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EPICS

Leukemia in 2022 and Beyond

Focus on AML & MDS

Full Report

September 21 and 26, 2022

Report Contents

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Content	Slide
Meeting Snapshot	3
Faculty Panel	4
Meeting Agenda	5
Strategic Recommendations	7
MDS: Low-Risk Disease	12
MDS: High-Risk Disease	20
AML: Newly Diagnosed Patients	31
AML: Relapsed/Refractory Patients	43
AML: The Current and Future Roles of Transplantation in Leukemias	51

Meeting Snapshot

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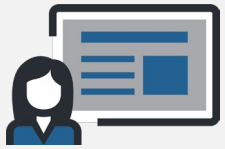
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
September 21 and 26, 2022



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in leukemia

- > 6 from US
- > 2 from Europe

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

Panel Consisting of 6 US and 2 European Leukemia Experts

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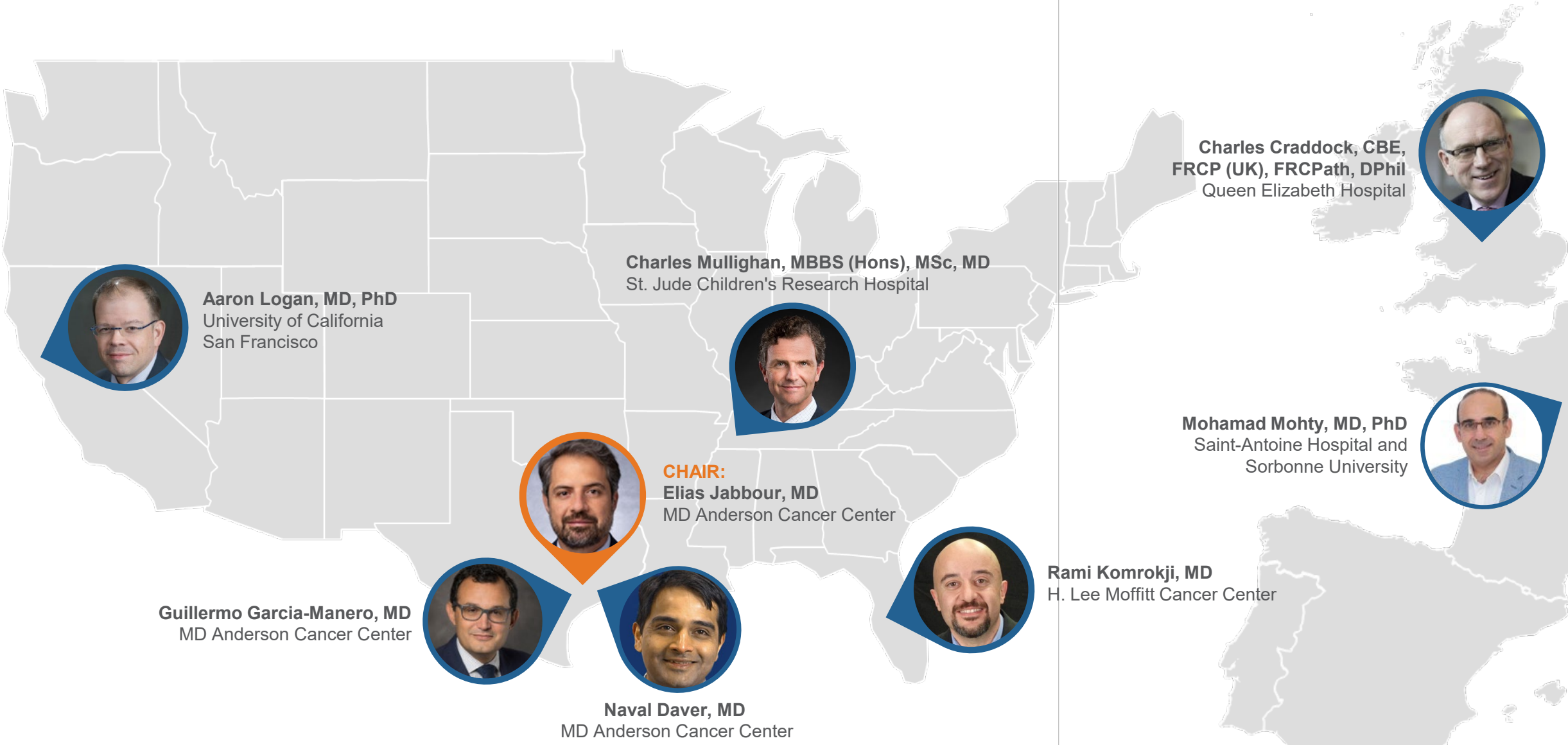

