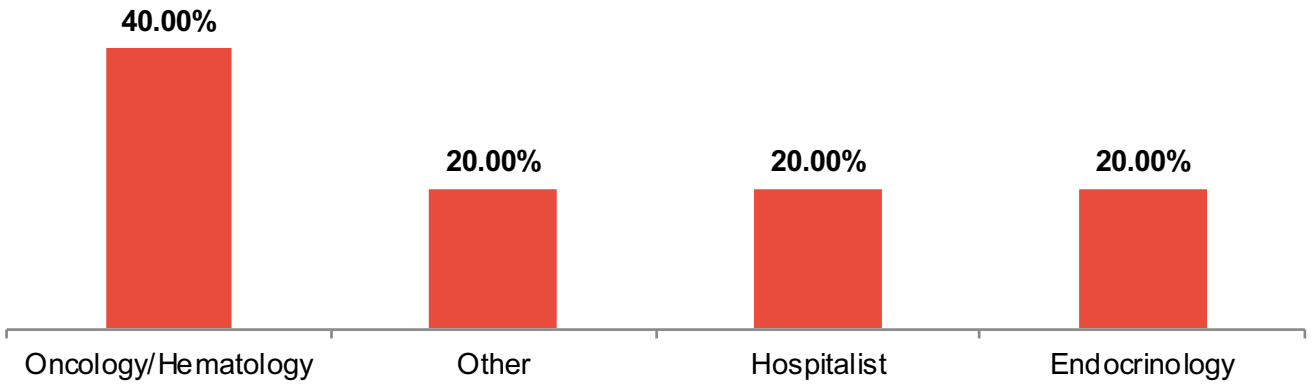
191
Total Attendees

1 Activity

N = 10 – 34

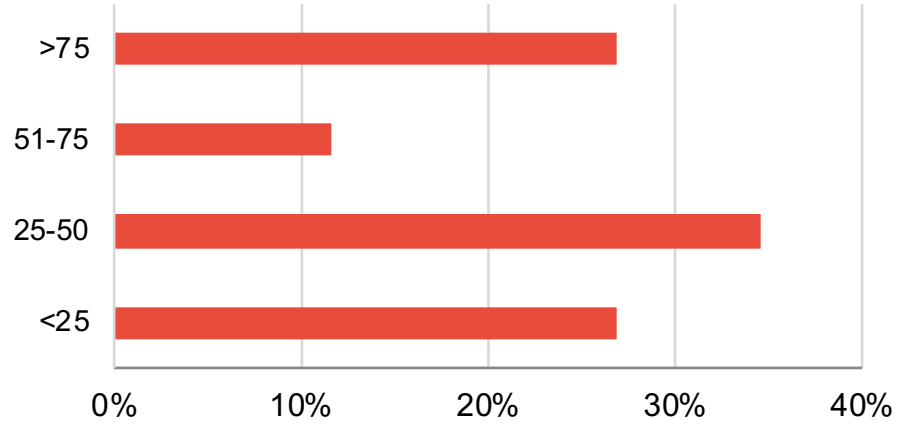
Level 1: Demographics and Patient Reach

Specialty



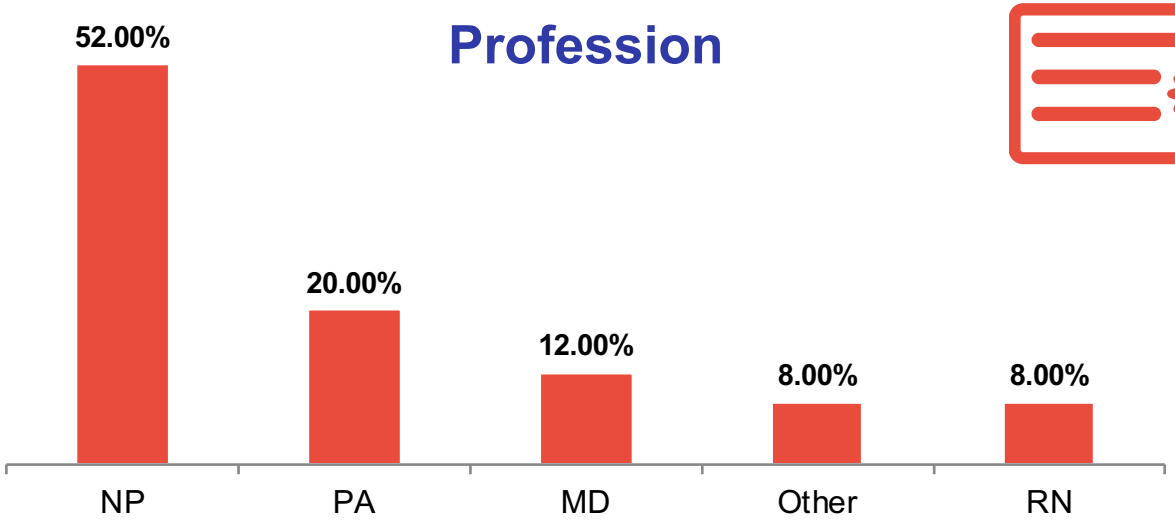
Patient Care Focus: 92%

Patients seen each week, in any clinical setting:

