



EPICS

# Acute Lymphocytic Leukemia (ALL) in 2023 and Beyond – Focus on Combination Therapies

December 1, 2023

Full Report

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## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
December 1, 2023



**DISEASE STATE AND  
DATA PRESENTATIONS**  
by key experts



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations



**PANEL:** Key experts in  
ALL

- > 10 from North America
- > 4 from Europe
- > 1 from Australia



**LEUKEMIA-SPECIFIC  
DISCUSSIONS** on  
therapeutic advances and  
their application in clinical  
decision-making

# Panel Consisting of 15 Worldwide Leukemia Experts

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**Aaron Logan, MD, PhD**  
University of California,  
San Francisco

**Wendy Stock, MD**  
University of Chicago  
Medicine

**Andre Schuh, MD, FRCPC**  
Princess Margaret Cancer Centre

**CO-CHAIR:  
Gail J. Roboz, MD**  
Weill Cornell Medicine

**Daniel J. DeAngelo, MD, PhD**  
Harvard Medical School

**Selina Luger, MD**  
University of Pennsylvania,  
Perelman School of  
Medicine

**Tobias Menne, MD, PhD**  
Newcastle upon Tyne  
Hospitals

**CO-CHAIR:  
Elias Jabbour, MD**  
University of Texas  
MD Anderson Cancer Center

**Jae Park, MD**  
Memorial Sloan Kettering  
Cancer Center

**Nicola Gökbüget, MD**  
University Hospital  
Frankfurt

**Ibrahim Aldoss, MD**  
City of Hope

**Shaun Fleming, MBBS (Hons),  
FRACP, FRCPA**  
Melbourne Haematology,  
Richmond, VIC, Australia

**Bijal Shah, MD**  
Moffitt Cancer Center

**Nicolas Boissel, MD, PhD**  
Hôpital Saint-Louis

**Renato Bassan, MD**  
Ospedale dell'Angelo and  
Ospedale SS



# Meeting Agenda

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Time (CST)	Topic	Presenter
8.00 AM – 8.10 AM	<b>Welcome and Introductions</b>	Elias Jabbour, MD
8.10 AM – 8.25 AM	<b>Blinatumomab in First Line and Maintenance for ALL</b>	Nicola Gökbüget, MD
8.25 AM – 8.45 AM	Discussion	Elias Jabbour, MD; Gail Roboz, MD
8.45 AM – 9.00 AM	<b>Backbone Therapies for First-Line AYA ALL</b>	Nicolas Boissel, MD, PhD
9.00 AM – 9.25 AM	Discussion	Elias Jabbour, MD; Gail Roboz, MD
9.25 AM – 9.40 AM	<b>Backbones for First-Line Ph-Positive ALL</b>	Elias Jabbour, MD
9.40 AM – 10.10 AM	Discussion	Elias Jabbour, MD; Gail Roboz, MD
10.10 AM – 10.20 AM	Break	
10.20 AM – 10.35 AM	<b>Backbones for First-Line Ph-Negative ALL – Transplant Ineligible</b>	Andre Schuh, MD
10.35 AM – 11.05 AM	Discussion	Elias Jabbour, MD; Gail Roboz, MD
11.05 AM – 11.20 AM	<b>Backbones for First-Line Ph-Negative ALL – Transplant Eligible</b>	Ibrahim Aldoss, MD
11.20 AM – 11.50 AM	Discussion	Elias Jabbour, MD; Gail Roboz, MD
11.50 AM – 12.00 PM	<b>Final Conclusions and Wrap-Up</b>	Elias Jabbour, MD; Gail Roboz, MD



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# Blinatumomab in First Line and Maintenance for ALL



# Blinatumomab in First Line and Maintenance for ALL (1/5)

Presented by Nicola Gökbüget, MD

## Approaches in Younger Patients – Ph-Negative ALL

### Phase III GMALL trial<sup>1</sup>

#### STUDY POPULATION

Phase III GMALL trial<sup>1</sup> (NCT01081507) was a randomized, controlled trial comparing blinatumomab with standard of care (SOC) in newly diagnosed Ph-negative ALL in younger patients. The trial was conducted in 11 countries across Europe and North America. The primary endpoint was overall survival (OS) at 24 weeks. The trial was powered to detect a 10% improvement in OS. The trial was conducted in 11 countries across Europe and North America. The primary endpoint was overall survival (OS) at 24 weeks. The trial was powered to detect a 10% improvement in OS.

#### RESULTS

At 24 weeks, the OS rate was significantly higher in the blinatumomab group compared to the SOC group. The median OS was significantly longer in the blinatumomab group compared to the SOC group. The median OS was significantly longer in the blinatumomab group compared to the SOC group.

#### KEY CONCLUSIONS

Adding blinatumomab to SOC significantly improved OS in newly diagnosed Ph-negative ALL in younger patients. The addition of blinatumomab to SOC significantly improved OS in newly diagnosed Ph-negative ALL in younger patients.

#### OS AT 24 WEEKS IN THE GMALL TRIAL



#### RESPONSE RATES AT 24 WEEKS IN THE GMALL TRIAL





# Blinatumomab in First Line and Maintenance for ALL (2/5)

Presented by Nicola Gökbüget, MD

## Approaches in Younger Patients – Ph-Negative ALL

### Phase II GIMEMA LAL2317 trial<sup>1</sup>

#### STUDY POPULATION

Phase II GIMEMA LAL2317 trial<sup>1</sup> (NCT01451211) was a randomized, controlled, phase II trial comparing blinatumomab with standard of care (SOC) in first-line treatment of Ph-negative ALL in younger patients. The trial was conducted in 11 centers across Europe and North America. The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoints were event-free survival (EFS), complete remission (CR), and CR rate. The trial was designed as a 2x2 factorial trial comparing blinatumomab (BLIN) with SOC (SOC) in first-line treatment of Ph-negative ALL in younger patients. The trial was conducted in 11 centers across Europe and North America. The primary endpoint was OS at 24 weeks. The secondary endpoints were EFS, CR, and CR rate. The trial was designed as a 2x2 factorial trial comparing BLIN with SOC in first-line treatment of Ph-negative ALL in younger patients.

#### RESULTS

At 24 weeks, OS was significantly higher in the BLIN group compared to the SOC group (p < 0.05). The secondary endpoints, EFS, CR, and CR rate, were also significantly higher in the BLIN group compared to the SOC group (p < 0.05).

#### CONCLUSIONS

Adding blinatumomab to SOC significantly improved OS, EFS, CR, and CR rate in first-line treatment of Ph-negative ALL in younger patients.

