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LEUKEMIA IN 2021 AND BEYOND

FULL REPORT

September 8 and 13, 2021

Report Contents

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Content	Slide
Meeting Snapshot	3
Faculty Panel	4
Meeting Agenda	5
Strategic Recommendations	7
CML: First-Line Treatment	9
CML: Treatment of Resistant/Refractory Patients	14
ALL: Genetic Subsets	18
ALL: Role of Monoclonal and Bispecific Antibodies	22
ALL: Role of CAR T Cells	27
MDS: Low-Risk Disease	32
MDS: High-Risk Disease	37
AML: Newly Diagnosed Patients	42
AML: Relapse/Refractory Patients	47

Meeting Snapshot

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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

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Daniel DeAngelo, MD, PhD
Dana-Farber Cancer Institute

Eunice Wang, MD
Roswell Park Comprehensive Cancer Center

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

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

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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)

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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 *FLT3*- and *IDH1/2*-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 *FLT3*- and *IDH1/2*-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

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

ELN 2020 Treatment Recommendations in First Line

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Key Insights

CML: First-Line Treatment (1/2)

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TKIs

> TKIs continue to be an excellent treatment for patients with CML

[redacted]

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CML: First-Line Treatment (2/2)

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)

Presented by Neil Shah, MD, PhD

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> Despite the advances in CML treatment, there remains a portion of patients with advanced-phase disease, particularly blast phase, that will not respond durably.

[redacted]

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Key Insights

CML: Treatment of Resistant/Refractory Patients and New Targets

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Assessment of TFR

- Highly sensitive technologies include digital PCR

[redacted]

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ALL: Genetic Subsets

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

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Lineage ambiguous acute leukemia

> Most cases of ALL can be classified by genomics, particularly transcriptomics: "*It's really*

Varying classification/immunophenotypic criteria

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Key Insights

ALL: Genetic Subsets

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

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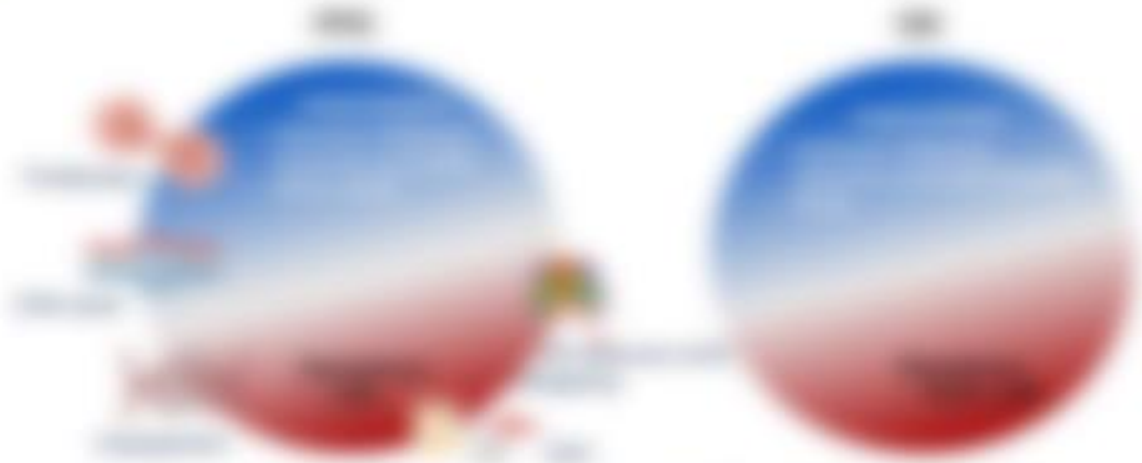
Target Antigens in ALL

- 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

ALL: Role of Monoclonal and Bispecific Antibodies (1/2)

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Sequencing

> Blina and Ino are superior to standard chemo in first and second relapse

[redacted]

ALL: Role of Monoclonal and Bispecific Antibodies (2/2)

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MRD

> The goal of therapy should always be achievement of MRD– status "*It is the MRD– patients, even in the relapsed-refractory setting, who do*

[redacted]

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ALL: Role of CAR T Cells

Presented by Jae Park, MD

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- 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

[redacted]

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Key Insights

ALL: Role of CAR T Cells (1/2)

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Sequencing

> Ino and Blina are already used upfront; therefore, the place for CAR T will be on relapse after treatment with either of these

[redacted]

ALL: Role of CAR T Cells (2/2)

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Transplant after CAR T therapy

> A definitive study providing this answer is lacking, and these studies are hard to design

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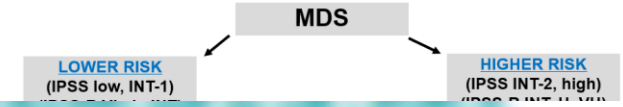
MDS: Low-Risk Disease

Presented by Guillermo Garcia-Manero, MD

Proposed treatment algorithm for patients with MDS 2021



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Key Insights

MDS: Low-Risk Disease (1/2)

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

MDS: Low-Risk Disease (2/2)

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Emerging agent roxadustat (HIFα inhibitor)

> *"The data suggest that this would be another drug for anemia"*

[redacted]

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MDS: High-Risk Disease

Presented by Rami Komrokji, MD

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Upfront HMA Combinations

Drug	MOA	ORR	CR	AE	DUR	unique	study	Ongoing stud
venetoclax	Anti-BCL2	79%	39.7%	myelosuppression	12.9	Median OS 27 mo	Garcia JS et al. ASH 2020.	VERONA

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Key Insights

MDS: High-Risk Disease (1/2)

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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

MDS: High-Risk Disease (2/2)

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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

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

STUDY POPULATION

- [illegible]

OUTCOME

- [illegible]

EXPERT CONCLUSIONS

[illegible]

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Key Takeaways

AML: Newly Diagnosed Patients (1/2)

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Patients ineligible for intensive chemo

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

[redacted]

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AML: Newly Diagnosed Patients (2/2)

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AML-MRC and t-AML subsets

> Opinions were split between usage of CPX-351 or HMA-Ven as bridge to transplant for fit patients

[redacted]

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

Presented by Naval Daver, MD

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Targeting *FLT3* mutations

FLAG-IDA + VEN: Efficacy and Summary

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Key Insights

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

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***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

[redacted]

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

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Bispecifics

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

[redacted]

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