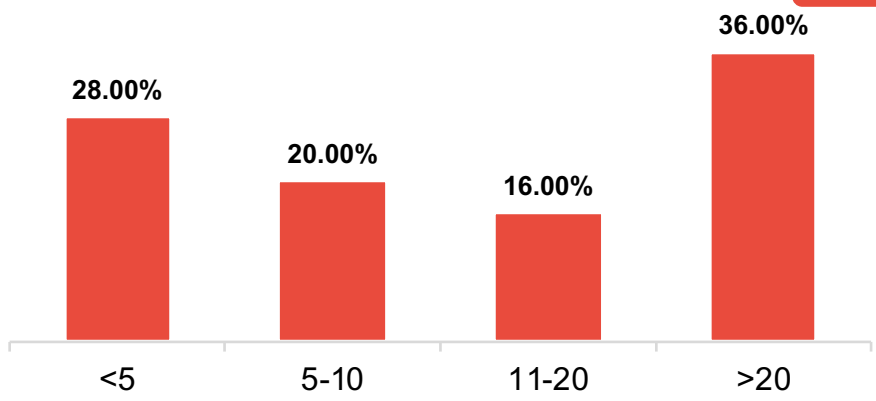


Average number of patients seen each week per clinician: 47

Profession

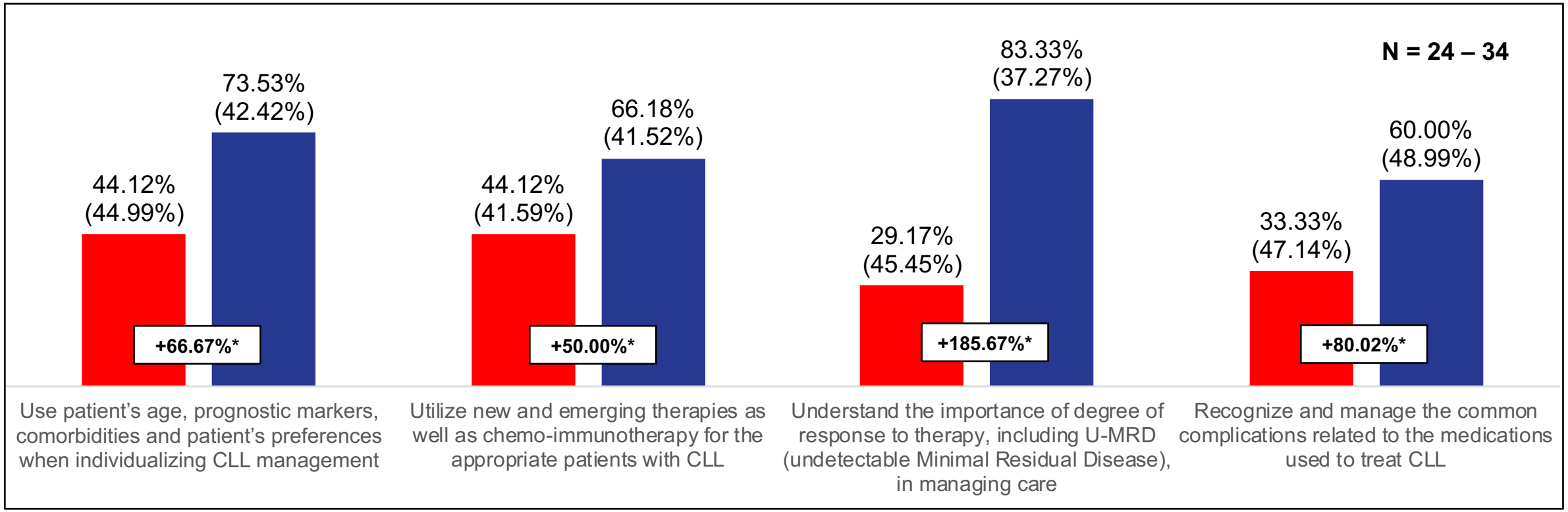


Years in Practice



Level 2-5:
Outcomes Metrics

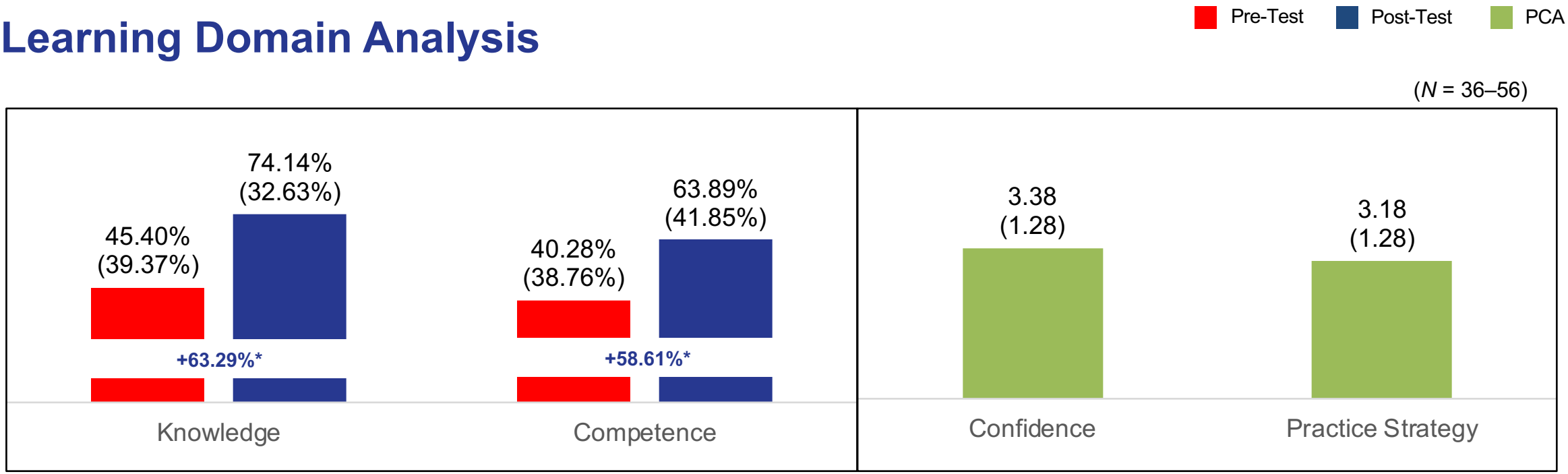
Learning Objective Analysis



- On each of the four curriculum Learning Objectives, learners achieved substantial and significant improvements, from Pre- to Post-Test
- The strongest improvements, and highest scores at Post-Test, were measured on understanding the importance of degree of response to therapy, including U-MRD
  - This improvement was driven by a single Knowledge item, which asked how U-MRD is defined in CLL
- On each of the three other Objectives, low and moderate Post-Test scores (< 74%) represent opportunities for further education in this area

Note: data are matched.
* indicates significance, $p < 0.05$.

