Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes – A Review of the 2022 ASCO Annual Meeting and EHA Congress

Wednesday, July 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard M Stone, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from Astellas, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, and Novartis.

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, the parent company of GHI, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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Data and Safety Monitoring Board/Committee	Epizyme Inc, Takeda Pharmaceuticals USA Inc

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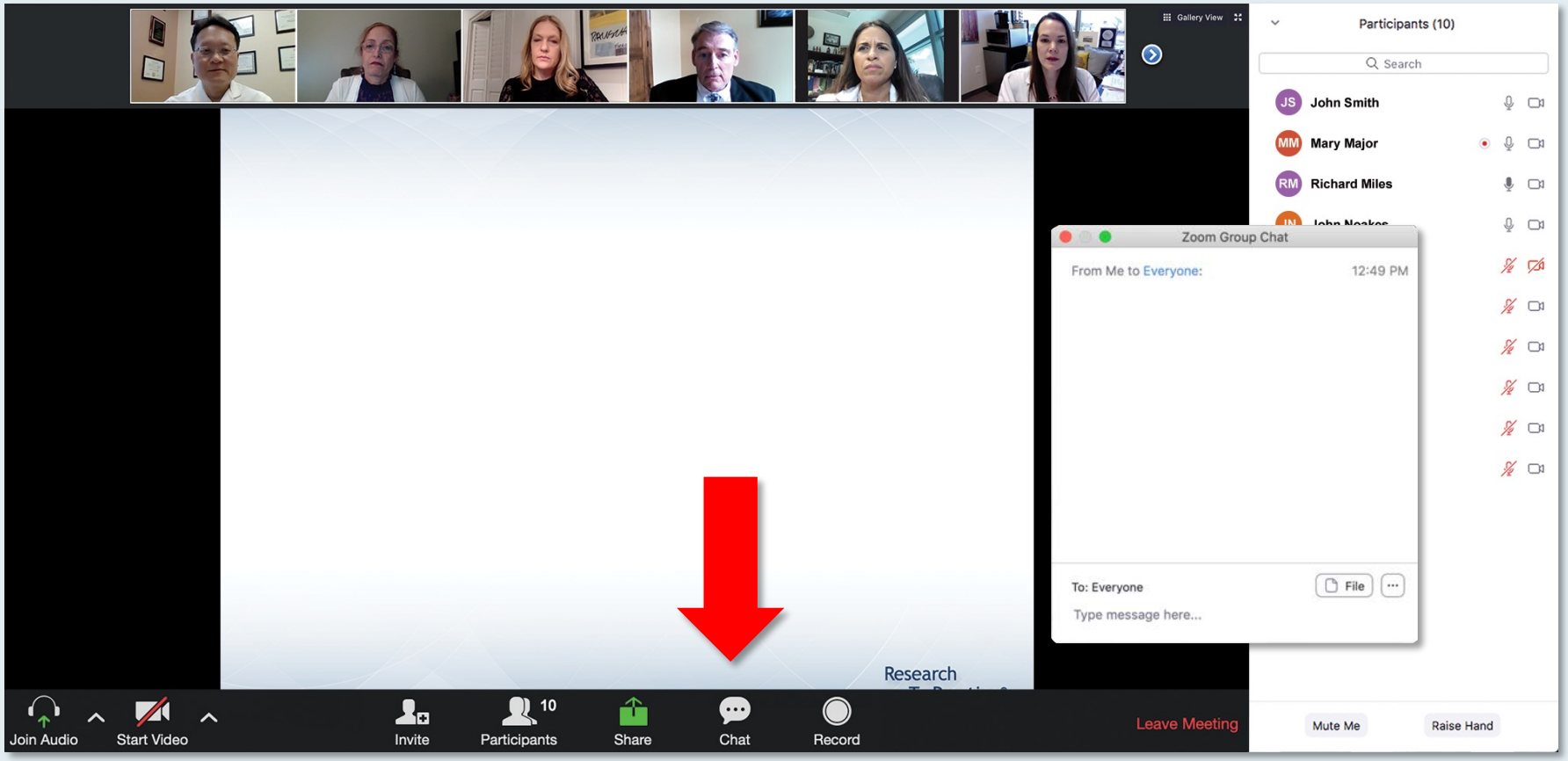
We Encourage Clinicians in Practice to Submit Questions



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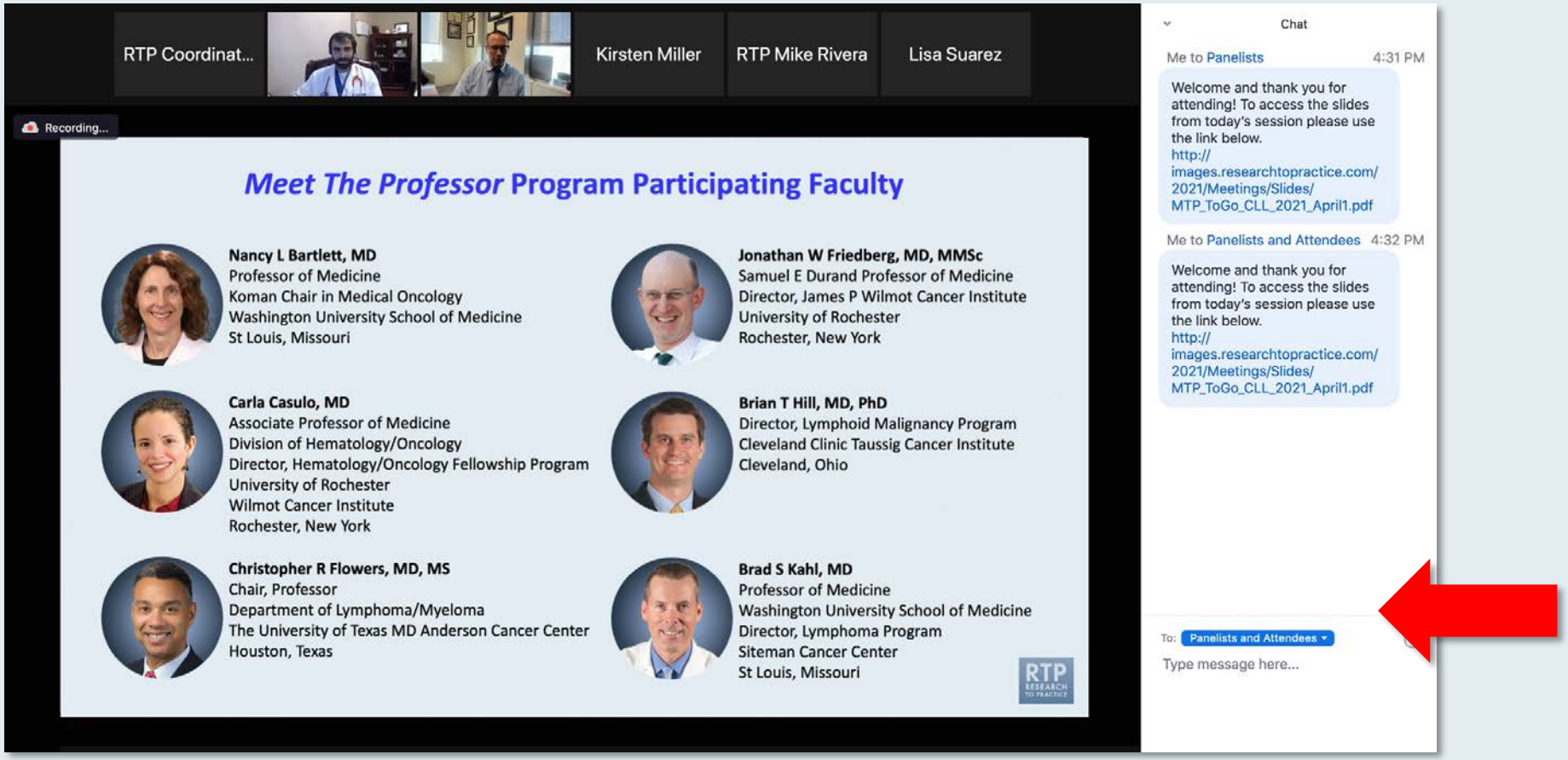
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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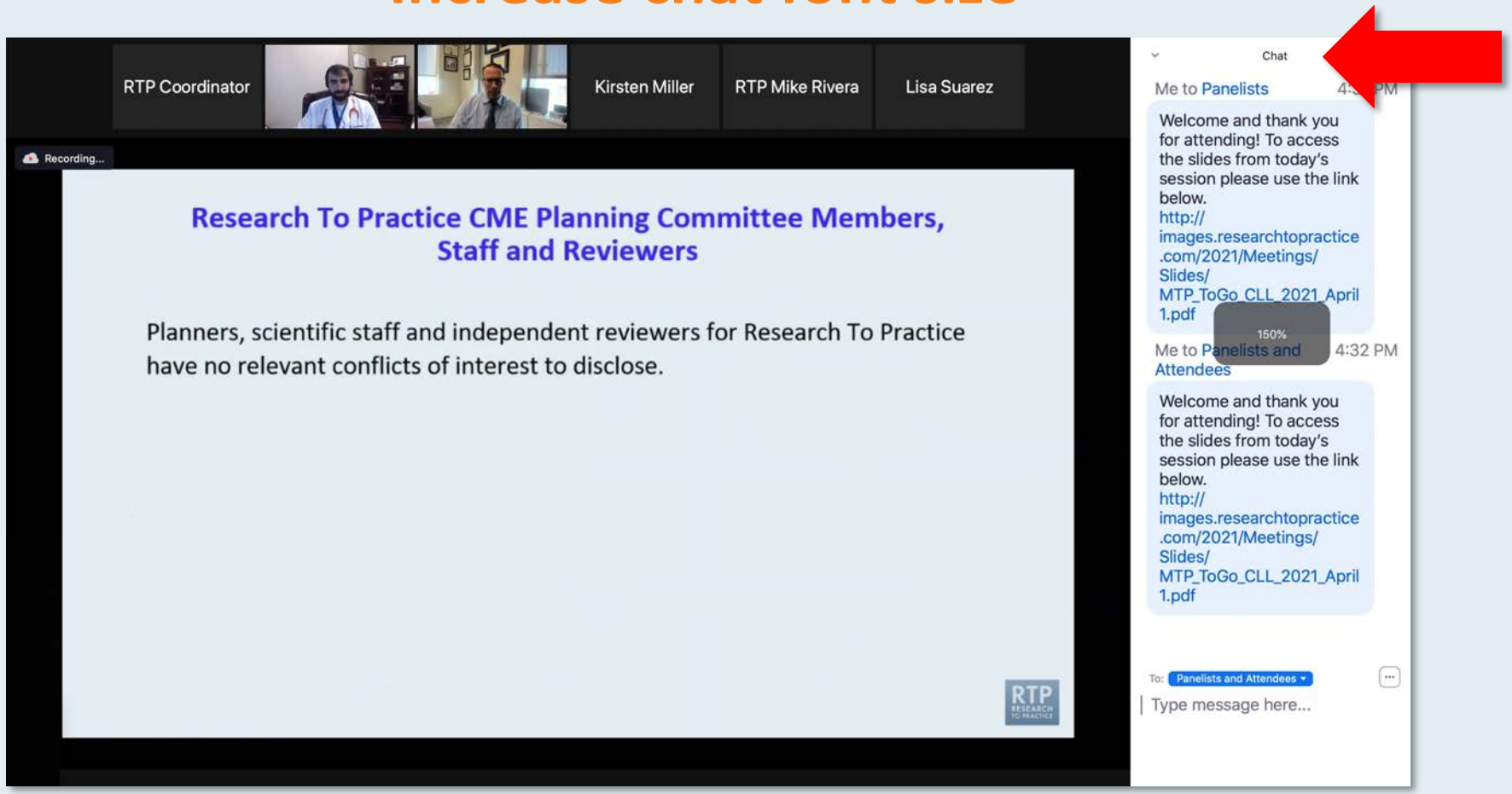
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Acute Myeloid Leukemia and Myelodysplastic Syndromes from ASH 2021

DR ANDREW BRUNNER

MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

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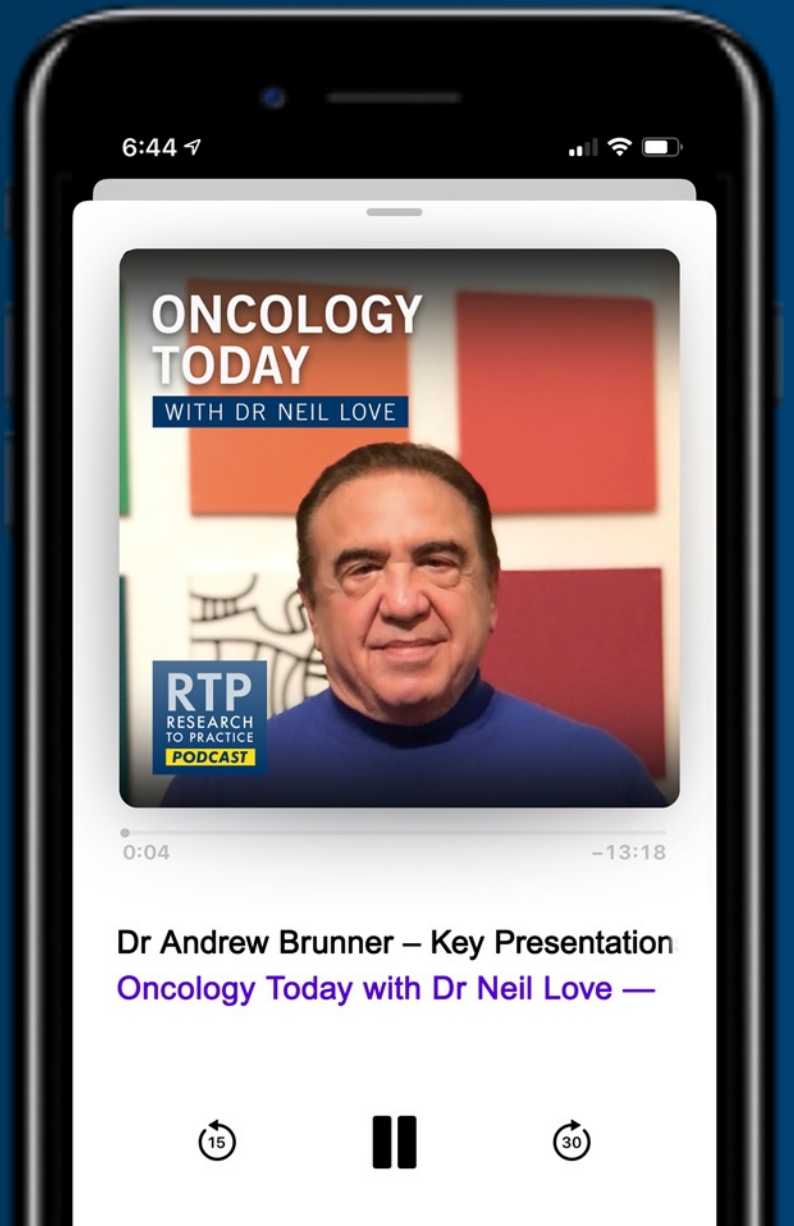

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, July 19, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel J DeAngelo, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Robin K Kelley, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, August 3, 2022
5:00 PM – 6:00 PM ET

Faculty

Prof Jonathan A Ledermann

Moderator

Neil Love, MD

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TO PRACTICE

Recent Advances in Medical Oncology:
A daylong CME hybrid (live/online) event

Saturday, August 6, 2022

9:00 AM – 4:30 PM PT (12:00 PM – 7:30 PM ET)

Bellagio Las Vegas | Las Vegas, Nevada

Faculty

Neeraj Agarwal, MD
Harold J Burstein, MD, PhD
Ibiayi Dagogo-Jack, MD
Rafael Fonseca, MD
Brad S Kahl, MD
Rutika Mehta, MD, MPH
Craig Moskowitz, MD
Joyce O'Shaughnessy, MD
Krina Patel, MD, MSc
Philip A Philip, MD, PhD, FRCP
Suresh S Ramalingam, MD
Sandy Srinivas, MD

Moderator

Neil Love, MD

In Partnership with the American Oncology Network

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Tuesday, August 9, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

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

MODERATOR
Neil Love, MD
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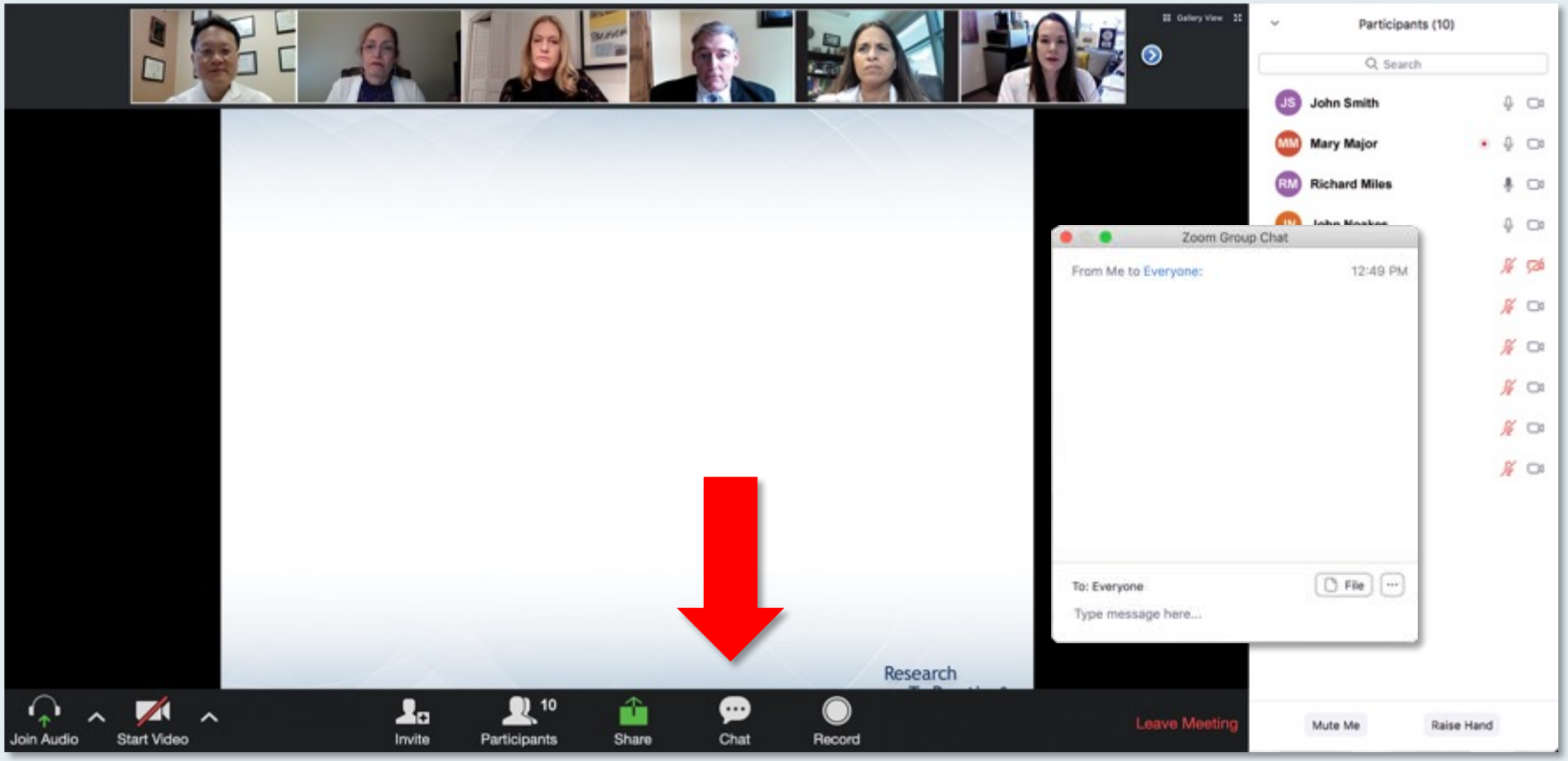

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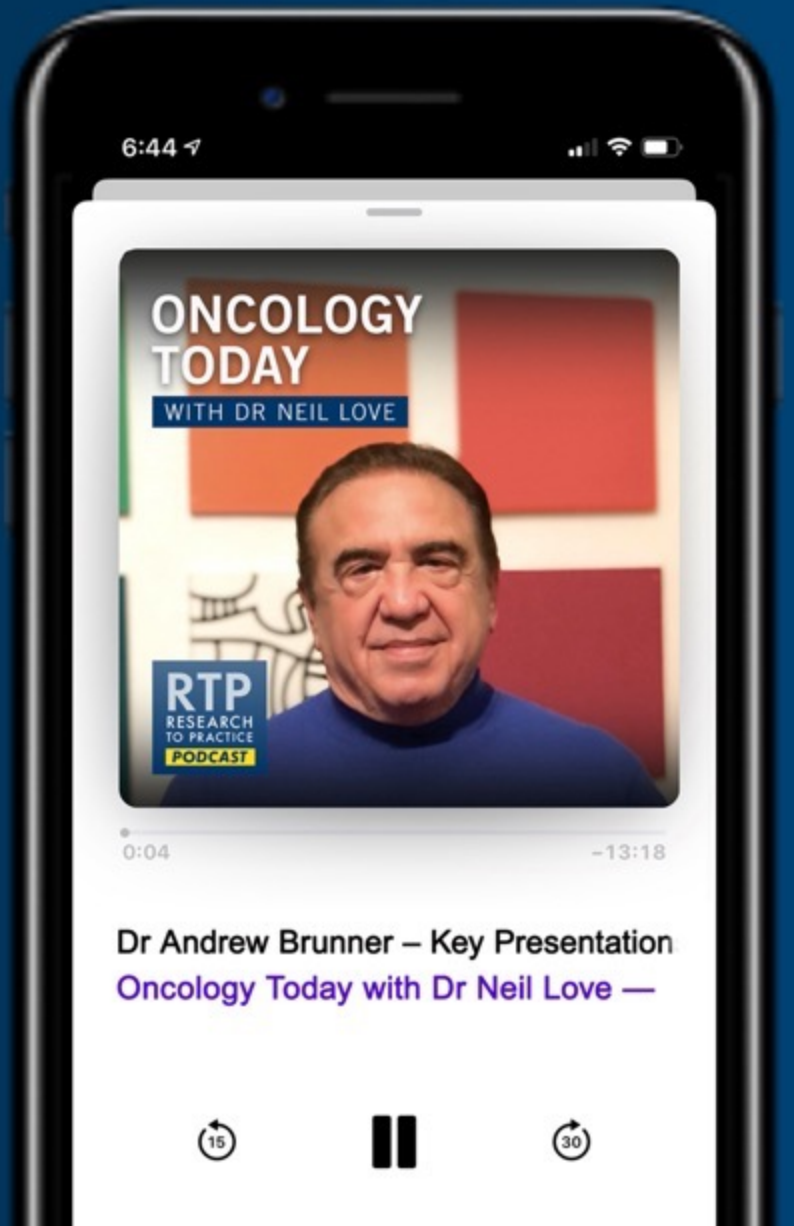

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Research To Practice CME Planning Committee Members, Staff and Reviewers

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Data and Safety Monitoring Board/Committee	Epizyme Inc, Takeda Pharmaceuticals USA Inc

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Lunch with the Investigators: Acute Myeloid Leukemia and Myelodysplastic Syndromes

A CME Hybrid Symposium Held in Conjunction with the 2022 ASCO Annual Meeting

Friday, June 3, 2022
11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Courtney D DiNardo, MD, MSCE
Michael R Savona, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

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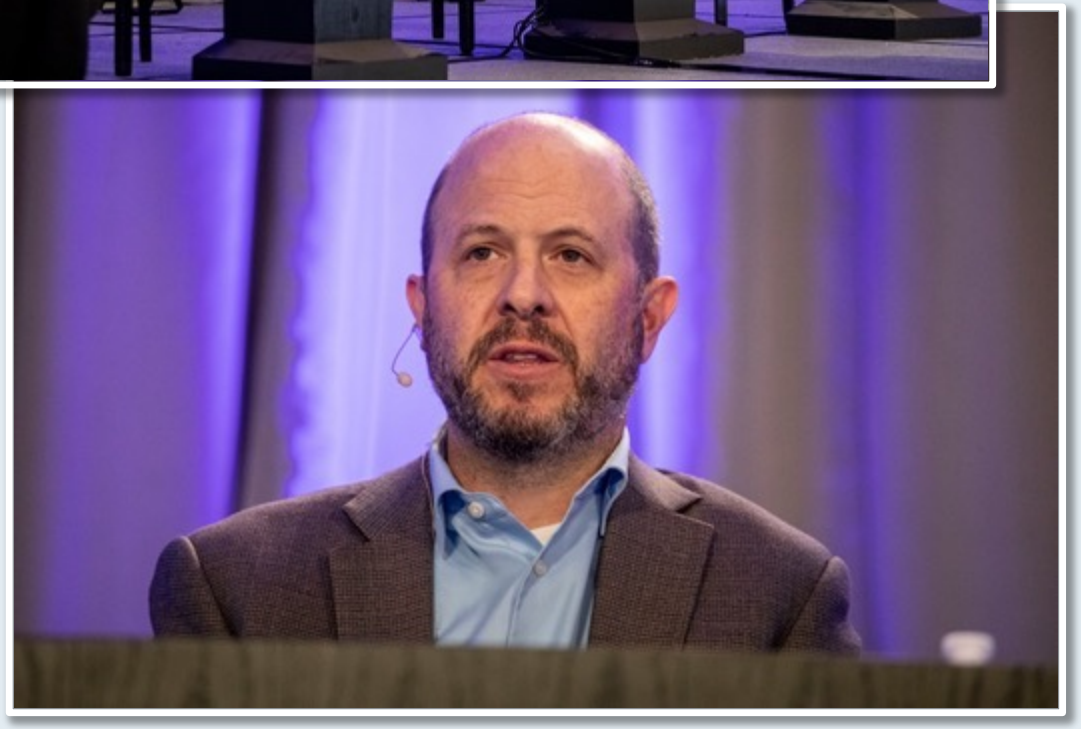
Agenda

Module 1 – Selection of Therapy for Older and Younger Patients with Acute Myeloid Leukemia (AML)

Module 2 – Therapy for Patients with AML and Targetable Mutations

Module 3 – Current and Future Management of Myelodysplastic Syndromes




Case 1 – Courtney D DiNardo,
Transplant is critical for survival regardless of initial treatment


Case 1 – Courtney D DiNardo, MD, MSCE
Real-world outcomes with CPX-351 vs VEN/AZA in NO AML

Agenda

Introduction – RATIFY Trial in Perspective

Module 1 – FLT3 Inhibitors

Module 2 – Anti-CD47 Antibody: Magrolimab

Module 3 – Anti-TIM-3 Antibody: Sabatolimab

Module 4 – CAR T-Cell Therapy

Module 5 – IDH Inhibitors

Module 6 – New Myelodysplastic Syndromes Classification System

Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

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ASH | 57th Annual Meeting & Exposition
Orlando, FL • December 5-8, 2015

6 The Multi-Kinase Inhibitor Midostaurin (M) Prolongs Survival Compared with Placebo (P) in Combination with Daunorubicin (D)/Cytarabine (C) Induction (ind), High-Dose C Consolidation (consol), and As Maintenance (maint) Therapy in Newly Diagnosed Acute Myeloid Leukemia (AML) Patients (pts) Age 18-60 with *FLT3* Mutations (muts): An International Prospective Randomized (rand)P-Controlled Double-Blind Trial (CALGB 10603/RATIFY [Alliance])

Plenary
Program: General Sessions
Session: Plenary Scientific Session

Sunday, December 6, 2015, 2:00 PM-4:00 PM
Hall D, Level 2 (Orange County Convention Center)

Richard M. Stone, MD[1], *Sumithra Mandrekar*[2*], *Ben L Sanford, MS*[3*], *Susan Geyer, PhD*[4,5*], *Clara D. Bloomfield, MD*[6], *Konstanze Dohner, M.D.*[7], *Christian Thiede, MD*[8], *Guido Marcucci, MD*[9], *Francesco Lo-Coco*[10*], *Rebecca B. Klisovic, MD*[11], *Andrew Wei, MBBS, PhD*[12], *Jorge Sierra, MD, PhD*[13], *Miguel A. Sanz, MD, PhD*[14], *Joseph M. Brandwein, MD, FRCPC*[15], *Theo de Witte, MD*[16], *Dietger Niederwieser, MD*[17], *Frederick R. Appelbaum, MD*[18], *Bruno C. Medeiros, MD*[19], *Martin S Tallman, MD*[20*], *Jurgen Krauter, MD*[21*], *Richard F. Schlenk, MD*[7], *Arnold Ganser, M.D.*[22], *Hubert Serve*[23], *Gerhard Ehninger, MD*[24], *Sergio Amadori, MD*[25], *Richard A. Larson, MD*[26] *and Hartmut Dohner, MD*[7]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a *FLT3* Mutation

R.M. Stone, S.J. Mandrekar, B.L. Sanford, K. Laumann, S. Geyer, C.D. Bloomfield, C. Thiede, T.W. Prior, K. Döhner, G. Marcucci, F. Lo-Coco, R.B. Klisovic, A. Wei, J. Sierra, M.A. Sanz, J.M. Brandwein, T. de Witte, D. Niederwieser, F.R. Appelbaum, B.C. Medeiros, M.S. Tallman, J. Krauter, R.F. Schlenk, A. Ganser, H. Serve, G. Ehninger, S. Amadori, R.A. Larson, and H. Döhner

N Engl J Med 2017;377(5):454-64.

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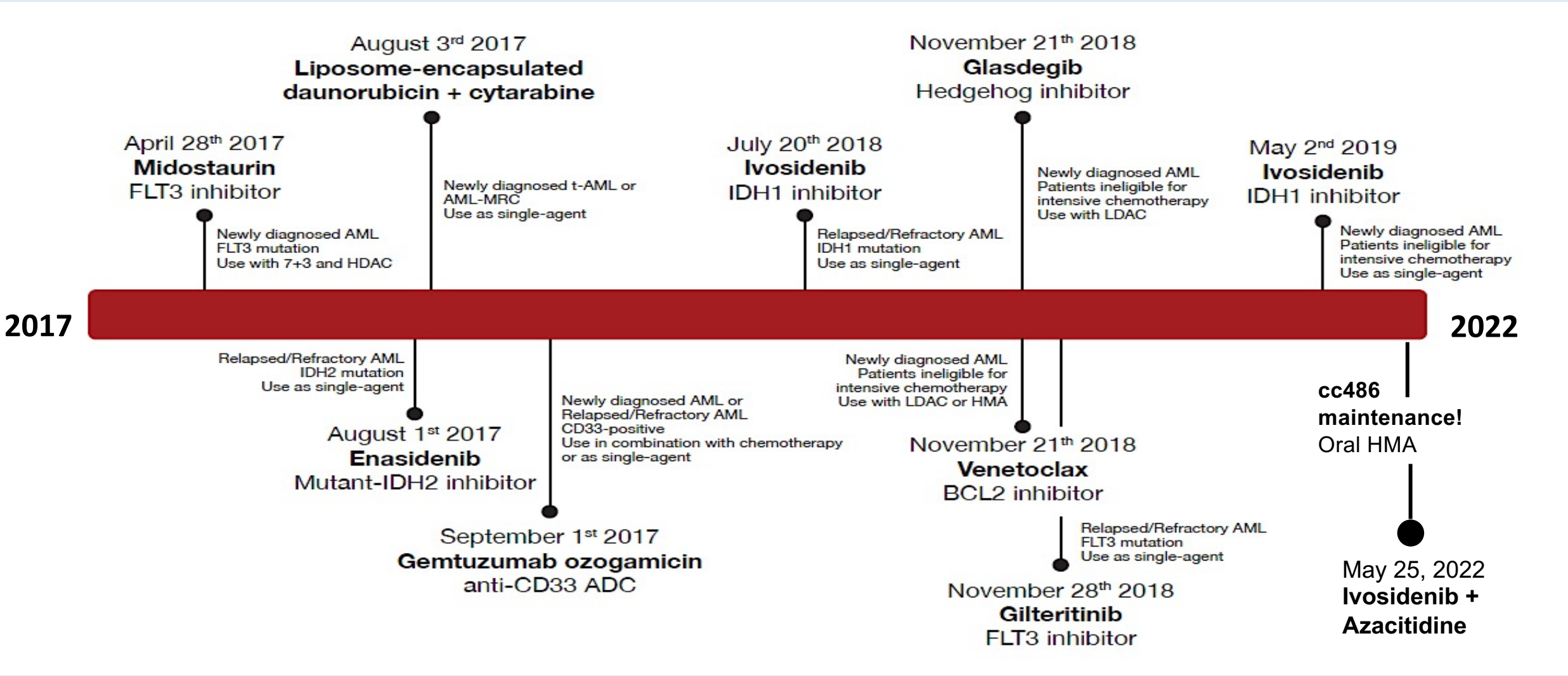
The Rapidly Evolving Treatment Landscape of AML: FDA Approvals



Richard-Carpentier G, DiNardo CD. *Hematology Am Soc Educ Program* 2019(1):548-56.

Content Courtesy of Courtney D DiNardo, MD, MSCE

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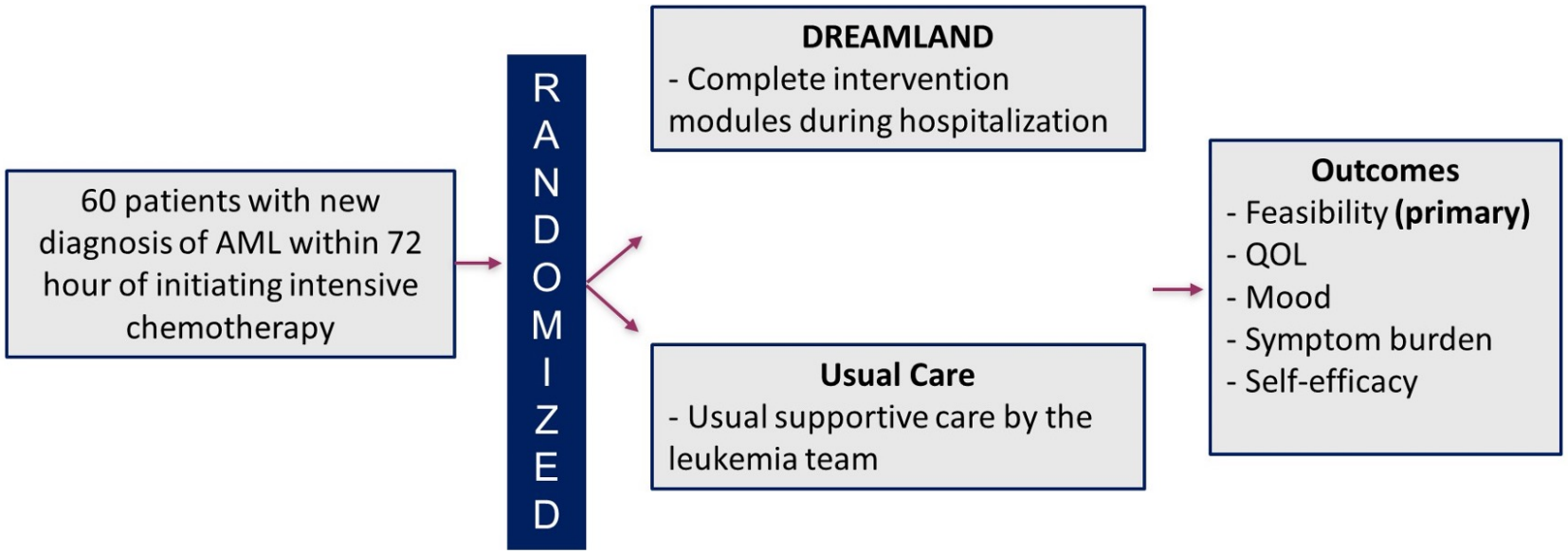
ASCO 2022 | Abstract 12018

Psychological Mobile App for Patients with Acute Myeloid Leukemia (AML): A Randomized Clinical Trial

Areej El-Jawahri, Marlise Rachael Luskin, Joseph A. Greer, Mitchell W. Lavoie, Dagny Vaughn, Daniel Yang, Kofi Boateng, Richard Newcomb, Amir Tahmasb Fathi, Gabriela Hobbs, Andrew Mark Brunner, Gregory A. Abel, Richard M. Stone, Daniel J. DeAngelo, Martha Wadleigh, Jennifer S. Temel

DREAMLAND Trial Design



El-Jawahri, A, manuscript under review

MGH 1811

CORE

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El-Jawahri A et al. ASCO 2022;Abstract 12018.

Patient Eligibility

Inclusion Criteria

- Age ≥ 18 years
- New diagnosis of AML
- Hospitalized for intensive chemotherapy requiring a 4-6 week hospitalization

Exclusion Criteria

- Unable to comprehend English
- Uncontrolled psychiatric disorders or other conditions, which the treating oncologist believed prohibited the ability to provide informed consent

El-Jawahri A et al. ASCO 2022;Abstract 12018.

El-Jawahri A et al. ASCO 2022;Abstract 12018.

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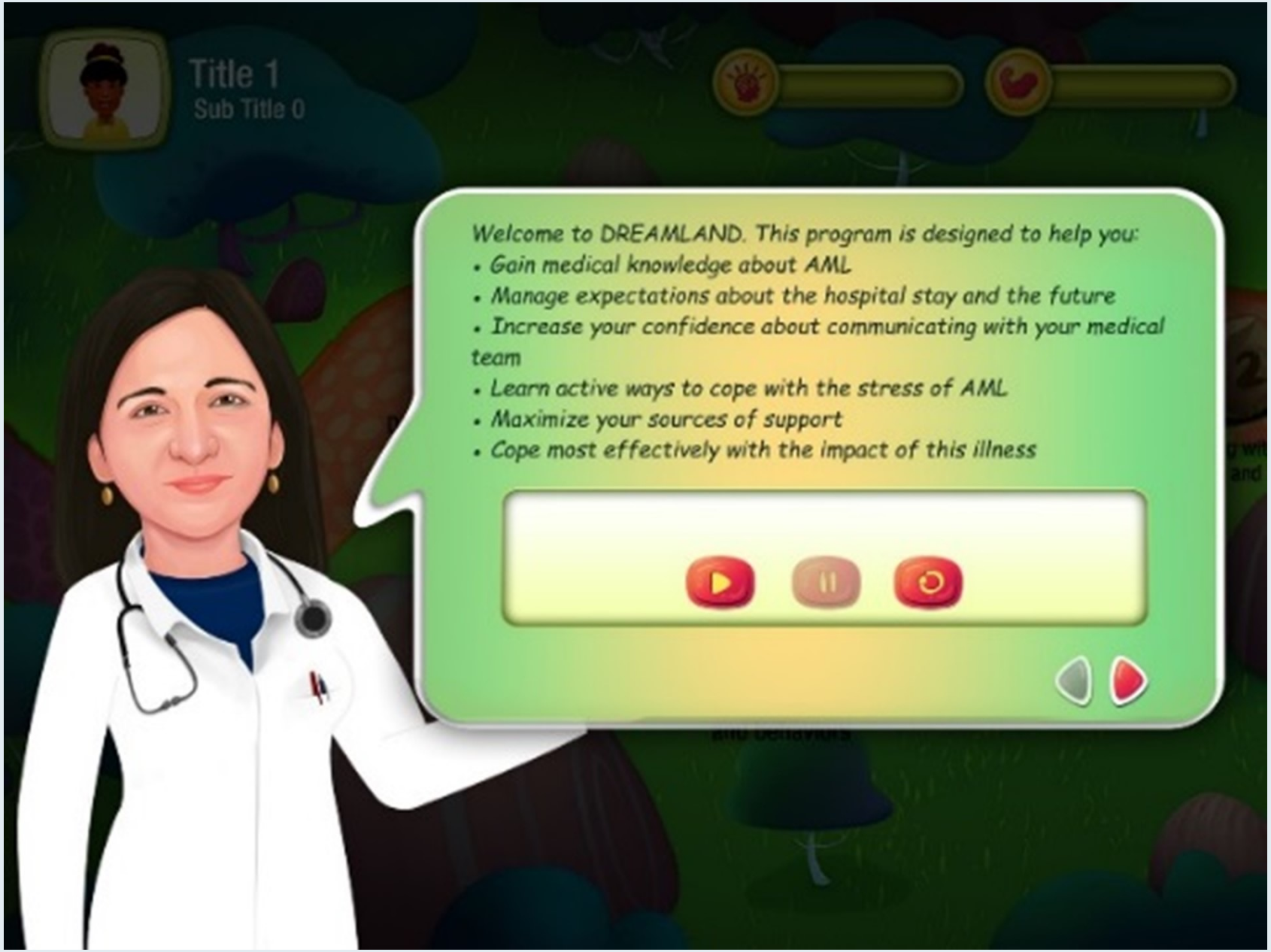
El-Jawahri A et al. ASCO 2022;Abstract 12018.

El-Jawahri A et al. ASCO 2022;Abstract 12018.

El-Jawahri A et al. ASCO 2022;Abstract 12018.



