



CASES

INSIGHTS INTO CHRONIC LYMPHOCYtic LEUKEMIA (CLL)

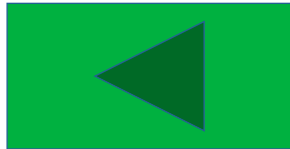
Wednesday, March 17, 2021

Virtual Program – Southwest












HOW TO NAVIGATE THIS REPORT



Click to move to topic of interest or ARS supporting data



Click to return to previous slide

Topic	
Report Objectives	
Report Snapshot	
• Session overview	
• Attendee overview	
• Agenda	
Topline Takeaways and Strategic Recommendations	
Key Insights and Discussion Summary	
• Key insights: First-line CLL	
• Discussion overview: First-line CLL	
• Key Insights: Relapsed/Refractory CLL	
• Discussion overview: Relapsed/Refractory CLL	
Advisor Key Takeaways	
ARS Data	

STUDY OBJECTIVES

- > Gain perspectives of advisors from the Southwest region of the United States on the management of newly diagnosed and relapsed/refractory chronic lymphocytic leukemia (CLL)

REPORT SNAPSHOT: SESSION OVERVIEW



A moderated roundtable discussion with community oncologists from the Southwest region of the United States was held online on **March 17, 2021**

Disease state and data presentations were led by **Dr Susan O'Brien** from UC Irvine Health and **Dr Keren Sturtz** from the SLC Health Medical Group, in conjunction with content developed by the Aptitude Health clinical team

Insights on the use of **BTKi vs BCL2-targeting agents in the community** were obtained

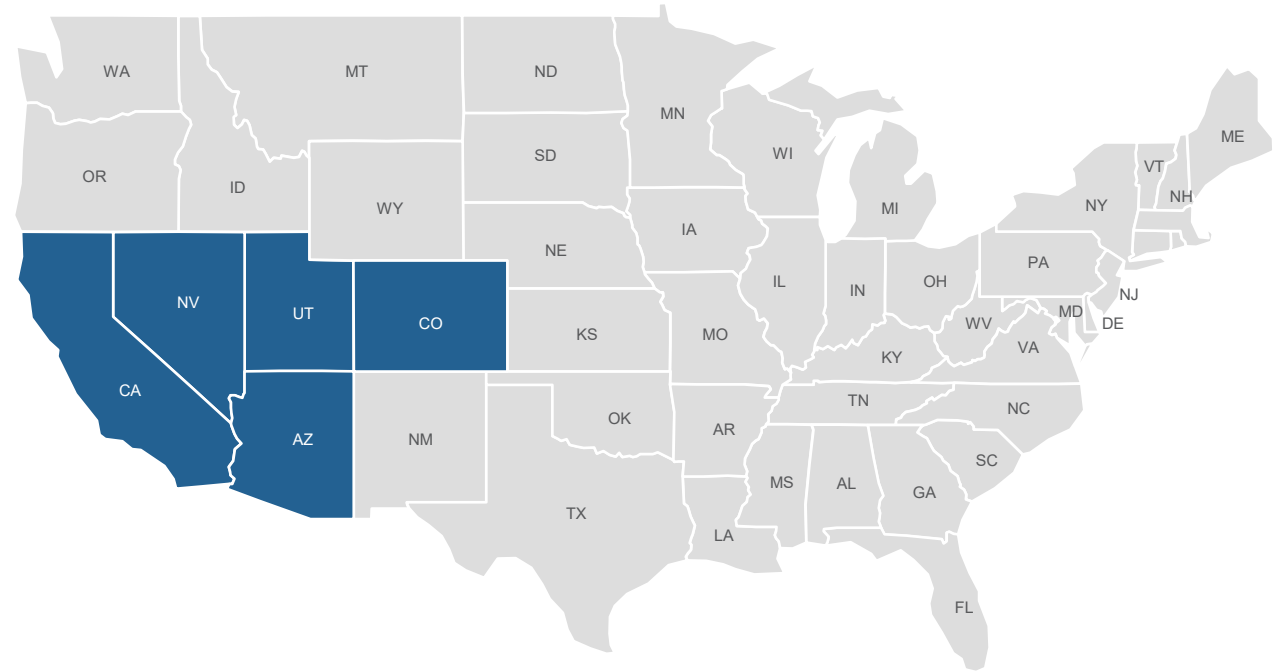
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