Learning Domain Analysis

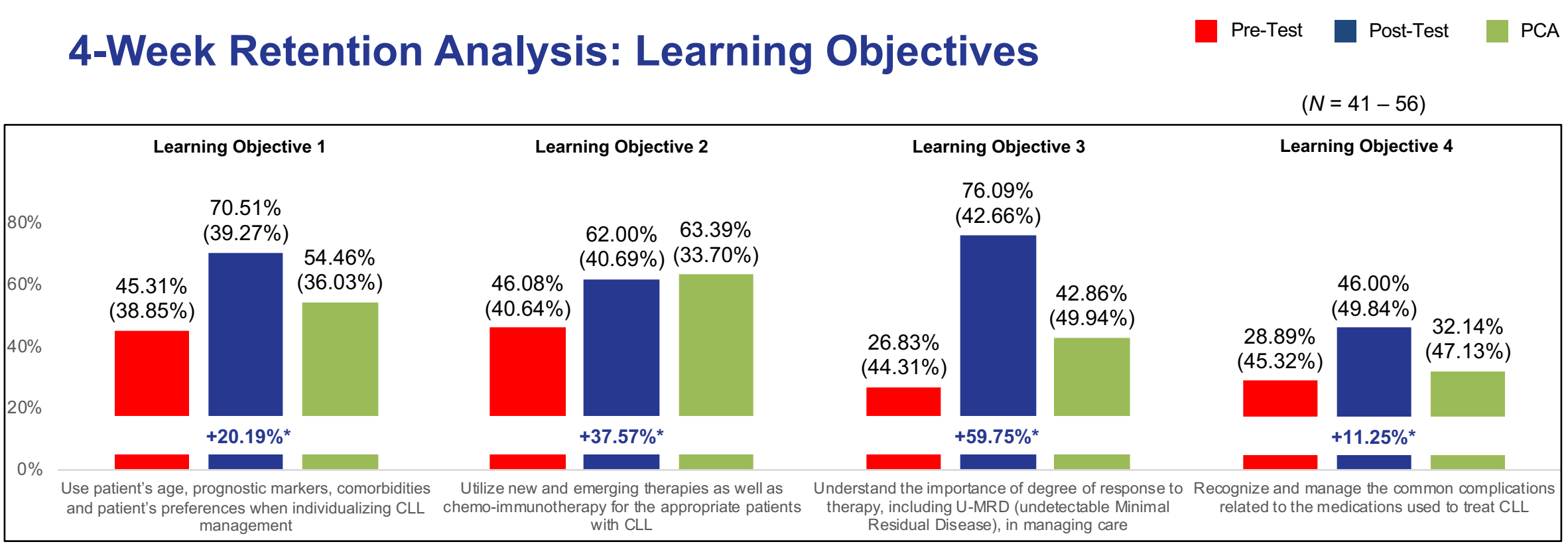


- Substantial and significant improvements were measured from Pre- to Post-Test in both Knowledge and Competence
- Post-Test scores in both Knowledge and Competence varied from low to moderate, but uniformly represented strong increases from low Pre-Test scores
- Confidence and practice strategy ratings, collected only at follow-up, were moderate. Learners indicated increased confidence in understanding how to select targeted therapy for individual patients with CLL and understanding how to anticipate and manage complications of targeted therapy for CLL. Learners also reported increasing risk stratification using prognostic and predictive factors for managing treatment of patients diagnosed with CLL

Note: data for Knowledge and Competence is matched; learners with a score for the given domain on both the Pre-Test and Post-Test are included