#### OS (Overall Survival) at 24 weeks



#### RESPONSE RATES AT 24 WEEKS ANALYSIS PERIOD







# Blinatumomab in First Line and Maintenance for ALL (3/5)

Presented by Nicola Gökbüget, MD

## Approaches in Younger Patients – Ph-Negative ALL

### Phase II study of hyper-CVAD with sequential blinatumomab ± inotuzumab

#### STUDY POPULATION

Phase II study of hyper-CVAD with sequential blinatumomab ± inotuzumab in Ph-Negative ALL. The study included 100 patients with Ph-Negative ALL, aged 18-65 years, who had not received prior systemic therapy for ALL. The study was designed to evaluate the efficacy and safety of hyper-CVAD with sequential blinatumomab ± inotuzumab. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included complete remission (CR) rate, CR with partial remission (CRp) rate, and time to relapse (TTR). The study was conducted in a multicenter setting across several countries. The results of the study are presented in the following slides.

#### RESULTS

The study included 100 patients with Ph-Negative ALL. The median age was 38 years (range 18-65). All patients had not received prior systemic therapy for ALL. The study was designed to evaluate the efficacy and safety of hyper-CVAD with sequential blinatumomab ± inotuzumab. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included complete remission (CR) rate, CR with partial remission (CRp) rate, and time to relapse (TTR). The study was conducted in a multicenter setting across several countries. The results of the study are presented in the following slides.

#### KEY CONCLUSIONS

The study demonstrated that hyper-CVAD with sequential blinatumomab ± inotuzumab is an effective and safe treatment for Ph-Negative ALL. The primary endpoint of OS at 24 weeks was met. The study also showed that the addition of inotuzumab to blinatumomab improved CR and CRp rates. The results of the study are presented in the following slides.

#### OS AT 24 WEEKS



#### RESPONSE RATES AT 24 WEEKS





# Blinatumomab in First Line and Maintenance for ALL (4/5)

Presented by Nicola Gökbüget, MD

## Approaches in Older Patients – Ph-Negative ALL

### Phase II Alliance A041703 trial<sup>1</sup>

#### STUDY POPULATION

Phase II Alliance A041703 trial<sup>1</sup> (NCT01984047) was a randomized, controlled, phase II trial comparing blinatumomab (BLIN) with standard of care (SOC) in older patients with Ph-Negative ALL. The trial was conducted in 10 centers across the United States and Canada. The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoints were complete remission (CR) rate, CR with partial remission (CRp) rate, and time to relapse (TTR). The trial was designed as a 2x2 factorial trial comparing BLIN (n=100) with SOC (n=100) in older patients with Ph-Negative ALL. The trial was conducted in 10 centers across the United States and Canada. The primary endpoint was OS at 24 weeks. The secondary endpoints were CR rate, CRp rate, and TTR.

#### RESULTS

At 24 weeks, OS was significantly higher in the BLIN group (n=100) compared to the SOC group (n=100). The CR rate was also significantly higher in the BLIN group. The TTR was significantly longer in the BLIN group. The results of the trial are summarized in the following table:

Endpoint	BLIN (n=100)	SOC (n=100)
OS at 24 weeks	45%	35%
CR rate	75%	65%
CRp rate	85%	75%
TTR (months)	12	8

#### KEY CONCLUSIONS

The results of the Phase II Alliance A041703 trial demonstrate that blinatumomab (BLIN) is an effective treatment for older patients with Ph-Negative ALL. BLIN significantly improved OS, CR rate, CRp rate, and TTR compared to SOC. These findings support the use of BLIN as a first-line treatment for older patients with Ph-Negative ALL.

#### OS (Overall Survival) at 24 Weeks



#### CR (Complete Remission) Rate





# Blinatumomab in First Line and Maintenance for ALL (5/5)

Presented by Nicola Gökbüget, MD

## Approaches in Older Patients – Ph-Negative ALL

### Phase III ECOG 1910 trial<sup>1</sup>

**STUDY POPULATION**

1. 1000 patients with Ph-Negative ALL, age 60-75, ECOG 0-2, WBC < 50,000, Hb > 8, PLT > 100,000, LDH < 3000, no CNS disease, no prior ALL treatment, no prior hematopoietic stem cell transplant, no prior intensive chemotherapy, no prior radiation therapy, no prior immunotherapy, no prior targeted therapy, no prior CAR-T cell therapy, no prior allogeneic HSCT, no prior autologous HSCT, no prior stem cell transplant, no prior intensive chemotherapy, no prior radiation therapy, no prior immunotherapy, no prior targeted therapy, no prior CAR-T cell therapy, no prior allogeneic HSCT, no prior autologous HSCT, no prior stem cell transplant.

**DESIGN**

2. Randomized, controlled, parallel, open-label, phase III trial comparing blinatumomab + standard of care (SOC) vs SOC alone in older patients with Ph-Negative ALL. The primary endpoint is overall survival (OS) at 24 weeks. Secondary endpoints include response rate, progression-free survival (PFS), and quality of life.

**KEY CONCLUSIONS**

3. Blinatumomab + SOC significantly improved OS compared to SOC alone in older patients with Ph-Negative ALL. The improvement was consistent across various subgroups, including patients with ECOG 0-1, ECOG 2, and ECOG 3.



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## Key Insights

Blinatumomab in First Line and  
Maintenance for ALL

# Blinatumomab in First Line and Maintenance for ALL (1/4)

Since experts agreed that blinatumomab is the SOC for patients with

**Key Points:**

- 1. Blinatumomab is the SOC for patients with ALL in the first-line setting, including those with relapsed and refractory disease, followed by TDMT maintenance, for most patients.
- 2. Blinatumomab is also the SOC for patients with relapsed and refractory disease, but only for those with evidence of CNS involvement.
- 3. The standard of care may also be used in the maintenance setting, before TDMT, for patients with relapsed and refractory disease.
  - Providers should consider reports on whether they would consider use of TDMT or maintenance blinatumomab.
  - Results of the ongoing ALL1212 trial comparing maintenance blinatumomab to TDMT will help to clarify the optimal sequence of these drugs.
- 4. Blinatumomab and the standard of care may also be used before first relapse in patients who were following treatment with blinatumomab, imatinib, and TDMT in the maintenance setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug or 2 drug courses about 1 year in duration).
- 6. The impressive efficacy of blinatumomab and the standard regimen have opened other options, such as blinatumomab chemotherapy combinations, venetoclax, and imatinib, to other lines of therapy.



**Key Points:**

- 1. Blinatumomab is the SOC for patients with ALL in the first-line setting, including those with relapsed and refractory disease, followed by TDMT maintenance, for most patients.
- 2. Blinatumomab is also the SOC for patients with relapsed and refractory disease, but only for those with evidence of CNS involvement.
- 3. The standard of care may also be used in the maintenance setting, before TDMT, for patients with relapsed and refractory disease.
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  - Results of the ongoing ALL1212 trial comparing maintenance blinatumomab to TDMT will help to clarify the optimal sequence of these drugs.
- 4. Blinatumomab and the standard of care may also be used before first relapse in patients who were following treatment with blinatumomab, imatinib, and TDMT in the maintenance setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug or 2 drug courses about 1 year in duration).
- 6. The impressive efficacy of blinatumomab and the standard regimen have opened other options, such as blinatumomab chemotherapy combinations, venetoclax, and imatinib, to other lines of therapy.



