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CASES

Insights Into Acute Lymphoblastic Leukemia (ALL)

June 24, 2024

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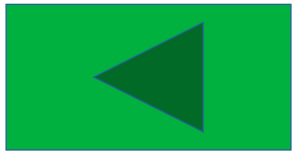
Click to move to topic of interest or ARS supporting data



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Report Objectives

STUDY OBJECTIVES

Gain physicians' perspectives on

- Frontline therapies for AYA patients with ALL
- Management options in relapsed/refractory (R/R) ALL
- Treatment challenges in AYA patients with ALL
- Drivers and barriers to adopting new therapies in the community setting

Report Snapshot: Session Overview

A moderated roundtable discussion was held with oncologists in the United States on **June 24, 2024**

Disease state and data presentations and moderation were led by **Michael R. Grunwald, MD, FACP,** from Atrium Health Levine Cancer Institute, Charlotte, NC, in conjunction with content developed by the Aptitude Health clinical team

Insights were obtained on **current treatment approaches for the management of ALL in young adults**, including their experience with **ASP-containing regimens** in the frontline setting

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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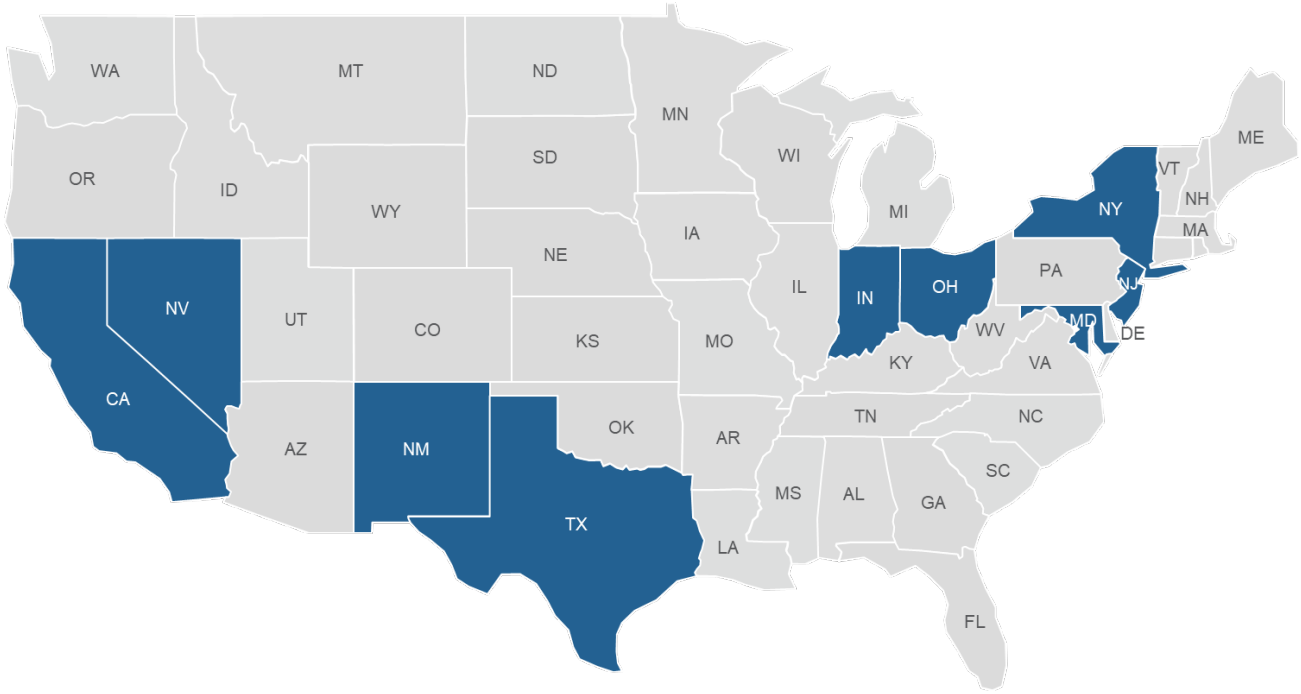
> The group of physicians comprised 12 oncologists from the United States, representing both academic and community setups

Practice	City	State
Advanced Care Oncology & Hematology Associates	Springfield	MD
Texas Oncology	Dallas	TX
University Hospitals Seidman Cancer Center	Parma	OH
Lovelace Health System	Albuquerque	NM
Riverside Medical Center	Riverside	CA
Regional Cancer Care Associates	Riverdale	NJ
Hematology Oncology of Indiana	Indianapolis	IN
New York Oncology Hematology	Hudson	NY
Jefferson Health Sidney Kimmel Cancer Center	Sewell	NJ
Kaiser Permanente Riverside Medical Center	Riverside	CA
Comprehensive Cancer Centers	Las Vegas	NV
Alta Bates Summit Medical Center	Berkeley	CA



Report Snapshot: Participant Demographics

In the past 12 months, approximately how many newly diagnosed AYA (18–39 years old) patients with B-cell ALL have you personally treated or managed care for? (n = 11*)

Approximately how many of your newly diagnosed patients with ALL in the past 12 months were Ph-negative? (n = 11*)

*One physician did not respond.