**significant at the p ≤ 0.05 level, matched data*

4-Week Retention Analysis: Learning Objectives

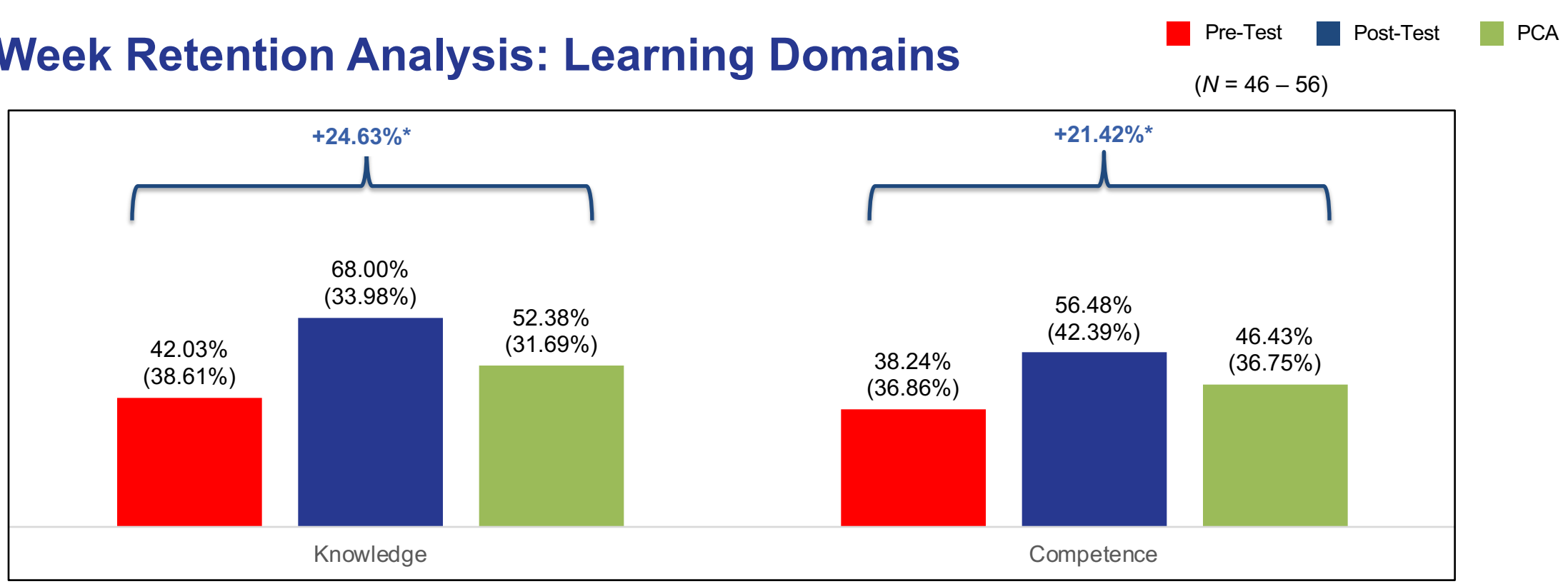


- In addition to collecting follow-up Confidence and Practice data for the curriculum, the Post Curriculum Assessment (PCA) repeated questions from the Knowledge and Competence domains
- Significant improvements in score between Pre-Test and PCA observations were measured for all curriculum Learning Objectives
- On all but one Learning Objective, some score slippage was seen between the Post-Test and PCA
  - On utilizing new and emerging therapies and chemo-immunotherapy for CLL patients, learners demonstrated ongoing improvements from Post-Test to PCA
- Low scores (32% to 63%) across curriculum Learning Objectives on the PCA reflect a need for further reinforcement in this area

Note: data is not matched due to sample size

significant at the p ≤ 0.05 level

4-Week Retention Analysis: Learning Domains



At follow-up:

- A statistically significant net gain was measured from Pre-Test to the Post Curriculum Assessment (PCA) in both Knowledge (25%) and Competence (21%)
- In both Knowledge and Competence, some score slippage from Post-Test to PCA was observed, reflecting an opportunity for further reinforcement of curriculum content

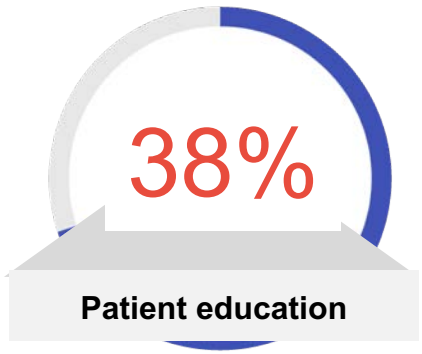
Note: data is matched; learners with a score for the given domain on both the Pre-Test and PCA are included

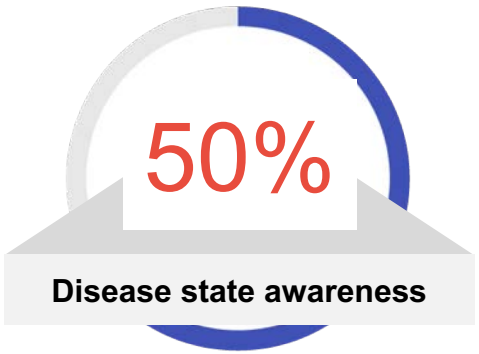
significant at the p ≤ 0.05 level

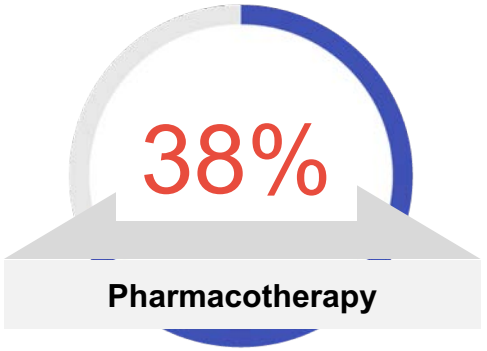
(4-week Post Assessment)

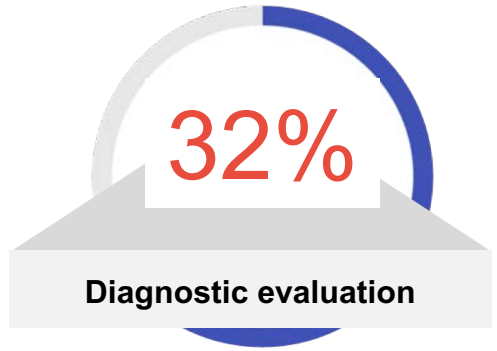
Please select the specific areas of *skills, or practice behaviors*, you have improved regarding the treatment of patients with CLL since this CME activity. (Select all that apply.)