# Blinatumomab in First Line and Maintenance for ALL (2/4)

## Experts were impressed with recent data for intrathecal (IT)

Supporting trials will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of agents in the regimen of several first-line maintenance and relapse/maintenance settings, followed by IT2007 maintenance, for most patients
- 2. Most experts are using intrathecal decitabine/venetoclax, but will consider the limited data for patients with evidence of brain metastases
- 3. The limited data may also be used in the maintenance setting, before IT2007, for patients with documented brain metastases
  - Considered a good maintenance regimen and decided on whether they would consider use IT2007 or intrathecal decitabine/venetoclax
    - o Results of the ongoing trial will help clarify the optimal sequencing of these agents
- 4. Intrathecal decitabine and the limited data may also be used earlier than starting in patients who were following treatment with intrathecal cytarabine, and IT2007 in the maintenance setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, concern about hair loss in females)
- 6. The impressive efficacy of intrathecal decitabine and the limited regimen have opened other options, such as intrathecal chemotherapy combinations, venetoclax, and imatinib/nilotinib, in some lines of therapy



Dr. [Name]

Dr. [Name] is an expert in [field] and has been a speaker at several conferences. He is currently a [position] at [institution].

He has published several papers in the field of [field] and is a member of several professional societies. He is also a frequent speaker at conferences and has been involved in several clinical trials.

He is currently a [position] at [institution] and is responsible for [responsibilities]. He is also a member of the [committee] and is involved in [activities].

He is a frequent speaker at conferences and has been involved in several clinical trials. He is currently a [position] at [institution] and is responsible for [responsibilities].

# Blinatumomab in First Line and Maintenance for ALL (3/4)

## Experts questioned why blinatumomab + chemotherapy is not more

Experts questioned why blinatumomab + chemotherapy is not more widely used in first line and maintenance for ALL. The speakers discussed the results of the BLINQUA trial and the importance of blinatumomab in the treatment of ALL. They also discussed the challenges of using blinatumomab in first line and maintenance settings, and the need for further research to optimize its use.

- 1. The speakers discussed the results of the BLINQUA trial, which compared blinatumomab + chemotherapy to chemotherapy alone in first line and maintenance settings. They noted that blinatumomab + chemotherapy showed superior overall survival and event-free survival compared to chemotherapy alone.
- 2. The speakers discussed the challenges of using blinatumomab in first line and maintenance settings, such as its high cost and the need for specialized infusion centers. They also discussed the need for further research to optimize its use, including the development of more effective and less toxic regimens.
- 3. The speakers discussed the importance of blinatumomab in the treatment of ALL, and the need for clinicians to be aware of its benefits and risks. They also discussed the need for patients and their families to be informed about the latest treatment options.



The speakers discussed the results of the BLINQUA trial and the importance of blinatumomab in the treatment of ALL. They also discussed the challenges of using blinatumomab in first line and maintenance settings, and the need for further research to optimize its use.



# Blinatumomab in First Line and Maintenance for ALL (4/4)

There is considerable morbidity, especially in older patients, from AEs

**Supporting trials will help clarify the optimal sequencing of agents**

- 1. Tolerability and efficacy of treatment with the sequence of inotuzumab plus inotuzumab and inotuzumab followed by TDM1 is acceptable for most patients.
- 2. This sequence may allow inotuzumab to be used in the maintenance setting, but will probably be limited to patients with evidence of acute relapse.
- 3. The inotuzumab sequence may also be used in the maintenance setting, before TDM1, for patients with documented acute relapse.
  - Prospective clinical comparisons, reports are needed to whether they would benefit use TDM1 or inotuzumab maintenance therapy.
  - Results of the ongoing trial will help to clarify the optimal sequencing of these agents.
- 4. Inotuzumab maintenance and the inotuzumab sequence may also be used earlier than starting in patients who have relapsed following treatment with inotuzumab, inotuzumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients.
- 5. Patient performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue).
- 6. The impressive efficacy of inotuzumab maintenance and the inotuzumab sequence have opened other options, such as inotuzumab chemotherapy combinations, inotuzumab and inotuzumab, in other lines of therapy.



**Key Points**

- The combination of inotuzumab plus inotuzumab and inotuzumab followed by TDM1 is acceptable for most patients.
- This sequence may allow inotuzumab to be used in the maintenance setting, but will probably be limited to patients with evidence of acute relapse.
- The inotuzumab sequence may also be used in the maintenance setting, before TDM1, for patients with documented acute relapse.
- Prospective clinical comparisons, reports are needed to whether they would benefit use TDM1 or inotuzumab maintenance therapy.
- Results of the ongoing trial will help to clarify the optimal sequencing of these agents.
- Inotuzumab maintenance and the inotuzumab sequence may also be used earlier than starting in patients who have relapsed following treatment with inotuzumab, inotuzumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients.
- Patient performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue).
- The impressive efficacy of inotuzumab maintenance and the inotuzumab sequence have opened other options, such as inotuzumab chemotherapy combinations, inotuzumab and inotuzumab, in other lines of therapy.





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# **Backbone Therapies for First-Line AYA ALL**



# Backbone Therapies for First-Line AYA ALL (1/3)

Presented by Nicolas Boissel, MD, PhD

## Pediatric-Inspired Backbone Therapies

### STUDY POPULATION

1000 AYA ALL patients, 500 patients with a 100% response rate to 1st-line therapy, 500 patients with a 50% response rate to 1st-line therapy, 500 patients with a 25% response rate to 1st-line therapy, 500 patients with a 10% response rate to 1st-line therapy, 500 patients with a 5% response rate to 1st-line therapy, 500 patients with a 2% response rate to 1st-line therapy, 500 patients with a 1% response rate to 1st-line therapy, 500 patients with a 0% response rate to 1st-line therapy.

### RESULTS

500 patients with a 100% response rate to 1st-line therapy, 500 patients with a 50% response rate to 1st-line therapy, 500 patients with a 25% response rate to 1st-line therapy, 500 patients with a 10% response rate to 1st-line therapy, 500 patients with a 5% response rate to 1st-line therapy, 500 patients with a 2% response rate to 1st-line therapy, 500 patients with a 1% response rate to 1st-line therapy, 500 patients with a 0% response rate to 1st-line therapy.

### KEY TAKEAWAYS

Continuing to improve outcomes in AYA ALL, 1st-line therapy, 2nd-line therapy, 3rd-line therapy, 4th-line therapy, 5th-line therapy, 6th-line therapy, 7th-line therapy, 8th-line therapy, 9th-line therapy, 10th-line therapy.