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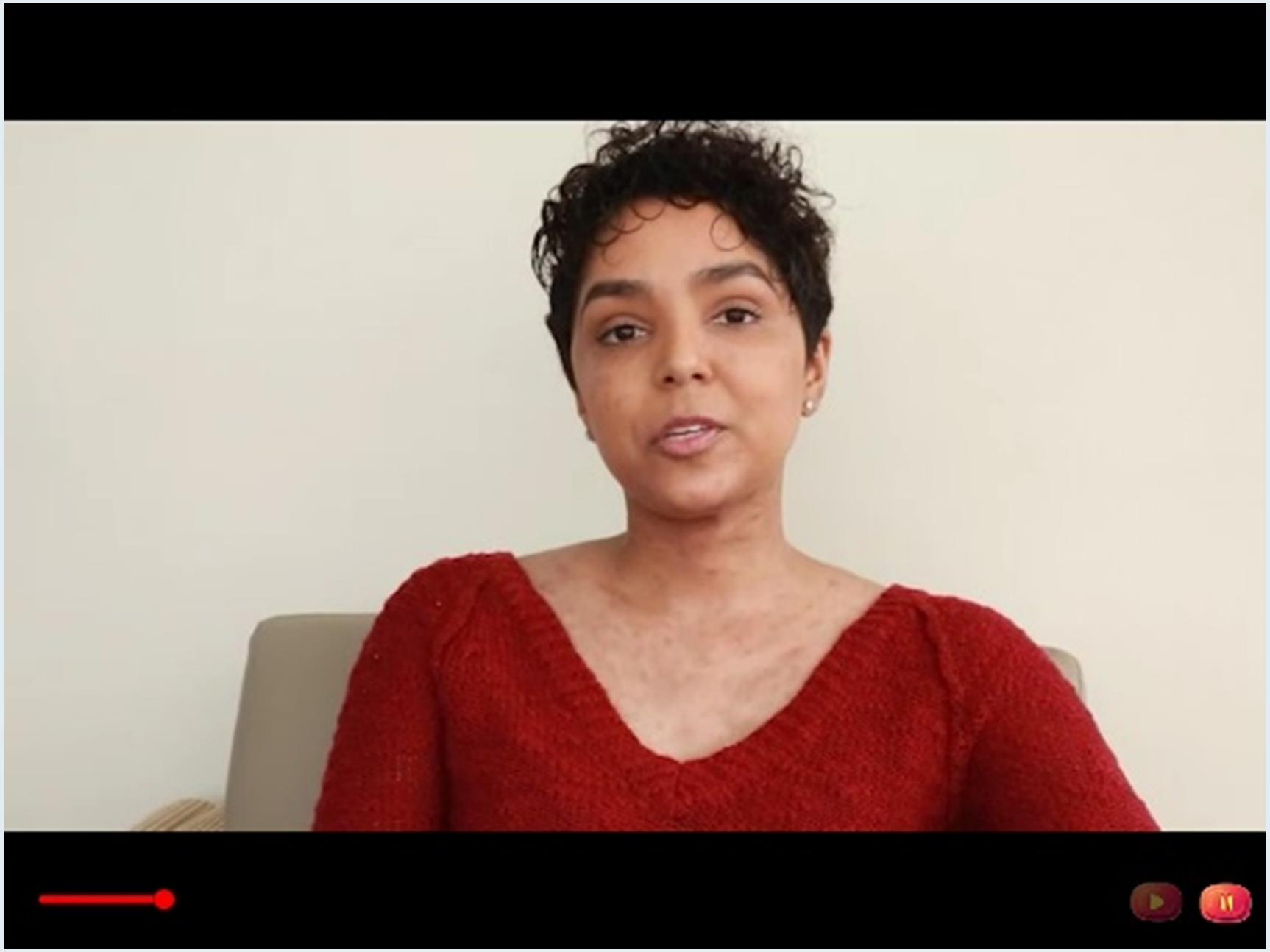

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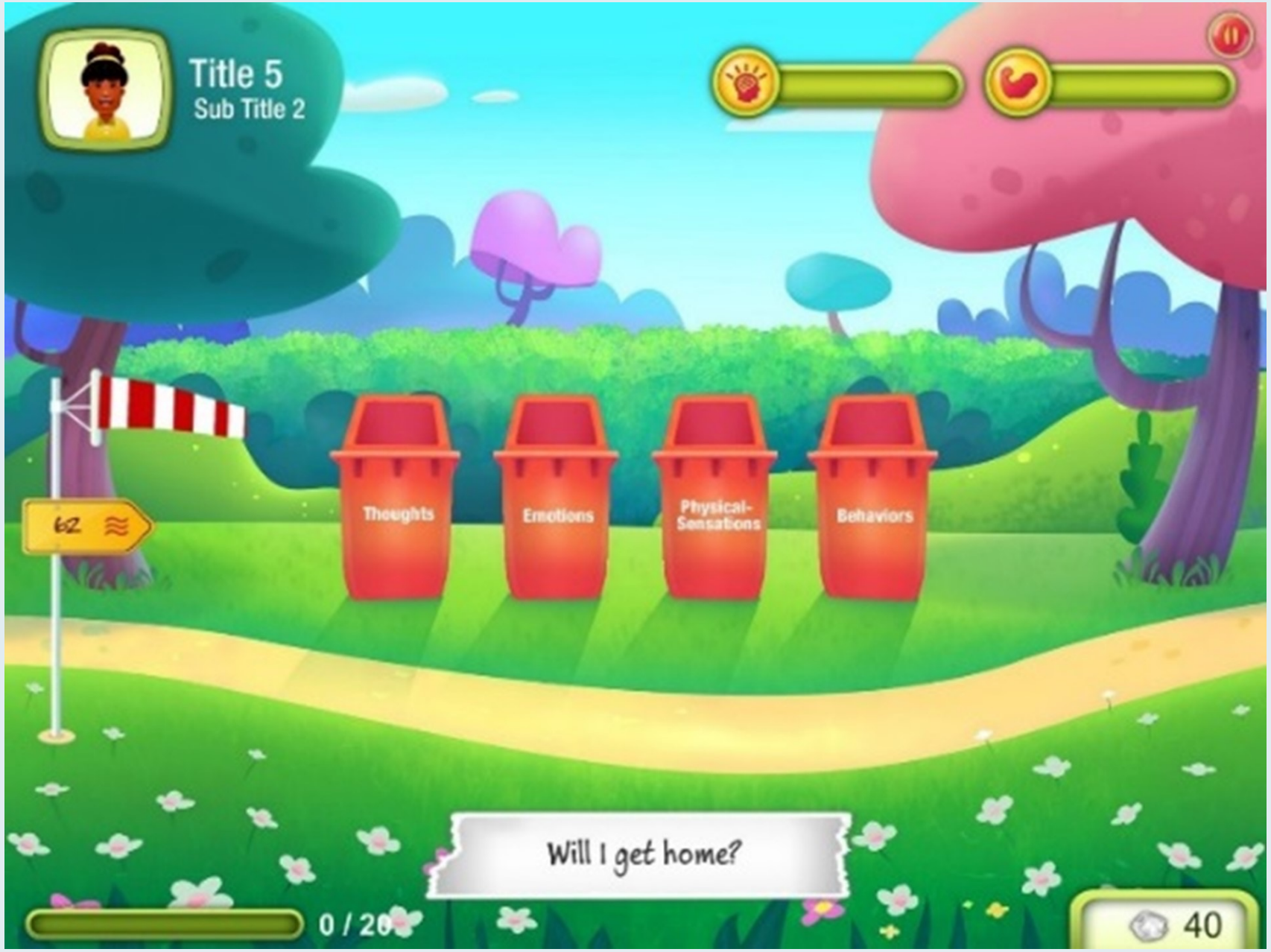

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Agenda

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Module 8 – CPX-351

Module 9 – Other Key Datasets

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HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION
2022

P523 MIDOSTAURIN PLUS INTENSIVE CHEMOTHERAPY IN FLT3 MUTATED AML. "REAL LIFE" DATA VERSUS THE RATIFY STUDY

Topic: 04. Acute myeloid leukemia - Clinical

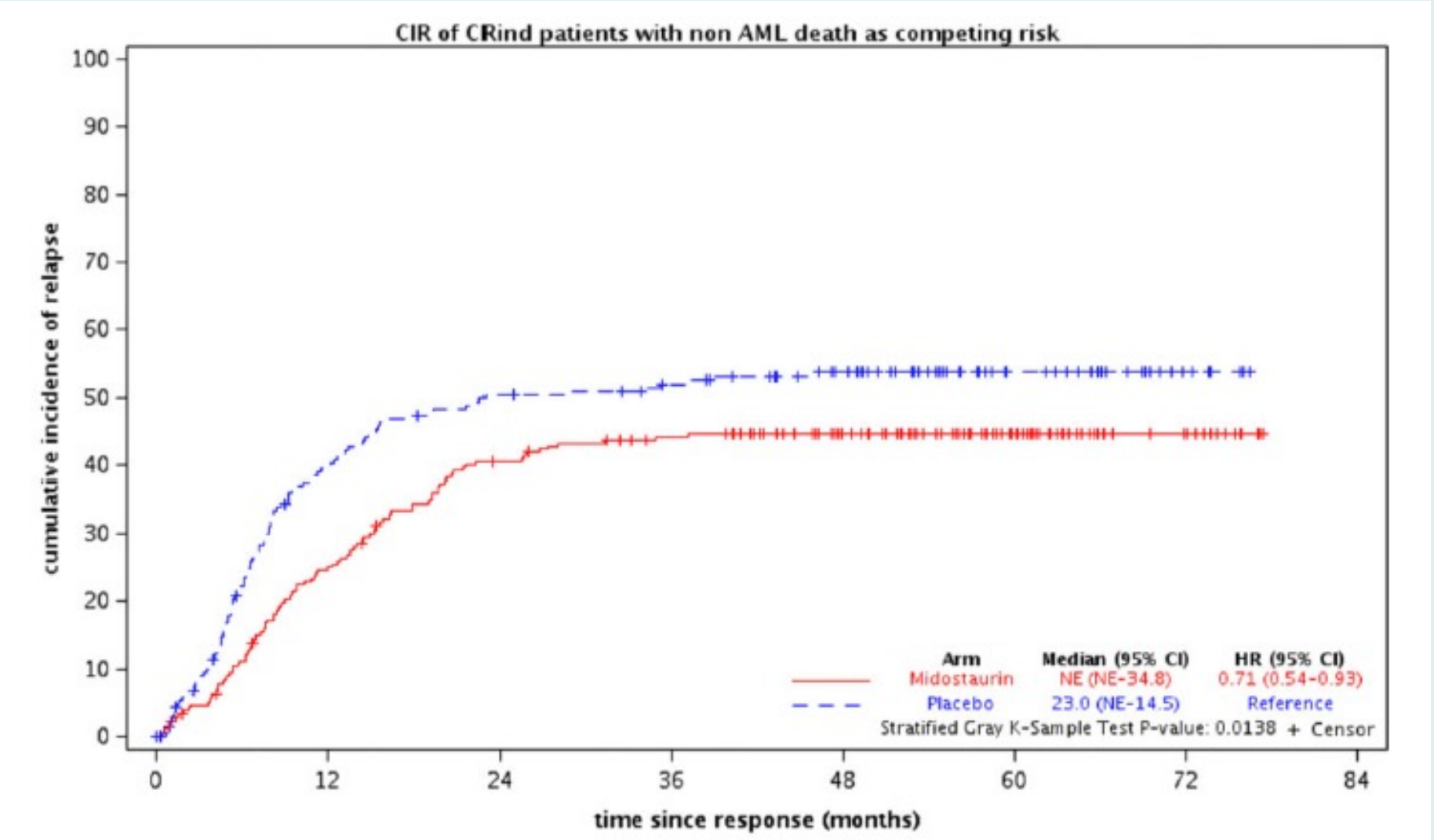
Adolfo De La Fuente[1, 1], Marina Diaz Beya[2], Paola Beneit[3], Carmen Botella[4], Ainhoa Fernandez Moreno[5], Antonia Sampol[6], Montserrat Arnan Sangerman[7], Ana Yeguas Bermejo[8], Maria de la Luz Amigo[9], Jorge Labrador[10], Antoni Garcia Guinon[11], Ana Garrido[12], Josefina Serrano[13], Susana Vives Polo[14], Maria Garcia Fortes[15], Maria Jose Sayas[16], Juan Miguel Bergua[17], Maria Teresa Olave[18], Ferra Vall LLovera[19], Juan Bargay[20], Maria Pereiro Sanchez[21], Raimundo Garcia Boyero[22], Antonio Diaz Lopez[23], Mar Tormo[24]

Midostaurin reduces relapse in *FLT3*-mutant acute myeloid leukemia: the Alliance CALGB 10603/RATIFY trial

Richard A. Larson[1], Sumithra J. Mandrekar[2,3], Lucas J. Huebner[3], Ben L. Sanford[4], Kristina Laumann[3], Susan Geyer[3], Clara D. Bloomfield[5], Christian Thiede[6], Thomas W. Prior[5], Konstanze Döhner[7], Guido Marcucci[8], Maria Teresa Voso[9], Rebecca B. Klisovic[10], Ilene Galinsky[11], Andrew H. Wei[12], Jorge Sierra[13], Miguel A. Sanz[14], Joseph M. Brandwein[15], Theo de Witte[16], Dietger Niederwieser[17], Frederick R. Appelbaum[18], Bruno C. Medeiros[19], Martin S. Tallman[20], Jürgen Krauter[21], Richard F. Schlenk[7,22], Arnold Ganser[21], Hubert Serve[23], Gerhard Ehninger[6], Sergio Amadori[9], Insa Gathmann[24], Hartmut Döhner[7], Richard M. Stone[11]

Leukemia 2021;35(9):2539-51.

RATIFY: Cumulative Incidence of Relapse in Patients Achieving Complete Response During Induction (CRind)



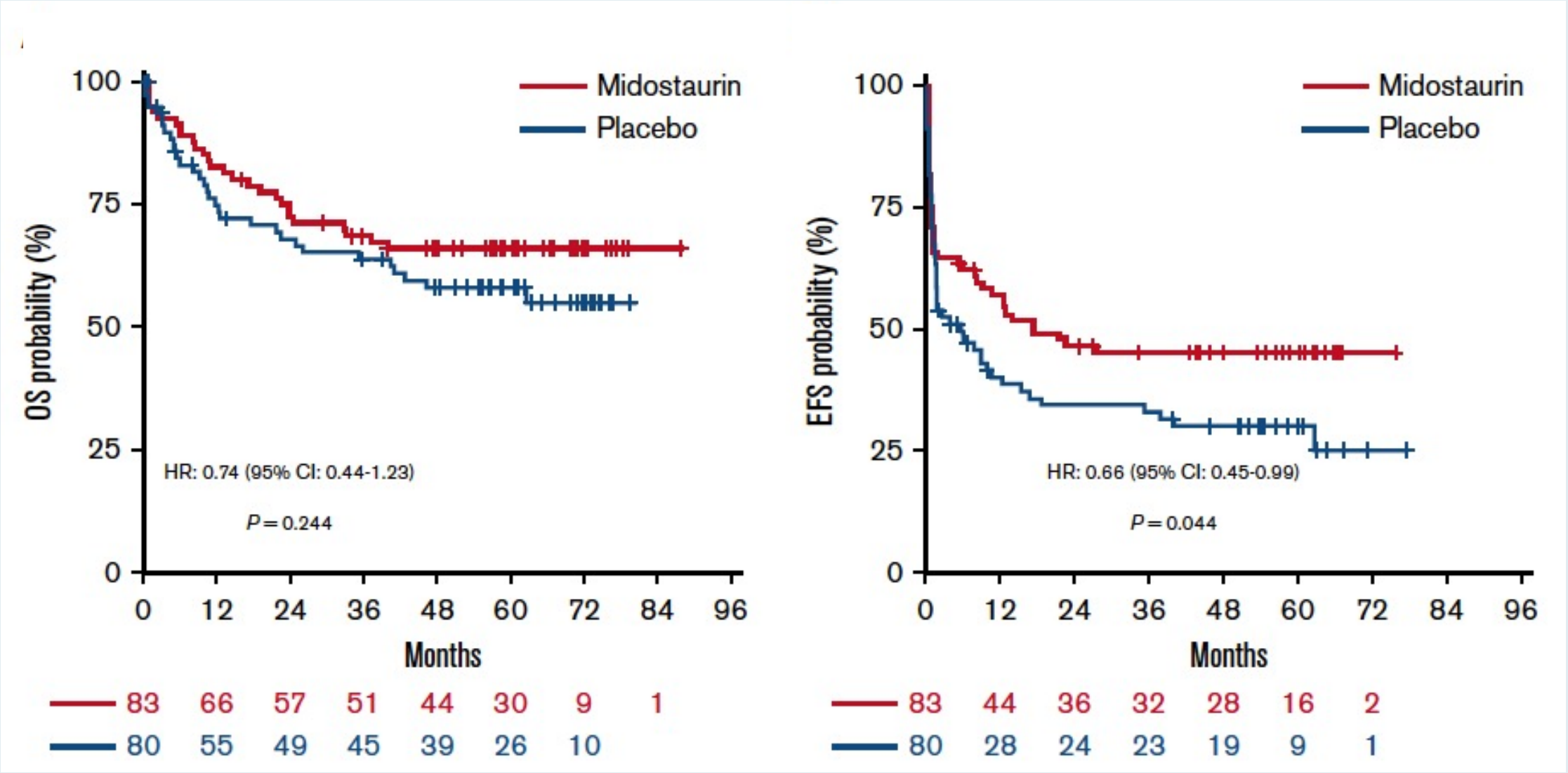
Lawson RA et al. *Leukemia* 2021;35(9):2539-51.

Midostaurin in patients with acute myeloid leukemia and *FLT3*-TKD mutations: a subanalysis from the RATIFY trial

Maria Teresa Voso,[1] Richard A. Larson,[2] Dan Jones,[3] Guido Marcucci,[3] Thomas Prior,[3] Jürgen Krauter,[4,5] Michael Heuser,[4] Serena Lavorgna,[1] Josep Nomdedeu,[6] Susan M. Geyer,[7] Alison Walker,[3] Andrew H. Wei,[8] Jorge Sierra,[6] Miguel A. Sanz,[9,10] Joseph M. Brandwein,[11] Theo M. de Witte,[12] Joop H. Jansen,[12] Dietger Niederwieser,[13] Frederick R. Appelbaum,[14] Bruno C. Medeiros,[15] Martin S. Tallman,[16] Richard F. Schlenk,[17-19] Arnold Ganser,[4] Sergio Amadori,[1] Yuan Cheng,[20] YinMiao Chen,[20] Celine Pallaud,[21] Ling Du,[22] Alfonso Piciocchi,[23] Gerhard Ehninger,[24] John Byrd,[3] Christian Thiede,[24] Konstanze Döhner,[17] Richard M. Stone,[25] Hartmut Döhner,[17,*] Clara D. Bloomfield,[3,*] and Francesco Lo-Coco[1,*]

***Blood Adv* 2020;4(19):4945-54.**

RATIFY: Survival in Patients with AML and FLT3-TKD mutations



Voso MT et al. *Blood Adv* 2020;4(19):4945-54.

Quizartinib Prolonged Survival vs Placebo Plus Intensive Induction and Consolidation Therapy Followed by Single-Agent Continuation in Patients Ages 18-75 Years With Newly Diagnosed *FLT3*-ITD+ AML

Harry P. Erba,[1] Pau Montesinos,[2] Radovan Vrhovac,[3] Elzbieta Patkowska,[4] Hee-Je Kim,[5] Pavel Zak,[6] Po-Nan Wang,[7] Tsvetomir Mitov,[8] James Hanyok,[9] Li Liu,[9] Aziz Benzohra,[9] Arnaud Lesegretain,[9] Jorge Cortes,[10] Alexander Perl,[11] Mikkael Sekeres,[12] Hervé Dombret,[13] Sergio Amadori,[14] Jianxiang Wang,[15] Mark Levis,[16] Richard F. Schlenk[17]

[1]Duke Cancer Institute, Durham, NC, USA; [2]La Fe University and Polytechnic Hospital, Valencia, Spain; [3]University Hospital Centre Zagreb, Zagreb, Croatia; [4]Institute of Hematology and Blood Transfusion, Warsaw, Poland; [5]Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea; [6]University Hospital Hradec Kralove, Hradec Kralove, Czechia; [7]Chang Gung Medical Foundation, Linkou, Taiwan; [8]Daiichi Sankyo UK Ltd, Uxbridge, United Kingdom; [9]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [10]Augusta University Medical Center, Augusta, GA, USA; [11]University of Pennsylvania, Philadelphia, PA, USA; [12]Sylvester Cancer Center, University of Miami Health System, Miami, FL, USA; [13]Saint Louis Hospital, University of Paris, Paris, France; [14]Tor Vergata Polyclinic Hospital Rome, Rome, Italy; [15]Institute of Hematology and Blood Diseases Hospital, Tianjin, China; [16]Johns Hopkins University, Baltimore, MD, USA; [17]Heidelberg University Hospital and German Cancer Research Center, Heidelberg, Germany

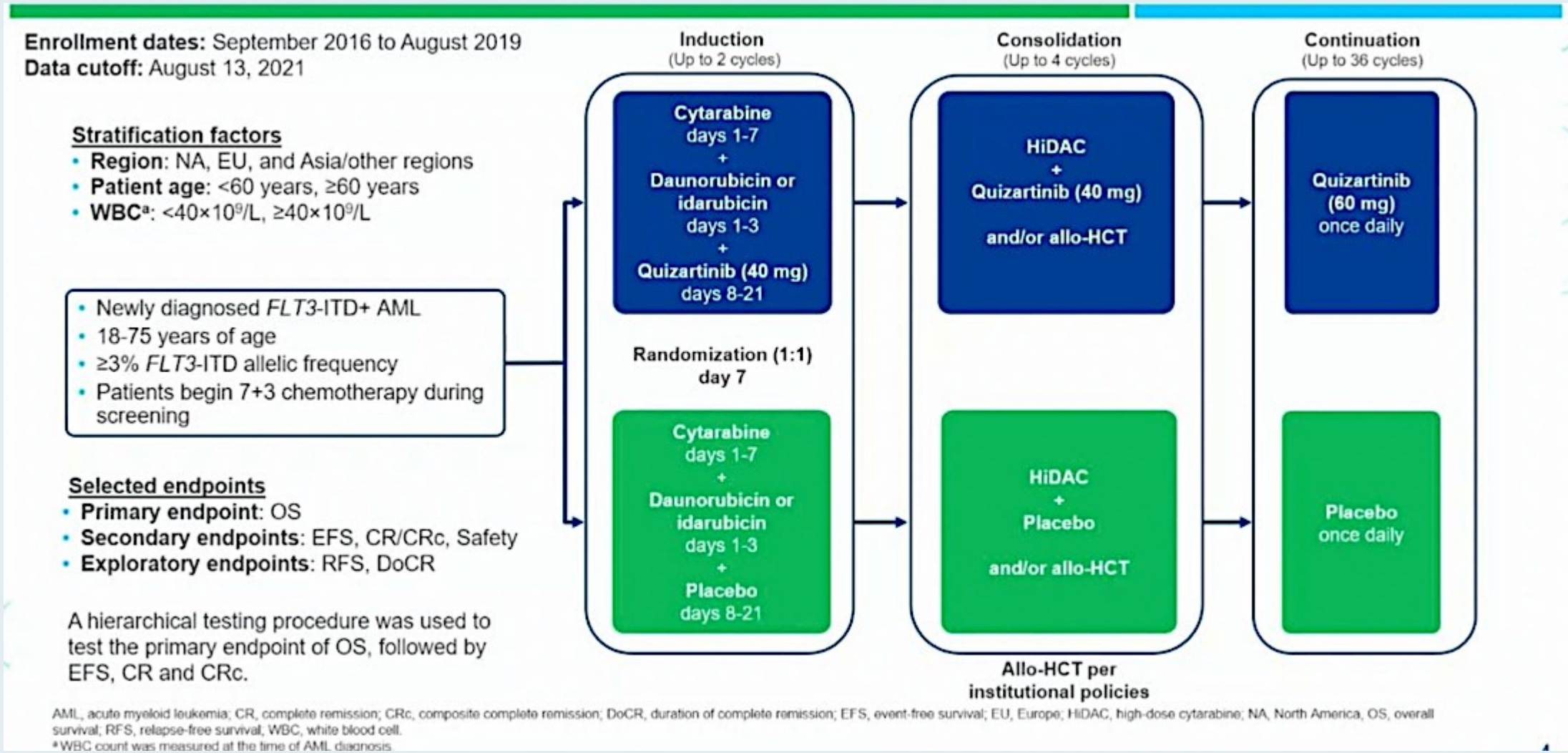
QuANTUM-FIRST STUDY

AML, acute myeloid leukemia; FLT3, fms related receptor tyrosine kinase 3; ITD+, internal tandem duplication positive.

EHA 2022;Abstract S100.

RTP RESEARCH TO PRACTICE

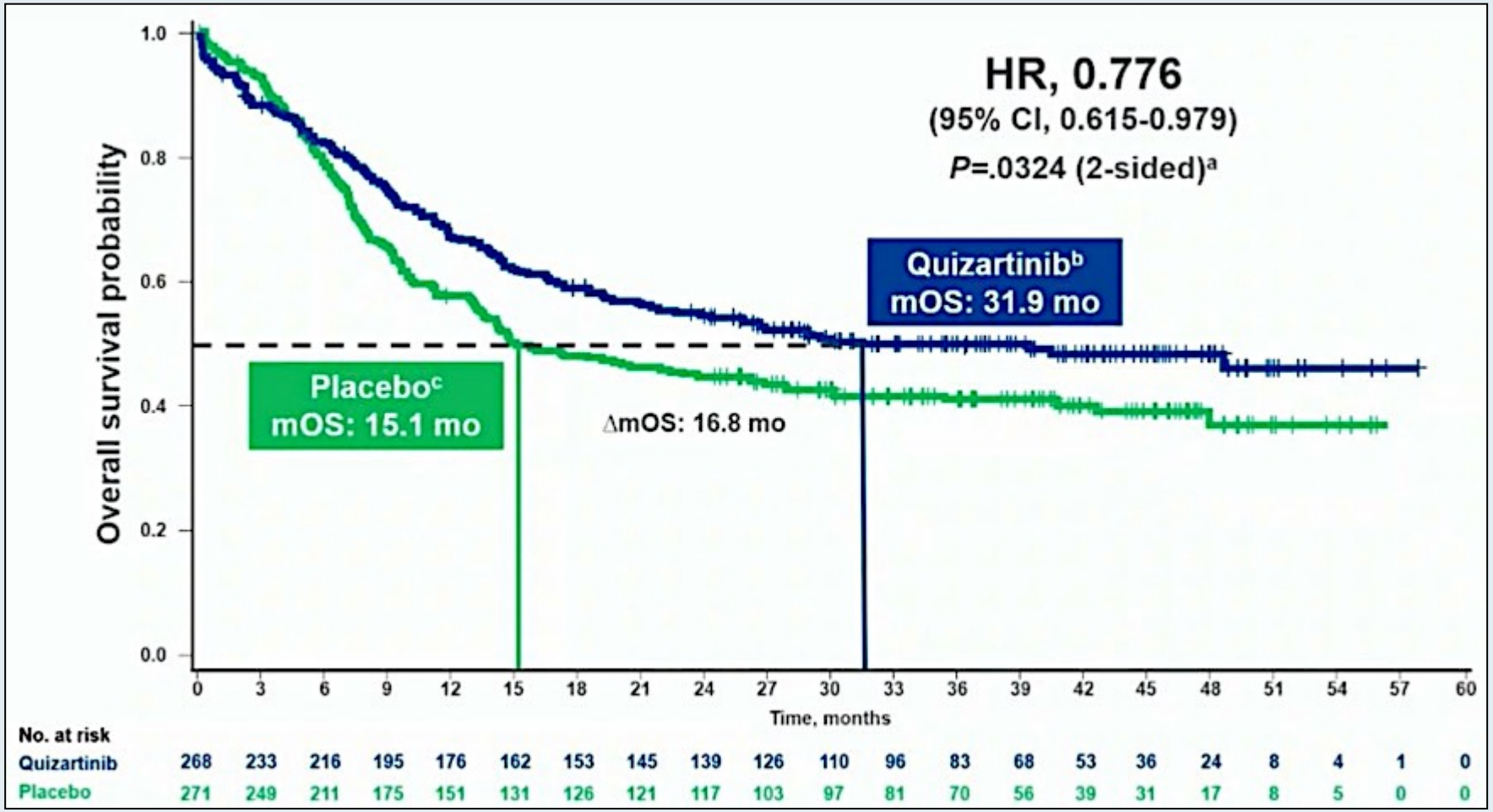
QuANTUM-First Phase III Trial (NCT02668653): Quizartinib with Standard Induction Chemotherapy and Consolidation Followed by Single-Agent Quizartinib



AML, acute myeloid leukemia; CR, complete remission; CRc, composite complete remission; DoCR, duration of complete remission; EFS, event-free survival; EU, Europe; HiDAC, high-dose cytarabine; NA, North America, OS, overall survival; RFS, relapse-free survival, WBC, white blood cell.
[a]WBC count was measured at the time of AML diagnosis

Erba H et al. EHA 2022;Abstract S100.

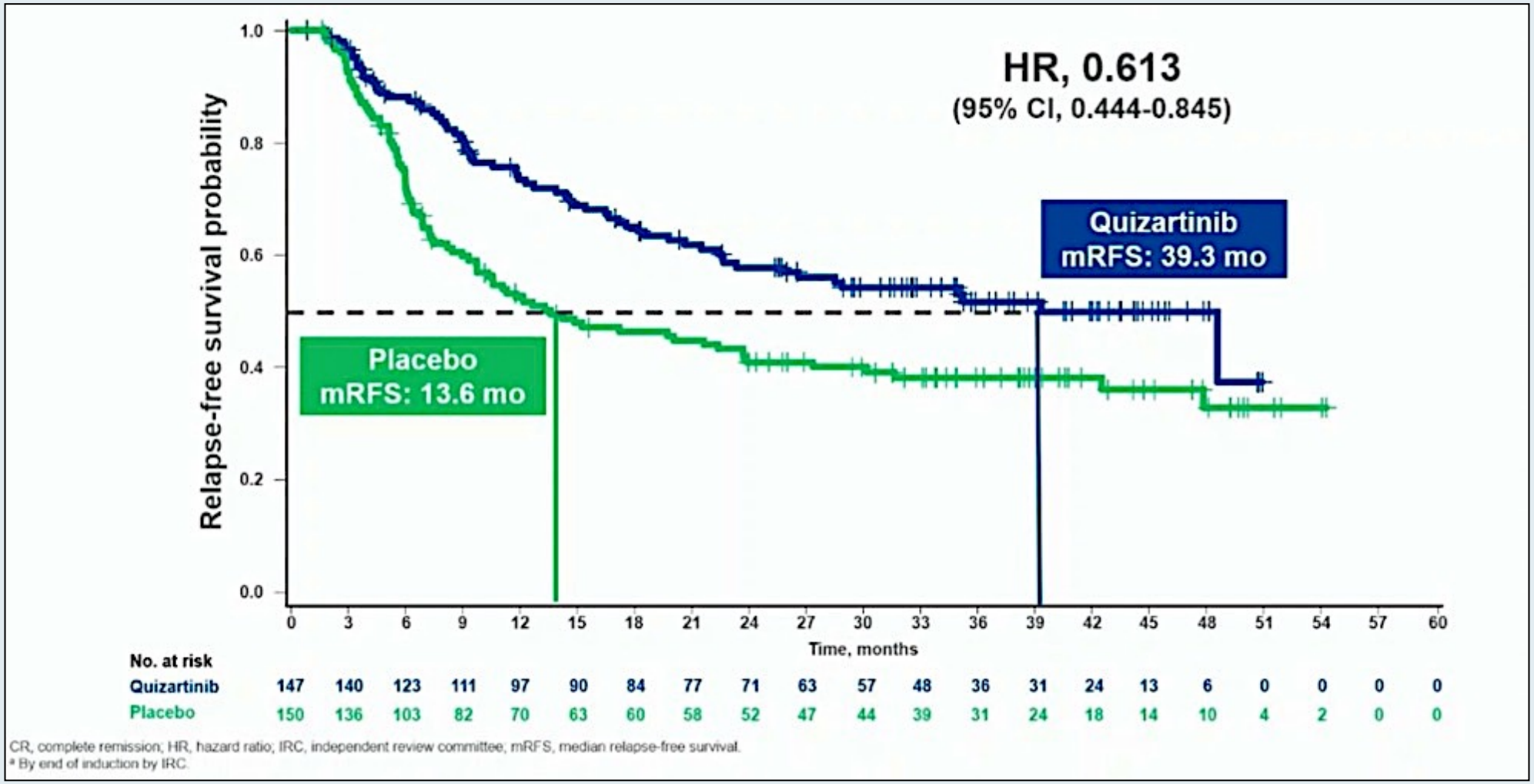
QuANTUM-First: Overall Survival



Erba H et al. EHA 2022;Abstract S100.

RTP RESEARCH TO PRACTICE

QuANTUM-First: Relapse-Free Survival



CR, complete remission; HR, hazard ratio; IRC, independent review committee; mRFS, median relapse-free survival.
[a] By end of induction by IRC.

Erba H et al. EHA 2022;Abstract S100.

RTP RESEARCH TO PRACTICE

QuANTUM-First: Summary of Treatment-Emergent Adverse Events (TEAEs) Occurring in ≥20% of Patients

TEAEs, %	Quizartinib (N=265)[a]		Placebo (N=268)[a]	
Hematologic adverse events	All Grades	Grade ≥3	All Grades	Grade ≥3
Febrile neutropenia	44.2	43.4	42.2	41.0
Neutropenia	20.4	18.1	10.1	8.6
Non-hematologic adverse events	All Grades	Grade ≥3	All Grades	Grade ≥3
Pyrexia	42.3	4.5	40.7	4.9
Diarrhea	37.0	3.8	35.1	3.7
Hypokalemia	35.1	18.9	35.8	16.4
Nausea	34.0	1.5	31.3	1.9
Headache	27.5	0	19.8	0.7
Rash	26.0	3.0	24.6	1.1
Vomiting	24.5	0	19.8	1.5
Stomatitis	21.5	4.5	20.9	3.0
Constipation	21.1	0.4	25.7	0

Erba H et al. EHA 2022;Abstract S100.

QUIZARTINIB WITH DECITABINE AND VENETOCLAX (TRIPLET) IS ACTIVE IN PATIENTS WITH FLT3-ITD MUTATED ACUTE MYELOID LEUKEMIA – A PHASE I/II STUDY

Musa Yilmaz, Muharrem Muftuoglu, Hagop Kantarjian, Courtney DiNardo, Tapan Kadia, Marina Konopleva, Gautam Borthakur, Naveen Pemmaraju, Nicholas J. Short, Yesid Alvarado, Abhishek Maiti, Lucia Masarova, Guillermo Montalban-Bravo, Sanam Loghavi, Keyur Patel, Steven Kornblau, Elias Jabbour, Guillermo Garcia-Manero, Farhad Ravandi, Michael Andreeff, Naval Daver

Department of Leukemia, MD Anderson Cancer Center
Houston, Texas, USA

EHA 2022;Abstract S127.

Decitabine (DAC) with Venetoclax (VEN) and Quizartinib for AML with a FLT-ITD Mutation

DAC + VEN + Quizartinib – Response

Response*, N (%)	Relapsed/Refractory (n=28)	Frontline (n=7)
CRc	**23 (82)**	**7 (100)**
CR	3 (11)	4 (57)
CRi	8 (28)	3 (43)
MLFS	12 (43)	0 (0)
Day 14 BM blasts ≤5%¥	13 (46)	7 (100)
Best MRD, anytime		
Flow Cytometry (-)	5/20 (25)	4/6 (66)
FLT3 PCR (-)	6/18 (33)	6/7 (86)
30-day mortality	0 (0)	0 (0)
60-day mortality	**3 (11)**	**0 (0)**
Bridge to ASCT	**12 (43)**	**3 (43)**

*Response assessment by modified IWG criteria – Cheson et al. J Clin Oncol. 2003 Dec 15;21(24):4642-9
¥Including acellular or aplastic bone marrow

Yilmaz M et al. EHA 2022;Abstract S127.

Decitabine with Venetoclax and Quizartinib: Adverse Events

Non-hematological	Grade 3-5	Grade 1-2
Febrile Neutropenia	15 (39)	0 (0)
Lung infection	15 (39)	0 (0)
Infection - other	11 (29)	6 (16)
Sepsis	6 (16)	0 (0)
Hypermagnesemia	2 (5)	8 (21)
Syncope	2 (5)	0 (0)
Hyperbilirubinemia	2(5)	16 (42)
Hypocalcemia	1 (3)	31 (81)
Hypokalemia	0 (0)	29 (76)
Dyspnea	0 (0)	20 (53)
Diarrhea	0 (0)	19 (50)
Hypophosphatemia	0 (0)	18 (47)
Increased creatinine	0 (0)	18 (47)
Hypomagnesemia	0 (0)	15 (39)
Elevated ALT	1 (1)	14 (36)
Nausea	0 (0)	14 (36)
Vomiting	0 (0)	11 (30)
QTcF Prolongation	1 (3)	6 (16)

Yilmaz M et al. EHA 2022;Abstract S127.

Follow-up of patients with R/R *FLT3*-mutation–positive AML treated with gilteritinib in the phase 3 ADMIRAL trial

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]; Naoko Hosono[14]; Masahiro Onozawa[15]; Shigeru Chiba[16]; Hee-Je Kim[17]; Nahla Hasabou[18]; Qiaoyang Lu[18]; Ramon Tiu[18]; Mark J. Levis[19]

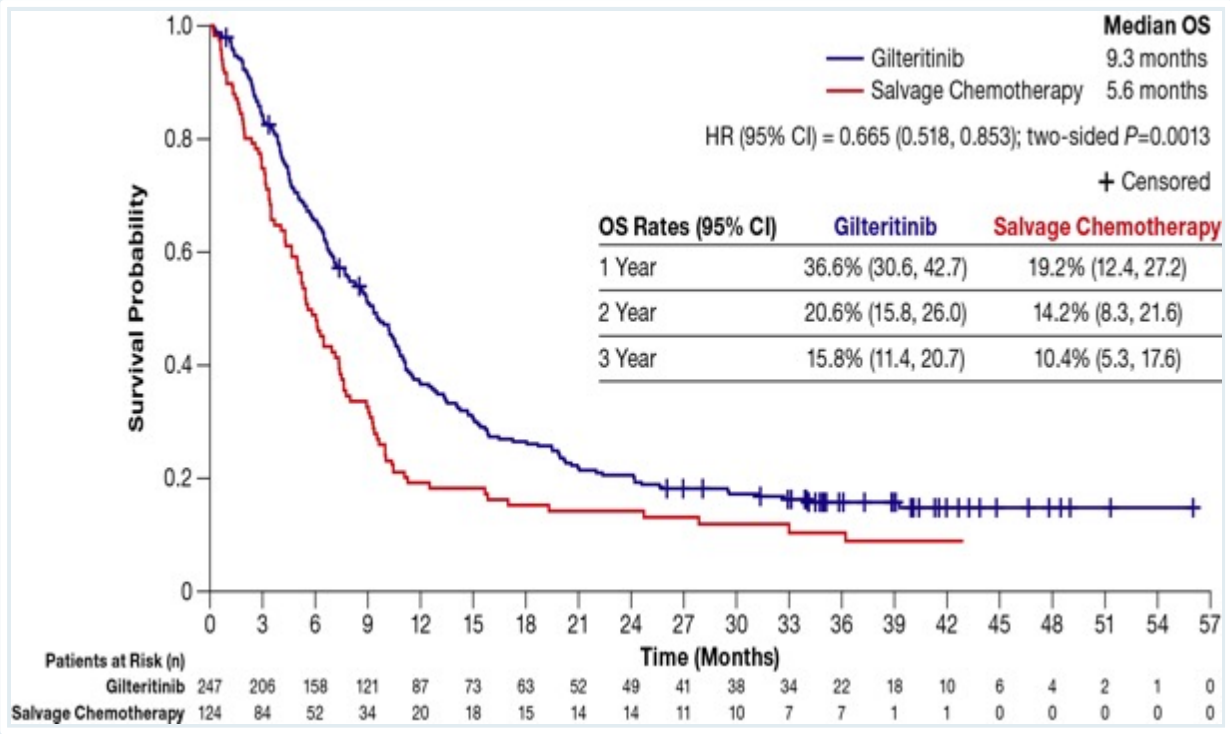
[1]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [2]University of Chicago, Chicago, IL; [3]Yale School of Medicine, New Haven, CT, USA; [4]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [5]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [6] Medical College of Wisconsin, Division of Hematology and Oncology, Froedtert Hospital, Milwaukee, WI, USA; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [8]IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" – IRST S.r.l., Meldola, Italy; [9]Universitätsklinikum Giessen und Marburg GmbH, Marburg, Germany; [10]Hospital de la Santa Creu I Sant Pau and Josep Carreras Leukemia Research Institute, Barcelona, Spain; [11]University Hospital La Fe, Valencia, Spain; [12]Centre Hospitalier Universitaire de Toulouse, Institut Universitaire du Cancer deToulouse Oncopole, Université de Toulouse 3 Paul Sabatier, Toulouse, France; [13]Seoul National University Hospital, Seoul, Republic of Korea; [14]University of Fukui, Fukui, Japan; [15]Hokkaido University, Sapporo, Japan; [16]Department of Hematology, University of Tsukuba, Tsukuba, Japan; [17]Catholic Hematology Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; [18]Astellas Pharma US, Inc., Northbrook, IL; [19]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA

Blood 2022;[Online ahead of print].

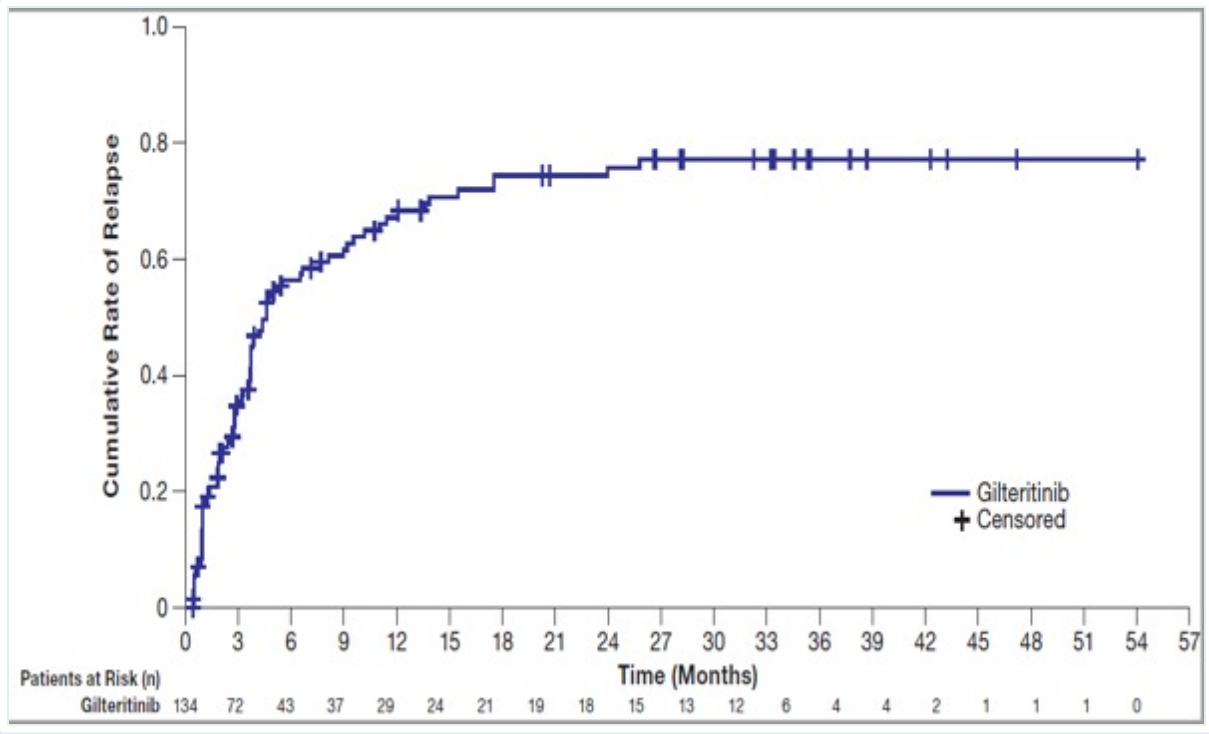
RTP RESEARCH TO PRACTICE

ADMIRAL: Updated Overall Survival and Cumulative Relapse Rate

Overall survival for relapsed/refractory AML with FLT3 mutations (ITT population; N = 371)



Cumulative incidence of relapse in patients experiencing composite complete remission (CRc) with gilteritinib

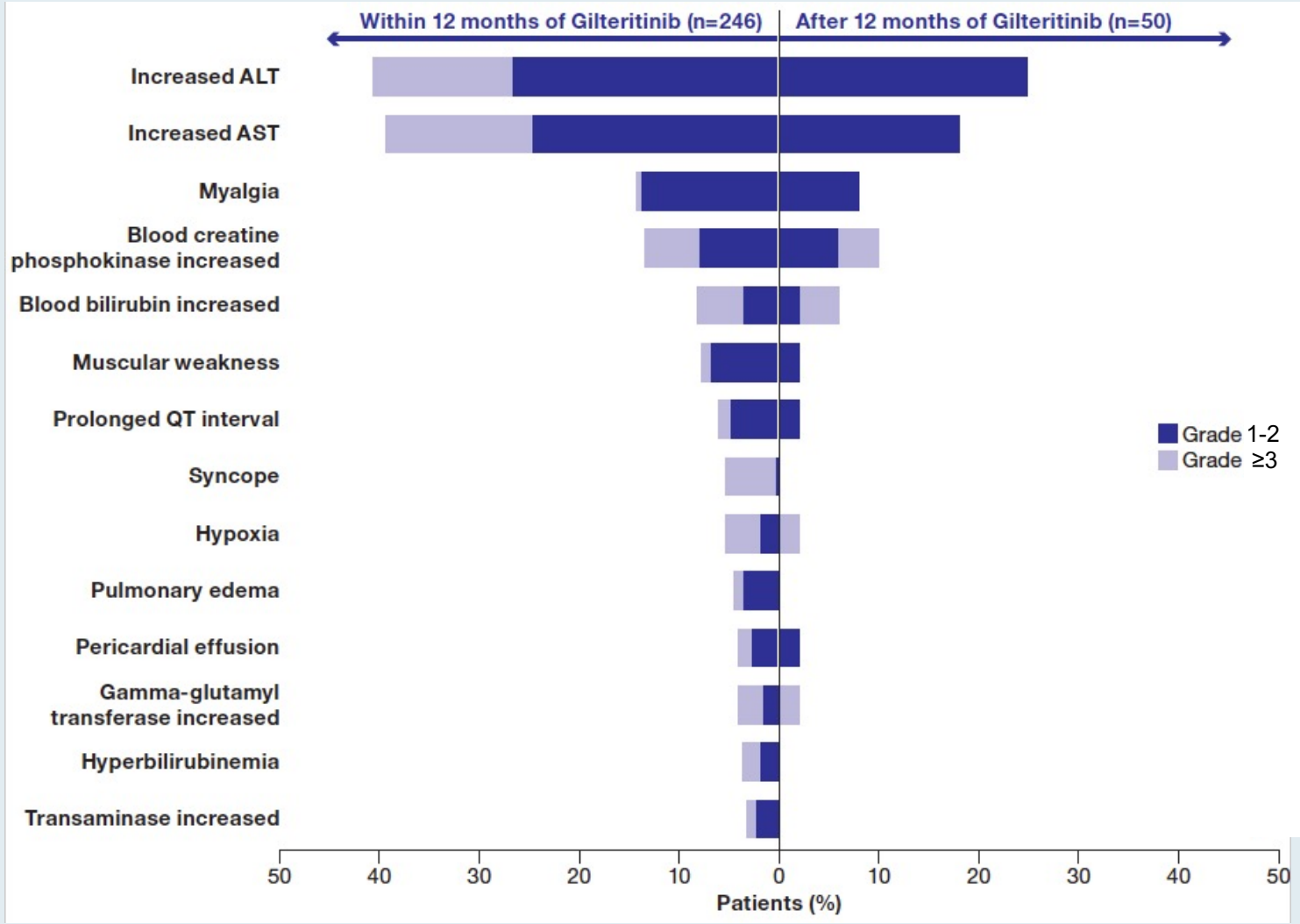


- With a median follow-up of 37.1 months, the median overall survival remained longer with gilteritinib than with salvage chemotherapy
- Most relapses after CRc occurred within 12 months and rarely occurred after 18 months

Perl AE et al. *Blood* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ADMIRAL: Adverse Events of Interest After First Year of Gilteritinib Therapy



Perl AE et al. *Blood* 2022;[Online ahead of print].

