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INSIGHTS INTO CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Wednesday, March 17, 2021

Virtual Program – Southwest

HOW TO NAVIGATE THIS REPORT

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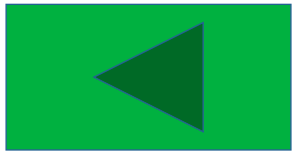
Click to move to topic of interest or ARS supporting data



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REPORT OBJECTIVES

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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

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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

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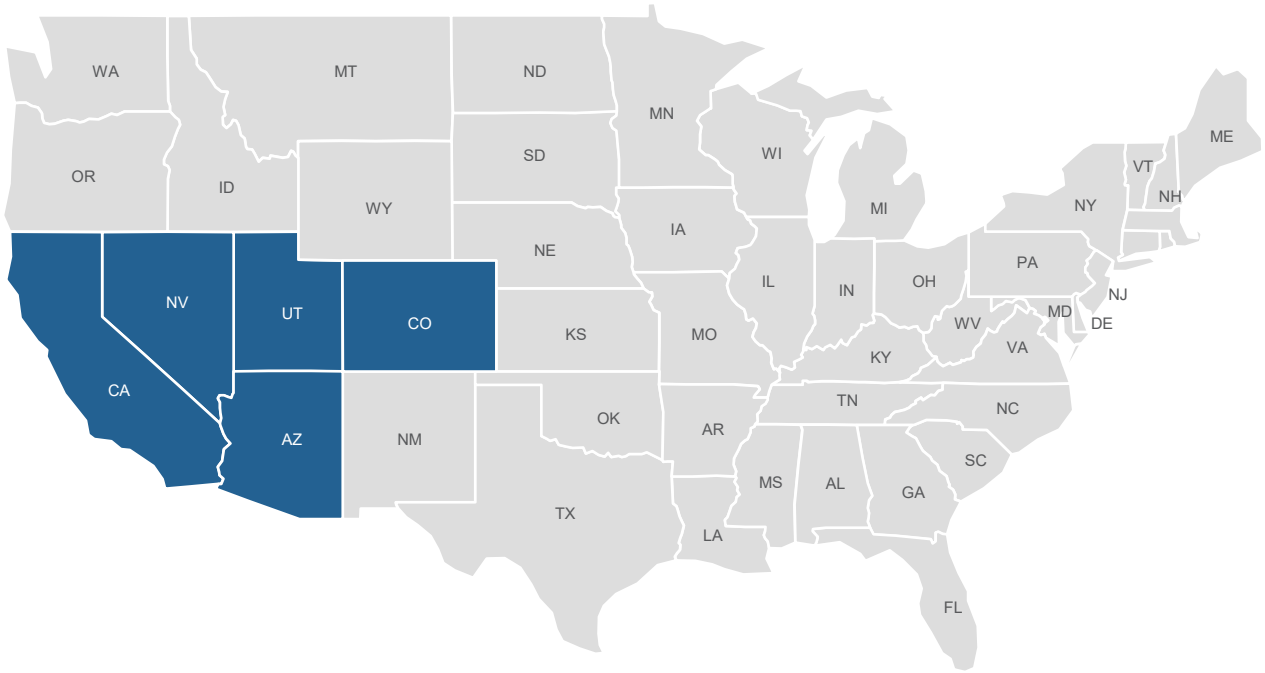
- The group of advisors comprised 12 community oncologists from across the United States
  - Attendees of the roundtable represented community oncologists from Arizona, California, Colorado, Nevada, and Utah

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



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REPORT SNAPSHOT: AGENDA

Time (EST)	Topic
5.00 PM – 5.15 PM	Introduction and ARS Questions • Program overview • ARS questions
5.15 PM – 6.25 PM	First-Line Treatment of CLL • Overview of treatment options • Reaction and discussion
6.25 PM – 6.35 PM	*Break*
6.35 PM – 7.45 PM	Treatment of Relapsed/Refractory CLL • 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

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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

