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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Faculty

Courtney D DiNardo, MD, MSCE
Associate Professor, Department of Leukemia
Division of Cancer Medicine
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Eunice S Wang, MD
Chief, Leukemia Service
Professor of Oncology
Roswell Park Comprehensive Cancer Center
Buffalo, New York

Michael R Savona, MD
Section Head, Hematology, Cellular Therapy and Stem Cell Transplantation
Beverly and George Rawlings Directorship in Hematology Research
Professor of Medicine and Cancer Biology
Department of Internal Medicine
Vanderbilt University School of Medicine
Nashville, Tennessee

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Friday June 3	**Acute Myeloid Leukemia and Myelodysplastic Syndromes** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Lung Cancer 6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)
Saturday June 4	**Prostate Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Gastrointestinal Cancers 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Sunday June 5	**Ovarian Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Monday June 6	**Urothelial Bladder Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Breast Cancer 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Tuesday June 7	**Multiple Myeloma** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Exciting CME Events in Chicago You Do Not Want to Miss

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

Acute Myeloid Leukemia and Myelodysplastic Syndromes

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

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

Prostate Cancer

Saturday, June 4, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Andrew J Armstrong, MD, ScM
Alan H Bryce, MD
Alicia K Morgans, MD, MPH

Lung Cancer

Friday, June 3, 2022
6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)

Faculty
Justin F Gainor, MD
Corey J Langer, MD
Luis Paz-Ares, MD, PhD
Heather Wakelee, MD
Jared Weiss, MD
Helena Yu, MD

Gastrointestinal Cancers

Saturday, June 4, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP
John Strickler, MD
Eric Van Cutsem, MD, PhD

Exciting CME Events in Chicago You Do Not Want to Miss

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

Ovarian Cancer

Sunday, June 5, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Antonio González-Martín, MD, PhD
Joyce F Liu, MD, MPH
Kathleen N Moore, MD, MS

Urothelial Bladder Cancer

Monday, June 6, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Yohann Loriot, MD, PhD
Elizabeth R Plimack, MD, MS
Jonathan E Rosenberg, MD

Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma

Sunday, June 5, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Ian W Flinn, MD, PhD
Brian T Hill, MD, PhD
John P Leonard, MD
Matthew Lunning, DO
Laurie H Sehn, MD, MPH
Mitchell R Smith, MD, PhD

Breast Cancer

Monday, June 6, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Javier Cortés, MD, PhD
Matthew P Goetz, MD
Erika Hamilton, MD
Ian E Krop, MD, PhD
Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Exciting CME Events in Chicago You Do Not Want to Miss

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

Multiple Myeloma

Tuesday, June 7, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Ajai Chari, MD
Elizabeth O'Donnell, MD
Robert Z Orlowski, MD, PhD

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.

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

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Dr DiNardo — Disclosures

Advisory Committee	Foghorn Therapeutics, Gilead Sciences Inc, Immune-Onc Therapeutics Inc, Novartis, Takeda Pharmaceuticals USA Inc
Consulting Agreements	AbbVie Inc, Agios Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Genentech, a member of the Roche Group, GlaxoSmithKline
Contracted Research	AbbVie Inc, Agios Pharmaceuticals Inc, Astex Pharmaceuticals, Bristol-Myers Squibb Company, Calithera Biosciences, Celgene Corporation, Cleave Therapeutics, Daiichi Sankyo Inc, Immune-Onc Therapeutics Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company
Scientific Advisory Board with Stock Options	Notable Labs

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Dr Savona — Disclosures

Advisory Committee	AbbVie Inc, Bristol-Myers Squibb Company, CTI BioPharma Corp, Geron, Karyopharm Therapeutics, Novartis, Ryvu Therapeutics, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc
Consulting Agreements and Ownership Interest	Karyopharm Therapeutics, Ryvu Therapeutics
Contracted Research	ALX Oncology, Incyte Corporation, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc
Data and Safety Monitoring Board/Committee	Bristol-Myers Squibb Company, Sierra Oncology, TG Therapeutics Inc

Dr Wang — Disclosures

Advisory Committee	AbbVie Inc, Amgen Inc, Astellas, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Jazz Pharmaceuticals Inc, Kite, A Gilead Company, Kura Oncology, Novartis, PharmaEssentia, Stemline Therapeutics Inc
Consulting Agreements	Mana Therapeutics, Rafael Pharmaceuticals Inc
Data and Safety Monitoring Board/Committee	AbbVie Inc, Rafael Pharmaceuticals Inc
Speakers Bureau	Astellas, DAVA Oncology, Kura Oncology, Stemline Therapeutics Inc

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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

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

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Case 1 — Courtney D DiNardo, MD, MSCE

- **71yo**
  - **Type 2 DM, well controlled**
  - **HTN and HL**
  - **Coronary artery disease s/p stent placement several years ago**
  - **History of prostate cancer s/p XRT 2.5 yrs ago, cancer NED**
  - **Retired, supportive wife. Remote smoking history.**
  - **ECOG PS 1 – progressive fatigue and shortness of breath**

  - **Referred to hematology for CBC results performed by PCP:**
    - **WBC 2.9K, Hgb 8.2 g/dL, Plts 34K. ANC 800.**
    - **Bone marrow demonstrates AML with underlying MDS related changes. RUNX1 and ASXL1 mutations with -7 cytogenetics.**

Case 1 — Courtney D DiNardo, MD, MSCE

- **HMA + VEN vs CPX-351?**
- **Admit for treatment?**

<u>Additional questions specific to HMA + VEN:</u>

- **He is neutropenic – should you start prophylaxis?**
- **When to do the bone marrow to assess response?**
- **OK to use GCSF?**
- **Transplant?**

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Case 1 — Courtney D DiNardo, MD, MSCE

Real-world outcomes with CPX-351 vs VEN/AZA in ND AML

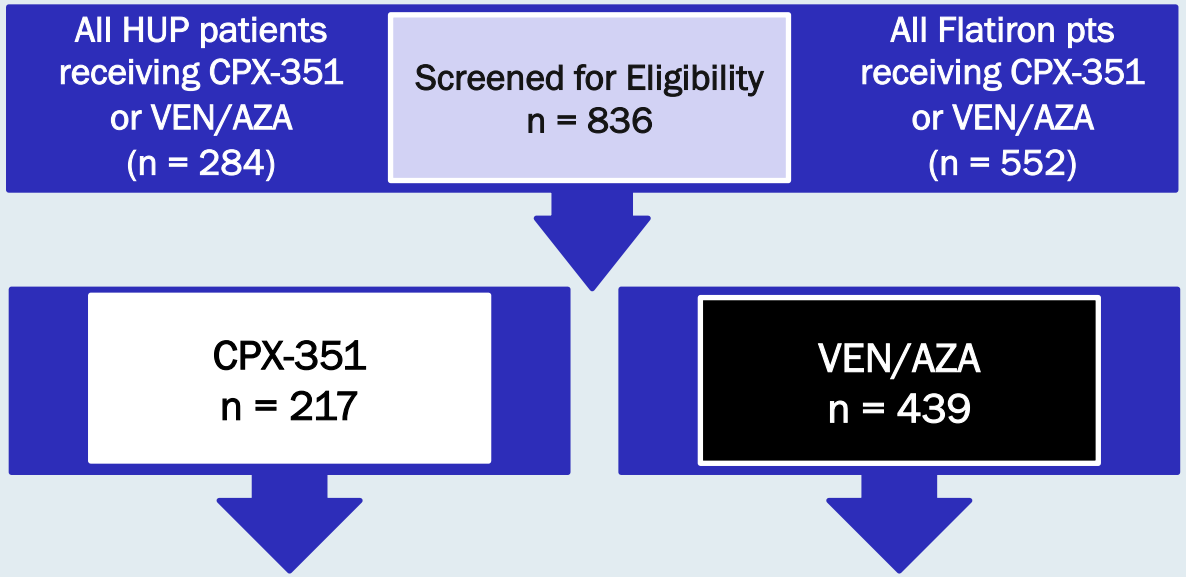
Key Eligibility Criteria

- AML (based on BM or PB blasts > 20%)
- Therapy started between 1/1/2017 to 12/31/2020
- Frontline VEN/AZA or CPX-351
- No mixed-phenotype leukemia or APL
- ECOG PS 0 to 2

2 data sources

1. UPHS (HUP) EHR: a 5-hospital system spanning inpatient and outpatient settings
2. Flatiron Health database: a nationwide compilation of de-identified EHR-derived clinical, biomarker, treatment and mortality data for 2.2 million patients at 800 sites of care

Primary endpoint: OS (time 0 at diagnosis)



EHR, electronic health record; HUP, Hospital of the University of Pennsylvania; UHPS, University of Pennsylvania Health System.

Matthews A, et al. Blood. 2021;138: Abstract 795.