2022 ASCO® ANNUAL MEETING

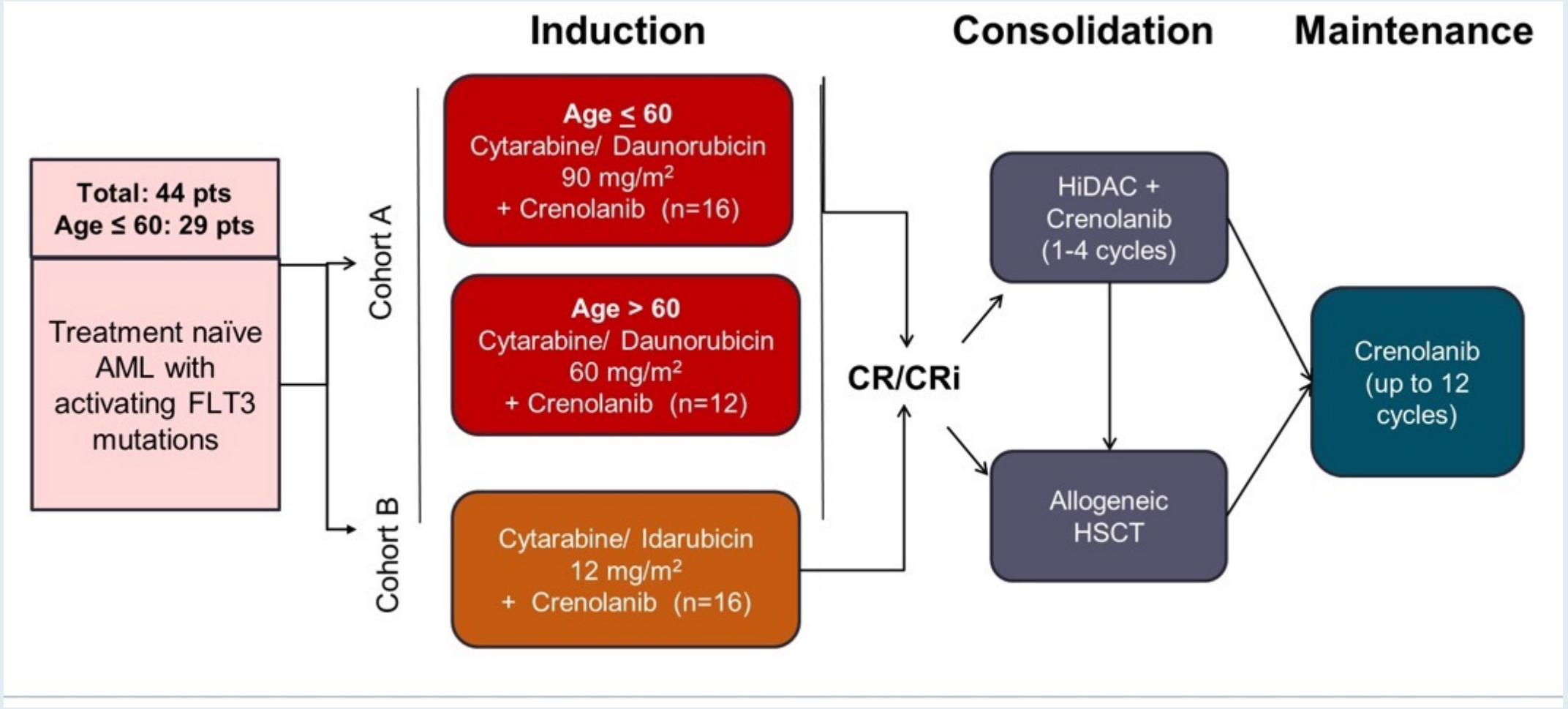
Long-term Results of a Phase 2 Trial of Crenolanib Combined with 7+3 Chemotherapy in Adults with Newly Diagnosed FLT3 Mutant AML

Eunice S. Wang[1], Aaron D. Goldberg[2], Roland B. Walter[3], Robert Collins[4], Richard M. Stone[5]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [2] Memorial Sloan Kettering Cancer Center, New York, NY; [3] Fred Hutchinson Cancer Research Center, Seattle, WA; [4] University of Texas Southwestern, Dallas, TX; [5] Dana-Farber Cancer Institute, Boston, MA

Abstract 7007.

Crenolanib with 7 + 3 Chemotherapy for Newly Diagnosed AML with a FLT3 Mutation: Study Design



Wang E et al. ASCO 2022;Abstract 7007.

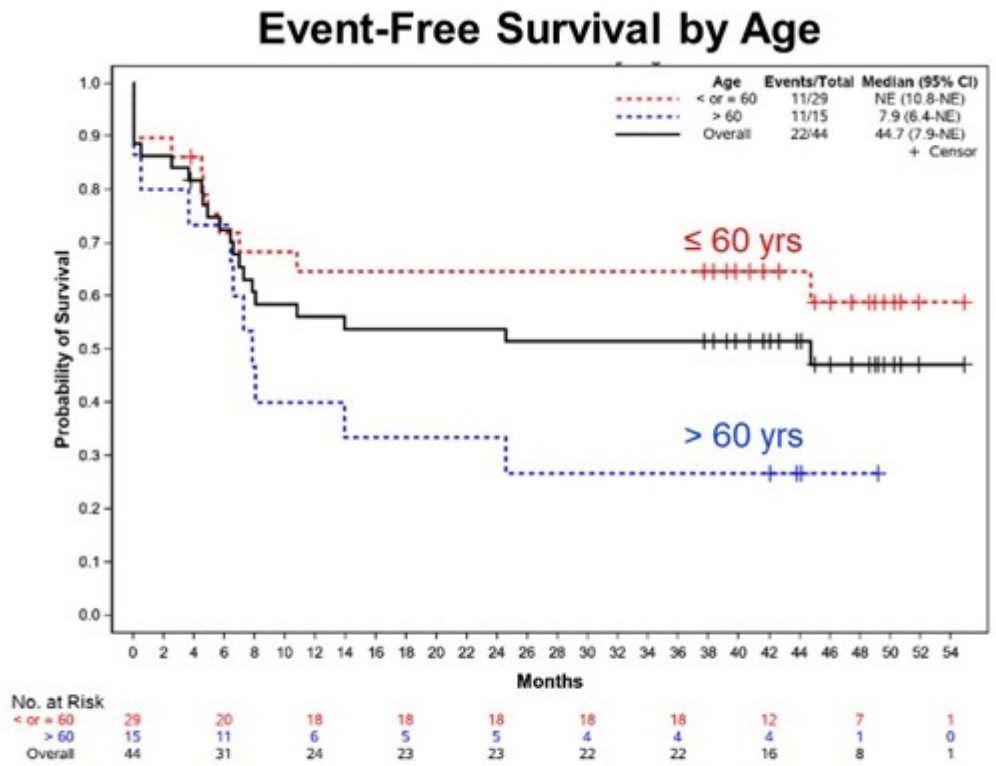
Crenolanib with 7 + 3 Chemotherapy for Newly Diagnosed AML with a FLT3 Mutation: Overall Response Rates After Induction

Age Group	CR/CRi After Induction 1	Overall CRc
Age ≤ 60 years (n=29)	**22/29 (76%)**	**26/29 (90%)**
MRD- CR (flow cytometry) (n=18)	16/18 (89%)	16/18 (89%)
Age > 60 years (n=15)	**10/15 (67%)**	**12/15 (80%)**
MRD- CR (flow cytometry) (n=11)	5/11 (45%)	5/11 (45%)
Total (n=44)	**32/44 (73%)**	**38/44 (86%)**

- 4 patients achieved CR/CRi after re-induction
- 2 patients went to consolidation in PR (1 each HSCT/HiDAC) and achieved CR/CRi on study

Wang E et al. ASCO 2022;Abstract 7007.

Crenolanib with 7 + 3 Chemotherapy for Newly Diagnosed AML with a FLT3 Mutation: Event-Free Survival (EFS) by Age



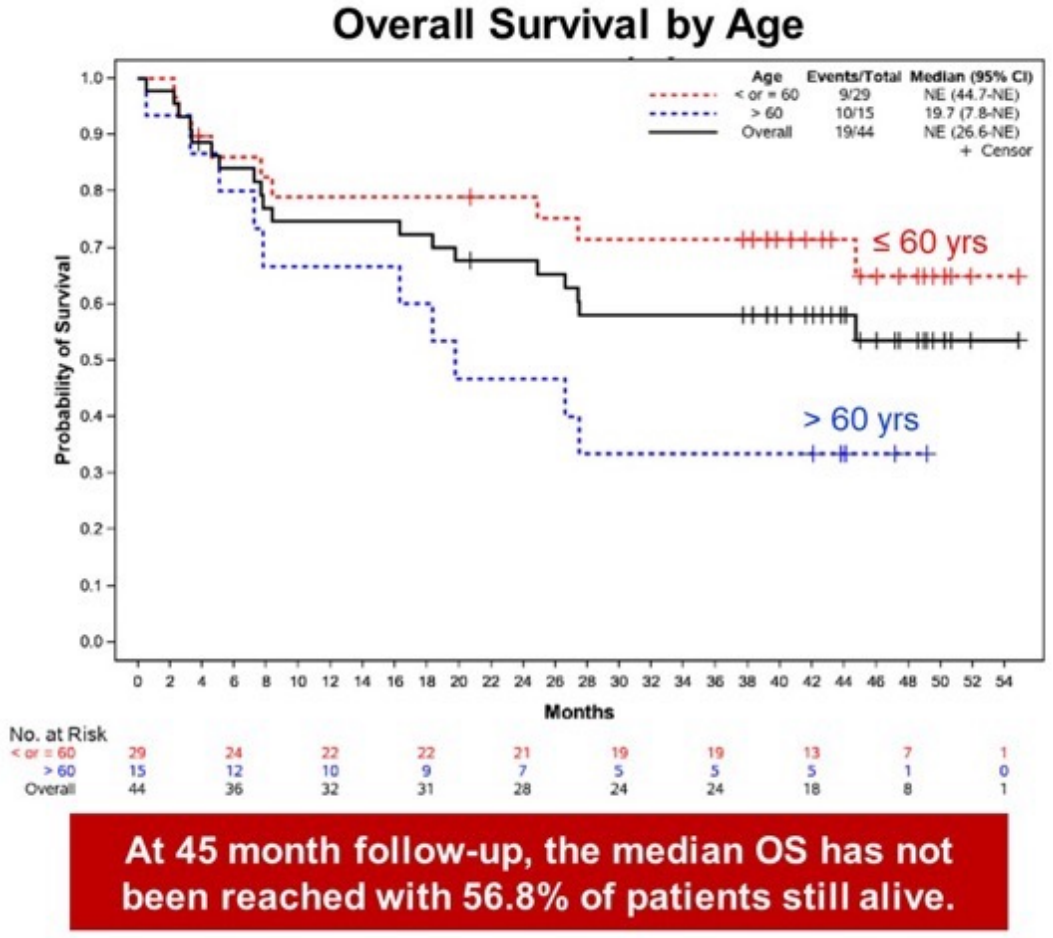
At 45 month follow-up, the median EFS for all patients (18 -75 yrs) was 45 months.

Duration of EFS (months)	Age ≤ 60 yo N=29	Age > 60 yo N=15	Total N=44
Median	**NE**	**7.9**	**44.7**
95% CI	10.8, NE	6.4, NE	7.9, NE
Min, Max	0.03, 54.9	0.03, 49.2	0.03, 54.9
Event (n, %)	11 (37.9)	11 (73.3)	22 (50)
Censored (n, %)	18 (62.1)	4 (26.7)	22 (50)
EFS Estimates (%, 95%CI)			
1-year	**64.7** (44.2, 79.2)	**40.0** (16.5, 62.8)	**56.1** (40.1, 69.3)
2-year	**64.7** (44.2, 79.2)	**33.3** (12.2, 56.4)	**53.8** (37.9, 67.2)
3-year	**64.7** (44.2, 79.2)	**26.7** (8.3, 49.6)	**51.4** (35.7, 65.1)

EFS was defined as time from enrollment to relapse or death of any cause. Failure to achieve CR/CRi on study was calculated as EFS on Day 1

Wang E et al. ASCO 2022;Abstract 7007.

Crenolanib with 7 + 3 Chemotherapy for Newly Diagnosed AML with a FLT3 Mutation: Overall Survival (OS) by Age



At 45 month follow-up, the median OS has not been reached with 56.8% of patients still alive.

Duration of OS (months)	Age ≤ 60 yo N=29	Age > 60 y0 N=15	Total N=44
Median	**NE**	**19.7**	**NE**
95% CI	44.7, NE	7.8, NE	26.6, NE
Min, Max	2.23, 54.89	0.49, 49.18	0.49, 54.89
Event (n, %)	9 (31.0)	10 (66.7)	19 (43.2)
Censored (n, %)	20 (69.0)	5 (33.3)	25 (56.8)
OS Estimates (%, 95%CI)			
1-year	**78.9** (58.9, 89.9)	**66.7** (37.5, 84.6)	**74.6** (58.9, 85.1)
2-year	**78.9** (58.9, 89.9)	**46.7** (21.2, 68.7)	**67.6** (51.5, 79.4)
3-year	**71.4** (50.8, 84.6)	**33.3** (12.2, 56.4)	**58.0** (41.8, 71.1)

Wang E et al. ASCO 2022;Abstract 7007.

Agenda

Introduction – RATIFY Trial in Perspective

Module 1 – FLT3 Inhibitors

Module 2 – Anti-CD47 Antibody: Magrolimab

Module 3 – Anti-TIM-3 Antibody: Sabatolimab

Module 4 – CAR T-Cell Therapy

Module 5 – IDH Inhibitors

Module 6 – New Myelodysplastic Syndromes Classification System

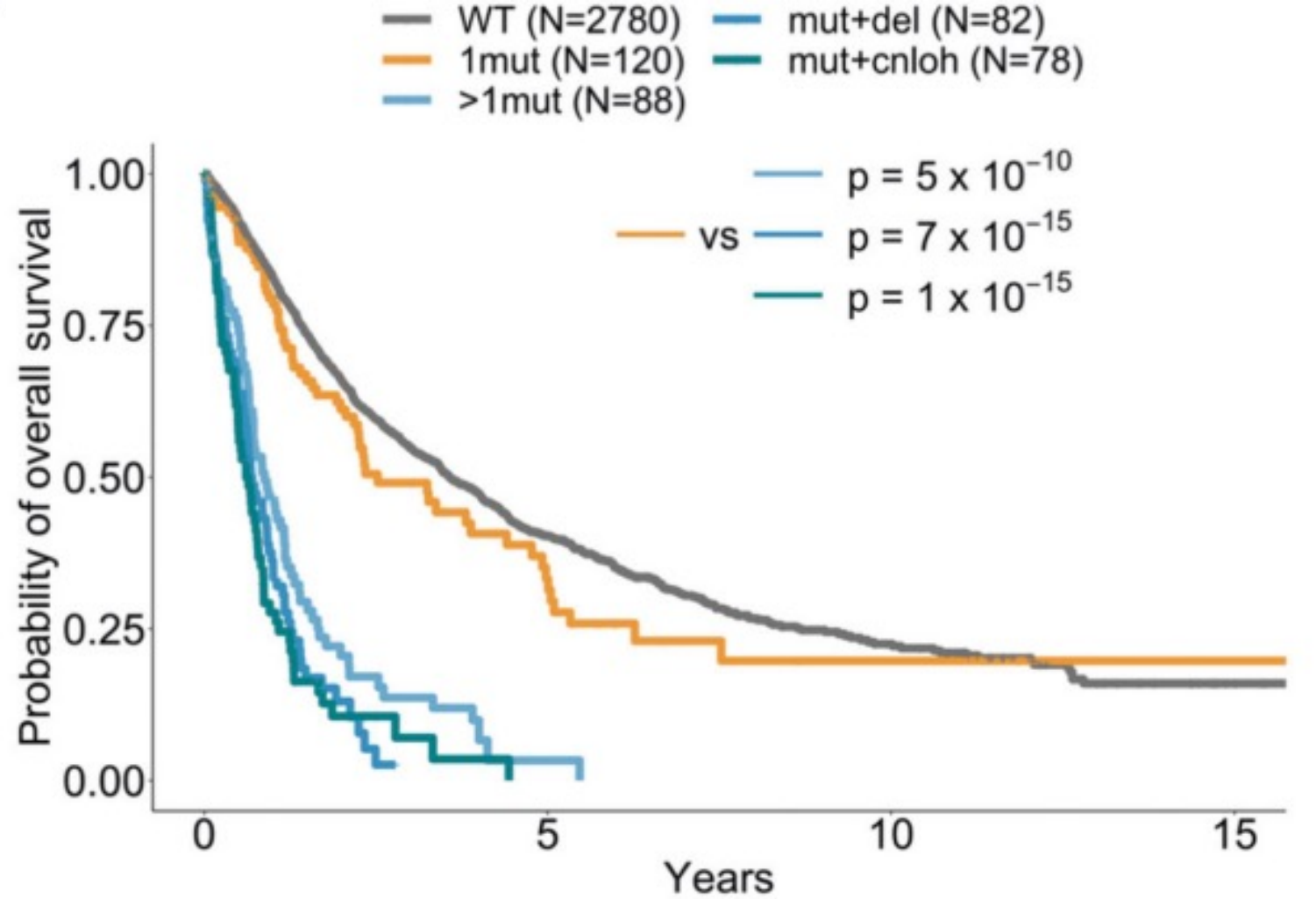
Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

RTP
RESEARCH
TO PRACTICE

TP53 Mutational Status Informs Risk in MDS

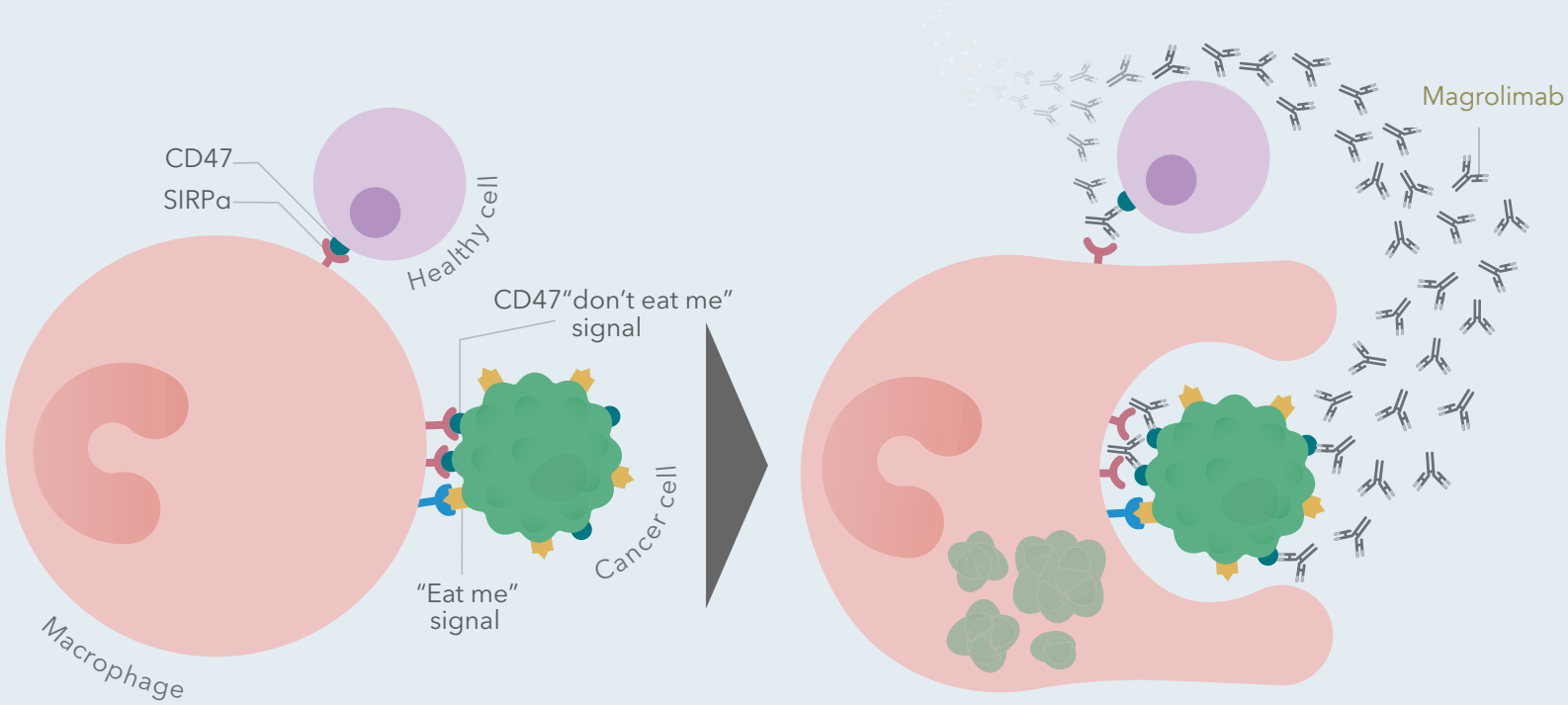


Bernard E et al. *Nat Med* 2020;26(10):1549-56.

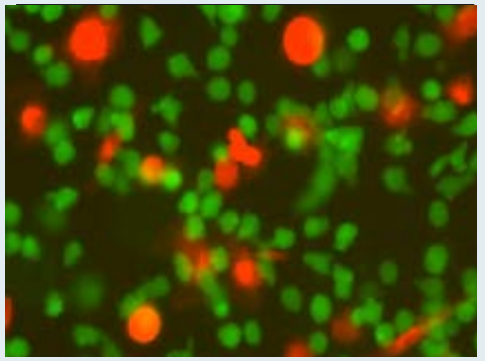
Content Courtesy of Michael R Savona, MD

RTP RESEARCH TO PRACTICE

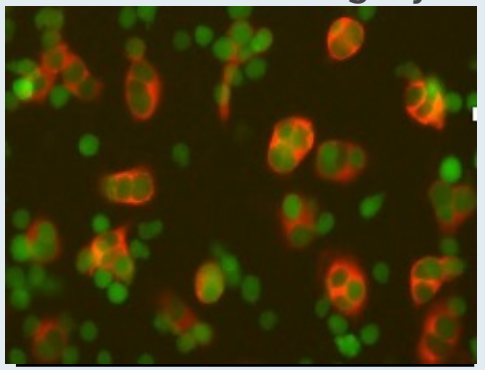
Magrolimab Is a Macrophage Immune Checkpoint Inhibitor Targeting CD47



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

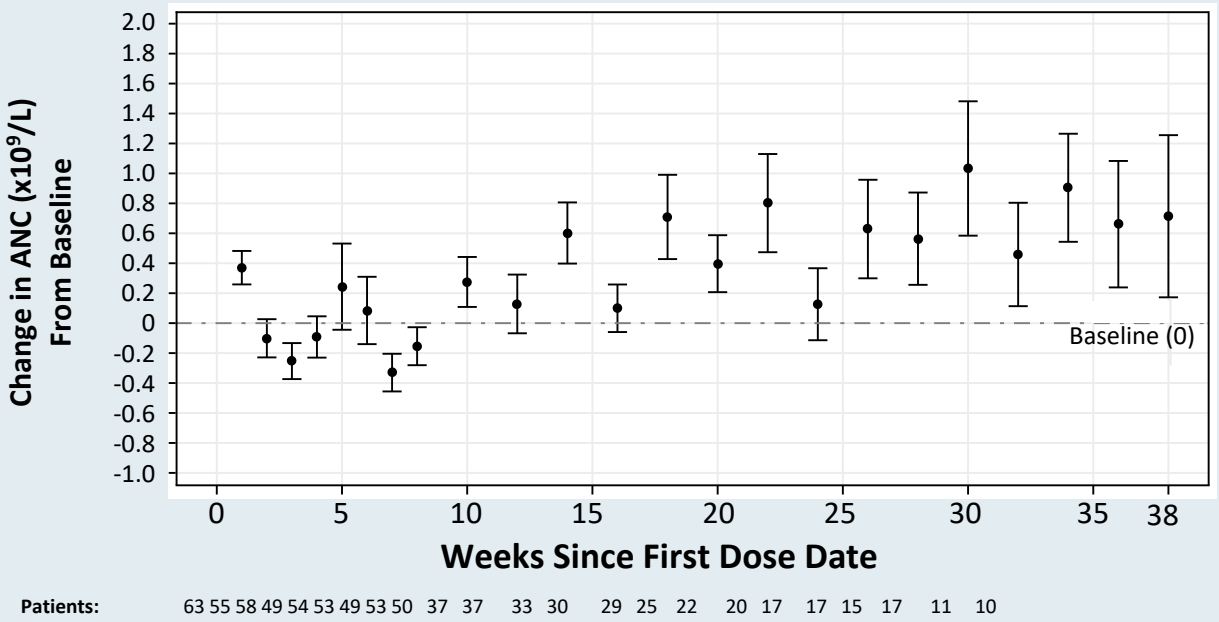
Sallman D et al. ASCO 2020;Abstract 7507.

Content Courtesy of Michael R Savona, MD

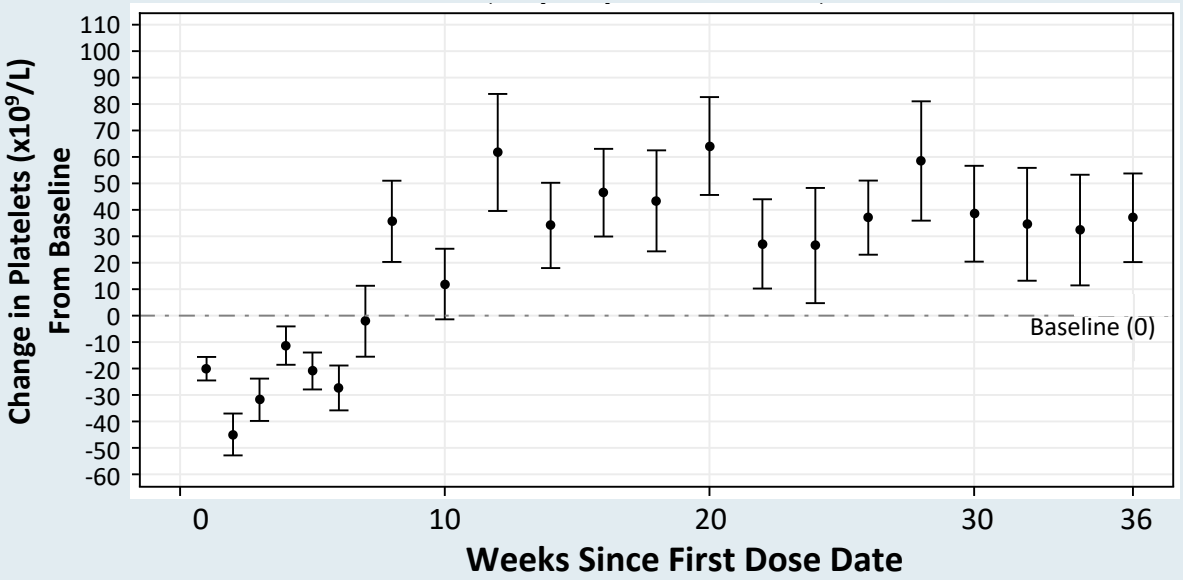
RTP RESEARCH TO PRACTICE

Magrolimab May Lead to Transient Hematologic Toxicities on the Way to Hematologic Response

Neutrophil Changes on Therapy



Platelet Changes on Therapy

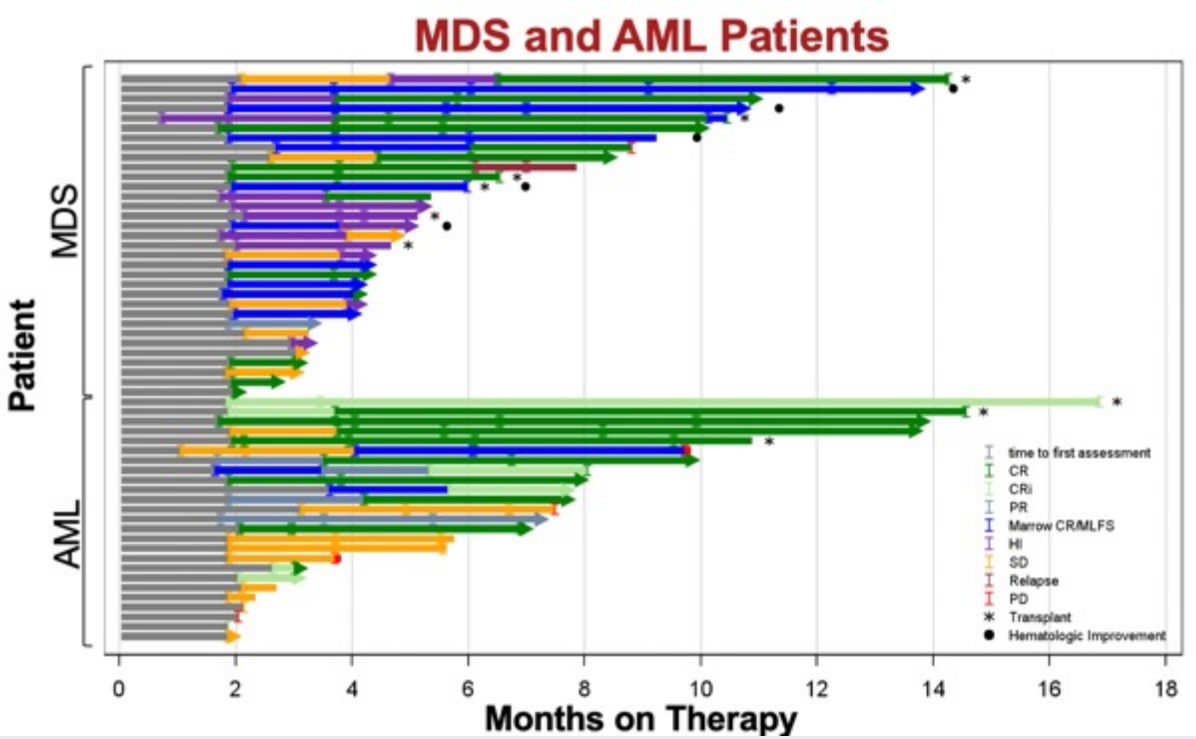


Sallman et al. ASCO 2020;Abstract 7507.

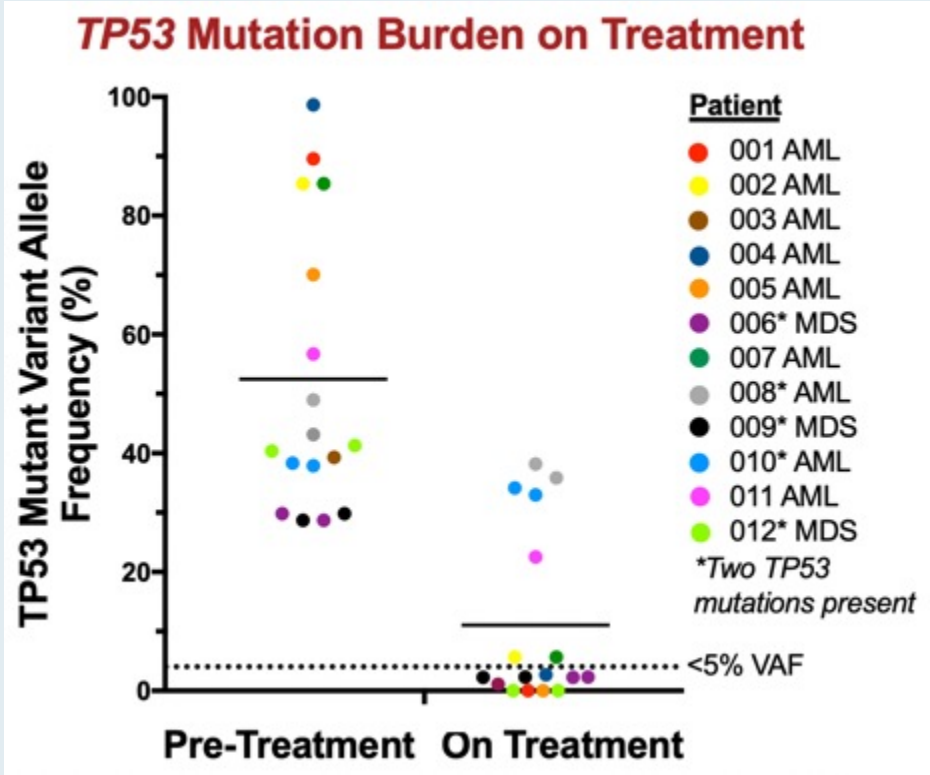
Content Courtesy of Michael R Savona, MD

RTP RESEARCH TO PRACTICE

Magrolimab Leads to Responses in Disease with TP53 Mutation



91% objective response rate for MDS



75% overall response rate in 16 patients with AML/MDS and a TP53 mutation

Sallman et al. ASCO 2020;Abstract 7507.

Content Courtesy of Michael R Savona, MD

RTP RESEARCH TO PRACTICE

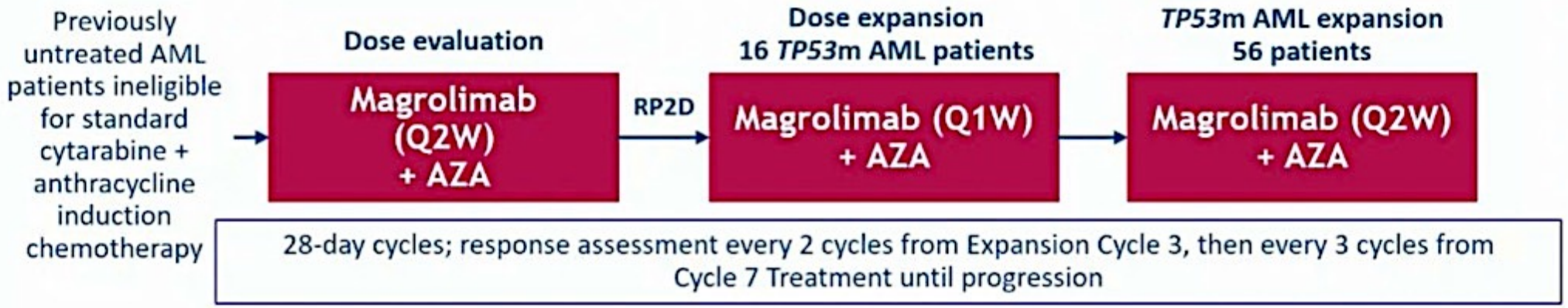
Tolerability and Efficacy of the First-in-Class Anti-CD47 Antibody Magrolimab Combined with Azacitidine in Frontline Patients with *TP53*-Mutated Acute Myeloid Leukemia: Phase 1b Results

Naval G. Daver[1], Paresh Vyas[2], Suman Kambhampati[3], Monzr M. Al Malki[4], Richard Larson[5], Adam Asch[6], Gabriel Mannis[7], Wanxing Chai-Ho[8], Tiffany Tanaka[9], Terrence Bradley[10], Deepa Jeyakumar[11], Eunice Wang[12], Guan Xing[13], Mark Chao[13], Giri Ramsingh[13], Camille Renard[13], Indu Lal[13], Joshua Zeidner[14], David A. Sallman[15]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]University of Oxford, Oxford, UK; [3]Healthcare Midwest, Kansas City, MO, USA; [4]City of Hope National Medical Center, Duarte, CA, USA; [5]University of Chicago, Chicago, IL, USA; [6]University of Oklahoma, Oklahoma City, OK, USA; [7]Stanford University, Stanford, CA, USA; [8]University of California Los Angeles, Los Angeles, CA, USA; [9]University of California San Diego, San Diego, CA, USA; [10]University of Miami, Miami, FL, USA; [11]University of California Irvine, Irvine, CA, USA; [12]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [13]Gilead Sciences, Inc, Foster City, CA, USA; [14]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA; [15]Moffitt Cancer Center, Tampa, FL, USA

EHA 2022;Abstract S132.

5F9005: Magrolimab in Combination with Azacitidine for AML — Study Design



- 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

IV = intravenously; MRD = minimal residual disease; Q1W = weekly; Q2W = every other week; RO = receptor occupancy; RP2D = recommended Phase 2 dose; SC = subcutaneously.

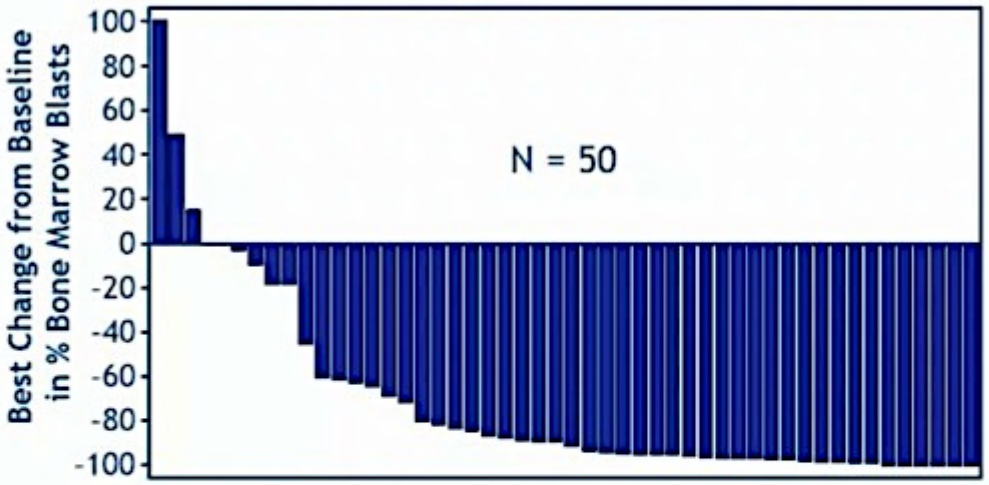
Daver N et al. EHA 2022;Abstract S132.

5F9005: Magrolimab/Azacitidine for AML with a TP53 Mutation — Response Rates

Efficacy Endpoints (Intent-to-Treat Analysis)

Outcome	N = 72
ORR, % (95% CI)	**48.6 (36.7, 60.7)**
CR, % (95% CI)	**33.3 (22.7, 45.4)** (n = 24/72)
MRD— CR*, % (95% CI)	50.0 (29.1, 70.9) (n = 12/24)
CRi/CRh, n (%)	6 (8.3)
PR, n (%)	4 (5.6)
MLFS, n (%)	1 (1.4)
DOR, median (95% CI), mo	**8.7 (6.5, 10.4)**
DCR, median (95% CI), mo	7.7 (4.7, 10.9)
TOR/TCR, median (range), mo	2.0 (1.0, 5.7) / 3.0 (1.8, 9.6)
CCyR, n/N† (%)	10/31 (32.3)
PFS, median (95% CI), mo	7.3 (3.7, 9.7)

Best Change from Baseline in % Bone Marrow Blasts

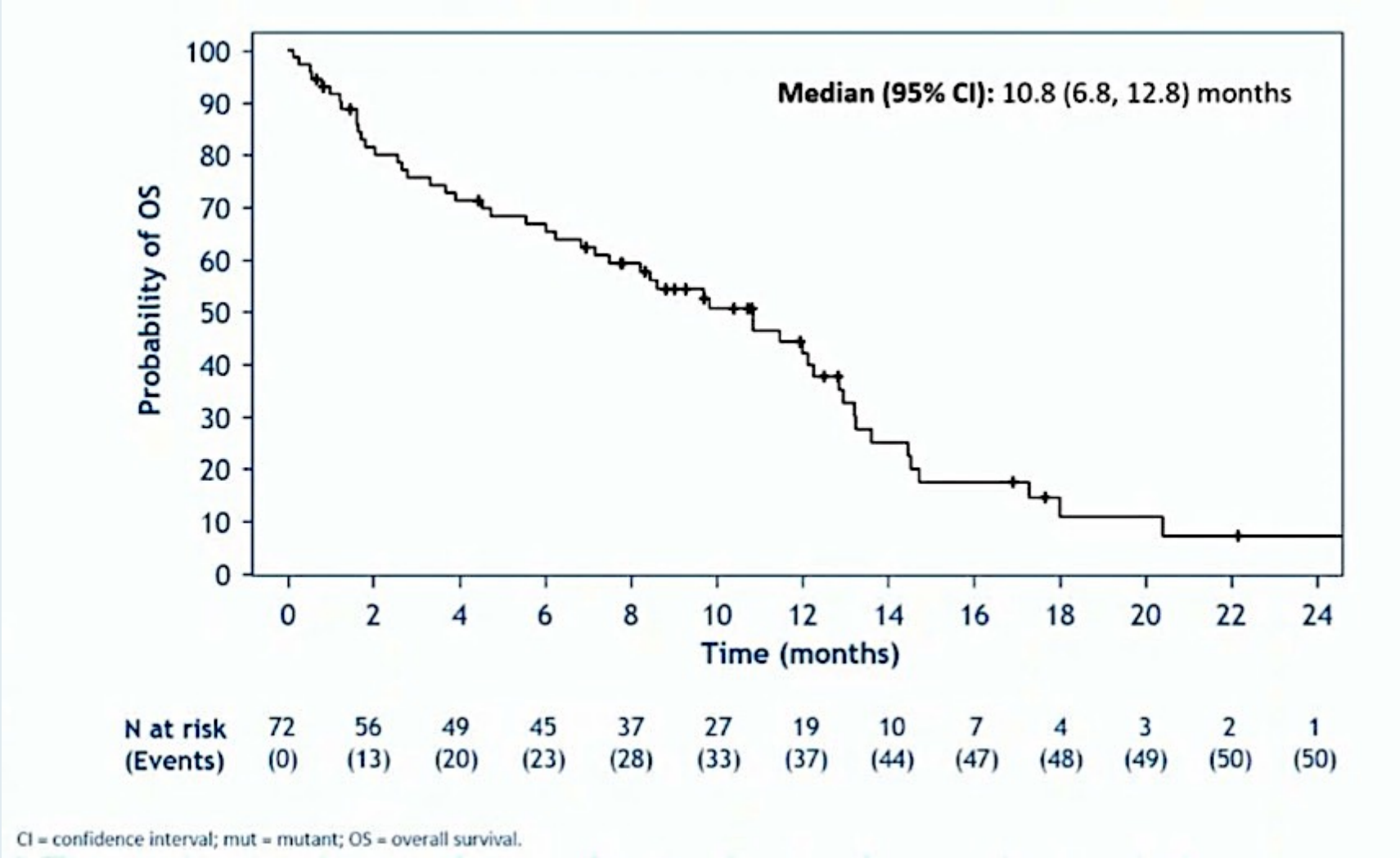


- CR was achieved by 33.3% of patients with half of CR patients being MRD–.
- 30 (41.7%) patients achieved CR/CRi.
- 29.7% and 45.8% of baseline transfusion-dependent patients converted to RBC and platelet transfusion independence,‡ respectively.

*MRD was assessed in bone marrow samples by a central laboratory using multiparameter flow cytometry with a lower limit of detection of 0.02%. †N = number with abnormal cytogenetics at baseline who achieved objective response. ‡RBC and platelet transfusion independence were defined as ≥8 consecutive weeks without transfusion. CCyR = complete cytogenetic response; CR = complete remission; CRh = CR with partial hematologic recovery; CRi = CR with incomplete blood count recovery; DCR = duration of CR; DOR = duration of response; MLFS = morphologic leukemia-free state; MRD = minimal residual disease; ORR = objective response rate; PFS = progression-free survival; PR = partial remission; TCR = time to CR; TOR = time to objective response.

Daver N et al. EHA 2022;Abstract S132.

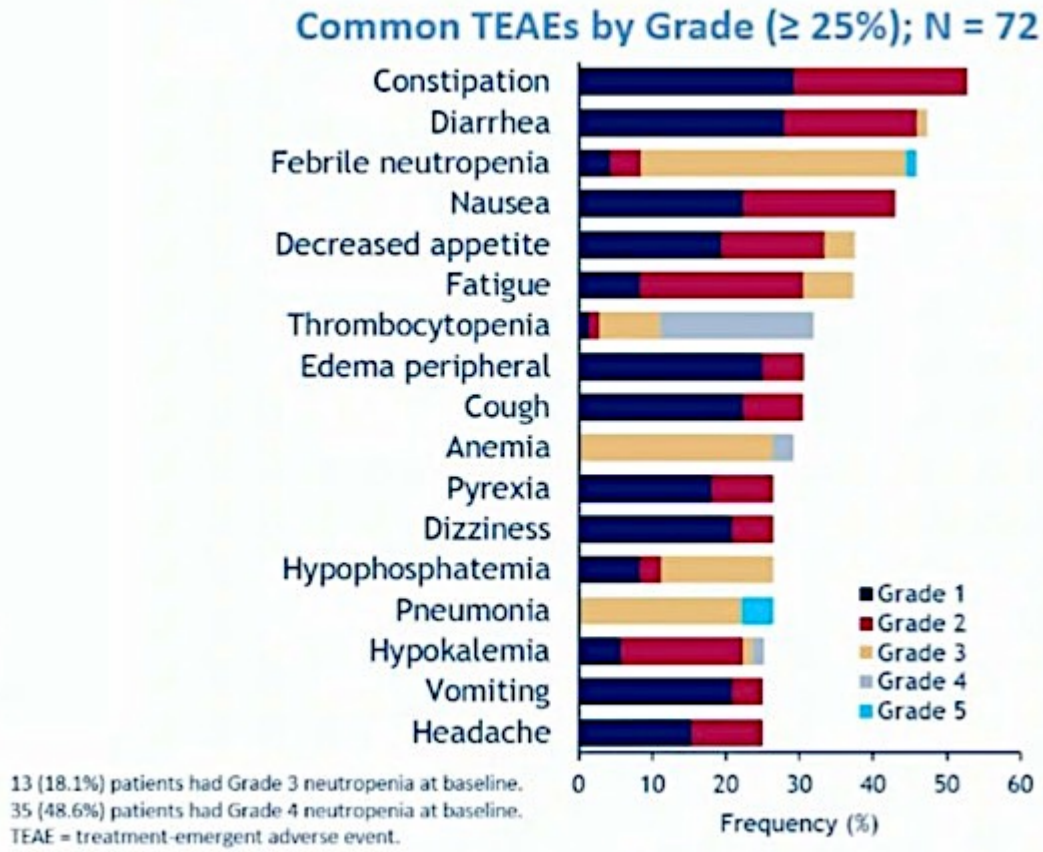
5F9005: Magrolimab/Azacitidine for AML with a TP53 Mutation — OS



CI = confidence interval; mut = mutant; OS = overall survival.

