



EPICS

**LEUKEMIA IN 2021
AND BEYOND**

FULL REPORT

September 8 and 13, 2021

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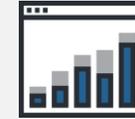
VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
September 8 and
13, 2021



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
leukemia
> 10 from US



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

Panel Consisting of 10 US Leukemia Experts

Neil Shah, MD, PhD
UCSF Helen Diller Family Comprehensive Cancer Center

Eunice Wang, MD
Roswell Park Comprehensive Cancer Center

Daniel DeAngelo, MD, PhD
Dana-Farber Cancer Institute

Charles Mullighan, MBBS (Hons), MSc, MD
St. Jude Children's Research Hospital

Jae Park, MD
Memorial Sloan Kettering Cancer Center

CHAIR: Elias Jabbour, MD
MD Anderson Cancer Center

Naval Daver, MD
MD Anderson Cancer Center

Jorge Cortes, MD
Georgia Cancer Center

Rami Komrokji, MD
H. Lee Moffitt Cancer Center

Guillermo Garcia-Manero, MD
MD Anderson Cancer Center

Meeting Agenda (Day 1)

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Time (CST)	Topic	Speaker/Moderator
4.00 PM – 4.10 PM	Welcome, Introductions, and Meeting Objectives	Elias Jabbour, MD
4.10 PM – 4.20 PM	CML: First-Line Treatment	Jorge Cortes, MD
4.20 PM – 4.40 PM	Discussion	
4.40 PM – 4.45 PM	Key Takeaways	Elias Jabbour, MD; Jorge Cortes, MD
4.45 PM – 4.55 PM	CML: Treatment of Resistant/Refractory Patients and New Targets (including mutation testing)	Neil Shah, MD, PhD
4.55 PM – 5.15 PM	Discussion	
5.15 PM – 5.20 PM	Key Takeaways	Elias Jabbour, MD; Neil Shah, MD, PhD
5.20 PM – 5.30 PM	ALL: Genetic Subsets	Charles Mullighan, MBBS (Hons), MSc, MD
5.30 PM – 5.45 PM	Discussion	
5.45 PM – 5.50 PM	Key Takeaways	Elias Jabbour, MD; Charles Mullighan, MBBS (Hons), MSc, MD
5.50 PM – 6.00 PM	ALL: Role of Monoclonal and Bispecific Antibodies	Daniel DeAngelo, MD, PhD
6.00 PM – 6.20 PM	Discussion	
6.20 PM – 6.25 PM	Key Takeaways	Elias Jabbour, MD; Daniel DeAngelo, MD, PhD
6.25 PM – 6.35 PM	ALL: Role of CAR T Cells	Jae Park, MD
6.35 PM – 6.50 PM	Discussion	
6.50 PM – 6.55 PM	Key Takeaways	Elias Jabbour, MD; Jae Park, MD
6.55 PM – 7.00 PM	Wrap-up and Overview	Elias Jabbour, MD



Meeting Agenda (Day 2)

EPICS

Time (CST)	Topic	Speaker/Moderator
4.00 PM – 4.05 PM	Agenda Review	Elias Jabbour, MD
4.05 PM – 4.15 PM	MDS: Low-Risk Disease	Guillermo Garcia-Manero, MD
4.15 PM – 4.35 PM	Discussion	
4.35 PM – 4.40 PM	Key Takeaways	Elias Jabbour, MD; Guillermo Garcia-Manero, MD
4.40 PM – 4.50 PM	MDS: High-Risk Disease	Rami Komrokji, MD
4.50 PM – 5.10 PM	Discussion	
5.10 PM – 5.15 PM	Key Takeaways	Elias Jabbour, MD; Rami Komrokji, MD
5.15 PM – 5.30 PM	AML: Newly Diagnosed Patients (including <i>FLT3</i>- and <i>IDH1/2</i>-mutated disease)	Eunice Wang, MD
5.30 PM – 5.50 PM	Discussion	
5.50 PM – 5.55 PM	Key Takeaways	Elias Jabbour, MD; Eunice Wang, MD
5.55 PM – 6.10 PM	AML: Relapsed/Refractory Patients (including <i>FLT3</i>- and <i>IDH1/2</i>-mutated disease)	Naval Daver, MD
6.10 PM – 6.30 PM	Discussion	
6.30 PM – 6.35 PM	Key Takeaways	Elias Jabbour, MD; Naval Daver, MD
6.35 PM – 6.45 PM	Wrap-up and Overview	Elias Jabbour, MD