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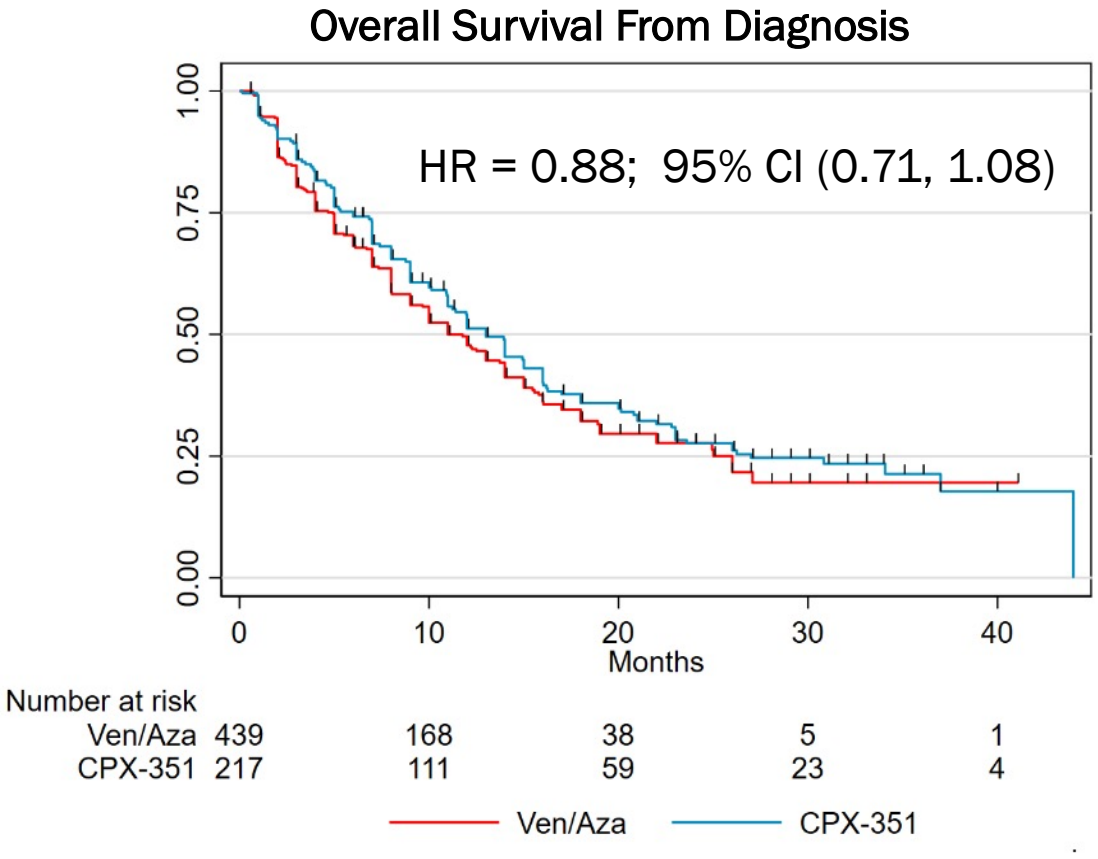
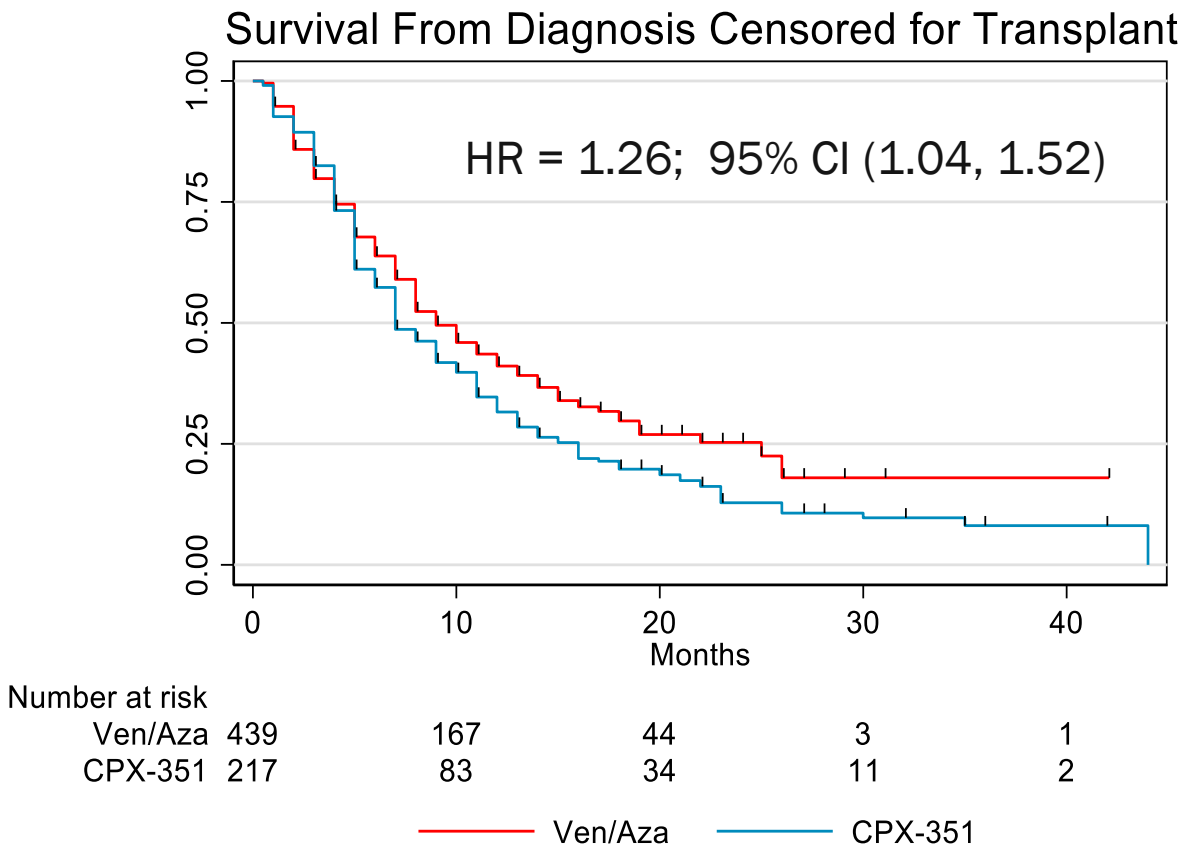
Case 1 — Courtney D DiNardo, MD, MSCE

VEN/AZA and CPX-351 showed similar overall survival





Matthews A et al. *Blood* 2021;138;Abstract 795.

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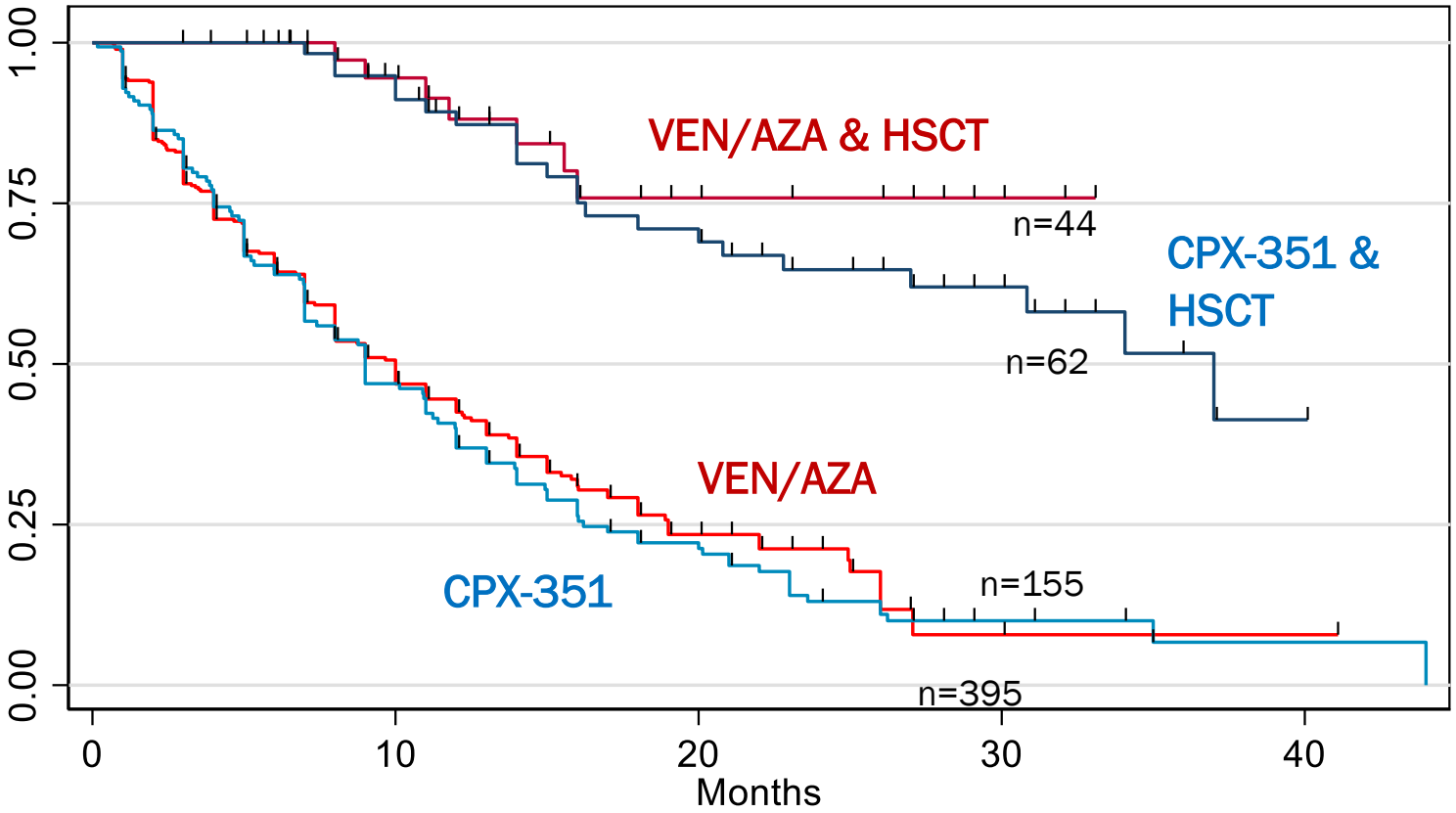
Case 1 — Courtney D DiNardo, MD, MSCE

Transplant is critical for survival regardless of initial treatment



	VEN/AZA	CPX-351
Number (%)	**44 (10%)**	**61 (28%)**
Median Time to Transplant (range)	186 days (87 to 578)	171 days (34 to 903)
Median OS w/ HSCT	NR	37 mos
Median OS w/o HSCT	10 mos	9 mos

Matthews A et al. *Blood* 2021;138;Abstract 795.