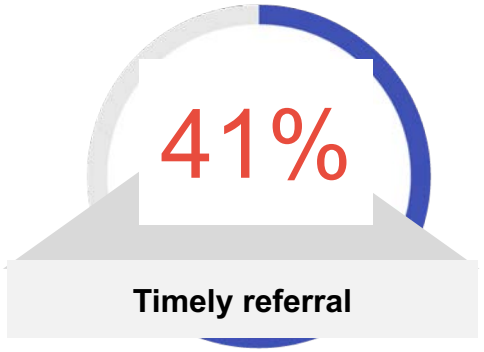
N=56

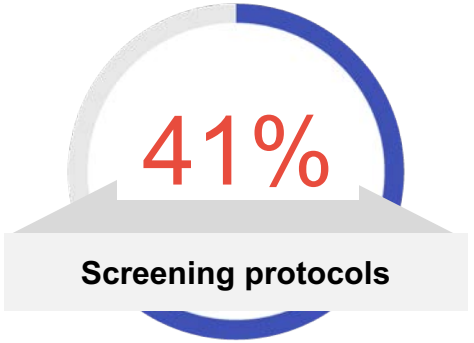


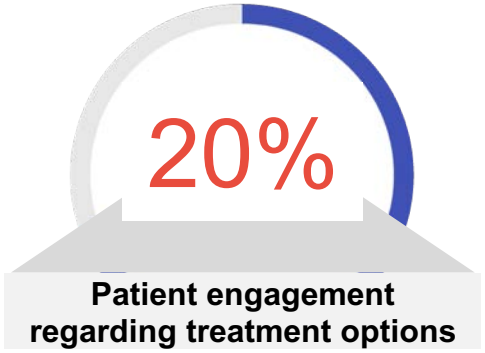








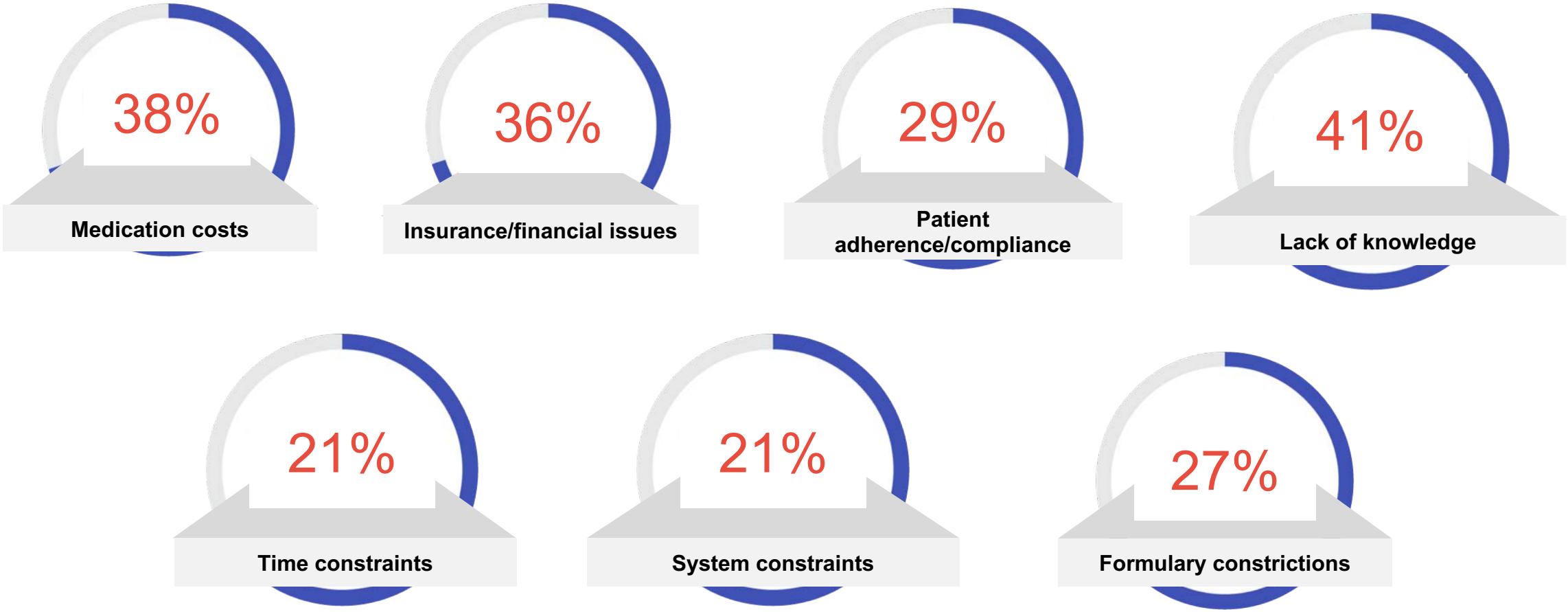




(4-week Post Assessment)

What specific *barriers* have you encountered that may have prevented you from successfully implementing strategies for patients with CLL since this CME activity? (Select all that apply.)

N=56



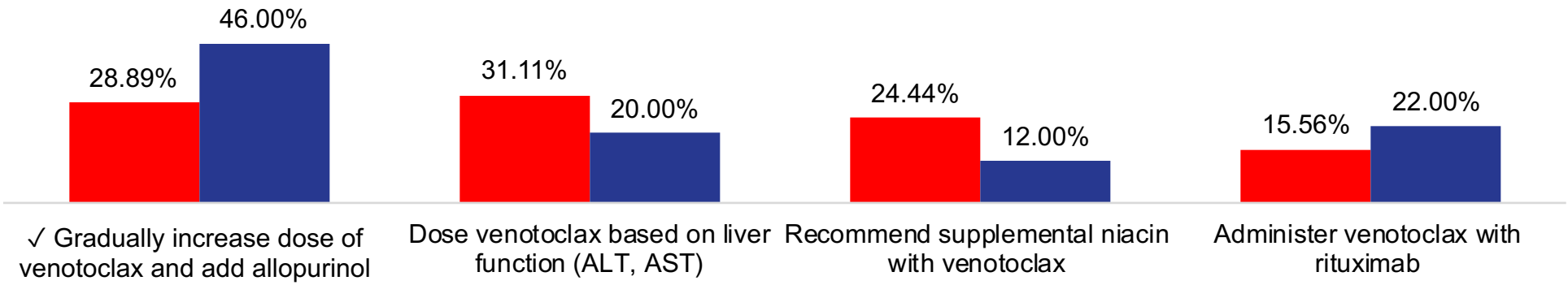
Identified Learning Gap, 1 of 3:
Managing risk of tumor lysis syndrome in treatment resistant CLL patients

On a Competence question presenting the case of a patient who becomes symptomatic after two years of ibrutinib treatment, learners struggled at Post-Test to identify the correct treatment action to reduce risk for tumor lysis syndrome.