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CML: First-Line Treatment



Presented by Jorge Cortes, MD

> **Imatinib, dasatinib, nilotinib, and bosutinib** are all approved TKIs for frontline

ELN 2020 Treatment Recommendations in First Line

- Imatinib** is approved for the treatment of chronic myeloid leukemia (CML) in patients with BCR-ABL1 positive disease. It is also approved for the treatment of gastrointestinal stromal tumors (GIST) and differentiated thyroid cancer (DTC).

 - The approval is based on efficacy, safety, and quality of life data from a phase III study of imatinib versus interferon- α in patients with CML.
- Dasatinib** is approved for the treatment of CML in patients with BCR-ABL1 positive disease. It is also approved for the treatment of acute myeloid leukemia (AML) in combination with cytarabine.

 - The approval is based on efficacy, safety, and quality of life data from a phase III study of dasatinib versus imatinib in patients with CML.
- Nilotinib** is approved for the treatment of CML in patients with BCR-ABL1 positive disease. It is also approved for the treatment of GIST.

 - The approval is based on efficacy, safety, and quality of life data from a phase III study of nilotinib versus imatinib in patients with CML.
- Bosutinib** is approved for the treatment of CML in patients with BCR-ABL1 positive disease. It is also approved for the treatment of GIST.

 - The approval is based on efficacy, safety, and quality of life data from a phase III study of bosutinib versus imatinib in patients with CML.



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Key Insights

TFR in frontline (cont.)

> Dose de-escalation is not required to stop therapy. Once the treatment is discontinued, patient follow-up should occur

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**CML: Treatment of
Resistant/Refractory Patients
and New Targets (including
mutation testing)**

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Key Insights

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ALL: Genetic Subsets



Presented by Charles Mullighan, MBBS (Hons), MSc, MD



Lineage ambiguous acute leukemia

> Most cases of ALL can be classified by genomics, particularly transcriptomics: "It's really DNA sequencing that's revolutionized the classification. This is a new paradigm"

Varying classification/immunophenotypic criteria

EPIC POPULATION

EPIC is a study of 1000 patients with ALL... (text is blurred)

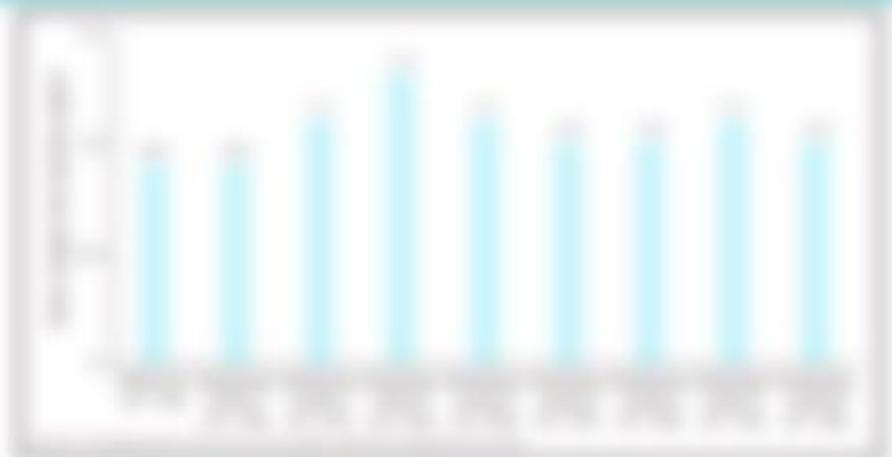
RESULTS

85% of 1000 patients achieved CR... (text is blurred)