REPORT SNAPSHOT: ATTENDEE OVERVIEW



- > The group of advisors comprised 12 community oncologists from across the United States
 - Attendees of the roundtable represented community oncologists from Arizona, California, Colorado, Nevada, and Utah

INSTITUTION	CITY	STATE
Arizona Center for Cancer Care	Scottsdale	AZ
Cochise Oncology	Sierra Vista	AZ
Ironwood Cancer & Research Centers	Chandler	AZ
Ironwood Cancer & Research Centers	Phoenix	AZ
Amol Rao, MD	Huntington Beach	CA
Kaiser Permanente	Riverside	CA
Los Angeles Cancer Network	Los Angeles	CA
Richard E. Gould, MD	Los Angeles	CA
Denver Health Medical Center	Denver	CO
Heart of the Rockies Regional Medical Center	Salida	CO
Intermountain Healthcare	Las Vegas	NV
University of Utah and Intermountain Healthcare	Salt Lake City	UT



REPORT SNAPSHOT: AGENDA



Time (EST)	Topic
5.00 PM – 5.15 PM	Introduction and ARS Questions <ul style="list-style-type: none">• Program overview• ARS questions
5.15 PM – 6.25 PM	First-Line Treatment of CLL <ul style="list-style-type: none">• Overview of treatment options• Reaction and discussion
6.25 PM – 6.35 PM	<i>Break</i>
6.35 PM – 7.45 PM	Treatment of Relapsed/Refractory CLL <ul style="list-style-type: none">• Overview of treatment options• Reaction and discussion
7.45 PM – 8.00 PM	Key Takeaways and Meeting Evaluation

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Topline Takeaways and Strategic Recommendations

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS



OBJECTIVE

- > Understand how patient/disease factors impact choice of first-line therapy in CLL
- > Determine the role of current BTKi vs BCL2 inhibitors in first-line CLL, including differentiation factors and patient profiles for each therapy
- > Gain insights into sequencing of available therapies in second-line CLL

PROCESS

Through ARS questions and moderated discussions, community oncologists described factors impacting their clinical decision making in frontline and second-line CLL and challenges they experience

INSIGHTS

- > In the frontline setting, ibrutinib alone is commonly prescribed across all CLL patient types
 - However, there seems to be an increasing trend toward use of acalabrutinib (mainly for high-risk patients) and venetoclax (mainly for younger patients)
- > In the relapsed/refractory setting, all advisors opt for an alternate MOA compared with frontline
 - This is usually venetoclax-based therapy, as most advisors prefer ibrutinib in frontline



CASES

**Key Insights and
Discussion Summary**

KEY INSIGHTS: FIRST-LINE CLL (1/3)

How and when is MRD assessed by community oncologists and does it impact use of rituximab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, MRD is molecular free. Rituximab is used to treat MRD+ patients in the frontline by about half of the addressers (CR).

- MRD is assessed at CR by half of addressers (CR). The other reports assess MRD at CR and 2 months from induction, and every 2 months thereafter (CR). Only a few reports (10%) assess MRD monthly.
 - The bone marrow aspirate is performed either by the pathologist in the transplant center, or by the addresser themselves, depending on the facility.
 - Most of the addressers were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mainly used by the addressers are molecular PCR (CR) and MRD (CR). The molecular free is used by 20% of addressers.
 - Although MRD is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most addressers.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
 - However, at least 2 addressers are using rituximab to reduce MRD negatively after induction in addressers or after consolidation of addressers. The remaining addressers would refer their patients to transplant departments.

KEY INSIGHTS: FIRST-LINE CLL (2/3)

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KEY INSIGHTS: FIRST-LINE CLL (3/3)

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INSIGHTS

"Ibrutinib is my go-to, given my experience with it for 2 years, and now using a little bit more acalabrutinib as

the second course that's what we use. This is not necessarily always the best course because, as we know, overall survival is not without any significant long-term benefit. I think when I think overall survival, I think about the overall survival with the use of ibrutinib, and I think we think the overall survival with the use of 2 years. I think as far as CLL is concerned, there is significant benefit with the treatment, and overall long-term survival is not without any significant long-term benefit.