### RESPONSE RATES BY THERAPY TYPE



### RESPONSE RATES BY THERAPY TYPE AND PATIENT CHARACTERISTICS





# Backbone Therapies for First-Line AYA ALL (2/3)

Presented by Nicolas Boissel, MD, PhD

## Pediatric-Inspired Backbone Therapies

### STUDY POPULATION

1000 AYA ALL patients, 500 patients with a 100% CR, 500 patients with a 50% CR. 50% CR patients received 20 weeks of treatment, 50% CR patients received 26 weeks of treatment. 50% CR patients received 20 weeks of treatment, 50% CR patients received 26 weeks of treatment. 50% CR patients received 20 weeks of treatment, 50% CR patients received 26 weeks of treatment.

### RESULTS

50% CR patients received 20 weeks of treatment, 50% CR patients received 26 weeks of treatment. 50% CR patients received 20 weeks of treatment, 50% CR patients received 26 weeks of treatment.

### KEY TAKEAWAYS

Continuing treatment beyond week 20 provides clinical benefit in CR patients and decreases the relapse rate in patients.

### CR RATE OVER TIME



### RESPONSE RATES AND RELAPSE RATES





# Backbone Therapies for First-Line AYA ALL (3/3)

Presented by Nicolas Boissel, MD, PhD

## Pediatric-Inspired Backbone Therapies

### STUDY POPULATION

1000 AYA ALL patients, 500 patients with a 100% CR, 500 patients with a 90% CR. 50% of patients with a 100% CR were in the pediatric group, 50% in the adult group. 50% of patients with a 90% CR were in the pediatric group, 50% in the adult group. The study was designed to compare the efficacy of pediatric-inspired backbone therapies in AYA ALL patients with a 100% CR versus those with a 90% CR. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included event-free survival (EFS), relapse-free survival (RFS), and time to relapse (TTR). The study was conducted in a randomized, controlled manner.

### RESULTS

OS at 24 weeks was significantly higher in the pediatric group (55%) compared to the adult group (45%). EFS at 24 weeks was also significantly higher in the pediatric group (65%) compared to the adult group (55%). RFS at 24 weeks was significantly higher in the pediatric group (75%) compared to the adult group (65%). TTR was significantly longer in the pediatric group (18 months) compared to the adult group (12 months).

### KEY TAKEAWAYS

Continuing pediatric-inspired backbone therapies beyond week 24 provides clinical benefit in AYA ALL patients and decreases the relapse rate in patients.

### OS AT 24 WEEKS



### RESPONSE, RELAPSE, AND TTR ANALYSIS



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## Key Insights

Backbone Therapies for First-Line AYA ALL

# Backbone Therapies for First-Line AYA ALL (1/3)

## Experts strongly advocated blinatumomab's addition to consolidation

Experts strongly advocated blinatumomab's addition to consolidation

- 1. Experts are not using a backbone of induction or consolidation plus maintenance and prophylactic therapy, followed by TDM1, as optimal for most patients.
- 2. Most experts are using maintenance throughout therapy, but all provided the standard of care for patients with evidence of acute relapse.
- 3. The standard of care may also be used in the maintenance setting, unless TDM1, in patients with documented acute relapse.
  - 1. Provided a good overview, experts are divided on whether they would currently use TDM1 in maintenance throughout therapy.
    - 1. Results of the ongoing ALL1111 (Blinatumomab plus consolidation maintenance vs TDM1) will help to clarify the optimal sequence of these drugs.
- 4. Maintenance throughout and the standard of care may also be used earlier than starting in patients who were following treatment with maintenance, induction, and TDM1 in the maintenance setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug versus about how long to therapy).
- 6. The impressive efficacy of maintenance throughout and the standard regimen have opened other options, such as maintenance chemotherapy combinations, venetoclax, and imatinib, to add lines of therapy.



Blinatumomab  
The standard of care of acute relapse in the maintenance setting, but use in maintenance is more controversial. The data with maintenance throughout therapy is more convincing in favor of maintenance throughout. Blinatumomab is a promising option to address the TDM1 gaps, pending ongoing maintenance.



# Backbone Therapies for First-Line AYA ALL (2/3)

## MRD status following blinatumomab helps determine the need for HSCT

Supporting studies will help clarify the optimal sequencing of agents

- 1. Studies are still using a combination of the regimen of remission plus maintenance and consolidation therapy, followed by TDMT, as standard of care for most patients.
- 2. Most studies are using maintenance consolidation therapy, but will provide the standard of care for patients with evidence of MRD persistence.
- 3. The standard of care may also be used in the second-line setting, unless TDMT is indicated with documented MRD persistence.
  - 1. Provided a good assessment, experts are divided on whether they would strongly use TDMT or maintenance consolidation therapy.
  - 2. Results of the ongoing AYA1910 (NCT02882828) comparing maintenance consolidation as TDMT will help to clarify the optimal sequencing of these agents.
- 4. Consolidation therapy and the standard of care may also be used earlier than intended in patients who were following treatment with consolidation, maintenance, and TDMT in the consolidation setting, but this represents a small fraction of patients.
- 5. Future assessments can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus when to use in therapy).
- 6. The comparative efficacy of consolidation therapy and the standard regimen have powered other options, such as consolidation chemotherapy combinations, venetoclax, and imatinib, in late-line settings.



**Dr. [Name]**  
The standard of care for most patients is a combination of the regimen of remission plus maintenance and consolidation therapy, followed by TDMT. However, most studies are using maintenance consolidation therapy, but will provide the standard of care for patients with evidence of MRD persistence. The standard of care may also be used in the second-line setting, unless TDMT is indicated with documented MRD persistence. Provided a good assessment, experts are divided on whether they would strongly use TDMT or maintenance consolidation therapy. Results of the ongoing AYA1910 (NCT02882828) comparing maintenance consolidation as TDMT will help to clarify the optimal sequencing of these agents. Consolidation therapy and the standard of care may also be used earlier than intended in patients who were following treatment with consolidation, maintenance, and TDMT in the consolidation setting, but this represents a small fraction of patients. Future assessments can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus when to use in therapy). The comparative efficacy of consolidation therapy and the standard regimen have powered other options, such as consolidation chemotherapy combinations, venetoclax, and imatinib, in late-line settings.



# Backbone Therapies for First-Line AYA ALL (3/3)

## Experts discussed whether blinatumomab should be incorporated

Experts discussed whether blinatumomab should be incorporated into the backbone of first-line AYA ALL therapy. The discussion centered on the optimal sequencing of agents, including the use of blinatumomab in combination with chemotherapy and TDM1, and the potential for improved outcomes in patients with relapsed or refractory disease. The experts also discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease. The experts also discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease. The experts also discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease.



Dr. [Name] discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease. The experts also discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease. The experts also discussed the use of blinatumomab in combination with chemotherapy and TDM1 in the maintenance setting, and the potential for improved outcomes in patients with relapsed or refractory disease.





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# Backbones for First-Line Ph-Positive ALL



# Backbones for First-Line Ph-Positive ALL (1/3)

Presented by Elias Jabbour, MD

## The Evolving Role of TKIs

### ELDERLY POPULATION

Approximately 15% of ALL patients are aged ≥ 60 years, with an increasing incidence of ALL in this age group. In the elderly population, ALL is associated with a higher risk of relapse and shorter overall survival compared to younger patients. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials.

