



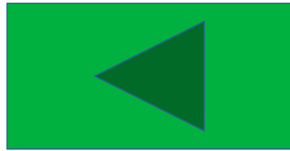
Insights Into Acute Lymphoblastic Leukemia (ALL)

June 24, 2024











How to Navigate This Report



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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

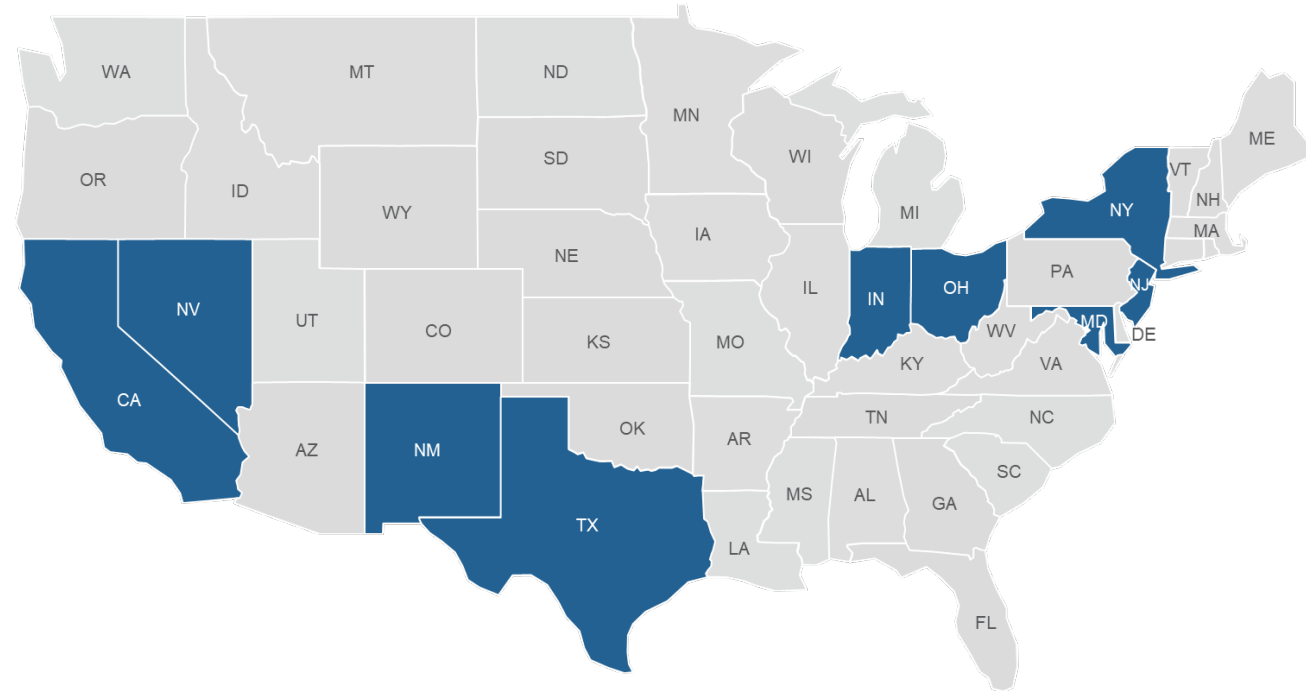
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

