# *Meet The Professor*

# Optimizing the Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

**Tuesday, September 19, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Naval Daver, MD**

## Moderator

**Neil Love, MD**

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# Commercial Support

This activity is supported by educational grants from Daiichi Sankyo Inc, Gilead Sciences Inc, and Taiho Oncology Inc.

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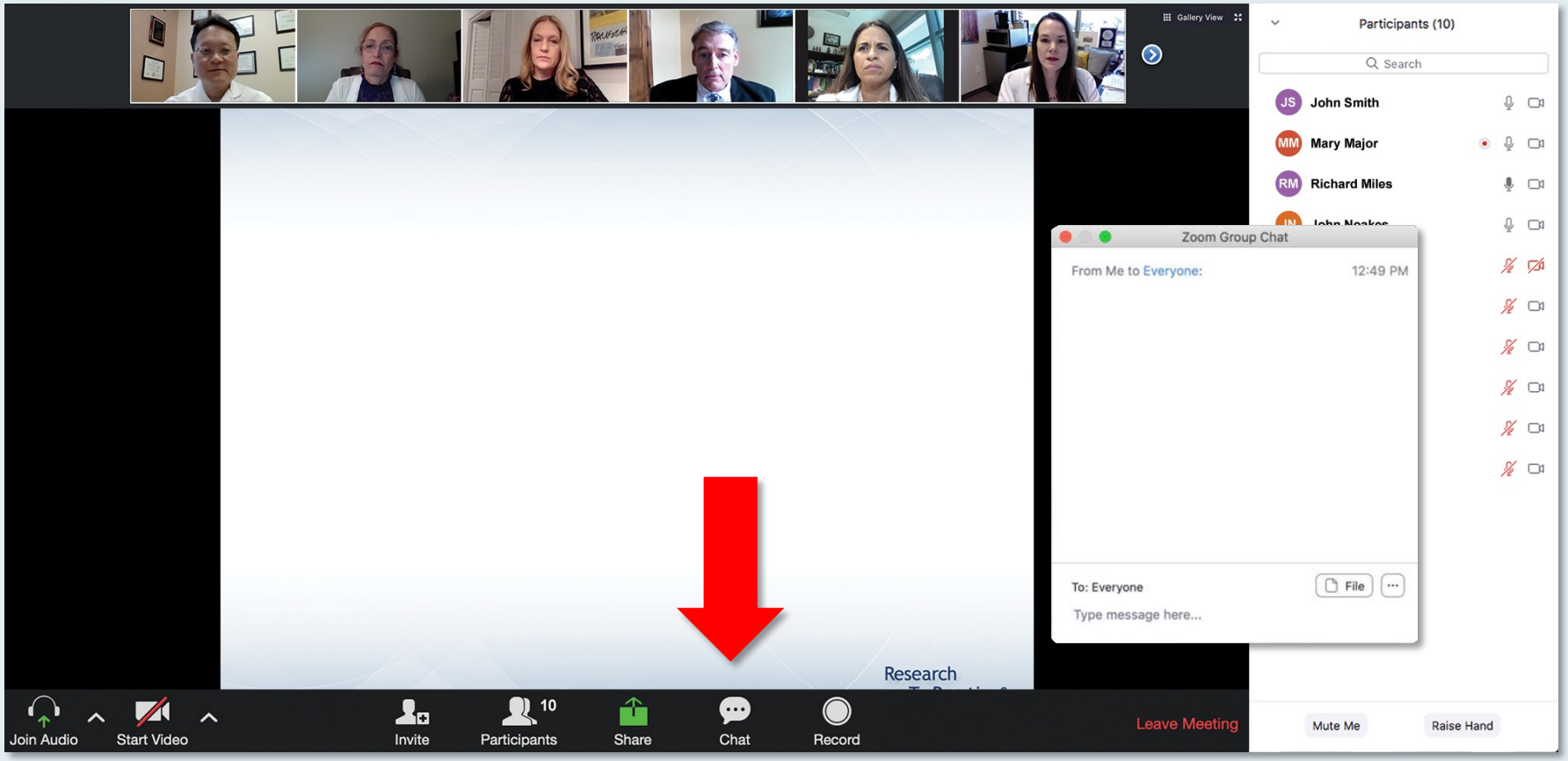
# We Encourage Clinicians in Practice to Submit Questions

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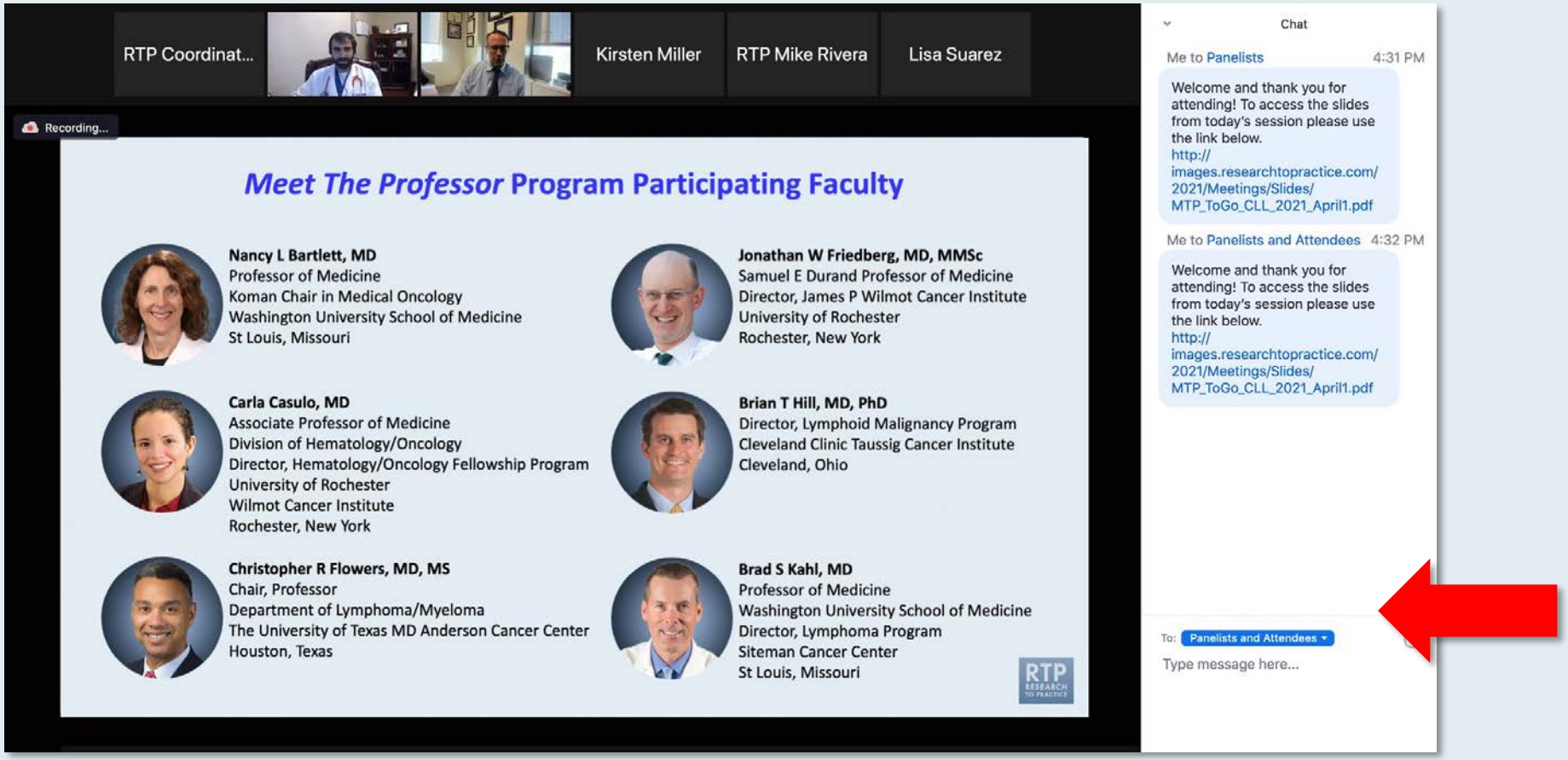


**Drag the white line above the submission box up to create more space for your message.**

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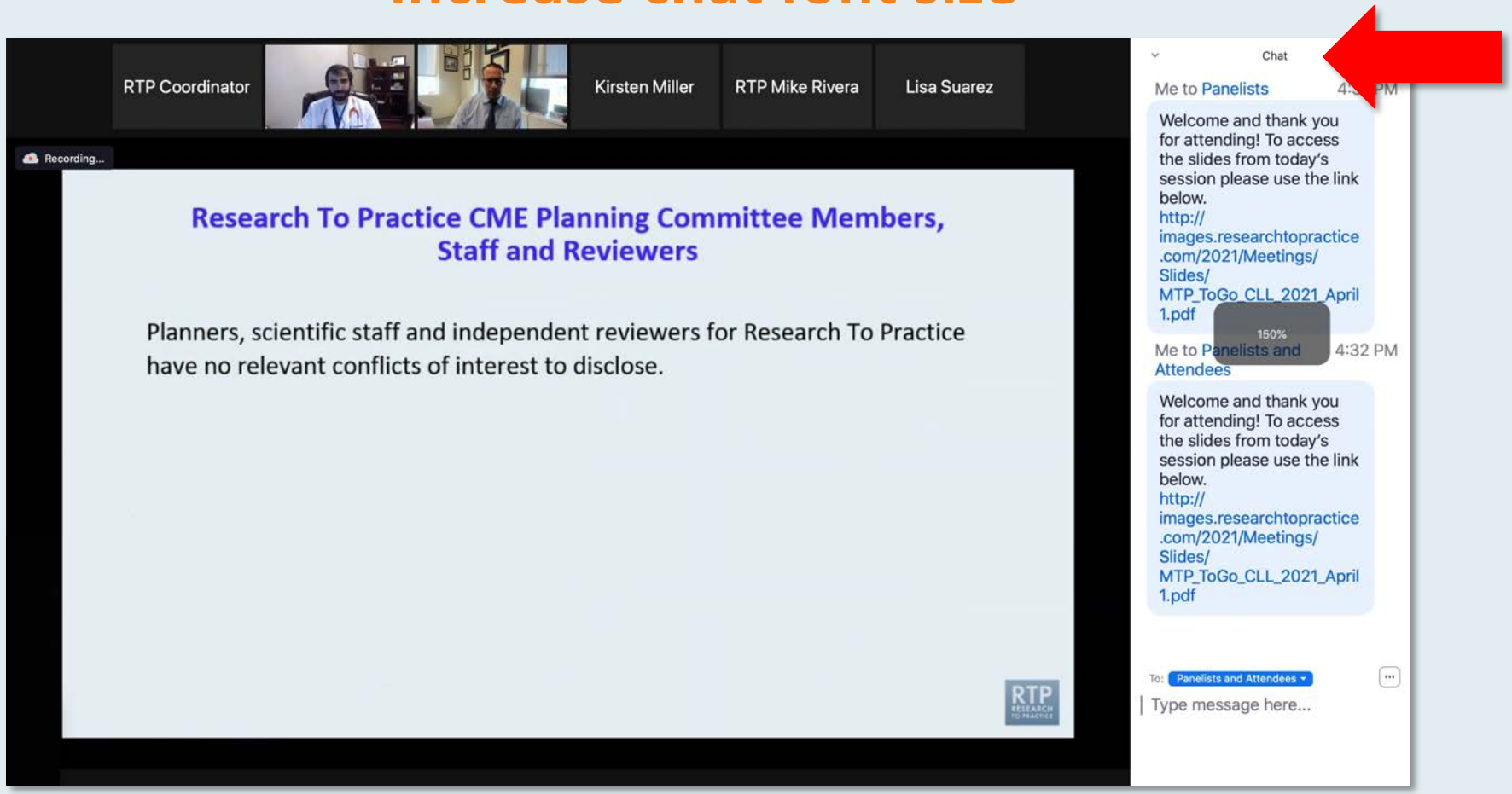
## Increase chat font size

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**You may do this as many times as you need for readability.**

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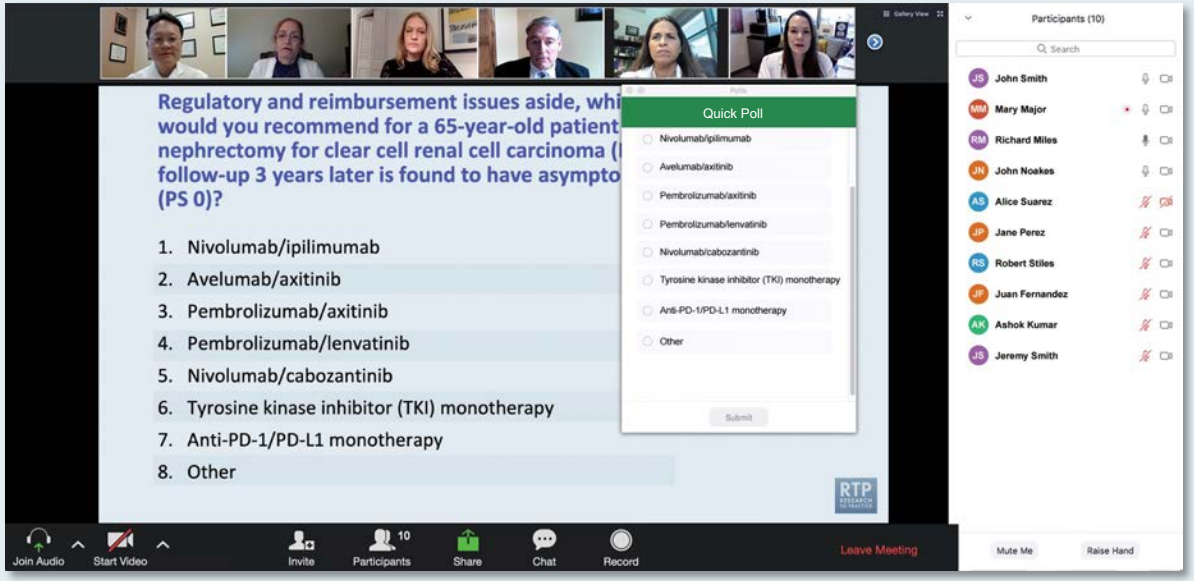


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## WITH DR NEIL LOVE

## Novel Agents, Approaches and Strategies in the Management of Higher-Risk Myelodysplastic Syndromes

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THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

DR DAVID SALLMAN
MOFFITT CANCER CENTER

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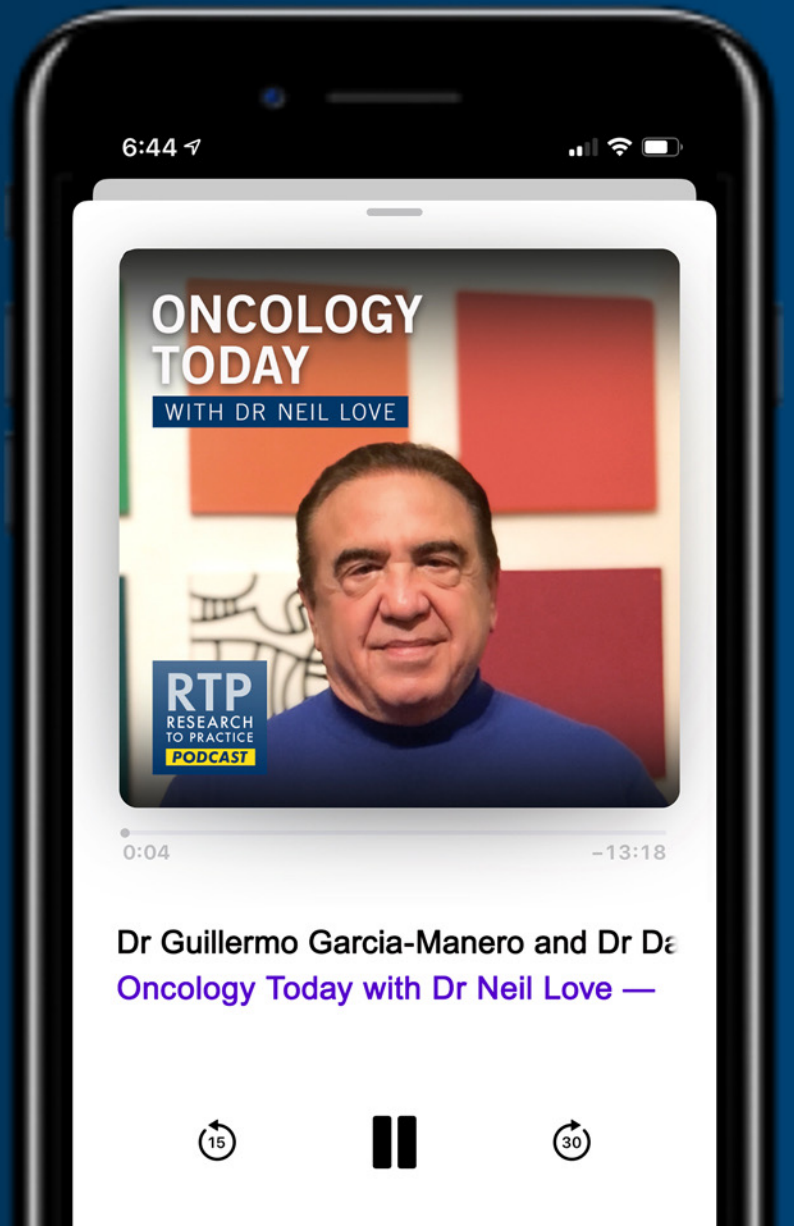

# Practical Perspectives: Investigators Discuss Current Management and Actual Cases of Relapsed/Refractory Metastatic Colorectal Cancer

*A CME/MOC-Accredited Virtual Event*

**Wednesday, September 20, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Kristen K Ciombor, MD, MSCI**
**J Randolph Hecht, MD**

## Moderator

**Neil Love, MD**

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# Inside the Issue: Integrating Targeted and Immunotherapy into the Management of Localized Non-Small Cell Lung Cancer

*A CME/MOC-Accredited Live Webinar*

**Thursday, September 21, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Jamie E Chaft, MD**
**John V Heymach, MD, PhD**

## Moderator

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# What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

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**Brad S Kahl, MD**

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# Optimizing the Management of Gastroesophageal Cancers

**Thursday, September 28, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Peter C Enzinger, MD**

## Moderator

**Neil Love, MD**

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# Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

*A CME/MOC-Accredited Live Webinar*

**Tuesday, October 3, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Nikhil I Khushalani, MD**
**Anna C Pavlick, DO, MBA**

## Moderator

**Neil Love, MD**

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# Current Approaches and Future Strategies in Oncology

***A Multitumor Educational Symposium in Partnership with Florida Cancer Specialists & Research Institute***

## Saturday, October 7, 2023

### ER-Positive Breast Cancer

**7:15 AM – 8:15 AM ET**

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### Lymphoma

**9:30 AM – 10:30 AM PT**
**(12:30 PM – 1:30 PM ET)**

**Faculty**

**Christopher R Flowers, MD, MS**
**Ann S LaCasce, MD, MMSc**

### Urothelial Bladder Cancer and Renal Cell Carcinoma

**10:30 AM – 11:30 AM PT**
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**Thomas E Hutson, DO, PharmD**
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**3:50 PM – 4:50 PM PT**
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*Thank you for joining us!*

*CME and MOC credit information will be emailed to each participant within 5 business days.*

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# *Meet The Professor*

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**Naval Daver, MD**
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Professor
Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

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# *Meet The Professor* Program Participating Faculty

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Director, Leukemia Research Alliance Program
Professor
Department of Leukemia
The University of Texas
MD Anderson Cancer Center
Houston, Texas

**Richard M Stone, MD**
Lunder Family Chair in Leukemia
Chief of Staff
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

**Gail J Roboz, MD**
Director, Clinical and Translational Leukemia Programs
Professor of Medicine
Weill Cornell Medical College
NewYork-Presbyterian Hospital
New York, New York

**MODERATOR**
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Research To Practice
Miami, Florida

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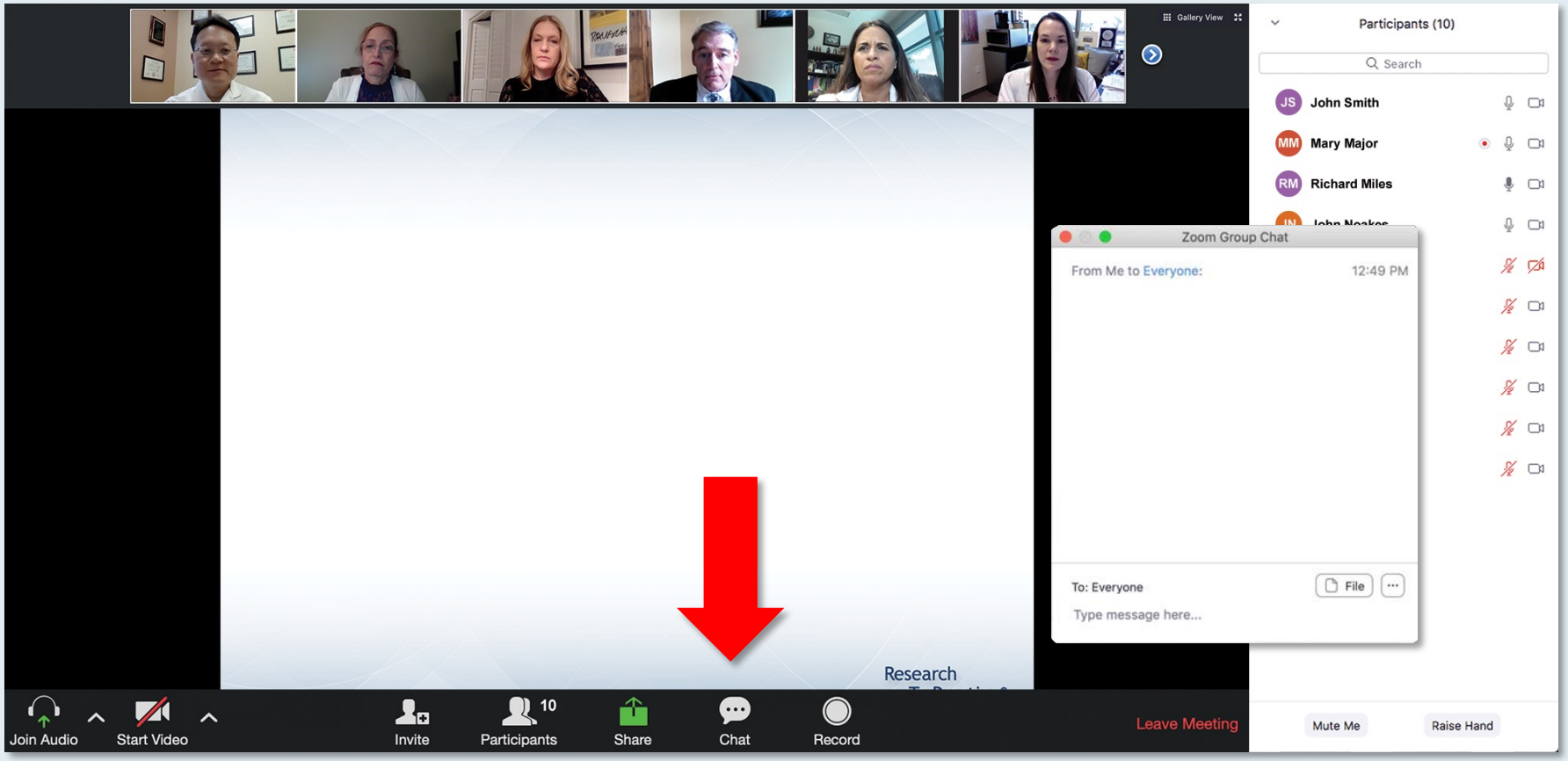