Daver N et al. EHA 2022;Abstract S132.

5F9005: Magrolimab/Azacitidine for AML with a TP53 Mutation — Safety



- 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 N et al. EHA 2022;Abstract S132.

Magrolimab in Combination with Azacitidine for Untreated Higher Risk Myelodysplastic Syndromes (HR-MDS): 5F9005 Phase 1b Study Results

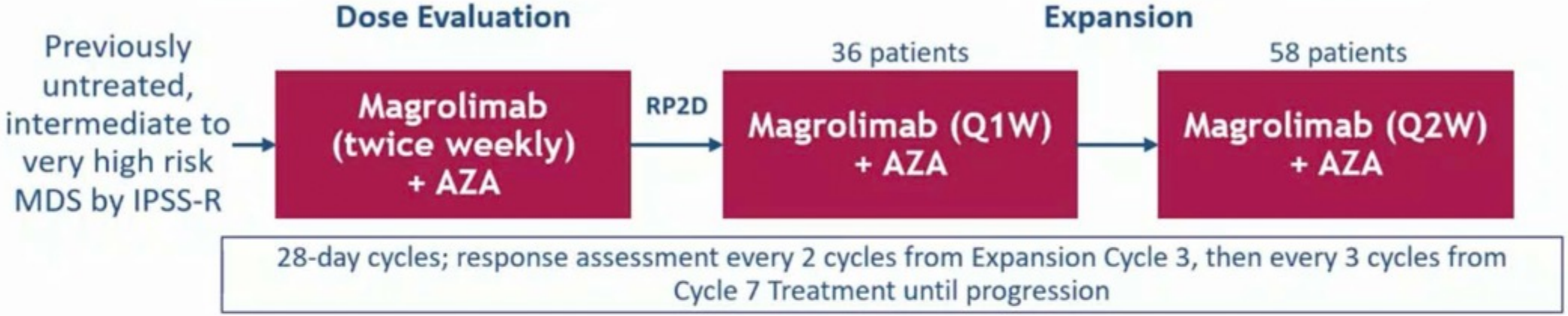
David A. Sallman[1], Monzr M. Al Malki[2], Adam S. Asch[3], Eunice S. Wang[4], Joseph G. Jurcic[5], Terrence J. Bradley[6], Ian W. Flinn[7], Daniel A. Pollyea[8], Suman Kambhampati[9], Tiffany N. Tanaka[10], Joshua F. Zeidner[11], Guillermo Garcia-Manero[12], Deepa Jeyakumar[13], Lin Gu[14], Anderson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

[1]Moffitt Cancer Center, Tampa, FL; [2]City of Hope National Medical Center, Duarte, CA; [3]Stephenson Cancer Center, Oklahoma University Health, Oklahoma City, OK; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [5]Columbia University Medical Center, New York, NY; [6]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL; [7]Tennessee Oncology, Nashville, TN; [8]University of Colorado School of Medicine, Denver, CO; [9]Sarah Cannon Research Institute, Kansas City, MO; [10]University of California San Diego Moores Cancer Center, San Diego, CA; [11]University of North Carolina, Lineberger Comprehensive Cancer Center, Chapel Hill, NC; [12]The University of Texas MD Anderson Cancer Center, Houston, TX; [13]University of California Irvine, Orange, CA; [14]Gilead Sciences, Inc., Foster City, CA; [15]Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, UK

Presented by: David A. Sallman

Sallman DA et al. EHA 2022;Abstract 166.

5F9005: Magrolimab with Azacitidine for Higher-Risk Myelodysplastic Syndromes (HR-MDS) — Study Design



– Patients received magrolimab IV as a 1 mg/kg priming dose on Days 1 and 4, then ramp-up to 30 mg/kg QW or Q2W maintenance; AZA dose was SC or IV 75 mg/m^2 on Days 1-7 of each cycle.

Primary objectives

Safety, tolerability and efficacy (CR rate) of magrolimab + azacitidine in HR-MDS

Secondary objectives

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

Exploratory objectives

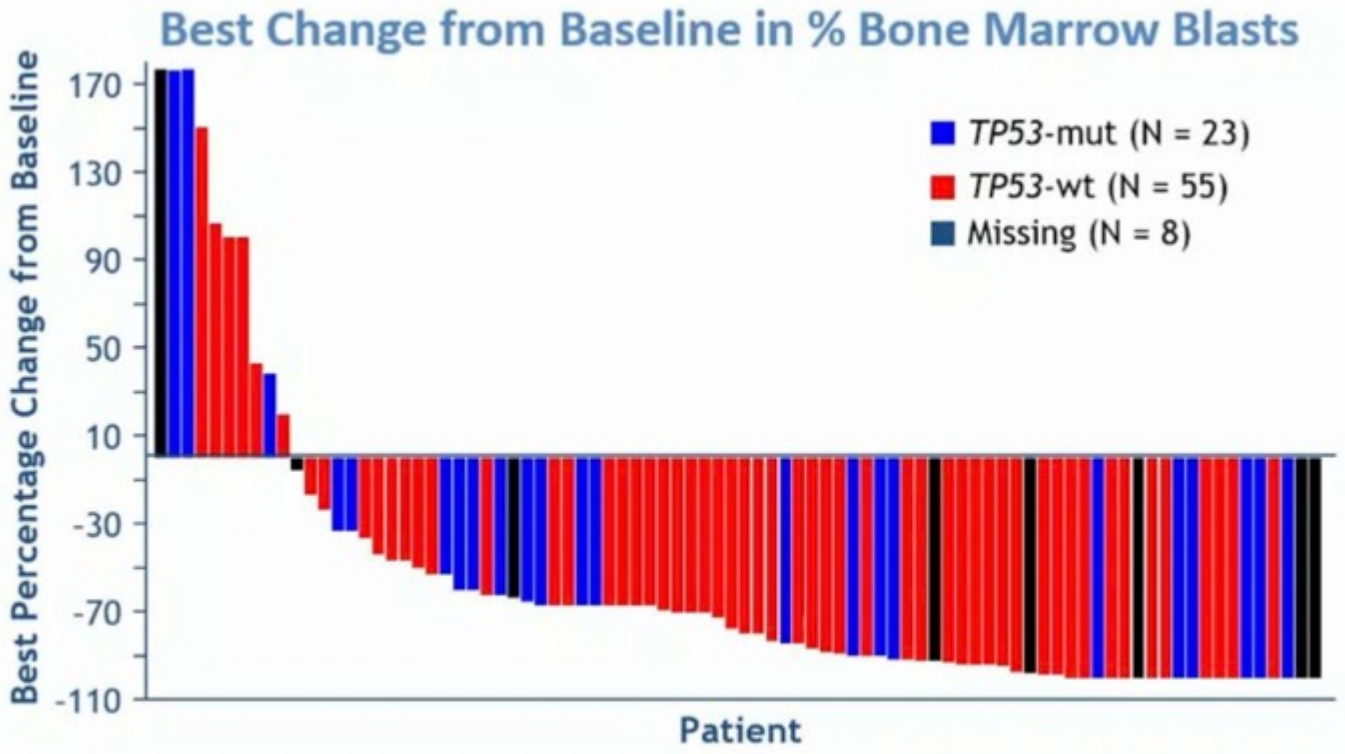
CD47 RO, Biomarkers, Efficacy in molecular subtypes of MDS

CR = complete remission; IPSS-R = Revised International Prognostic Scoring System; IV = intravenous; MRD = minimal residual disease; RO = receptor occupancy; RP2D = recommended Phase 2 dose; SC = subcutaneous; Q1W = weekly;

Sallman DA et al. EHA 2022;Abstract 166.

5F9005: Magrolimab with Azacitidine for HR-MDS — Responses

Outcome	All (N = 95)*	*TP53*-wt (N = 61)	*TP53*-mut (N = 25)
ORR, %*	74.7	78.7	68.0
CR, % (95% CI)	32.6 (23.4, 43.0)	31.1 (19.9, 44.3)	40.0 (21.1, 61.3)
DCR, median (95% CI), mo	11.1 (7.6, 13.4)	12.9 (8.0, NR)	7.6 (3.1, 13.4)
DOR, median (95% CI), mo	9.8 (8.8, 12.9)	9.8 (8.5, 18.5)	9.2 (5.0, 12.2)
CCyR, n/N† (%)	19/65 (29.2)	13/41 (31.7)	6/20 (30)



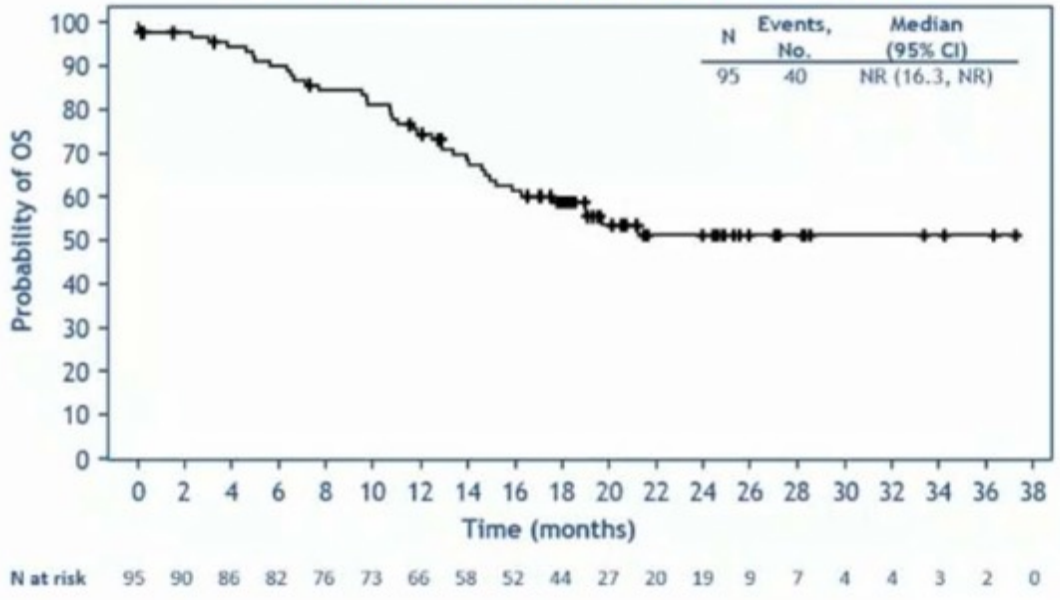
- CR rate was 32.6% and ORR was 74.6%, with response rates similar in *TP53*-mut and *TP53*-wt.

Sallman DA et al. EHA 2022;Abstract 166.

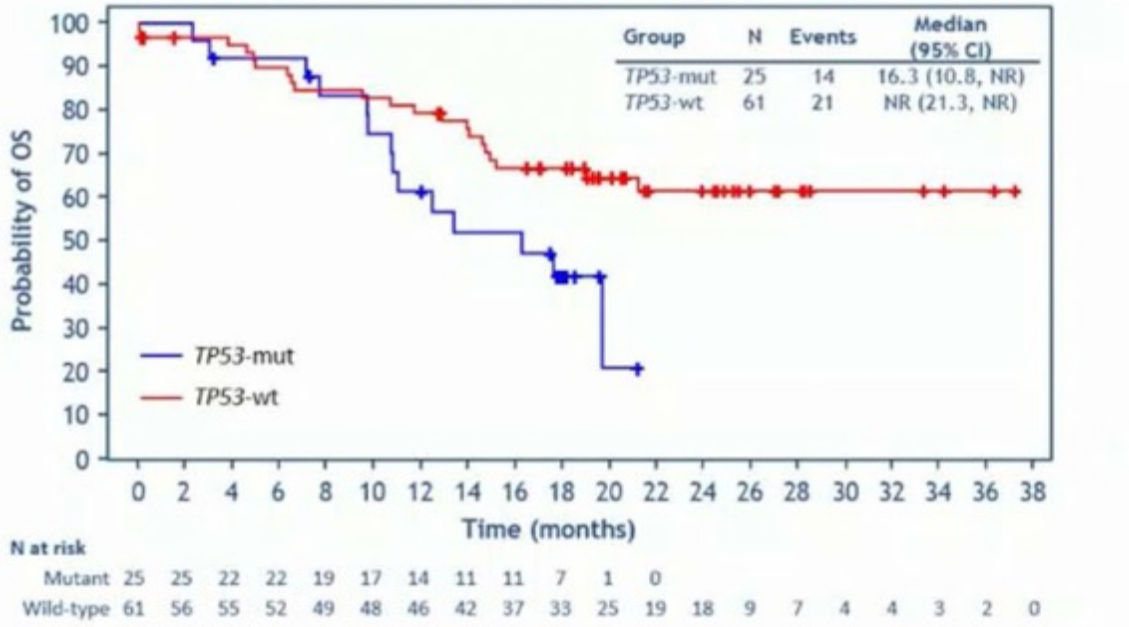
5F9005: Magrolimab with Azacitidine for HR-MDS — Overall Survival (OS)

- With a median follow-up of 17.1 months, median OS was not reached and was 16.3 months in *TP53*-mut MDS.

Overall Survival in All Patients



Overall Survival By *TP53* Mutation Status

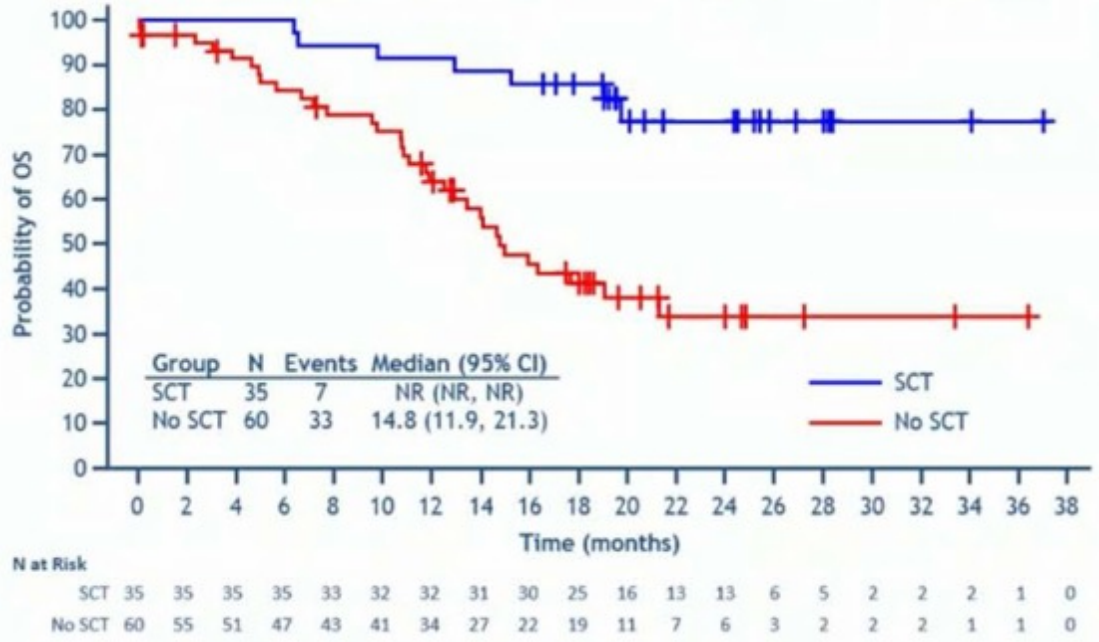


Sallman DA et al. EHA 2022;Abstract 166.

RTP RESEARCH TO PRACTICE

5F9005: Magrolimab with Azacitidine for HR-MDS — Stem Cell Transplant Outcomes

Overall Survival with and Without SCT



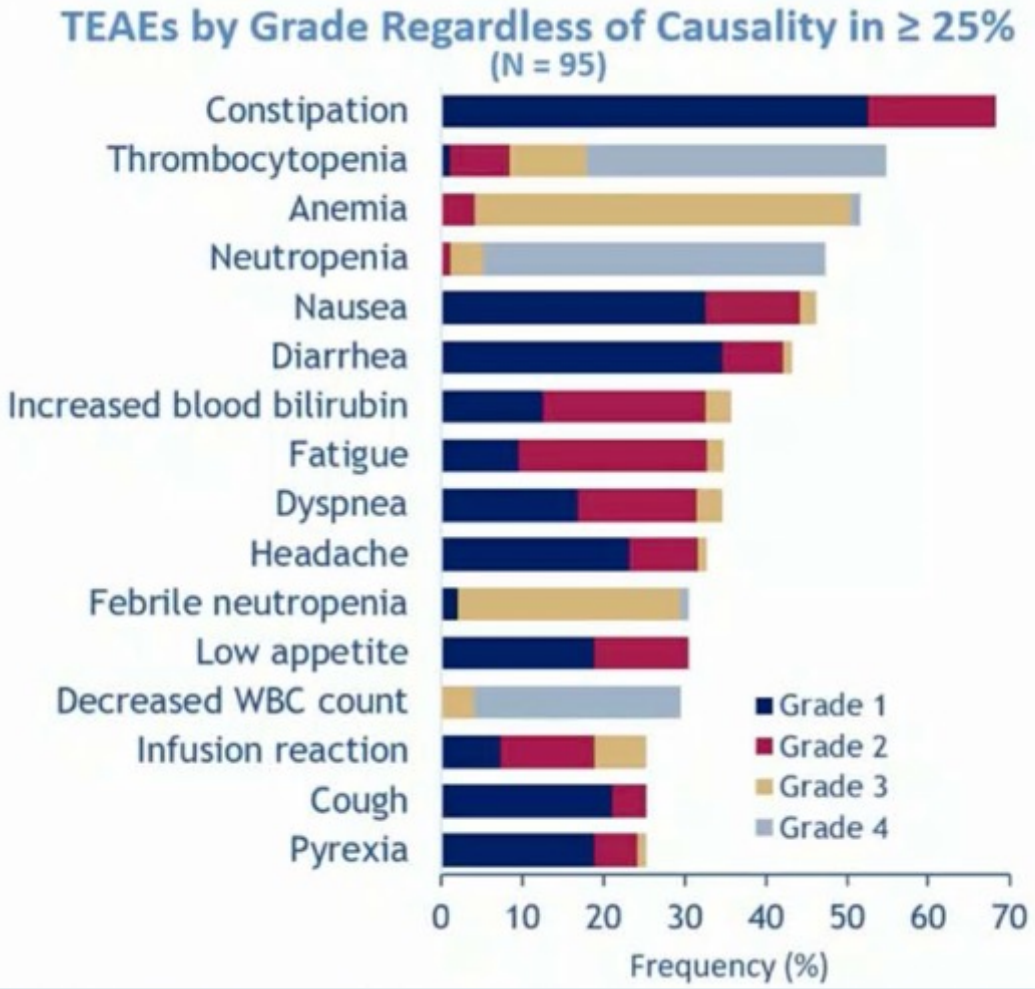
Kaplan–Meier Survival Estimates

All Patients	SCT (N = 35)	No SCT (N = 60)
Median follow-up, months	19.6	12.9
Median OS (95% CI)	NR (NR, NR)	14.8 (11.9, 21.3)
1-year OS, % (95% CI)	91.4 (75.7, 97.2)	64.0 (49.9, 75.1)
2-year OS, % (95% CI)	77.3 (57.3, 88.8)	33.9 (20.0, 48.3)

Sallman DA et al. EHA 2022;Abstract 166.

RTP RESEARCH TO PRACTICE

5F9005: Magrolimab with Azacitidine for HR-MDS — Safety



- 30-day mortality was 2.1%, no additional deaths at 60 days.
- TEAEs led to magrolimab dose delays in 52.6% (no dose reductions), and to AZA dose delays in 49.5% (17.9% had dose reductions).
- One Grade 4 anemia occurred in Cycle 4.
- Infusion-related reaction in 25.3%, Grade 3 in 6.3%.
- Magrolimab discontinuation due to AEs in 6.3% and AZA discontinuation due to AEs in 7.4% of patients.

Sallman DA et al. EHA 2022;Abstract 166.

Agenda

Introduction – RATIFY Trial in Perspective

Module 1 – FLT3 Inhibitors

Module 2 – Anti-CD47 Antibody: Magrolimab

Module 3 – Anti-TIM-3 Antibody: Sabatolimab

Module 4 – CAR T-Cell Therapy

Module 5 – IDH Inhibitors

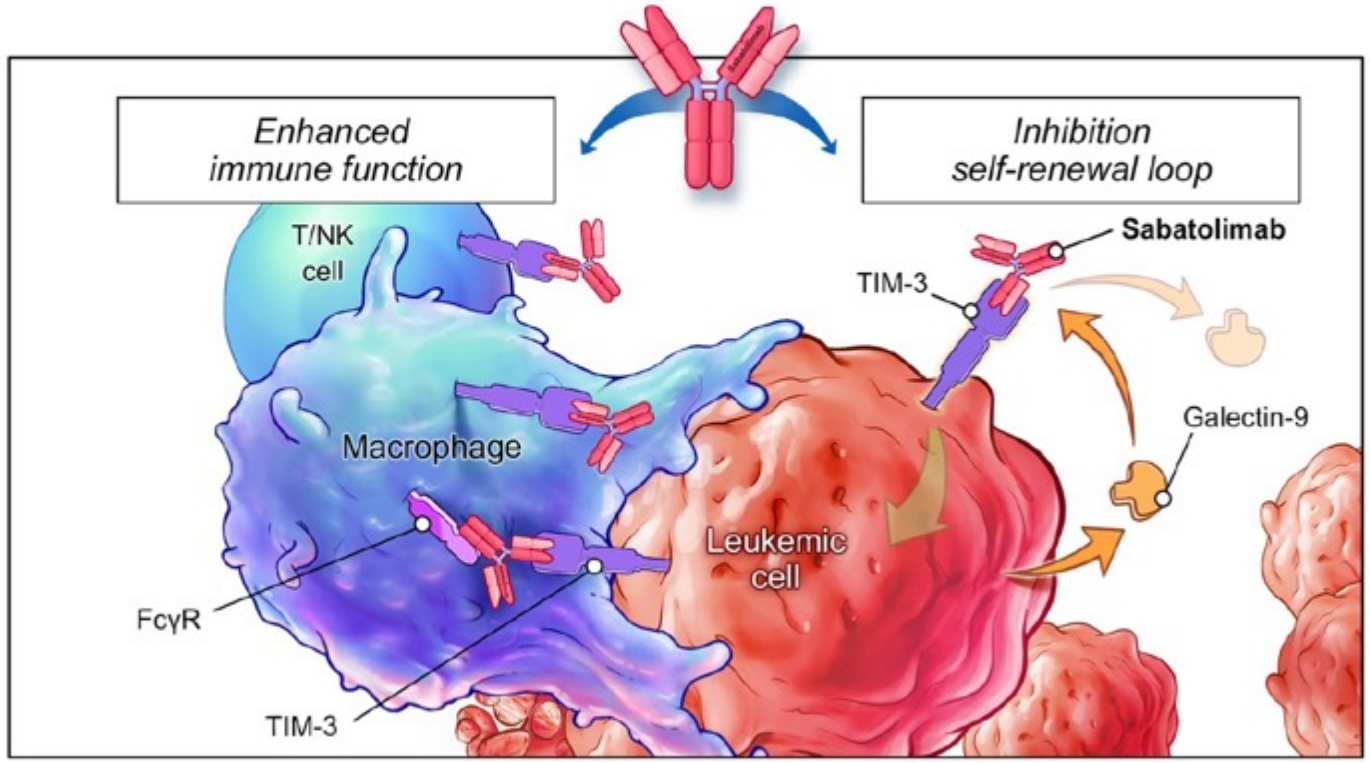
Module 6 – New Myelodysplastic Syndromes Classification System

Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

Sabatolimab targets TIM-3 on immune and leukemic cells: A novel immuno-myeloid therapy



- Sabatolimab binds TIM-3 on immune cells, which enhances antileukemic immune function and phagocytic killing of LSCs and blasts[1-4]
- Sabatolimab directly targets TIM-3 on LSCs, inhibiting TIM-3/galectin-9–driven self-renewal[1,2]

1. Acharya N, et al. *J Immunother Cancer*. 2020;8(1):e000911; 2. Sabatos-Peyton C, et al. SITC 2020. Abstract 439; 3. Borate U, et al. *HemaSphere*. 2020;4(suppl 1):Abstract S185; 4. Borate U, et al. EHA 2020. Oral presentation.

LSC = leukemic stem cell

Brunner AM et al. ASH 2021;Abstract 244.

Efficacy and Safety of Sabatolimab in Combination with Hypomethylating Agents in Patients with Very High/High-Risk Myelodysplastic Syndrome and Acute Myeloid Leukemia: Final Analysis from a Phase Ib Study

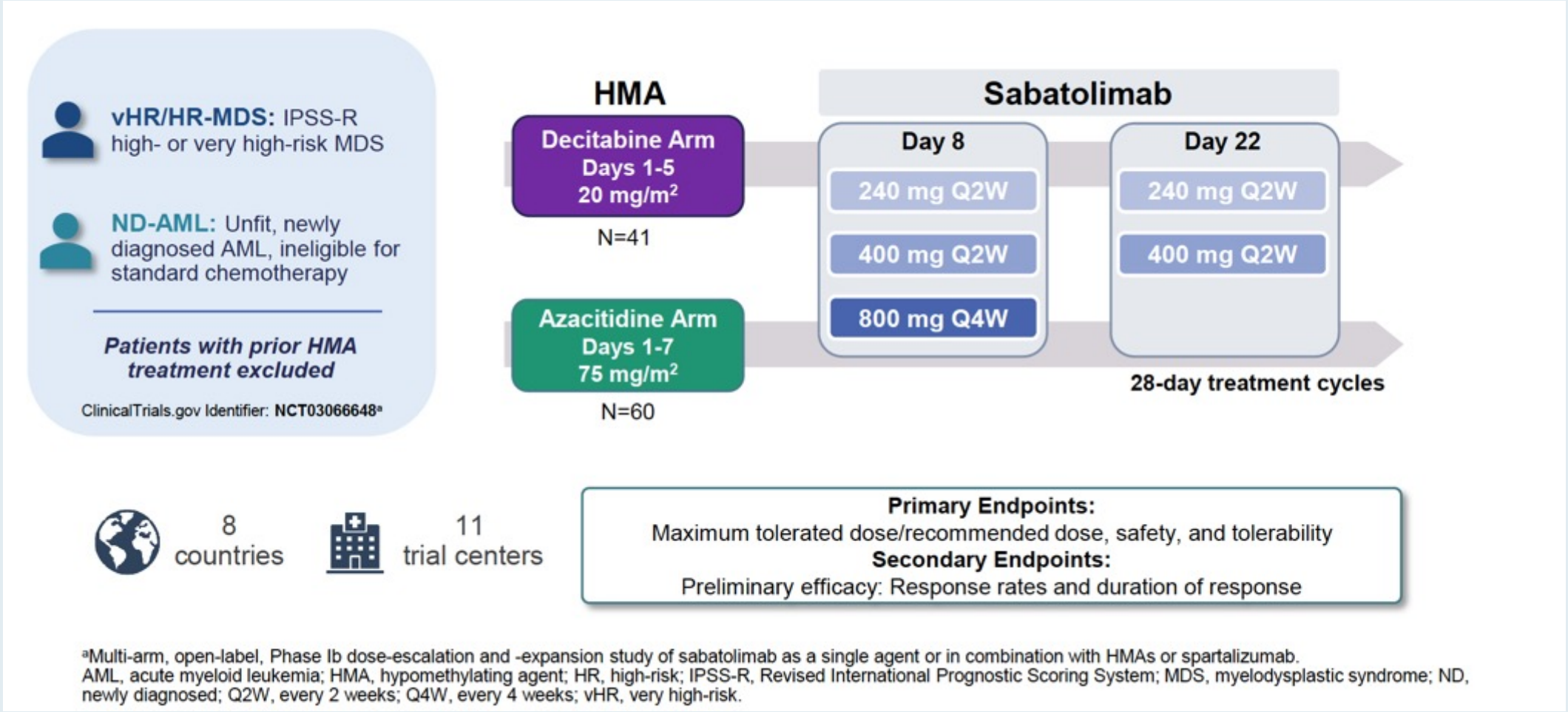
Andrew M. Brunner,[1] Jordi Esteve,[2] Kimmo Porkka,[3] Steve Knapper,[4] Elie Traer,[5] Sebastian Scholl,[6] Guillermo Garcia-Manero,[7] Norbert Vey,[8] Martin Wermke,[9] Jeroen Janssen,[10] Rupa Narayan,[1] Sun Loo,[11] Natalia Tovar,[2] Mika Kontro,[3] Oliver Ottmann,[4] Purushotham Naidu,[12] Marc Pelletier,[13] Andrew Lewandowski,[13] Na Zhang,[13] Anisa Mohammed,[12] Mikael L. Rinne,[13] Uma Borate,[5*] Andrew H. Wei[14*]

*Co-senior authors Uma Borate and Andrew H. Wei contributed equally to this work.

[1]Massachusetts General Hospital, Boston, MA, USA; [2]Hospital Clínic, Barcelona, Spain; [3]Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; [4]Cardiff University, Cardiff, UK; [5]Oregon Health & Science University, Portland, OR, USA; [6]University Hospital Jena, Jena, Germany; [7]MD Anderson Cancer Center, Houston, TX, USA; [8]Institut Paoli-Calmettes, Marseille, France; [9]University Hospital Dresden, Dresden, Germany; [10]Amsterdam University Medical Centers, location VUmc, Amsterdam, The Netherlands; [11]The Alfred Hospital, Melbourne, Victoria, Australia; [12]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [13]Novartis Institutes for BioMedical Research, Cambridge, MA, USA; [14]The Alfred Hospital and Monash University, Melbourne, Australia

ASH 2021;Abstract 244.

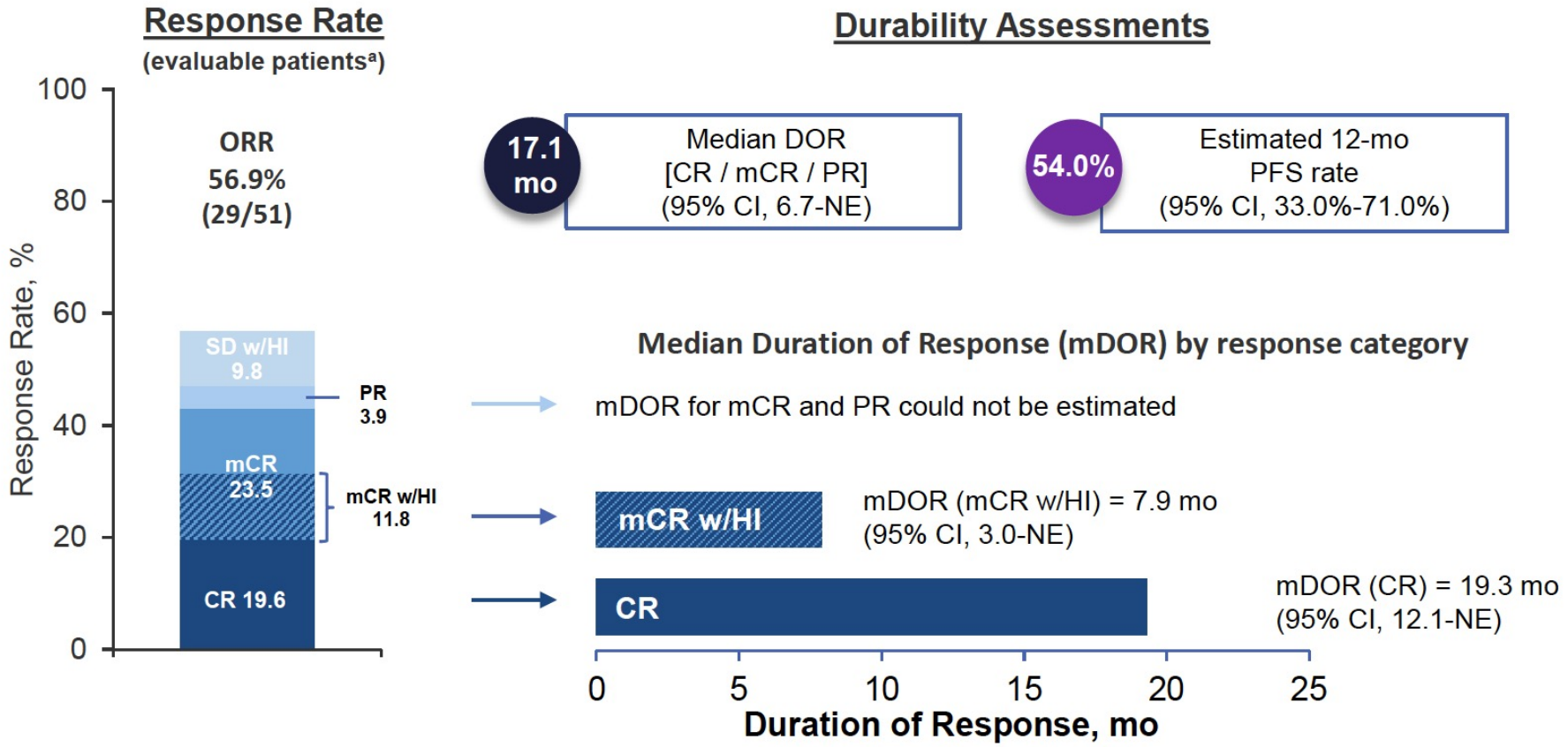
Phase Ib Trial Design of Sabatolimab Combined with Hypomethylating Agents (HMA) for MDS and AML



[a]Multi-arm, open-label, Phase Ib dose-escalation and -expansion study of sabatolimab as a single agent or in combination with HMAs or spartalizumab.
AML, acute myeloid leukemia; HMA, hypomethylating agent; HR, high-risk; IPSS-R, Revised International Prognostic Scoring System; MDS, myelodysplastic syndrome; ND, newly diagnosed; Q2W, every 2 weeks; Q4W, every 4 weeks; vHR, very high-risk.

Brunner AM et al. ASH 2021;Abstract 244.

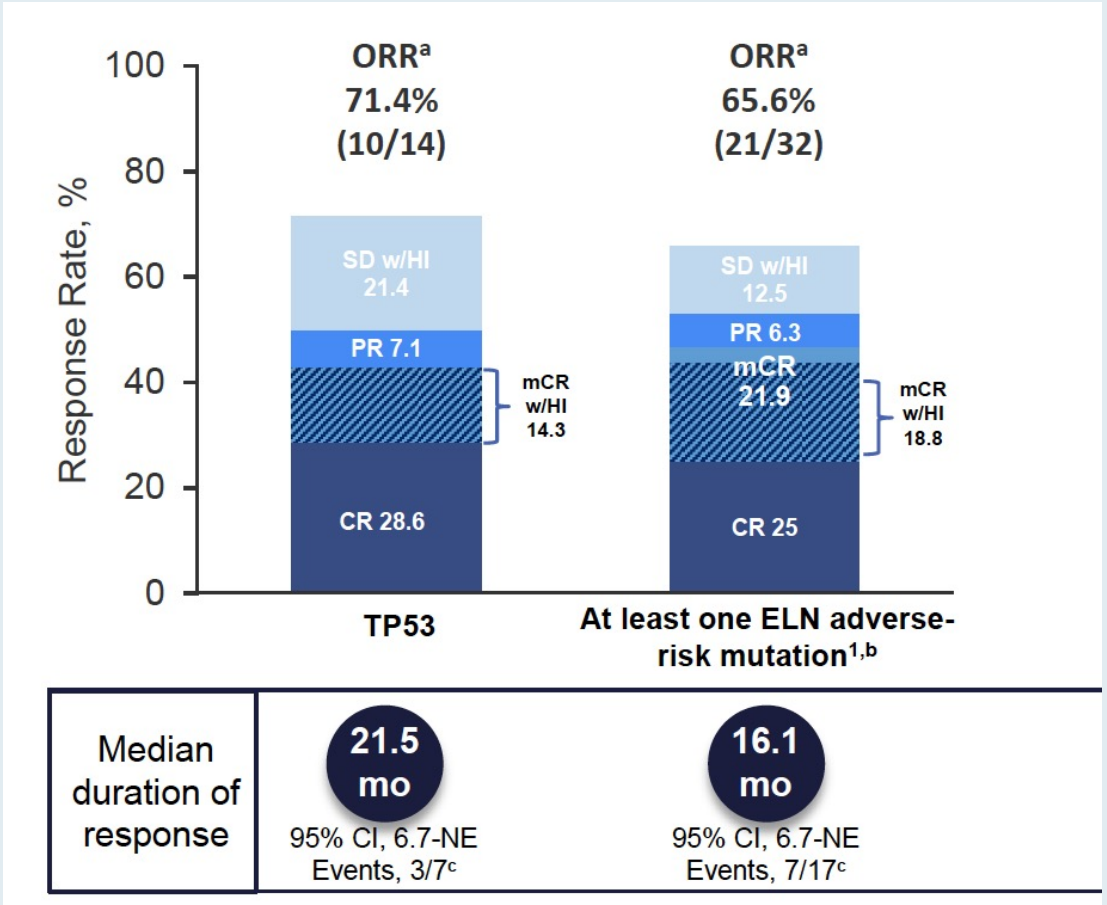
Clinical Responses Associated with Sabatolimab Combined with HMA for Very High-Risk (vHR) or High-Risk (HR) MDS



[a]Evaluable patients, including patients with a valid baseline and at least 1 postbaseline bone marrow assessment or if they had disease progression or disease-related death prior to the first marrow assessment.
CR, complete remission; DOR, duration of response; HI, hematologic improvement; mCR, bone marrow CR; mDOR, median duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial remission; SD, stable disease.

Brunner AM et al. ASH 2021;Abstract 244.

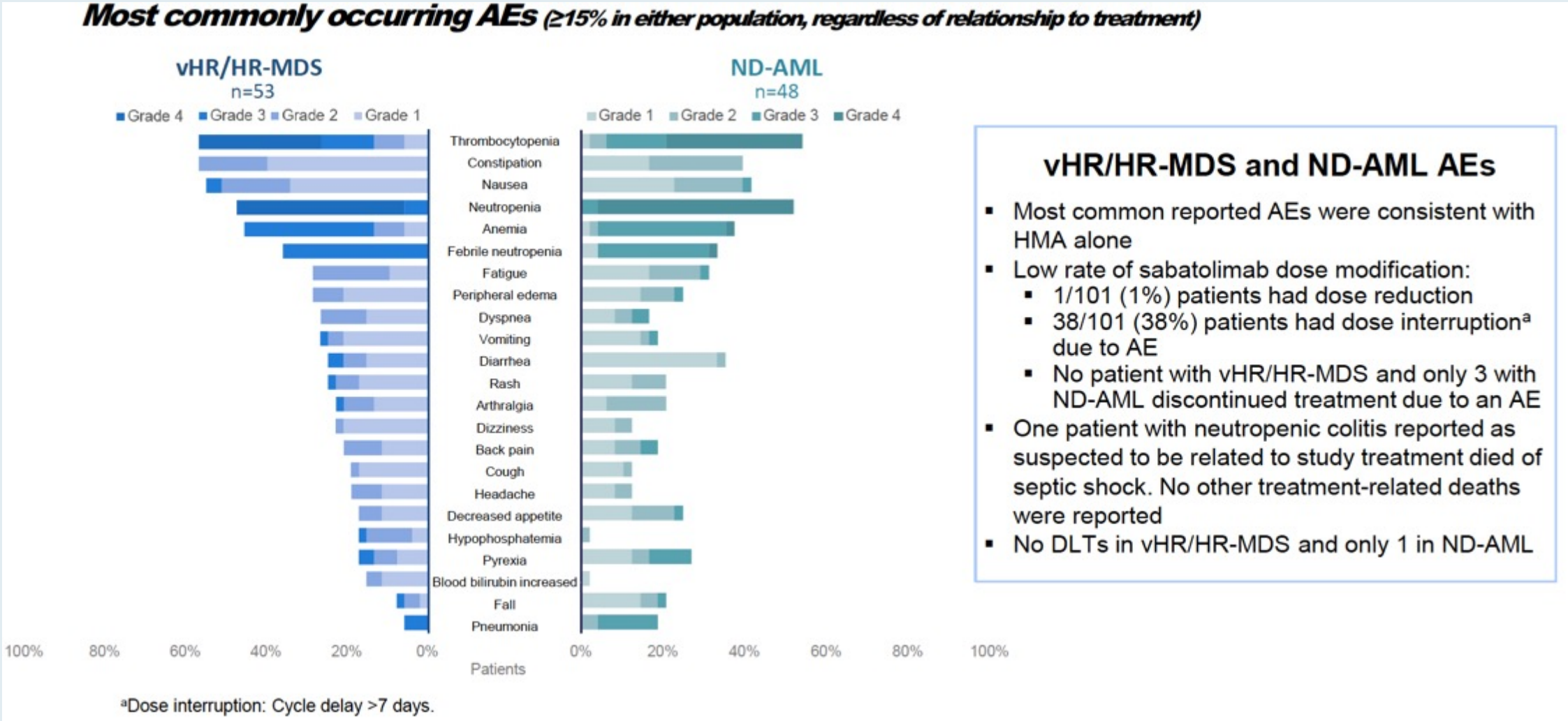
Durability of Responses Associated with Sabatolimab Combined with HMA for vHR/HR MDS



[a] ORR (overall response rate) for patients with MDS was defined as CR + mCR + PR + SD with HI; [b] ELN adverse-risk mutations: TP53, ASXL1, and RUNX1; [c] DOR events (including progression/relapse and death) reported out of the number of patients with a BOR of CR, mCR, or PR (forMDS). [1] Döhner H et al. *Blood* 2017;129(4):424-47.

Brunner AM et al. ASH 2021;Abstract 244.

Adverse Events Associated with Sabatolimab Combined with HMA for MDS and AML



vHR/HR-MDS and ND-AML AEs

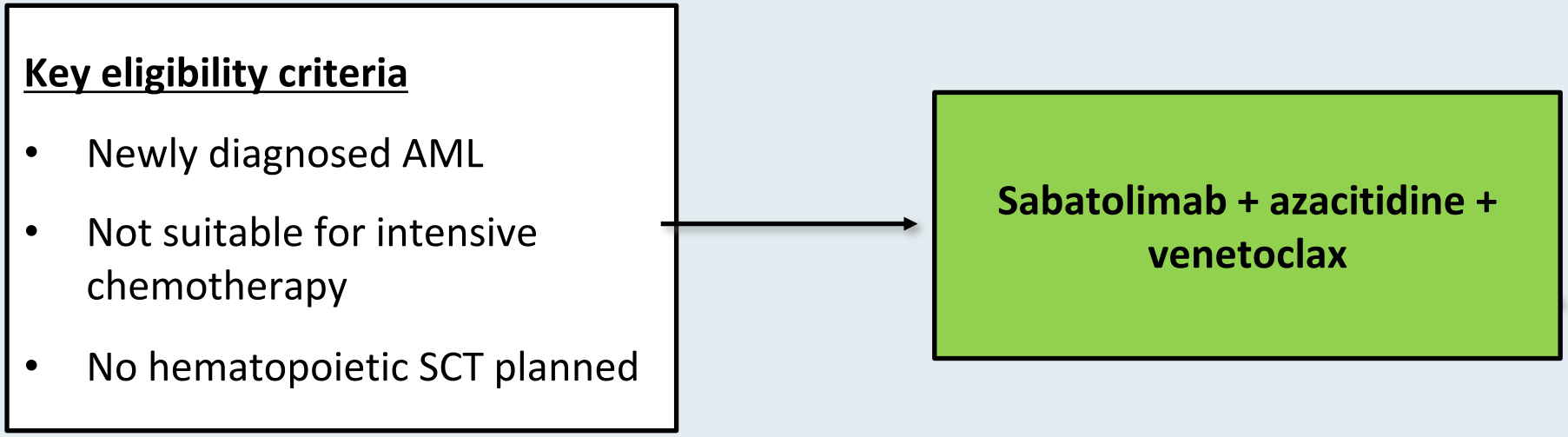
- Most common reported AEs were consistent with HMA alone
- Low rate of sabatolimab dose modification:
  - 1/101 (1%) patients had dose reduction
  - 38/101 (38%) patients had dose interruption[a] due to AE
  - No patient with vHR/HR-MDS and only 3 with ND-AML discontinued treatment due to an AE
- One patient with neutropenic colitis reported as suspected to be related to study treatment died of septic shock. No other treatment-related deaths were reported
- No DLTs in vHR/HR-MDS and only 1 in ND-AML

ND-AML = newly diagnosed AML; AEs = adverse events; DLTs = dose-limiting toxicities

Brunner AM et al. ASH 2021;Abstract 244.

STIMULUS-AML1: A Phase II Trial of Sabatolimab in Combination with Venetoclax and Azacitidine for Patients with AML Not Eligible for Chemotherapy

Trial Identifier: NCT04150029 (Open)



- **Primary endpoints:** Dose-limiting toxicities, complete remission

www.clinicaltrials.gov. Accessed July 2022.

RTP RESEARCH TO PRACTICE

STIMULUS: Clinical Trial Program for Sabatolimab for MDS

Trial identifier	Phase	Setting	Study arms
STIMULUS-MDS1 (NCT03946670)	II	IPSS-R Intermediate-, High- or Very High-risk MDS	• Sabatolimab + HMA • Placebo + HMA
STIMULUS-MDS2 (NCT04266301)	III	High- or Very High-risk MDS	• Sabatolimab + azacitidine • Placebo + azacitidine
STIMULUS-MDS3 (NCT04812548)	II	High- or Very High-risk MDS	• Sabatolimab + azacitidine + venetoclax

www.clinicaltrials.gov. Accessed March 8, 2022.