Report Snapshot: Attendee Overview



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

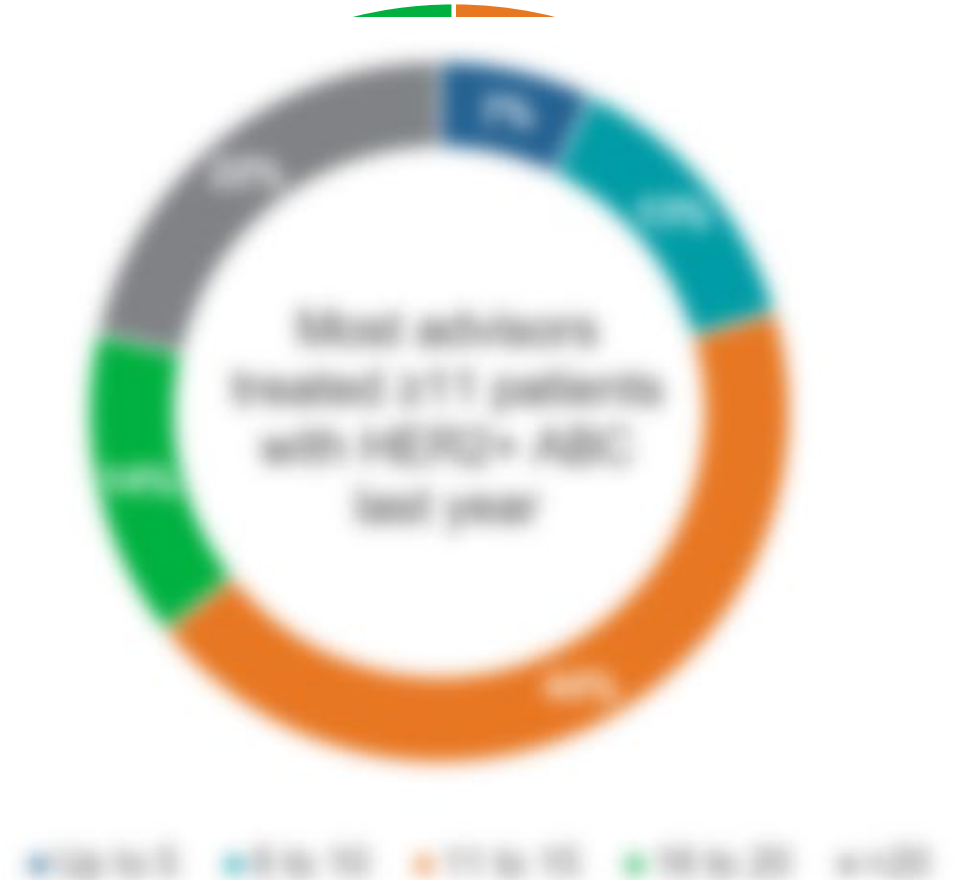
Practice	City	State
Advanced Care Oncology & Hematology Associates	Springfield	MD
Texas Oncology	Dallas	TX
University Hospitals Seidman Cancer Center	Parma	OH
Lovelace Health System	Albuquerque	NM
Riverside Medical Center	Riverside	CA
Regional Cancer Care Associates	Riverdale	NJ
Hematology Oncology of 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*)



Report Snapshot: Agenda



Time (CT)	Topic
6.00 PM – 6.15 PM	Introduction <ul style="list-style-type: none">• 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





Discussion Summary

Frontline Management Options in ALL

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

1. Treatment success in frontline B-ALL

The overall survival that's seen in acute B-ALL is not necessarily disease-free or overall survival, so we need overall survival. I think overall survival is a better endpoint, but I think we should also use a frontline endpoint rather than using OS or DFS, and I think we should be looking at the disease-free rate at 1 year. I think we should also be looking at overall survival with the treatment, and overall drug-free survival.

2. Data needed to support front-line B-ALL in frontline

That's all a lot of things that we need to see, looking at both the B-ALL and the overall survival, with both B-ALL patients and the overall survival. I think we should be looking at overall survival, but I think we should also be looking at the disease-free rate at 1 year. I think we should also be looking at overall survival with the treatment, and overall drug-free survival. I think we should also be looking at the disease-free rate at 1 year. I think we should also be looking at overall survival with the treatment, and overall drug-free survival.

INSIGHTS AND DATA

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

the overall survival that's what we want. This is not necessarily disease-free or overall survival, so we want overall survival.”

“I would not use significant response levels. I think what I would consider I would rather use a frontline response rate that's using CR or PR, and I would use that to measure the rate of 1 year. I believe as that CR is important I think is significant mostly with the treatment, and overall going from something like 10%.”

“That's all a lot of things have been said, nothing is better than 100% CR and PR, I think that's what we want to see. I think that's what we want to see.”

“I would use a CR or PR. I would not use CR or PR as a measure of overall survival, I would use CR or PR as a measure of something that's more important and we want to see that.”

“If the overall survival rate is low, I think a response rate of 100% or better would be something that would be better.”