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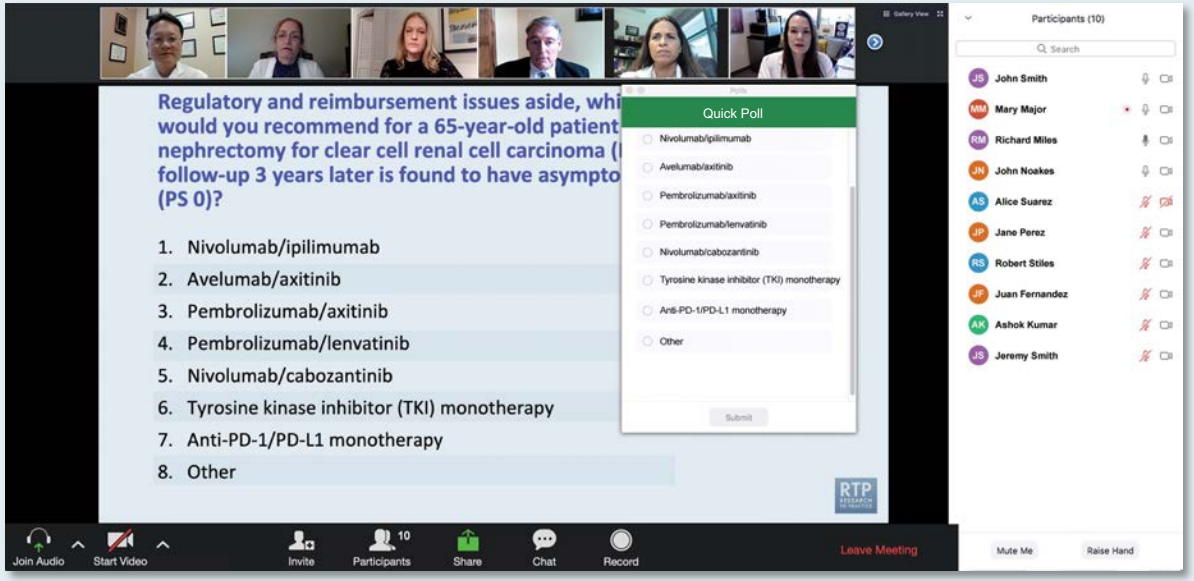


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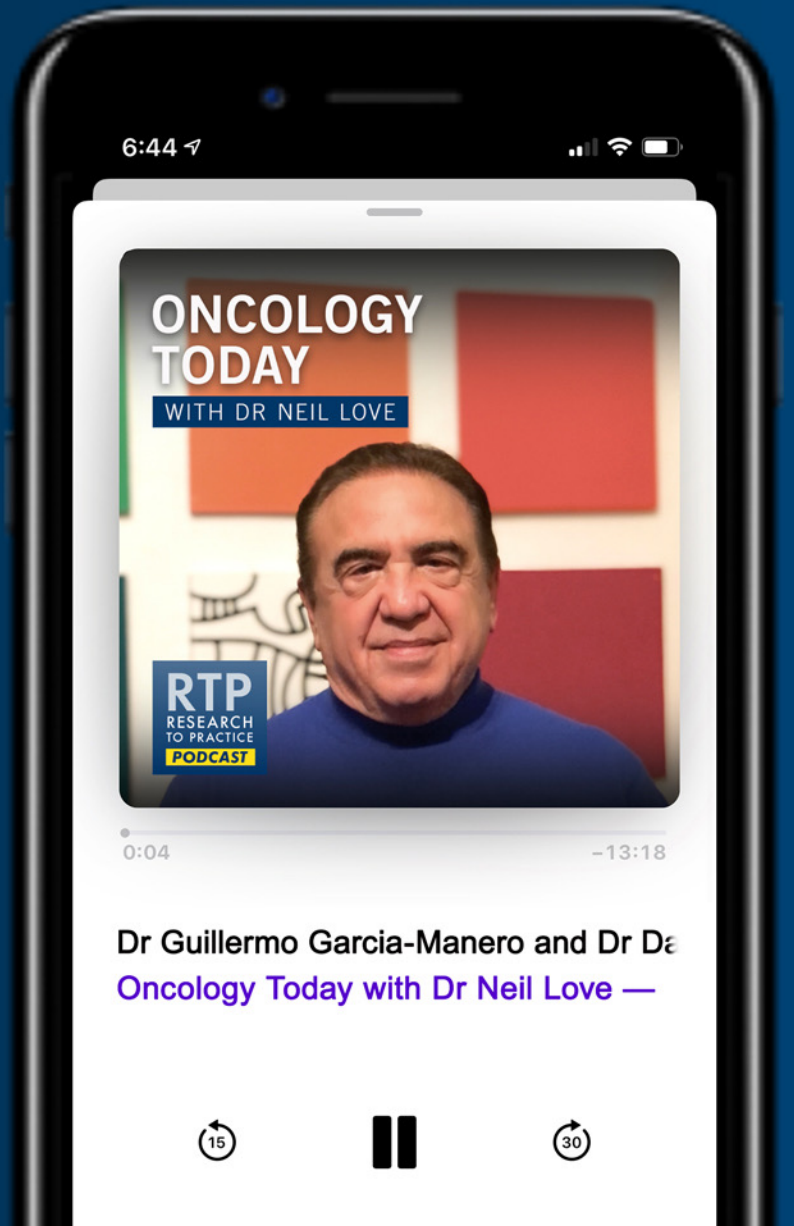

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**Bhavana (Tina) Bhatnagar, DO**
West Virginia University Cancer Institute Schiffler Cancer Center
Wheeling, West Virginia

**Anna Halpern, MD**
Fred Hutch Cancer Center
Seattle, Washington

**Rachel J Cook MD**
Oregon Health and Science University
Portland, Oregon

**Amany R Keruakous, MD, MS**
Georgia Cancer Center
Augusta University
Augusta, Georgia

**Ranju Gupta, MD**
Cancer Institute
Lehigh Valley Health Network
Bethlehem, Pennsylvania

**Khuda Dad Khan, MD, PhD**
Norton Cancer Institute
Prospect, Kentucky

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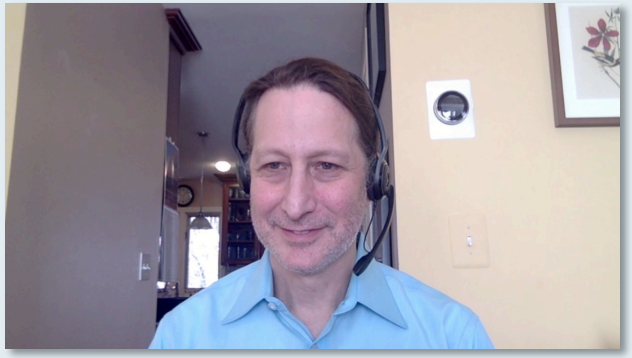

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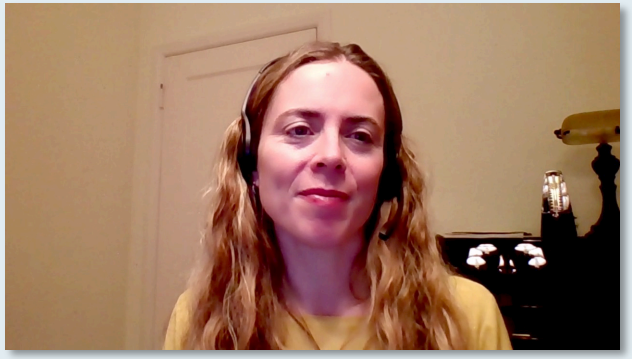
Atlantic Health System
Summit, New Jersey

**Erik Rupard, MD**
The Reading Hospital
West Reading, Pennsylvania



**Rebecca L Olin, MD, MSCE**
University of California, San Francisco
San Francisco, California

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# Meet The Professor with Dr Daver

**INTRODUCTION: Biology, Classification, p53, Magrolimab**

**MODULE 1: Case Presentations**

**MODULE 2: Journal Club with Dr Daver**

**MODULE 3: Appendix**

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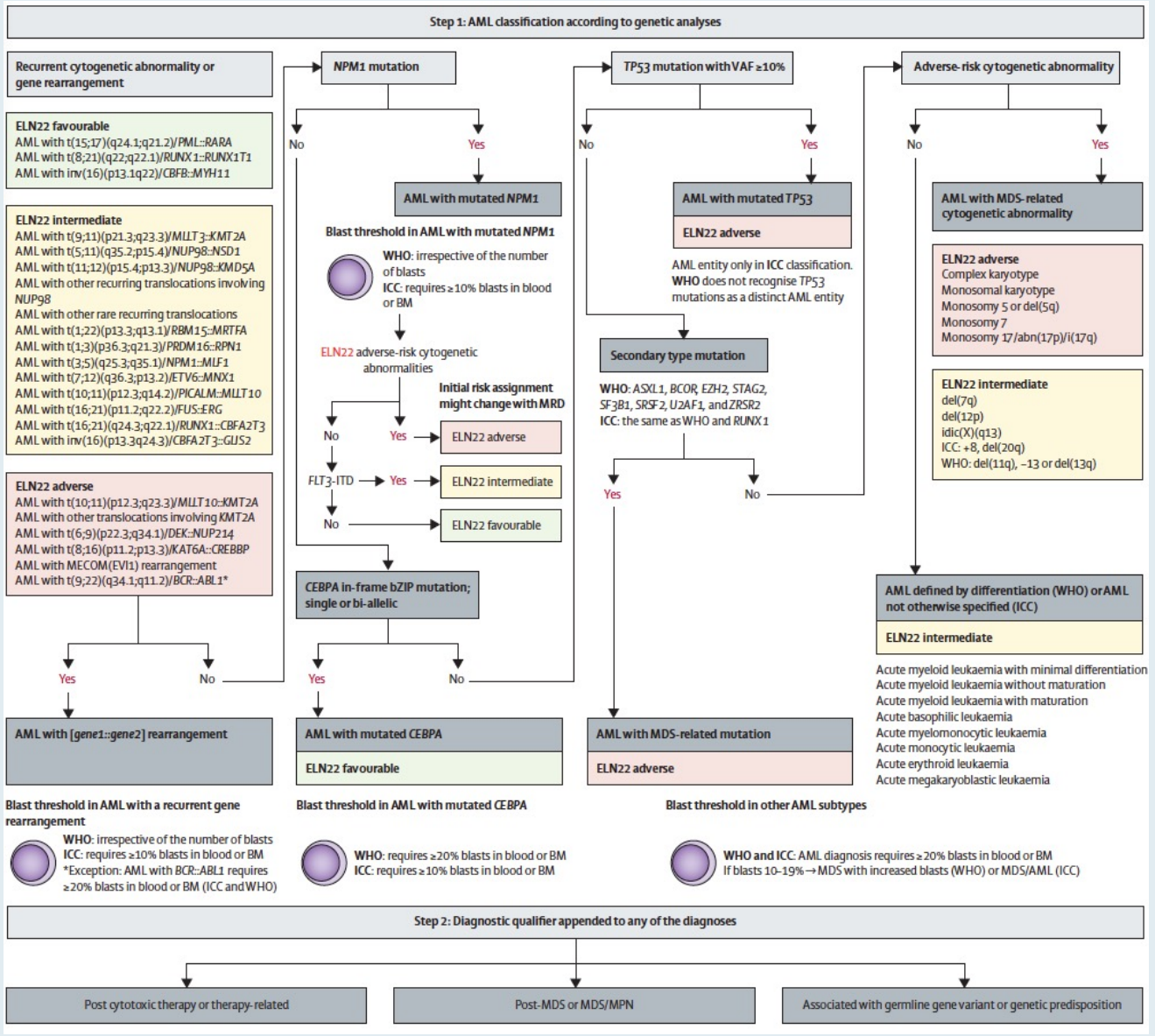
Viewpoint

# Standardising acute myeloid leukaemia classification systems: a perspective from a panel of international experts

*Rory M Shallis, Naval Daver, Jessica K Altman, Rami S Komrokji, Daniel A Pollyea, Talha Badar, Jan P Bewersdorf, Vijaya R Bhatt, Stéphane de Botton, Adolfo de la Fuente Burguera, Hetty E Carraway, Pinkal Desai, Richard Dillon, Nicolas Duployez, Firas El Chaer, Amir T Fathi, Sylvie D Freeman, Ivana Gojo, Michael R Grunwald, Brian A Jonas, Marina Konopleva, Tara L Lin, Gabriel N Mannis, John Mascarenhas, Laura C Michaelis, Alice S Mims, Pau Montesinos, Olga Pozdnyakova, Keith W Pratz, Andre C Schuh, Mikkael A Sekeres, Catherine C Smith, Maximilian Stahl, Marion Subklewe, Geoffrey L Uy, Maria Teresa Voso, Roland B Walter, Eunice S Wang, Joshua F Zeidner, Andrius Žučenka, Amer M Zeidan*

***Lancet Haematol* 2023;10(9):e767-76.**

# Current Unified Approach to the Classification of Acute Myeloid Leukemia




Shallis RM et al. *Lancet Haematol* 2023;10(9):e767-76.

Contents lists available at ScienceDirect

Blood Reviews

journal homepage: www.elsevier.com/locate/issn/0268960X

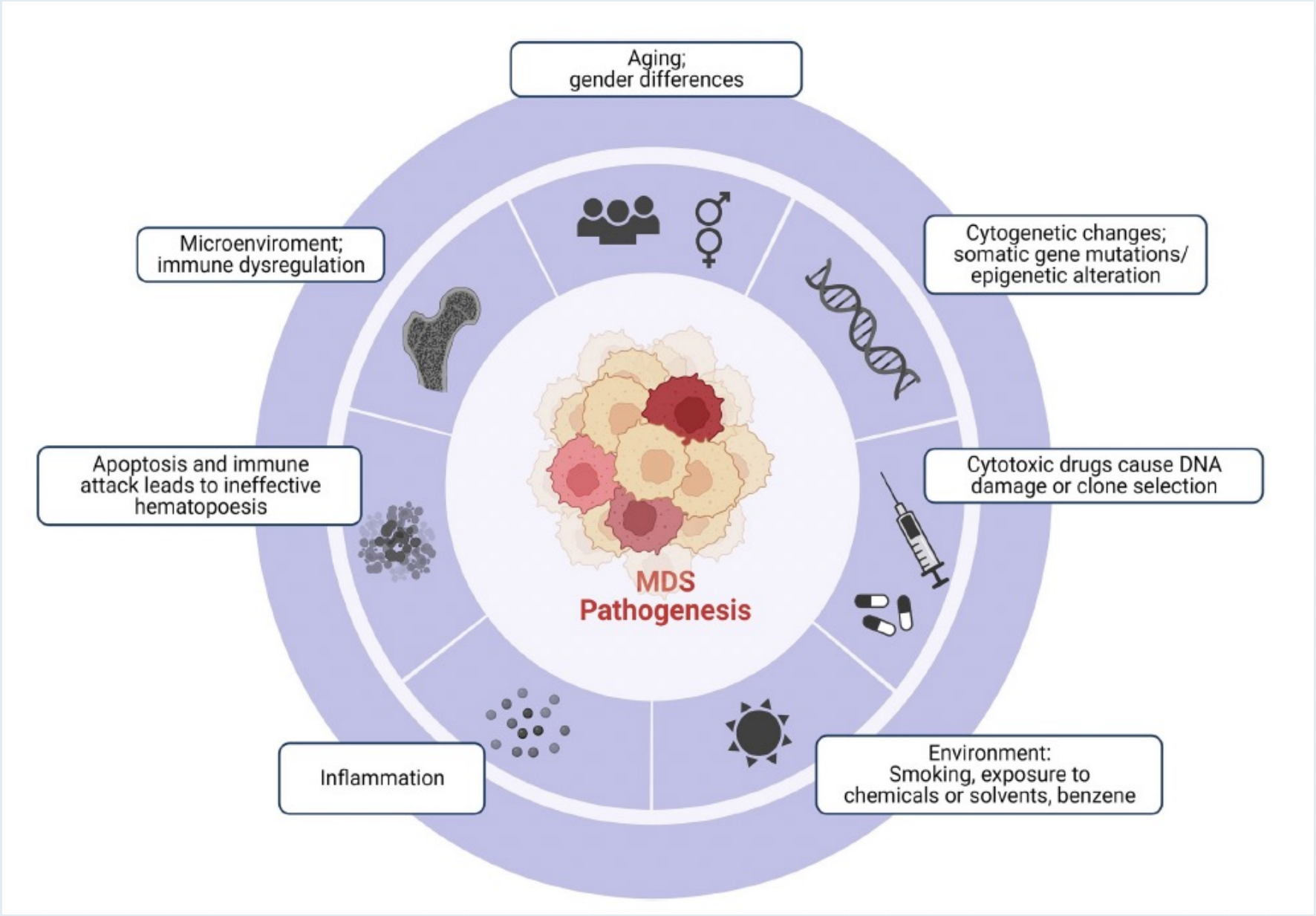
Review

# Current landscape of translational and clinical research in myelodysplastic syndromes/neoplasms (MDS): Proceedings from the 1st International Workshop on MDS (iwMDS) Of the International Consortium for MDS (icMDS)

Jan Philipp Bewersdorf[a], Zhuoer Xie[b], Rafael Bejar[c], Uma Borate[d], Jacqueline Boultwood[e], Andrew M. Brunner[f], Rena Buckstein[g], Hetty E. Carraway[h], Jane E. Churpek[i], Naval G. Daver[j], Matteo Giovanni Della Porta[k], Amy E. DeZern[l], Pierre Fenaux[m], Maria E. Figueroa[n], Steven D. Gore[o], Elizabeth A. Griffiths[p], Stephanie Halene[q], Robert P. Hasserjian[r], Christopher S. Hourigan[s], Tae Kon Kim[t], Rami Komrokji[b], Vijay K. Kuchroo[u], Alan F. List[v], Sanam Loghavi[w], Ravindra Majeti[x], Olatoyosi Odenike[y], Mrinal M. Patnaik[z], Uwe Platzbecker[aa], Gail J. Roboz[ab], David A. Sallman[b], Valeria Santini[ac], Guillermo Sanz[ad,ae,af], Mikkael A. Sekeres[n], Maximilian Stahl[ag], Daniel T. Starczynowski[ah], David P. Steensma[ai], Justin Taylor[n], Omar Abdel-Wahab[a], Mina L. Xu[aj], Michael R. Savona[t], Andrew H. Wei[ak], Amer M. Zeidan[q,*]