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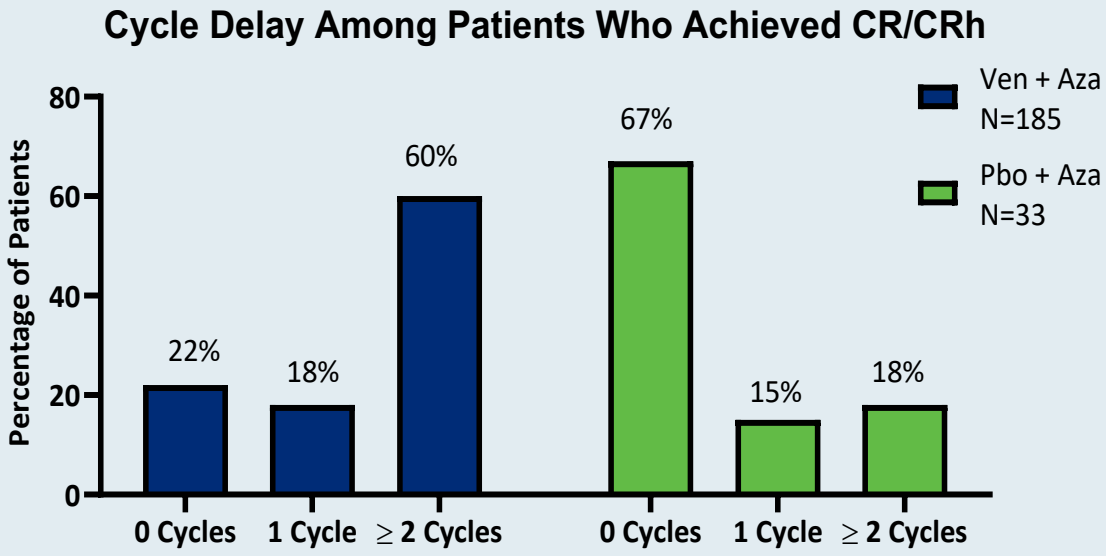
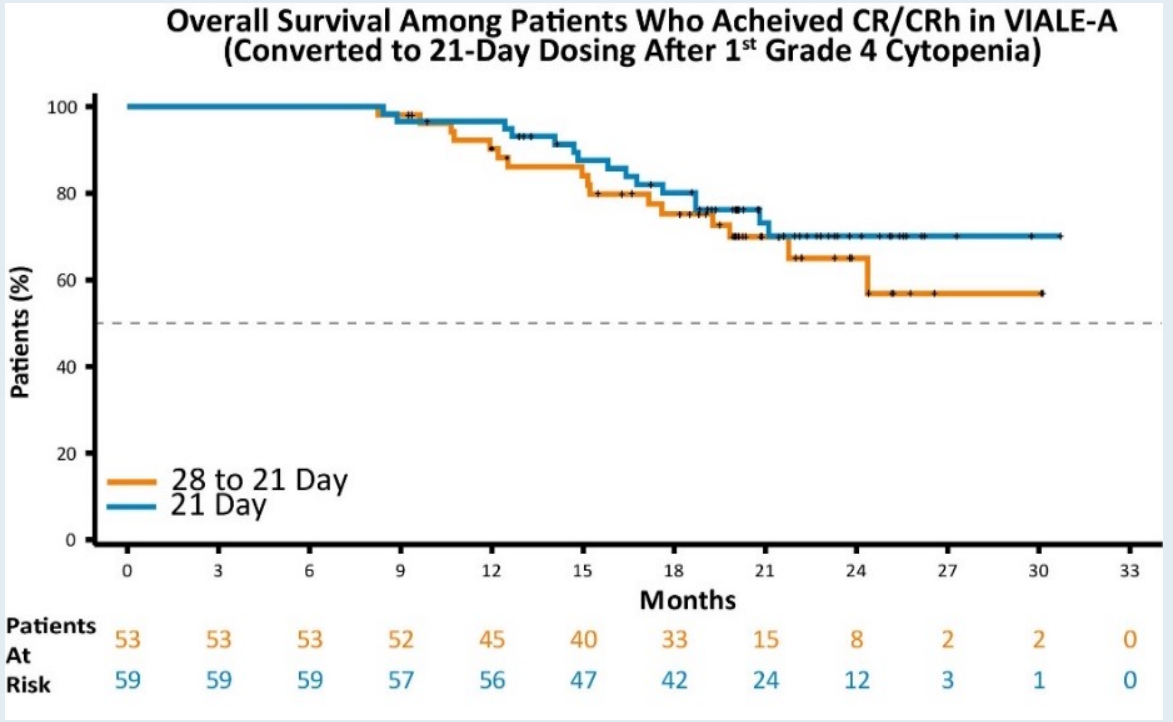
Case 1 — Courtney D DiNardo, MD, MSCE

Cytopenia management with AZA + VEN

Patients with CR or CRh with a post-remission Grade 4 cytopenia ≥7 days, n (%)	Ven + Aza (n=185)	Pbo + Aza (n=33)
0 events	24 (13)	18 (55)
1 event	36 (19)	8 (24)
≥2 events	**125 (68)**	7 (21)



VIALE-A was not designed to evaluate differences between 21/28 day and 28/28 day dosing per cycle



Pratz K et al. ASH 2020;Abstract 1944.

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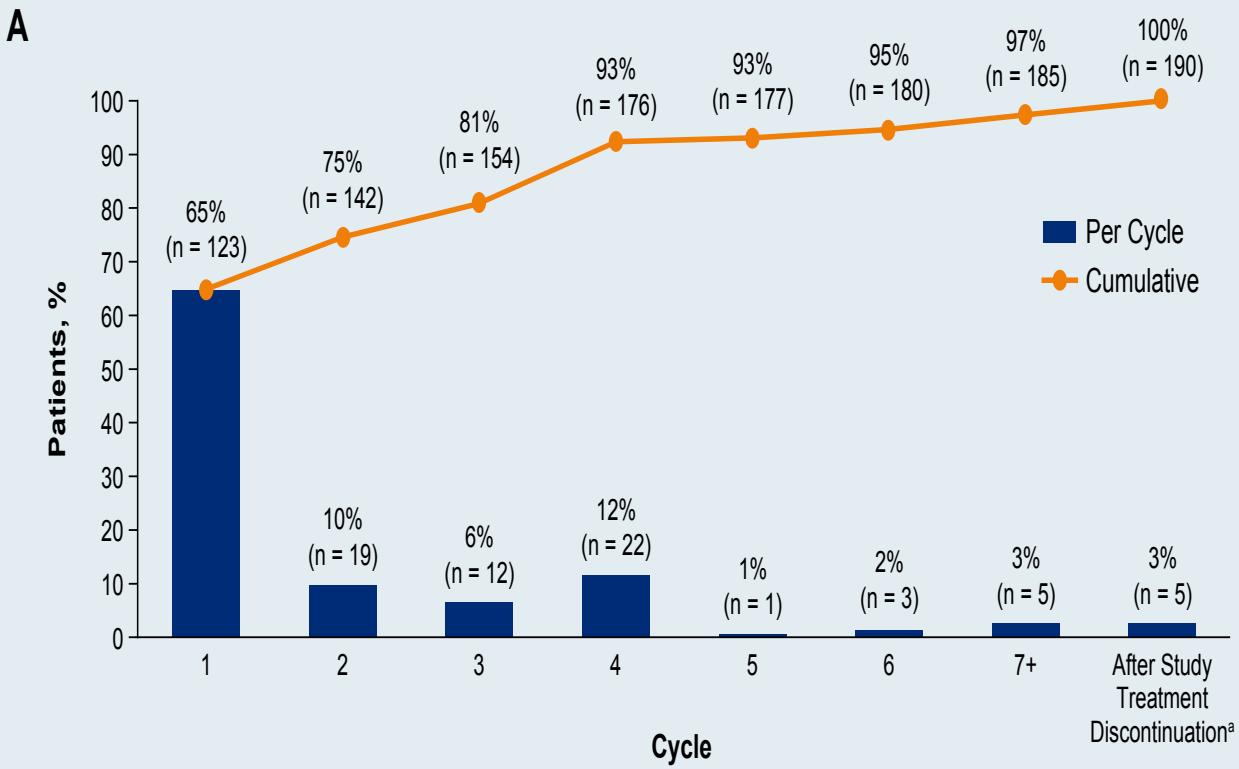
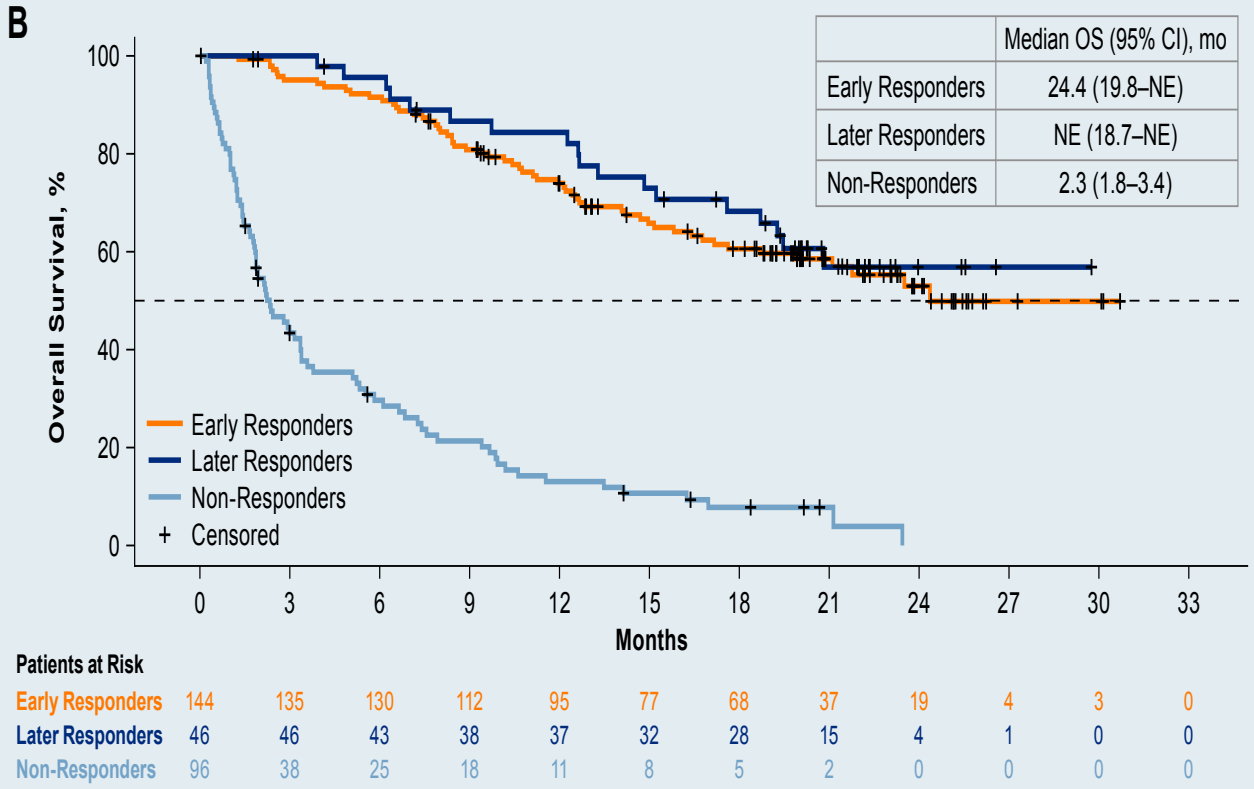
Case 1 — Courtney D DiNardo, MD, MSCE