Competence: A 65 y/o woman with del17p CLL becomes symptomatic after 2 years of treatment with ibrutinib. ECOG performance status is 1. Her clinician recommends venotoclax for second-line therapy. Which of the following may help reduce risk for tumor lysis syndrome in this patient?

Results:

- At Post-Test, only 46% of learners correctly answered: “Gradually increase dose of venotoclax and add allopurinol”



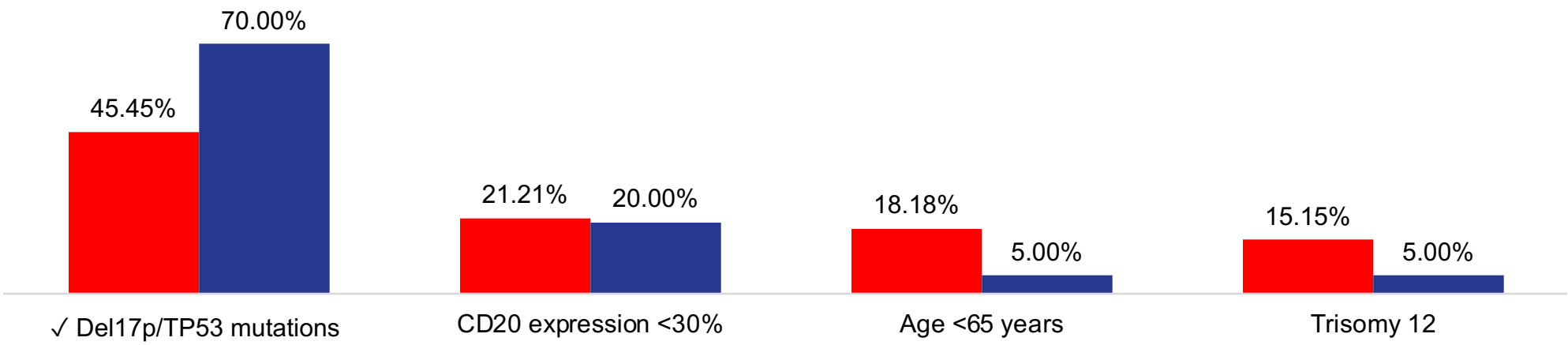
Identified Learning Gap, 2 of 3:
Factors associated with poor outcomes in CLL patients

On a Knowledge item asking learners to identify a prognostic factor associated with poor outcomes in patients with CLL, low scores were measured at Post-Test.

Knowledge: Which of the following is a prognostic factor associated with poorer outcome in CLL?

Results:

- At Post-Test, 70% of learners correctly answered: “Del17p/TP53 mutations”



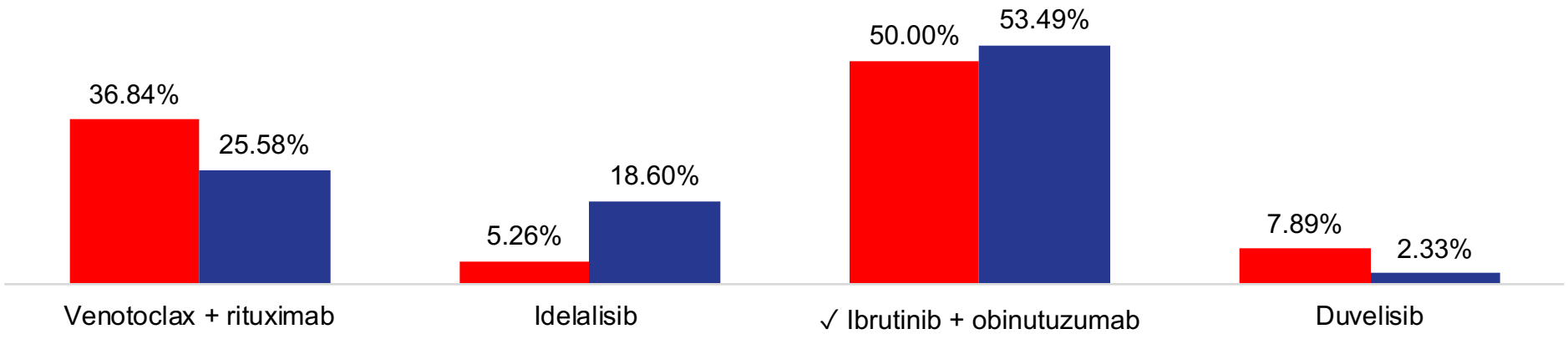
Identified Learning Gap, 3 of 3:
First-line therapy for CLL

On a Knowledge item asking learners struggled at Post-Test to identify the correct first-line therapy for CLL.

Knowledge: Which of the following agents/combinations is indicated for first-line therapy of CLL?