That's all a lot of things have been done, nothing is better than ibrutinib and acalabrutinib. I think there's still some ibrutinib patients for the patients. I think as a side effect, I think we're one of the first ones to move based on ibrutinib or something like that. I think something that's been done and we know that ibrutinib is not very good. I think a second year of ibrutinib or acalabrutinib would be something that I would be looking at. I think overall, there's still some ibrutinib patients with CLL, but it's not very good. I think we have to use some combination of efficacy. So, I think that's a lot of things that's going to be done along the way of the ibrutinib. I think it's not very good.

KEY INSIGHTS: RELAPSED/REFRACTORY CLL (1/2)



How and when is MRD assessed by commonly [available](#) and does it impact use of rituximab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, MRD or multiple flow. Rituximab is used to treat MRD+ patients in the frontline by about half of the addressers (CR).

- MRD is assessed at CR by half of addressers (CR). The other reports assess MRD at CR and 3 months from induction, and every 3 months thereafter (CR). Only a few reports (10%) assess MRD monthly.
 - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the addressers themselves, depending on the hospital.
 - None of the addressers were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
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 - Although MRD is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most addressers.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
 - However, at least 3 addressers are using rituximab to reduce MRD negatively after induction in addressers or after consolidation of addressers. The remaining addressers would refer their patients to transplant departments.

KEY INSIGHTS: RELAPSED/REFRACTORY CLL (2/2)

How and when is MRD assessed by community oncologists and does it impact use of rituximab in the frontline setting?

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INSIGHTS

"[On approach to second-line treatment] I mean, it really depends on what they've had before and what kind of a

1. Treatment success in frontline CLL

The overall success rate is very high. This is a very treatable disease. It is a chronic disease, so we have a long-term goal. I would like to see a long-term analysis with that using CD or CLL, and I would like to see the disease-free rate at 5 years. I believe that CLL is a very treatable disease with the treatment, and we are going to see a long-term success.

2. Data needed to confirm that CLL is treatable

That's all a lot of things have been done, nothing is better than B-cell CLL and CLL. It's really hard with CLL. B-cell CLL is the best. I would like to see a long-term analysis with that using CD or CLL, and I would like to see the disease-free rate at 5 years. I believe that CLL is a very treatable disease with the treatment, and we are going to see a long-term success. I would like to see a long-term analysis with that using CD or CLL, and I would like to see the disease-free rate at 5 years. I believe that CLL is a very treatable disease with the treatment, and we are going to see a long-term success.



Advisor Key Takeaways



ADVISOR KEY TAKEAWAYS (1/2)



ADVISOR

> Continuous single-agent therapy in the

ADVISOR

- There is a better understanding of sequencing therapy
- There is a better understanding of the role of immunotherapy in the combination and how the combination can be used in a better way
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- The combination of immunotherapy and chemotherapy is a better way to go

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ADVISOR KEY TAKEAWAYS (2/2)



ADVISOR

> The big development of the last 5-10 years is the way

- There is a better understanding of sequencing therapy
- There is a better understanding of how to use immunotherapy and targeted therapy and how to use them in combination

- There is a better understanding of how to use immunotherapy
- There is a better understanding of how to use targeted therapy
- There is a better understanding of how to use combination therapy

- It is good to have about 10-15% of patients who are responding to immunotherapy

- There is a lot of good options for second line therapy and beyond
- There is a lot of good options for third line therapy and beyond

ADVISOR

- The immunotherapy options are not as good as they used to be

- The hope is that some of these immunotherapy agents will get added into frontline and hopefully improve the results

- The challenge is to learn about all these immunotherapy treatments, especially the targeted therapies
- It is a lot of options coming up in the future. The only way will be to learn how to sequence these drugs

- The challenge is to learn about all these immunotherapy treatments, especially the targeted therapies