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Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

OFF-THE-SHELF CD33 CAR-NK CELL THERAPY FOR RELAPSE/REFRACTORY AML: FIRST-IN-HUMAN, PHASE I TRIAL

Ruihao Huang, Qin Wen, Xiaoqi Wang, Hongju Yan, Yingying Ma, Maihong Wang, Xiao Han, Li Gao, Lei Gao, Cheng Zhang, Xi Zhang*

Medical Center of Hematology, Xinqiao Hospital of Army Medical University, State Key Laboratory of Trauma, Burns and Combined Injury.

Chongqing China.

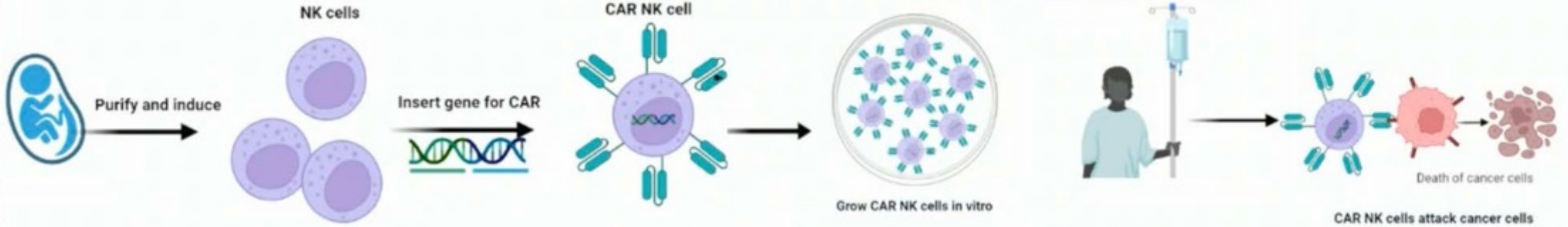
EHA 2022;Abstract 133.

CD33 CAR NK cell Design

CD33 CAR and sIL-15 to enhance the anti-leukemia efficacy of UBC derived NK cells

CAR Design

Treating Procedure



Huang R et al. EHA 2022;Abstract 133.

Efficacy of CD33 CAR NK cell therapy

The ORR is promising especially for patients with low tumor burden(<40%)

ORR:80% (4/5)
CRR(MRD-):80% (4/5)

In dose 2
patient 4 bridging to allo-HSCT maintains CR until the presentation.
Patient 5 have received 91 days MRD- CR without other treatment.

Huang R et al. EHA 2022;Abstract 133.

Safety of CD33 CAR NK Cell Therapy

Mild CAR NK cell therapy related AE

Adverse events	Subjects N (%) Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Management	Outcomes
CRS	1 (20%)	1 (20%)	0	0	0	Antipyretic treatment with NO.5: dexamethasone 5mg	Cure
ICANS	0	0	0	0	0	-	-

No lasting severe bone marrow depression

- Fever and nausea were the most common

Grade 1-2 AEs occurred which is self limiting 5

Adverse events	Subjects N (%) Grade 3	Grade 4	Average duration (d)
Leukopenia	1(20%)	4(80%)	26
Lymphopenia	1(20%)	4(80%)	20
Neutropenia	0	5(100%)	27
Thrombocytopenia	0	5(100%)	20
Anemia	5(100%)	0	25

Huang R et al. EHA 2022;Abstract 133.

Comparing with CD33 CAR-T Cell Therapy

	CD33 CAR T	CD33 CAR NK
Cell source	Autologous T cell	UCB/ healthy donor/ iPSCs cells
Availability	Customed(at least 7 days)	Off- the- shelf
CRS	High risk	Low risk
ICANS	High risk	Low risk
Bone marrow depression	Lasting and refractory	Temporary
Proliferation	Better	Limited
Future aspect	Complications management	Proliferation and anti-leukemia efficacy

Huang R et al. EHA 2022;Abstract 133.

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Module 8 – CPX-351

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RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

A phase Ib/II study of ivosidenib with venetoclax +/- azacitidine in *IDH1*-mutated hematologic malignancies

Curtis Andrew Lachowiez, M.D.[1], Zhihong Zeng, M.D., M.S., M.S.E. [2], Sanam Loghavi, M.D.[3], Gautam Borthakur, M.D.[2], Rebecca S. S. Tidwell, M.S[4]. Tapan M. Kadia, M.D.[2], Lucia Masarova, M.D.[2], George Dono Tippett, B.S.N., R.N.[2], Jacqueline S. Garcia, M.D.[5], Prithviraj Bose, M.D.[2], Elias Jabbour, M.D.[2], Farhad Ravandi, M.D.[2], Naval Guastad Daver, M.D.[2], Guillermo Garcia-Manero, M.D.[2], Koichi Takahashi, M.D., Ph.D.[2], Bilyana Stoilova, B.Sc., M.Sc., Ph.D.[6], Paresh Vyas, M.R.C.P, F.R.C.P, F.R.C. Path.[6,7,8], Hagop M. Kantarjian, M.D.[2], Marina Konopleva, M.D. Ph.D.[2], Courtney Denton DiNardo, M.D., M.S.C.E.[2]

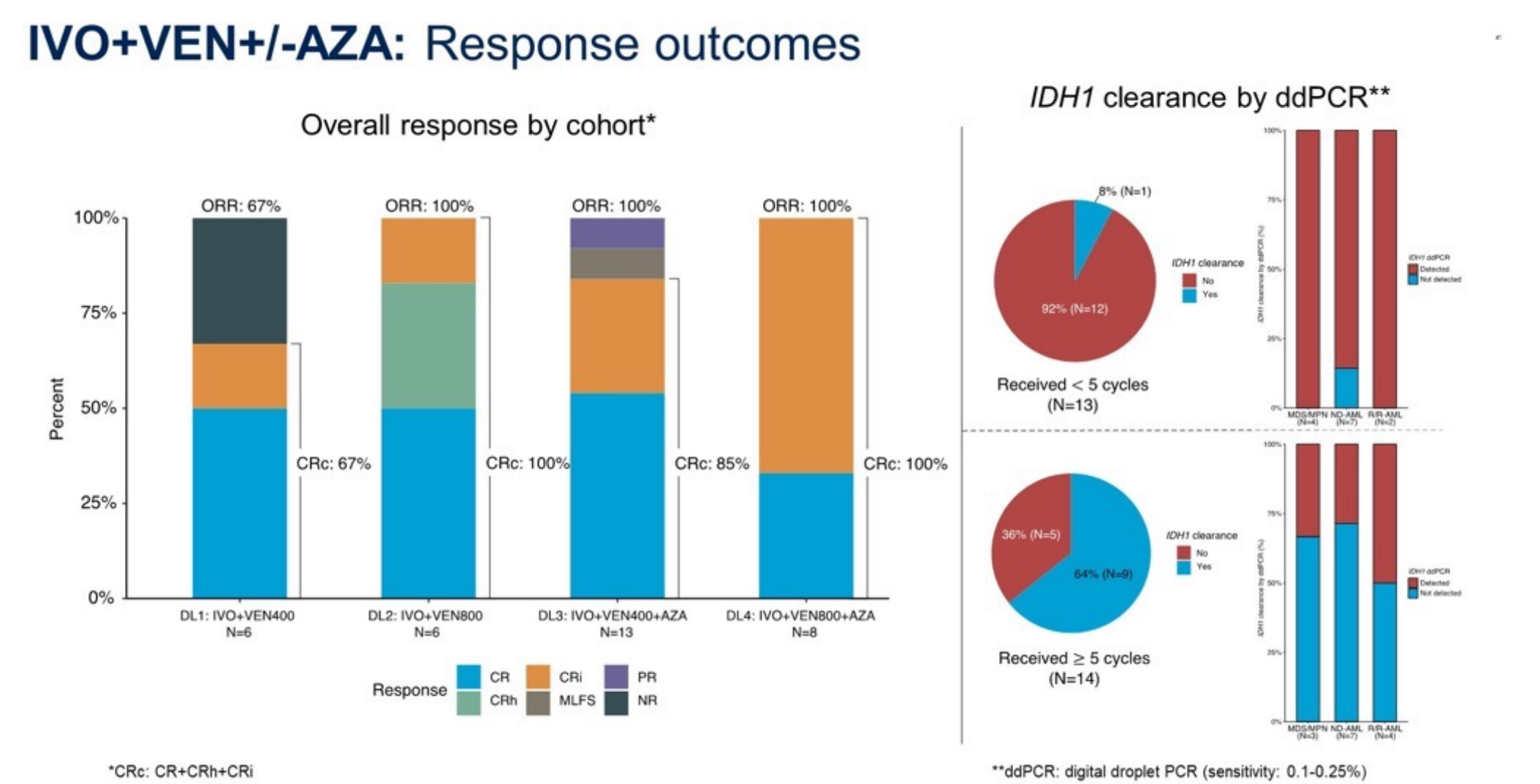
[1]Division of Cancer Medicine, [2]Department of Leukemia, [3]Department of Hematopathology, Department of Biostatistics[4], The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030; [5]Dana-Farber Cancer Institute, Leukemia Program, 450 Brookline Avenue, Boston, MA 02215; [6]MRC Molecular Haematology Unit, MRC Weatherall Institute of Molecular Medicine, [7]Oxford Biomedical Research Centre, University of Oxford, Oxford, UK; [8]Department of Hematology, OUH NHS Trust, Oxford, UK

PRESENTED BY:

Curtis Andrew Lachowiez, M.D.

Abstract 7018.

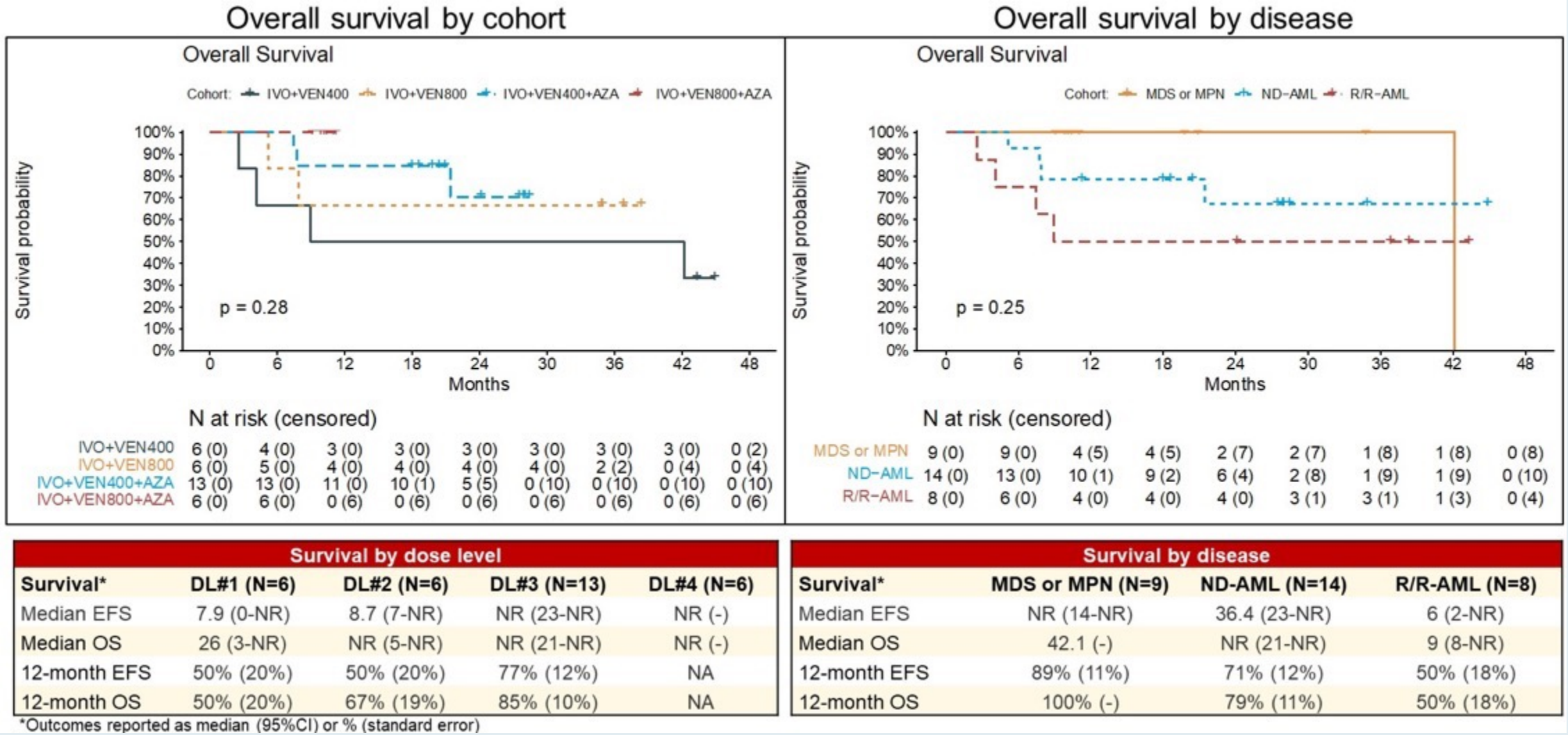
Ivosidenib and Venetoclax with or without Azacitidine: Response Outcomes



Lachowiez CA et al. ASCO 2022;Abstract 7018.

RTP RESEARCH TO PRACTICE

Ivosidenib and Venetoclax with or without Azacitidine: Survival Outcomes



Survival by dose level

Survival*	DL#1 (N=6)	DL#2 (N=6)	DL#3 (N=13)	DL#4 (N=6)
Median EFS	7.9 (0-NR)	8.7 (7-NR)	NR (23-NR)	NR (-)
Median OS	26 (3-NR)	NR (5-NR)	NR (21-NR)	NR (-)
12-month EFS	50% (20%)	50% (20%)	77% (12%)	NA
12-month OS	50% (20%)	67% (19%)	85% (10%)	NA

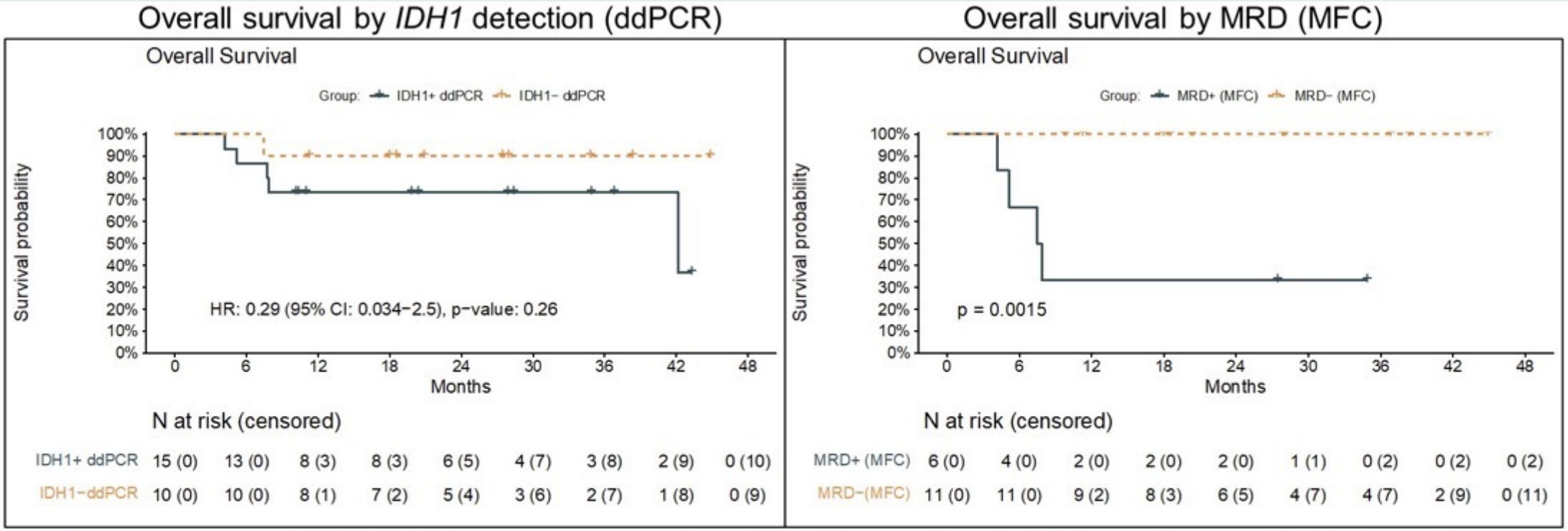
Survival by disease

Survival*	MDS or MPN (N=9)	ND-AML (N=14)	R/R-AML (N=8)
Median EFS	NR (14-NR)	36.4 (23-NR)	6 (2-NR)
Median OS	42.1 (-)	NR (21-NR)	9 (8-NR)
12-month EFS	89% (11%)	71% (12%)	50% (18%)
12-month OS	100% (-)	79% (11%)	50% (18%)

*Outcomes reported as median (95%CI) or % (standard error)

Lachowiez CA et al. ASCO 2022;Abstract 7018.

Ivosidenib and Venetoclax with or without Azacitidine: Survival Outcomes by IDH1 and MRD-MFC

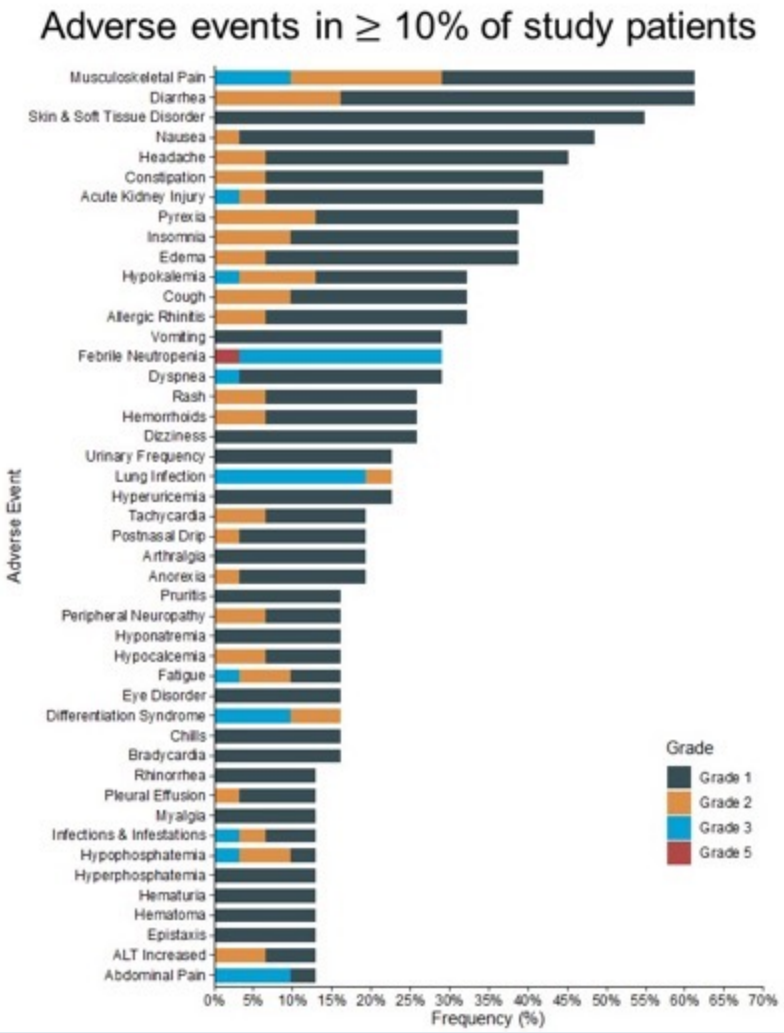


MRD outcomes	Doublet	Triplet	p-value
MRD-negative (MFC)	4/8 (50%)	6/8 (75%)	0.608
IDH1 clearance (ddPCR)	3/10 (30%)	7/17 (41%)	0.6919
IDH1 clearance cycle 5+ (ddPCR)	3/7 (43%)	6/7 (86%)	0.2657
MRD-negative/*IDH1* undetected (N=16)	5/8 (63%)		

*MRD-MFC: measurable residual disease via multiparameter flow cytometry (sensitivity 10^{-3}-10^{-4})

Lachowiez CA et al. ASCO 2022;Abstract 7018.

Ivosidenib and Venetoclax with or without Azacitidine: Safety and Tolerability



Grade 3-5 adverse events*				
Adverse event	**Overall (N = 31)**	**Grade 3**	**Grade 4**	**Grade 5**
Febrile neutropenia	9 (29%)	8 (26%)	-	1 (3%)
Lung infection	6 (19%)	6 (19%)	-	-
Abdominal pain	3 (10%)	3 (10%)	-	-
Differentiation syndrome (IDH-DS)	3 (10%)	3 (10%)	-	-
Musculoskeletal pain	3 (10%)	3 (10%)	-	-
Otitis media	2 (6.5%)	2 (6.5%)	-	-
Tumor lysis syndrome (TLS)	2 (6.5%)	2 (6.5%)	-	-

AE of special interest*	Onset days (range)	Grade 1/2	Grade 3/4	DLT
TLS (N=2)	14 (0-27)	-/-	2/0	1 (50%)
IDH-DS (N=4)	39 (17-95)	0/1	3/0	0 (0%)

*All variables reported as N (%) or median (range); One patient in DL3 experienced G3 TLS attributed as a DLT

No 30- or 60-day mortality occurred on study.

One death secondary to febrile neutropenia and pneumonia occurred in a patient with R/R-AML in DL#1 who relapsed on study treatment

Lachowiez CA et al. ASCO 2022;Abstract 7018.

2022 ASCO® ANNUAL MEETING

Overall survival by *IDH2* mutant allele (R140 or R172) in patients with late-stage mutant-*IDH2* relapsed or refractory acute myeloid leukemia treated with enasidenib or conventional care regimens in the phase 3 IDHENTIFY trial

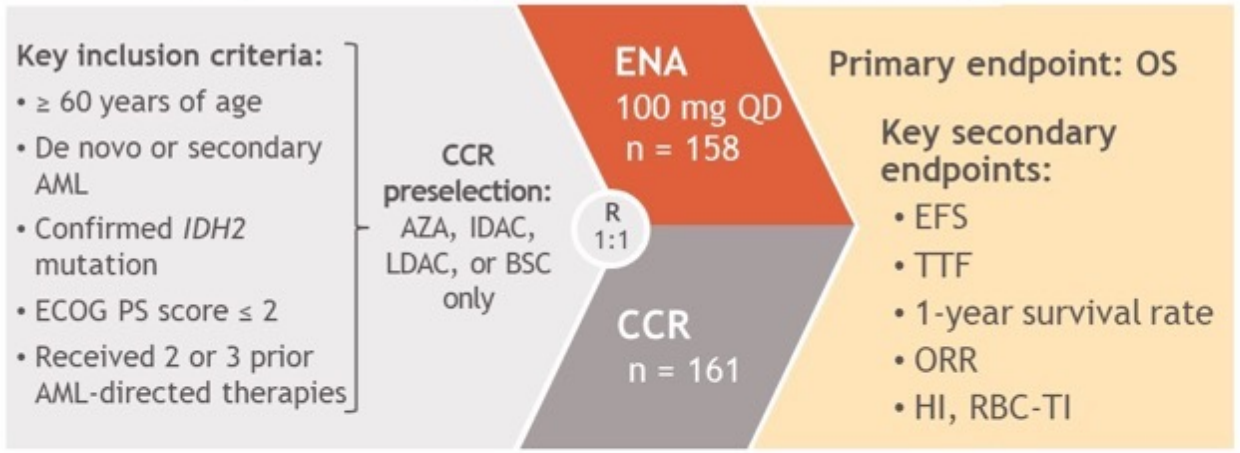
Stéphane de Botton,[1] Alberto Risueño,[2] Andre C. Schuh,[3] Bob Löwenberg,[4] Hee-Je Kim,[5] Paresh Vyas,[6] Andrew H. Wei,[7,8] Eytan M. Stein,[9] Hartmut Döhner,[10] Amir T. Fathi,[11,12] Courtney D. DiNardo,[13] Patricia Martin-Regueira,[14] Lilia Taningco,[14] Iryna Bluemmert,[14] Xin Yu,[14] Wendy L. See,[14] Maroof Hasan[14]

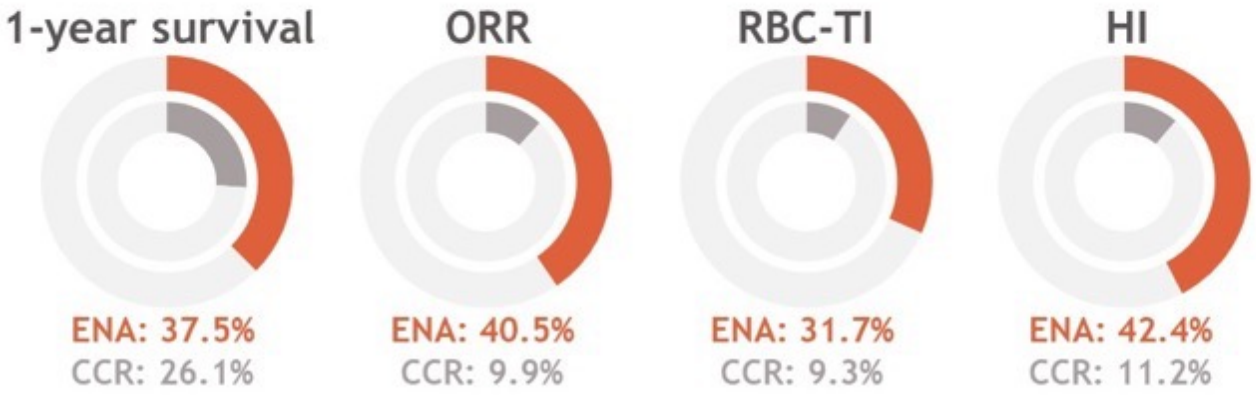
[1]Gustave Roussy, Villejuif, France; [2]BMS Center for Innovation and Translational Research Europe (CITRE), a Bristol-Myers Squibb Company, Seville, Spain; [3]Princess Margaret Cancer Centre, Toronto, ON, Canada; [4]Erasmus University Medical Center, Rotterdam, Netherlands; [5]Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; [6]Oxford Biomedical Research Centre and Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [7]The Alfred Hospital, Melbourne, VIC, Australia; [8]Monash University, Melbourne, VIC, Australia; [9]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [10]Universitätsklinikum Ulm, Ulm, Germany; [11]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [12]Harvard Medical School, Boston, MA, USA; [13]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [14]Bristol Myers Squibb, Princeton, NJ, USA

Presentation Number 7005

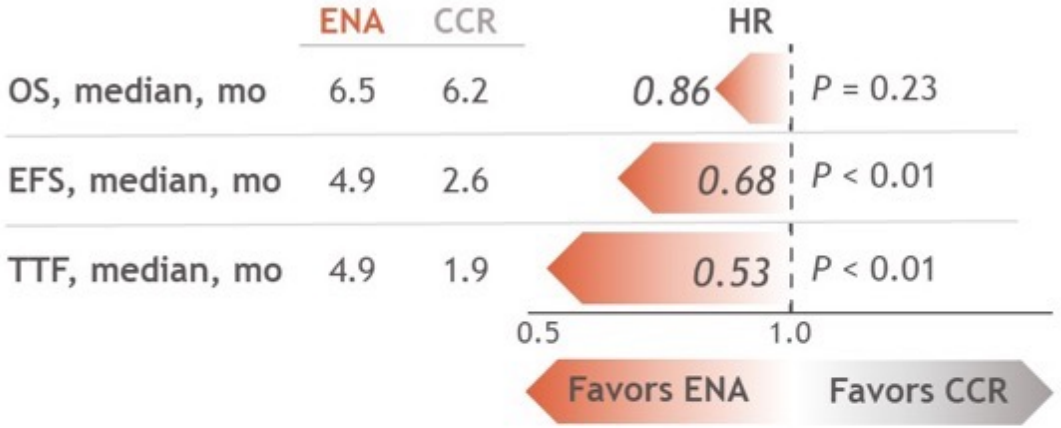
IDHentify: Study Design and Overall Results in the ITT Population

Phase 3, open-label, preselection study design





KM-estimated survival outcomes



- OS was likely confounded by early Tx discontinuation and use of subsequent therapy during OS follow-up, which were more frequent in the CCR arm[1]

ENA = enasidenib; CCR = conventional care regimens

De Botton et al. ASCO 2022;Abstract 7005.

IDHentify: Clinical Responses

- ORR was greater with ENA compared with CCR within both the R140 and R172 subgroups, as were rates of CR, HI, and RBC and platelet TI

R140	ENA n = 115	CCR n = 114
ORR,[a] n (%)	42 (36.5)	13 (11.4)
OR (95% CI); *P* value	4.3 (2.2-8.6); < 0.0001	
CR rate,[a] n (%)	21 (18.3)	4 (3.5)
P value	0.0005	
TI,[b,c] n/N (%)		
RBC	15/76 (19.7)	4/69 (5.8)
Platelet	14/66 (21.2)	7/58 (12.1)
Any HI,[b] n (%)	42 (36.5)	14 (12.3)

R172	ENA n = 43	CCR n = 45
ORR,[a] n (%)	22 (51.2)	3 (6.7)
OR (95% CI); *P* value	15.0 (3.9-56.9); < 0.0001	
CR rate,[a] n (%)	16 (37.2)	2 (4.4)
P value	0.0001	
TI,[b,c] n/N (%)		
RBC	18/28 (64.3)	5/28 (17.9)
Platelet	12/22 (54.5)	1/16 (6.3)
Any HI,[b] n (%)	25 (58.1)	4 (8.9)

ENA = enasidenib; CCR = conventional care regimens

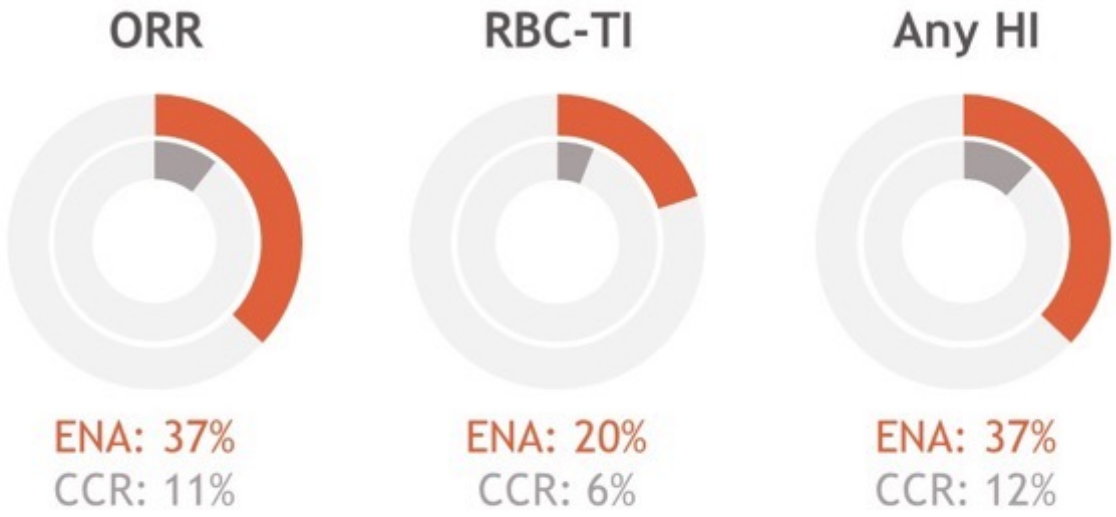
De Botton et al. ASCO 2022;Abstract 7005.

RTP RESEARCH TO PRACTICE

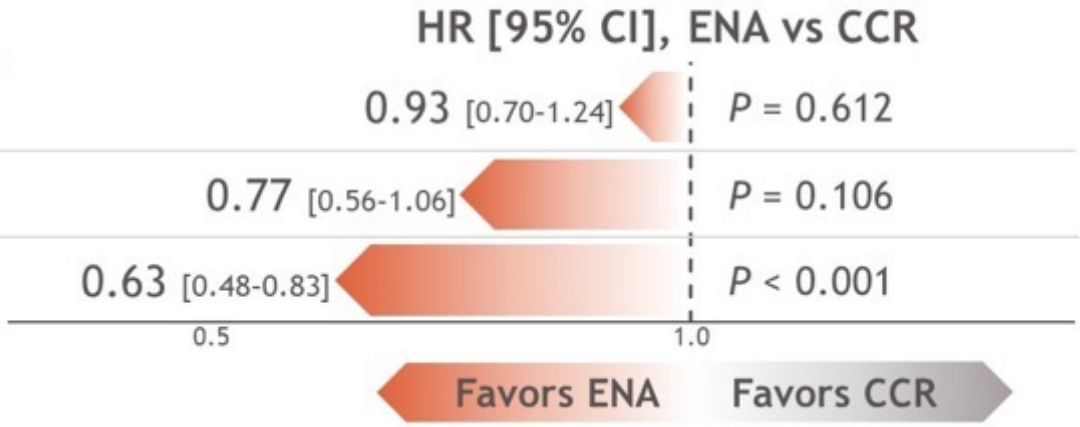
IDHentify: R140 Subgroup Summary

Baseline mutations:

- Median 5 (range, 1-11) gene mutations
- Most common co-mutations: *RUNX1*, *SRSF2*
- The R140 group was enriched (vs R172) with generally poor-risk mutations, including *FLT3* (-ITD and -TKD), *NRAS*, and *RUNX1*



	ENA	CCR
OS, median, mo	5.7	5.7
EFS, median, mo	3.9	1.9
TTF, median, mo	4.3	1.6



ENA = enasidenib; CCR = conventional care regimens

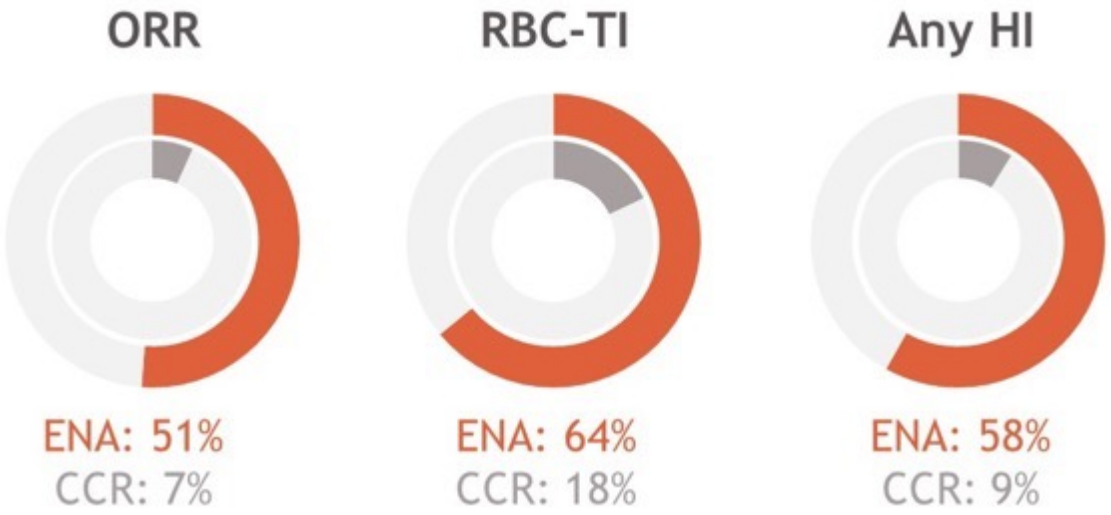
De Botton et al. ASCO 2022;Abstract 7005.

RTP RESEARCH TO PRACTICE

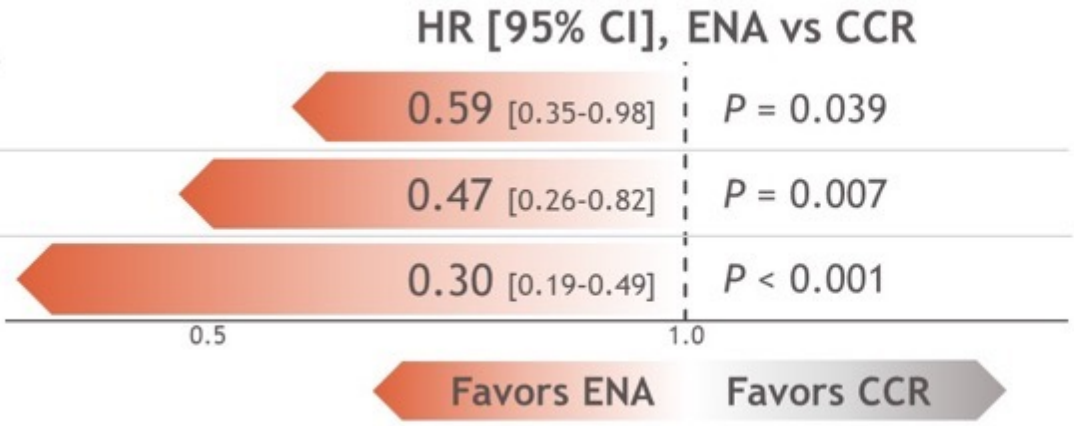
IDHentify: R172 Subgroup Summary

Baseline mutations:

- Median 4 (range, 2-8) gene mutations
- Most common co-mutations: *DNMT3A*, *RUNX1*
- The R172 group was enriched (vs R140) with *DNMT3A* and *TP53*



	ENA	CCR
OS, median, mo	14.6	7.8
EFS, median, mo	10.1	2.7
TTF, median, mo	7.5	2.2



ENA = enasidenib; CCR = conventional care regimens

De Botton et al. ASCO 2022;Abstract 7005.

RTP RESEARCH TO PRACTICE

IDHentify: Grade ≥3 Treatment-Related Adverse Events in ≥10% of Patients in the R140 and R172 Subgroups

Preferred term, n (%)	R140		R172	
	ENA n = 115	CCR n = 101	ENA n = 42	CCR n = 40
Thrombocytopenia	8 (7)	8 (8)	8 (19)	4 (10)
Neutropenia	4 (3)	10 (10)	5 (12)	5 (13)
Febrile neutropenia	2 (2)	12 (12)	2 (5)	5 (13)
Increased blood bilirubin	12 (10)	0	1 (2)	0

ENA = enasidenib; CCR = conventional care regimens

De Botton et al. ASCO 2022;Abstract 7005.

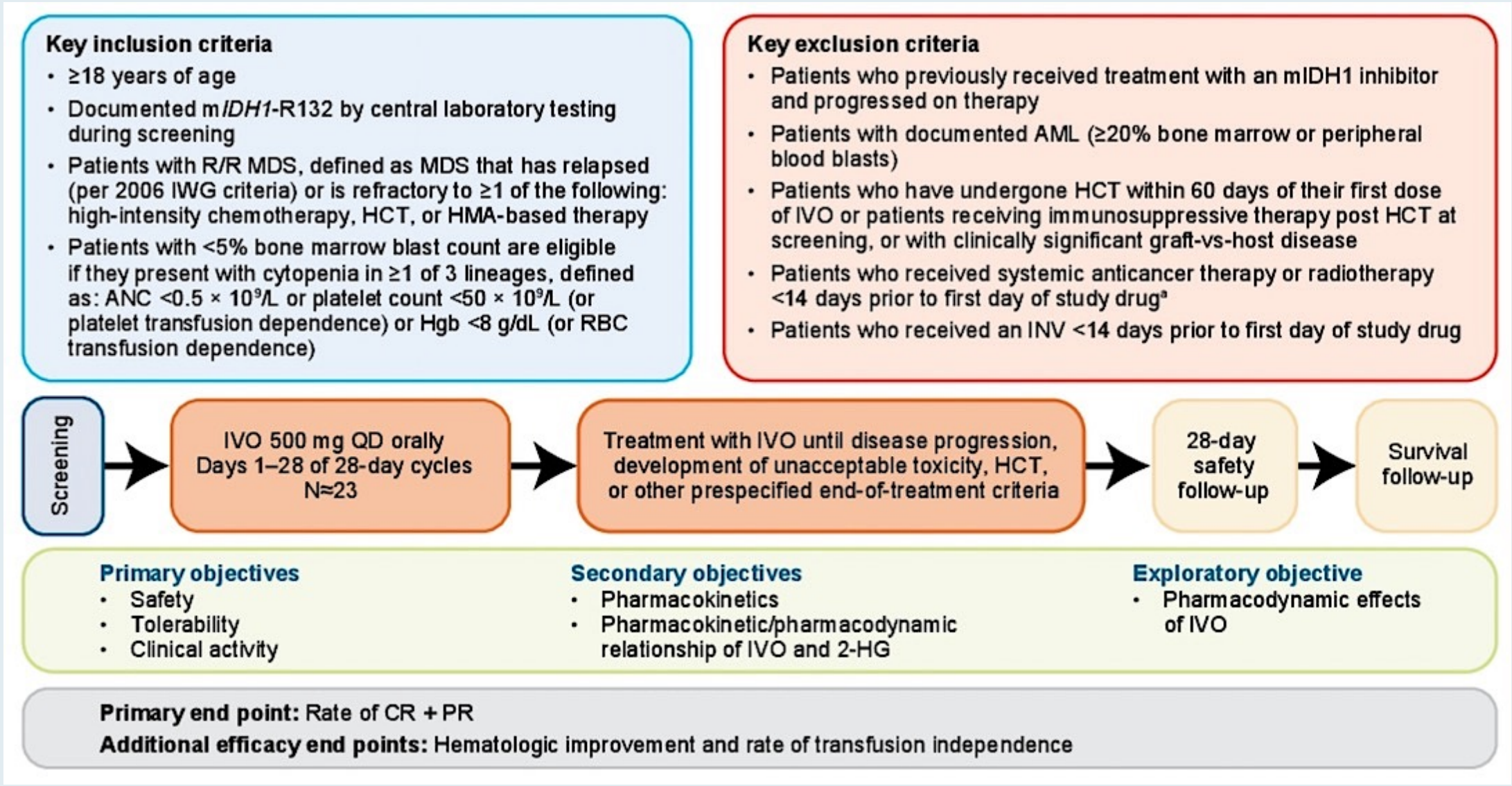
RTP RESEARCH TO PRACTICE

Ivosidenib in Patients with IDH-Mutant Relapsed/Refractory Myelodysplastic Syndrome (R/R MDS): Updated Enrollment and Results of a Phase 1 Dose Escalation and Expansion Substudy

Sallman DA et al.

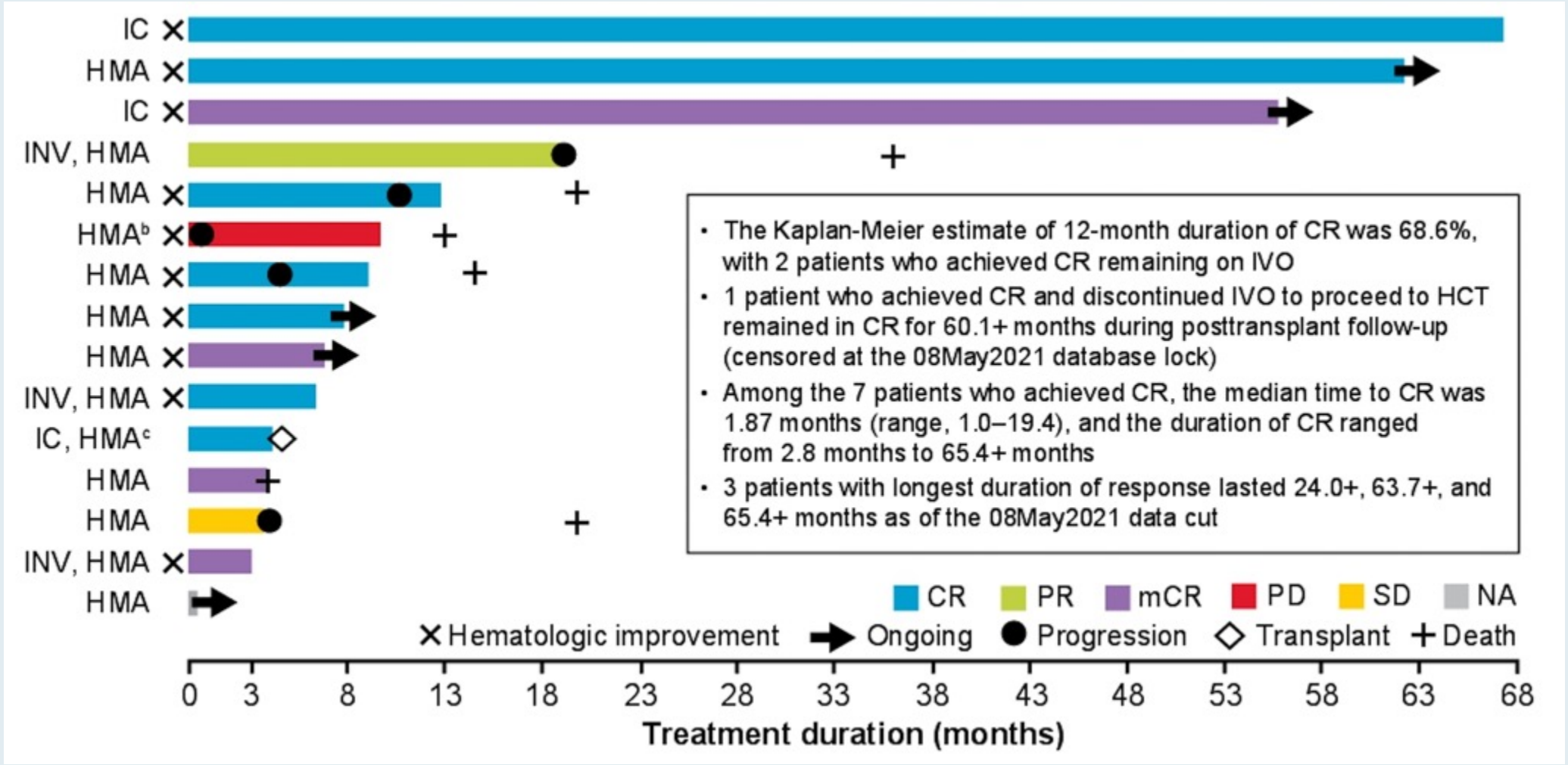
ASCO 2022;Abstract 7053.