Aaron Logan, MD, PhD
University of California
San Francisco

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

CHAIR:
Elias Jabbour, MD
MD Anderson Cancer Center

Guillermo Garcia-Manero, MD
MD Anderson Cancer Center

Naval Daver, MD
MD Anderson Cancer Center

Rami Komrokji, MD
H. Lee Moffitt Cancer Center

Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
Queen Elizabeth Hospital

Mohamad Mohty, MD, PhD
Saint-Antoine Hospital and
Sorbonne University

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Meeting Agenda Day 1: September 21

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Time (CST)	Topic	Speaker/Moderator
12.00 PM – 12.10 PM	Welcome and Introductions	Elias Jabbour, MD
12.10 PM – 12.20 PM	MDS: Low-Risk Disease	Rami Komrokji, MD
12.20 PM – 12.40 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
12.40 PM – 12.45 PM	Key Takeaways	Rami Komrokji, MD
12.45 PM – 12.55 PM	MDS: High-Risk Disease	Guillermo Garcia-Manero, MD
12.55 PM – 1.20 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
1.20 PM – 1.25 PM	Key Takeaways	Guillermo Garcia-Manero, MD
1.25 PM – 1.35 PM	Break	
1.35 PM – 1.45 PM	ALL: Genetic Subsets	Charles Mullighan, MBBS (Hons), MSc, MD
1.45 PM – 2.05 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
2.05 PM – 2.10 PM	Key Takeaways	Charles Mullighan, MBBS (Hons), MSc, MD
2.10 PM – 2.20 PM	ALL: Role of Monoclonal and Bispecific Antibodies	Aaron Logan, MD, PhD
2.20 PM – 2.45 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
2.45 PM – 2.50 PM	Key Takeaways	Aaron Logan, MD, PhD
2.50 PM – 3.00 PM	Wrap-up and Overview	Elias Jabbour, MD

Meeting Agenda Day 2: September 26

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Time (CST)	Topic	Speaker/Moderator
12.00 PM – 12.10 PM	Agenda Review	Elias Jabbour, MD
12.10 PM – 12.20 PM	AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease)	Naval Daver, MD
12.20 PM – 12.50 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
12.50 PM – 12.55 PM	Key Takeaways	Naval Daver, MD
12.55 PM – 1.05 PM	AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease)	Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
1.05 PM – 1.35 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
1.35 PM – 1.40 PM	Key Takeaways	Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
1.40 PM – 1.50 PM	The Current and Future Roles of Transplantation in Leukemias	Mohamad Mohty, MD, PhD
1.50 PM – 2.20 PM	Key Questions and Topics for Discussion	Moderator: Elias Jabbour, MD
2.20 PM – 2.25 PM	Key Takeaways	Mohamad Mohty, MD, PhD
2.25 PM – 2.30 PM	Wrap-up and Overview	Elias Jabbour, MD

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MDS: Low-Risk Disease

MDS: Low-Risk Disease (1/4)

Presented by Rami Komrokji, MD

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Treatment goals and classification of low-risk MDS

MDS: Low-Risk Disease (2/4)

Presented by Rami Komrokji, MD

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Ongoing evolution of low-risk MDS therapies

MDS: Low-Risk Disease (3/4)

Presented by Rami Komrokji, MD

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Ongoing evolution of low-risk MDS therapies (cont.)

MDS: Low-Risk Disease (4/4)

Presented by Rami Komrokji, MD

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Possible treatment map for low-risk MDS

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Key Insights

MDS: Low-Risk Disease (1/2)

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Unmet need for treating cytopenias and low-risk MDS

[redacted]

MDS: Low-Risk Disease (2/2)

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Luspatercept as an emerging agent

[redacted]

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MDS: High-Risk Disease

MDS: High-Risk Disease (1/7)

Presented by Guillermo Garcia-Manero, MD

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Proposed treatment algorithm for patients with MDS 2020

MDS: High-Risk Disease (2/7)

Presented by Guillermo Garcia-Manero, MD

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Hypomethylating Agents (HMAs)

STUDY POPULATION

- [illegible]

OUTCOME

- [illegible]

EXPERT CONCLUSIONS

[illegible]

MDS: High-Risk Disease (3/7)

Presented by Guillermo Garcia-Manero, MD

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Venetoclax + Azacitidine

84% of patients who received RP2D Ven + Aza (N=51) responded to treatment

• Median time to response:

MDS: High-Risk Disease (4/7)

Presented by Guillermo Garcia-Manero, MD

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Venetoclax + ASTX727

Venetoclax in combination with oral ASTX727 (cedazuridine-decitabine)