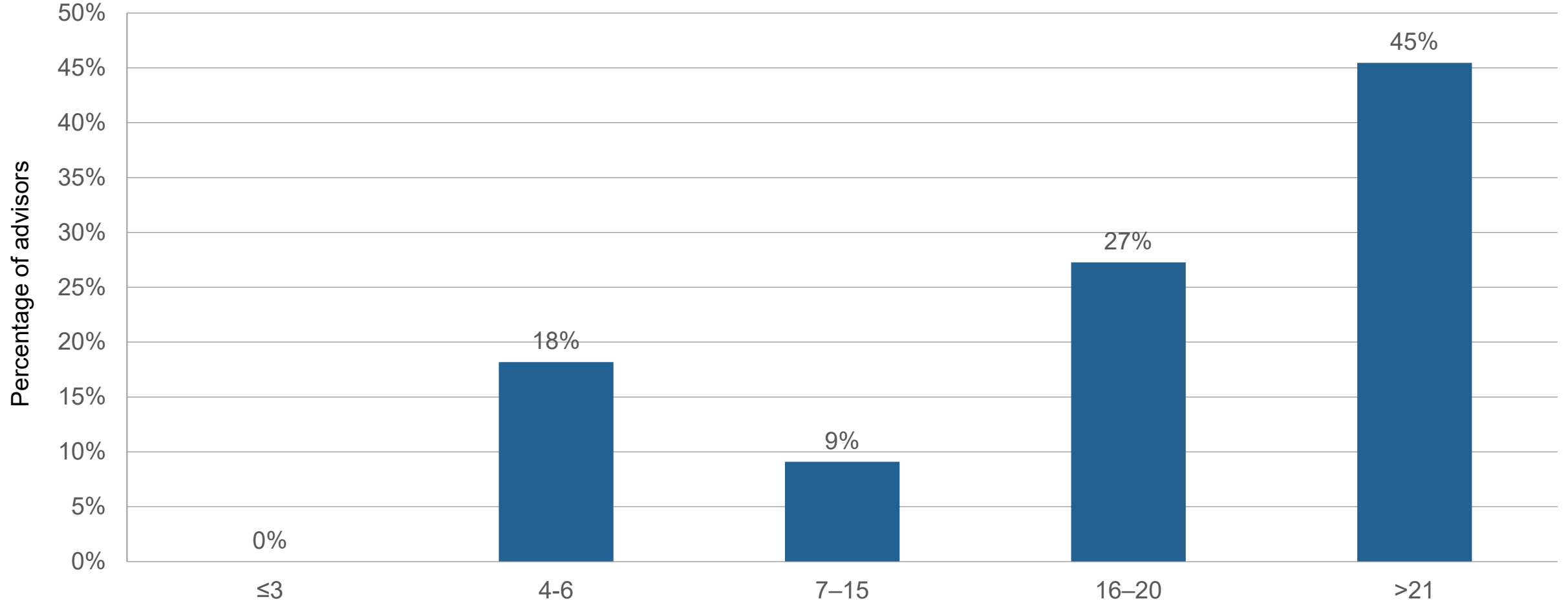
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ARS Data

NEARLY THREE-FOURTHS OF THE ADVISORS CURRENTLY FOLLOW ≥ 16 UNIQUE CLL PATIENTS



How many unique patients with CLL are you currently following? (N = 11*)



TWO-THIRDS OF ADVISORS REPORTED THAT VERY FEW OF THEIR PATIENTS ($\leq 20\%$) HAVE DEL(17P) AND/OR *TP53* MUTATIONS



What percentage of your CLL patients have del(17p) and/or *TP53* mutations? (N = 9*)

FOR EXAMPLE PURPOSES ONLY



AGE AND COMORBIDITIES HAVE THE BIGGEST IMPACT ON CHOOSING FIRST-LINE THERAPY, FOLLOWED BY DEL(17P) MUTATION STATUS

On a scale of 1–5 (1 is very little, 5 is a great deal), how much does each of the following patient characteristics impact your first-line therapy choice for your CLL patients? (N = 10*)

FOR EXAMPLE PURPOSES ONLY



PFS WAS SELECTED BY MOST ADVISORS AS THE MOST IMPORTANT EFFICACY-RELATED OUTCOME WHEN DETERMINING FIRST-LINE THERAPY

Which of the following efficacy-related outcomes do you consider most important when determining first-line therapy for your CLL patients? (Please select your top 2) (N = 10*)

FOR EXAMPLE PURPOSES ONLY



ONE-THIRD OF ADVISORS FEEL THAT THE ABILITY TO STOP THERAPY WITHOUT DISEASE PROGRESSION OR TOXICITY IS VERY IMPORTANT



How important is the ability to stop therapy (without disease progression or toxicity) in your first-line therapy consideration? (N = 11*)

FOR EXAMPLE PURPOSES ONLY



HALF OF THE ADVISORS CHOSE VENETOCLAX + OBINUTUZUMAB AS THEIR PREFERRED OPTION FOR A YOUNG AND FIT PATIENT WHO HAD NO MUTATIONS

What first-line regimen do you routinely use for a **50-year-old** PS 0 patient with no major comorbidities (without del[17p]/TP53 mutation or IGHV mutation)? (N = 10*)