Report Snapshot: Agenda

Time (CT)	Topic
6.00 PM – 6.15 PM	**Introduction** • Program overview • ARS questions
6.15 PM – 7.50 PM	**Frontline Management Options in ALL**
7.50 PM – 8.00 PM	**Break**
8.00 PM – 8.50 PM	**Management Options in Relapsed/Refractory (R/R) ALL**
8.50 PM – 9.00 PM	**Key Takeaways and Meeting Evaluation**

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Discussion Summary

Frontline Management Options in ALL

Discussion: Frontline Management Options in ALL (1/9)

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INSIGHTS AND DATA

"We normally see maybe 5 to 10 [patients with B-ALL] at the most. We get a lot of them through emergency room

- Treatment success in frontline DLBCL

- Data needed to switch from BCIC in frontline

Discussion: Frontline Management Options in ALL (2/9)

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INSIGHTS AND DATA

"If these patients do need to be hospitalized due to complications, they're not really served very well in a local-

- Treatment success in frontline DLBCL

- Data needed to switch from SOC in frontline

Discussion: Frontline Management Options in ALL (3/9)

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INSIGHTS AND DATA

"We treat everything. We use pediatric regimens. We do not have a relationship with pediatric hematologists, but

- Treatment success in frontline DLBCL

"We overall survival, that's what we need. This is not metastatic disease, this is curable disease, so we need overall survival."
"... cure without any significant long-term toxicity. ... I think when I define success, I would rather use a landmark endpoint rather than using OS or PFS, and I would say what's the disease-free rate at 2 years. I definitely do think OS is important if there is significant toxicity with the treatment, and people dying from competing comorbidities."

- Data needed to switch from SOC in frontline

"First of all, a lot of things have been tried, nothing is better than R-CHOP, and frankly, I'm pretty happy with how R-CHOP performs for my patients."
"I would be a late adopter. I would not be one of the first ones to move based on PFS or anything like that. I want something that's tried and true and we know how well it works."
"If the toxicities are not very severe, I think a hazard ratio of 0.85 or better would be something that I would be looking at."
"Overall survival data, that's ideal, but in this disease state OS is hard to come by, so you do have to use some surrogates of efficacy. So, I do think that a 2- or 3-year event-free survival kind of story is likely what's going to start driving my use of any regimen. ... PFS is NOT sufficient."

Discussion: Frontline Management Options in ALL (4/9)

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INSIGHTS AND DATA

"We treat up to the age of 39. The majority of us will use the CALGB protocol, but there are some who talk to MD

- Treatment success in frontline (ALL)

- Data needed to switch from 3C/C in frontline

Discussion: Frontline Management Options in ALL (5/9)

INSIGHTS AND DATA

"Years ago, I had to use Erwinia only once, because of a bad reaction to E.coli. We didn't have access at that time

- [redacted]

- [redacted]

Discussion: Frontline Management Options in ALL (6/9)

INSIGHTS AND DATA

"But, from the asparaginase [point of view], it looks like the recombinant product should be the way to go . . .

- [illegible]

- [illegible]

Discussion: Frontline Management Options in ALL (7/9)

INSIGHTS AND DATA

[Is the CALGB10403 study practice changing, this 2019 study from Dr. Stock and colleagues showing

- Treatment success in frontline (b-ALL)

- Data needed to switch from 3C/C in frontline

Discussion: Frontline Management Options in ALL (8/9)

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INSIGHTS AND DATA

"The problem is with the community hospitals, they often have difficulty approving, especially the PEG-

- [illegible]

[illegible]

- [illegible]

[illegible]

Discussion: Frontline Management Options in ALL (9/9)

INSIGHTS AND DATA

"I think one of the problems that we also have is fertility preservation in younger people. We have had patients in

- [illegible]

- [illegible]

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Discussion Summary

Management Options in R/R ALL

Discussion: Management Options in R/R ALL (1/2)

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INSIGHTS AND DATA

"If they got chemo in the beginning, then your options will be the bispecifics or the inos, and refer them to

- Treatment success in frontline (blinatumomab, inotuzumab ozogamicin)
- Data needed to switch from blinatumomab, inotuzumab ozogamicin in frontline

Discussion: Management Options in R/R ALL (2/2)

INSIGHTS AND DATA

[How often are you checking the MRD status of patients?] "Every three months . . . bone marrow . . . we do not have

- Treatment success in frontline (blinatumomab)

- Data needed to switch from blinatumomab in frontline

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Participant Key Takeaways

Physician Key Takeaways (1/2)

ADVISOR	ADVISOR
> It was insightful to learn about the data on the advent of asparaginase and its application in pediatric protocols.	> Anticipated changes include the use of blinatumomab and inotuzumab as first-line therapies, with CAR T potentially
1	6
2	6
3	7
4	8

Physician Key Takeaways (2/2)

ADVISOR	ADVISOR
> Main points include the importance of dose intensification in	> Given the robust data on asparaginase-based protocols, I
1	5
2	6
3	7
4	8

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ARS Results

Frontline Management Options in ALL

All Physicians See Overall Survival as Most Important in Considering First-Line Therapy Options for AYA Patients With ALL, Followed by High Cure Rate and Durable Remission

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*One physician did not respond.