Phase I Dose Escalation Substudy of Ivosidenib for Relapsed/Refractory (R/R) Myelodysplastic Syndromes (MDS)



Sallman DA et al. ASCO 2022;Abstract 7053.

Phase I Dose Escalation Substudy of Ivosidenib for R/R MDS: Treatment Duration and Best Overall Response (n = 15)



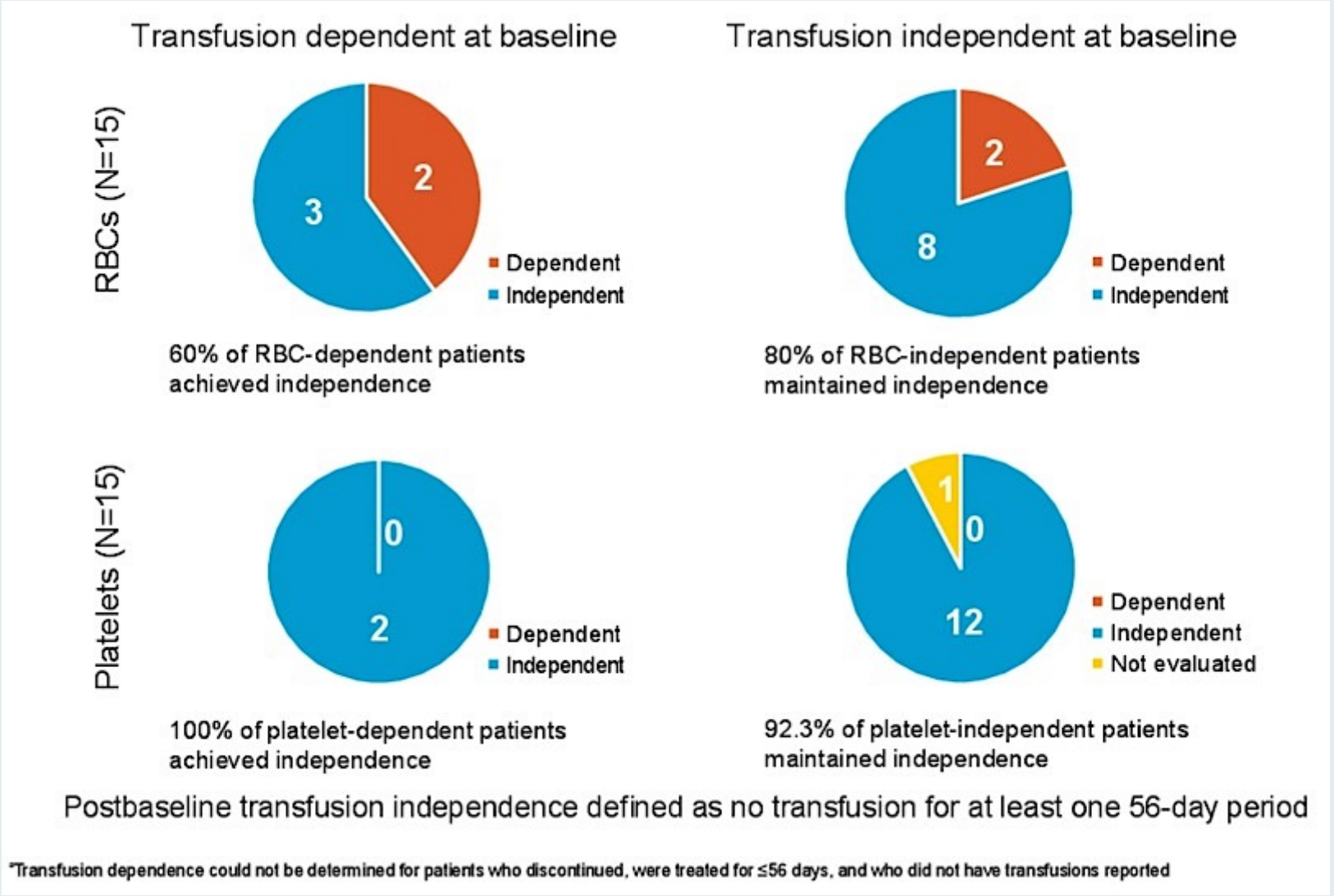
Sallman DA et al. ASCO 2022;Abstract 7053.

Phase I Dose Escalation Substudy of Ivosidenib for R/R MDS: Best Overall Responses Reported by Investigators Using the IWG 2006 MDS Response Criteria

	Patients with R/R MDS receiving IVO 500 mg N=15[a]
CR + PR rate, n (%) [95% CI]	8 (53.3) [26.6, 78.7]
ORR, n (%) [95% CI]	12 (80.0) [51.9, 95.7]
Best response[b], n (%)	
CR	7 (46.7)
PR	1 (6.7)
mCR	4 (26.7)
SD	1 (6.7)
PD	1 (6.7)
Time to CR + PR,[c] median (min, max), months	2.32 (1.0, 19.4)

Sallman DA et al. ASCO 2022;Abstract 7053.

Phase I Dose Escalation Substudy of Ivosidenib for R/R MDS: Platelet and RBC Transfusion Independence



Sallman DA et al. ASCO 2022;Abstract 7053.

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Module 1 – FLT3 Inhibitors

Module 2 – Anti-CD47 Antibody: Magrolimab

Module 3 – Anti-TIM-3 Antibody: Sabatolimab

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Module 5 – IDH Inhibitors

Module 6 – New Myelodysplastic Syndromes Classification System

Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

NEJM Evidence

Published June 12, 2022
NEJM Evid 2022; 1 (7)
DOI: 10.1056/EVIDoa2200008

ORIGINAL ARTICLE

Molecular International Prognostic Scoring System for Myelodysplastic Syndromes

Elsa Bernard, Ph.D.,[1] Heinz Tuechler, Peter L. Greenberg, M.D.,[2] Robert P. Hasserjian, M.D.,[3] Juan E. Arango Ossa, M.S.,[1] Yasuhito Nannya, M.D., Ph.D.,[4,5] Sean M. Devlin, Ph.D.,[1] Maria Creignou, M.D.,[6] Philippe Pinel, M.S.,[1] Lily Monnier, M.S.,[1] Gunes Gundem, Ph.D.,[1] Juan S. Medina-Martinez, M.S.,[1] Dylan Domenico, B.S.,[1] Martin Jädersten, M.D., Ph.D.,[6] Ulrich Germing, M.D.,[7] Guillermo Sanz, M.D., Ph.D.,[8,9,10] Arjan A. van de Loosdrecht, M.D., Ph.D.,[11] Olivier Kosmider, M.D., Ph.D.,[12] Matilde Y. Follo, Ph.D.,[13] Felicitas Thol, M.D.,[14] Lurdes Zamora, Ph.D.,[15] Ronald F. Pinheiro, Ph.D.,[16] Andrea Pellagatti, Ph.D.,[17] Harold K. Elias, M.D.,[18] Detlef Haase, M.D., Ph.D.,[19] Christina Ganster, Ph.D.,[19] Lionel Ades, M.D., Ph.D.,[20] Magnus Tobiasson, M.D., Ph.D.,[6] Laura Palomo, Ph.D.,[21] Matteo Giovanni Della Porta, M.D.,[22] Akifumi Takaori-Kondo, M.D., Ph.D.,[23] Takayuki Ishikawa, M.D., Ph.D.,[24] Shigeru Chiba, M.D., Ph.D.,[25] Senji Kasahara, M.D., Ph.D.,[26] Yasushi Miyazaki, M.D., Ph.D.,[27] Agnes Viale, Ph.D.,[28] Kety Huberman, B.S.,[28] Pierre Fenaux, M.D., Ph.D.,[20] Monika Belickova, Ph.D.,[29] Michael R. Savona, M.D.,[30] Virginia M. Klimek, M.D.,[18] Fabio P. S. Santos, M.D., Ph.D.,[31] Jacqueline Boultwood, Ph.D.,[17] Ioannis Kotsianidis, M.D., Ph.D.,[32] Valeria Santini, M.D.,[33] Francesc Solé, Ph.D.,[21] Uwe Platzbecker, M.D.,[34] Michael Heuser, M.D.,[14] Peter Valent, M.D.,[35,36] Kazuma Ohyashiki, M.D., Ph.D.,[37] Carlo Finelli, M.D.,[38] Maria Teresa Voso, M.D.,[39] Lee-Yung Shih, M.S.,[40] Michaela Fontenay, M.D., Ph.D.,[12] Joop H. Jansen, Ph.D.,[41] José Cervera, M.D., Ph.D.,[42] Norbert Gattermann, M.D.,[7] Benjamin L. Ebert, M.D., Ph.D.,[43] Rafael Bejar, M.D., Ph.D.,[44] Luca Malcovati, M.D.,[45] Mario Cazzola, M.D.,[45] Seishi Ogawa, M.D., Ph.D.,[4,46,47] Eva Hellström-Lindberg, M.D., Ph.D.,[6] and Elli Papaemmanuil, Ph.D.[1]

MDS Risk Assessment Calculators

The IWG-PM under the aegis of the MDS Foundation, Inc. has developed two prognostic tools, the IPSS-M and IPSS-R Calculators, to determine a patient's risk of progressing to Acute Myeloid Leukemia (AML).

NEW IPSS-M Calculator

The IPSS-M is the newest MDS prognosis calculator that combines genomic profiling with hematologic and cytogenetic parameters, improving the risk stratification of patients with MDS. This is a valuable tool for clinical decision-making, offering the prospect of tailoring diagnosis and therapeutic interventions to each patient's molecular profile.

Click below to access the calculator. iOS and Android apps coming soon.

IPSS-M Calculator

IPSS-M R Package

https://www.mds-foundation.org/mds-iwg-pm/

RTP RESEARCH TO PRACTICE

INTEGRATED GENETIC DIAGNOSTICS OF PATIENTS WITH EARLY ONSET OF *DE NOVO* MYELODYSPLASTIC SYNDROMES

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Department of Biomedicine and Prevention, University of Rome "Tor Vergata", Rome, Italy
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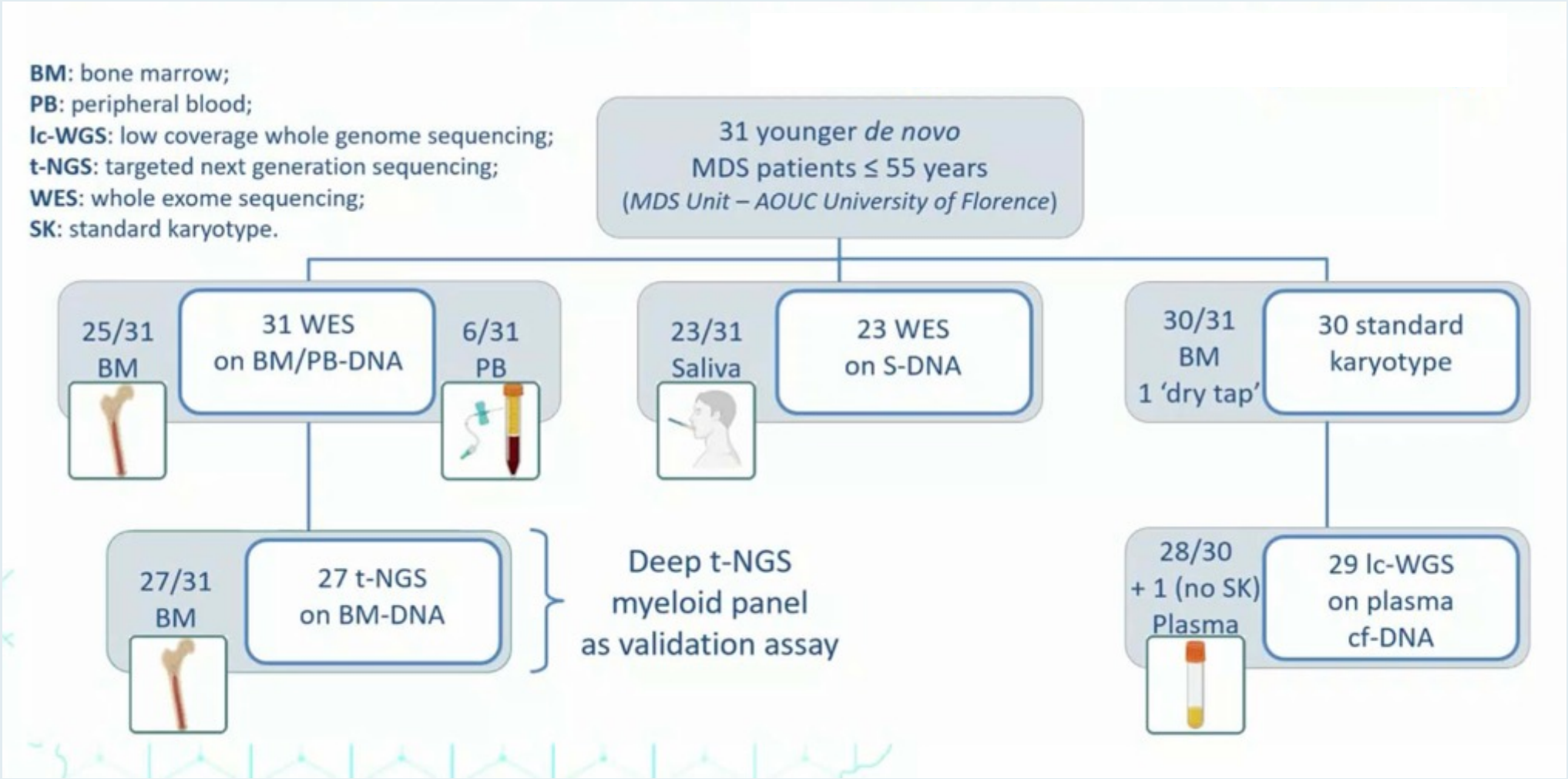
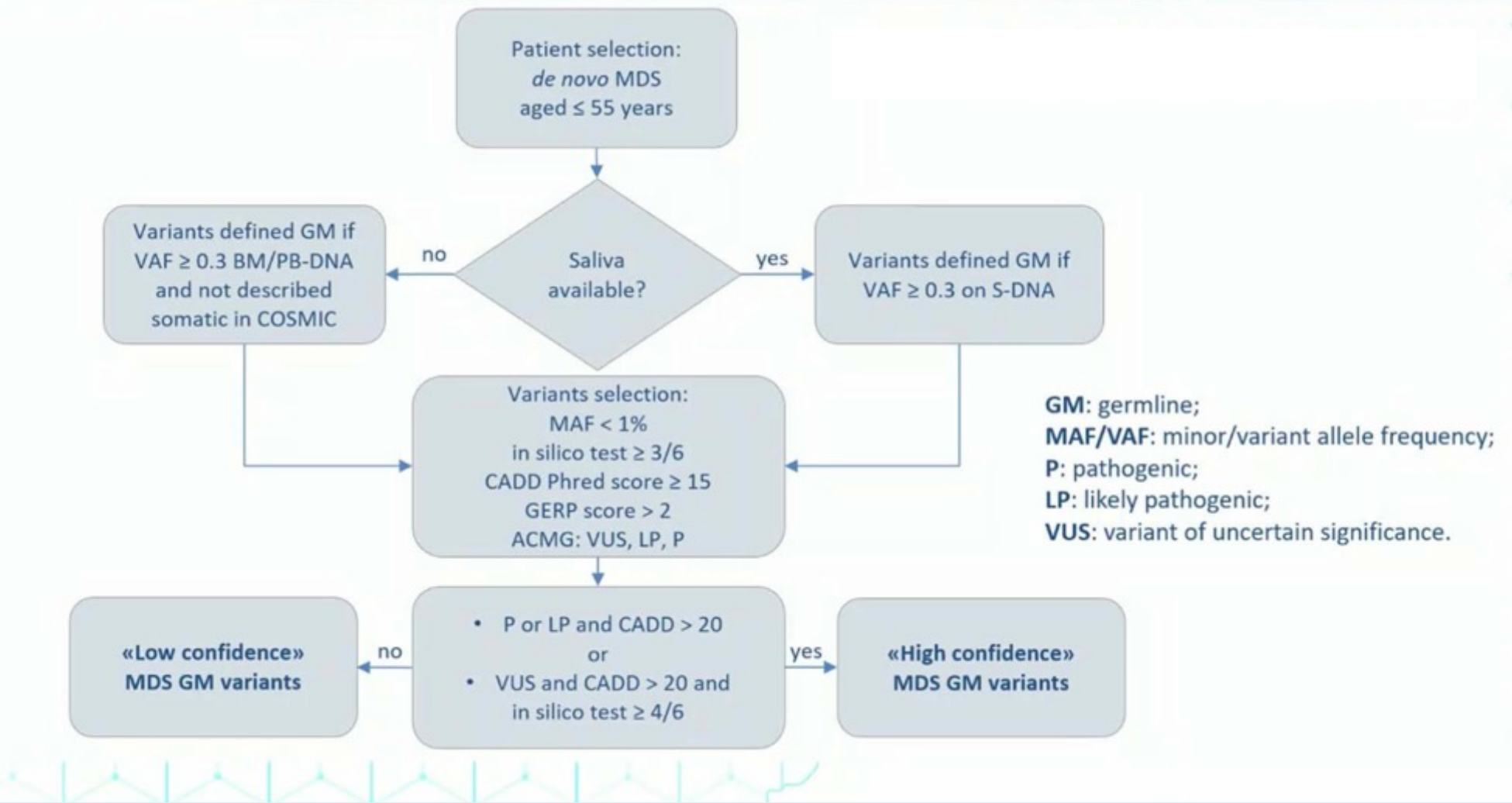
EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes: Next-Generation Sequencing



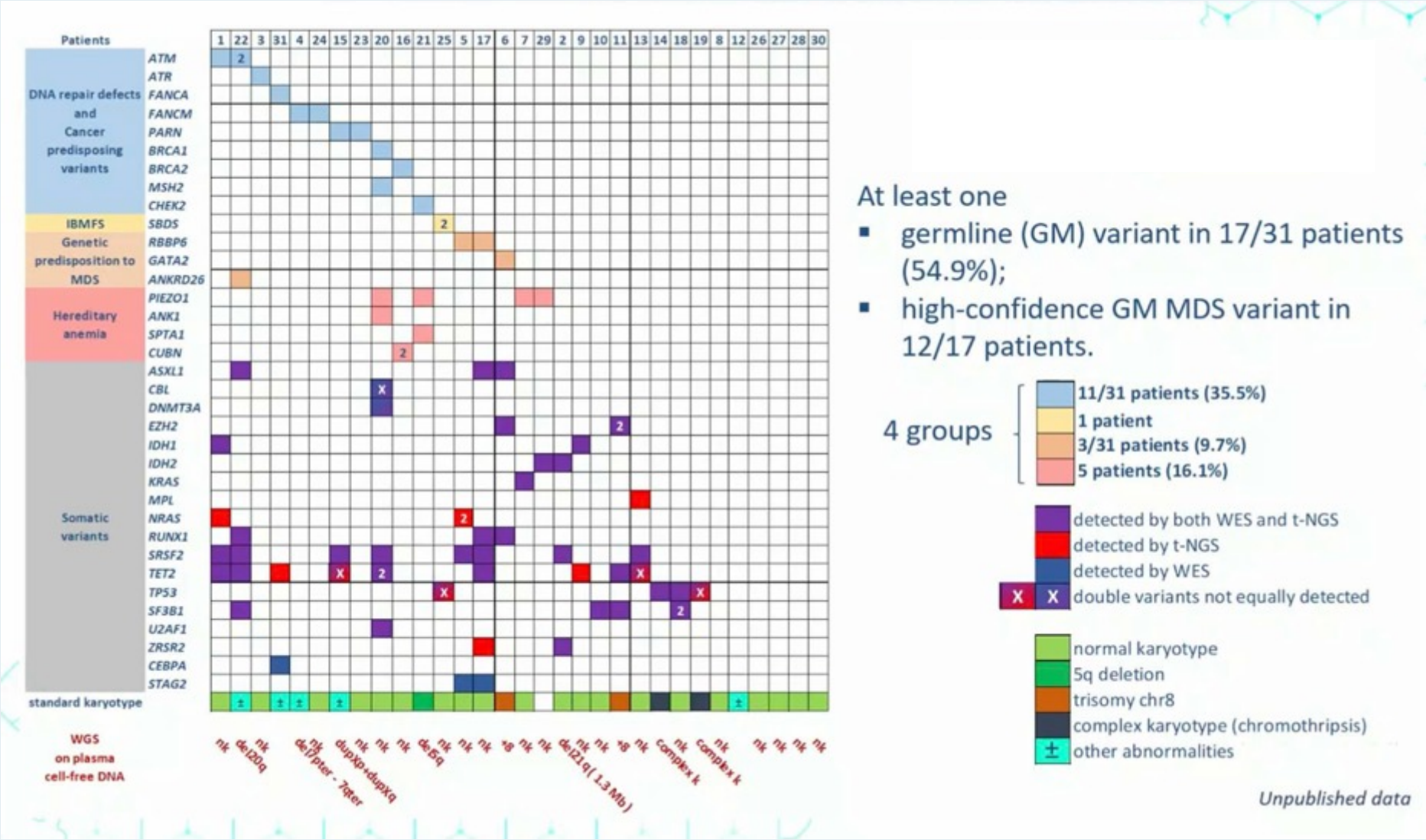
Attardi E et al. EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes: Variant Selection



Attardi E et al. EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes



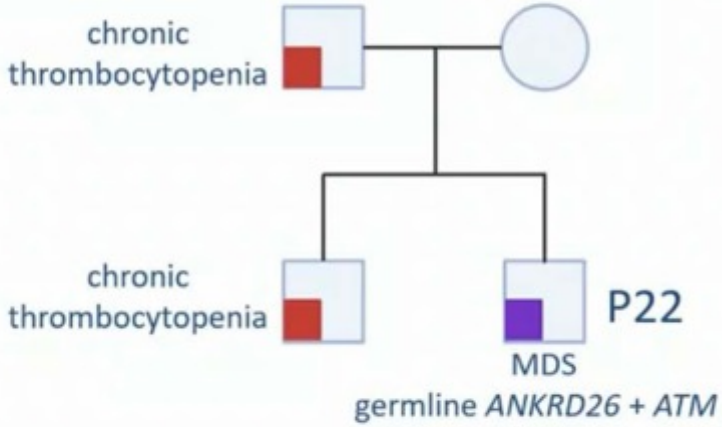
Attardi E et al. EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes: Multilocus Inheritance

multi-locus inheritance: 4/17 patients:

- i.e. P22: 2 compound heterozygous variants in *ATM* gene

  familial thrombocytopenia → screening of the 5'UTR of *ANKRD26*: *ANKRD26* c.-128G>A;



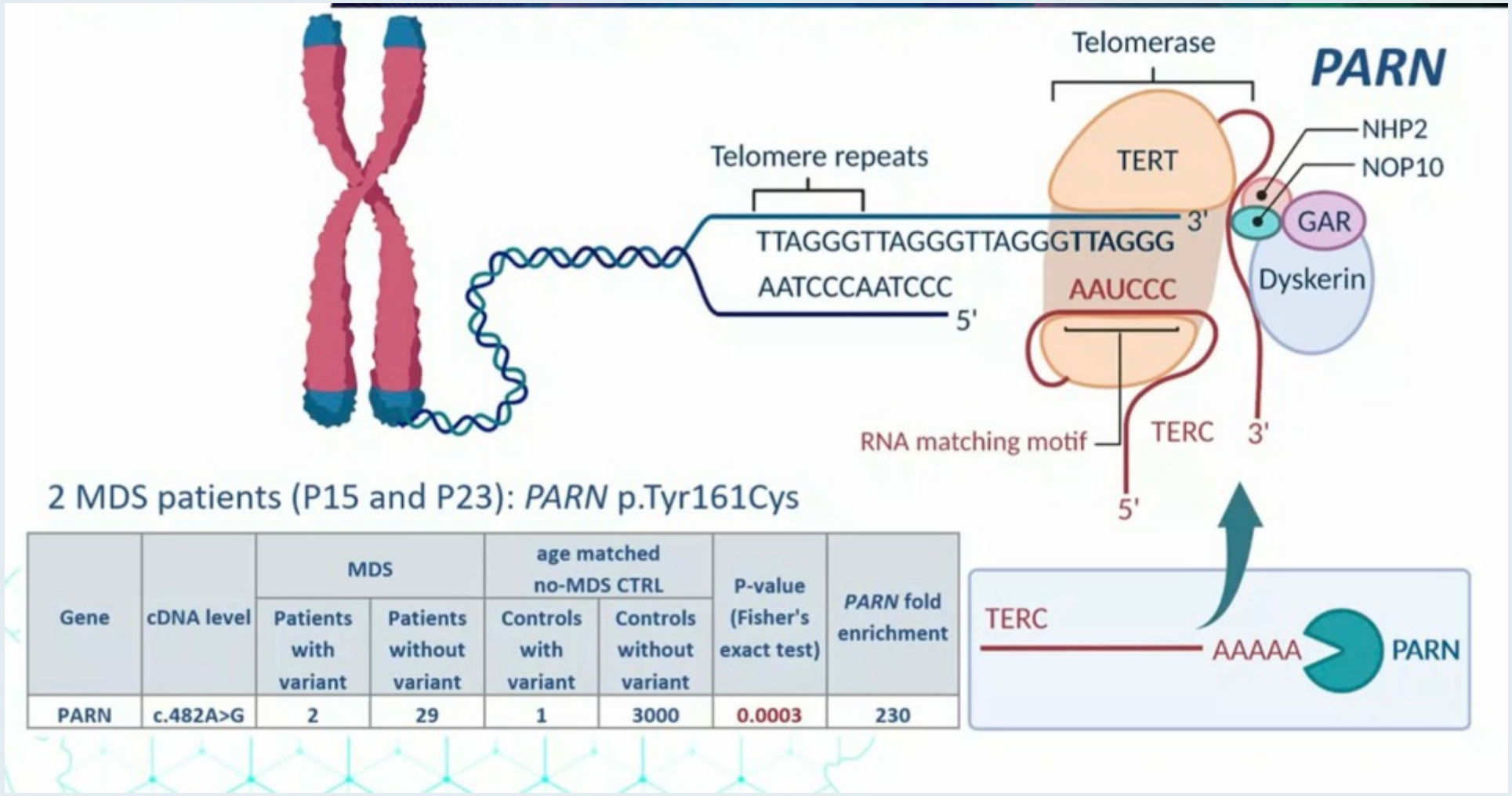
positive familial history in 11/31 patients → 9/11 patients presented at least one GM variant.

"familial history" as predictive parameter for GM predisposition (p-value = 0.03).

Unpublished data

Attardi E et al. EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes



2 MDS patients (P15 and P23): *PARN* p.Tyr161Cys

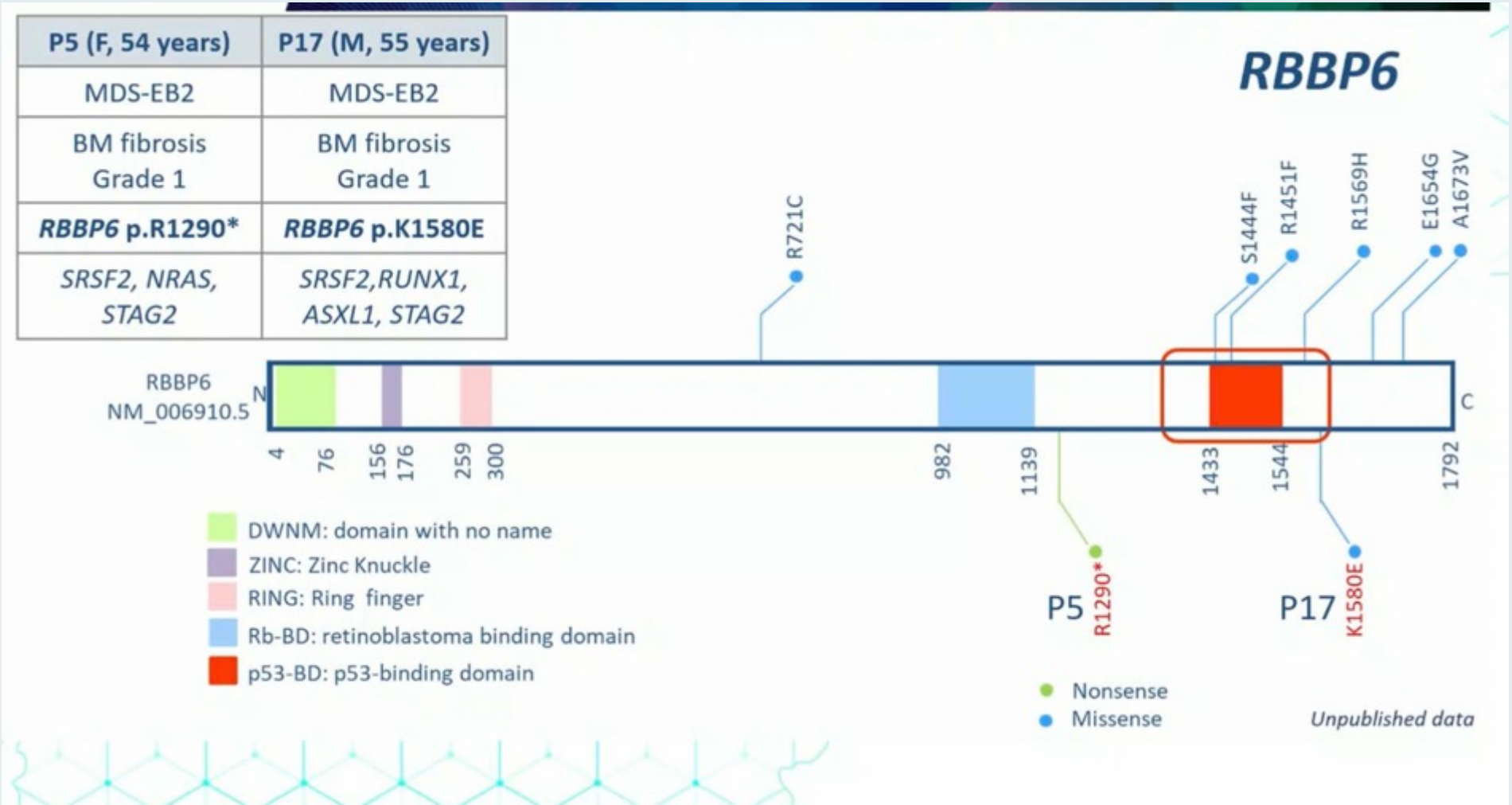
Gene	cDNA level	MDS		age matched no-MDS CTRL		P-value (Fisher's exact test)	*PARN* fold enrichment
		Patients with variant	Patients without variant	Controls with variant	Controls without variant		
PARN	c.482A>G	2	29	1	3000	0.0003	230

Attardi E et al. EHA 2022;Abstract 165.

RTP RESEARCH TO PRACTICE

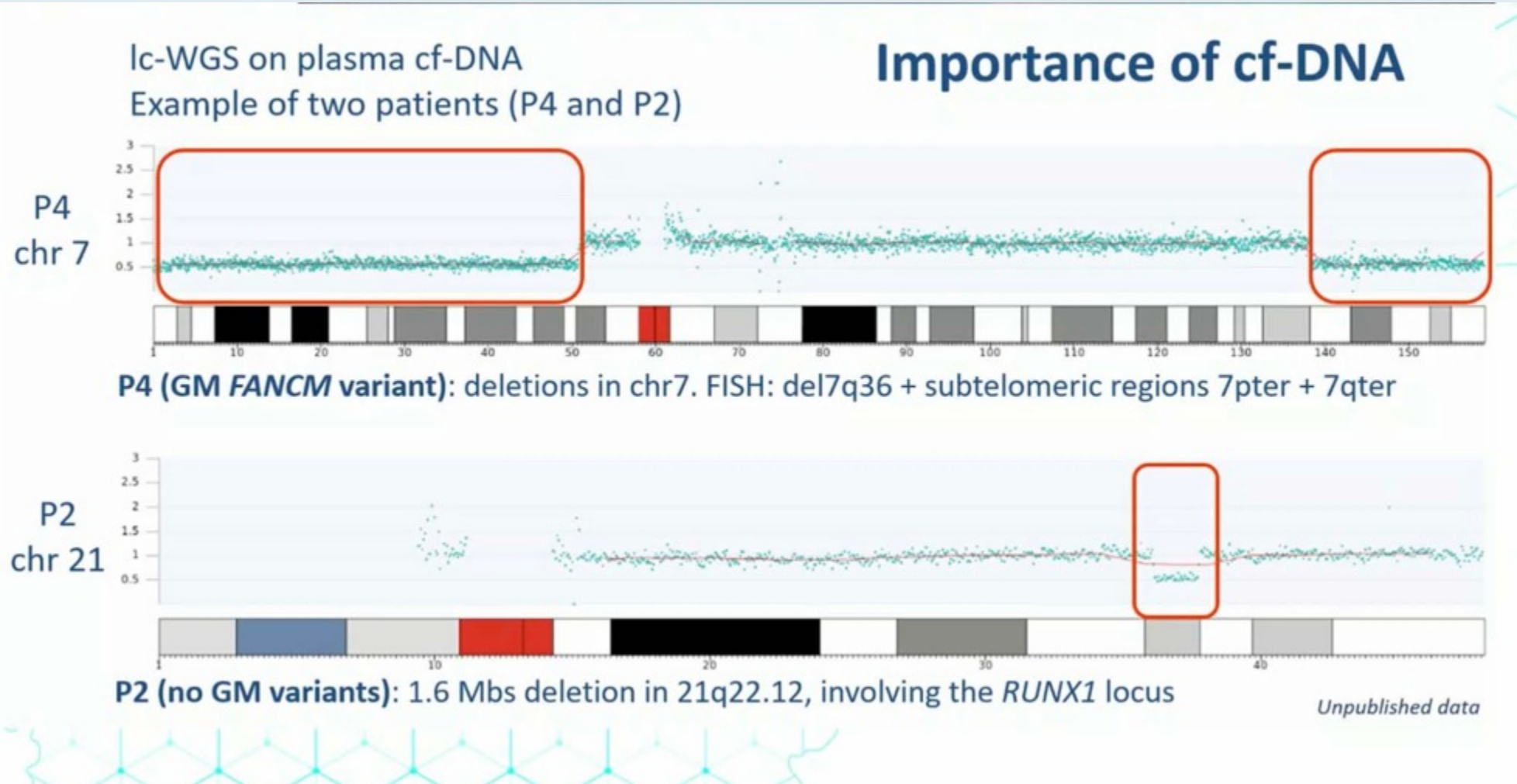
Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes

P5 (F, 54 years)	P17 (M, 55 years)
MDS-EB2	MDS-EB2
BM fibrosis Grade 1	BM fibrosis Grade 1
RBBP6* p.R1290	***RBBP6* p.K1580E**
SRSF2, NRAS, STAG2	*SRSF2,RUNX1, ASXL1, STAG2*



Attardi E et al. EHA 2022;Abstract 165.

Integrated Genetic Diagnostics of Patients with Early Onset of de Novo Myelodysplastic Syndromes: Importance of cf-DNA



Attardi E et al. EHA 2022;Abstract 165.

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RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

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617-29.

Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia

C.D. DiNardo, B.A. Jonas, V. Pullarkat, M.J. Thirman, J.S. Garcia, A.H. Wei, M. Konopleva, H. Döhner, A. Letai, P. Fenaux, E. Koller, V. Havelange, B. Leber, J. Esteve, J. Wang, V. Pejsa, R. Hájek, K. Porkka, Á. Illés, D. Lavie, R.M. Lemoli, K. Yamamoto, S.-S. Yoon, J.-H. Jang, S.-P. Yeh, M. Turgut, W.-J. Hong, Y. Zhou, J. Potluri, and K.W. Pratz

Blood Cancer Journal *Blood Cancer J* 2021;11(10):163. www.nature.com/bcj

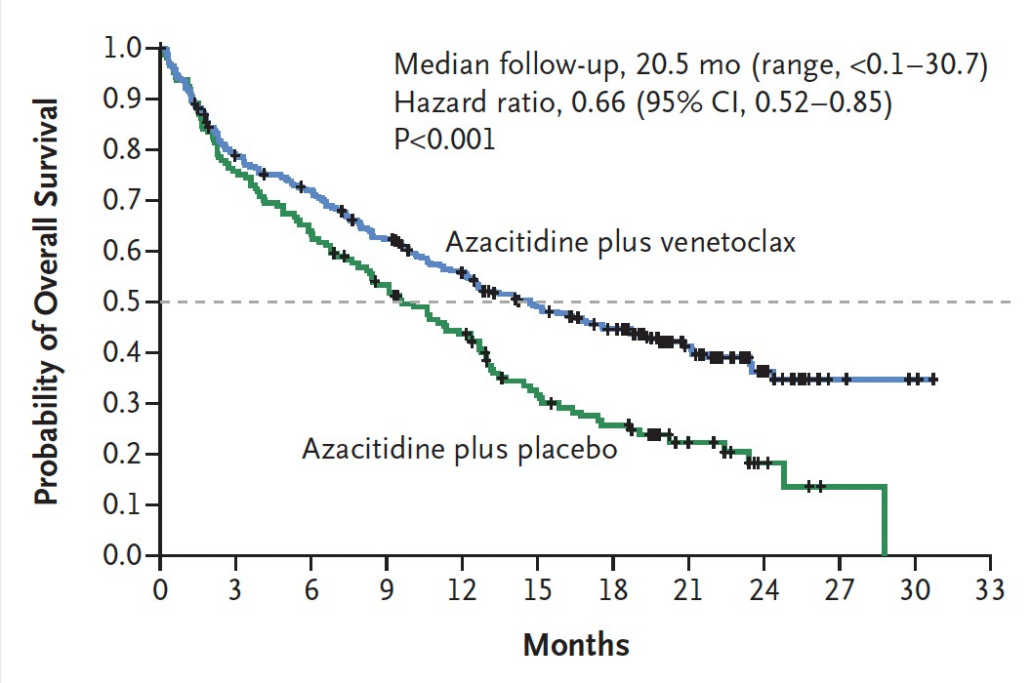
ARTICLE

6-month follow-up of VIALE-C demonstrates improved and durable efficacy in patients with untreated AML ineligible for intensive chemotherapy

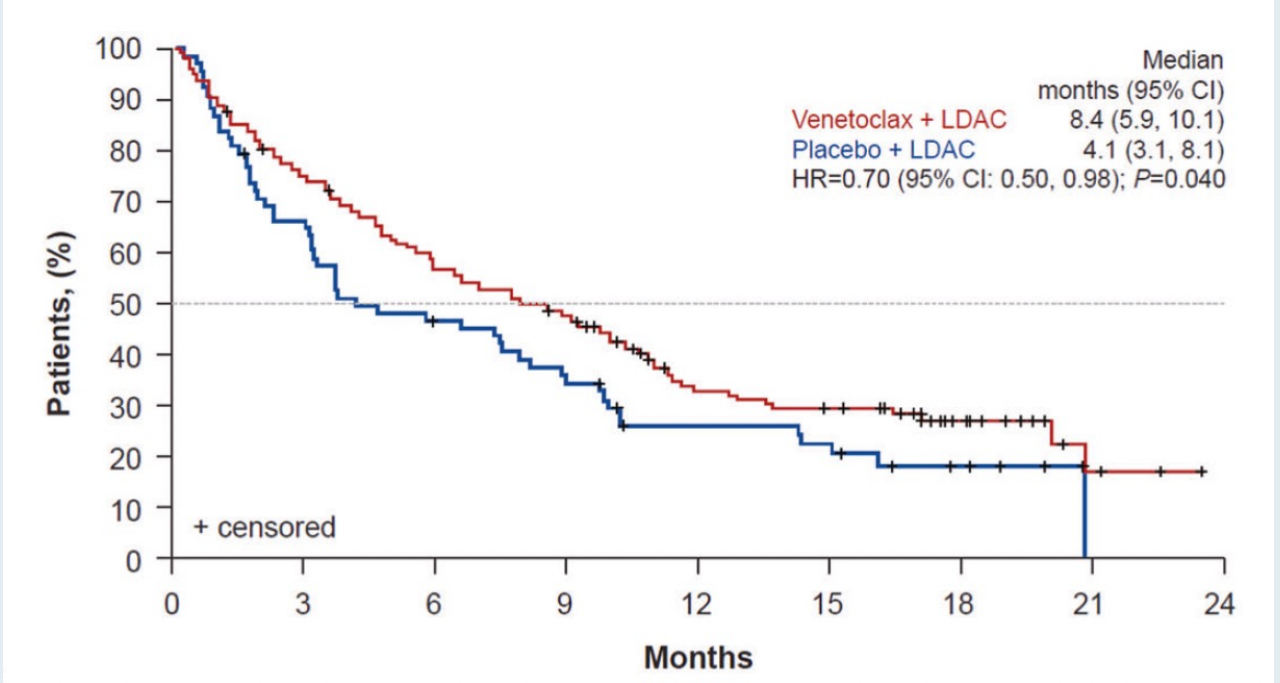
Andrew H. Wei[1], Panayiotis Panayiotidis[2], Pau Montesinos[3,4], Kamel Laribi[5], Vladimir Ivanov[6], Inho Kim[7], Jan Novak[8], Don A. Stevens[9], Walter Fiedler[10], Maria Pagoni[11], Julie Bergeron[12], Stephen B. Ting[13], Jing-Zhou Hou[14], Achilles Anagnostopoulos[15], Andrew McDonald[16], Vidhya Murthy[17], Takahiro Yamauchi[18], Jianxiang Wang[19], Brenda Chyla[20], Yan Sun[20], Qi Jiang[20], Wellington Mendes[20], John Hayslip[20] and Courtney D. DiNardo[21]

Overall Survival with Venetoclax in Combination with Azacitidine (VIALE-A) or LDAC (VIALE-C)

VIALE-A[1]



VIALE-C[2]



LDAC = low-dose cytarabine

[1]DiNardo CD et al. *N Engl J Med* 2020;383(7):617-29; [2] Wei AH et al. *Blood Cancer J* 2021;11(10):163.

VIALE-A and VIALE-C: Select Grade ≥3 Adverse Events (AEs)

Adverse event (AE)	VIALE-A[1]		VIALE-C[2]	
	VEN + AZA (n = 283)	AZA + PBO (n = 144)	VEN + LDAC (n = 142)	LDAC + PBO (n = 68)
Thrombocytopenia	45%	38%	46%	38%
Neutropenia	42%	28%	49%	18%
Febrile neutropenia	42%	19%	32%	29%
Anemia	26%	20%	27%	22%
Diarrhea	5%	3%	3%	0
Nausea	2%	1%	1%	0

VEN = venetoclax; AZA = azacitidine; PBO = placebo; LDAC = low-dose cytarabine

[1] DiNardo CD et al. *N Engl J Med* 2020;383(7):617-29; [2] Wei AH et al. *Blood Cancer J* 2021;11(10):163.