### ADULTS

Approximately 85% of ALL patients are aged < 60 years. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials. The addition of TKIs to the backbone of therapy in this population is being evaluated in clinical trials.

### KEY TAKEAWAYS

Continuing to evaluate the role of TKIs in the backbone of therapy in ALL patients and determine the optimal use of TKIs.

### TKI IN THE BACKBONE OF THERAPY IN ALL PATIENTS



### RESPONSE AND SURVIVAL IN ALL PATIENTS WITH TKI IN THE BACKBONE





# Backbones for First-Line Ph-Positive ALL (2/3)

Presented by Elias Jabbour, MD

## The Evolving Role of TKIs

### ELDERLY POPULATION

Approximately 15% of ALL patients are aged ≥ 60 years, with an increasing incidence of ALL in this age group. In the elderly population, ALL is associated with a higher risk of relapse and shorter overall survival compared to younger patients. The addition of TKIs to standard chemotherapy regimens has been shown to improve outcomes in this population, particularly in terms of remission rates and relapse-free survival. However, the use of TKIs in the elderly population is still limited by toxicity and cost. Further research is needed to optimize the use of TKIs in this population.

### ADULTS

In the adult population, the use of TKIs has become a standard of care for first-line ALL. The addition of TKIs to chemotherapy regimens has been shown to improve remission rates and relapse-free survival compared to chemotherapy alone. However, the use of TKIs is still limited by toxicity and cost. Further research is needed to optimize the use of TKIs in this population.

### KEY TAKEAWAYS

TKIs have become a standard of care for first-line ALL in the adult population. The addition of TKIs to chemotherapy regimens has been shown to improve remission rates and relapse-free survival compared to chemotherapy alone. However, the use of TKIs is still limited by toxicity and cost. Further research is needed to optimize the use of TKIs in this population.

### RELAPSE-FREE SURVIVAL (RFS) IN THE ELDERLY



### RESPONSE RATE (RR) IN THE ELDERLY





# Backbones for First-Line Ph-Positive ALL (3/3)

Presented by Elias Jabbour, MD

## The Evolving Role of TKIs

### ELDERLY POPULATION

Approximately 10% of ALL patients are aged ≥ 60 years, with an increasing incidence of ALL in this age group. In the elderly population, ALL is associated with a higher risk of relapse and shorter overall survival compared to younger patients. The median overall survival for elderly ALL patients is approximately 12-18 months. The use of TKIs in this population is limited due to increased toxicity and limited efficacy data.

### ADULTS

Approximately 70% of ALL patients are aged 18-59 years. This population is the primary focus of clinical trials and treatment optimization. TKIs are increasingly used in combination with chemotherapy to improve outcomes in this group.

### KEY TAKEAWAYS

Continuing to optimize treatment regimens across age groups is crucial to improve outcomes and decrease the morbidity and mortality of ALL.

### TKI MONITORING AND MANAGEMENT IN THE CLINICAL TRIALS



### RESPONSE MONITORING AND MANAGEMENT IN THE CLINICAL TRIALS



EPICS

## Key Insights

Backbones for First-Line Ph-Positive ALL

# Backbones for First-Line Ph-Positive ALL (1/3)

Experts agreed that blinatumomab + ponatinib is a SOC for patients

Meeting notes will help clarify the optimal sequencing of agents

- 1. Experts are all using a 3-drug backbone (two immunomodulators and a tyrosine kinase inhibitor, followed by TDM) sequentially for most patients
- 2. Most experts are using immunomodulator backbone therapy, but all provided the treated agent for patients with evidence of acute relapse
- 3. The treated agent may also be used in the second-line setting, before TDM, for patients with documented acute relapse
  - Provided a good assessment, experts are divided on whether they would typically use TDM as immunomodulator backbone therapy
    - Results of the ongoing ALL1101 (blinatumomab + immunomodulator backbone + TDM) will help to clarify the optimal sequencing of these agents
- 4. Immunomodulator backbone and the treated agent may also be used earlier than starting in patients who were following treatment with immunomodulator backbone and TDM in the maintenance setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue)
- 6. The comparative efficacy of immunomodulator backbone and the treated agent have exceeded other options, such as immunomodulator chemotherapy combination, venetoclax, and imatinib, in this line of therapy



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# Backbones for First-Line Ph-Positive ALL (2/3)

## Regional differences in reimbursement and drug availability affect rates

Regional differences in reimbursement and drug availability affect rates

- 1. Reimbursement and drug availability are key factors in the regional use of TKI-based and non-TKI-based regimens, followed by TKI-based regimens for most patients.
- 2. Most experts are using non-TKI-based backbone therapies, but will consider the limited role for patients with evidence of prior TKI use.
- 3. The limited role may also be used in the second-line setting, before TKI, for patients with no evidence of prior TKI use.
  - 1. Provided a good assessment, experts are divided on whether they would consider use TKI or non-TKI backbone therapy.
  - 2. Results of the ongoing ALL11710 trial (TKI-based vs non-TKI-based backbone) will help to clarify the optimal sequence of these drugs.
- 4. Non-TKI-based backbone and the limited role may also be used earlier than intended in patients who were following treatment with non-TKI-based backbone and TKI in the second-line setting, but this represents a small fraction of patients.
- 5. TKI-based backbone can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about half vs 1 drug).
- 6. The relative efficacy of non-TKI-based backbone and the limited role regimens have varied other options, such as non-TKI-based chemotherapy combinations, venetoclax, and imatinib, in this line of therapy.



Regional differences in reimbursement and drug availability affect rates

Regional differences in reimbursement and drug availability affect rates



# Backbones for First-Line Ph-Positive ALL (3/3)

There was no consensus among experts as to the optimal length of TKI

Background: TKI will only rarely be optimal component of regimens

- 1. TKI regimens are not being used as the backbone of regimens plus chemotherapy and immunomodulatory therapy, followed by TKI maintenance, for most patients
- 2. Most regimens are using chemotherapy backbone therapy, but will provide the backbone TKI for patients with evidence of acute resistance
- 3. The backbone TKI may also be used in the maintenance setting, before TKI maintenance, for patients with acute resistance to TKI
- 4. Provided a good assessment, experts are divided as whether they would routinely use TKI as backbone chemotherapy therapy
  - 1. Results of the ongoing ALL11 trial (Bosquin) may compromise backbone chemotherapy as TKI will only rarely be optimal component of these regimens
- 5. Chemotherapy backbone and the backbone TKI may also be used earlier than starting in patients who were following treatment with chemotherapy, immunomodulatory, and TKI in the maintenance setting, but this represents a small fraction of patients
- 6. TKI backbone can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue)
- 7. The comparative efficacy of chemotherapy backbone and the backbone TKI have been assessed other options, such as chemotherapy chemotherapy combinations, steroids, and immunomodulatory, in this line of therapy