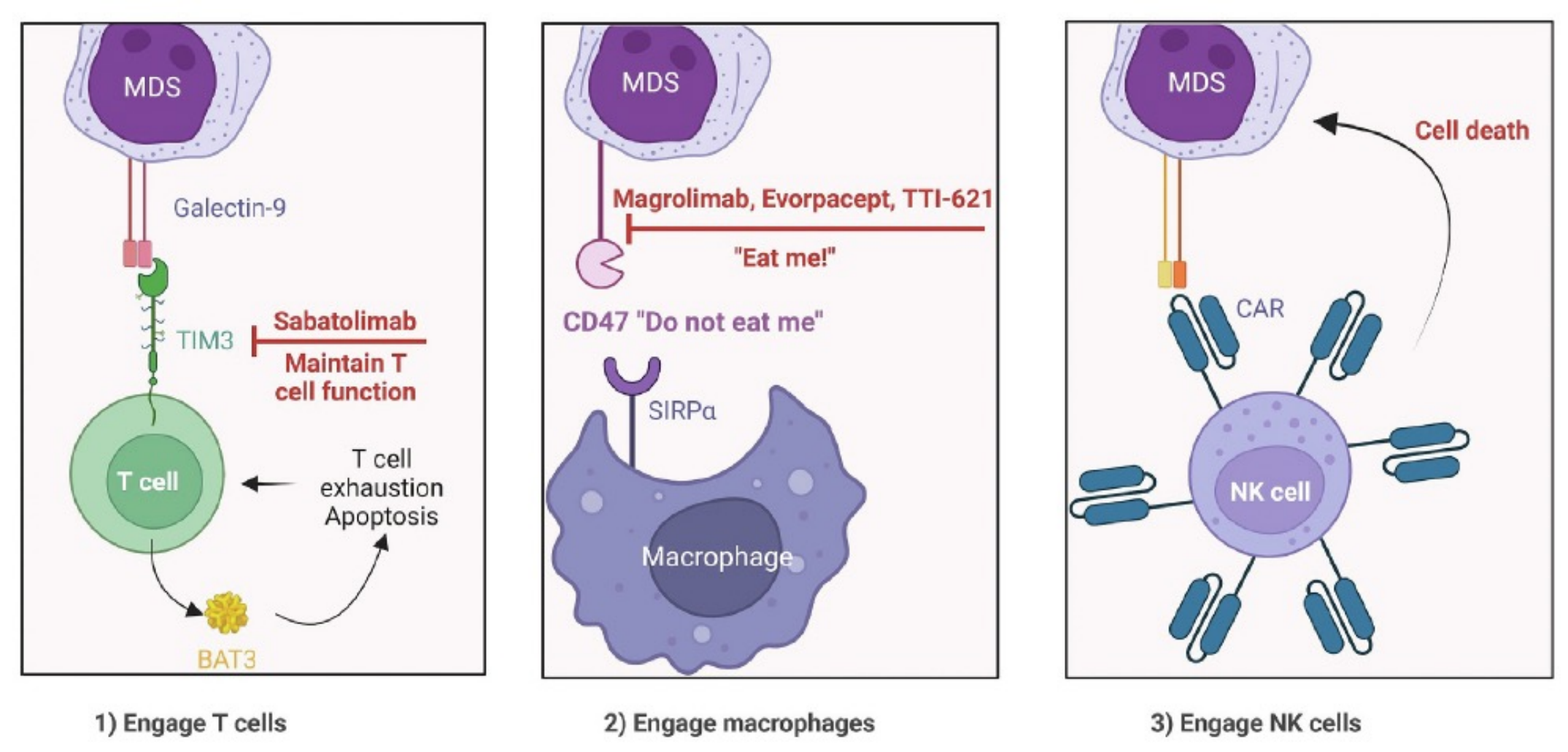
*Blood Rev* 2023;60:101072

# Overview of Myelodysplastic Syndromes Pathophysiology



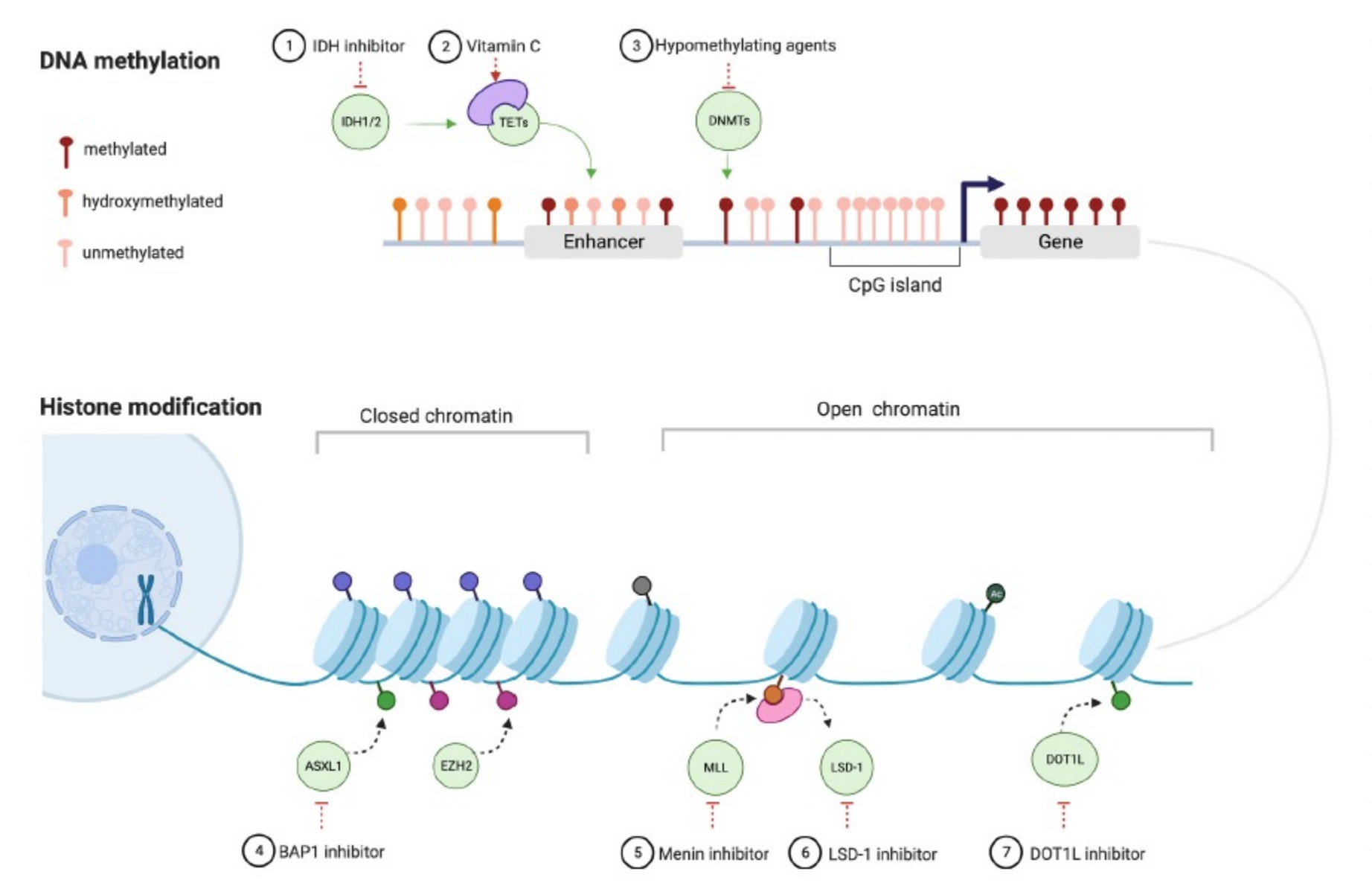

Bewersdorf JP et al. *Blood Rev* 2023;60:101072.

# Novel Immunotherapy Targets for Myelodysplastic Syndromes (MDS)




Bewersdorf JP et al. *Blood Rev* 2023;60:101072.

# Epigenetic Therapeutics for MDS




Bewersdorf JP et al. *Blood Rev* 2023;60:101072.

# Case Presentation: 70-year-old man with TP53-mutant AML-MRC with complex cytogenetics, s/p CPX-351; azacitidine/ venetoclax, now in palliative care

Dr Anna Halpern (Seattle, Washington)

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REVIEW

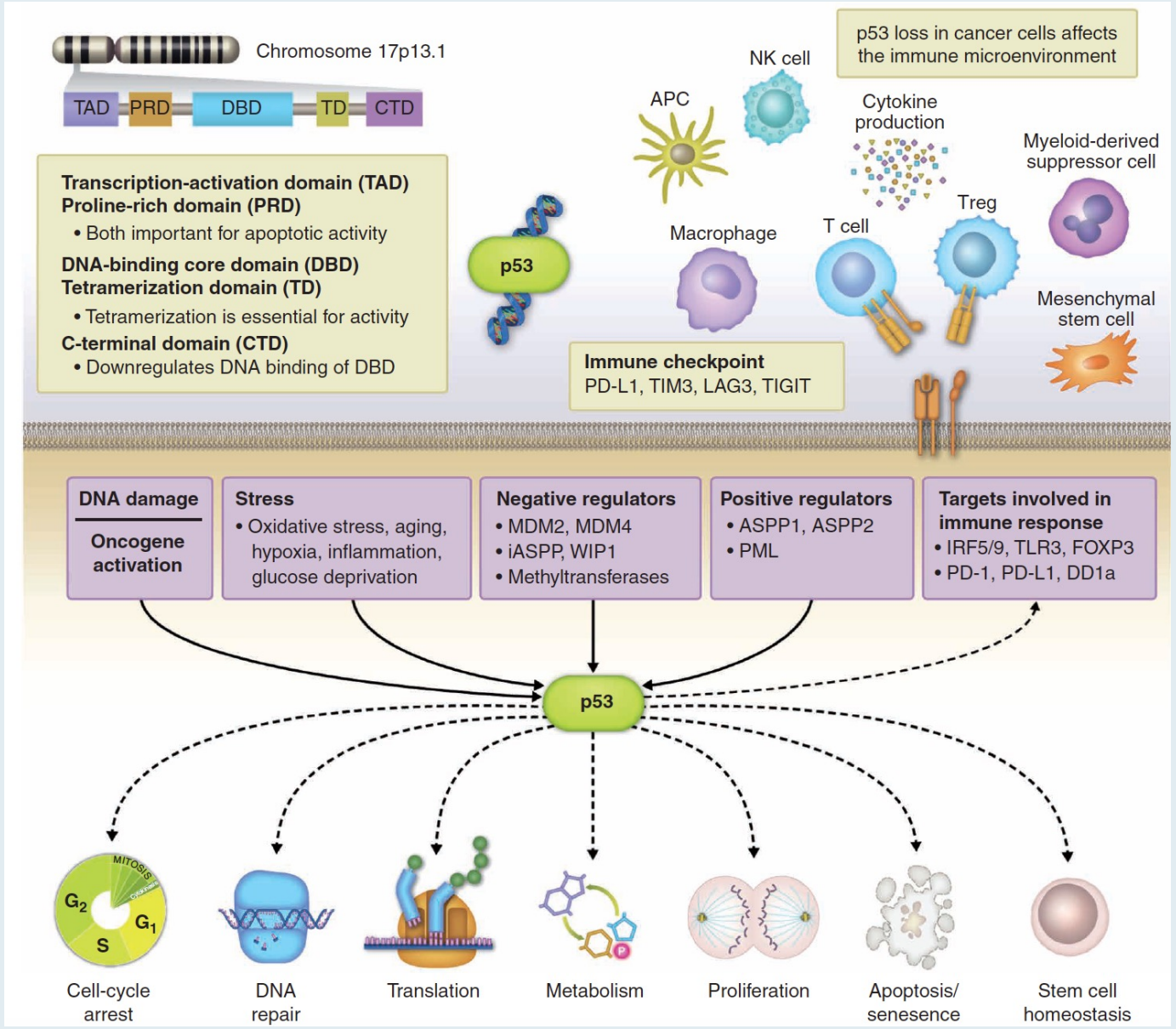
# *TP53*-Mutated Myelodysplastic Syndrome and Acute Myeloid Leukemia: Biology, Current Therapy, and Future Directions

Naval G. Daver[1], Abhishek Maiti[1], Tapan M. Kadia[1], Paresh Vyas[2], Ravindra Majeti[3], Andrew H. Wei[4], Guillermo Garcia-Manero[1], Charles Craddock[5], David A. Sallman[6], and Hagop M. Kantarjian[1]

*Cancer Discov* 2022;12(11):2516-29.

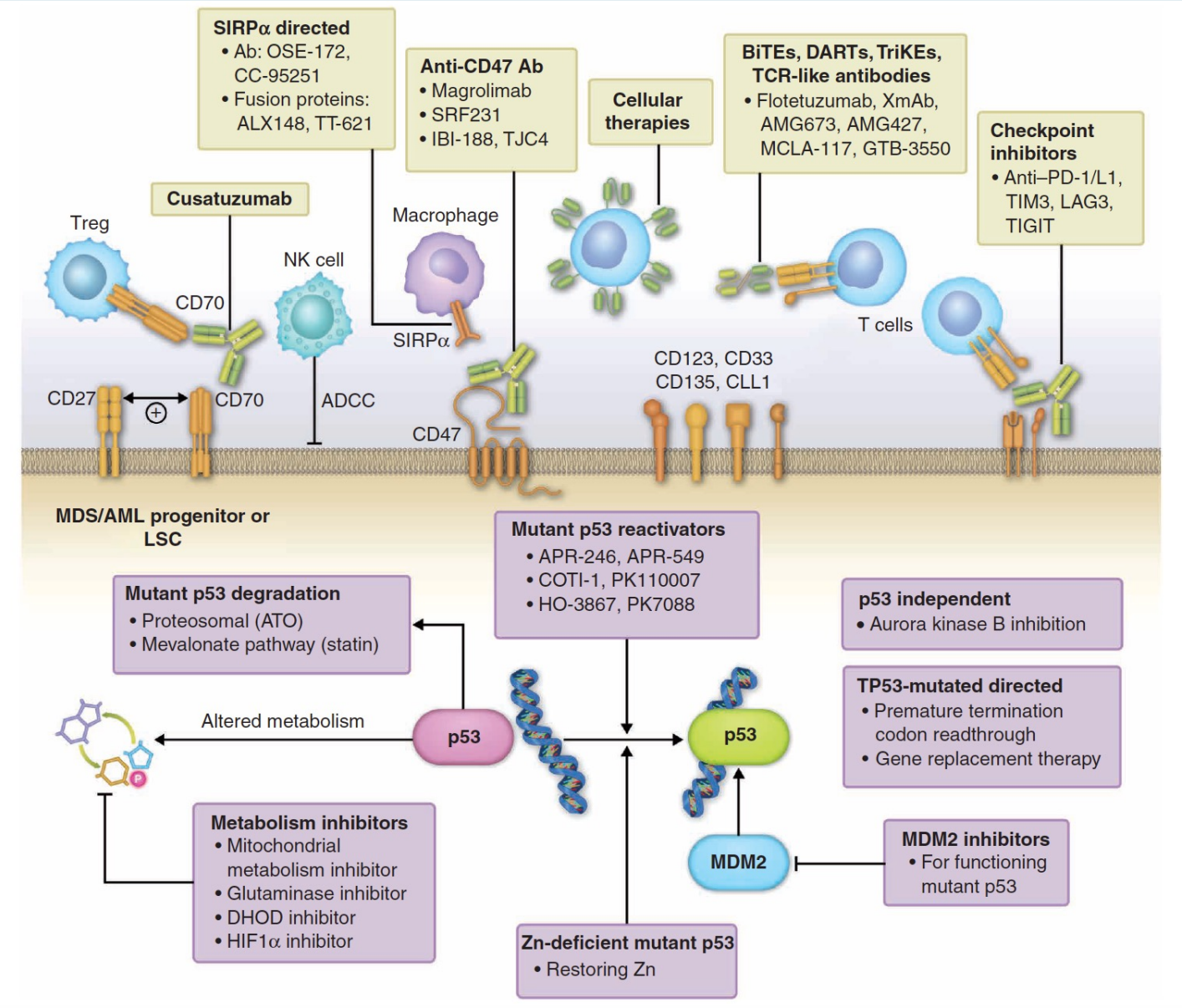
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

# p53 Signaling Pathways



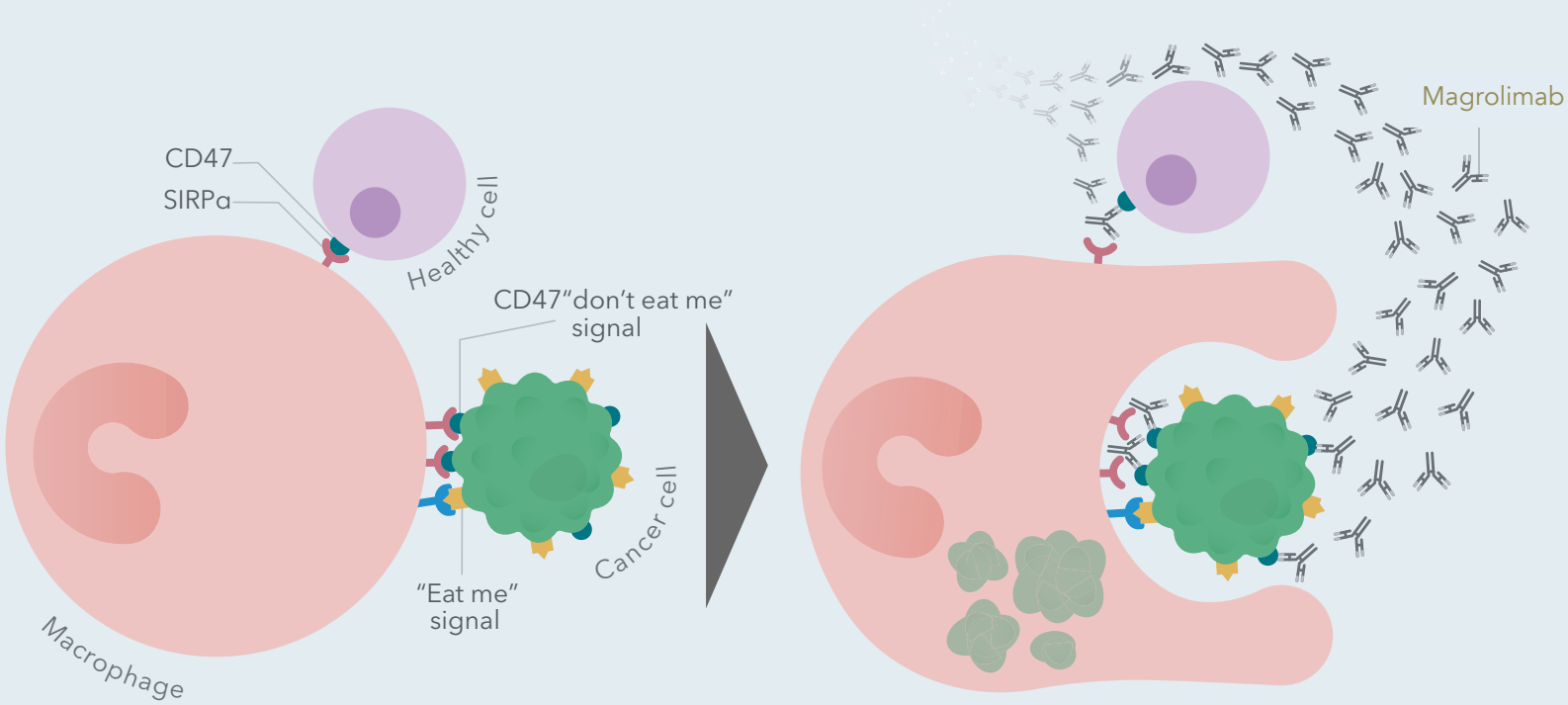

Daver NG et al. *Cancer Discov* 2022;12(11):2516-29.

# Novel Therapies for TP53-Mutated MDS and AML

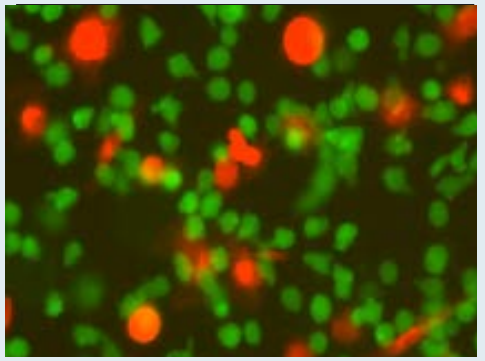



Daver NG et al. *Cancer Discov* 2022;12(11):2516-29.

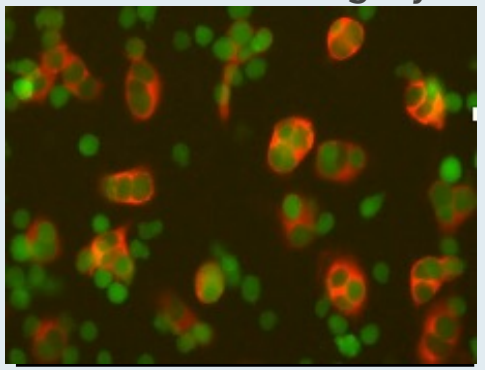
# Magrolimab Is a Macrophage Immune Checkpoint Inhibitor Targeting CD47




Control mAb: No Phagocytosis



Anti-CD47 mAb: Phagocytosis



Macrophages Cancer cells

- Magrolimab is an IgG4 anti-CD47 monoclonal antibody (mAb) that eliminates tumor cells through macrophage phagocytosis
- Magrolimab is being investigated for multiple cancers with >500 patients dosed

Sallman D et al. ASCO 2020;Abstract 7507.

Content Courtesy of Michael R Savona, MD

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# FDA Places Partial Clinical Hold on Magrolimab for AML

## Press Release: August 21, 2023

"[T]he US Food and Drug Administration (FDA) has placed a partial clinical hold on the initiation of new patients in US studies evaluating magrolimab to treat acute myeloid leukemia (AML).

The FDA action follows the previously announced discontinuation of the Phase 3 ENHANCE study of magrolimab in higher-risk myelodysplastic syndromes (HR-MDS).

Effective immediately, screening and enrollment of new study participants under the US investigational new drug application (IND 147229) and US Expanded Access Program will be paused. Patients already enrolled in AML clinical studies may continue to receive treatment and be monitored, according to the current study protocol. Global regulatory authorities and clinical trial investigators involved in the studies have been informed of the FDA's decision. Studies of magrolimab in solid tumors continue without any impact from the FDA action."

https://www.gilead.com/news-and-press/press-room/press-releases/2023/8/gilead-announces-partial-clinical-hold-for-magrolimab-studies-in-aml

# Discontinuation of the Phase III ENHANCE Trial of Magrolimab with Azacitidine for Higher-Risk MDS

## Press Release: July 21, 2023

"[T]he Phase 3 ENHANCE study in higher-risk myelodysplastic syndromes (MDS) has been discontinued due to futility based on a planned analysis. The safety data seen in this study is consistent with the known magrolimab profile and adverse events that are typical in this patient population. Gilead recommends discontinuing treatment with magrolimab in patients with MDS."

https://www.gilead.com/news-and-press/press-room/press-releases/2023/7/gilead-to-discontinue-phase-3-enhance-study-of-magrolimab-plus-azacitidine-in-higher-risk-mds

# Meet The Professor with Dr Daver

## INTRODUCTION

## MODULE 1: Case Presentations

- Dr Bhatnagar: 59-year-old woman with multiple comorbidities and FLT3-ITD-positive AML s/p PD on azacitidine/venetoclax, now on gilteritinib
- Dr Keruakous: 70-year-old woman with FLT3-ITD- and IDH1-mutant AML receives an HMA with ivosidenib
- Dr Khan: 61-year-old man with newly diagnosed MDS-RS receives oral decitabine/cedazuridine
- Dr Cook: 66-year-old man presents with copper deficiency and ringed sideroblasts; genetic analysis reveals SF3B1 and DNMT3A mutations
- Dr Gupta: 71-year-old woman with PMH of extensively treated follicular lymphoma develops AML and receives CPX-351
- Dr Olin: 78-year-old woman with newly diagnosed AML receives decitabine/venetoclax with concurrent voriconazole
- Dr Rupard: 97-year-old woman is diagnosed with multiple myeloma and del(5q) MDS
- Dr Morganstein: 70-year-old woman with low-grade MDS-RS receives luspatercept

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# Case Presentation: 59-year-old woman with multiple comorbidities and FLT3-ITD-positive AML s/p PD on azacitidine/venetoclax, now on gilteritinib

Dr Tina Bhatnagar (Wheeling, West Virginia)

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# FDA Approves Quizartinib for Newly Diagnosed AML

## Press Release: July 20, 2023

"On July 20, 2023, the Food and Drug Administration approved quizartinib with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive, as detected by an FDA-approved test.

FDA also approved LeukoStrat CDx FLT3 Mutation Assay as a companion diagnostic for quizartinib.