VIALE-A: Time to CR/CRi response





	Median OS (95% CI), mo
Early Responders	24.4 (19.8–NE)
Later Responders	NE (18.7–NE)
Non-Responders	2.3 (1.8–3.4)

Note that all later responders who had a CR/CRi beyond Cycle 6 had achieved MLFS before Cycle 6

Jonas B. AJH 2022. In press.

RTP RESEARCH TO PRACTICE

Received: 29 September 2020 | Revised: 22 October 2020 | Accepted: 25 October 2020

DOI: 10.1002/ajh.26039

RESEARCH ARTICLE

Venetoclax with azacitidine or decitabine in patients with newly diagnosed acute myeloid leukemia: Long term follow-up from a phase 1b study

Daniel A. Pollyea[1] | Keith Pratz[2] | Anthony Letai[3] | Brian A. Jonas[4] | Andrew H. Wei[5] | Vinod Pullarkat[6] | Marina Konopleva[7] | Michael J. Thirman[8] | Martha Arellano[9] | Pamela S. Becker[10,11] | Brenda Chyla[12] | Wan-Jen Hong[13] | Qi Jiang[12] | Jalaja Potluri[12] | Courtney D. DiNardo[7]

Am J Hematol 2021;96:208-17.

Long-Term Follow-Up of a Phase Ib Trial of Venetoclax in Combination with Azacitidine or Decitabine for Newly Diagnosed AML

Clinical endpoint	Venetoclax 400 mg	
	AZA (n = 84)	DEC (n = 31)
Complete response (CR)	37 (44%)	17 (55%)
CR/CRi	60 (71%)	23 (74%)
Duration of response	21.9 mo	15.0. mo
Median overall survival	16.4 mo	16.2 mo

CRi = CR with incomplete blood count recovery

- 46% (AZA) and 32% (DEC) of patients achieved CR/CRi prior to initiation of cycle 2 therapy
- Key Grade ≥3 adverse events (AZA and DEC) were febrile neutropenia (39% and 65%), anemia (30% and 26%), thrombocytopenia (25% and 23%) and neutropenia (20% and 10%)

Pollyea DA et al. *Am J Hematol* 2021;96:208-17.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 13, 2020 VOL. 383 NO. 7

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;11:163 www.nature.com/bcj

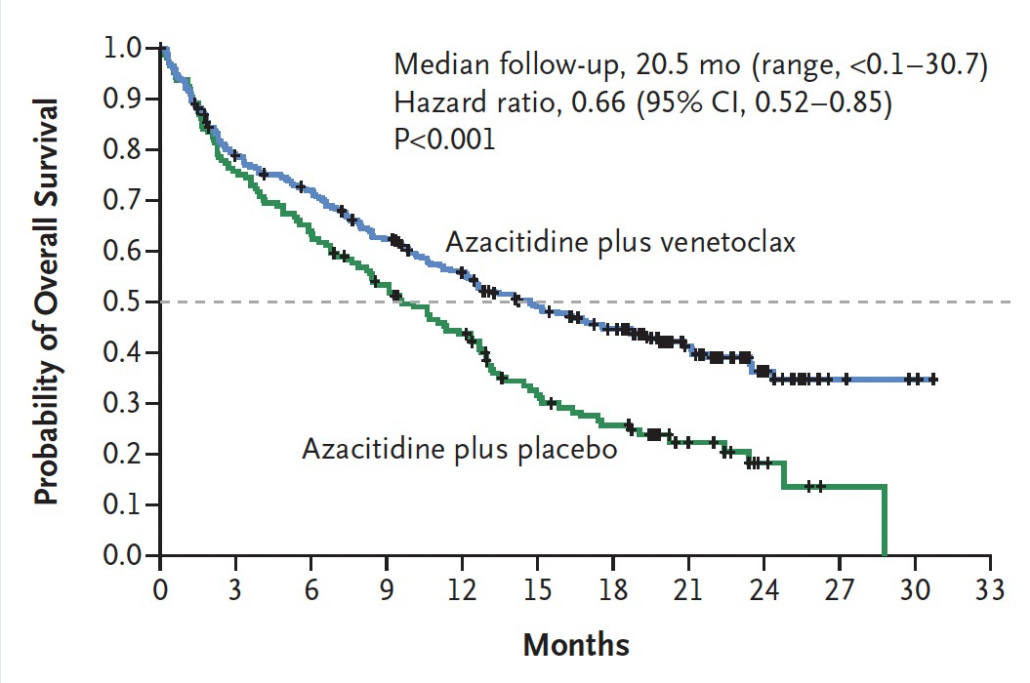
ARTICLE

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

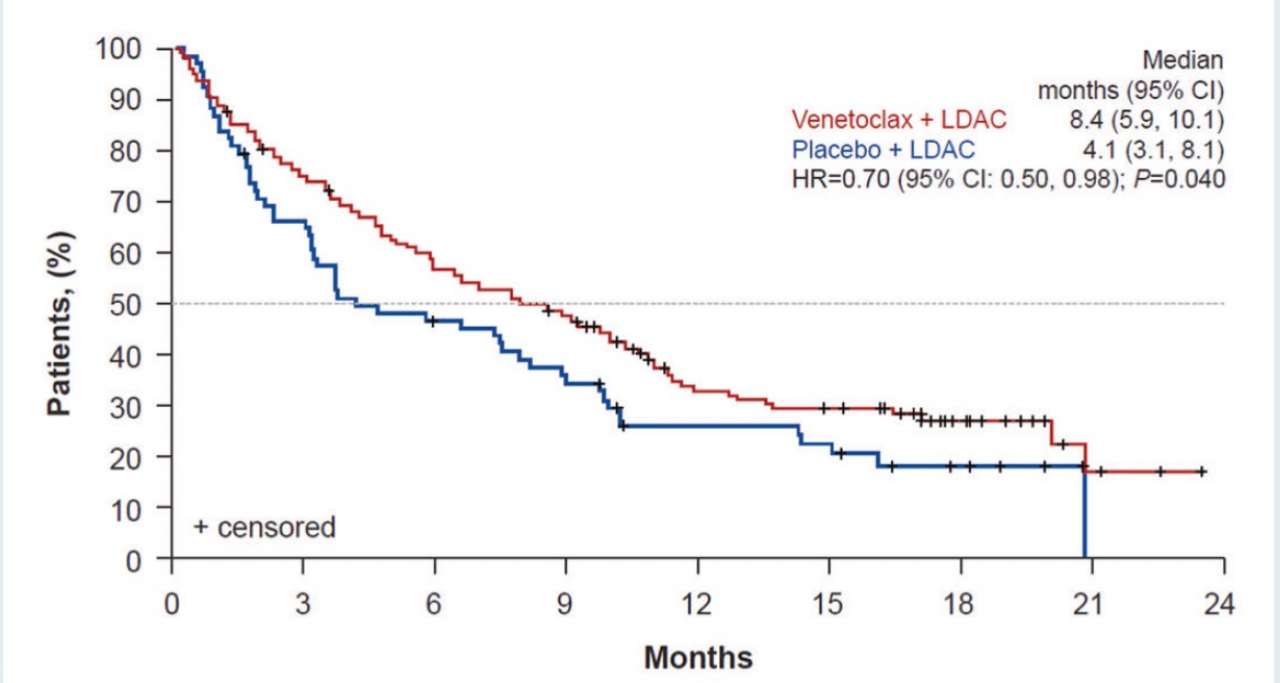
Andrew H. Wei[1✉], Panayiotis Panayiotidis[2], Pau Montesinos[3,4], Kamel Laribi[5], Vladimir Ivanov[6], Inho Kim[7], Jan Novak[8], Don A. Stevens[9], Walter Fiedler[10], Maria Pagoni[11], Julie Bergeron[12], Stephen B. Ting[13], Jing-Zhou Hou[14], Achilles Anagnostopoulos[15], Andrew McDonald[16], Vidhya 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;383:617-29; [2]Wei AH et al. *Blood Cancer J* 2021;11:163.