KEY CONCLUSIONS

Continuing to improve treatment beyond week 20... (text is blurred)

EPIC POPULATION



RESPONSE RATES BY ALL SUBTYPE



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Key Insights

Genomic features

> ALL is best classified using genetic-based approaches. Although these are not available in all centers, they can be streamlined into 1 main

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ALL: Role of Monoclonal and Bispecific Antibodies

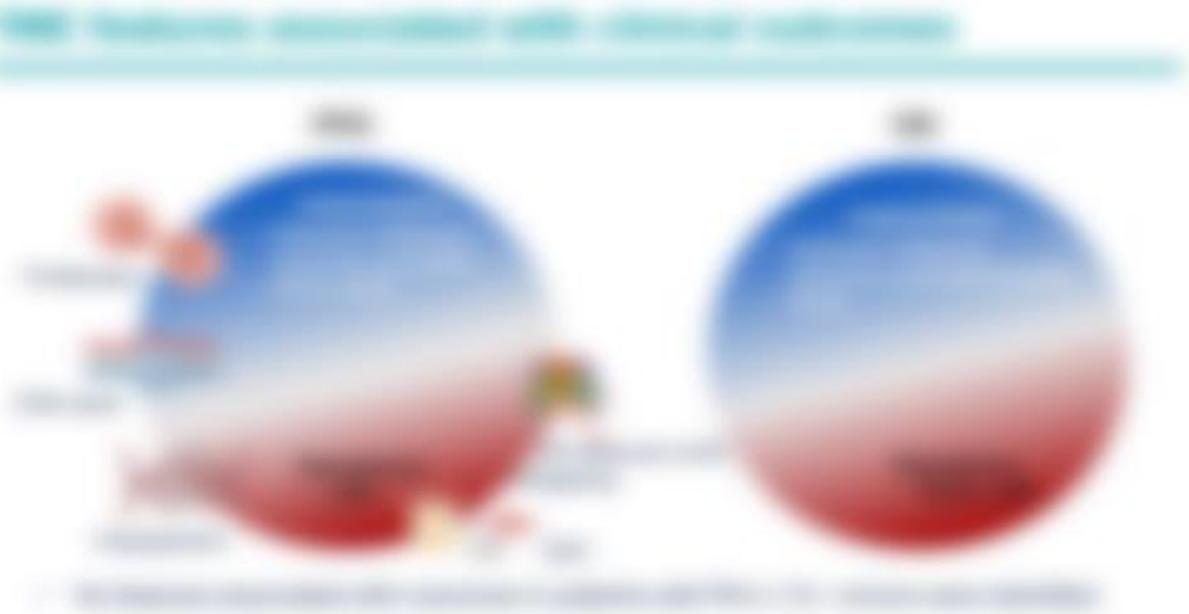


Presented by Daniel DeAngelo, MD, PhD

Target Antigens in ALL

- > The 3 most common targets in ALL are
 - CD19, ubiquitously expressed throughout development of the B-cell from the pro B to the

Pro-B Pre-B1 Immature B Mature B Plasma



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Key Insights

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ALL: Role of CAR T Cells



Presented by Jae Park, MD

- > Despite Blina and Ino, median OS for R/R B-ALL remains low, at 7–8 months
- > Blina and Ino have lower curative potential as monotherapy in R/R ALL

Phase 1/2 study of blinatumab + inotuzumab in relapsed B-ALL

- Shows that the combination of monoclonal antibodies is possible to use here, and these combinations can potentially be targeted

Phase 1/2 study of blinatumab + inotuzumab in relapsed B-ALL

- The regimen is seen as effective, working well, and broadly applicable to many patients

Phase 1/2 study of blinatumab + inotuzumab in relapsed B-ALL

- The approach is seen as a good solution for a patient population in which giving conventional therapy is difficult. It is seen as effective and safe