Efficacy of quizartinib with chemotherapy was evaluated in QuANTUM-First (NCT02668653), a randomized, double-blind, placebo-controlled trial of 539 patients with newly diagnosed FLT3-ITD positive AML. FLT3-ITD status was determined prospectively with a clinical trial assay and verified retrospectively with the companion diagnostic LeukoStrat CDx FLT3 Mutation Assay."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-quizartinib-newly-diagnosed-acute-myeloid-leukemia

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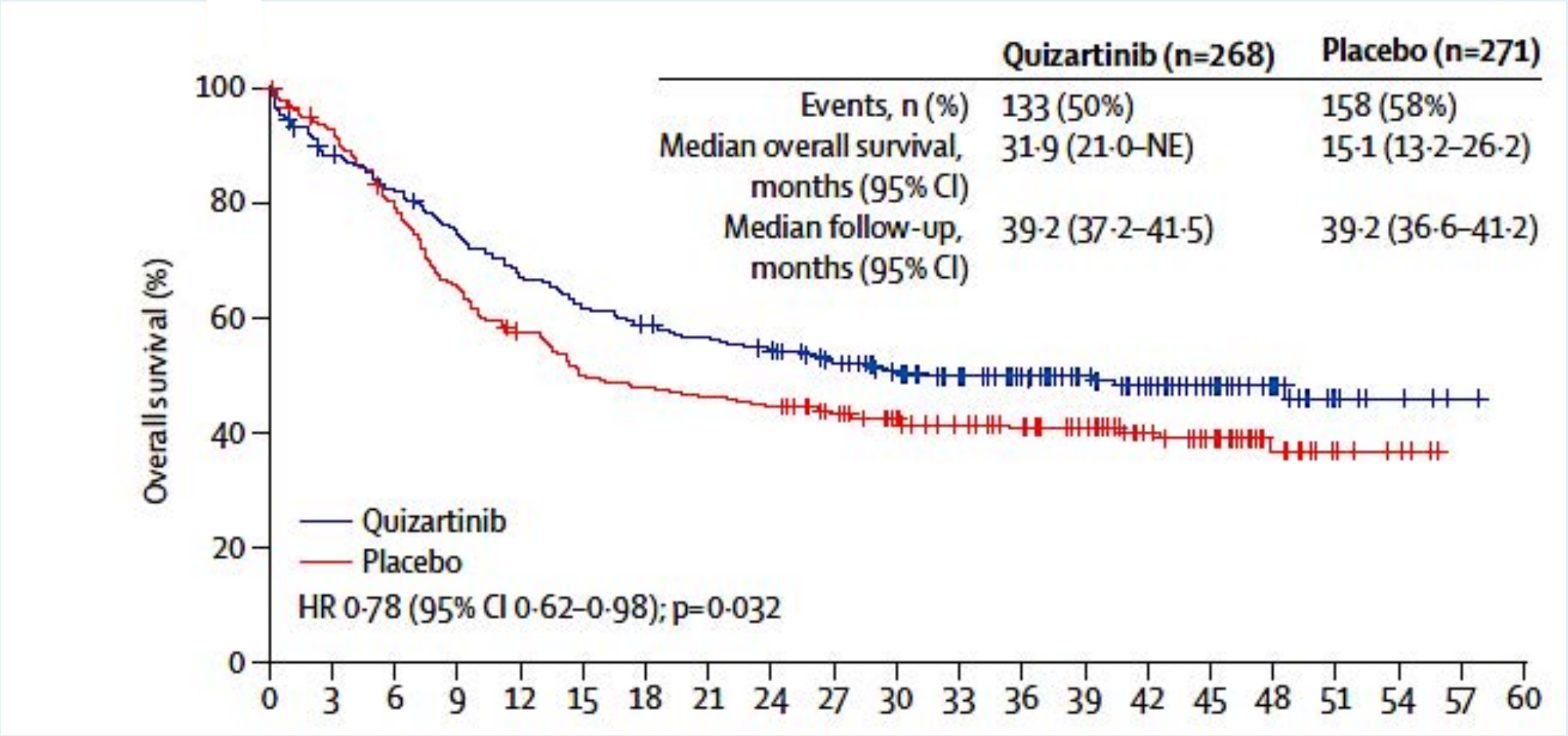
*Lancet* 2023;401:1571-83

Articles

# Quizartinib plus chemotherapy in newly diagnosed patients with *FLT3*-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial

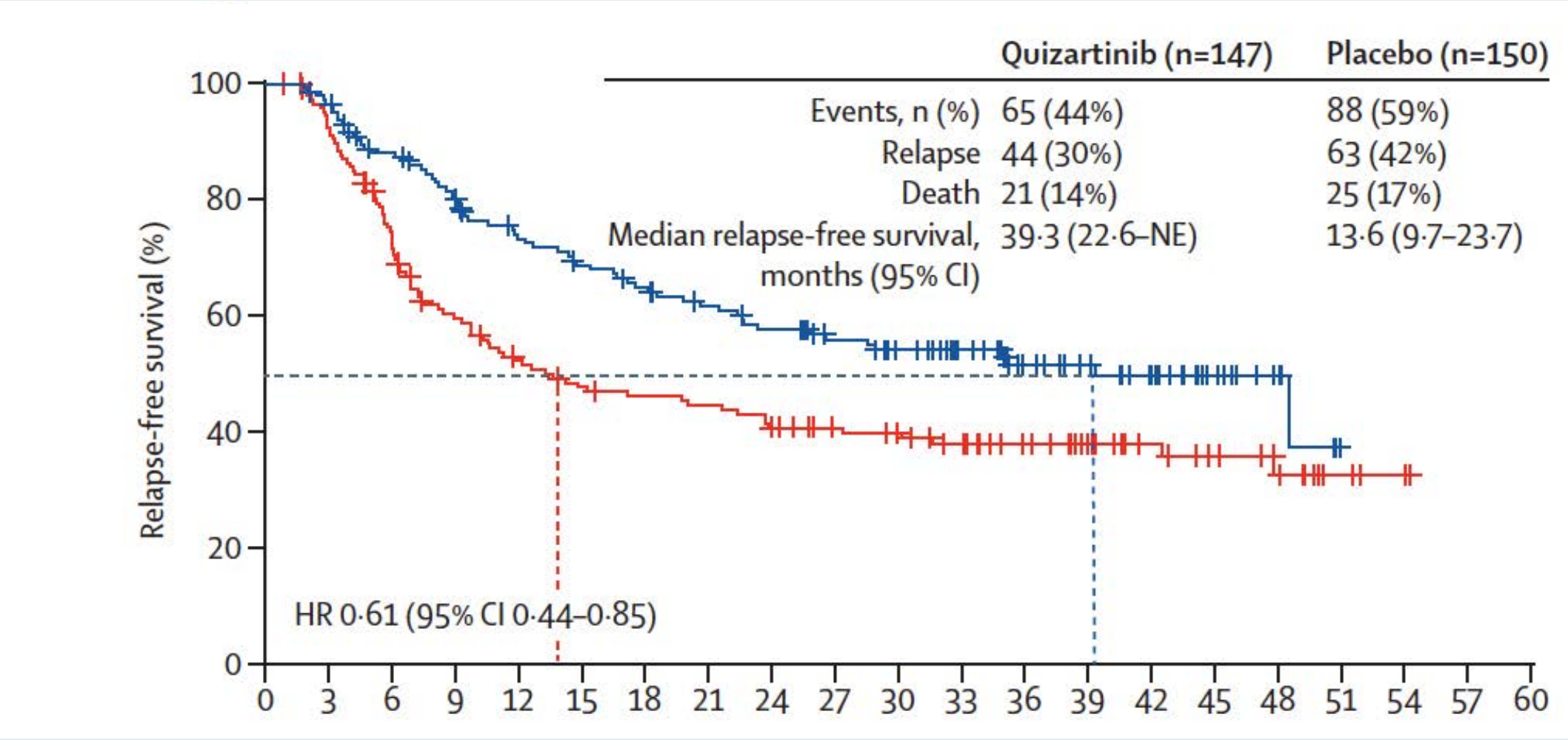
*Harry P Erba, Pau Montesinos, Hee-Je Kim, Elżbieta Patkowska, Radovan Vrhovac, Pavel Žák, Po-Nan Wang, Tsvetomir Mitov, James Hanyok, Yasser Mostafa Kamel, Jaime E Connolly Rohrbach, Li Liu, Aziz Benzohra, Arnaud Lesegretain, Jorge Cortes, Alexander E Perl, Mikkael A Sekeres, Hervé Dombret, Sergio Amadori, Jianxiang Wang, Mark J Levis, Richard F Schlenk, on behalf of the QuANTUM-First Study Group*

# QuANTUM-First: Overall Survival with Quizartinib in Combination with Chemotherapy



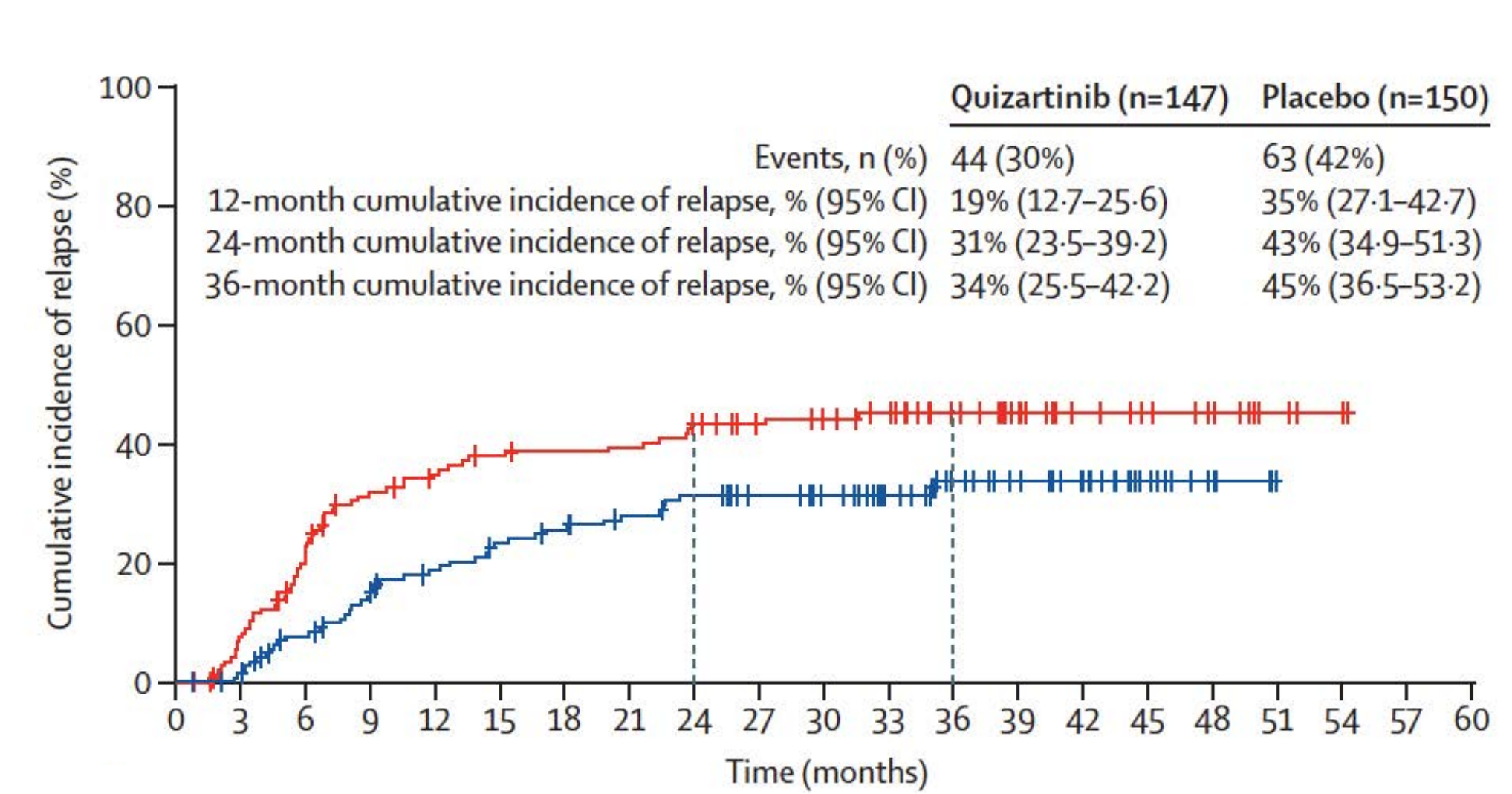

Erba HP et al. *Lancet* 2023;401:1571-83.

# QuANTUM-First: Relapse-Free Survival with Quizartinib in Combination with Chemotherapy




Erba HP et al. *Lancet* 2023;401:1571-83.

# QuANTUM-First: Cumulative Incidence of Relapse with Quizartinib in Combination with Chemotherapy




Erba HP et al. *Lancet* 2023;401:1571-83.

# Impact of Allogeneic Hematopoietic Cell Transplantation in First Complete Remission plus FLT3 Inhibition with Quizartinib in Acute Myeloid Leukemia with FLT3-ITD: Results from QuANTUM-First

Schlenk R F et al.

EHA 2023;Abstract S137

# A Randomised Assessment of the Sequential Addition of the Kinase Inhibitor Quizartinib to Intensive Chemotherapy in Older Acute Myeloid Leukaemia (AML) Patients: Results from the NCRI AML18 Trial

Knapper S et al.

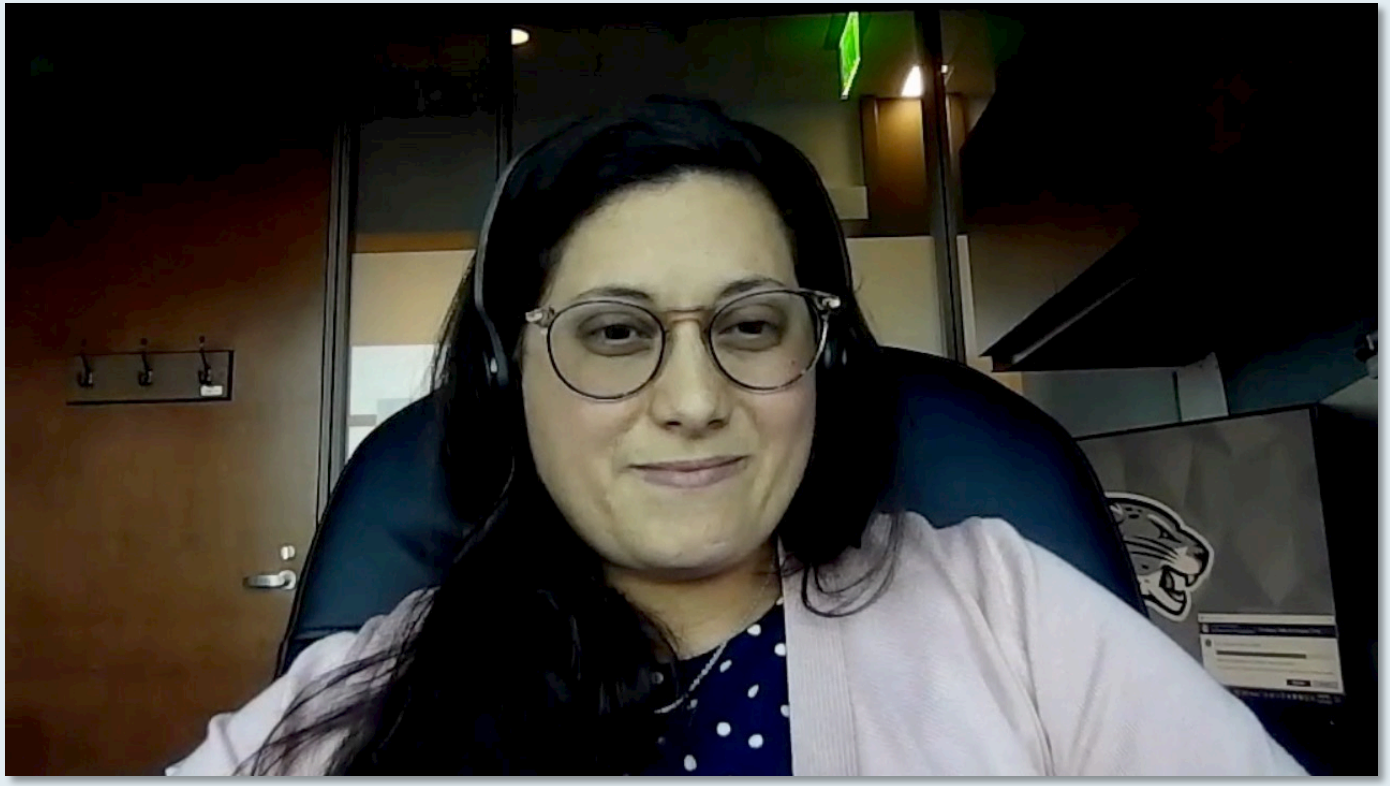
EHA 2023;Abstract S131.

# Updated Results of VEN-A-QUI Study: A Phase 1-2 Trial to Assess the Safety and Efficacy of Triplets for Newly Diagnosed Unfit AML Patients: Azacitidine or Low-Dose Cytarabine with Venetoclax and Quizartinib

Burgues MB et al.

EHA 2023;Abstract S132.

# Case Presentation: 70-year-old woman with FLT3-ITD- and IDH1-mutant AML receives an HMA with ivosidenib



Dr Amany Keruakous (Augusta, Georgia)

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# Case Presentation: 61-year-old man with newly diagnosed MDS-RS receives oral decitabine/cedazuridine

**Dr Khuda Khan (Prospect, Kentucky)**

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# Pharmacokinetic Exposure Equivalence and Preliminary Efficacy and Safety from a Randomized Crossover Phase 3 Study of an Oral Hypomethylating Agent, ASTX727 (DEC-C), Compared to IV Decitabine

Geissler K et al.

EHA 2022;Abstract P573.

# ASCERTAIN (ASTX727-02) Trial AML Cohort: Preliminary Efficacy Response

| Response category | All Treated Subjects (N=87) n (%) | 95% CI |
|---|---|---|
| Complete response (CR) | 19 (21.8) | (13.7, 32.0) |
| CR with incomplete blood count recovery (CRi) | 5 (5.7) | (1.9, 12.9) |
| CR with incomplete platelet recovery (CRp) | 2 (2.3) | (0.3, 8.1) |
| Partial response (PR) | 4 (4.6) | (1.3, 11.4) |
| Stable disease | 33 (37.9) | (27.7, 49.0) |
| Not Evaluable (NE)* | 26 (29.9) | (20.5, 40.6) |
| Composite Response (CR + CRi + PR) | 28 (32.2) | (22.6, 43.1) |

* Subjects who did not have a valid post-treatment efficacy assessment (ie, no post-treatment BM/PB sample or the quality of BM/PB sample was not adequate for an assessment of efficacy) were classified as NE for response classification.

- Median CR duration was 5.8 months
- Median time to best response was 3.4 months
- 38% of the 37 subjects who were RBC transfusion dependent at baseline were RBC transfusion independent for any consecutive ≥56-day period post-baseline

Geissler K et al. EHA 2022;Abstract P573.

# ASCERTAIN (ASTX727-02) AML Cohort: Treatment-Emergent Adverse Events in >5% of Patients

| Preferred Term | Phase 3 Total (N=87, n[%]) | Phase 3 Total Grade 3 or higher |
|---|---|---|
| Thrombocytopenia | 22 (25.3) | 20 (23.0) |
| Neutropenia | 14 (16.1) | 14 (16.1) |
| Anemia | 14 (16.1) | 12 (13.8) |
| Febrile neutropenia | 10 (11.5) | 10 (11.5) |
| Nausea | 9 (10.3) | 0 |
| Constipation | 6 (6.9) | 0 |
| Asthenia | 6 (6.9) | 4 (4.6) |
| Decreased Appetite | 6 (6.9) | 0 |
| Diarrhea | 5 (5.7) | 0 |

*Events attributed to oral decitabine/cedazuridine

- Safety profile consistent with that of decitabine
- Most grade 3 or higher events related to myelosuppression
- GI system adverse events following ASTX727 were generally grade 1-2

Geissler K et al. EHA 2022;Abstract P573.