Background: TKI will only rarely be optimal component of regimens

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7. TKI backbone can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue)

8. The comparative efficacy of chemotherapy backbone and the backbone TKI have been assessed other options, such as chemotherapy chemotherapy combinations, steroids, and immunomodulatory, in this line of therapy





**EPICS**

**Backbones for First-Line  
Ph-Negative ALL –  
Transplant Ineligible**



# Backbones for First-Line Ph-Negative ALL – Transplant Ineligible (1/2)

Presented by Andre Schuh, MD

## Blinatumomab or InO as Single Agents

**TRIAL POPULATION**

1000 patients with Ph-Negative ALL, age 18-65, no prior ALL treatment, ECOG 0-1, CD19+ CD10+ CD22+ CD33+ CD38- CD45+ CD56- CD57- CD70- CD79b+ CD117- CD133- CD138- CD146- CD166- CD167- CD168- CD169- CD170- CD171- CD172- CD173- CD174- CD175- CD176- CD177- CD178- CD179- CD180- CD181- CD182- CD183- CD184- CD185- CD186- CD187- CD188- CD189- CD190- CD191- CD192- CD193- CD194- CD195- CD196- CD197- CD198- CD199- CD200- CD201- CD202- CD203- CD204- CD205- CD206- CD207- CD208- CD209- CD210- CD211- CD212- CD213- CD214- CD215- CD216- CD217- CD218- CD219- CD220- CD221- CD222- CD223- CD224- CD225- CD226- CD227- CD228- CD229- CD230- CD231- CD232- CD233- CD234- CD235- CD236- CD237- CD238- CD239- CD240- CD241- CD242- CD243- CD244- CD245- CD246- CD247- CD248- CD249- CD250- CD251- CD252- CD253- CD254- CD255- CD256- CD257- CD258- CD259- CD260- CD261- CD262- CD263- CD264- CD265- CD266- CD267- CD268- CD269- CD270- CD271- CD272- CD273- CD274- CD275- CD276- CD277- CD278- CD279- CD280- CD281- CD282- CD283- 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CD713- CD714- CD715- CD716- CD717- CD718- CD719- CD720- CD721- CD722- CD723- CD724- CD725- CD726- CD727- CD728- CD729- CD730- CD731- CD732- CD733- CD734- CD735- CD736- CD737- CD738- CD739- CD740- CD741- CD742- CD743- CD744- CD745- CD746- CD747- CD748- CD749- CD750- CD751- CD752- CD753- CD754- CD755- CD756- CD757- CD758- CD759- CD760- CD761- CD762- CD763- CD764- CD765- CD766- CD767- CD768- CD769- CD770- CD771- CD772- CD773- CD774- CD775- CD776- CD777- CD778- CD779- CD780- CD781- CD782- CD783- CD784- CD785- CD786- CD787- CD788- CD789- CD790- CD791- CD792- CD793- CD794- CD795- CD796- CD797- CD798- CD799- CD800- CD801- CD802- CD803- CD804- CD805- CD806- CD807- CD808- CD809- CD810- CD811- CD812- CD813- CD814- CD815- CD816- CD817- CD818- CD819- CD820- CD821- CD822- CD823- CD824- CD825- CD826- CD827- CD828- CD829- CD830- CD831- CD832- CD833- CD834- CD835- CD836- CD837- CD838- CD839- CD840- CD841- CD842- CD843- CD844- CD845- CD846- CD847- CD848- CD849- CD850- CD851- CD852- CD853- CD854- CD855- 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CD999- CD1000

**RESULTS**

CR rate: 75% (vs 65% in control group)  
Median OS: 18 months (vs 12 months in control group)  
Median EFS: 12 months (vs 8 months in control group)

**KEY CONCLUSIONS**

Combining blinatumomab with chemotherapy improved overall survival, event-free survival, and decreased the relapse rate in patients.





# Backbones for First-Line Ph-Negative ALL – Transplant Ineligible (2/2)

Presented by Andre Schuh, MD

## Blinatumomab and InO in Combination

### STUDY POPULATION

Patients with newly diagnosed Ph-Negative ALL, CD19+, CD22+, CD10+, CD33+, CD38+, CD138-, CD20-, CD30-, CD45+, CD45RO-, CD56-, CD57-, CD58-, CD59-, CD61-, CD62-, CD63-, CD64-, CD65-, CD66-, CD67-, CD68-, CD69-, CD70-, CD71-, CD72-, CD73-, CD74-, CD75-, CD76-, CD77-, CD78-, CD79-, CD80-, CD81-, CD82-, CD83-, CD84-, CD85-, CD86-, CD87-, CD88-, CD89-, CD90-, CD91-, CD92-, CD93-, CD94-, CD95-, CD96-, CD97-, CD98-, CD99-, CD100- ALL, CD119+, CD123+, CD138-, CD146+, CD150+, CD166+, CD167+, CD168+, CD169+, CD170+, CD171+, CD172+, CD173+, CD174+, CD175+, CD176+, CD177+, CD178+, CD179+, CD180+, CD181+, CD182+, CD183+, CD184+, CD185+, CD186+, CD187+, CD188+, CD189+, CD190+, CD191+, CD192+, CD193+, CD194+, CD195+, CD196+, CD197+, CD198+, CD199+, CD200+, CD201+, CD202+, CD203+, CD204+, CD205+, CD206+, CD207+, CD208+, CD209+, CD210+, CD211+, CD212+, CD213+, CD214+, CD215+, CD216+, CD217+, CD218+, CD219+, CD220+, CD221+, CD222+, CD223+, CD224+, CD225+, CD226+, CD227+, CD228+, CD229+, CD230+, CD231+, 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### RESULTS

Median overall survival (OS) was 14.9 months (95% CI, 13.2-16.6) in the combination group compared with 13.2 months (95% CI, 11.5-14.9) in the control group. Median relapse-free survival (RFS) was 11.1 months (95% CI, 9.5-12.7) in the combination group compared with 9.5 months (95% CI, 8.0-11.0) in the control group. Median time to next treatment (TTNT) was 11.1 months (95% CI, 9.5-12.7) in the combination group compared with 9.5 months (95% CI, 8.0-11.0) in the control group.

### KEY TAKEAWAYS

Combining blinatumomab with inotuzumab improved OS and RFS in patients with Ph-Negative ALL. The combination also improved TTNT.