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

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

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

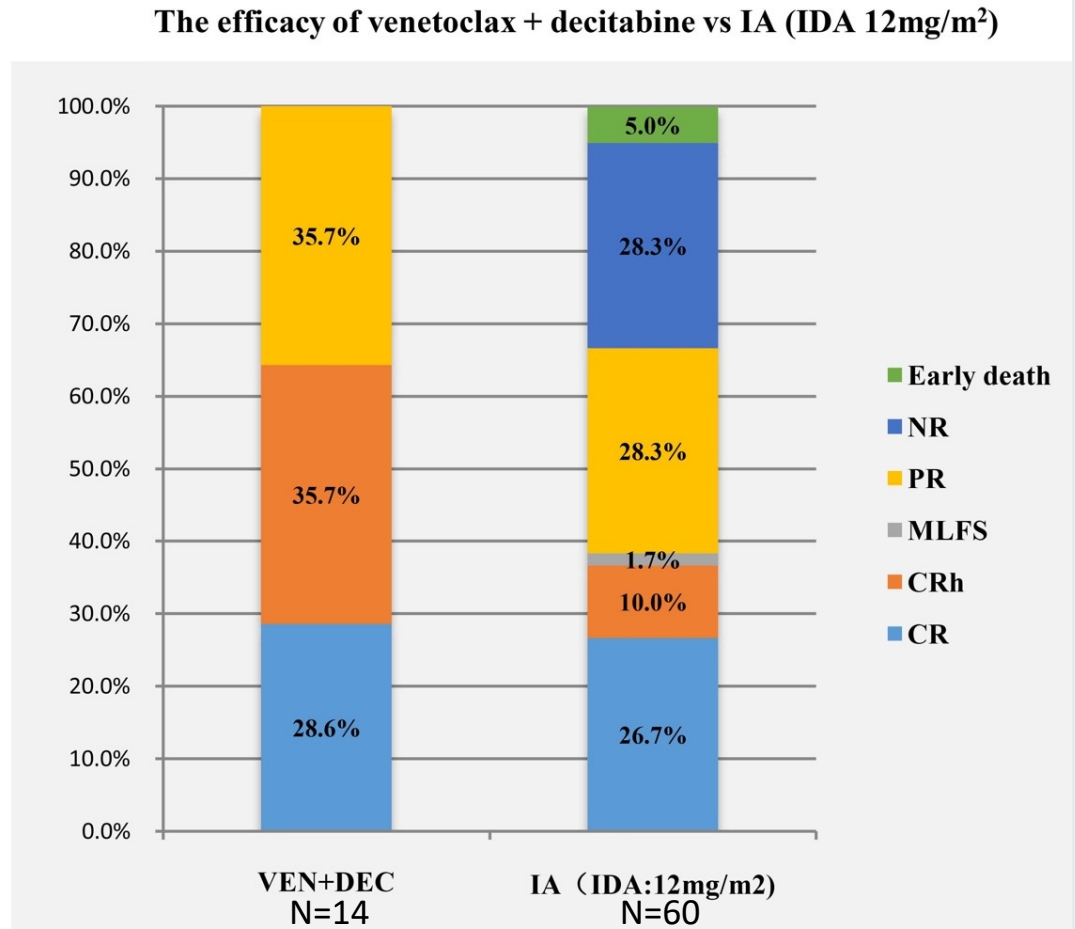
Venetoclax plus Decitabine for Young Adults with Newly Diagnosed ELN Adverse-Risk Acute Myeloid Leukemia: Interim Analysis of a Prospective, Multicenter, Single-Arm, Phase 2 Trial

Chen S et al.

ASH 2021;Abstract 35.

Interim Analysis of a Phase II Trial of Venetoclax with Decitabine for Young Adults with Newly Diagnosed European LeukemiaNet Adverse-Risk AML

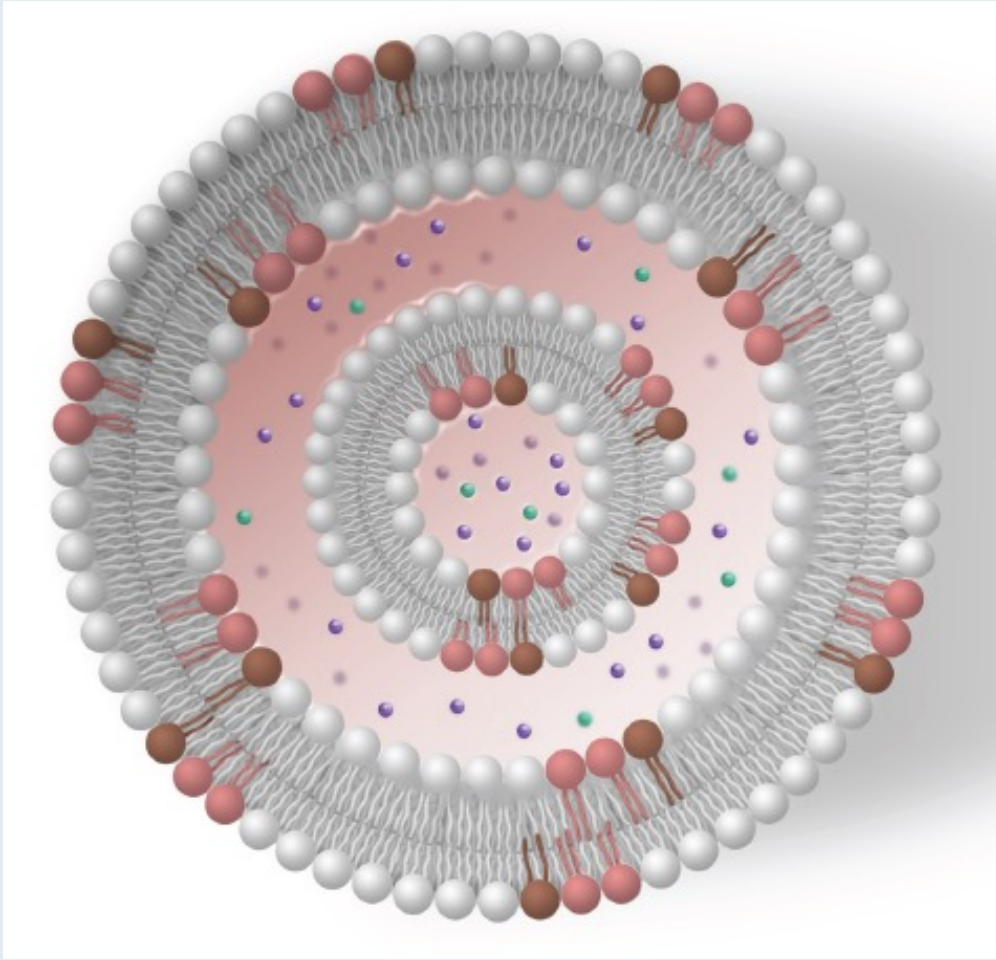
- Primary endpoint: Superiority of composite remission versus historic control of cytarabine + idarubicin (12 mg/m^2)



Chen S et al. ASH 2021;Abstract 35

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.

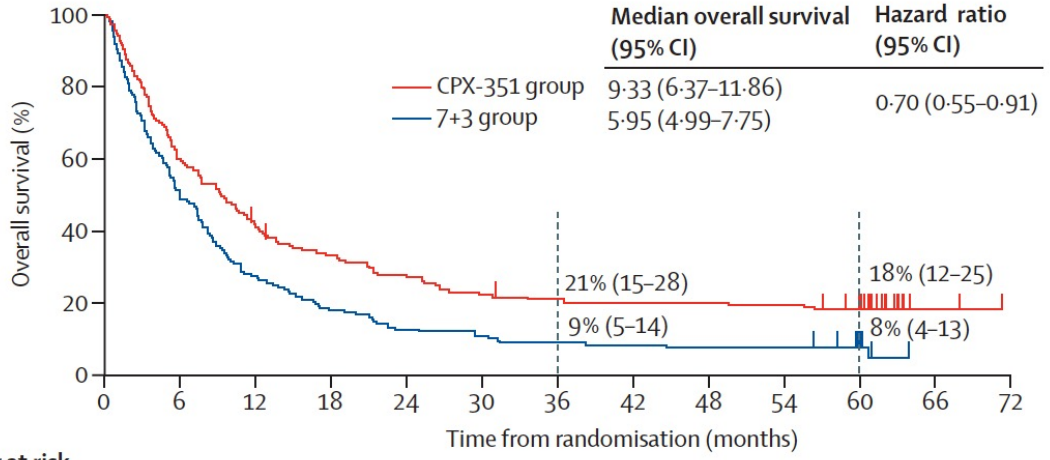
Lancet Haematol 2021;8:e481-91.

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

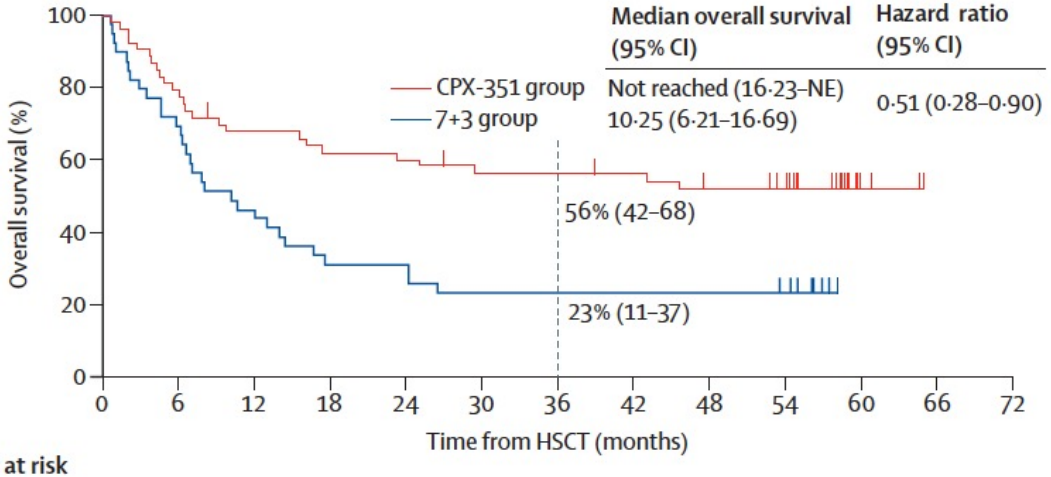
OS



Number at risk (number censored)

CPX-351 group	153	92	62	49	40	33	30	29	29	28	22	2	0
	(0)	(0)	(1)	(2)	(2)	(2)	(3)	(3)	(3)	(3)	(7)	(27)	(29)
7+3 group	156	77	43	28	20	17	14	13	12	12	5	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(11)	(11)