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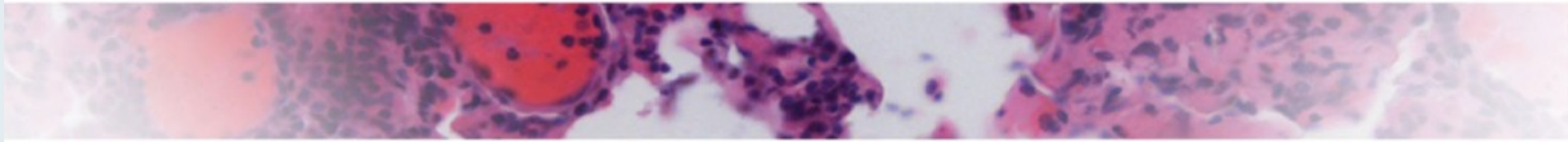
2022;Abstract 461



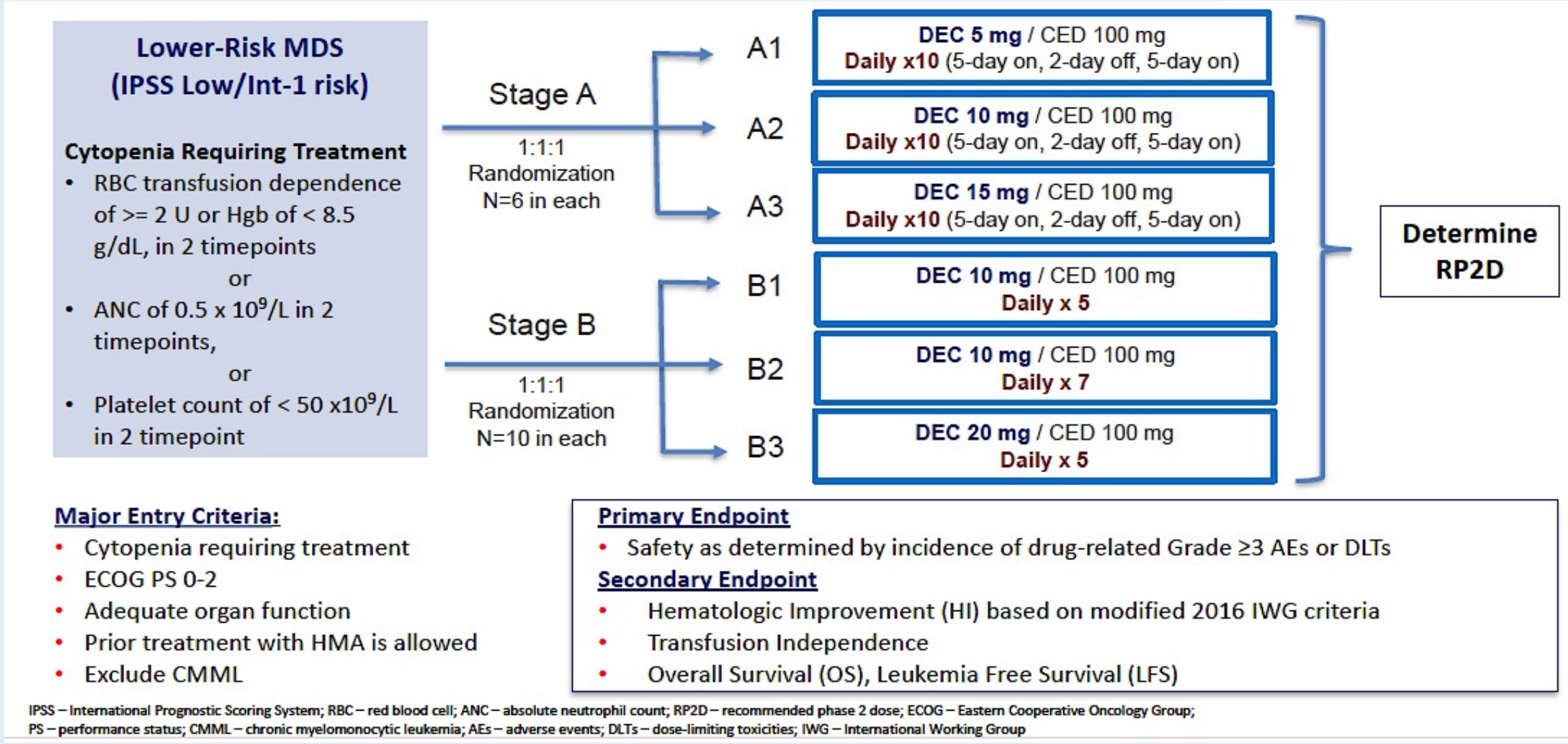
# ASTX727-03: Phase 1 Study Evaluating Oral Decitabine/Cedazuridine (ASTX727) Low-Dose (LD) in Lower-Risk Myelodysplastic Syndromes (LR-MDS) Patients

**On behalf of the ASTX727-03 Investigators Team**

Guillermo Garcia-Manero[1], Kimo Bachiashvili[2], Harshad Amin[3], Elie Traer[4], Daniel A. Pollyea[5], David Sallman[6], Aref Al-Kali[7], Larry Cripe[8], Jesus Berdeja[9], Elizabeth A. Griffiths[10], Sanjay Mohan[11], Yuri Sano[12], Aram Oganesian[12], Harold Keer[12], Abdulraheem Yacoub[13]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL; [3]Boca Raton Cancer Research, Boca Raton, FL; [4]Oregon Health and Science University, Portland, OR; [5]University of Colorado Cancer Center, Denver, CO; [6]Moffitt Cancer Center, Tampa, FL; [7]Mayo Clinic, Rochester, Rochester, MN; [8]Indiana University Health, Indianapolis, IN; [9]Sarah Cannon Research Institute, Nashville, TN; [10]Roswell Park Comprehensive Cancer Center, New York, NY; [11]Vanderbilt-Ingram Cancer Center, Nashville, TN; [12]Astex Pharmaceuticals, Inc., Pleasanton, CA; [13]The University of Kansas Clinical Cancer Research Center

# ASTX727-03: Phase I Study Design




**Major Entry Criteria:**

- Cytopenia requiring treatment
- ECOG PS 0-2
- Adequate organ function
- Prior treatment with HMA is allowed
- Exclude CMML

**Primary Endpoint**

- Safety as determined by incidence of drug-related Grade ≥3 AEs or DLTs

**Secondary Endpoint**

- Hematologic Improvement (HI) based on modified 2016 IWG criteria
- Transfusion Independence
- Overall Survival (OS), Leukemia Free Survival (LFS)

IPSS – International Prognostic Scoring System; RBC – red blood cell; ANC – absolute neutrophil count; RP2D – recommended phase 2 dose; ECOG – Eastern Cooperative Oncology Group; PS – performance status; CMML – chronic myelomonocytic leukemia; AEs – adverse events; DLTs – dose-limiting toxicities; IWG – International Working Group

Garcia-Manero G et al. ASH 2022;Abstract 461.

# ASTX727-03: Treatment-Emergent Adverse Events with Oral Decitabine/Cedazuridine

| Preferred Term | Cohort A1 5mg 10-day (N=10) | Cohort A2 10mg 10-day (N=4) | Cohort B1 10mg 5-day (N=11) | Cohort B2 10mg 7-day (N=11) | Cohort B3 20mg 5-day (N=11) | Total (N=47) |
|---|---|---|---|---|---|---|
| **Subjects with any AE** | 10 (100) | 4 (100) | 11 (100) | 11 (100) | 11 (100) | 47 (100) |
| **Total number of AEs** | 162 | 54 | 290 | 265 | 317 | 1093 |
| Fatigue | 6 (60.0) | 2 (50.0) | 4 (36.4) | 5 (45.5) | 4 (36.4) | 21 (44.7) |
| Neutropenia | 3 (30.0) | 3 (75.0) | 5 (45.5) | 5 (45.5) | 3 (27.3) | 19 (40.4) |
| Neutrophil count decreased | 1 (10.0) | 2 (50.0) | 2 (18.2) | 5 (45.5) | 8 (72.7) | 18 (38.3) |
| Anaemia | 1 (10.0) | 2 (50.0) | 5 (45.5) | 3 (27.3) | 5 (45.5) | 16 (34.0) |
| Constipation | 2 (20.0) | 1 (25.0) | 3 (27.3) | 6 (54.5) | 4 (36.4) | 16 (34.0) |
| Diarrhoea | 1 (10.0) | 1 (25.0) | 3 (27.3) | 3 (27.3) | 5 (45.5) | 13 (27.7) |
| Decreased appetite | 0 | 2 (50.0) | 3 (27.3) | 4 (36.4) | 3 (27.3) | 12 (25.5) |
| Cough | 2 (20.0) | 3 (75.0) | 3 (27.3) | 1 (9.1) | 3 (27.3) | 12 (25.5) |
| Pyrexia | 3 (30.0) | 1 (25.0) | 4 (36.4) | 2 (18.2) | 1 (9.1) | 11 (23.4) |
| Platelet count decreased | 2 (20.0) | 0 | 3 (27.3) | 3 (27.3) | 3 (27.3) | 11 (23.4) |
| Oedema peripheral | 2 (20.0) | 1 (25.0) | 4 (36.4) | 1 (9.1) | 3 (27.3) | 11 (23.4) |
| Dyspnoea | 0 | 2 (50.0) | 4 (36.4) | 2 (18.2) | 2 (18.2) | 10 (21.3) |

- Safety profile consistent with that of standard (approved) DEC-C dosing
- No significant safety differences between the cohorts, with the exception of increase of AE frequency of decreased neutrophil counts observed in regiments with higher DEC doses per cycle (A2, B2, & B3)
- No clinically significant incidence of GI events at all the investigated doses were attributed to oral DEC-C

Garcia-Manero G et al. ASH 2022;Abstract 461.

EHA 2023;Abstract S172

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
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# Phase 1/2 study of oral decitabine/cedazuridine in combination with venetoclax in treatment-naïve higher-risk myelodysplastic syndromes or chronic myelomonocytic leukemia

Alex Bataller, Guillermo Montalban-Bravo, Alexandre Bazinet, Yesid Alvarado, Kelly Chien, Sangeetha Venugopal, Jo Ishizawa, Danielle Hammond, Mahesh Swaminathan, Koji Sasaki, Ghayas C. Issa, Nicholas J. Short, Lucia Masarova, Naval G. Daver, Tapan M. Kadia, Simona Colla, Wei Qiao, Xuelin Huang, Rashmi Kanagal-Shamanna, Stephany Hendrickson, Farhad Ravandi, Elias Jabbour, Hagop Kantarjian, Guillermo Garcia-Manero

Leukemia Department, The University of Texas MD Anderson Cancer Center, Houston (TX, USA)

June 10th 2023
s424 Clinical updates in MDS

## Conclusions

- Combination of oral decitabine with venetoclax is a tolerable totally oral treatment for HR-MDS and CMML
- Oral decitabine/cedazuridine with venetoclax is an active combination, achieving an ORR of 95%, with a CR rate of 36% and a mCR of 59%
- Up to 49% of patients with HR-MDS and CMML could undergo HSCT after achieving response with this combination
- Definitive conclusions regarding the benefit of venetoclax with HMA in HR-MDS await completion of the phase 3 randomized trial VERONA (NCT04401748)



Bataller Aet al. EHA 2023;Abstract S172.

# Case Presentation: 66-year-old man presents with copper deficiency and ringed sideroblasts; genetic analysis reveals SF3B1 and DNMT3A mutations

Dr Rachel Cook (Portland, Oregon)

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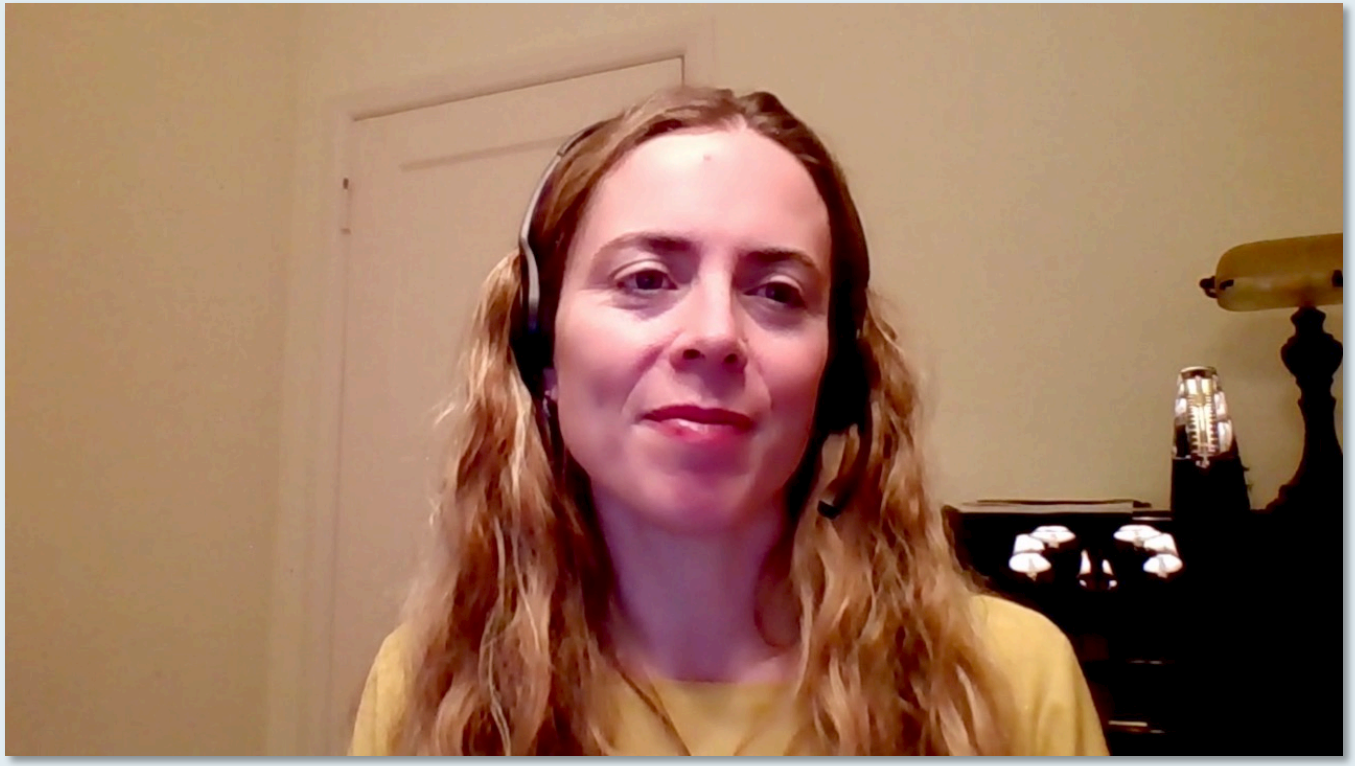
# Case Presentation: 71-year-old woman with PMH of extensively treated follicular lymphoma develops AML and receives CPX-351

Dr Ranju Gupta (Bethlehem, Pennsylvania)

# Case Presentation: 78-year-old woman with newly diagnosed AML receives decitabine/venetoclax with concurrent voriconazole



Dr Rebecca Olin (San Francisco, California)

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# Case Presentation: 97-year-old woman is diagnosed with multiple myeloma and del(5q) MDS

Dr Erik Rupard (West Reading, Pennsylvania)

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# Case Presentation: 70-year-old woman with low-grade MDS-RS receives luspatercept

**Dr Neil Morganstein (Summit, New Jersey)**

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# Meet The Professor with Dr Daver

**INTRODUCTION: Biology, Classification, p53, Magrolimab**

**MODULE 1: Case Presentations**

**MODULE 2: Journal Club with Dr Daver**

**MODULE 3: Appendix**

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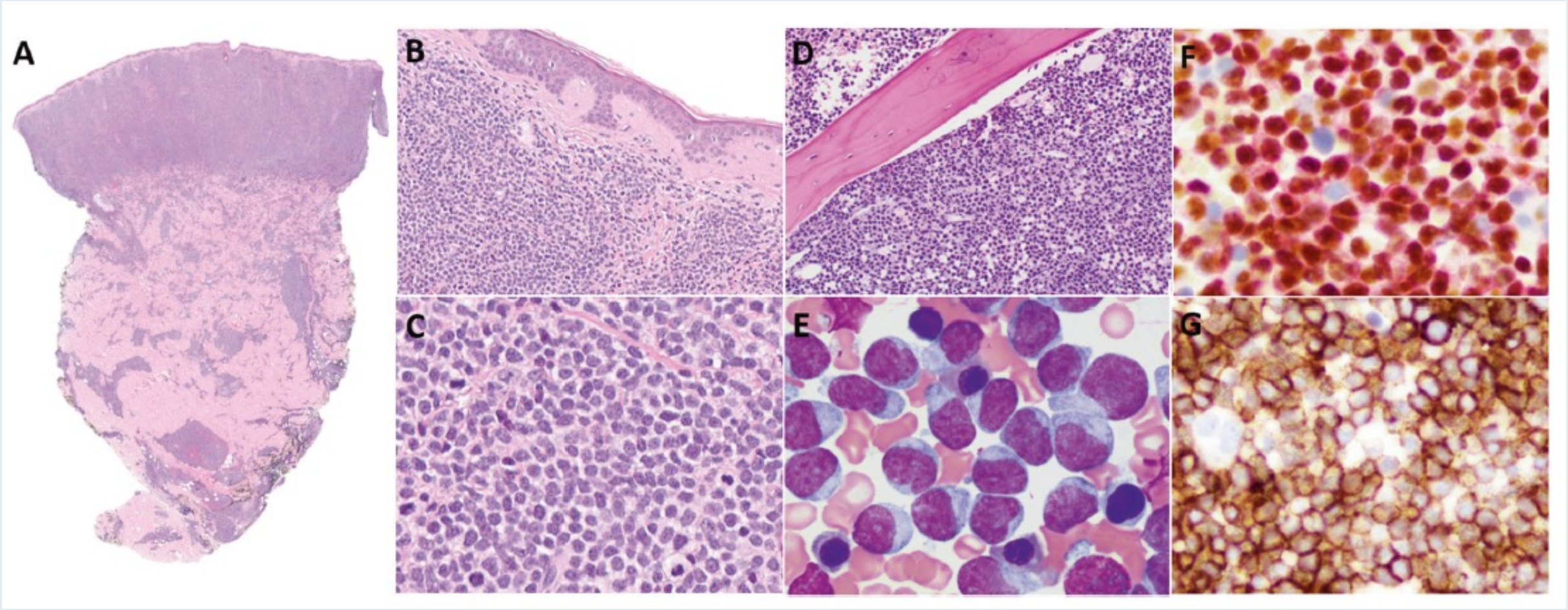
# Blastic plasmacytoid dendritic cell neoplasm: a comprehensive review in pediatrics, adolescents, and young adults (AYA) and an update of novel therapies

Branko Cuglievan[1,14]✉, Jeremy Connors[1,14], Jiasen He[1], Sajad Khazal[2], Sireesha Yedururi[3], Julia Dai[4], Sofia Garces[5], Andres E. Quesada[5], Michael Roth[1], Miriam Garcia[1], David McCall[1], Amber Gibson[1], Dristhi Ragoonanan[2], Demetrios Petropoulos[2], Priti Tewari[2], Cesar Nunez[1], Kris M. Mahadeo[6], Sarah K. Tasian[7], Adam J. Lamble[8], Anna Pawlowska[9], Danielle Hammond[10], Abhishek Maiti[10], Fadi G. Haddad[10], Jayatsu Senapati[10], Naval Daver[10], Naseema Gangat[11], Marina Konopleva[12], Soheil Meshinchi[13] and Naveen Pemmaraju[10]

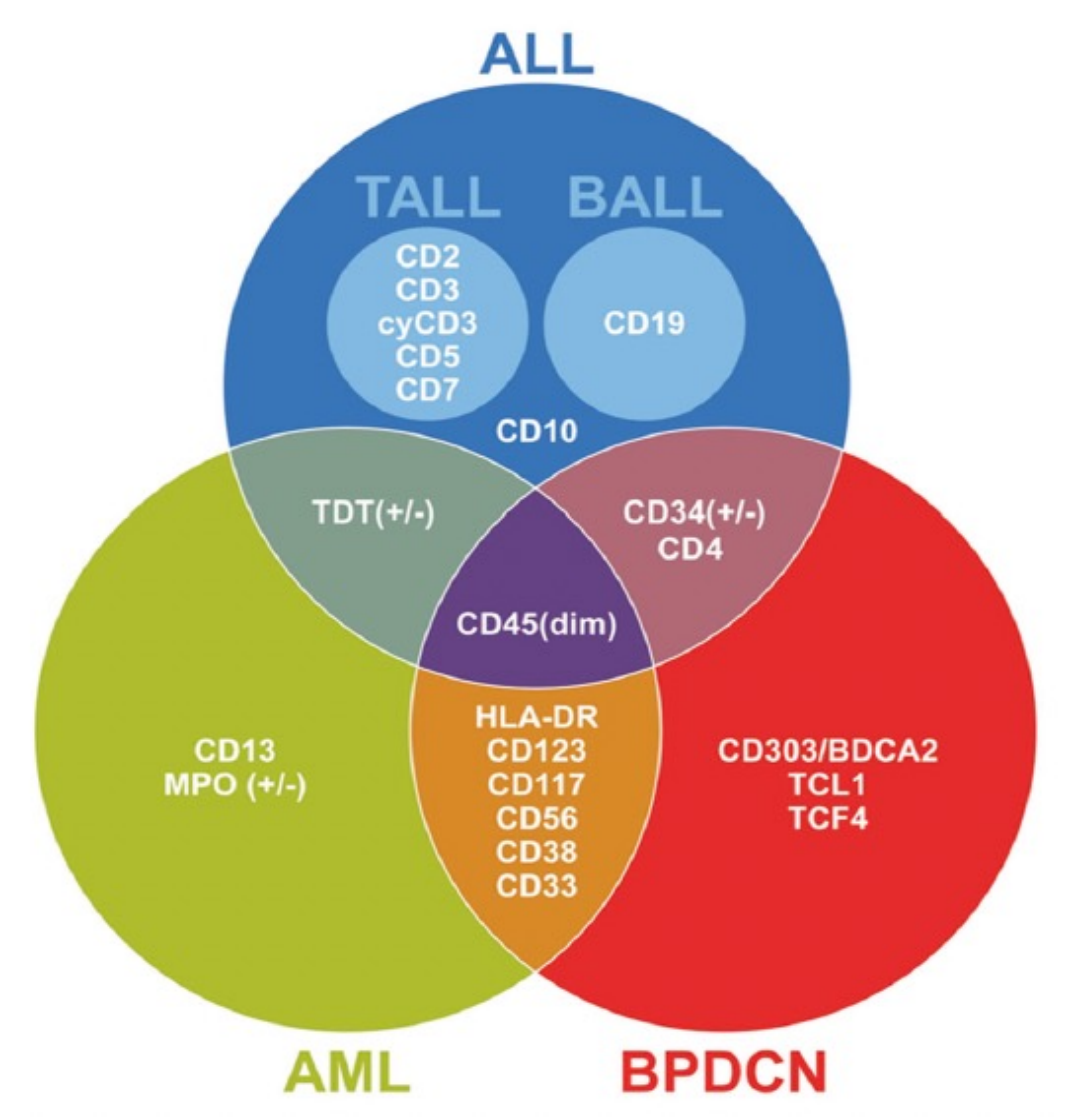
*Leukemia* 2023;37(9):1767-78

# Histologic Presentation Patterns of Blastic Plasmacytoid Dendritic Cell Neoplasm




Cuglievan B et al. *Leukemia* 2023;37(9):1767-78.

# Typical Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) Cell Surface Markers and Their Overlap with Other Hematologic Cancers




Cuglievan B et al. *Leukemia* 2023;37(9):1767-78.