“Overall survival rate, that's what we want to see. I think that's what we want to see. I think that's what we want to see. I think that's what we want to see. I think that's what we want to see.”

INSIGHTS AND DATA

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

1. Treatment outcomes in frontline ALL

The overall survival (OS) rates are low. This is not necessarily because this is a curable disease, as we have several options. I think we have significant long-term toxicity. I think we have a better overall survival rate using CR1 or CR2, and I would say that the disease-free rate at 5 years is actually as high as a reported 70% in significant toxicity with the treatment, and people going from something like 70%.

2. Data needed to support front-line ALL

That's all a lot of things have been done, nothing is really new. I think we need to really focus on how to improve outcomes for the patients. I would like to see a study that would not be one of the first ones to come based on CR1 or something like that. I want something that's not just a trial and see how that goes. If the toxicity is not very severe, I think a longer trial of CR1 or CR2 would be something that would be helpful. I think overall, there's a lot of things that we can do to improve outcomes, but I think that's a lot of things that we're going to start doing in the next 5-10 years. I think it's not sufficient.

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 Anderson, and they’ll do the mini-MOGAD like PLINOXTO.”

1. Treatment success in frontline ALL

... The overall survival rate is not as good. This is not necessarily because the disease is more aggressive, or we have a more aggressive regimen. ... There are some people who would rather use a frontline protocol rather than going to MD or NCI, and I would say that the disease-free rate at 1 year ... is similar to that of a regimen that is significantly better with the treatment, and people going from something ...

2. Data needed to support front ALL in frontline

... That’s what a lot of things have been about, getting a better idea of what’s going on and being ... to really focus with how to control patients for the future. ... I would be a little bit more ... to really focus on the first year or two ... of something like that ... something that’s not as good and not as well as the ... of the disease ... a better idea of what’s going on ... something that ... of the disease ... to really focus on the first year or two ... of something like that ... something that’s not as good and not as well as the ...

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

1. Treatment success in Frontline (2010)

The overall success rate was very high. This is not necessarily because the disease is easily treated, as we have several options. I think what really helped was the fact that we had access to the best drugs, and I think we were able to use a treatment protocol with that drug. I think we were able to use the drug for up to 10 years. I think we were able to use it as a treatment if there is significant toxicity with the treatment, and we were going from something else.

2. Data needed to support from 2010 in Frontline

That's all a lot of things have been done, nothing is really that difficult and hard. It's really hard, with how difficult patients are to handle. I think we have a lot of things that we can do to make sure we are able to use the drug for up to 10 years. I think we were able to use it as a treatment if there is significant toxicity with the treatment, and we were going from something else. I think we were able to use the drug for up to 10 years. I think we were able to use it as a treatment if there is significant toxicity with the treatment, and we were going from something else. I think we were able to use the drug for up to 10 years. I think we were able to use it as a treatment if there is significant toxicity with the treatment, and we were going from something else.

INSIGHTS AND DATA

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

1. Treatment success in Frontline ALL (2012)

The overall success rate is about 40%. This is not necessarily because there is a problem with the drug, but because of the way the drug is used. The drug is used in a way that is not optimal. The drug is used in a way that is not optimal. The drug is used in a way that is not optimal.

2. Data needed to support from 2012 in Frontline

This slide is all things that have been done. Nothing is better than 40000 and there is a really big gap with the 40000 patients for the system. The data needed to support from 2012 in Frontline is all things that have been done. Nothing is better than 40000 and there is a really big gap with the 40000 patients for the system.

INSIGHTS AND DATA

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

1. Treatment success in frontline ALL

The overall survival (OS) rates were similar. This is not necessarily unusual. It is possible that the OS rates were similar because of the overall survival benefit. The overall survival benefit was not statistically significant. The overall survival benefit was not statistically significant. The overall survival benefit was not statistically significant.

2. Data needed to support front ALL in frontline

There are a lot of things that have been done. Nothing is better than the CALGB10403 and the overall survival benefit. The overall survival benefit was not statistically significant. The overall survival benefit was not statistically significant. The overall survival benefit was not statistically significant.