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DOI: 10.1002/ajh.26600

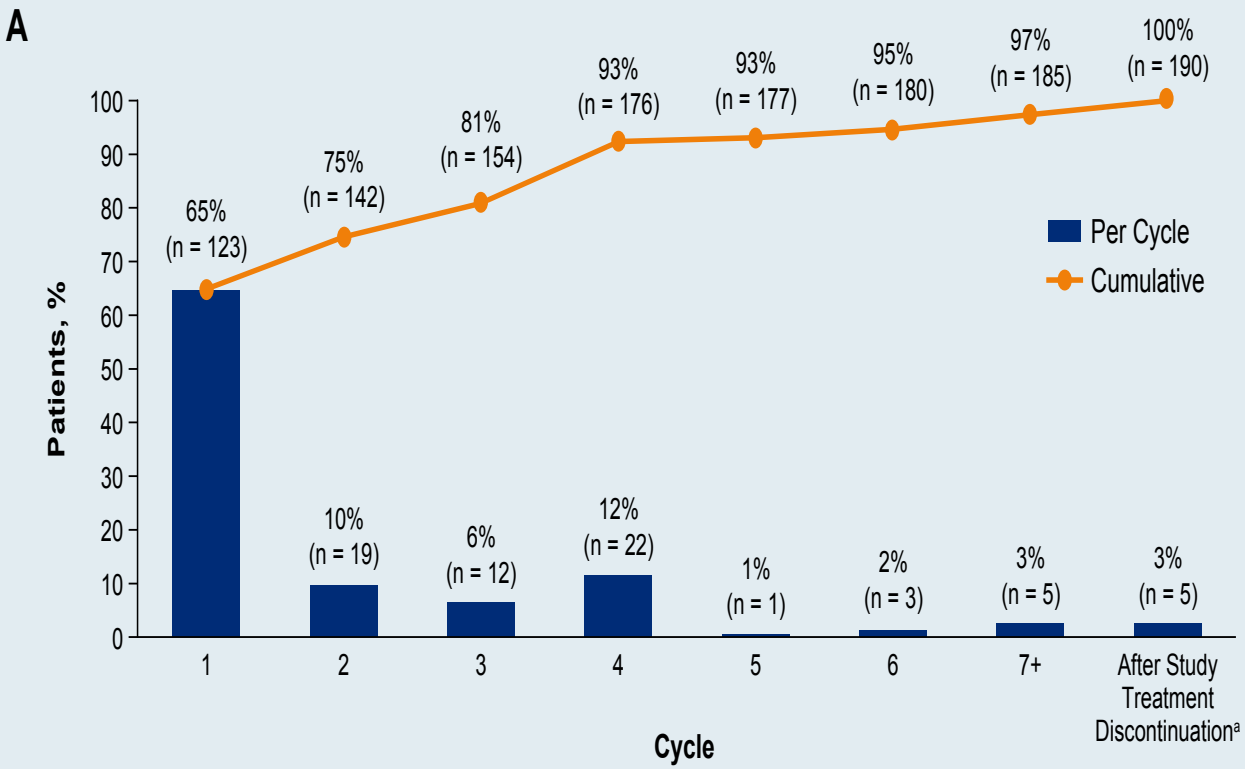
CORRESPONDENCE

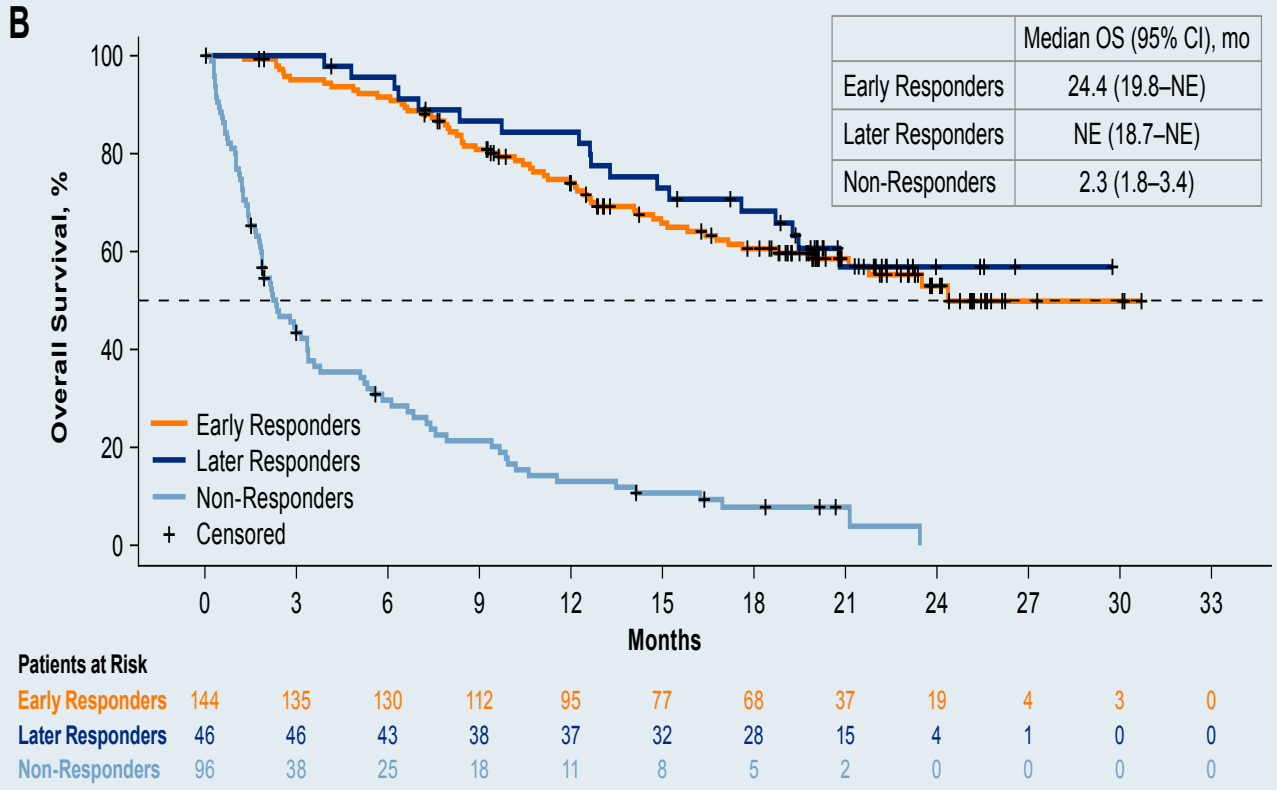
Timing of response with venetoclax combination treatment in patients with newly diagnosed acute myeloid leukemia

Brian A. Jonas[1], Andrew H. Wei[2], Christian Recher[3,4], Courtney D. DiNardo[5], Jun-Ho Jang[6], Keith Pratz[7], Panayiotis Panayiotidis[8], Pau Montesinos[9], Su-Peng Yeh[10], Vladimir Ivanov[11], Walter Fiedler[12], Takahiro Yamauchi[13], Yinghui Duan[14], Wellington Mendes[15], Jalaja Potluri[16], Björn Tews[17], Yishai Ofran[18]

Am J Hematol 2022;97(8):E299-303.

VIALE-A: Time to CR/CRi Response





Note that all later responders who had a complete remission (CR)/CR with incomplete blood count recovery (CRi) beyond Cycle 6 had achieved morphologic leukemia-free state before Cycle 6

Jonas BA et al. *Am J Hematol* 2022;97(8):E299-303.

original reports

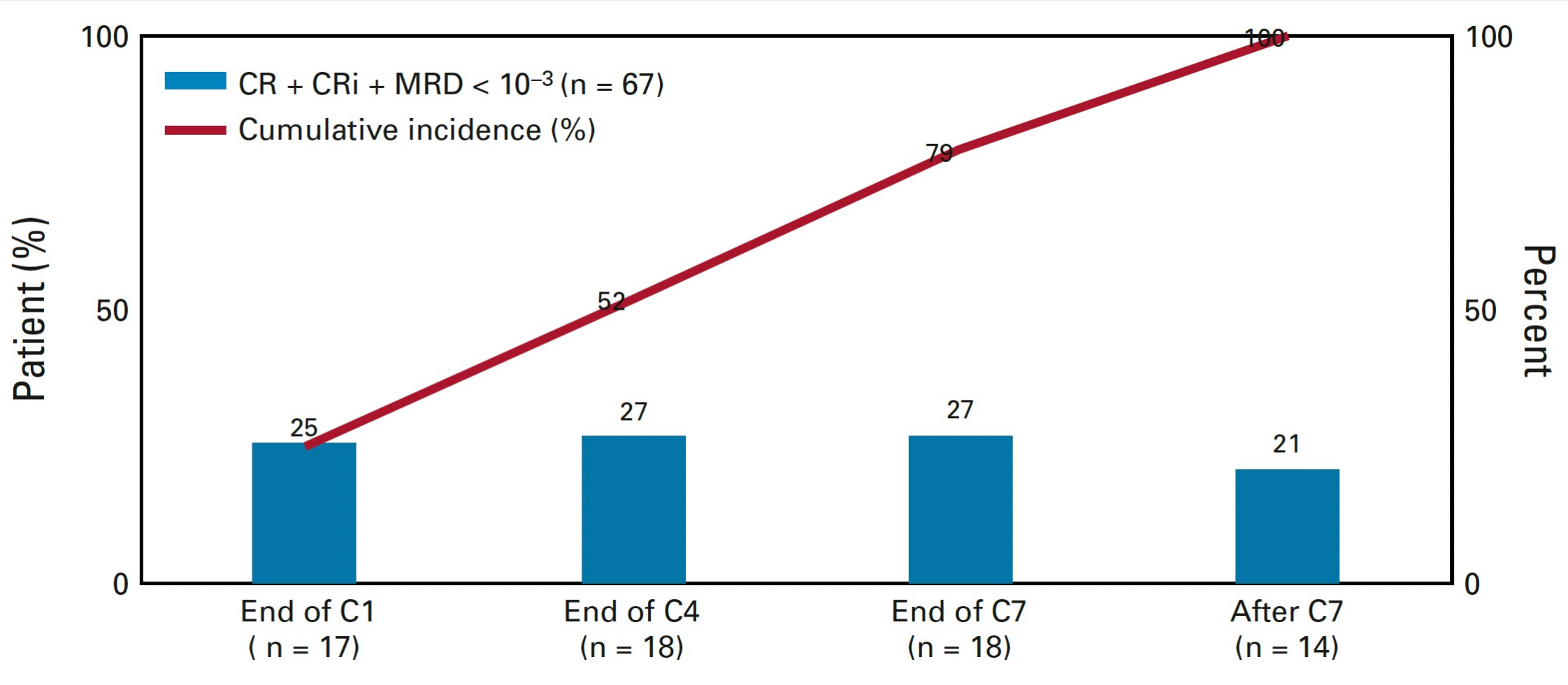
Measurable Residual Disease Response and Prognosis in Treatment-Naïve Acute Myeloid Leukemia With Venetoclax and Azacitidine

Keith W. Pratz, MD[1]; Brian A. Jonas, MD[2]; Vinod Pullarkat, MD[3]; Christian Recher, MD[4]; Andre C. Schuh, MD[5]; Michael J. Thirman, MD[6]; Jacqueline S. Garcia, MD[7]; Courtney D. DiNardo, MD[8]; Vladimir Vorobyev, MD[9]; Nicola S. Fracchiolla, MD[10]; Su-Peng Yeh, MD[11]; Jun Ho Jang, MD[12]; Muhit Ozcan, MD[13]; Kazuhito Yamamoto, MD[14]; Arpad Illes, MD[15]; Ying Zhou, PhD[16]; Monique Dail, PhD[17]; Brenda Chyla, PhD[16]; Jalaja Potluri, MD[16]; and Hartmut Döhner, MD[18]

J Clin Oncol 2022;40(8):855-65.

RTP RESEARCH TO PRACTICE

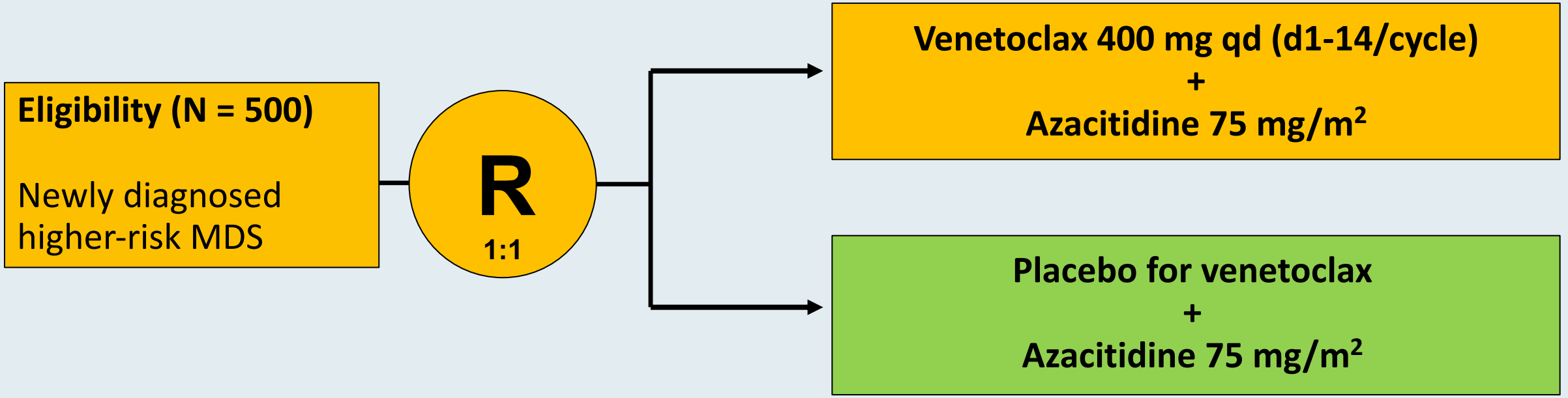
VIALE-A: MRD by Treatment Cycle and Cumulative Incidence



MRD = measurable residual disease; CR = complete remission; CRi = CR with incomplete hematologic recovery

Pratz KW et al. *J Clin Oncol* 2022;40(8):855-65.

VERONA Phase III Study Design



Until relapse, progression or unacceptable toxicity

Dual primary endpoints: Complete remission and OS

Secondary endpoints: RBC and platelet transfusion independence for patients who are transfusion-dependent at baseline, change from baseline in fatigue, time to deterioration of physical functioning and overall response

www.clinicaltrials.gov, Accessed July, 2022.

Agenda

Introduction – RATIFY Trial in Perspective

Module 1 – FLT3 Inhibitors

Module 2 – Anti-CD47 Antibody: Magrolimab

Module 3 – Anti-TIM-3 Antibody: Sabatolimab

Module 4 – CAR T-Cell Therapy

Module 5 – IDH Inhibitors

Module 6 – New Myelodysplastic Syndromes Classification System

Module 7 – Hypomethylating Agents/Venetoclax

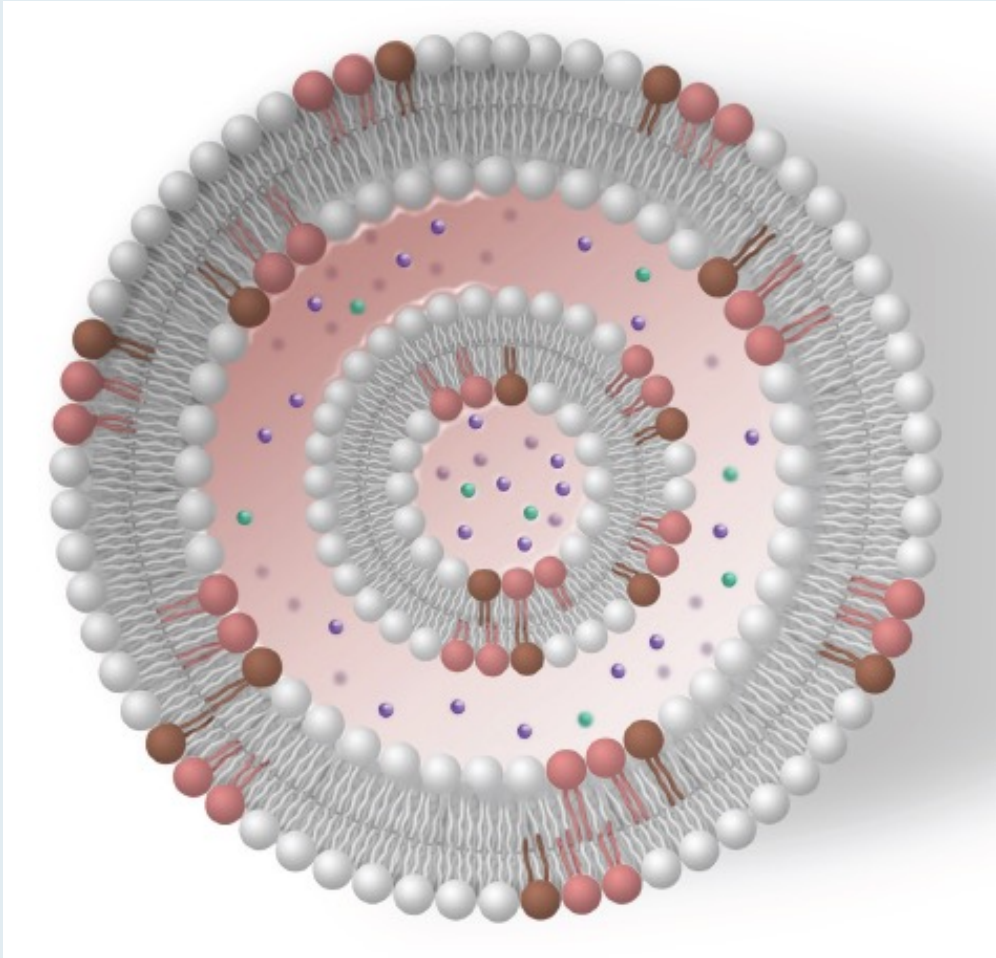
Module 8 – CPX-351

Module 9 – Other Key Datasets

RTP RESEARCH TO PRACTICE

CPX-351

- CPX-351 is a liposomal coformulation of cytarabine and daunorubicin designed to achieve synergistic antileukemia activity
  - 5:1 molar ratio of cytarabine to daunorubicin provides synergistic leukemia cell killing in vitro[1]
  - In patients, CPX-351 preserved delivery of the 5:1 drug ratio for over 24 hours, with drug exposure maintained for 7 days[2]
  - Selective uptake of liposomes by bone marrow leukemia cells was demonstrated in xenograft models[3]



[1] Tardi P et al. *Leuk Res* 2009;33(1):129-39. [2] Feldman EJ et al. *J Clin Oncol* 2011;29(8):979-85.
[3] Lim WS et al. *Leuk Res* 2010;34(9):1214-23.

blood advances

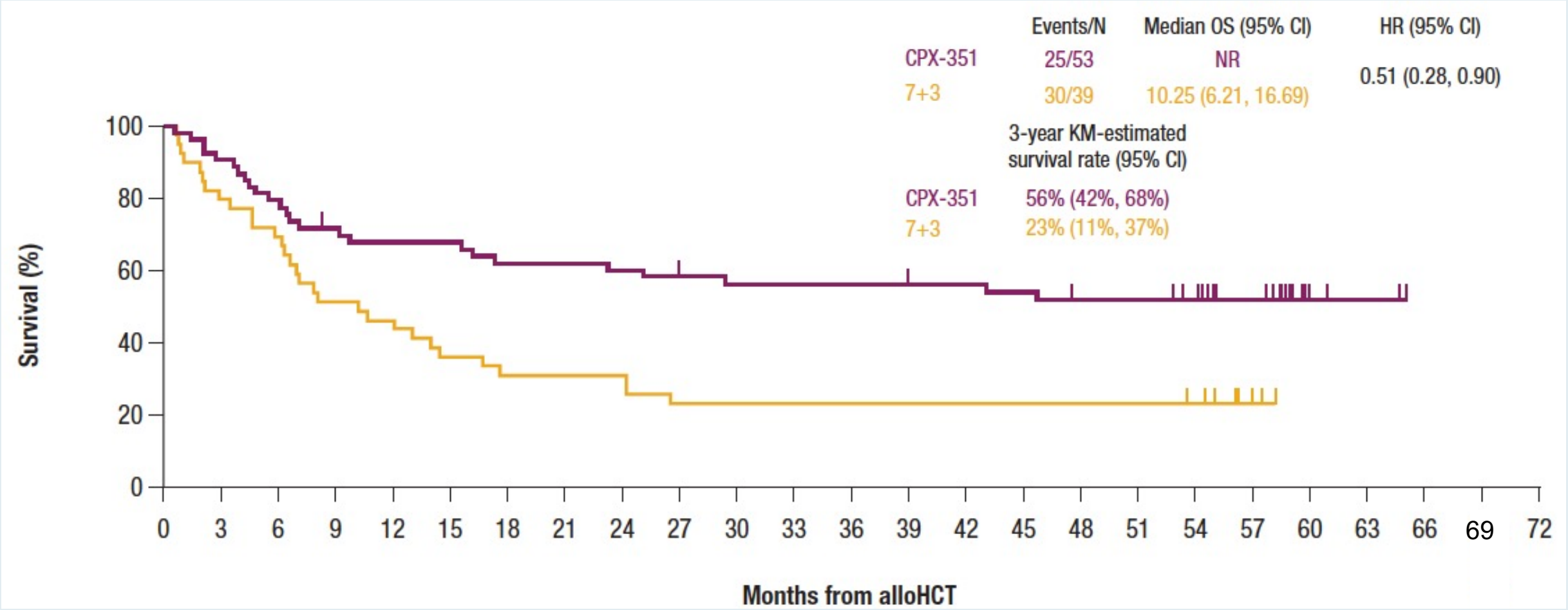
Transplant Outcomes After CPX-351 vs 7+3 in Older Adults With Newly Diagnosed High-risk and/or Secondary AML

Tracking no: ADV-2021-006468R1

Geoffrey Uy (Division of Oncology, Washington University School of Medicine, United States) Laura Newell (OHSU, United States) Tara Lin (University of Kansas, United States) Stuart Goldberg (John Theurer Cancer Center at Hackensack University Medical Center, United States) Matthew Wieduwilt (University of Oklahoma Stephenson Cancer Center, United States) Robert Ryan (Jazz Pharmaceuticals, Inc., United States) Stefan Faderl (Jazz Pharmaceuticals, United States) Jeffrey Lancet (Moffitt Cancer Center, United States)

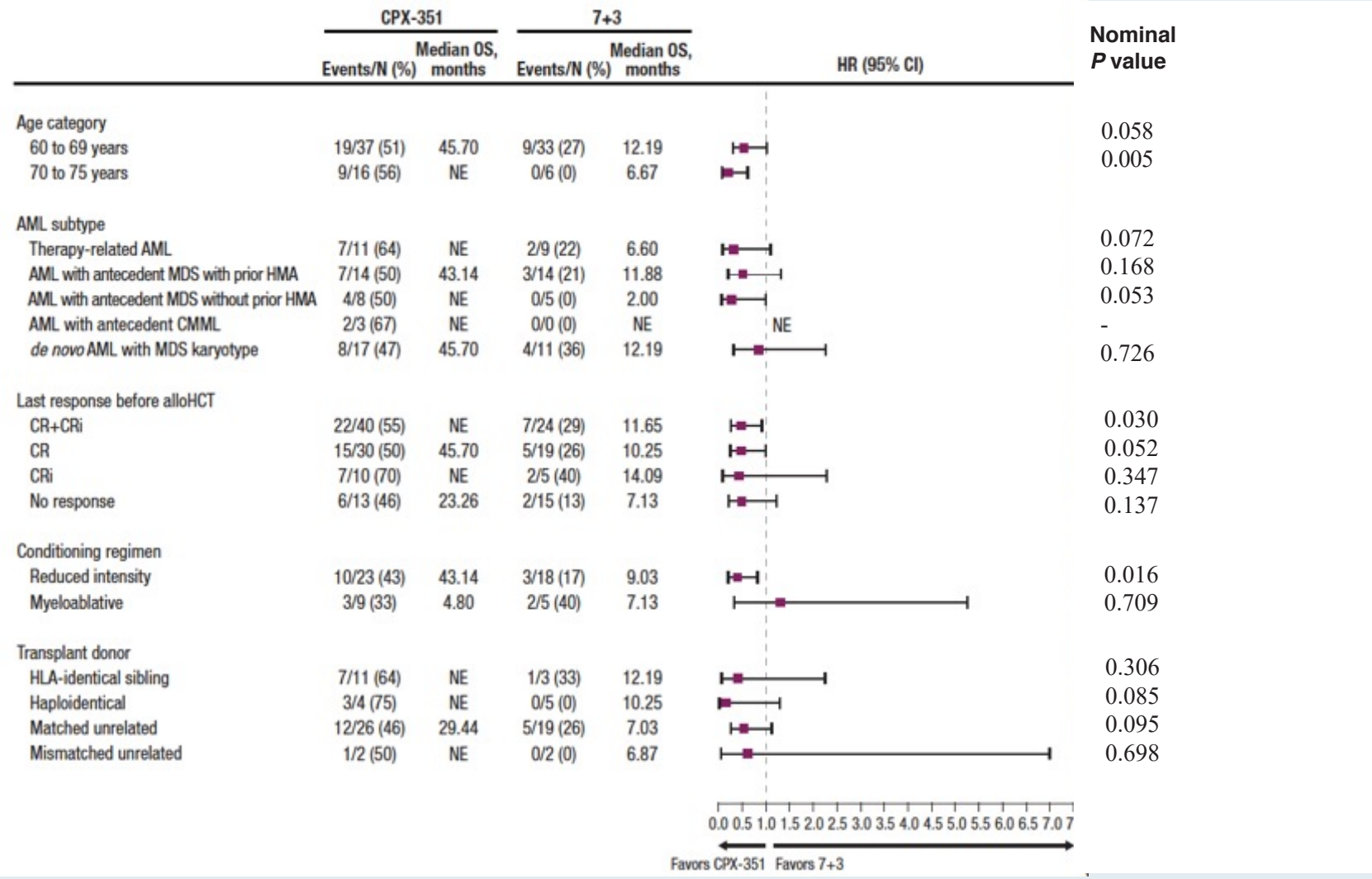
Blood Adv **2022;[Online ahead of print].**

Transplant Outcomes After CPX-351 versus 7 + 3 in Older Patients with Newly Diagnosed, High-Risk and/or Secondary AML: Overall Survival (OS) Landmarked from the alloHCT Date



Uy G et al. *Blood Adv* 2022;[Online ahead of print].

Transplant Outcomes After CPX-351 versus 7 + 3 in Older Patients with Newly Diagnosed, High-Risk and/or Secondary AML: Subgroup Analyses OS Landmarked from the alloHCT Date



Uy G et al. *Blood Adv* 2022;[Online ahead of print].

A RANDOMISED COMPARISON OF CPX-351 AND FLAG-IDA IN HIGH RISK ACUTE MYELOID LEUKAEMIA. RESULTS FROM THE NCRI AML19 TRIAL

Nigel Russell, Charlotte Wilhelm-Benartzi, Steve Knapper, Leona Batten, Joanna Canham, Emily Hinson, Ulrik Malthe Overgaard, Jad Othman, Richard Dillon, Priyanka Mehta, Panos Kottaridis, Jamie Cavenagh, Claire Hemmaway, Claire Arnold, Mike Dennis on behalf of the NCRI AML Working Group

EHA 2022;Abstract S128.

AML19: Response After Course 1 and Overall Response

RESPONSE	FLAG-Ida	CPX-351	
CR	51.2%	40.0%	
CRi	13.4%	11.4%	
PR	6.1%	16.2%	
Resistant Disease	14.6%	21.0%	
ORR post Course 2	75.6%	63.8%	HR: 0.54, 95%CI 0.28-1.04 p=0.06).

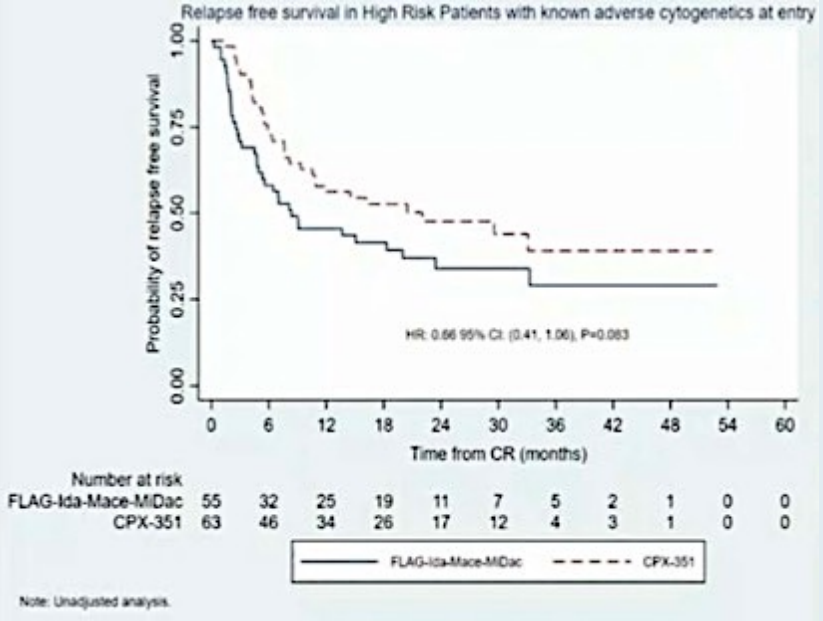
CR = complete response; CRi = CR with incomplete blood count recovery; PR = partial response

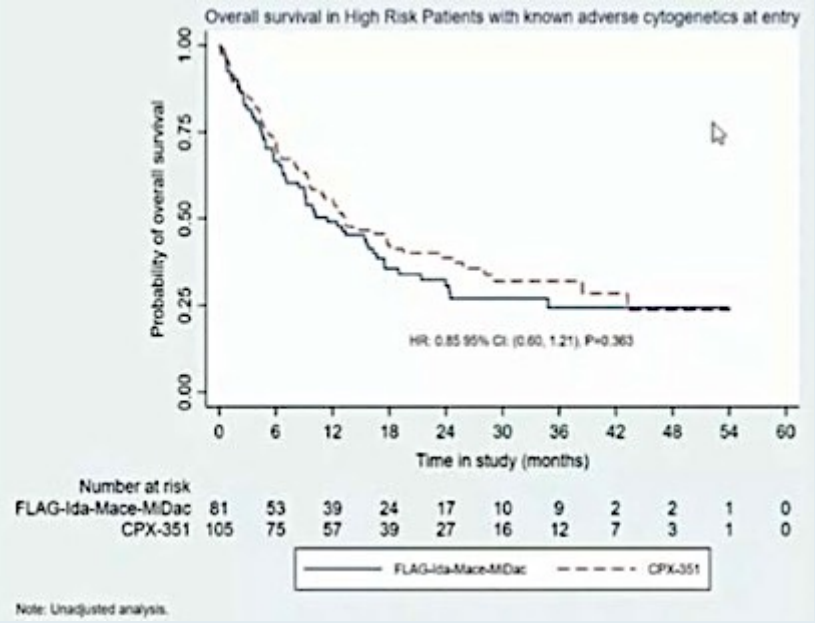
- Median duration of remission favored CPX-351 and was 510 days for CPX-351 vs 391 days for FLAG-IDA (p = 0.24)

Russell N et al. EHA 2022;Abstract S128.

AML19: Relapse-Free and Overall Survival

- Overall survival (OS) at 3 years was 32% and 25%; median OS was 13.3 months versus 11.4 months for CPX-351 and FLAG-IDA respectively.
- Event-free survival (EFS) at 3 years was 25% and 24%; median EFS was 7.1 months versus 5.95 months for CPX-351 and FLAG-IDA respectively.
- Relapse-free survival (RFS) at 3 years was 39% and 29%; median RFS was 22.1 months versus 8.4 months for CPX-351 and FLAG-IDA respectively.
- RFS was significant when adjusting for NPM1 mutation status or FLT3 mutations status using multivariable Cox regression model, with RFS being better with CPX-351 compared to FLAG-IDA (HR 0.58, 95% CI 0.36-0.93, p = 0.03).





Russell N et al. EHA 2022;Abstract S128.

RTP RESEARCH TO PRACTICE

AML19: Hematological Toxicity

	FLAG-Ida	CPX-351	
COURSE 1	Days	Days	
Neutrophils 1.0 x 10^9/L	30	32	P = 0.11
Platelets 100x 10^9/L	29	34	P =0.0008
COURSE 2			
Neutrophils 1.0 x 10^9/L	46	31	P =0.0001
Platelets 100 x 10^9/L	36	31	P =0.20

Russell N et al. EHA 2022;Abstract S128.

Lancet Haematol 2021;8(7):e481-91.

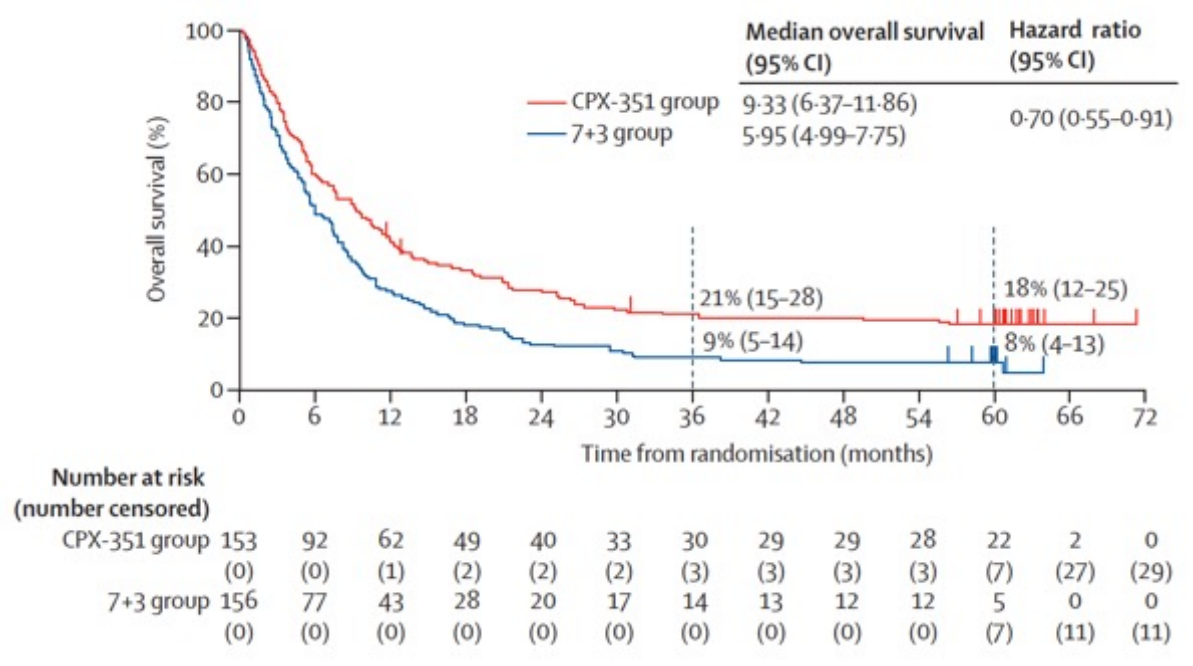
Articles

CPX-351 versus 7+3 cytarabine and daunorubicin chemotherapy in older adults with newly diagnosed high-risk or secondary acute myeloid leukaemia: 5-year results of a randomised, open-label, multicentre, phase 3 trial

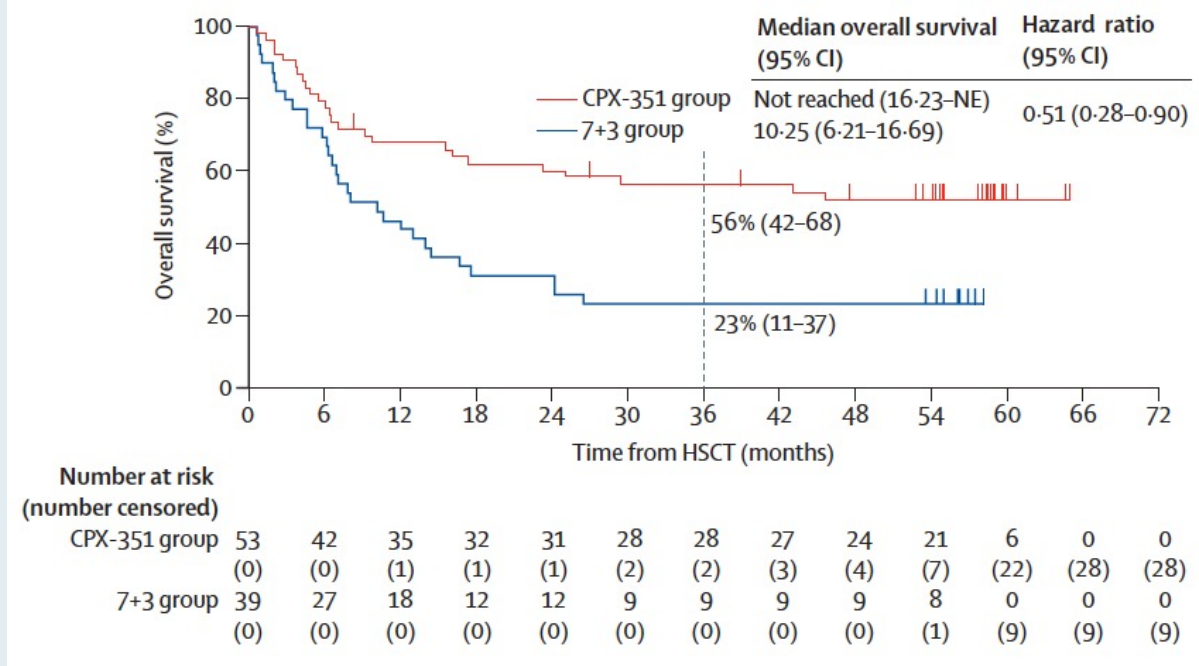
Jeffrey E Lancet, Geoffrey L Uy, Laura F Newell, Tara L Lin, Ellen K Ritchie, Robert K Stuart, Stephen A Strickland, Donna Hogge, Scott R Solomon, Dale L Bixby, Jonathan E Kolitz, Gary J Schiller, Matthew J Wieduwilt, Daniel H Ryan, Stefan Faderl, Jorge E Cortes

Phase III Trial of CPX-351 versus 7 + 3 Cytarabine and Daunorubicin for Older Patients with Newly Diagnosed High-Risk or Secondary AML: 5-Year Overall Survival Results

OS



OS landmarked from time of HSCT

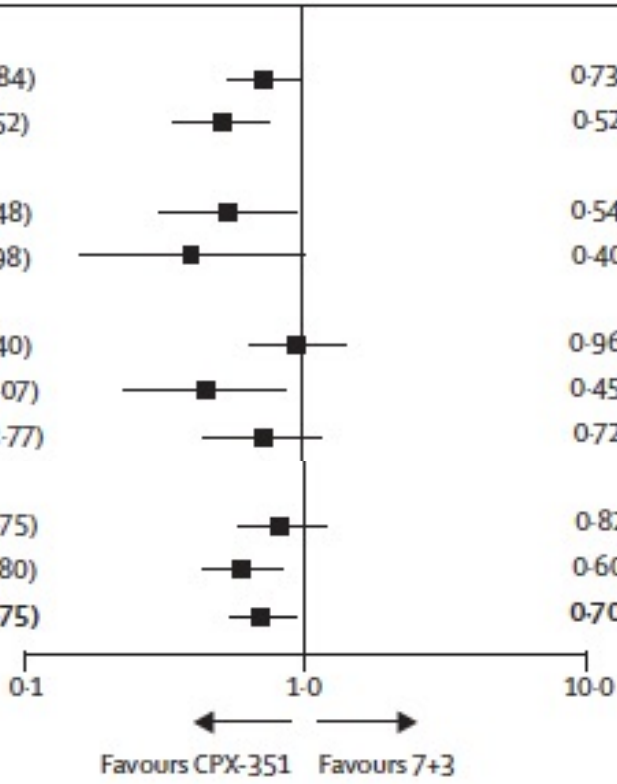


OS = overall survival; HSCT = hematopoietic stem cell transplant

Lancet JE et al. *Lancet Haematol* 2021;8(7):e481-91.

Phase III Trial of CPX-351 versus 7 + 3 Cytarabine and Daunorubicin for Older Patients with Newly Diagnosed High-Risk or Secondary AML: OS Analysis of Select Subroups

	CPX-351 group		7+3 group		Hazard ratio (95% CI) for death
	n/N	Median overall survival, (95% CI) months	n/N	Median overall survival, (95% CI) months	
Age					
60–69 years	76/96	9·59 (6·01–12·62)	91/102	6·87 (4·63–8·84)	0·73 (0·54–0·99)
70–75 years	48/57	8·87 (4·73–12·19)	54/54	5·62 (3·29–7·52)	0·52 (0·34–0·77)
AML subtype					
Therapy-related AML	23/30	12·17 (7·43–27·37)	30/33	5·95 (2·92–8·48)	0·54 (0·31–0·94)
AML with antecedent CMML	9/11	9·33 (1·94–23·98)	11/12	2·28 (0·72–3·98)	0·40 (0·16–1·01)
AML with antecedent MDS					
With previous HMA	43/50	5·65 (3·55–7·75)	52/55	7·43 (5·55–9·40)	0·96 (0·64–1·45)
Without previous HMA	16/21	15·74 (5·55–26·32)	19/19	5·13 (1·74–11·07)	0·45 (0·23–0·88)
De novo AML with MDS karyotype	33/41	9·66 (5·32–25·23)	33/37	7·36 (2·89–13·77)	0·72 (0·44–1·17)
Previous HMA treatment					
Yes	53/62	5·65 (3·55–7·75)	67/70	5·98 (4·63–7·75)	0·82 (0·57–1·18)
No	71/91	11·33 (9·17–18·69)	78/86	5·62 (3·88–8·80)	0·60 (0·43–0·83)
Overall study population	**124/153**	**9·33 (6·37–11·86)**	**145/156**	**5·95 (4·99–7·75)**	**0·70 (0·55–0·91)**



CMML = chronic myelomonocytic leukemia; MDS = myelodysplastic syndromes; HMA = hypomethylating agent

Lancet JE et al. *Lancet Haematol* 2021;8(7):e481-91.

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Agenda

Introduction – RATIFY Trial in Perspective

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Module 5 – IDH Inhibitors

Module 6 – New Myelodysplastic Syndromes Classification System

Module 7 – Hypomethylating Agents/Venetoclax

Module 8 – CPX-351

Module 9 – Other Key Datasets

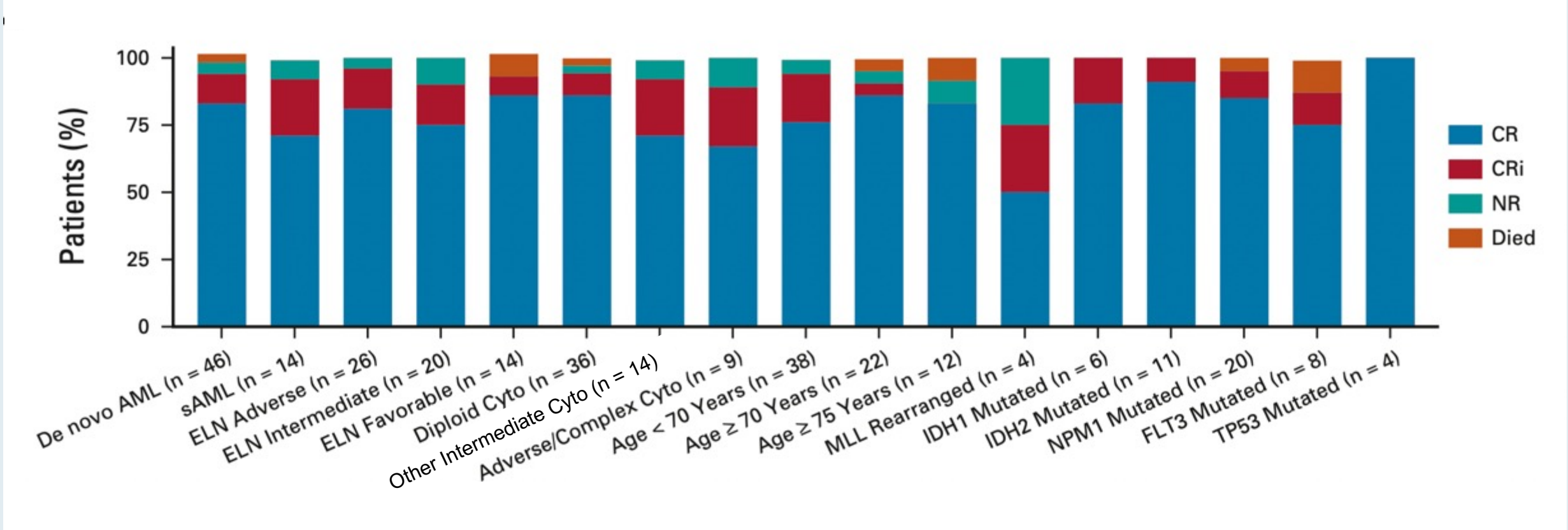
original reports

Phase II Study of Venetoclax Added to Cladribine Plus Low-Dose Cytarabine Alternating With 5-Azacitidine in Older Patients With Newly Diagnosed Acute Myeloid Leukemia

Tapan M. Kadia, MD[1]; Patrick K. Reville, MPH, MD[2]; Xuemei Wang, MS[3]; Caitlin R. Rausch, PharmD[4]; Gautam Borthakur, MD[1]; Naveen Pemmaraju, MD[1]; Naval G. Daver, MD[1]; Courtney D. DiNardo, MD, MSCE[1]; Koji Sasaki, MD, PhD[1]; Ghayas C. Issa, MD[1]; Maro Ohanian, MD[1]; Guillermo Montalban-Bravo, MD[1]; Nicholas J. Short, MD[1]; Nitin Jain, MD[1]; Alessandra Ferrajoli, MD[1]; Kapil N. Bhalla, MD[1]; Elias Jabbour, MD[1]; Koichi Takahashi, MD, PhD[1]; Rashmi Malla, BSN[1]; Kelly Quagliato, BS[1]; Rashmi Kanagal-Shamanna, MD[5]; Uday R. Popat, MD[6]; Michael Andreeff, MD, PhD[1]; Guillermo Garcia-Manero, MD[1]; Marina Y. Konopleva, MD, PhD[1]; Farhad Ravandi, MD[1]; and Hagop M. Kantarjian, MD[1]

J Clin Oncol 2022;[Online ahead of print].

Venetoclax with Cladribine and Low-Dose Cytarabine Alternating with 5-Azacitidine in Older Patients with Newly Diagnosed AML



CR = complete response; CRi = CR with incomplete blood count recovery; NR = not reported

Kadia TM et al. *J Clin Oncol* 2022;[Online ahead of print].