OS landmarked from time of HSCT



Number at risk (number censored)

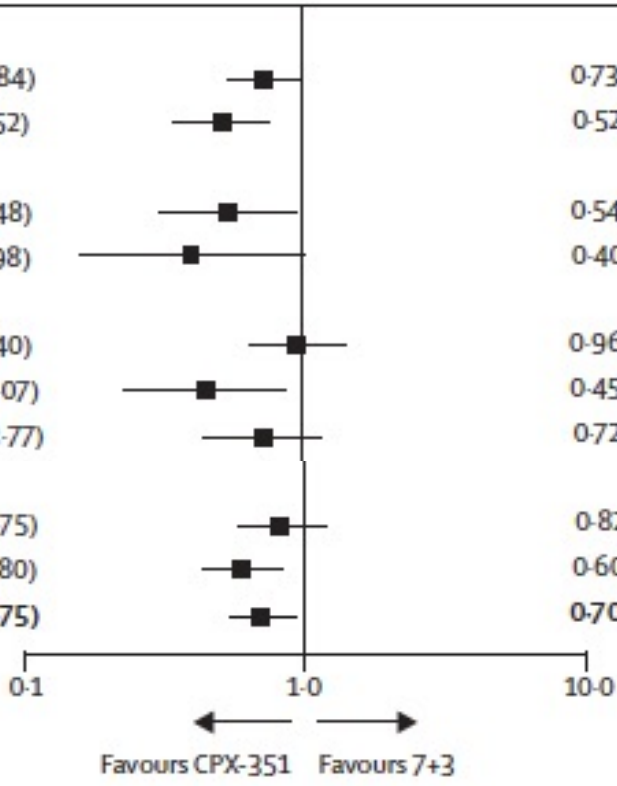
CPX-351 group	53	42	35	32	31	28	28	27	24	21	6	0	0
	(0)	(0)	(1)	(1)	(1)	(2)	(2)	(3)	(4)	(7)	(22)	(28)	(28)
7+3 group	39	27	18	12	12	9	9	9	9	8	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(9)	(9)	(9)

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

RTP RESEARCH TO PRACTICE

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 – 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)**



HMA = hypomethylating agent

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

Preliminary Results of V-FAST, a Phase 1b Master Trial to Investigate CPX-351 Combined With Targeted Agents in Newly Diagnosed AML

Presenter: Vinod Pullarkat

City of Hope Comprehensive Cancer Center, Duarte, CA

Vinod Pullarkat,[1] Mark Levis,[2] Gabriel Mannis,[3] Stephen A. Strickland,[4] Tara L. Lin,[5] Stefan Faderl,[6] Divya Chakravarthy,[6] Vijayalakshmi Chandrasekaran,[7] Ronald S. Cheung,[6] Harry P. Erba[8]

[1]City of Hope Comprehensive Cancer Center, Duarte, CA; [2]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [3]Stanford University Medical Center, Palo Alto, CA; [4]Vanderbilt-Ingram Cancer Center, Nashville, TN; [5]University of Kansas Medical Center, Kansas City, KS; [6]Jazz Pharmaceuticals, Palo Alto, CA; [7]Jazz Pharmaceuticals, Philadelphia, PA; [8]Duke University School of Medicine, Durham, NC.

ASCO 2021;Abstract 7026.

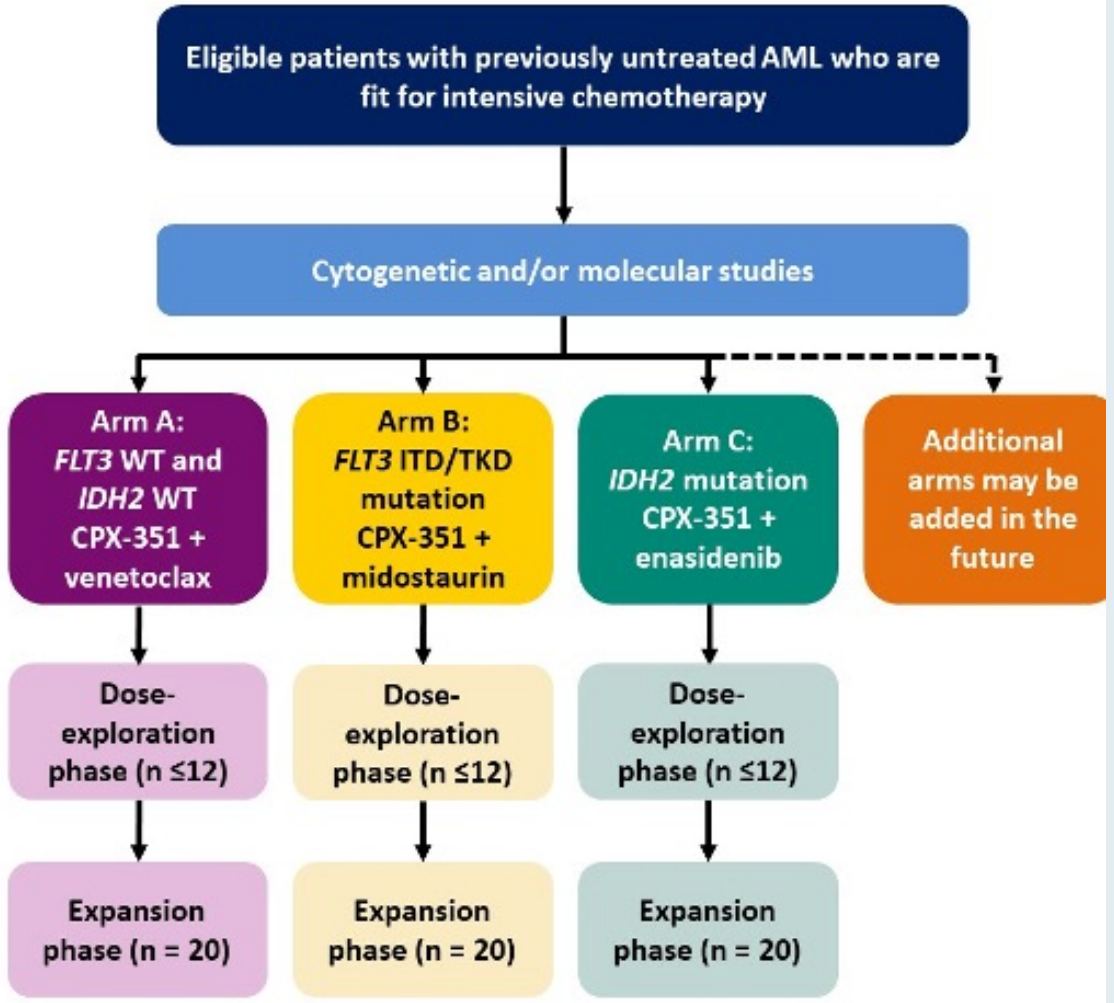
ASCO 2021; June 4-8, 2021

V-FAST Phase Ib Study Design

- The V-FAST (Vyxeos – First Phase ASsessment with Targeted Agents) trial aims to examine the safety and initial efficacy of CPX-351 combinations (eg, with venetoclax, midostaurin, or enasidenib) in adults with previously untreated AML who are fit for intensive chemotherapy
- V-FAST is an open-label, multicenter, multi-arm, nonrandomized, phase 1b master trial (ClinicalTrials.gov Identifier: NCT04075747)
- The flexible trial design permits additional combinations to be added in the future, under the same master protocol

Dose-exploration phase: 3+3 design to identify a RP2D and evaluate the safety of CPX-351 combination regimens

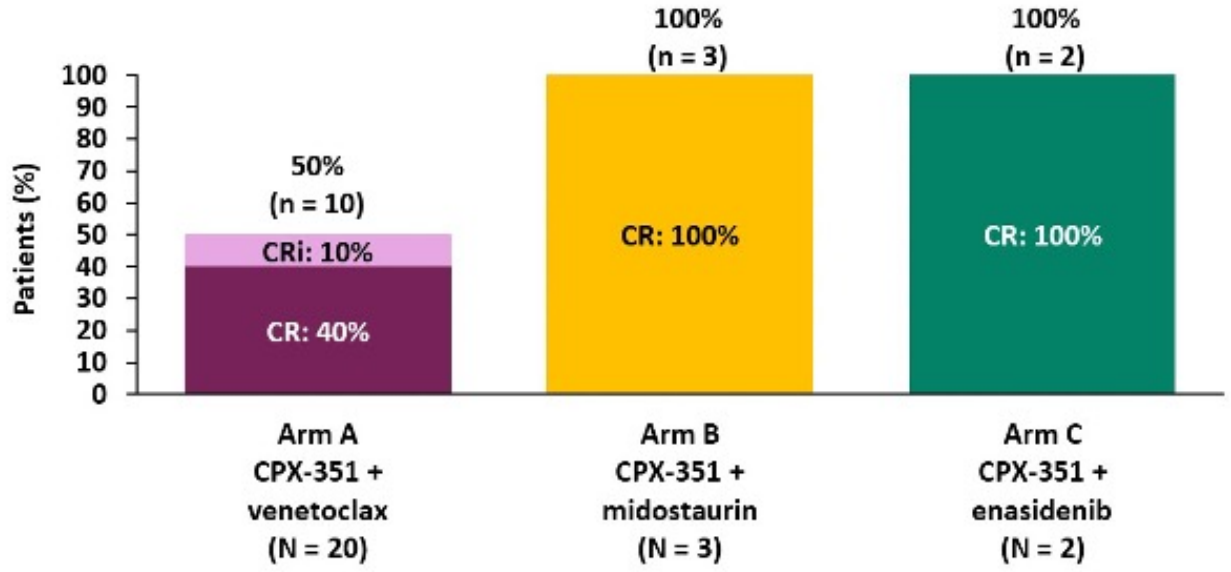
Expansion phase: Confirm the RP2D of CPX-351 combination regimens, further evaluate safety, and assess efficacy



RP2D, recommended phase 2 dose.

Pullarkat V et al. ASCO 2021;Abstract 7026.