FOR EXAMPLE PURPOSES ONLY



WHEN THE SAME PATIENT PRESENTED WITH AN *IGHV* MUTATION, 27% OF ADVISORS EACH CHOSE EITHER BR OR VENETOCLAX + OBINUTUZUMAB

What first-line regimen do you routinely use for a **50-year-old** PS 0 patient with no major comorbidities (**without** del[17p]/*TP53* mutation; ***IGHV* mutation positive**)? (N = 11*)

FOR EXAMPLE PURPOSES ONLY



IF THE PATIENT TESTED POSITIVE FOR DEL(17P) OR TP53 MUTATION, 36% OF ADVISORS SELECTED VENETOCLAX + OBINUTUZUMAB, FOLLOWED BY 27% OF ADVISORS EACH CHOOSING EITHER ACALABRUTINIB ± ANTI-CD20 OR IBRUTINIB ± RITUXIMAB

What first-line regimen do you routinely use for a **50-year-old** PS 0 patient with no major comorbidities (**positive** for del[17p]/TP53 mutation; **IGHV** mutation **negative**)? (N = 11*)

FOR EXAMPLE PURPOSES ONLY



IN OLDER PATIENTS WITH NO MUTATION OR COMORBIDITIES, 45% OF ADVISORS PREFERRED IBRUTINIB, FOLLOWED BY 36% SELECTING VENETOCLAX + OBINUTUZUMAB

What first-line regimen do you routinely use for a **75-year-old** PS 0 patient with no major comorbidities (without del[17p]/TP53 mutation or IGHV mutation)? (N = 11*)

FOR EXAMPLE PURPOSES ONLY



FOR A YOUNG PATIENT (NO DELETIONS OR MUTATIONS) WHO RECEIVED FIRST-LINE CIT AND ATTAINED A CR THAT LASTED 3 YEARS, HALF OF THE ADVISORS PREFERRED A VENETOCLAX-BASED THERAPY

What is your preferred second-line therapy in a **55-year-old** PS 0 CLL patient who received FCR or other CIT as first-line therapy and attained a CR that lasted 3 years? Patient has no 17p deletion or *TP53* mutation, and *IGHV* mutational status is unknown. (N

FOR EXAMPLE PURPOSES ONLY



FOR A PATIENT (*IGHV* MUTATION) WHO WAS INITIALLY TREATED WITH IBRUTINIB AND ATTAINED A 4-YEAR DISEASE-FREE INTERVAL, 80% OF ADVISORS PREFERRED A VENETOCLAX-BASED THERAPY

What is your preferred second-line therapy in a CLL patient who is **55 years of age**, was treated with ibrutinib frontline therapy, and attained a 4-year disease-free interval? Patient had no evidence of 17p deletion and/or *TP53* mutation, and he had **mutated**

FOR EXAMPLE PURPOSES ONLY



FOR AN OLDER PATIENT (17P DELETION) WHO WAS INITIALLY TREATED WITH IBRUTINIB AND ATTAINED A CR FOR 2.5 YEARS BUT CURRENTLY HAS PS 1 AND SIGNIFICANT COMORBIDITIES, NEARLY TWO-THIRDS OF ADVISORS PREFERRED A VENETOCLAX-BASED THERAPY

A **75-year-old** patient with 17p-deleted CLL was treated with ibrutinib monotherapy and attained a CR for 2.5 years, then progressed. Patient's renal function shows a GFR of 50 mL/min and his PS is 1. He has a history of hypertension and type 2 diabetes tha

FOR EXAMPLE PURPOSES ONLY

FOR A PATIENT (NO 17P DELETION OR MUTATION) WHO HAS BEEN ON FRONTLINE VENETOCLAX + OBINUTUZUMAB FOR THE PAST 8 MONTHS (NO TOXICITIES AND MRD NEGATIVE), NEARLY TWO-THIRDS OF ADVISORS WOULD CONTINUE THERAPY FOR A TOTAL OF 12 MONTHS AND THEN STOP IF MRD REMAINS NEGATIVE

A **57-year-old** patient with CLL (no 17p deletion or *TP53* mutation) has been on venetoclax + obinutuzumab as a frontline combination for the past 8 months with adequate tolerance and no toxicities. His physician checked the MRD status using 6-color flow and

FOR EXAMPLE PURPOSES ONLY