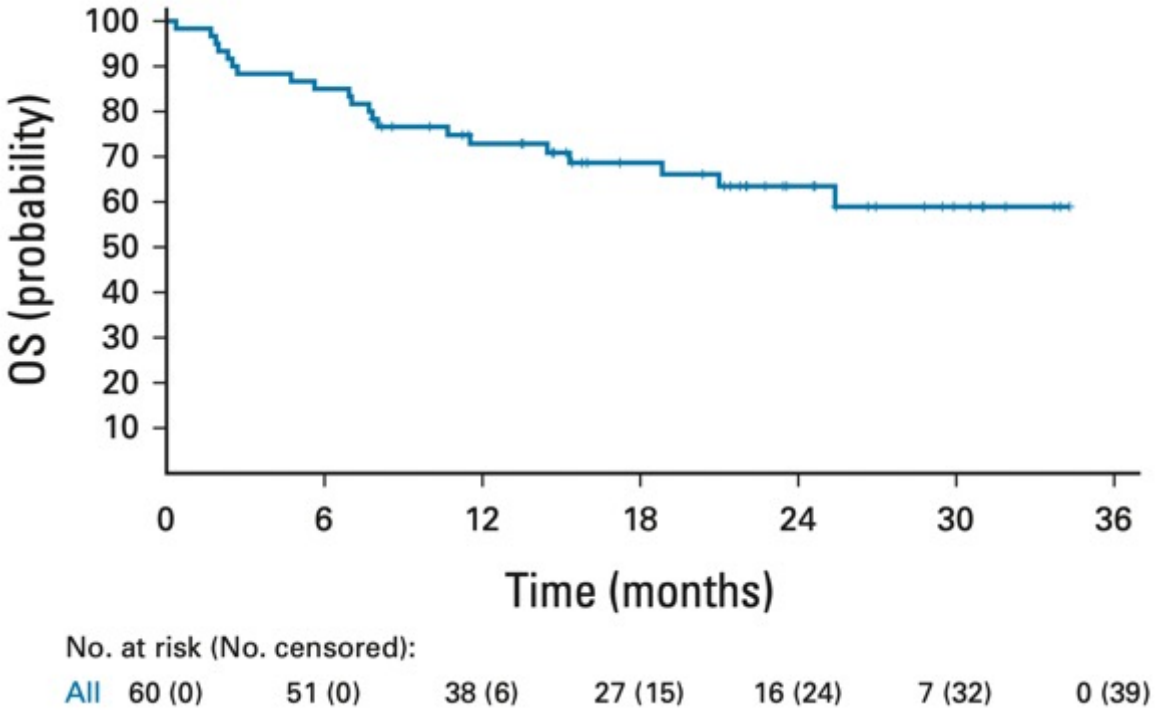
RTP RESEARCH TO PRACTICE

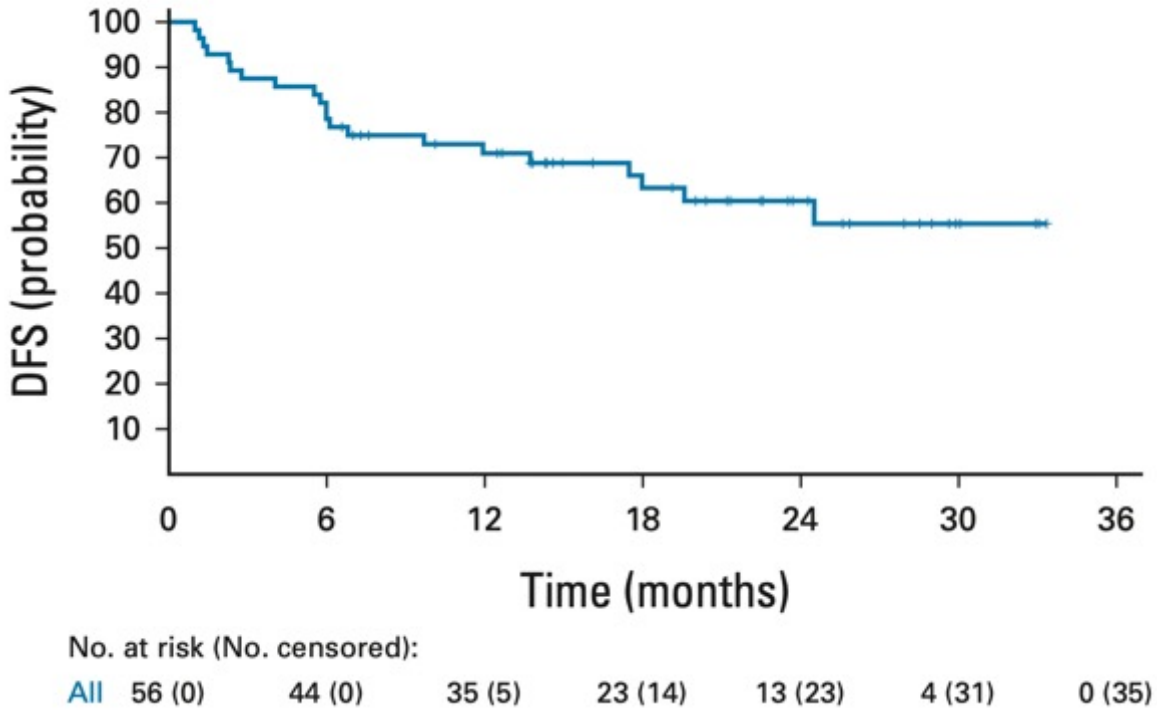
Venetoclax with Cladribine and Low-Dose Cytarabine Alternating with 5-Azacitidine in Older Patients with Newly Diagnosed AML: Response Rate and Early Mortality

Characteristic	N = 60; No. (%)
CRc rate (CR plus CRi)	56/60 (93)
Best response	
CR	48/60 (80)
CRi	8/60 (13)
NR	3/60 (5.0)
Died	1/60 (1.7)
Patients requiring reinduction cycle	4/57 (7)
MRD at response assessment (by flow)	
Negative	43/51 (84)
Positive	8/51 (16)
Total No. of course given, median (IQR)	3.0 [2.0-5.0]
Responders who received alloSCT	19/56 (34)
Mortality rate at 4 weeks	1/60 (1.7)
Mortality rate at 8 weeks	4/60 (6.7)

Kadia TM et al. *J Clin Oncol* 2022;[Online ahead of print].

Venetoclax with Cladribine and Low-Dose Cytarabine Alternating with 5-Azacitidine in Older Patients with Newly Diagnosed AML: Survival

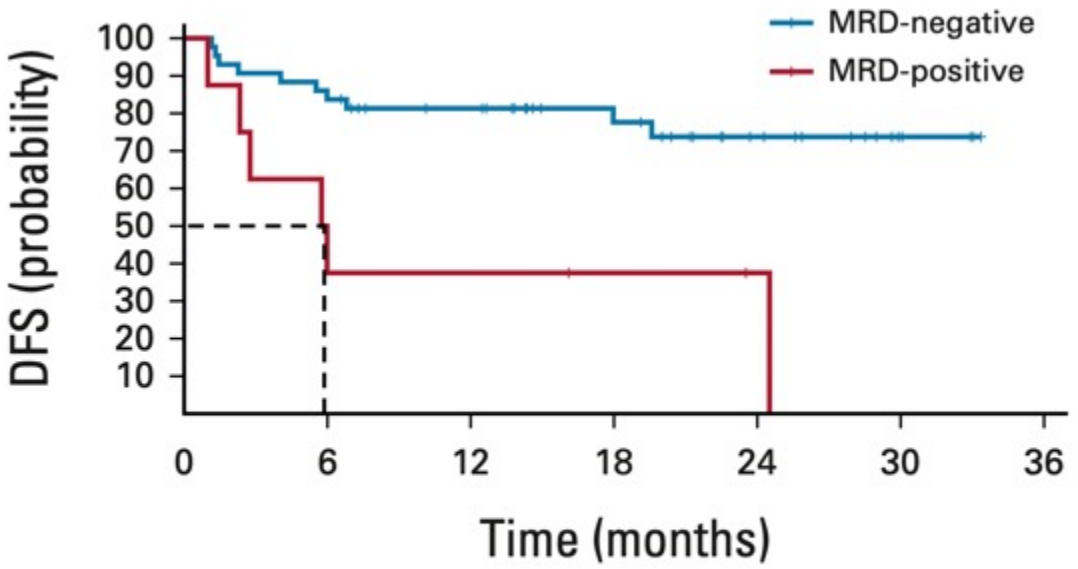




OS = overall survival; DFS = disease-free survival

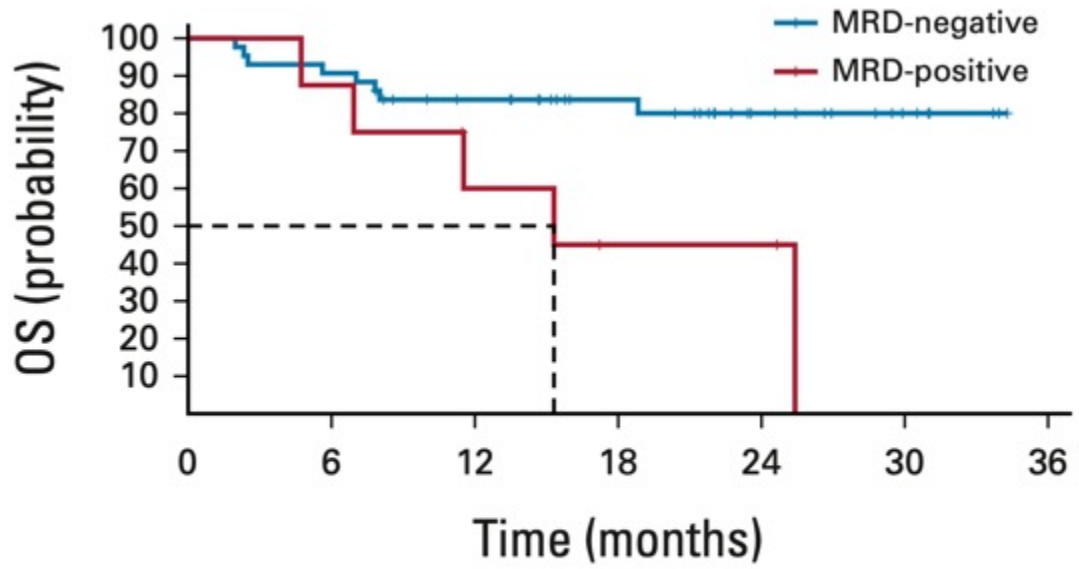
Kadia TM et al. *J Clin Oncol* 2022;[Online ahead of print].

Venetoclax with Cladribine and Low-Dose Cytarabine Alternating with 5-Azacitidine in Older Patients with Newly Diagnosed AML: Survival by MRD



No. at risk (No. censored):

MRD-negative	43 (0)	36 (0)	30 (5)	21 (13)	12 (21)	4 (29)	0 (33)
MRD-positive	8 (0)	3 (0)	3 (0)	2 (1)	1 (2)	0 (2)	0 (2)



No. at risk (No. censored):

MRD-negative	43 (0)	39 (0)	31 (5)	23 (13)	13 (22)	6 (29)	0 (35)
MRD-positive	8 (0)	7 (0)	4 (1)	2 (2)	2 (2)	0 (3)	0 (3)

MRD = measurable residual disease; DFS = disease-free survival; OS = overall survival

Kadia TM et al. *J Clin Oncol* 2022;[Online ahead of print].

2022 ASCO® ANNUAL MEETING

Pre-MEASURE:

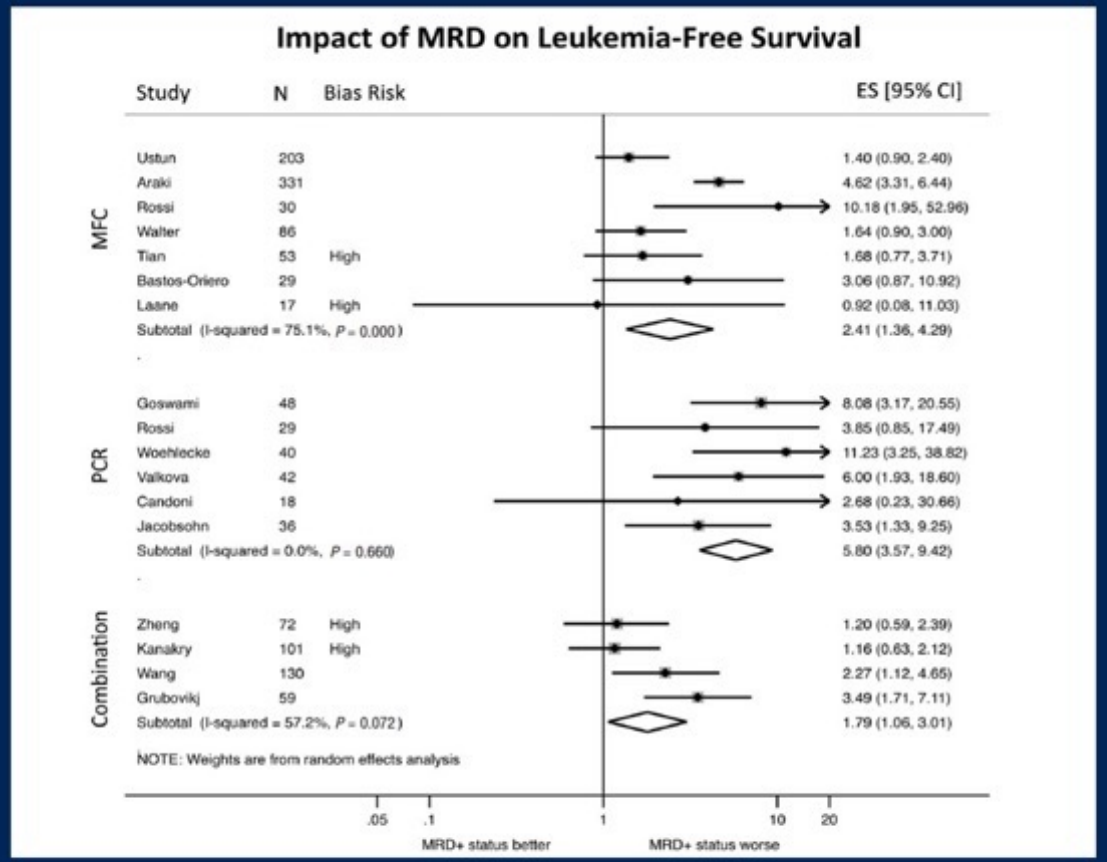
Multicenter evaluation of the prognostic significance of measurable residual disease testing prior to allogeneic transplantation for adult patients with AML in first remission

Christopher S. Hourigan DM DPhil FRCP
National Heart, Lung, and Blood Institute
on behalf of the co-authors

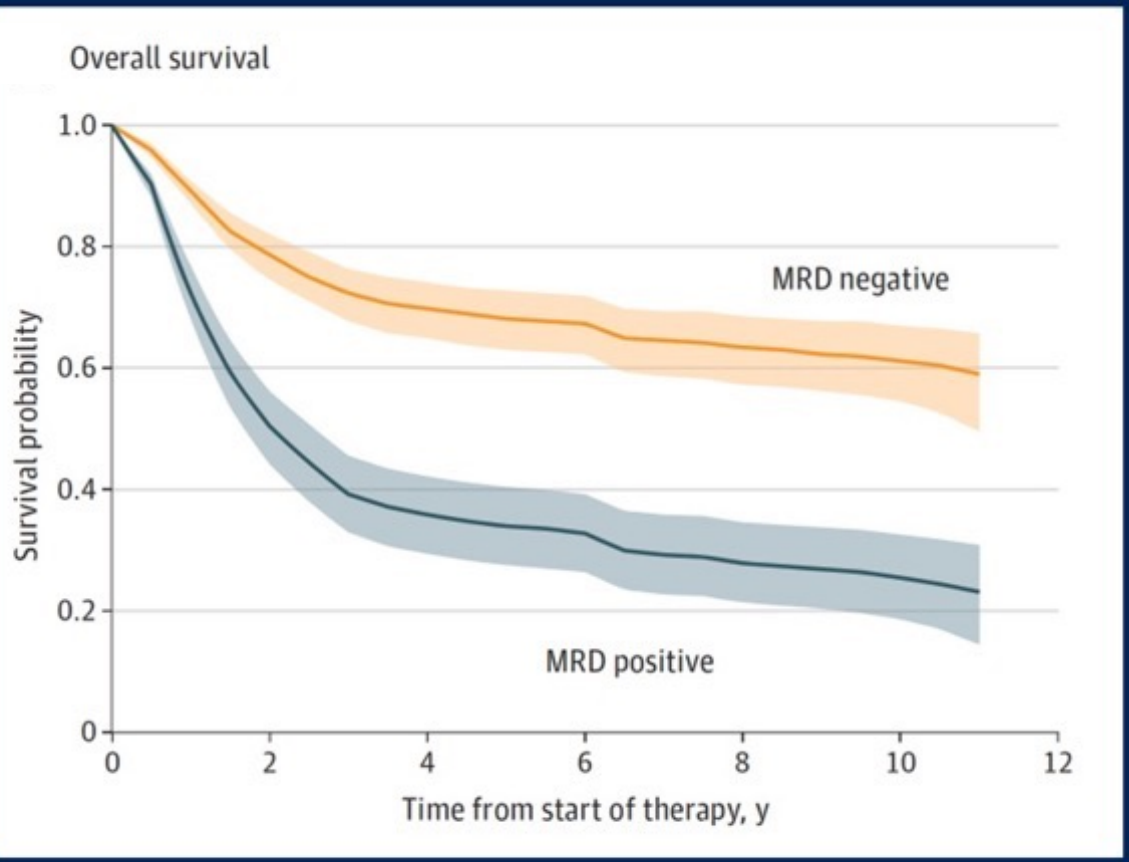
Abstract 7006.

RTP RESEARCH TO PRACTICE

Impact of Measurable Residual Disease (MRD) on Survival



Buckley…Hourigan…Walter Haematologica 2017

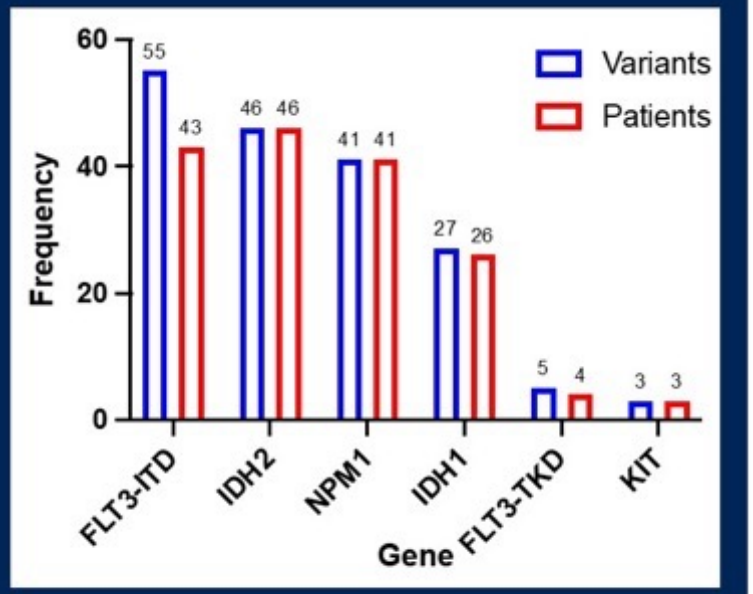


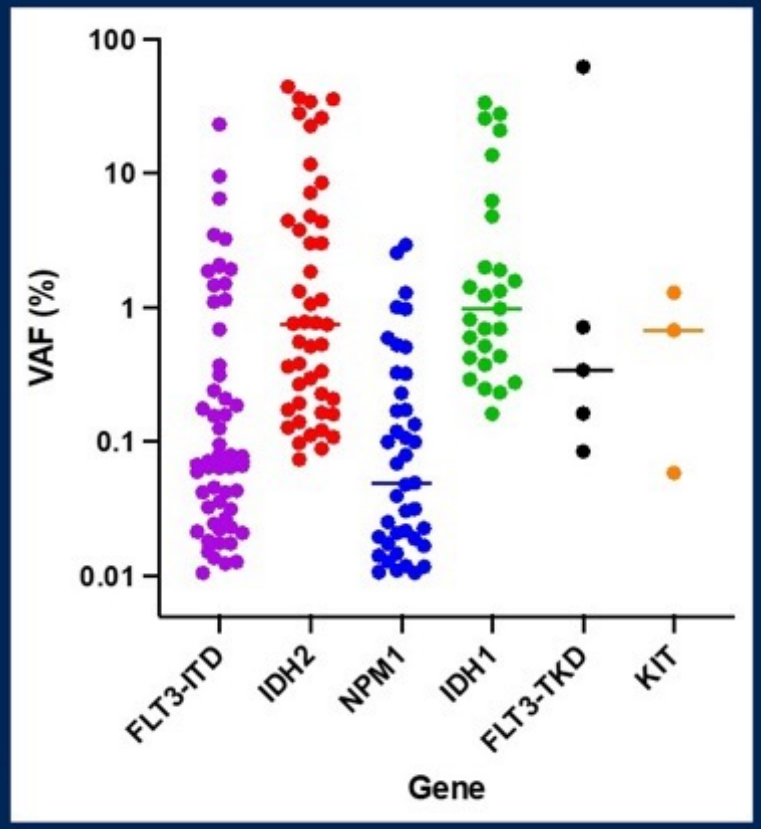
Short…Hourigan…Ravandi JAMA Oncology 2020

Hourigan CS et al. ASCO 2022;Abstract 7006.

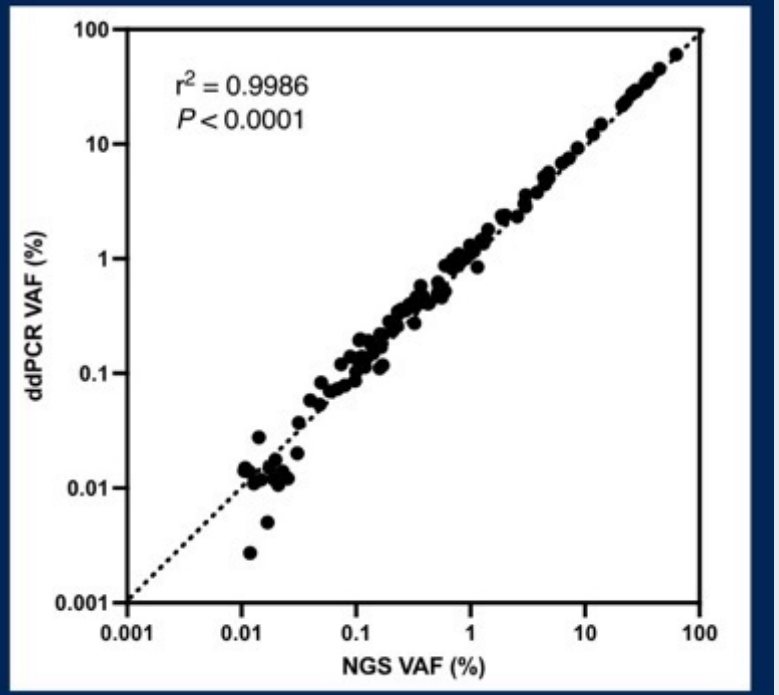
Next-Generation Sequencing for Measurable Residual Disease (NGS-MRD) Variant Detection Before Allogeneic Hematopoietic Cell Transplantation (AlloHCT)

177 variants
131/454 patients, 29% "MRD"+





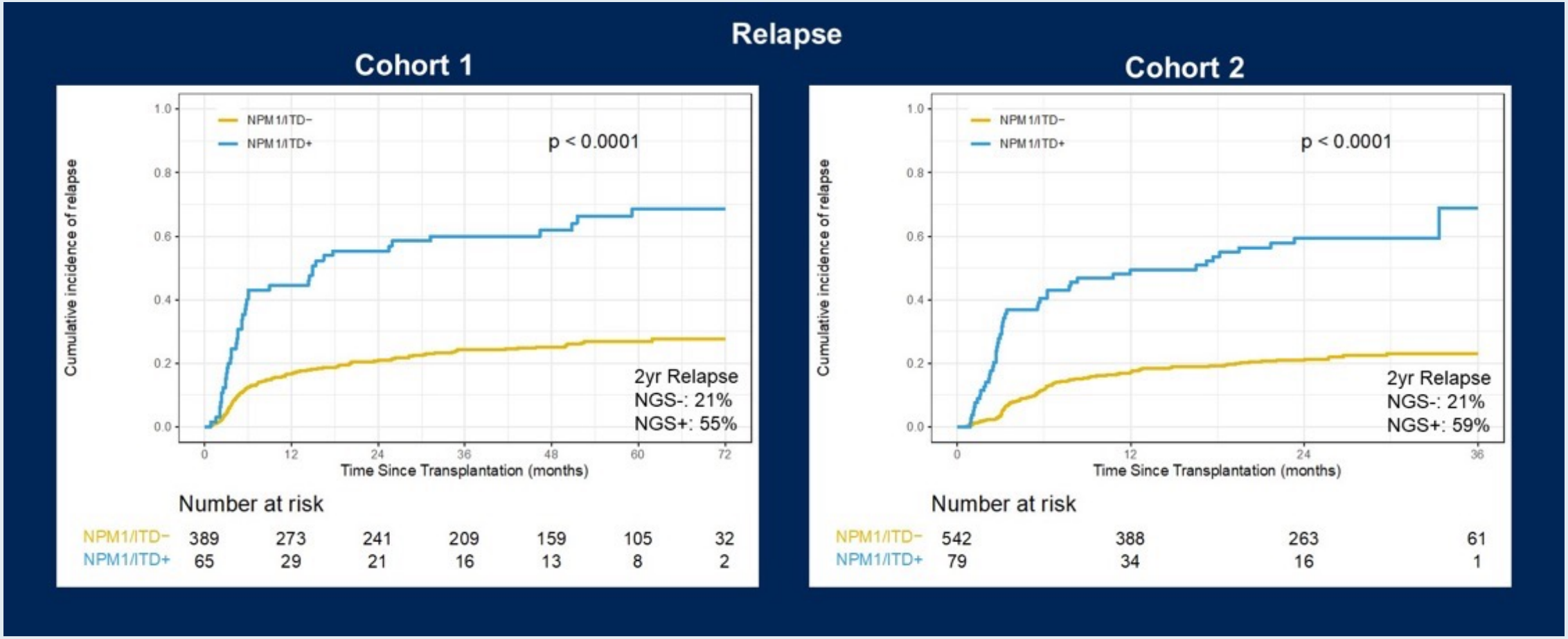
114 variants evaluated by ddPCR, 100% validation rate



Hourigan CS et al. ASCO 2022;Abstract 7006.

RTP RESEARCH TO PRACTICE

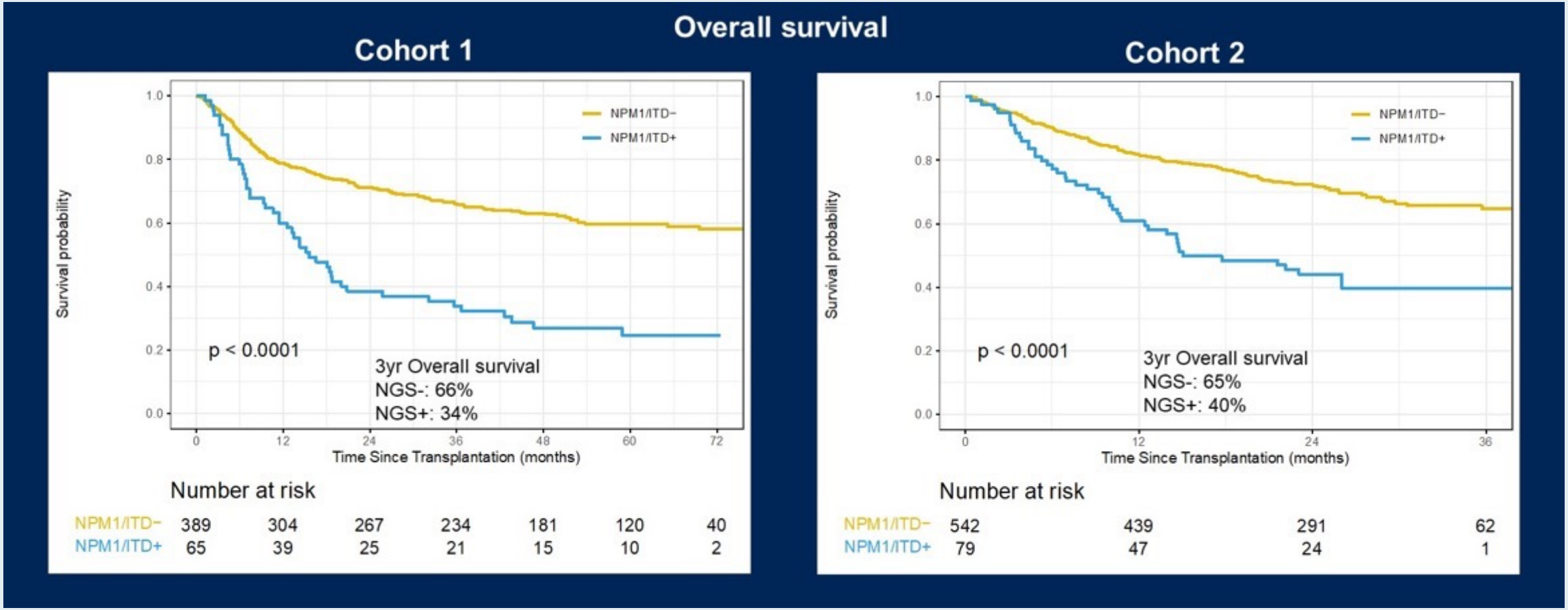
NGS-MRD Before AlloHCT for AML in First Complete Remission (CR1): Relapse



Hourigan CS et al. ASCO 2022;Abstract 7006.

RTP RESEARCH TO PRACTICE

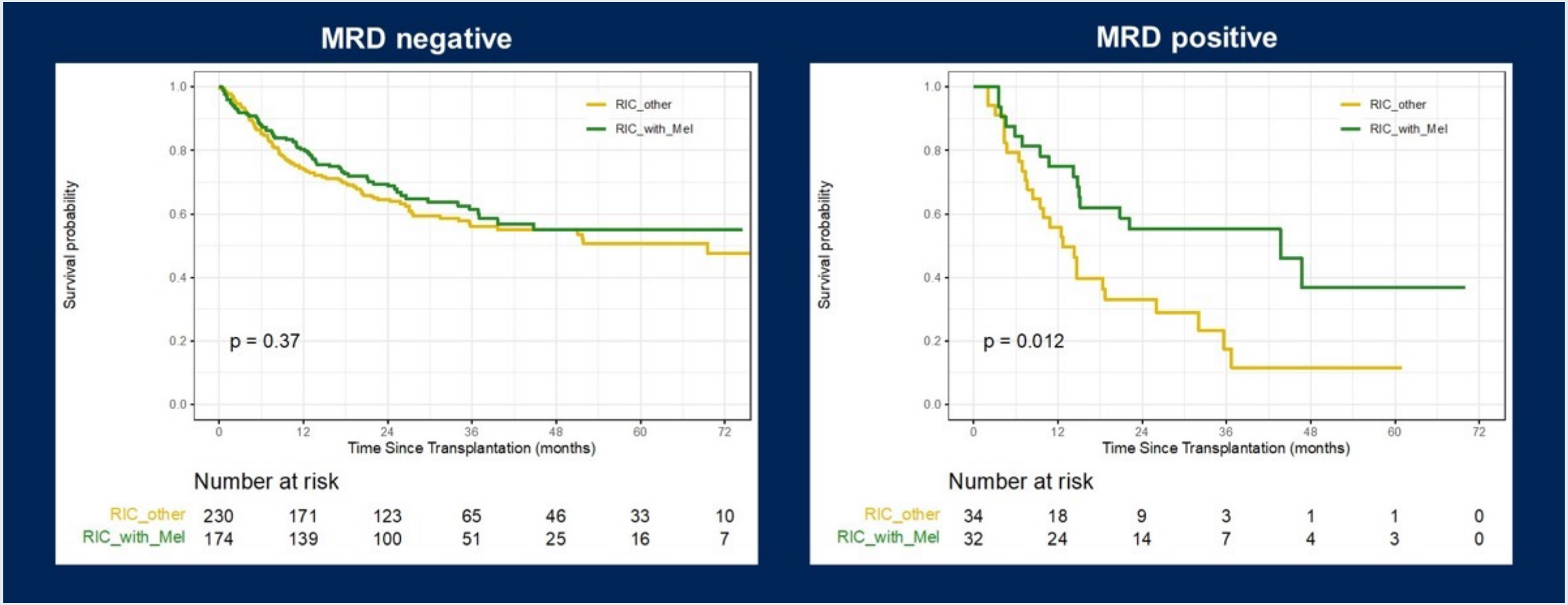
NGS-MRD Before AlloHCT for AML CR1: Overall Survival



Hourigan CS et al. ASCO 2022;Abstract 7006.

RTP RESEARCH TO PRACTICE

Melphalan-Based Condition: Overall Survival



Hourigan CS et al. ASCO 2022;Abstract 7006.

RTP RESEARCH TO PRACTICE

10-day decitabine versus conventional chemotherapy ("3+7") followed by allografting in AML patients ≥ 60 years: a randomized phase III study of the EORTC Leukemia Group, CELG, GIMEMA and German MDS Study Group

Lübbert M, Wijermans P, Kicinski M, Chantepie S, Van der Velden W, Noppeney R, Griskevicius L, Neubauer A, Crysandt M, Vrhovac R, Luppi M, Fuhrmann S, Audisio E, Candoni A, Vekhoff A, Foà R, Gaidano G, van Lammeren-Venema D, Posthuma E, Hoogendoorn M, Giraut A, M Stevens-Kroef, Jansen JH, Ammatuna E, Vilque JP, Wäsch R, Becker H, Blijlevens N, Dührsen U, Baron F, Suciu S, Amadori S, Venditti A, Huls G

fondazione GIMEMA FRANCO MANDELLI

EORTC

The future of cancer therapy

EHA 2022;Abstract 125.

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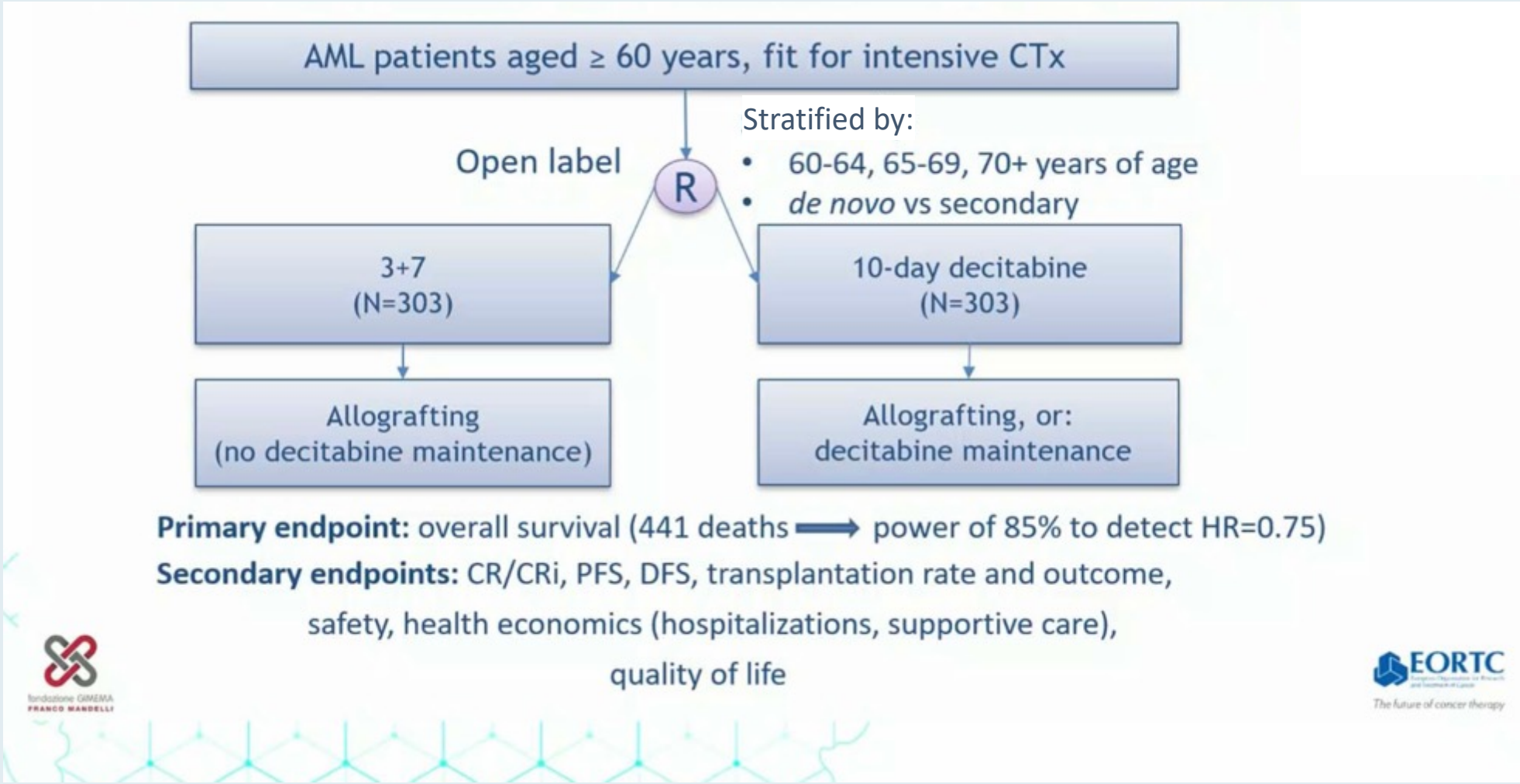
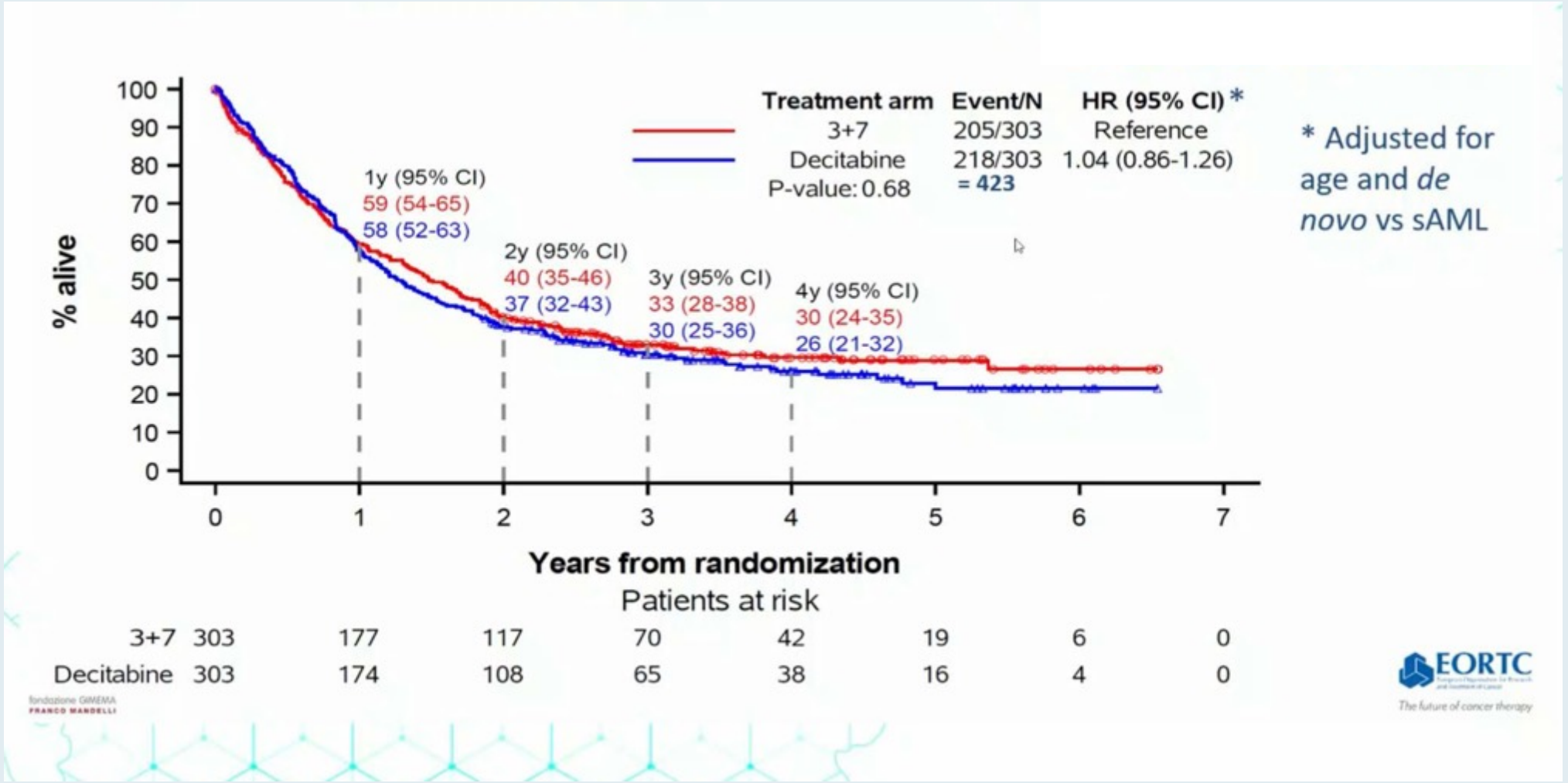
10-Day Decitabine versus Conventional Chemotherapy: Study Design



Lübbert M et al. EHA 2022;Abstract 125.

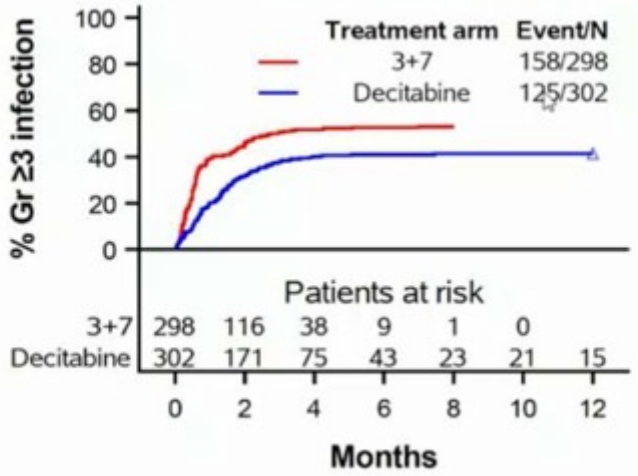
10-Day Decitabine versus Conventional Chemotherapy: Overall Survival

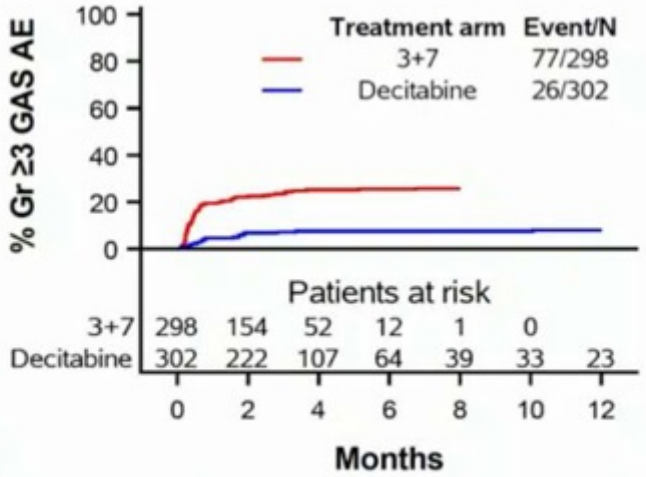


sAML = secondary AML

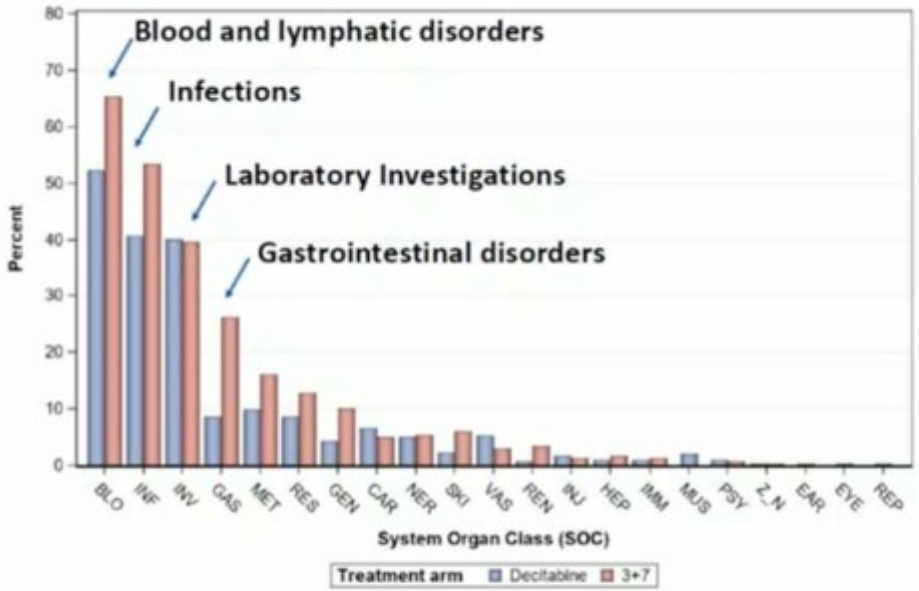
Lübbert M et al. EHA 2022;Abstract 125.

10-Day Decitabine versus Conventional Chemotherapy: Safety





Grade 3-5 adverse events during decitabine vs 3+7



	Decitabine (N=122)	3+7 (N=118)
Incidence of grade 5 treatment-related AE after HSCT	25%	22%

AE = adverse event; HSCT = hematopoietic stem cell transplant

Lübbert M et al. EHA 2022;Abstract 125.

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, July 19, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel J DeAngelo, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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