V-FAST: Remission Rates



N = number of patients who received >1 dose of study drug and had an evaluable bone marrow result.
n = number of patients who achieved CR or CRi in each treatment arm.

- In conclusion, these results suggest CPX-351 can be combined with venetoclax and midostaurin with a manageable safety profile in patients with newly diagnosed AML
- Preliminary remission rates are promising, particularly given the high-risk population enrolled in Arm A
- The study is currently ongoing and actively enrolling patients

Pullarkat V et al. ASCO 2021;Abstract 7026.

A Randomised Comparison of CPX-351 and FLAG-IDA in High-Risk Acute Myeloid Leukemia. Results from the NCRA AML19 Trial

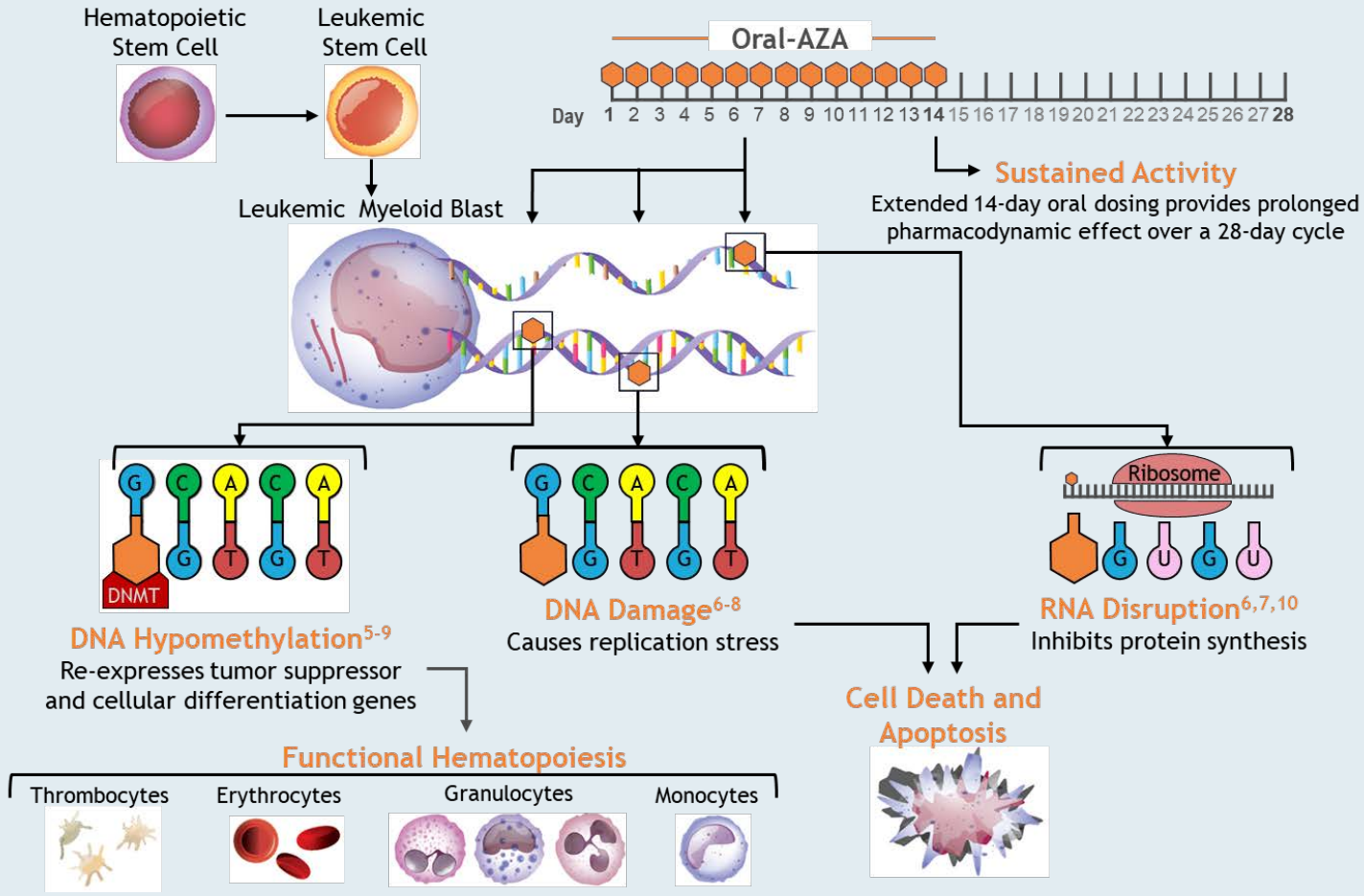
Russell N et al.

EHA 2022;Abstract S128 (Oral).

June 11, 2022

Oral Azacitidine (Oral-AZA, CC-486)

- **Oral HMA with a distinct PK/PD profile from injectable AZA; the two are not bioequivalent[1,2]**
- **Approved in the United States for continued Tx of adult pts with AML in first CR/CRi post-IC and not able to complete intensive curative therapy (eg, HSCT)[3]**
  - **Oral dosing allows for extended drug exposure during each Tx cycle to prolong AZA activity[1,2]**



1. Garcia-Manero et al. *J Clin Oncol*. 2011;29(18):2521–7. 2. Laille et al. *PLoS One*. 2015;10(8):e0135520. 3. ONUREG® (azacitidine) tablets [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; Rev. 9/2020. 4. Savona et al. *Am J Hematol*. 2018;93(10):1199–206. 5. Stresemann et al. *Mol Cancer Ther*. 2008;7:2998–3005. 6. Hollenbach et al. *PLoS One*. 2010;5(2):e9001. 7. Scott LJ. *Drugs*. 2016;76(8):889–900. 8. Stresemann C, Lyko F. *Int J Cancer*. 2008;123(1):8–13. 9. Aimiuwu et al. *Blood*. 2012;119(22):5229–38.

AML, acute myeloid leukemia; AZA, azacitidine; CR, complete remission; CRi, CR with incomplete blood count recovery; HMA, hypomethylating agent; HSCT, hematopoietic stem cell transplant; IC, intensive chemotherapy; PD, pharmacodynamic; PK, pharmacokinetic; pts, patients; Tx, treatment.

Courtesy of Richard M Stone, MD

The First-in-Class Anti-CD47 Antibody Magrolimab Combined with Azacitidine Is Well-Tolerated and Effective in AML Patients: Phase 1b Results

Sallman DA et al.

ASH 2020;Abstract 330.

Phase Ib Study of Magrolimab Combined with Azacitidine for Patients with Newly Diagnosed AML Who Are Not Eligible for Intensive Chemotherapy

Clinical endpoint	Magrolimab + AZA Pts evaluable for efficacy (n = 34)
Objective response	22 (65%)
CR/CRi	4 (12%)
CR	14 (44%)
Median time to response	2.0 mo

Treatment-related adverse events (≥15% of patients) with magrolimab + AZA were anemia (31%), fatigue (19%), blood bilirubin increase (19%), neutropenia (19%), thrombocytopenia (17%) and nausea (15%).

Sallman DA et al. ASH 2020;Abstract 330.

Tolerability and Efficacy of the First-in-Class Anti-CD47 Antibody Magrolimab Combined with Azacitidine in Frontline TP53m AML Patients: Phase Ib Results

Daver NG et al.

ASCO 2022;Abstract 7018 (Poster Discussion).

Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant
June 4, 2022
2:15 PM – 3:35 PM EDT

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 Ib Results

Daver N et al.

EHA 2022;Abstract S132 (Oral).

June 10, 2022

Phase I/II Study of Azacitidine (AZA) with Venetoclax (VEN) and Magrolimab (Magro) in Patients (pts) with Newly Diagnosed Older/Unfit or High-Risk Acute Myeloid Leukemia (AML) and Relapsed/Refractory (R/R) AML

Daver N et al.

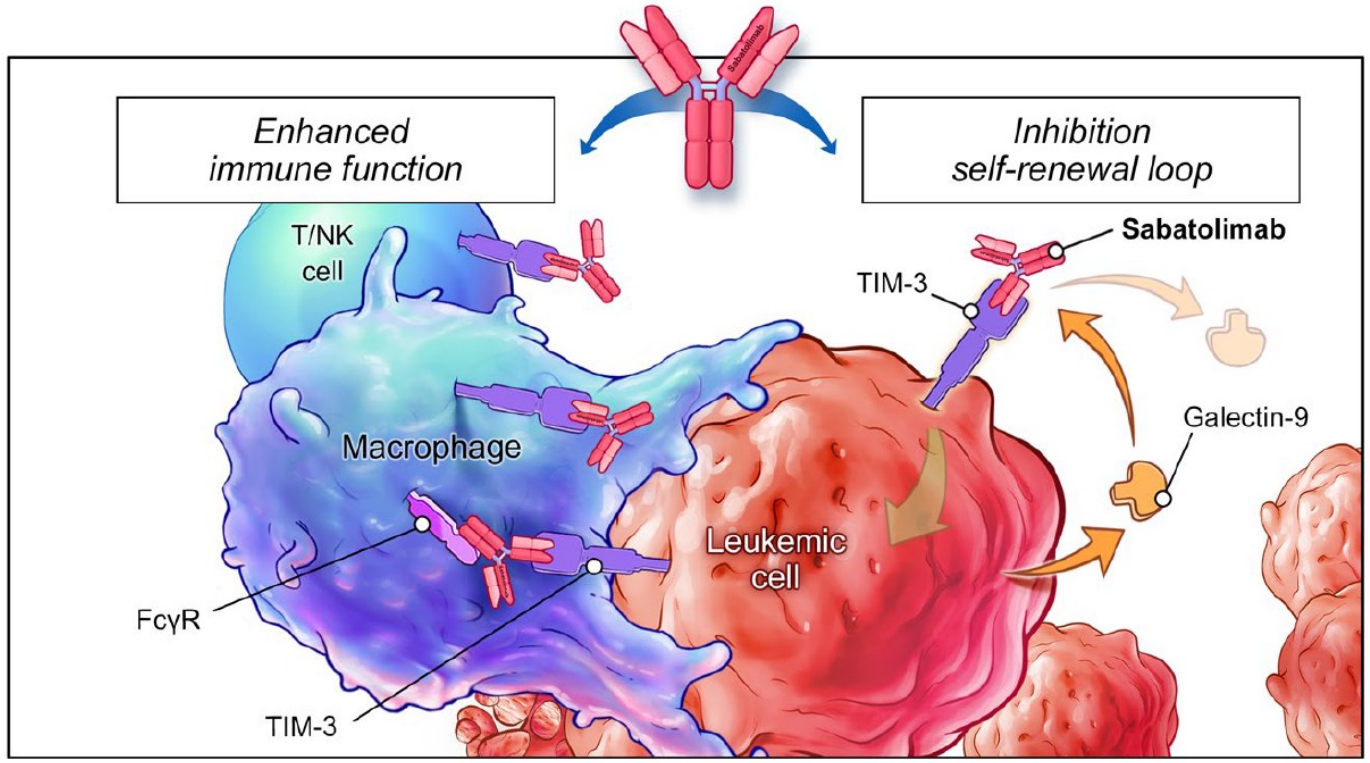
ASH 2021;Abstract 371.