Phase 1/2 study of blinatumab + inotuzumab in relapsed B-ALL

- Shows that the combination of monoclonal antibodies with rituximab is safe. However, they would like to see phase 2 data to confirm its activity in this setting

Phase 1/2 study of blinatumab + inotuzumab in relapsed B-ALL

- The 1:1000 regimen is seen as useful in the specific patient population with refractory disease. It was seen to be effective, very safe, and well-tolerated. Some of the responses were seen early, very quickly



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Key Insights

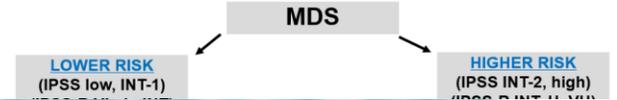
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MDS: Low-Risk Disease



Presented by Guillermo Garcia-Manero, MD

Proposed treatment algorithm for patients with MDS 2021



STUDY POPULATION

1. 100% of study, 1000 patients with either myelodysplasia or MDS with 2-5% blasts, with blasts in bone marrow, non-blastic MDS, intermediate to high, or high, average 10% blasts. Median age 75 years, 50% male. Treatment with disease-modifying agents (eg, 5-azacytidine, lenalidomide) or transfusion support (eg, 100% transfused, transfusion requirements > 100% of needs at 12w). The population, 1000 patients who did not receive 5-azacytidine or lenalidomide, 75% of all study by week 24 not continued treatment through week 48.

OUTCOME

1. 100% of 1000 patients achieved CR, 75% of weeks 24-48, median survival 100, 75% of weeks 24-48, median survival 100, 75% of weeks 24-48.

KEY POINT CONCLUSIONS

Continuing investigational treatment beyond week 24 provides clinical benefit in CRs responses and decreases the transfusion need in patients.



RESPONSE RATE OVER TIME



RESPONSE RATE OVER TIME IN HIGH RISK PATIENTS



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Key Insights

In low-risk disease, the goal of therapy is to impact the natural history of the disease, to improve outcomes. This can be achieved by

- > Altering the progression or clonal evolution of the disease by intervening early

[Faded content area containing multiple paragraphs and bullet points, likely representing clinical trial results or treatment options for low-risk MDS.]

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MDS: High-Risk Disease

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Key Insights

There is a need to have a better definition of high-risk MDS, as about 25% of low-risk MDS patients die within 2 years of diagnosis and they may qualify as high risk

- 1. Current criteria for classification of MDS are based on morphology, cytogenetics, and blast count, but these criteria are not predictive of prognosis
- 2. Promising investigational and off-label agents from phase I/II studies in an ongoing phase III study of combination with granulocyte colony-stimulating factor (G-CSF) – (NCT01880400)
- 3. The approach is seen as effective, working well, and broadly applicable to many patients
- 4. Investigational agents: investigational for intermediate patients with low-risk MDS, continue to show promising safety and efficacy with broader complete responses – (NCT01880400)
- 5. The approach is seen as a good option for a patient population in which going investigational is difficult. It is seen as effective and safe
- 6. Phase III study: a phase III, open-label, randomized study to assess safety of combination of combination 1 combination 2 combination 3 in addition to G-CSF in patients with newly diagnosed MDS – (NCT01880400)
- 7. Experts believe the combination of combination 1 combination 2 combination 3 with G-CSF is safe. However, they would like to see phase II data to confirm its safety in this setting
- 8. Long-term outcomes from a phase III study of combination 1 combination 2 combination 3 in patients with MDS – (NCT01880400)
- 9. The G-CSF approach is seen as useful in the specific patient population with refractory disease. It was seen to be effective, very safe, and well-tolerated. Some of the responses were seen with steady state G-CSF

Molecular signatures

> A molecular classification of MDS is much needed, and the data from thousands of patients will become available via the

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**AML: Newly Diagnosed
Patients (including *FLT3*- and
IDH1/2-mutated disease)**



Presented by Eunice Wang, MD

> In AML, patients now can be treated on the basis of cytogenetic and biologic features

STUDY POPULATION

Phase 3 study, 400 patients with $t(8;21)$ or $t(16;17)$ AML. 200 patients in each arm. 100 patients in each arm received standard of care (SOC) and 100 patients in each arm received SOC + ATRA. SOC + ATRA group had significantly higher overall survival (OS) and event-free survival (EFS) compared to SOC group. The SOC + ATRA group had significantly higher OS and EFS compared to SOC group. The SOC + ATRA group had significantly higher OS and EFS compared to SOC group.