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

INSIGHTS AND DATA

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

1. Treatment success in Frontline ALL

The overall success rate is about 30%. This is not necessarily because the disease is so hard to treat, it is because of the way we treat it. The success rate is low because we often use a treatment protocol with high doses of drugs, and we don't always have the disease-free survival rate of 30%. We think that the 30% is a reflection of the fact that we are not always using the best treatment, and we are not always using the best supportive care.

2. Data needed to support Frontline ALL

The data we need to support Frontline ALL is not just about the disease, it is about the way we treat it. We need to know what the best treatment is, and we need to know what the best supportive care is. We need to know what the best way to deliver the treatment is, and we need to know what the best way to deliver the supportive care is. We need to know what the best way to combine the treatment and the supportive care is. We need to know what the best way to monitor the disease is, and we need to know what the best way to manage the side effects is.

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

1. Treatment success in frontline ALL

The overall success rate is very high. This is a very heterogeneous disease. It is highly curable. In the past, overall survival was around 50%. Now it's around 70-80%. This is a significant improvement. This is due to the use of a frontline regimen with high-dose IT and CNS prophylaxis. The overall success rate is around 70-80%. This is a significant improvement. This is due to the use of a frontline regimen with high-dose IT and CNS prophylaxis.

2. Data needed to support front-line ALL

The data needed to support front-line ALL is very high. This is a very heterogeneous disease. It is highly curable. In the past, overall survival was around 50%. Now it's around 70-80%. This is a significant improvement. This is due to the use of a frontline regimen with high-dose IT and CNS prophylaxis. The overall success rate is around 70-80%. This is a significant improvement. This is due to the use of a frontline regimen with high-dose IT and CNS prophylaxis.



Discussion Summary

Management Options in R/R ALL

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

INSIGHTS AND DATA

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

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t.

1. Treatment success in frontline (N=200)	<p>The overall survival rate was 18%. This is a very low survival rate. The only overall survival data is from the overall survival.</p> <p>There was no significant difference in overall survival between the two groups. The only significant difference was in the overall survival rate. The overall survival rate was 18% in the control group and 18% in the experimental group. There was no significant difference in overall survival between the two groups.</p>
2. Data needed to support from R/R ALL in frontline	<p>The data is a bit messy. There are a lot of things that have been done. Nothing is really clear. The overall survival rate is 18%. This is a very low survival rate. The only overall survival data is from the overall survival.</p> <p>There was no significant difference in overall survival between the two groups. The only significant difference was in the overall survival rate. The overall survival rate was 18% in the control group and 18% in the experimental group. There was no significant difference in overall survival between the two groups.</p>

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

3. Treatment success in frontline CR MRD

“The overall success that I would expect is about 30-40% in frontline CR MRD. This is based on the overall success in CR MRD in the overall population. . . . we do not have . . .”

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4. Data needed to support front-line CR MRD in frontline

“That’s all a lot of things have been done, nothing is better than CR MRD and CR MRD. . . . we do not have . . .”



Participant Key Takeaways

Physician Key Takeaways (1/2)



ADVISOR

- > It was insightful to learn about the data on the advent of asparaginase and its application in pediatric protocols.

ADVISOR

- > Anticipated changes include the use of blinatumomab and inotuzumab as first-line therapies, with CAR T potentially

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

- There is a better understanding of sequencing therapy
- There is a better understanding of the importance of dose intensification
- There is a better understanding of the importance of the role of the physician

- The importance of having a good understanding of the role of the physician

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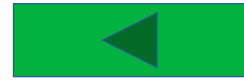
ARS Results

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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY



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

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

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



FOR EXAMPLE PURPOSES ONLY





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%

FOR EXAMPLE PURPOSES ONLY

*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,

FOR EXAMPLE PURPOSES ONLY

*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

FOR EXAMPLE PURPOSES ONLY

*Two physicians did not respond.



- > 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 (>90%) 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 2x 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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US 5901-B Peachtree Dunwoody Road
Suite 415, Atlanta, GA 30328, US

EU Laan van Nieuw Oost-Indië 133 F
2593 BM The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

[aptitudehealth.com](https://www.aptitudehealth.com)