Most Physicians (or their practices) Have Prescribing Rights at a Nearby Hospital or Infusion Center Where Patients Can Receive Myelosuppressive Intensive Chemotherapy like Hyper-CVAD; Nearly 30% Reported That Their Patients Have Access to Facilities Offering ASP-Containing Regimens

*One physician did not respond.

55% of Physicians Chose Hyper-CVAD ± Immunotherapy for Treating Newly Diagnosed Ph-Negative AYA Patients With ALL; Over a Third Opted for ASP-Containing or Modified BFM Backbone Therapy ± Immunotherapy

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*One physician did not respond.

Physicians Were Divided Equally in Their Evaluations of Toxicity Profiles; 45% Regard ASP-Containing or Modified BFM Backbone Therapy as Having the Least Favorable Toxicity, and 45% View Hyper-CVAD With Comparable Concern Regarding Its Toxicity

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*One physician did not respond.

73% of Physicians Had the Most Experience in Managing AEs Associated With the Hyper-CVAD Regimen for Ph-Negative B-ALL in AYA Patients. In Contrast, They Were Significantly Less Experienced With AEs Linked to ASP-Containing Regimens

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*One physician did not respond.

When Using ASP Regimens, Most Physicians (91%) Will Use It in the First Line for Their AYA Patients With B-ALL; Very Few Utilize It in the Second Line

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*One physician did not respond.

Almost All Physicians Agreed That ASP Regimens Are Suitable for 18- to 39-Year-Old Patients With ALL; Over Half Were Aware of Recent Guidance on AEs Associated With ASP-Based Treatments, and Nearly Half Recognized the Superiority Data of These "Pediatric-Inspired" Regimens Over Traditional "Adult" Regimens

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*One physician did not respond.

Nearly Half the Physicians Were Somewhat Familiar With the AALL1931 Study Results; 17% of Physicians Were Very Familiar With These Findings

67% of Physicians Would Discontinue ASP Therapy if Their AYA Patients Experienced Pancreatitis, 58% Would Stop Treatment Due to Cases of Transaminitis, and 50% Would Discontinue Due to Hypertriglyceridemia

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ARS Results

Management Options in R/R ALL

For 80% of Physicians, Comorbidities Are the Leading Influence on Therapeutic Decisions in the First-Relapse Setting, Closely Followed by Ph Status, Initial Induction Therapy Response, and Timing of Relapse, Each at 50%

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*Two physicians did not respond.

80% of Physicians Would Consider Changing the Treatment Approach If MRD Positivity Persists Across Any of the Treatment Stages Listed Below, Indicating a Strong Preference for an Adaptive Treatment Strategy Based on Ongoing MRD Assessment; 40% Opted to Change Treatment Protocols Early on,

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*Two physicians did not respond.

The Most Significant Challenges in Ordering MRD Testing Include Reimbursement Issues and Patient Refusal to Undergo Bone Marrow Aspirate, Each Reported by 29% of Physicians, Followed by 24% Indicating That Pathologists at Their Practices Do Not Offer MRD Testing

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*Two physicians did not respond.

Patient Case

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- A 35-year-old woman presents with a history of pre–B-ALL diploid cytogenetics

A 63-year-old man presents with a 4-week history of progressive back pain. Imaging reveals an 11-cm retroperitoneal mass. A core needle biopsy is obtained and is read as DLBCL, non-GCB by Hans methods. IHC for bcl-2 and myc show high expression (>80%) for each. FISH testing for bcl-2 and myc are both negative. FISH for bcl-6 is positive. PET imaging reveals widespread pathologic adenopathy with involvement of mediastinal, retroperitoneal, and mesenteric nodes. There are also 2 PET-avid mass lesions in the liver, and 1 lesion in the left kidney. The SUV_{max} is 28. Ki67 is 90%. There is no apparent marrow involvement by PET. The LDH is elevated at 3× the ULN. His PS is 1 and there are no significant comorbidities.

Most Physicians (90%) Would Opt for Blinatumomab as the Next Treatment Option for a Young Patient With Relapsed ALL, With a History of Pre–B-ALL, Positive for CD19 and CD22, Diploid Cytogenetics, and *CRLF2* Negativity, Who Had a CR With MRD Negativity Following Induction With R–Hyper-CVAD

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*Two physicians did not respond.

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