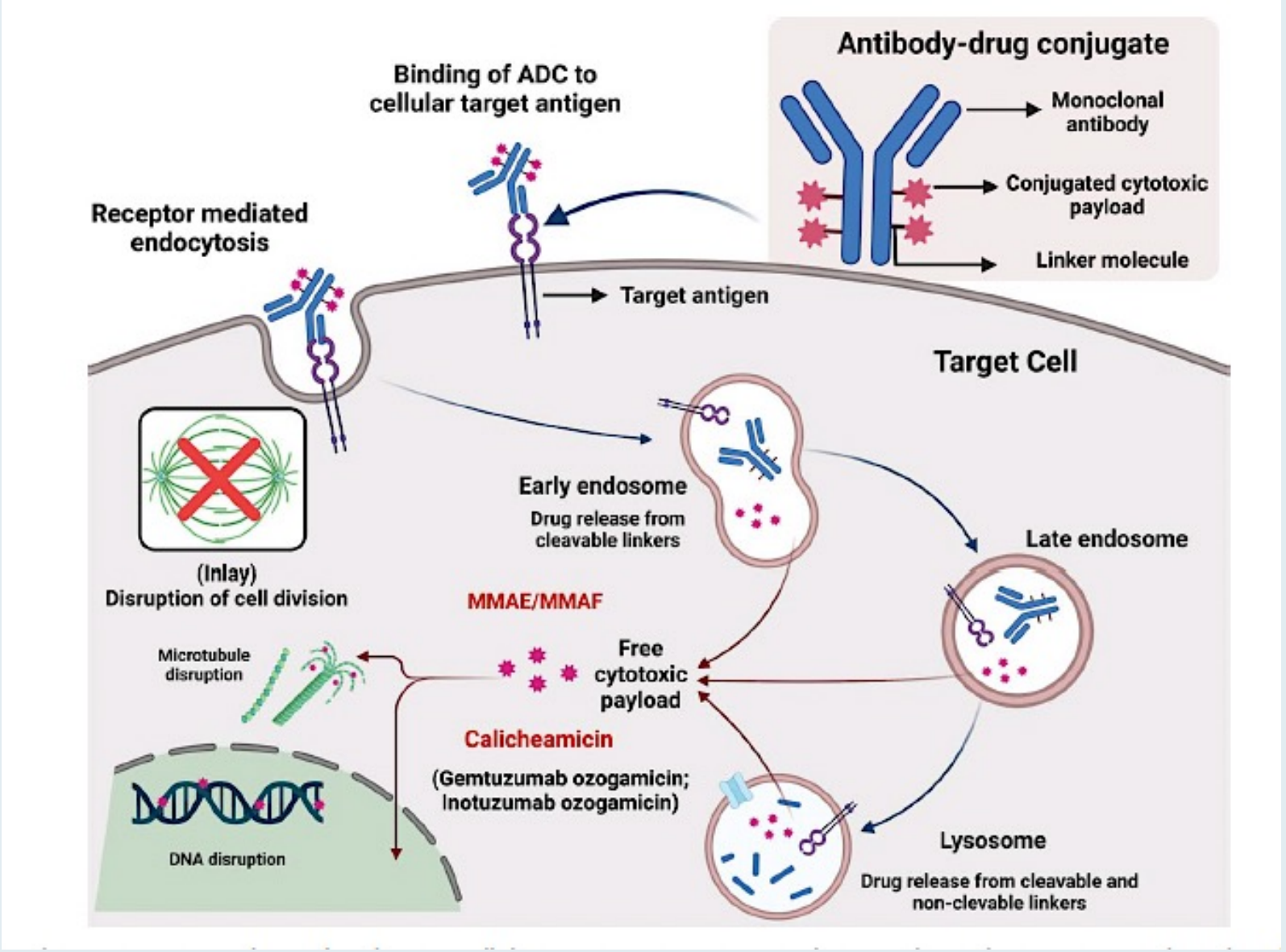
REVIEW ARTICLE

# Antibody-Drug Conjugates in Myeloid Leukemias

*Jayastu Senapati, MBBS, MD, DM, Naval G. Daver, MD, and Naveen Pemmaraju, MD*

***Cancer J* 2022;28(6):454-61**

# Antibody-Drug Conjugate (ADC) Mechanism of Action



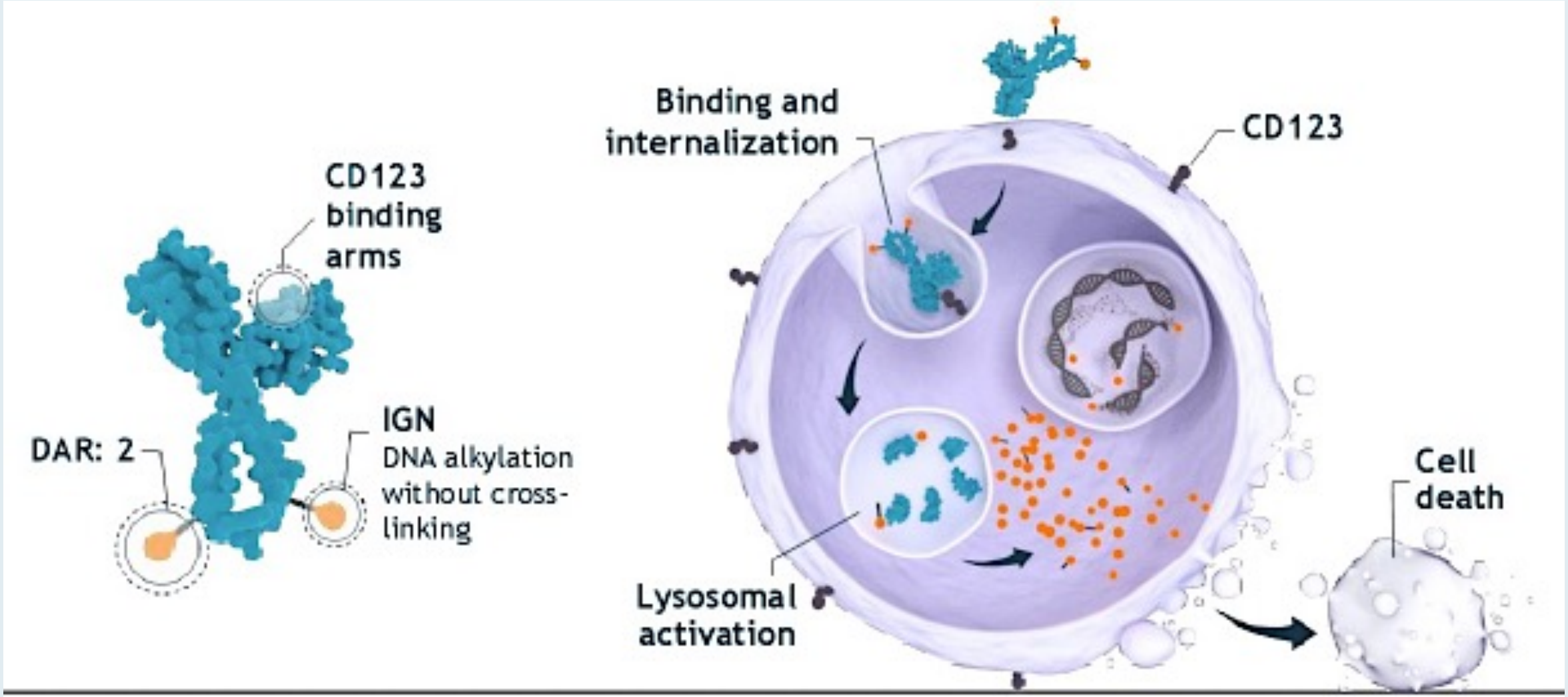

Senapati J et al. *Cancer J* 2022;28(6):454-61.

# A Phase 1b/2 Study of Pivekimab Sunirine (PVEK, IMGN632) in Combination with Venetoclax/Azacitidine or Magrolimab for Patients with CD123-Positive Acute Myeloid Leukemia (AML)

Daver NG et al.
ASCO 2023;Abstract TPS7073.

Daver NG et al.
EHA 2023;Abstract PB1888.

# Structure and Mechanism of Action of PVEK




Daver NG et al. ASCO 2023;Abstract TPS7073.

# A First-in-Human Study of CD123 NK Cell Engager SAR443579 in Relapsed or Refractory Acute Myeloid Leukemia, B-Cell Acute Lymphoblastic Leukemia or High Risk-Myelodysplasia

*Anthony Stein[1], Mojca Jongen-Lavrencic[2], Sylvain Garciaz[3], Gerwin A Huls[4], Abhishek Maiti[5], Nicolas Boissel[6], Stephane De Botton[7], Shaun Fleming[8], C. Michel Zwaan[9], David C. de Leeuw[10], Pinkal Desai[11], Martha Lucia Arellano[12], David Avigan[13], Saskia Langemeijer[14], Kyle Jensen[15], Timothy Wagenaar[15], Gu Mi[15], Giovanni Abbadessa[15], Ashish Bajel[16]*

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**Presented at American Society of Clinical Oncology (ASCO) Annual Meeting 2023 – Chicago, IL, June 02-06, 2023; #7005**

REVIEW ARTICLE

# Checkpoint Inhibitors and Other Immune-Based Therapies in Acute Myeloid Leukemia

*Fadi Haddad, MD,* Amer M. Zeidan, MBBS, MHS,† and Naval Daver, MD**

***Cancer J* 2022;28:43-50**

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

*"T cell-directed therapies have been investigated in AML with promising results. Novel BiTE and TriKE targets are being exploited in an effort to improve efficacy and limit adverse effects. Newer-generation CAR-T cells and more recently cCAR constructs are being designed with less off-target effects,which would potentially allow safer use in myeloid malignancies."*

Haddad F et al. *Cancer J* 2022;28:43-50.

# Immunologic Predictors for Clinical Responses during Immune Checkpoint Blockade in Patients with Myelodysplastic Syndromes

Sung-Eun Lee[1,2], Feng Wang[3], Maison Grefe[4], Abel Trujillo-Ocampo[4], Wilfredo Ruiz-Vasquez[4], Koichi Takahashi[3,5], Hussein A. Abbas[5], Pamella Borges[5,6], Dinler Amaral Antunes[6], Gheath Al-Atrash[1,4,5], Naval Daver[5], Jeffrey J. Molldrem[1,4,5], Andrew Futreal[3], Guillermo Garcia-Manero[4], and Jin S. Im[1,4,5]

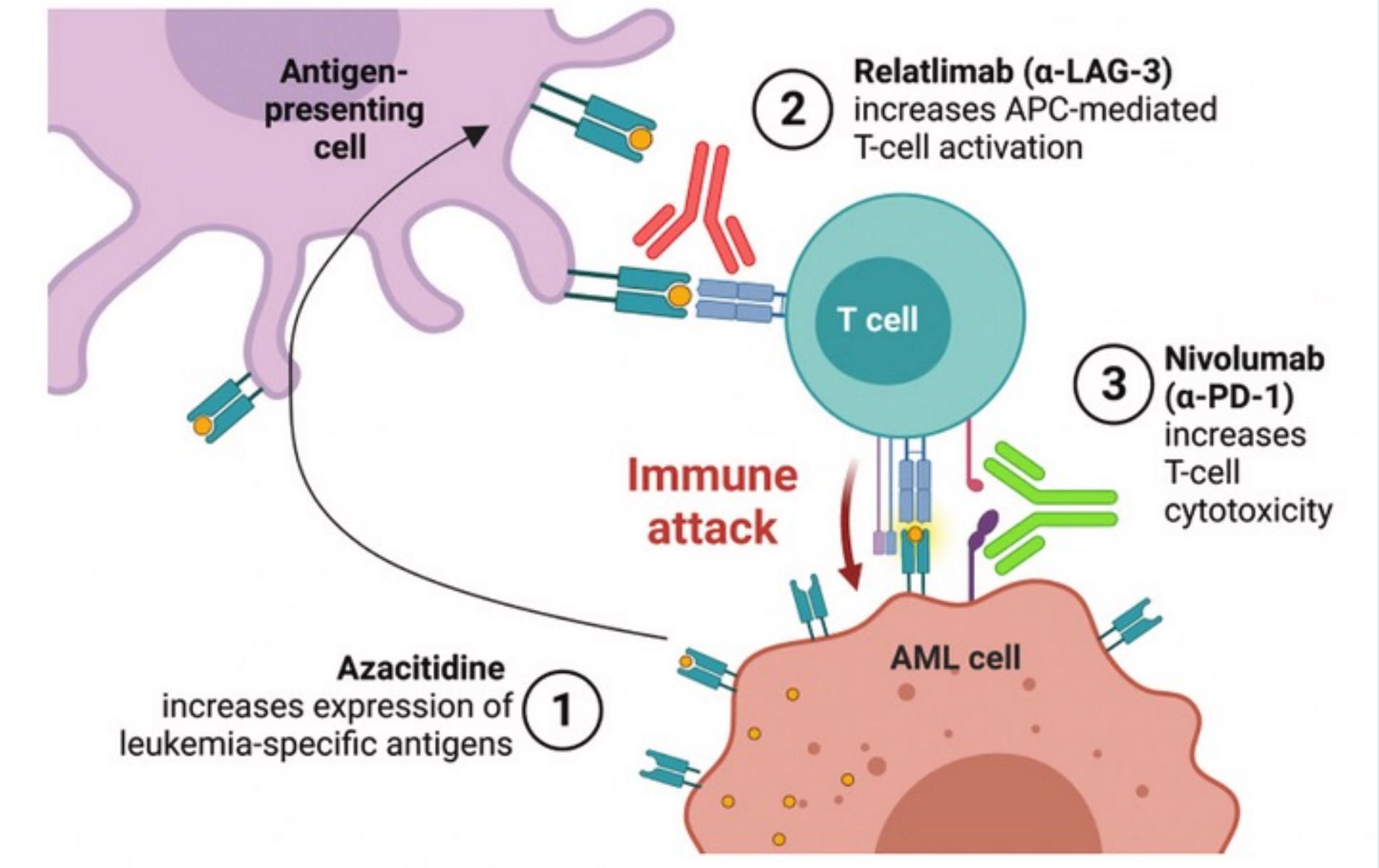
*Clin Cancer Res* 2023;29:1938-51

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

# Trial in Progress: An Open-Label Phase II Study of Relatlimab with Nivolumab in Combination with 5-Azacytidine for the Treatment of Patients with Relapsed/Refractory and Elderly Patients with Newly Diagnosed Acute Myeloid Leukemia (AARON)

Buecklein VL et al.
*Blood* 2022;140(Supplement 1):3227-28.

# Rationale for Combining 5-Azacitidine with Relatlimab and Nivolumab




Buecklein VL et al. ASH 2022.

blood advances

# Cigarette smoke exposure accelerates AML progression in FLT3-ITD models

Tracking no: ADV-2023-010111R2

Mary Figueroa (M.D. Anderson Cancer Center, United States) Huaxian Ma (MD Anderson, United States) Mansour Alfayez (MD Anderson Cancer Center, Saudi Arabia) Daniel Morales-Mantilla (Baylor College of Medicine, United States) Fei Wang (M.D. Anderson Cancer Center, United States) Yue Lu (MD Anderson Cancer Center, United States) Marcos Estecio (UT M,. D, Anderson Cancer Center, United States) Katherine King (Baylor College of Medicine, United States) Eugenie Kleinerman (The University of Texas M. D. Anderson Cancer Center, United States) Seyed Javad Moghaddam (The University of Texas M.D. Anderson Cancer Center, United States) Naval Daver (University of Texas, MD Anderson Cancer Center, United States) Michael Andreeff (The University of Texas M.D. Anderson Cancer Center, United States) Marina Konopleva (Albert Einstein College of Medicine, United States) Courtney DiNardo (UT MD Anderson Cancer Center, United States) Joya Chandra (M.D. Anderson Cancer Center, United States)

**2023; July 24 [Online ahead of print]**

# Microsatellite Instability Assessment by Immunohistochemistry in Acute Myeloid Leukemia: A Reappraisal and Review of the Literature

Siba El Hussein,[a,d] Naval Daver,[b] Jing-Lan Liu,[b,c] Steven Kornblau,[b] Hong Fang,[a] Sergej Konoplev,[a] Hagop Kantarjian,[b] Joseph D. Khoury[a]

***Clin Lymphoma Myeloma Leuk* 2022;22(6):e386-91.**

# Menin Inhibitor DS-1594b Drives Differentiation and Induces Synergistic Lethality in Combination with Venetoclax in AML Cells with MLL-Rearranged and NPM1 Mutation

Ciaurro V et al.

*Blood* 2022;140(Supplement 1):3082-83.

Received: 16 December 2021 | Revised: 2 February 2022 | Accepted: 3 February 2022

DOI: 10.1002/ajh.26496

RESEARCH ARTICLE

# Activity of decitabine as maintenance therapy in core binding factor acute myeloid leukemia

Jayastu Senapati[1] | Mahran Shoukier[1] | Guillermo Garcia-Manero[1] | Xuemei Wang[2] | Keyur Patel[3] | Tapan Kadia[1] | Farhad Ravandi[1] | Naveen Pemmaraju[1] | Maro Ohanian[1] | Naval Daver[1] | Courtney DiNardo[1] | Yesid Alvarado[1] | Jeffrey Aldrich[4] | Gautam Borthakur[1]

*Am J Hematol* 2022;97(5):574-82.

COMMENTARY

blood advances

TO THE EDITOR:

# An agenda to advance research in myelodysplastic syndromes: a TOP 10 priority list from the first international workshop in MDS

Maximilian Stahl,[1] Omar Abdel-Wahab,[2] Andrew H. Wei,[3] Michael R. Savona,[4] Mina L. Xu,[5] Zhuoer Xie,[6] Justin Taylor,[8] Daniel Starczynowski,[9] Guillermo F. Sanz,[10-12] David A. Sallman,[6] Valeria Santini,[13] Gail J. Roboz,[14] Mrinal M. Patnaik,[7] Eric Padron,[6] Olatoyosi Odenike,[15] Aziz Nazha,[16] Stephen D. Nimer,[8] Ravindra Majeti,[17] Richard F. Little,[18] Steven Gore,[18] Alan F. List,[19] Vijay Kutchroo,[20] Rami S. Komrokji,[6] Tae Kon Kim,[4] Nina Kim,[18] Christopher S. Hourigan,[21] Robert P. Hasserjian,[22] Stephanie Halene,[23] Elizabeth A. Griffiths,[24] Peter L. Greenberg,[17] Maria Figueroa,[8] Pierre Fenaux,[25] Fabio Efficace,[26] Amy E. DeZern,[27] Matteo G. Della Porta,[28] Naval G. Daver,[29] Jane E. Churpek,[30] Hetty E. Carraway,[31] Andrew M. Brunner,[32] Uma Borate,[33] John M. Bennett,[34] Rafael Bejar,[35] Jacqueline Boultwood,[36] Sanam Loghavi,[37] Jan Philipp Bewersdorf,[2] Uwe Platzbecker,[38] David P. Steensma,[39] Mikkael A. Sekeres,[8] Rena J. Buckstein,[40] and Amer M. Zeidan[23]

2023;7(12):2709-14

2023 ASCO ANNUAL MEETING

# Efficacy and safety results from the COMMANDS trial: a phase 3 study evaluating luspatercept vs epoetin alfa in erythropoiesis-stimulating agent-naive transfusion-dependent patients with lower-risk myelodysplastic syndromes

Guillermo Garcia-Manero,[1] Uwe Platzbecker,[2] Valer
Rami S. Komrokji,[6] Jake Shortt,[7] David Valcarcel,[8] A
Ing Soo Tiong,[11] Chien-Chin Lin,[12] Jiahui Li,[13] Sandra
Andrius Degulys,[15] Carlo Finelli,[16] Thomas Cluzeau,
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and Monash Health, Melbourne, VIC, Australia; [8]Hospital Universitari Vall d'Hebron, Barcelor
Prague, Czech Republic; [10]Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordea
Melbourne, VIC, Australia; [12]Department of Laboratory Medicine, National Taiwan University
Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [15]Hematology, Oncology and Tra
Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [16]IR
Bologna, Italy; [17]Département d'Hématologie Clinique, Université Cote d'Azur, CHU Nice, Ni
Biomedical Sciences, Humanitas University, Milan, Italy. *At the time the study was conduct

*Abstract number 7003*

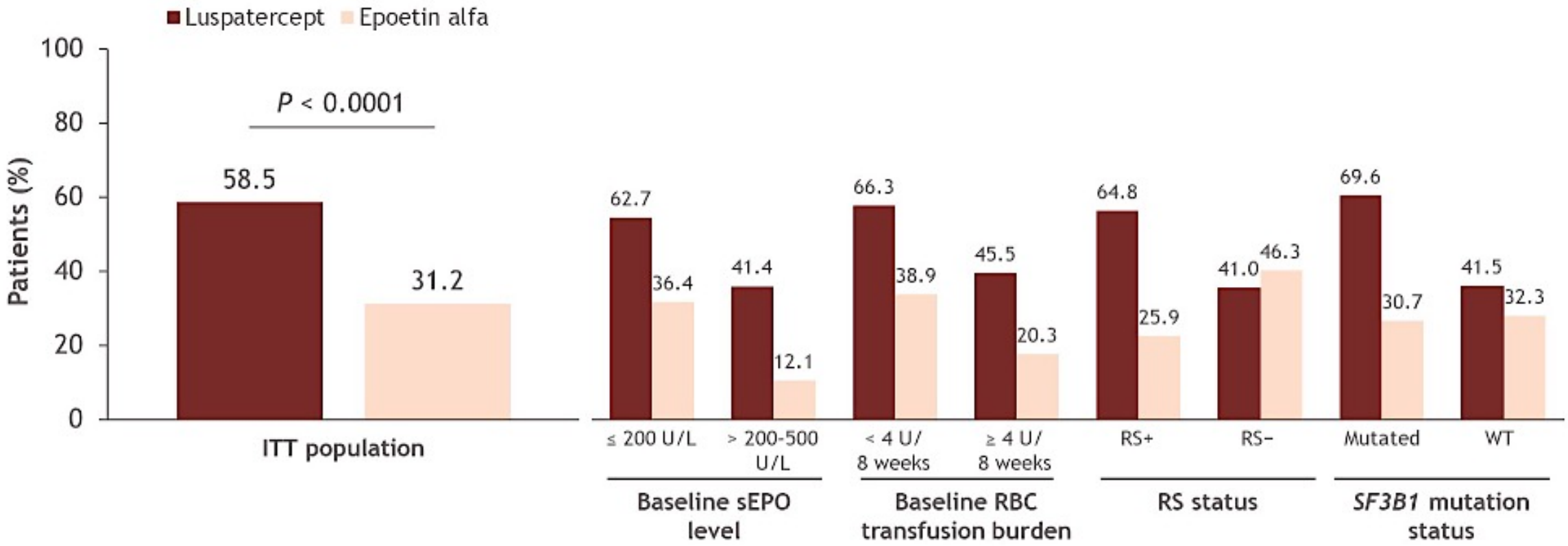
***Lancet* 2023;402:373-85.**

Articles

# Efficacy and safety of luspatercept versus epoetin alfa in erythropoiesis-stimulating agent-naive, transfusion-dependent, lower-risk myelodysplastic syndromes (COMMANDS): interim analysis of a phase 3, open-label, randomised controlled trial

*Uwe Platzbecker*, Matteo Giovanni Della Porta*, Valeria Santini, Amer M Zeidan, Rami S Komrokji, Jake Shortt, David Valcarcel, Anna Jonasova, Sophie Dimicoli-Salazar, Ing Soo Tiong, Chien-Chin Lin, Jiahui Li, Jennie Zhang, Ana Carolina Giuseppi, Sandra Kreitz, Veronika Pozharskaya, Karen L Keeperman, Shelonitda Rose, Jeevan K Shetty, Sheida Hayati, Sadanand Vodala, Thomas Prebet, Andrius Degulys, Stefania Paolini, Thomas Cluzeau, Pierre Fenaux†, Guillermo Garcia-Manero†*

# COMMANDS Composite Primary Endpoint: RBC Transfusion Independence for ≥12 Weeks with Concurrent Mean Hb Increase ≥1.5 g/dL

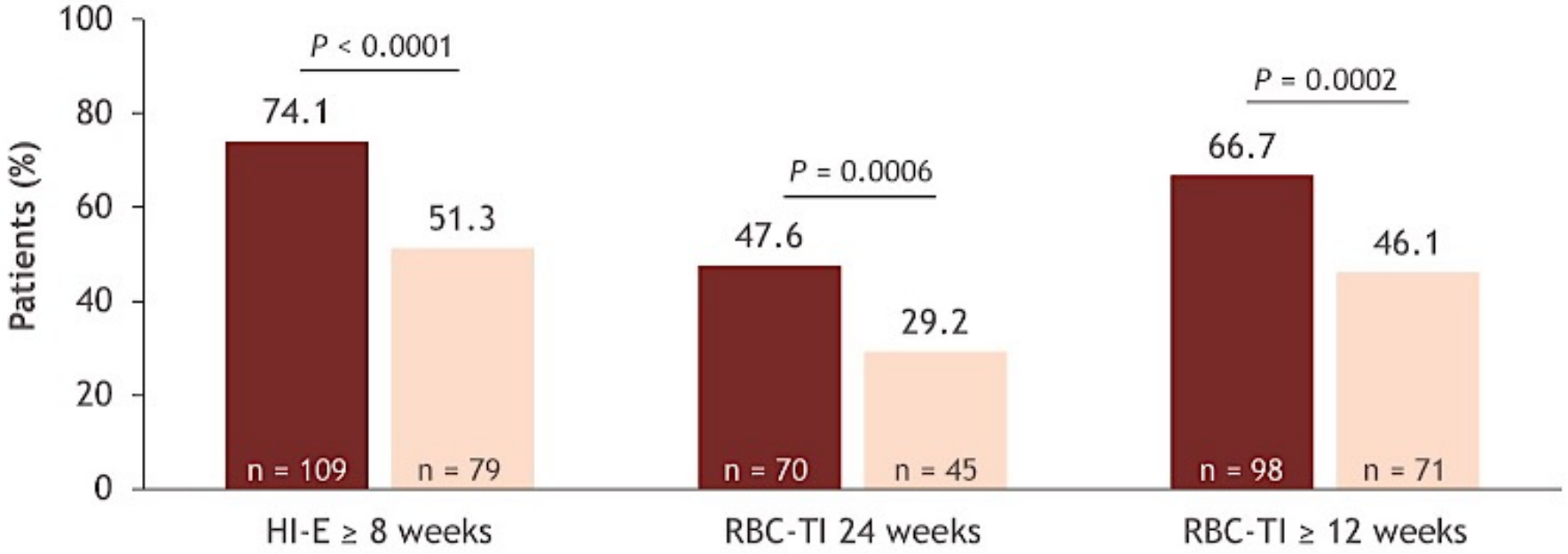



RS status, baseline sEPO level, and baseline RBC transfusion burden were prespecified factors for randomization. *SF3B1* mutation status was a post hoc subgroup analysis. WT, wild type.