MDS: High-Risk Disease (5/7)

Presented by Guillermo Garcia-Manero, MD

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Sabatolimab + HMA

Phase Ib study of sabatolimab + HMA in MDS and AML

MDS: High-Risk Disease (6/7)

Presented by Guillermo Garcia-Manero, MD

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Magrolimab + Azacitidine

Magrolimab + AZA in previously untreated HR-MDS

MDS: High-Risk Disease (7/7)

Presented by Guillermo Garcia-Manero, MD

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Targeted options in MDS

IDH inhibitors

> *IDH* mutations are less common than in MDS than in AML; *IDH2* mutations occur in approximately 3% to 5% of patients, and *IDH1*

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Key Insights

MDS: High-Risk Disease (1/2)

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Single-agent HMA is still the standard of care

- There is no clear understanding on how to obtain an optimal response in patients for whom HMA therapy has failed; one expert stated, *"In*

MDS: High-Risk Disease (2/2)

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Molecular signatures

- The new IPSS-M system serves as a powerful tool to stratify MDS risk categories

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

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (1/6)

Presented by Naval Daver, MD

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Treatment of core-binding factor (CBF) AML

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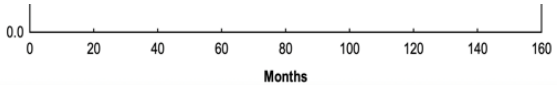
Timeline of FDA Approvals for HER2+ Breast Cancer



Am J Hematol;2022 Aug 26. doi:10.1002/ajh.26700.

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (2/6)

Presented by Naval Daver, MD

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Improving cytotoxic therapy, nontargeted approaches

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Kadia et al. *Lancet Haematol.* 2021;8(8):e552-e561.

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (3/6)

Presented by Naval Daver, MD

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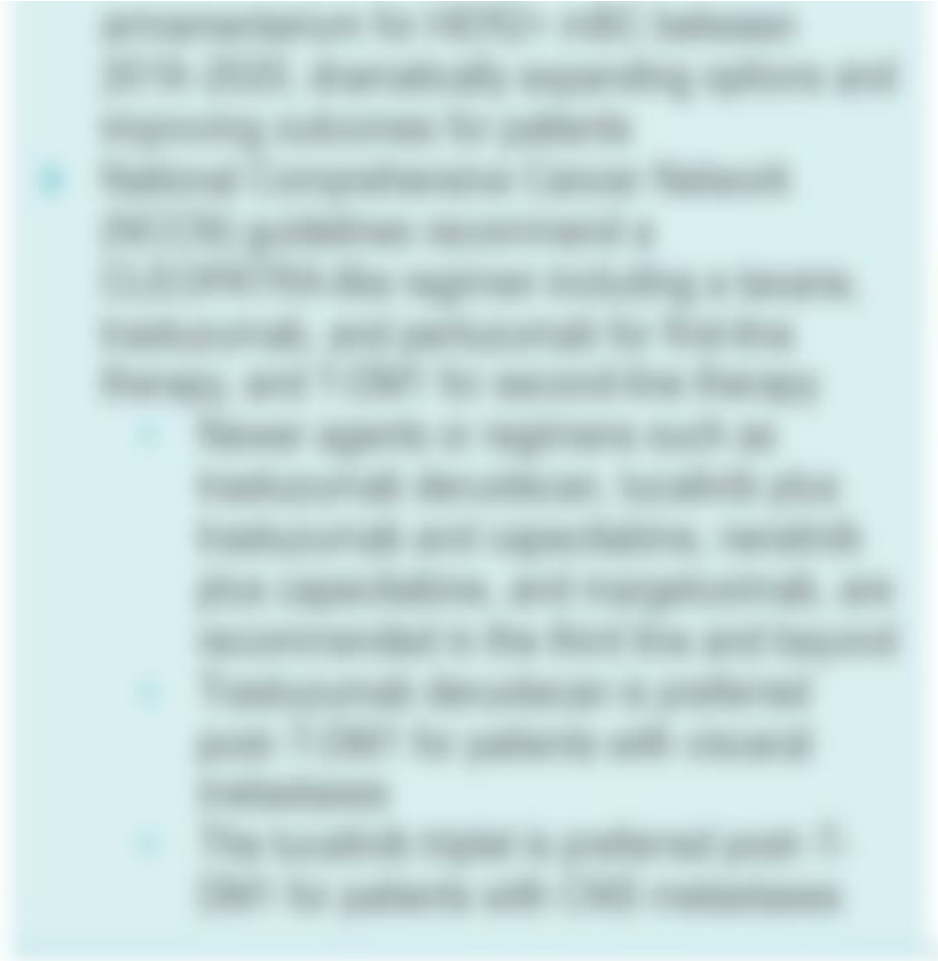
Treatment of frontline FIT *FLT3*-mutated AML and maintenance with FLT3 inhibitor posttransplant



AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (4/6)

Presented by Naval Daver, MD

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Management of older/unfit *FLT3* AML patients

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Time, mo

Yilmaz M, et al. Blood Cancer Journal, April 2022

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (5/6)

Presented by Naval Daver, MD

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Targeting *IDH1* and *IDH2* mutations

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (6/6)

Presented by Naval Daver, MD

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TP53 mutation-directed therapies and immune therapies in AML

AZA + VEN vs chemotherapy in all AML patients

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Key Takeaways

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (1/4)

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Patients eligible for intensive chemotherapy

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (2/4)

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Patients ineligible for intensive chemotherapy

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (3/4)

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IDH1/2-mutated AML patients

AML: Newly Diagnosed Patients (including *FLT3*- and *IDH1/2*-mutated disease) (4/4)

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MRD

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

AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (1/4)

Presented by Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil

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Impact of pretransplant MRD on patient outcomes

- A prospective, randomized study (Craddock C, et al. *J Clin Oncol*. 2021;39:768-778) with a reduced-intensity conditioning

Impact of Pre-transplant MRD Measured by Unsupervised

AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (2/4)

Presented by Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil

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FLT3-mutated R/R AML

- In the ADMIRAL trial, compared with intensive chemotherapy, R/R *FLT3*-mutated AML patients treated with gilteritinib achieved higher CR

AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (3/4)

Presented by Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil

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IDH1/2-mutated R/R AML

- IDH inhibitors are FDA approved in R/R AML: ivosidenib (IDH1 inhibitor) and enasidenib (IDH2 inhibitor)

AML: Relapsed/Refractory Patients (including *FLT3*- and *IDH1/2*-mutated disease) (4/4)

Presented by Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil

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R/R AML without actionable mutations

- Treatment with VEN + FLAG-IDA in R/R patients after intensive chemotherapy shows high response rates and deep CRs, with ~70%

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Key Insights

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

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It was strongly emphasized that sequentially testing at every relapse to identify actionable mutations is very important

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

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***IDH1/2*-mutant AML subset**

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AML: The Current and Future Roles of Transplantation in Leukemias

AML: The Current and Future Roles of Transplantation in Leukemias

Presented by Mohamad Mohty, MD, PhD

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Indications for allogeneic HCT

> Allo-HCT is so far the most powerful antileukemia treatment through conditioning

AML: The Current and Future Roles of Transplantation in Leukemias

Presented by Mohamad Mohty, MD, PhD

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Maintenance after allogeneic HCT

> Many patients (especially those with adverse genetics and/or

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Key Insights

AML: The Current and Future Roles of Transplantation in Leukemias (1/2)

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Allo-SCT, applied as consolidation in first complete remission, is associated with a significant reduction of relapse risk and improvement of survival in AML patients independent of karyotype

AML: The Current and Future Roles of Transplantation in Leukemias (2/2)

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In the future, the expectation is that more AML patients who are harder to treat, in advanced, refractory disease, will undergo allo-SCT

- KOLs are seeing more relapsed AML patients go into remission and then for transplant without intensive chemotherapy by using VEN +

randomized phase 2 study – (ICML) Zhang 408

- Experts believe the resolution of molecular phenotype is possible in real time, and these vulnerabilities can potentially be targeted

Promising tolerability and efficacy results from dose-escalation in an ongoing phase I/II study of inotuzumab with polatuzumab vedotin for relapsed/refractory B-cell NHL – (EHA) Ghosh #S222

- The regimen is seen as effective, exciting, safe, and broadly applicable to many patients

Blinatumomab (Amgen) monotherapy for elderly/unfit patients with first-line DLBCL continues to show promising safety and efficacy with durable complete responses – (EHA) Chaumeil #EP343

- This approach is seen as a great solution for a patient population in whom giving immunochemotherapy is difficult. It is viewed as effective and safe

FIRST-MIND: a phase Ib, open-label, randomized study to assess safety of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL – (EHA) Beriada #EP494

- Experts believe the combination of tafasitamab + lenalidomide with R-CHOP is safe. However, they would like to see phase III data to confirm its activity in this setting

Long-term analyses from L-MIND, a phase II study of tafasitamab plus lenalidomide (len) in patients with R/R DLBCL – (ICML) Duell #28

- The L-MIND regimen is seen as useful in the specific patient population with refractory disease. It was noted to be effective, very safe, and well tolerated. Some of the responses seen were clearly very durable

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