Results:

- At Post-Test, only 53% of learners correctly answered: “Ibrutinib + obinutuzumab”



Overall Educational Impact

- Significant increases in score were measured in both Knowledge and Competence, from Pre- to Post-Test
  - The strongest improvements in score (+184%) were on a Knowledge item about the definition of undetectable minimal residual disease (U-MRD) in CLL
  - Strong improvements (59% and 62%) were measured on both Competence items, though Pre- and Post-Test scores were low to moderate
  - Significant increases on all curriculum Learning Objectives were measured from Pre-Test to Post-Test
    - The highest Post-Test scores were measured on understanding the importance of degree of response to therapy, including undetectable Minimal Residual Disease (U-MRD)
  - Final scores on Confidence and practice strategy questions were moderate (3.38 and 3.18)
- The analysis of scored items in the curriculum identified three **persistent learning gaps related to the managing risk of tumor lysis syndrome in treatment resistant CLL patients, factors associated with poor outcomes in CLL patients, and first-line therapy for CLL**
  - Learners struggled on a Competence question asking them to select the correct treatment action for a patient who becomes symptomatic after two years of ibrutinib treatment
  - On a Knowledge item about prognostic factors associated with poor outcomes in CLL patients, low scores were measured at Post-Test
  - Learners also had low Post-Test scores on a Knowledge item on first-line therapy for CLL

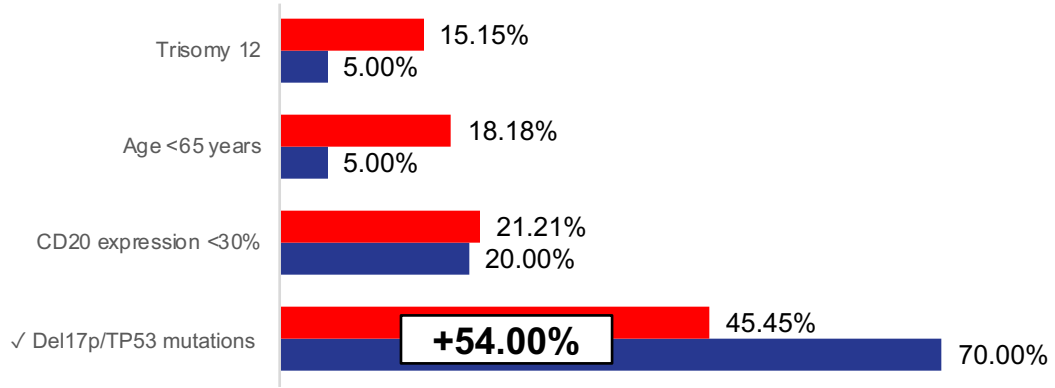
Appendix

Knowledge Items

Pre-Test
Post-Test

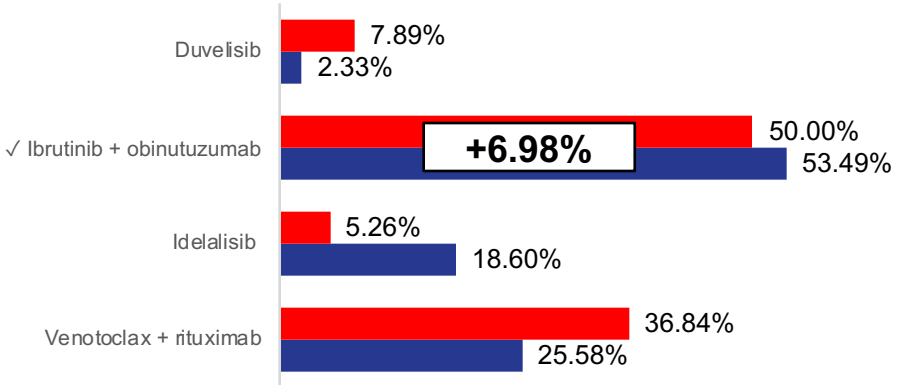
Which of the following is a prognostic factor associated with poorer outcome in CLL?

N = 33 – 40



Which of the following agents/combinations is indicated for first-line therapy of CLL?

N = 38 – 43

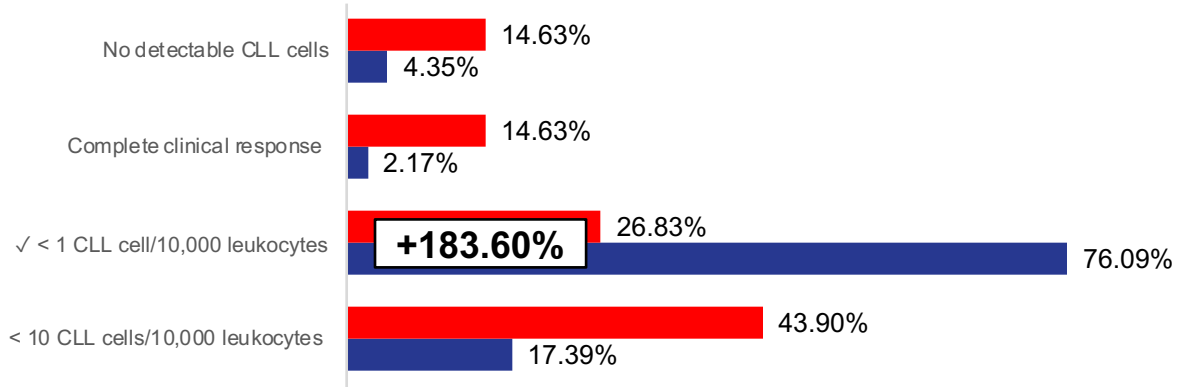


Note: data are matched.
Correct answer is designated by a ✓.

Knowledge Items

How is undetectable minimal residual disease (U-MRD) defined in CLL?