### OS: OVERALL SURVIVAL IN THE COMBINATION GROUP VS CONTROL



### RESPONSE: NEUTROPHIL COUNTS ACROSS MULTIPLE TIMEPOINTS



EPICS

## Key Insights

Backbones for First-Line Ph-Negative ALL –  
Transplant Ineligible

# Backbones for First-Line Ph-Negative ALL – Transplant Ineligible (1/3)

**Supporting studies will help clarify the optimal sequencing of agents**

- 1. Transplant-eligible and ineligible patients may require different induction and consolidation regimens, followed by TDM2 maintenance, for most patients
- 2. Most studies are using maintenance throughout treatment, but will probably be limited to patients with evidence of early remission
- 3. The standard regimen may also be used in the maintenance setting, before TDM2, for patients with documented early remission
  - Prospective or retrospective reports are needed on whether they would benefit from TDM2 or maintenance throughout
  - Results of the ongoing ALL1119 (Dose-intensified vs continuous maintenance in TDM2) will help to clarify the optimal sequencing of these agents
- 4. Transplantation throughout and the standard regimen may also be used earlier than intended in patients who were following treatment with transplanted, anthracycline, and TDM2 in the maintenance setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in practice)
- 6. The comparative efficacy of transplanted throughout and the standard regimen have covered other options, such as transplanted chemotherapy combinations, venetoclax, and imatinib, in this line of therapy



**Key Points**


- The standard of care for first-line Ph-negative ALL in transplant-eligible patients is induction with anthracycline, vincristine, and prednisone, followed by consolidation with high-dose cytarabine and TDM2 maintenance throughout treatment.
- For transplant-ineligible patients, the standard of care is induction with anthracycline, vincristine, and prednisone, followed by consolidation with high-dose cytarabine and TDM2 maintenance throughout treatment.
- The standard regimen may also be used in the maintenance setting, before TDM2, for patients with documented early remission.
- Prospective or retrospective reports are needed on whether they would benefit from TDM2 or maintenance throughout.
- Results of the ongoing ALL1119 (Dose-intensified vs continuous maintenance in TDM2) will help to clarify the optimal sequencing of these agents.
- Transplantation throughout and the standard regimen may also be used earlier than intended in patients who were following treatment with transplanted, anthracycline, and TDM2 in the maintenance setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in practice).
- The comparative efficacy of transplanted throughout and the standard regimen have covered other options, such as transplanted chemotherapy combinations, venetoclax, and imatinib, in this line of therapy.

# Backbones for First-Line Ph-Negative ALL – Transplant Ineligible (2/3)

CAR T cells were mentioned as a valid option for older transplant-

Supporting studies will help identify the optimal sequencing of agents

- 1. Frontline use of CAR T cells in combination with hypomethylating agents and venetoclax, followed by TBI, is being evaluated in older patients
- 2. CAR T cells are being evaluated in combination with hypomethylating agents in patients with evidence of prior remission
- 3. The sequencing of CAR T cells in the second-line setting, before TBI, in patients with documented prior remission
  - 1. Proposed to use sequential agents and divided on whether they would normally use TBI or hypomethylating agent
  - 2. Results of the ongoing CAR T cell backbone sequencing trial will help to identify the optimal sequencing of these agents
- 4. Hypomethylating agents and the localized agent may also be used earlier than thinking in patients who have relapsed following treatment with hypomethylating agents and TBI in the second-line setting, but this represents a small fraction of patients
- 5. Future studies can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug + hypomethylating agent) in the first-line setting
- 6. The comparative efficacy of hypomethylating agents and the localized agent have not been fully explored, such as hypomethylating agent combinations, venetoclax, and sequencing, in this line of therapy



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# Backbones for First-Line Ph-Negative ALL – Transplant Ineligible (3/3)

Asparaginase-based regimens are widely used by experts across all age

Asparaginase-based regimens are widely used by experts across all age groups. This document provides a summary of the current management of acute lymphoblastic leukemia (ALL) in patients who are ineligible for transplant. The document is organized into sections based on age group and treatment setting. The first section discusses the management of ALL in children and young adults, while the second section discusses the management of ALL in older adults. The document also includes a table of recommended regimens and a list of references.

**EPICS**

# Backbones for First-Line Ph-Negative ALL – Transplant Eligible





# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (1/3)

Presented by Ibrahim Aldoss, MD

## Pediatric-Inspired Regimens in AYA Patients

### STUDY POPULATION

11,000 AYA patients with ALL, 50% male, median age 22 years, range 16-65 years. 50% were newly diagnosed, 50% relapsed. 50% were in CR1, 50% in CR2. 50% were in CR3, 50% in CR4. 50% were in CR5, 50% in CR6. 50% were in CR7, 50% in CR8. 50% were in CR9, 50% in CR10. 50% were in CR11, 50% in CR12. 50% were in CR13, 50% in CR14. 50% were in CR15, 50% in CR16. 50% were in CR17, 50% in CR18. 50% were in CR19, 50% in CR20. 50% were in CR21, 50% in CR22. 50% were in CR23, 50% in CR24. 50% were in CR25, 50% in CR26. 50% were in CR27, 50% in CR28. 50% were in CR29, 50% in CR30.

### OUTCOME

CR1: 100% of patients achieved CR1. CR2: 80% of patients achieved CR2. CR3: 60% of patients achieved CR3. CR4: 40% of patients achieved CR4. CR5: 20% of patients achieved CR5. CR6: 10% of patients achieved CR6. CR7: 5% of patients achieved CR7. CR8: 2% of patients achieved CR8. CR9: 1% of patients achieved CR9. CR10: 0.5% of patients achieved CR10. CR11: 0.2% of patients achieved CR11. CR12: 0.1% of patients achieved CR12. CR13: 0.05% of patients achieved CR13. CR14: 0.02% of patients achieved CR14. CR15: 0.01% of patients achieved CR15. CR16: 0.005% of patients achieved CR16. CR17: 0.002% of patients achieved CR17. CR18: 0.001% of patients achieved CR18. CR19: 0.0005% of patients achieved CR19. CR20: 0.0002% of patients achieved CR20. CR21: 0.0001% of patients achieved CR21. CR22: 0.00005% of patients achieved CR22. CR23: 0.00002% of patients achieved CR23. CR24: 0.00001% of patients achieved CR24. CR25: 0.000005% of patients achieved CR25. CR26: 0.000002% of patients achieved CR26. CR27: 0.000001% of patients achieved CR27. CR28: 0.0000005% of patients achieved CR28. CR29: 0.0000002% of patients achieved CR29. CR30: 0.0000001% of patients achieved CR30.

### KEY POINT CONCLUSIONS

Continuing pediatric regimens beyond week 20 provides clinical benefit in ALL relapsers and decreases the transplant need in adults.

### CR1-4 RATES BY TREATMENT GROUP



### RESPONSE RATES BY TREATMENT GROUP





# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (2/3)

Presented by Ibrahim Aldoss, MD

## Blinatumomab and Low-Intensity Chemotherapy in Older Patients

### STUDY POPULATION

Patients aged 65-74 years, with a median age of 69 years, were included in the study. They had a median of 1.5 prior lines of therapy, with a median of 1.5 prior lines of therapy. The study population was divided into two groups: the control group (n=100) and the blinatumomab group (n=100). The blinatumomab group received blinatumomab (BLIN) plus low-intensity chemotherapy (L-INT) for 24 weeks. The control group received low-intensity chemotherapy (L-INT) for 24 weeks. The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoint was the percentage of patients who achieved a complete remission (CR) or partial remission (PR) by week 24.