RESULTS

OS: SOC + ATRA (n=100) vs SOC (n=100). SOC + ATRA group had significantly higher OS compared to SOC group. EFS: SOC + ATRA (n=100) vs SOC (n=100). SOC + ATRA group had significantly higher EFS compared to SOC group. CR: SOC + ATRA (n=100) vs SOC (n=100). SOC + ATRA group had significantly higher CR compared to SOC group.

KEY CONCLUSIONS

Adding ATRA to SOC significantly improved OS and EFS in patients with $t(8;21)$ or $t(16;17)$ AML. SOC + ATRA is the preferred treatment for these patients.

OS: SOC + ATRA vs SOC (n=400)



RESPONSE: SOC + ATRA vs SOC (n=400)



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Key Takeaways

Patients ineligible for intensive chemo

- > HMA-Ven is standard of care for patients (with no TP53 mutation) unfit for intensive chemo

[The following text is extremely faint and largely illegible. It appears to be a list of clinical trial descriptions or evidence supporting the use of HMA-Ven in specific patient populations.]

EPICS

**AML: Relapsed/Refractory
Patients (including *FLT3*- and
IDH1/2-mutated disease)**



Presented by Naval Daver, MD

Targeting *FLT3* mutations

FLAG-IDA + VEN: Efficacy and Summary

STUDY POPULATION

1000 patients with FLT3 mutations... (text is blurred)

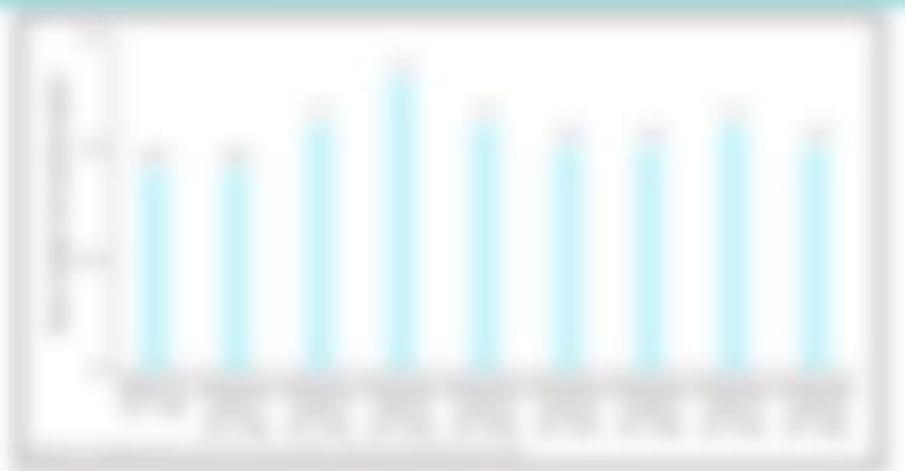
RESULTS

80% of patients achieved CR... (text is blurred)

KEY CONCLUSIONS

Continuing treatment beyond week 20... (text is blurred)

RESPONSE RATE OVER TIME



RESPONSE RATE OVER TIME BY FLT3 MUTATION



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Key Insights

AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (1/2)

FLT3-mutant AML subset

> In the relapse setting, *FLT3* inhibitor is used in combination, rather than as single agent. It is still unclear if the optimal combination regimen is with Ven plus

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AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (2/2)

Bispecifics

> Similar to cellular therapy, use of bispecifics can lead to 70%–80% CRS rates, requires close monitoring of patients, and inpatient

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