Garcia-Manero G et al. ASCO 2023;Abstract 7003; Platzbecker U et al. *Lancet* 2023;402:373-85.

# COMMANDS Secondary Endpoints: RBC Transfusion Independence (TI) for ≥12 Weeks and Hematological Improvement-Erythroid (HI-E) During Weeks 1-24

| | Luspatercept (N = 147) | Epoetin alfa (N = 154) |
|---|---|---|
| Time to first RBC transfusion (week 1-EOT), median (range), weeks | n = 93<br>168.0 (64.0-323.0) | n = 116<br>42.0 (22.0-55.0) |




Garcia-Manero G et al. ASCO 2023;Abstract 7003; Platzbecker U et al. *Lancet* 2023;402:373-85.

EHA 2023;Abstract S102

# Luspatercept versus epoetin alfa for treatment of anemia in ESA-naive lower-risk myelodysplastic syndromes patients requiring RBC transfusions: data from the phase 3 COMMANDS study

Matteo Giovanni Della Porta,[1,2] Uwe Platzbecker,[3] Valeria Santini,[4] Amer M. Zeidan,[5] Pierre Fenaux,[6] Rami S. Komrokji,[7] Jake Shortt,[8] David Valcarcel,[9] Anna Jonasova,[10] Sophie Dimicoli-Salazar,[11] Ing Soo Tiong,[12] Chien-Chin Lin,[13] Jiahui Li,[14] Jennie Zhang,[14] Ana Carolina Giuseppi,[14] Sandra Kreitz,[15] Veronika Pozharskaya,[14] Karen L. Keeperman,[14] Shelonitda Rose,[14] Jeevan K. Shetty,[15*] Sheida Hayati,[14] Sadanand Vodala,[14] Andrius Degulys,[16,17] Stefania Paolini,[18] Thomas Cluzeau,[19] Guillermo Garcia-Manero[20]

[1]Cancer Center IRCCS Humanitas Research Hospital, Milan, Italy; [2]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [3]Medical Clinic and Policlinic 1, Hematology and Cellular Therapy, University Hospital Leipzig, Leipzig, Germany; [4]MDS Unit, Hematology, University of Florence, AOUC, Florence, Italy; [5]Department of Internal Medicine, Yale School of Medicine and Yale Cancer Center, Yale University, New Haven, CT, USA; [6]Service d'Hématologie Séniors, Hôpital Saint-Louis, Université Paris 7, Paris, France; [7]Moffitt Cancer Center, Tampa, FL, USA; [8]Monash University and Monash Health, Melbourne, VIC, Australia; [9]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [10]Medical Department Hematology, Charles University General University Hospital, Prague, Czech Republic; [11]Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [12]Malignant Haematology & Stem Cell Transplantation, The Alfred, Melbourne, VIC, Australia; [13]Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]Celgene International Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [16]Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania; [17]Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania.; [18]IRCCS University Hospital of Bologna, "Seràgnoli" Institute of Hematology, Bologna, Italy; [19]Département d'Hématologie Clinique, Université Cote d'Azur, CHU Nice, Nice, France; [20]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, USA.
*At the time of the study

# FDA Expands Indication for Luspatercept as First-Line Treatment of Anemia in Lower-Risk MDS Regardless of Ring Sideroblast Status

## Press Release — August 28, 2023

"[It was] today announced that the US Food and Drug Administration (FDA) has approved luspatercept-aamt for the treatment of anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions.

This expanded indication to the first-line setting is based on interim results from the pivotal Phase 3 COMMANDS trial, in which luspatercept-aamt demonstrated superior efficacy of concurrent RBC transfusion independence and hemoglobin increase compared to epoetin alfa, an ESA, regardless of ring sideroblast status. These results underscore luspatercept-aamt's ability to address chronic anemia earlier in the treatment journey in a broader range of patients."

https://news.bms.com/news/details/2023/U.S.-FDA-Approves-Bristol-Myers-Squibbs-Reblozyl-luspatercept-aamt-as-First-Line-Treatment-of-Anemia-in-Adults-with-Lower-Risk-Myelodysplastic-Syndromes-MDS-Who-May-Require-Transfusions/default.aspx

RTP RESEARCH TO PRACTICE

# Meet The Professor with Dr Daver

**INTRODUCTION: Biology, Classification, p53, Magrolimab**

**MODULE 1: Case Presentations**

**MODULE 2: Journal Club with Dr Daver**

**MODULE 3: Appendix**

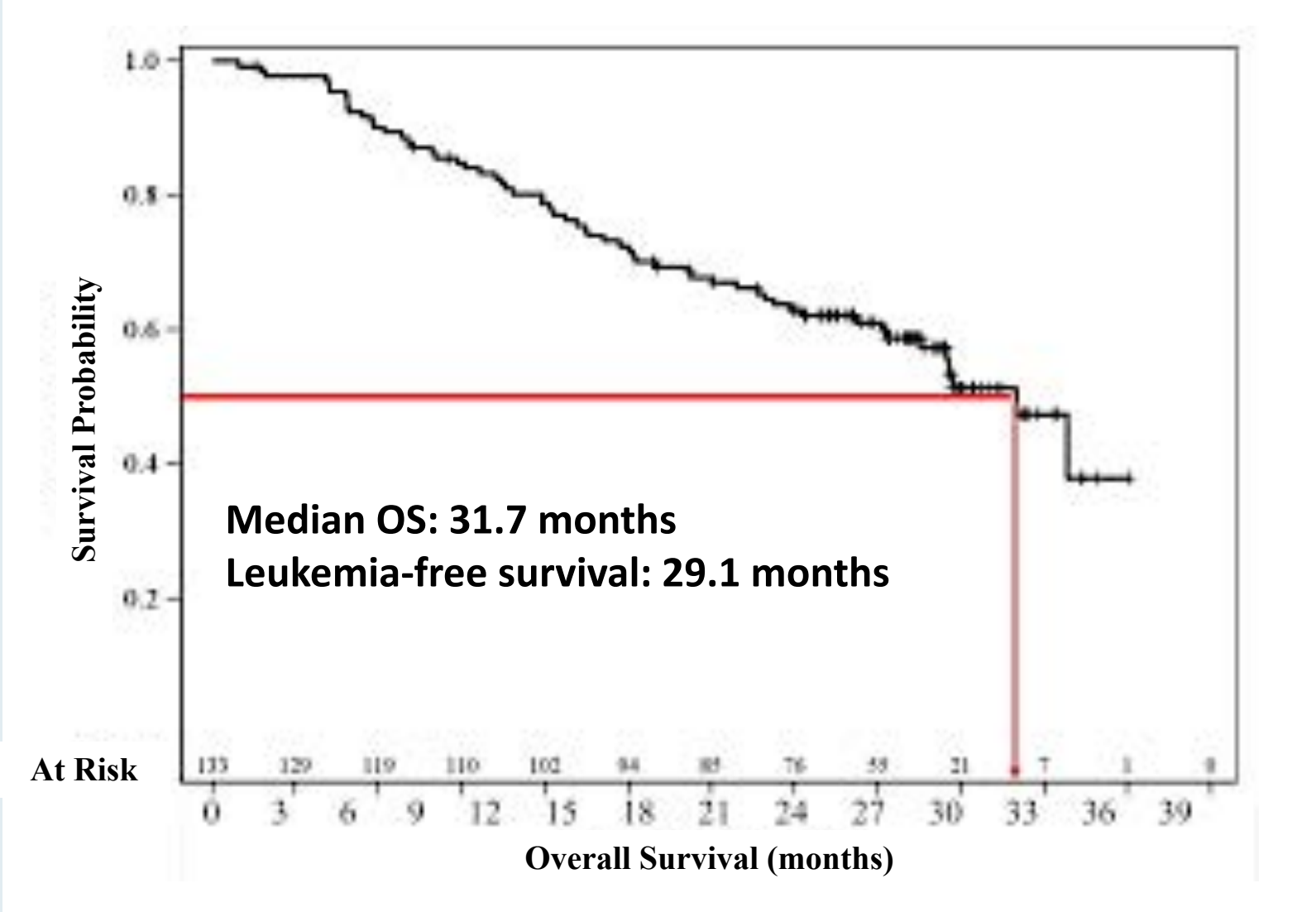
RTP
RESEARCH
TO PRACTICE

# Prolonged Survival Observed in 133 MDS Patients Treated with Oral Decitabine/Cedazuridine

Savona MR et al.
16th International Congress on Myelodysplastic Syndromes (MDS 2021);Abstract P48.

RTP RESEARCH TO PRACTICE

# ASCERTAIN: Updated Overall Survival with 32-Month Follow-Up




Savona MR et al. MDS 2021;Abstract P48.

RTP RESEARCH TO PRACTICE

Received: 27 January 2023 | Revised: 11 April 2023 | Accepted: 18 April 2023

DOI: 10.1002/ajh.26941

RESEARCH ARTICLE

# Clinical characteristics and overall survival among acute myeloid leukemia patients with *TP53* gene mutation or chromosome 17p deletion

Naval G. Daver[1] | Shahed Iqbal[2] | Julie Huang[2] | Camille Renard[2] | Joyce Lin[2] | Yang Pan[2] | Mellissa Williamson[2] | Giridharan Ramsingh[2]

*Am J Hematol* 2023;98(8):1176-84.

Received: 23 May 2022 | Revised: 28 July 2022 | Accepted: 19 September 2022

DOI: 10.1002/cncr.34535

CONSENSUS STATEMENT

# *TP53*-altered acute myeloid leukemia and myelodysplastic syndrome with excess blasts should be approached as a single entity

Rory M. Shallis MD[1] | Naval G. Daver MD[2] | Jessica K. Altman MD[3] | Robert P. Hasserjian MD[4] | Hagop M. Kantarjian MD[2] | Uwe Platzbecker MD[5] | Valeria Santini MD[6] | Andrew H. Wei MBBS, PhD, FRACP, FRCPA[7] | David A. Sallman MD[8] | Amer M. Zeidan MBBS, MHS[1]

***Cancer* 2023;129(2):175-80.**

Original Reports | Hematologic Malignancy

# Tolerability and Efficacy of the Anticluster of Differentiation 47 Antibody Magrolimab Combined With Azacitidine in Patients With Previously Untreated AML: Phase Ib Results

Naval G. Daver, MD[1]; Paresh Vyas, FRCP[2]; Suman Kambhampati, MD[3]; Monzr M. Al Malki, MD[4]; Richard A. Larson, MD[5]; Adam S. Asch, MD[6]; Gabriel Mannis, MD[7]; Wanxing Chai-Ho, MD[8]; Tiffany N. Tanaka, MD[9]; Terrence J. Bradley, MD[10]; Deepa Jeyakumar, MD[11]; Eunice S. Wang, MD[12]; Kendra Sweet, MD[13]; Hagop M. Kantarjian, MD[1]; Guillermo Garcia-Manero, MD[1]; Rami Komrokji, MD[13]; Guan Xing, PhD[14]; Giridharan Ramsingh, MD[14]; Camille Renard, MSc[14]; Joshua F. Zeidner, MD[15]; and David A. Sallman, MD[13]

*J Clin Oncol* 2023 September 13;[Online ahead of print]

# 5F9005 Study: Front-Line Magrolimab in Combination with Azacitidine for Previously Untreated AML — Response

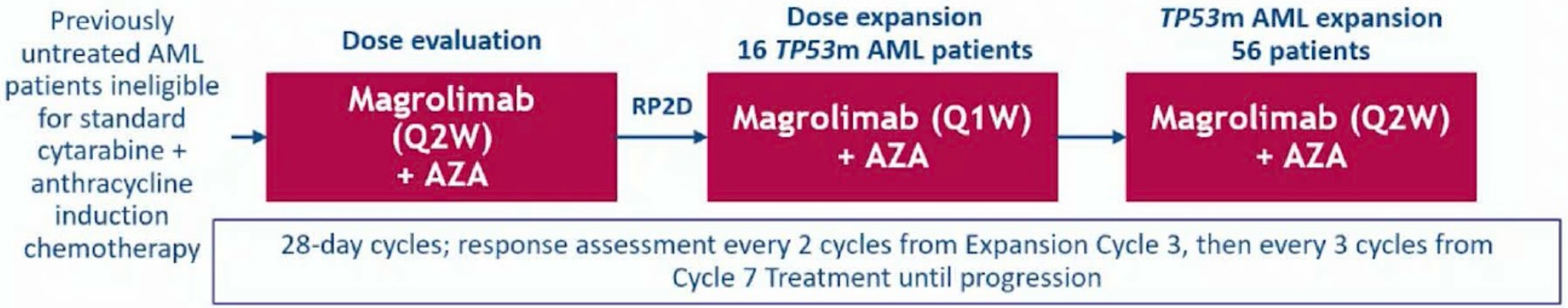
| Clinical endpoint | All patients (n = 87) | TP53 mutation (n = 72) | TP53 wild type (n = 15) |
|---|---|---|---|
| ORR, % | 47.1% | 47.2% | 46.7% |
| CR, % | 32.2% | 31.9% | 33.3% |
| CRi, No. (%) | 5 (5.7%) | 5 (6.9%) | 0 |
| Duration of CR/CRi, months | 9.6 mo | 7.7 mo | 31.3 mo |

ORR = objective response rate; CR = complete remission; Cri = CR with incomplete blood count recovery;
DCR = duration of complete remission

Daver NG et al. *J Clin Oncol* 2023 September 13;[Online ahead of print].

RTP RESEARCH TO PRACTICE

# 5F9005 Study Design: A Phase Ib Study of Magrolimab in Combination with Azacitidine for TP53-Mutated AML




- Patients received magrolimab IV as a 1 mg/kg priming dose on Days 1 and 4, then ramp-up to 30 mg/kg maintenance once or twice weekly. AZA dose was administered SC or IV, 75 mg/m$^2$ on Days 1-7 of each cycle.

**Primary objectives**

Safety, tolerability and efficacy of magrolimab + azacitidine in AML

**Secondary objectives**

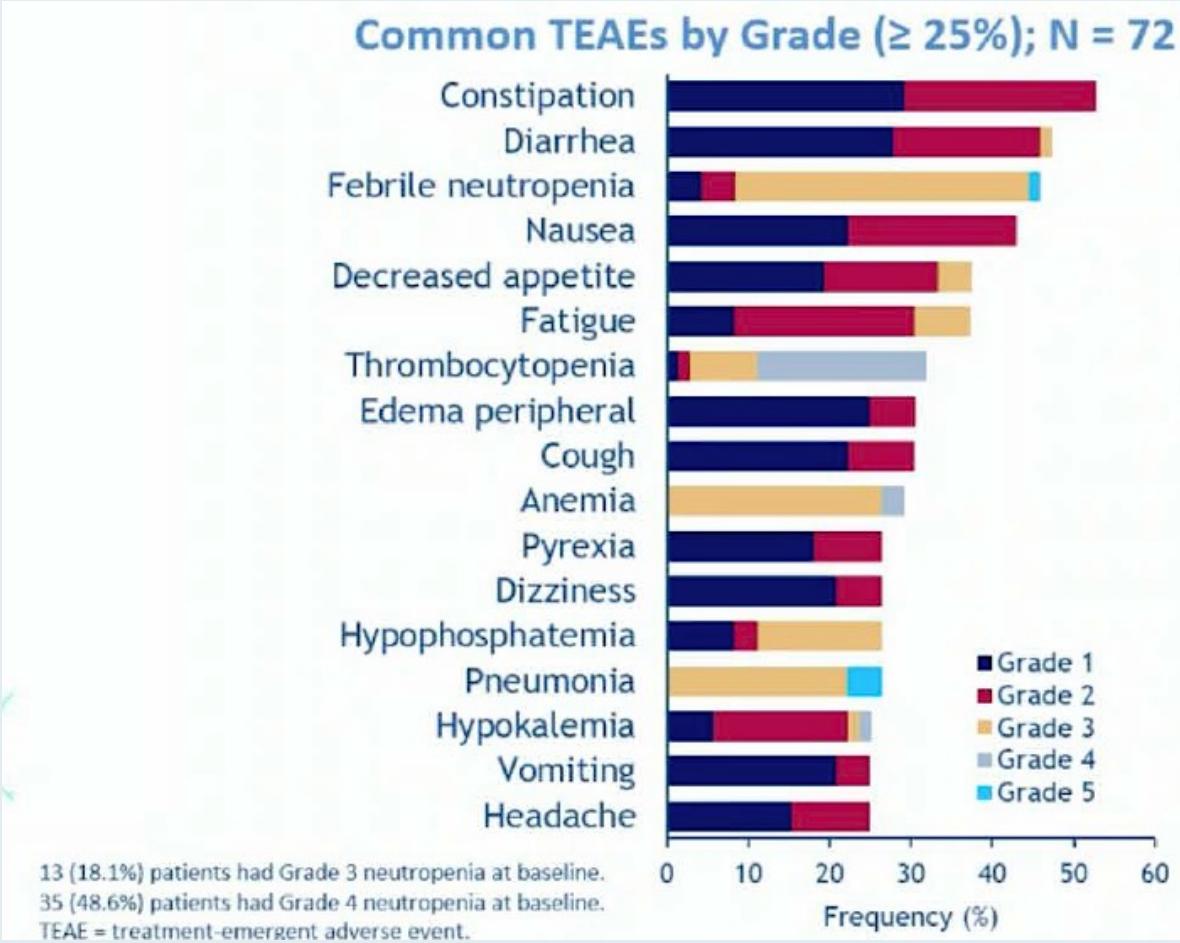
Efficacy of magrolimab + azacitidine; MRD negativity; PK profile; immunogenicity

**Exploratory objectives**

CD47 RO, biomarkers, efficacy in molecular subtypes of AML

Daver NG et al. EHA 2022;Abstract S132.

# 5F9005 Phase Ib Study of Front-Line Magrolimab in Combination with Azacitidine for TP53-Mutated AML: Safety Summary




- No patient had magrolimab dose reduction; magrolimab dose delays occurred in 45.8% of patients.
- TEAEs led to discontinuation of magrolimab in 22 (30.6%) and of AZA in 21 (29.2%) patients.
- 13 (18.1%) patients died within 60 days of the first study drug dose.
- Infusion-related reaction (all grades) in 22.2%, Grade 3+ in 1.4%.
- 19 (26.4%) patients had Grade 3 anemia, and 2 (2.8%) had Grade 4 anemia, regardless of attribution.

Daver NG et al. EHA 2022;Abstract S132.