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Key Insights and Discussion Summary

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

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

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS 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 advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 1 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors 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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DISCUSSION: FIRST-LINE CLL

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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

- [illegible]

- [illegible]

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

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- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

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

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DISCUSSION: RELAPSED/REFRACTORY CLL

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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

- [illegible]

[illegible]

- [illegible]

[illegible]

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Advisor Key Takeaways

ADVISOR KEY TAKEAWAYS (1/2)

ADVISOR		ADVISOR	
	> Continuous single-agent therapy in the		

ADVISOR KEY TAKEAWAYS (2/2)

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

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ARS Data

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

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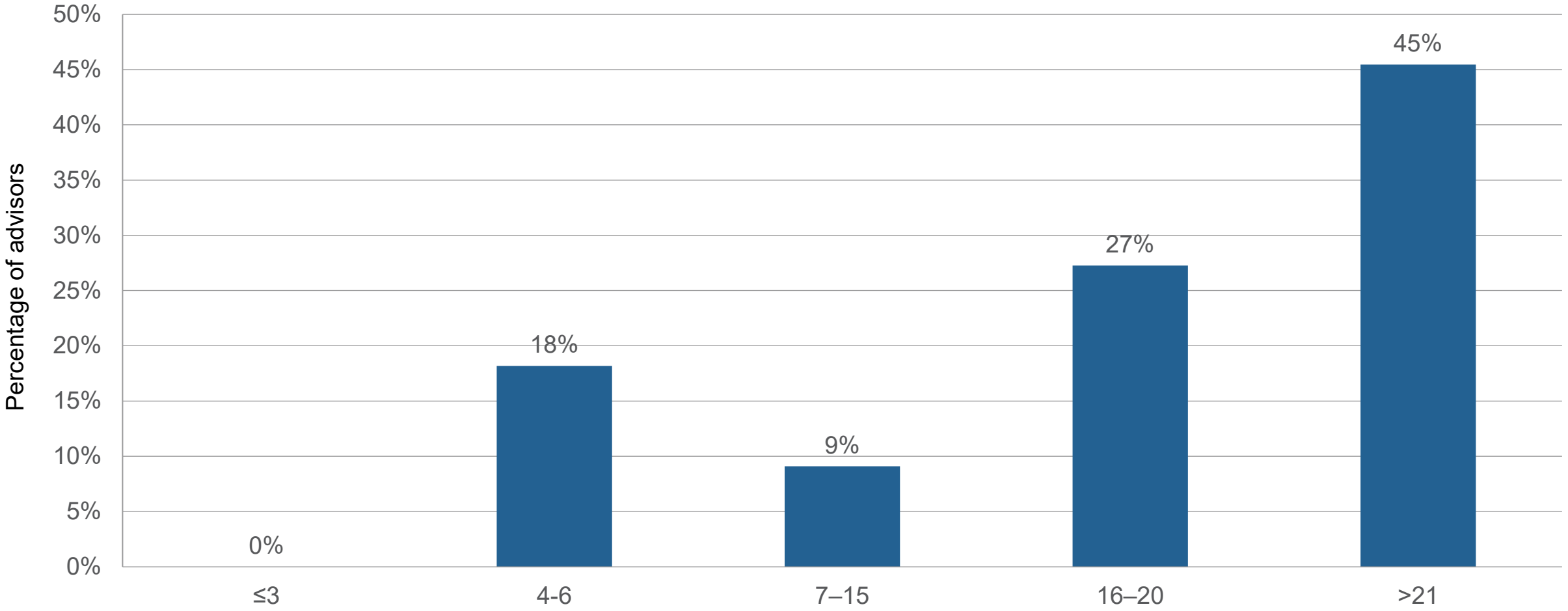
How many unique patients with CLL are you currently following? (N = 11*)



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*One advisor did not respond.

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

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

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*)

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*)

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*)

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*)

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

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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*)

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

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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*)

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

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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 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

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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 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

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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 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

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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 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

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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