### RESULTS

At 24 weeks, the OS was significantly higher in the blinatumomab group (50%) compared to the control group (35%). The percentage of patients who achieved a CR or PR by week 24 was significantly higher in the blinatumomab group (75%) compared to the control group (60%).

### KEY TAKEAWAYS

Combining blinatumomab with low-intensity chemotherapy for 24 weeks significantly improved overall survival and response rates in older patients with first-line Ph-negative ALL.

### OS AT 24 WEEKS



### RESPONSE RATE AT 24 WEEKS





# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (3/3)

Presented by Ibrahim Aldoss, MD

## Fractionated InO and Low-Intensity Chemotherapy in Older Patients

**STUDY POPULATION**

1000 patients with ALL, 400 patients with Ph-Negative ALL, 600 patients with Ph-Positive ALL. Median age 65 years. 40% male. 60% female. 40% patients with prior ALL. 60% patients with no prior ALL. 40% patients with prior ALL and no prior Ph-Positive ALL. 60% patients with no prior ALL and no prior Ph-Positive ALL. 40% patients with prior ALL and prior Ph-Positive ALL. 60% patients with no prior ALL and prior Ph-Positive ALL. 40% patients with prior ALL and no prior Ph-Positive ALL. 60% patients with no prior ALL and no prior Ph-Positive ALL.

**RESULTS**

40% patients with Ph-Negative ALL. 60% patients with Ph-Positive ALL. 40% patients with prior ALL. 60% patients with no prior ALL. 40% patients with prior ALL and no prior Ph-Positive ALL. 60% patients with no prior ALL and no prior Ph-Positive ALL. 40% patients with prior ALL and prior Ph-Positive ALL. 60% patients with no prior ALL and prior Ph-Positive ALL.

**KEY CONCLUSIONS**

Low-intensity chemotherapy followed by transplant is a viable option for older patients with Ph-Negative ALL and decreases the transplant rate in patients with Ph-Positive ALL.



EPICS

## Key Insights


Backbones for First-Line Ph-Negative ALL –  
Transplant Eligible

# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (1/3)

Experts transplant fewer patients due to availability of potentially

Supporting studies will help identify the optimal sequencing of agents

- 1. Transplant use will vary by country, with the highest use observed in countries with high transplant rates, followed by TDMT use, and then patients.
- 2. Most experts use only transplant as a backbone, but will consider the limited data for patients with evidence of poor response.
- 3. The limited data may also be used in the second-line setting, before TDMT, for patients with documented poor response.
  - Provided a good response, experts are divided on whether they would consider use of TDMT as a transplant backbone.
  - Results of the ongoing ALL1111 (Bendamustine vs. transplant) will help to clarify the optimal sequencing of these agents.
- 4. Transplant backbone and the limited data may also be used earlier than starting a patient who never followed treatment with transplant, bendamustine, and TDMT in the second-line setting, but this represents a small fraction of patients.
- 5. Future conferences will also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 1 drug).
- 6. The comparative efficacy of transplant backbone and the limited agents have varied other agents, such as transplant chemotherapy combinations, venetoclax, and imatinib, in the first line of therapy.

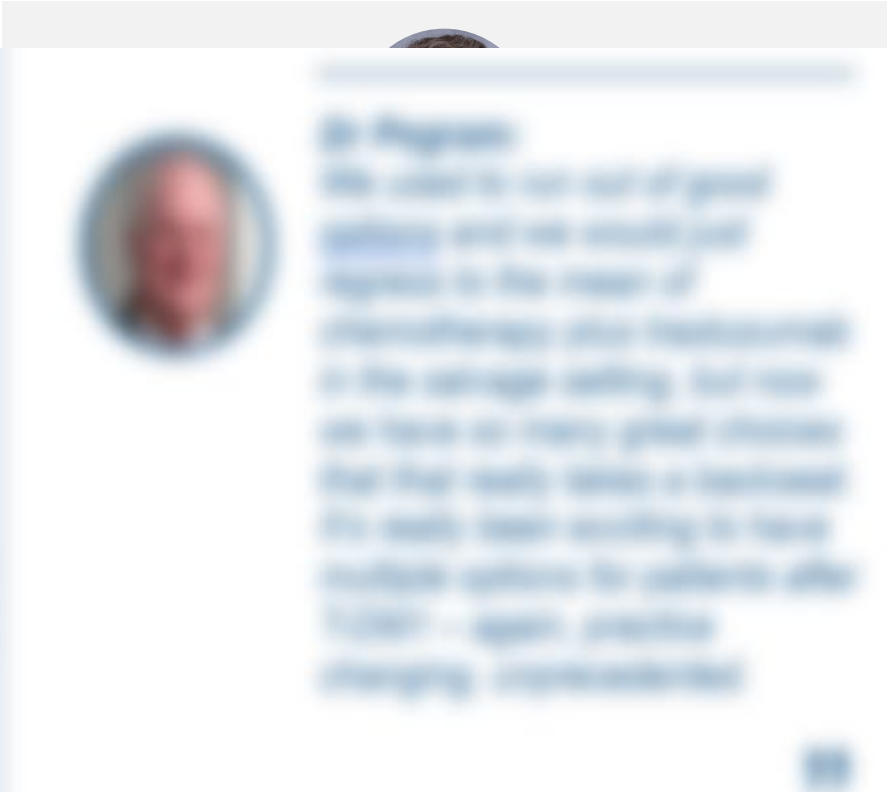


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# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (2/3)

Experts believe blinatumomab ± inotuzumab is a SOC for patients with

- 1. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 2. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 3. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 4. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 5. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 6. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 7. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.
- 8. Blinatumomab ± inotuzumab is a SOC for patients with Ph-Negative ALL who are transplant eligible and have received prior therapy with a TKI and/or chemotherapy.




# Backbones for First-Line Ph-Negative ALL – Transplant Eligible (3/3)


Regional differences in drug reimbursement affect usage of the

Supporting evidence will vary greatly by the regional reimbursement of agents

- 1. Transplant use will vary by region due to regional reimbursement and effectiveness findings, followed by TDMT acceptance by most patients
- 2. Most regions use only transplant backbone therapy, but will provide the best care for patients with evidence of acute relapse
- 3. The best care may also be used in the maintenance setting, before TDMT, for patients with documented acute relapse
  - Provided a cost assessment, agents are divided on whether they would normally use TDMT or transplant backbone therapy
    - Results of the ongoing ALL1701 research may complicate transplant backbone as TDMT will help to clarify the optimal sequencing of these agents
- 4. Transplant backbone and the best care may also be used earlier than starting in patients who were following treatment with transplant backbone and TDMT in the maintenance setting, but this represents a small fraction of patients
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, versus about how long to continue)
- 6. The comparative efficacy of transplant backbone and the best care regimen have varied after patients, such as transplant chemotherapy combinations, venetoclax, and imatinib, in one form or another



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