RTP RESEARCH TO PRACTICE

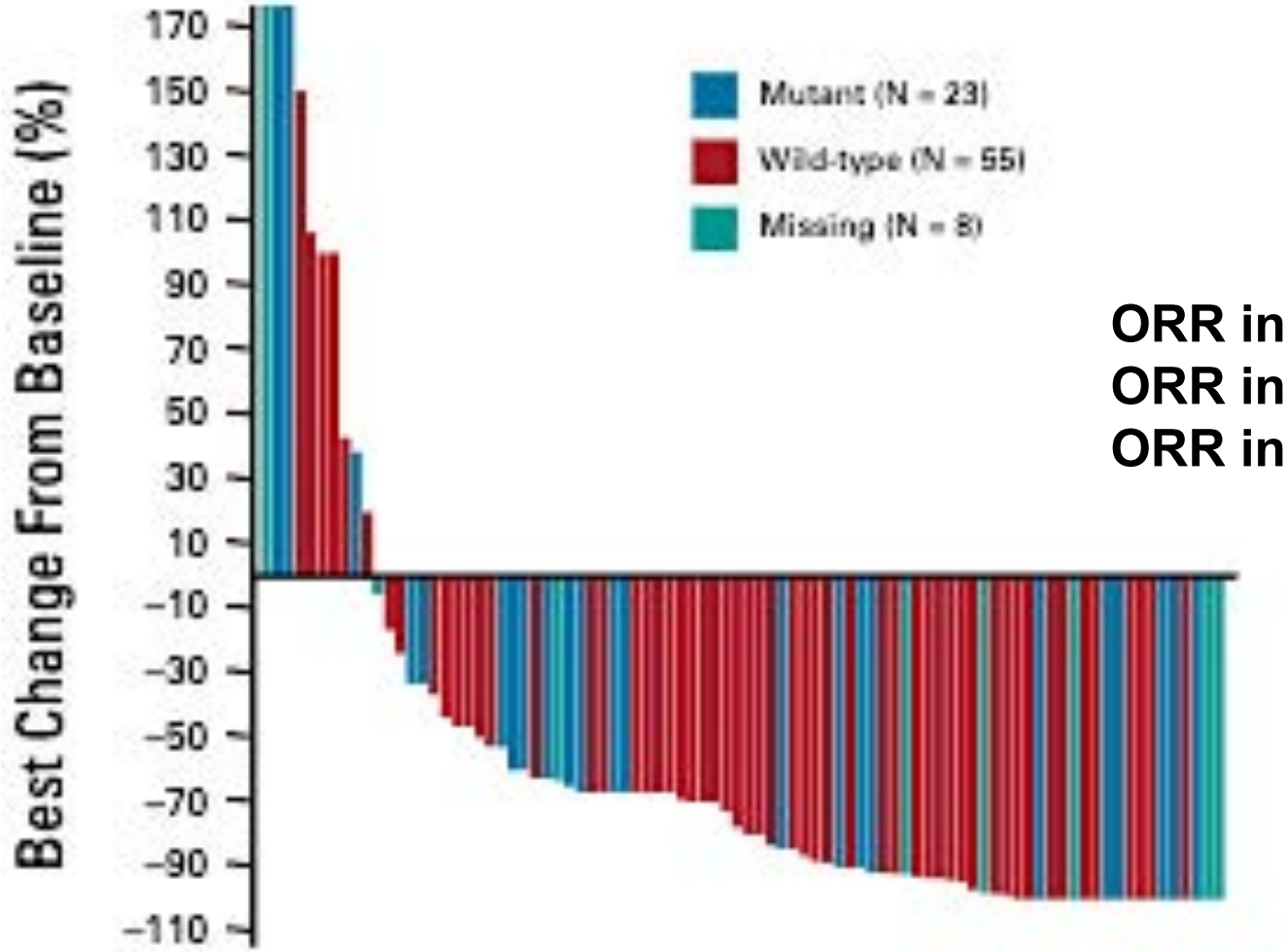
original reports

# Magrolimab in Combination With Azacitidine in Patients With Higher-Risk Myelodysplastic Syndromes: Final Results of a Phase Ib Study

David A. Sallman, MD[1]; Monzr M. Al Malki, MD[2]; Adam S. Asch, MD[3]; Eunice S. Wang, MD[4]; Joseph G. Jurcic, MD[5]; Terrence J. Bradley, MD[6]; Ian W. Flinn, MD[7]; Daniel A. Pollyea, MD, MS[8]; Suman Kambhampati, MD[9]; Tiffany N. Tanaka, MD[10]; Joshua F. Zeidner, MD[11]; Guillermo Garcia-Manero, MD[12]; Deepa Jeyakumar, MD[13]; Rami Komrokji, MD[1]; Jeffrey Lancet, MD[1]; Hagop M. Kantarjian, MD[12]; Lin Gu, MS[14]; Yajia Zhang, PhD[14]; Anderson Tan, PharmD, RPh[14]; Mark Chao, MD, PhD[14]; Carol O'Hear, MD, PhD[14]; Giridharan Ramsingh, MD[14]; Indu Lal, MD[14]; Paresh Vyas, MD, PhD[15]; and Naval G. Daver, MD[12]

*J Clin Oncol* 2023;41(15):2815-26

# 5F9005: Response to Magrolimab in Combination with Azacitidine for Higher-Risk MDS with and without TP53 Mutations




**ORR in all patients (N = 95): 74.7%**
**ORR in *TP53* wild-type (n = 61): 78.7%**
**ORR in *TP53* mutant (n = 25): 68.0%**

Sallman DA et al. *J Clin Oncol* 2023;41(15):2815-26.

# 5F9005: Select Treatment-Emergent Adverse Events (TEAEs) with Magrolimab in Combination with Azacitidine for Higher-Risk MDS (N = 95)

| TEAE (%) | Total | Grade 3 | Grade 4 |
|---|---|---|---|
| Constipation | 68.4 | — | — |
| Thrombocytopenia | 54.7 | 9.5 | 36.8 |
| Anemia | 51.6 | 46.3 | 1.1 |
| Neutropenia | 47.4 | 4.2 | 42.1 |
| Febrile neutropenia | 30.5 | 27.4 | 1.1 |
| WBC count decreased | 29.5 | 4.2 | 25.3 |
| Hypophosphatemia | 18.9 | 11.6 | — |

Immune-related reactions possibly/probably related to magrolimab were infrequent (2.1%; one Grade 2 pneumonitis and one Grade 3 pneumonitis).

Sallman DA et al. *J Clin Oncol* 2023; March 8;[Online ahead of print].

# ENHANCE Phase III Study Design

Study treatment may be continued, up to 5 years, until disease progression, loss of clinical benefit, or unacceptable toxicities occur

**Screening:**
Untreated MDS intermediate to very high risk by IPSS-R

1:1 Randomization (n=520)

- Magrolimab + Azacitidine*
- Placebo + Azacitidine*

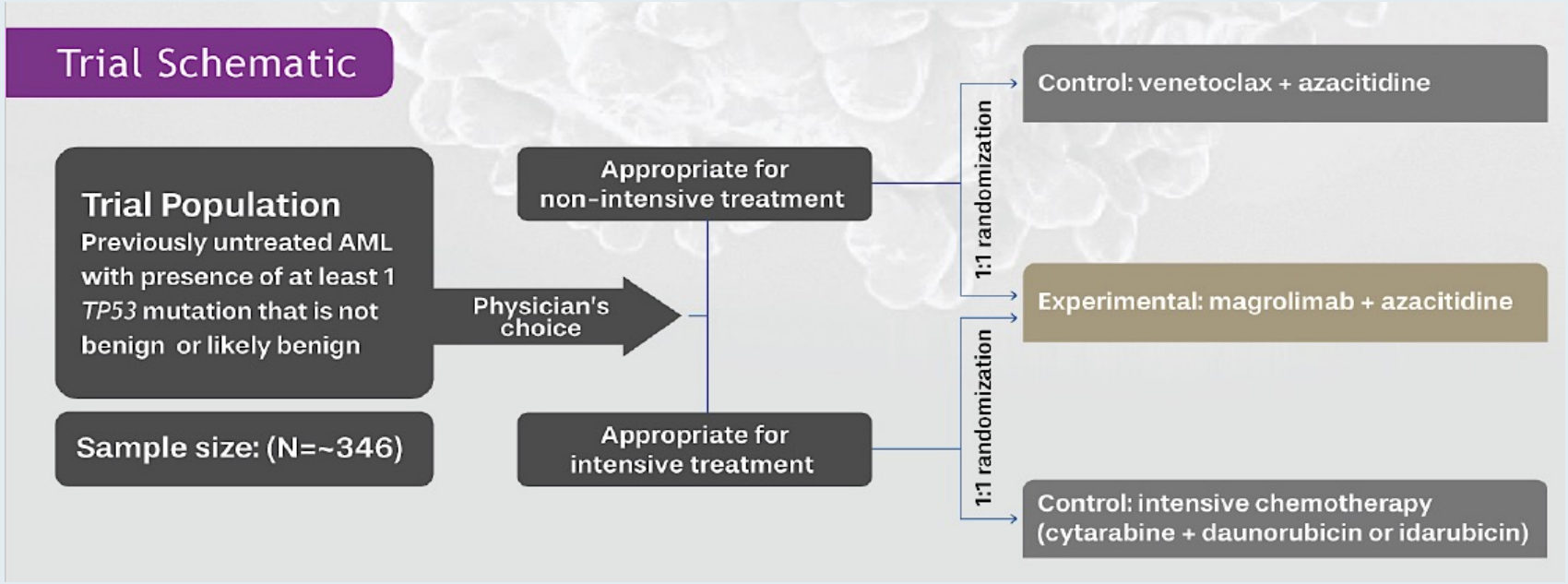
| Dosing | Cycle* 1 | Cycle 2 | Cycle 3 and Beyond |
|---|---|---|---|
| Magrolimab | Priming (1mg/kg) on Days 1 and 4<br>15 mg/kg on Day 8<br>30 mg/kg on Days 11, 15, 22 | 30 mg/kg on Days 1, 8, 15, 22 | 30 mg/kg Q2W on Days 1, 15 |
| Placebo (saline) | Days 1, 4, 8, 11, 15, 22 | Days 1, 8, 15, 22 | Days 1, 15 |
| Azacitidine | 75 mg/m$^2$ IV or SC on Days 1-7 (or Days 1-5 and 8-9) every cycle | | |

*Each cycle is 28 days.
IV, intravenous; SC, subcutaneous; Q2W, every 2 weeks.

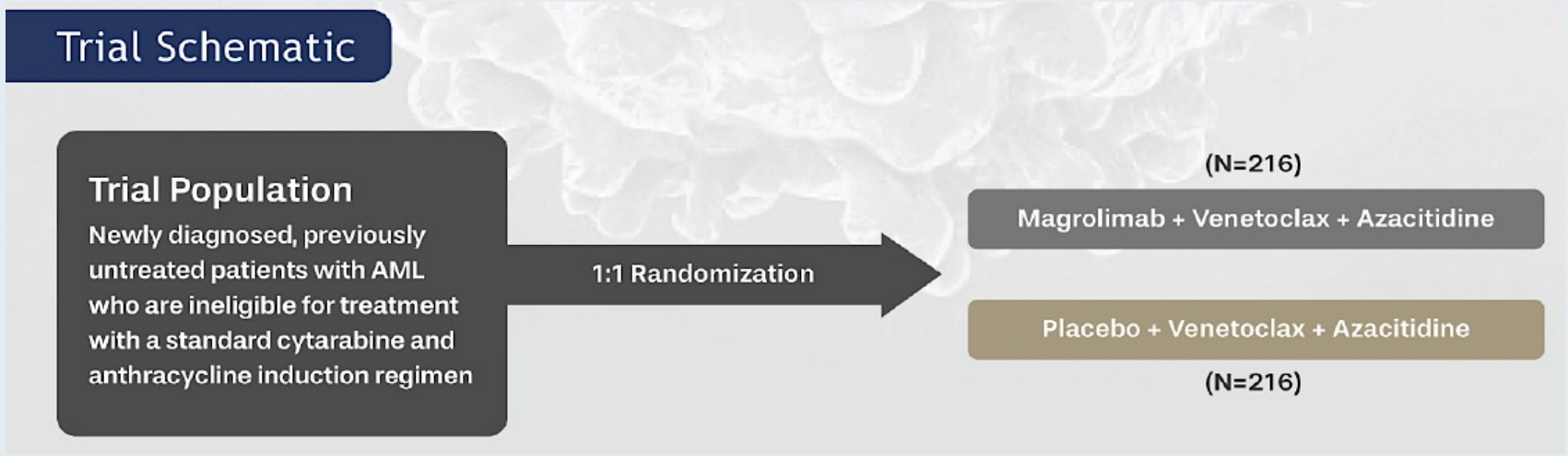
Garcia-Manero G et al. ASCO 2021;Abstract TPS 7055.

# Ongoing Phase III Studies of Magrolimab-Based Therapies for Newly Diagnosed AML

## ENHANCE-2




## ENHANCE-3




https://www.mds-foundation.org; www.clinicaltrials.gov. NCT04778397. Accessed September 2023; www.clinicaltrials.gov. NCT05079230. Accessed September 2023.

# Clinical and Molecular Characterization of Newly Diagnosed IDH/TP53 Co-Mutated AML and Impact of Genomically Sensitive Treatment Strategies

Venugopal S et al.
*Blood* 2022;140(Supplement 1):6328-30.

# Optimizing the Use of Targeted Therapy for Patients with AML and FLT3 or IDH Mutations

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# Hypomethylating agent and venetoclax with FLT3 inhibitor "triplet" therapy in older/unfit patients with *FLT3* mutated AML

Musa Yilmaz[1], Hagop Kantarjian[1], Nicholas J. Short[1], Patrick Reville[1], Marina Konopleva[1], Tapan Kadia[1], Courtney DiNardo[1], Gautam Borthakur[1], Naveen Pemmaraju[1], Abhishek Maiti[1], Elias Jabbour[1], Nitin Jain[1], Ghayas Issa[1], Koichi Takahashi[1], Koji Sasaki[1], Maro Ohanian[1], Sherry Pierce[1], Guillin Tang[2], Sanam Loghavi[2], Keyur Patel[2], Sa A. Wang[2], Guillermo Garcia-Manero[1], Michael Andreeff[1], Farhad Ravandi[1] and Naval Daver[1]✉

***Blood Cancer J*** **2022;12(5):77**

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

*Transplant Cell Ther*. 2023 April ; 29(4): 265.e1–265.e10. doi:10.1016/j.jtct.2022.12.006.

# Outcomes in Patients with *FLT3*-Mutated Relapsed/ Refractory Acute Myelogenous Leukemia Who Underwent Transplantation in the Phase 3 ADMIRAL Trial of Gilteritinib versus Salvage Chemotherapy

**Alexander E. Perl[1,*], Richard A. Larson[2], Nikolai A. Podoltsev[3], Stephen Strickland[4], Eunice S. Wang[5], Ehab Atallah[6], Gary J. Schiller[7], Giovanni Martinelli[8], Andreas Neubauer[9], Jorge Sierra[10], Pau Montesinos[11], Christian Recher[12], Sung-Soo Yoon[13], Yoshinobu Maeda[14], Naoko Hosono[15], Masahiro Onozawa[16], Takayasu Kato[17], Hee-Je Kim[18], Nahla Hasabou[19], Rishita Nuthethi[19], Ramon Tiu[19,†], Mark J. Levis[20]**

Original Reports | Hematologic Malignancy

# Gilteritinib in Combination With Induction and Consolidation Chemotherapy and as Maintenance Therapy: A Phase IB Study in Patients With Newly Diagnosed AML

Keith W. Pratz, MD[1]; Mohamad Cherry, MD, MS[2]; Jessica K. Altman, MD[3]; Brenda W. Cooper, MD[4]; Nikolai A. Podoltsev, MD, PhD[5]; Jose Carlos Cruz, MD[6]; Tara L. Lin, MD[7]; Gary J. Schiller, MD[8]; Joseph G. Jurcic, MD[9]; Adam Asch, MD[10]; Ruishan Wu, MS[11]; Jason E. Hill, PhD[11]; Stanley C. Gill, PhD[11]; Angela J. James, PhD[11]; Elizabeth Shima Rich, MD, PhD[11]; Nahla Hasabou, MD[11]; Alexander E. Perl, MD[1]; and Mark J. Levis, MD, PhD[12]

*J Clin Oncol* 2023;41(26):4236-46.

# Efficacy and Safety of Gilteritinib versus Sorafenib as Post-Transplant Maintenance in Patients with FLT3-ITD Acute Myeloid Leukemia

Yeh J et al.
*Blood* 2022;140(Supplement 1):7686-88.

# Next-Generation Sequencing-Based Measurable Disease Monitoring in Acute Myeloid Leukemia with FLT3 Internal Tandem Duplication Treated with Intensive Chemotherapy plus Midostaurin

Rucker F et al.

EHA 2023;Abstract S135.

# Characteristics of Select FLT3 Inhibitors

| FLT3 inhibitor | Inhibitory type | FLT3 kinase inhibition IC50 (nmol/L) | Non-FLT3 targets | FLT3-TKD mutation activity | Major toxicities |
|---|---|---|---|---|---|
| Sorafenib<br>400 mg BID | II | 58 | c-KIT<br>PDGFR<br>RAF<br>VEGFR | No | Rash<br>Hemorrhage<br>Myelosuppression |
| Midostaurin<br>50 mg BID | I | 6.3 | c-KIT<br>PDGFR<br>PKC<br>VEGFR | Yes | GI toxicity<br>Myelosuppression |
| Quizartinib<br>30-60 mg qd | II | 1.6 | c-KIT | No | QTc prolongation<br>Myelosuppression |
| Gilteritinib<br>120 mg qd | I | 0.29 | AXL<br>LTK<br>ALK | Yes | Elevated transaminases<br>Diarrhea |

Kiyoi H et al. *Cancer Science* 2019;[Online ahead of print];
Short NJ et al. *Ther Adv Hematol* 2019;10:2040620719827310.

# Key Clinical Trials of FLT3 Inhibitors

| Study | Agents | FLT3 inhibitor generation | Inhibits | N | Population | OS hazard ratio |
|---|---|---|---|---|---|---|
| SORAML<br>Phase II | Sorafenib<br>Placebo | First | ITD | 267 | Treatment naïve | 0.82, ns |
| RATIFY<br>Phase III | Midostaurin<br>Placebo | First | ITD, TKD | 717 | Treatment naïve | 0.78 |
| QuANTUM-First<br>Phase III | Quizartinib<br>Placebo | Second | ITD | 539 | Treatment naïve | 0.78 |
| QuANTUM-R<br>Phase III | Quizartinib<br>SC | — | — | 367 | R/R | 0.76 |
| ARO-021<br>Phase III | Crenolanib<br>Placebo | Second | ITD, TKD | 510 | Treatment naïve | Not yet reported |
| ADMIRAL<br>Phase III | Gilteritinib<br>SC | Second | ITD, TKD | 371 | R/R | 0.67 |

OS = overall survival; SC = salvage chemotherapy; R/R = relapsed/refractory

Novatcheva ED et al. *Clin Lymphoma Myeloma Leuk* 2021;[Online ahead of print]. Rollig C et al. *Leukemia* 2021;35:2517-25. Erba HP et al. *Lancet* 2023;401:1571-83. Perl AE et al. *Blood* 2022;139(23):3366-75.

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DOI: 10.1002/ajh.26694

RESEARCH ARTICLE

# Contemporary outcomes in *IDH*-mutated acute myeloid leukemia: The impact of co-occurring *NPM1* mutations and venetoclax-based treatment

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*Am J Hematol* 2022;97(11):1443-52.

# Pivotal Studies of IDH Inhibitor Monotherapy for AML with IDH Mutations

| IDH inhibitor | Enasidenib | Ivosidenib | | Olutasidenib |
|---|---|---|---|---|
| FDA approval | Aug 1, 2017 | July 20, 2018 | May 2, 2019 | December 1, 2022 |
| Setting | Relapsed/refractory | Relapsed/refractory | Newly diagnosed | Relapsed/refractory |
| Trial | AG221-C-001 | AG120-C-001 | AG120-C-001 | Study 2102-HEM-101 |
| IDH mutation | IDH2 | IDH1 | IDH1 | IDH1 |
| N | 109 | 179 | 28 | 147 |
| Dose | 100 mg qd | 500 mg qd | 500 mg qd | 150 mg BID |
| CR + CRh | 23% | 30.4% | 42.9% | 35% |
| Median duration of response | 8.2 mo | 8.2 mo | Not estimable | 25.9 mo |
| Median OS, ITT | 9.3 mo | 8.8 mo | 29.3 mo | Not reported |

CRh = CR with partial hematologic recovery; OS = overall survival; ITT = intent to treat

Stein EM et al. *Blood* 2017;130(6):722-31; Enasidenib PI, rev 11/2020; DiNardo CD et al. *N Engl J Med* 2018;378(25):2386; Roboz GJ et al. *Blood* 2020;135(7)463-71; Ivosidenib PI, rev 8/2021; de Botton S et al. ASCO 2023;Abstract 7012; Olutasidenib PI, rev 12/2022.

# FDA Approves Olutasidenib for Relapsed or Refractory Acute Myeloid Leukemia with a Susceptible IDH1 Mutation

## Press Release: December 1, 2022

"On December 1, 2022, the Food and Drug Administration approved olutasidenib capsules for adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.

[The] FDA also approved the RealTime IDH1 Assay to select patients for olutasidenib.

Approval was based on Study 2102-HEM-101 (NCT02719574), an open-label, single-arm, multicenter clinical trial that included 147 adult patients with relapsed or refractory AML with an IDH1 mutation confirmed using the above assay. Olutasidenib was given orally, 150 mg twice daily, until disease progression, unacceptable toxicity, or hematopoietic stem cell transplantation. Efficacy was established on the rate of complete remission (CR) plus complete remission with partial hematologic recovery (CRh), the duration of CR+CRh, and the rate of conversion from transfusion dependence to independence.

The prescribing information contains a Boxed Warning alerting health care professionals and patients about the risk of differentiation syndrome which can be fatal."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olutasidenib-relapsed-or-refractory-acute-myeloid-leukemia-susceptible-idh1-mutation

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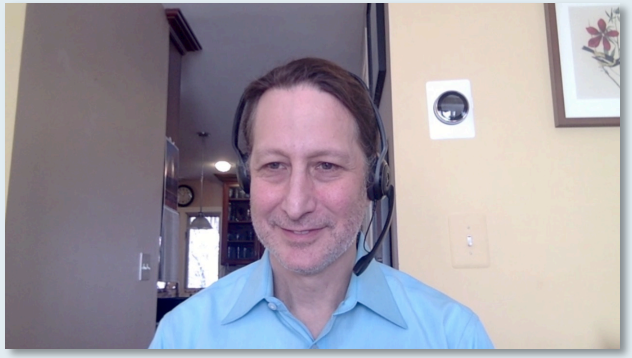

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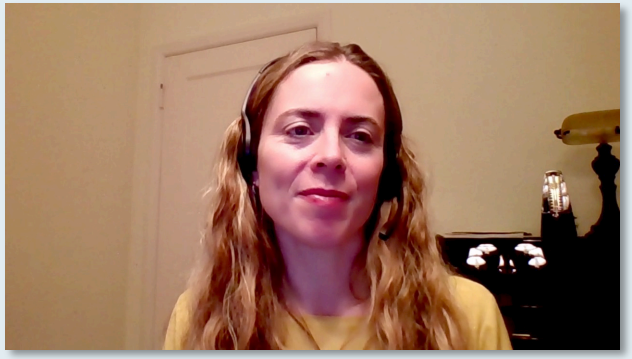

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# Practical Perspectives: Investigators Discuss Current Management and Actual Cases of Relapsed/Refractory Metastatic Colorectal Cancer

*A CME/MOC-Accredited Virtual Event*

**Wednesday, September 20, 2023**
**5:00 PM – 6:00 PM ET**

## Faculty

**Kristen K Ciombor, MD, MSCI**
**J Randolph Hecht, MD**

## Moderator

**Neil Love, MD**

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*Thank you for joining us!*

*Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.*

*CME and MOC credit information will be emailed to each participant within 5 business days.*

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