N = 41 – 46

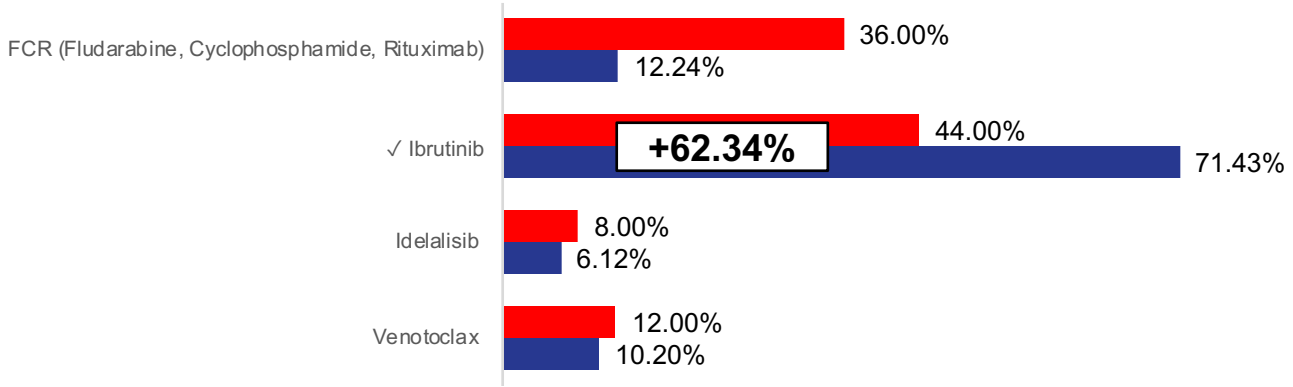


Note: data are matched.
Correct answer is designated by a ✓.

Competence Items

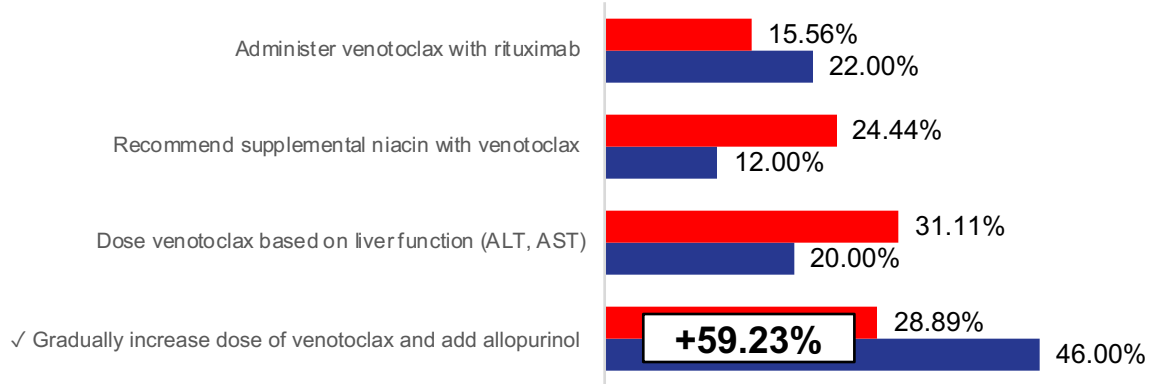
67-y/o man, diagnosed with CLL, reports fatigue and exertional dyspnea. Rai Stage IV. Labs: WBC 140k/μL, 94% lymphocytes, Hgb 10.4g/dL, Plts 90k/μL, FISH del17p, TP53 mutated (NGS), IGHV unmutated. ECOG performance status 1. He is treatment naïve with no other medical history. What treatment might be appropriate for this patient?

N = 49 – 50



A 65 y/o woman with del17p CLL becomes symptomatic after 2 years of treatment with ibrutinib. ECOG performance status is 1. Her clinician recommends venotoclax for second-line therapy. Which of the following may help reduce risk for tumor lysis syndrome in this patient?

N = 45 – 50



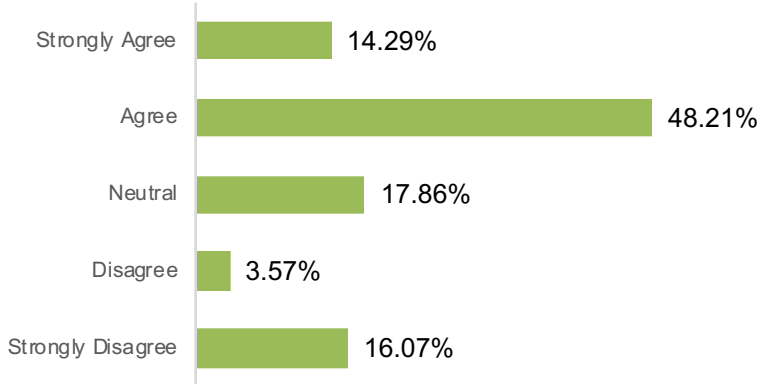
Note: data are matched.
Correct answer is designated by a ✓.

Confidence Items (given at 4 week follow-up)

PCA

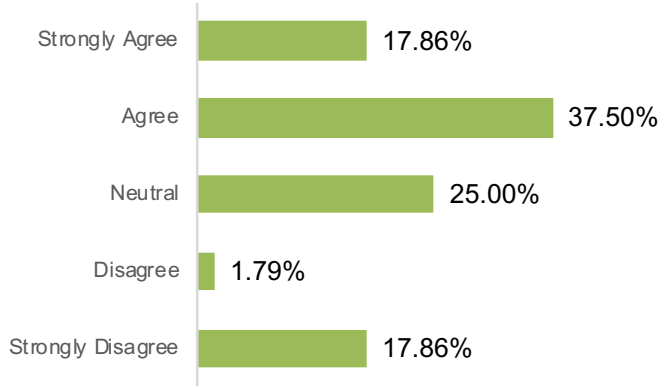
Please rate your level of agreement with the following statement: "I am much more confident in understanding how to select targeted therapy for individual patients with CLL."

N = 56



Please rate your level of agreement with the following statement: "I am much more confident in understanding how to anticipate and manage complications of targeted therapy for CLL."

N = 56



Practice Strategy Item (given at 4 week follow-up)

PCA

Please rate your level of agreement with the following statement: "I have increased risk stratification using prognostic and predictive factors for managing treatment of patients diagnosed with CLL."

N = 116