Phase I/II Study of Azacitidine with Venetoclax and Magrolimab for Newly Diagnosed AML in Older/Unfit Patients or Those at High Risk and for Relapsed/Refractory AML

Clinical endpoint	Front line (n = 16)	Relapsed/refractory	
		Venetoclax-naïve (n = 8)	Venetoclax failure (n = 11)
ORR	16 (100%)	6 (75%)	3 (27%)
CR/CRi	15 (94%)	5 (63%)	3 (27%)
CR	13 (81%)	3 (38%)	0
Time to best response	1.1 mo	1.5 mo	2.3 mo

Daver N et al. ASH 2021;Abstract 371.

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 (MBG453) in Combination with Hypomethylating Agents (HMAs) in Patients (Pts) with Very High/High-Risk Myelodysplastic Syndrome (vHR/HR-MDS) and Acute Myeloid Leukemia (AML): Final Analysis from a Phase Ib Study

Brunner AM et al.

ASH 2021;Abstract 244.

Phase Ib Study of Sabatolimab in Combination with HMAs for Newly Diagnosed AML

Response in evaluable patients	Sabatolimab + HMA* (n = 40)
ORR	42.5%
CR	25.0%
CRi	5.0%
Median duration of response	12.6 mo

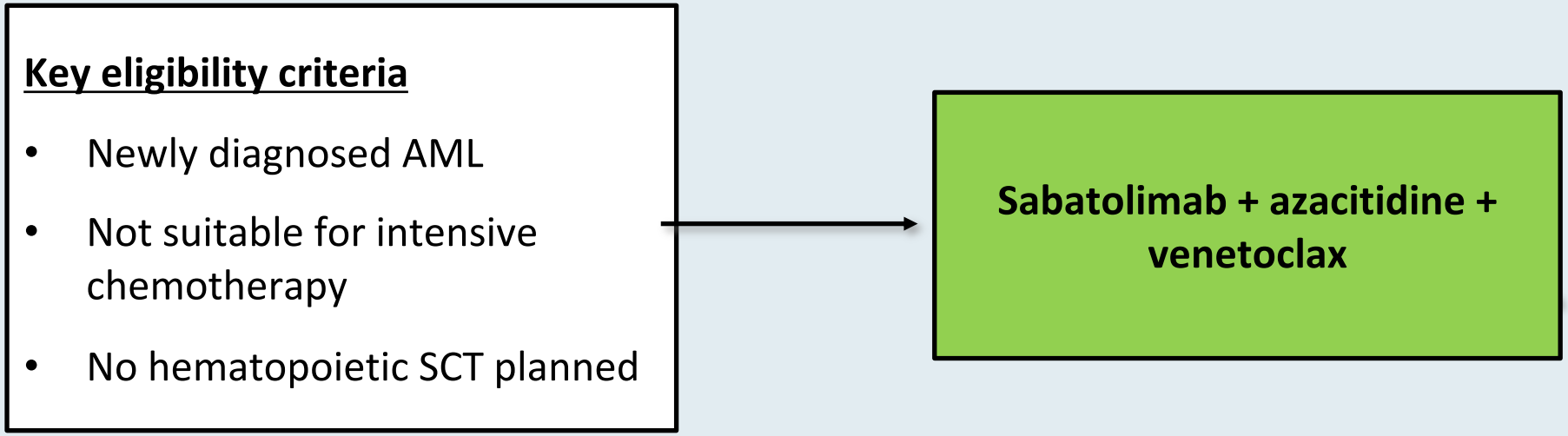
*Decitabine or azacitidine

Immune-mediated adverse events (imAEs) were uncommon (21% of patients), and no Grade 4/5 imAEs were observed.

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 May 2022.

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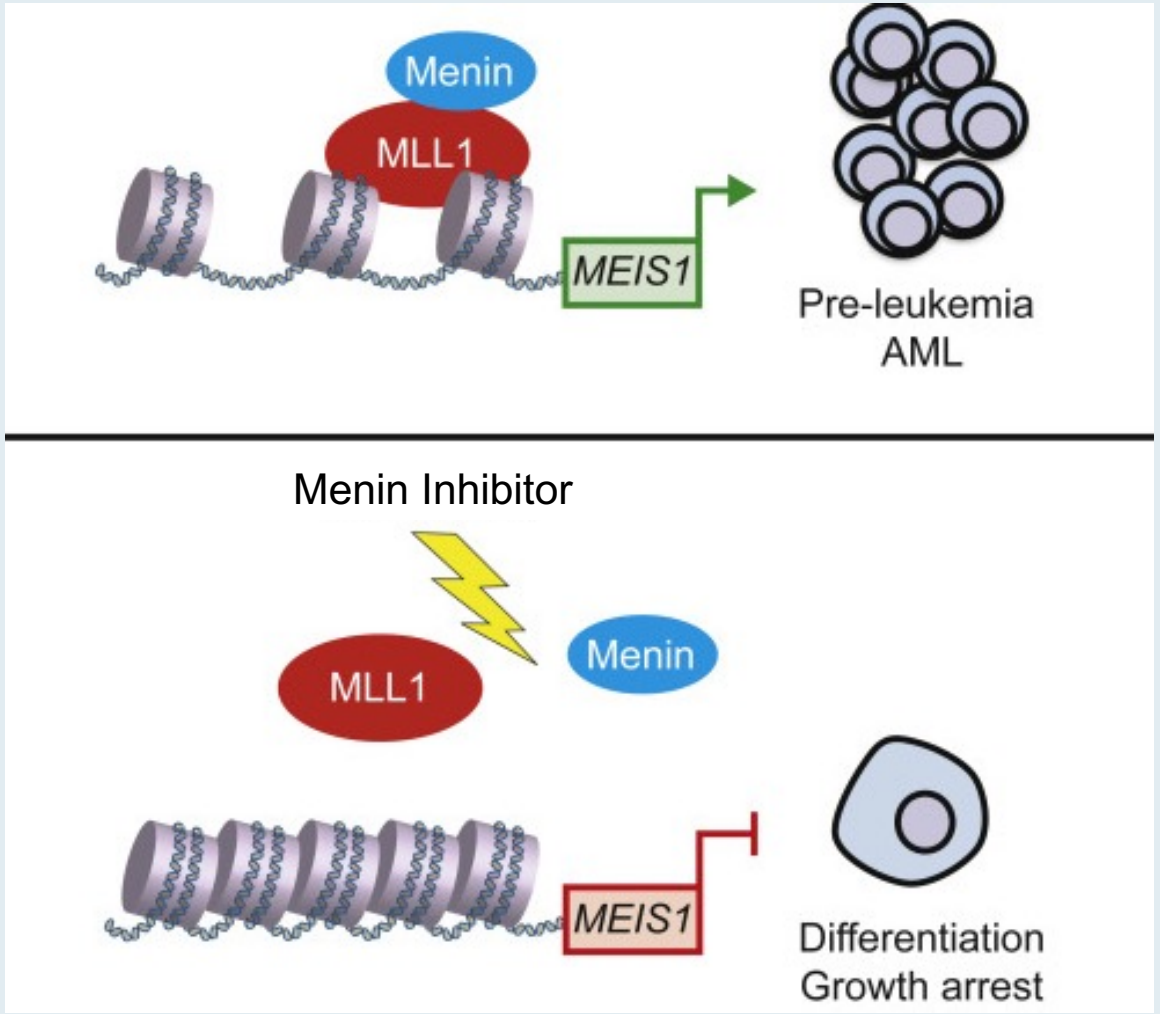
Menin Inhibitor Disruption of Menin-MLL Interaction



Gundry MC et al. *Cancer Cell* 2020;37(3):267-9.

RTP RESEARCH TO PRACTICE

Safety and Efficacy of Menin Inhibition in Patients (Pts) with MLL-Rearranged and NPM1 Mutant Acute Leukemia: A Phase (Ph) 1, First-in-Human Study of SNDX-5613 (AUGMENT 101)

Stein EM et al.

ASH 2021;Abstract 699.

AUGMENT 101: Phase I Results with SNDX-5613 for R/R Acute Leukemia Harboring an MLL Rearrangement or an NPM1 Mutation

Best overall response	SNDX-5613
Overall CRc (CR + CRh + CRp + CRi/MLFS)	20/45 (40%)
CRc in patients with MLLr leukemia	17/35 (49%)
CRc in patients with mNPM1 leukemia	3/10 (33%)

- The MTD was 276 mg q12h in Arm A (pts not taking strong CYP3A4 inhibitors) and 163 mg q12h in Arm B (pts taking strong CYP3A4 inhibitors)
- The only DLTs were Grade 3 prolonged QTc in 3/38 patients (8%); all events were clinically asymptomatic and no ventricular arrhythmias were reported
- Other common (>10%) treatment-related AEs were nausea (n = 12; 22%), vomiting (n = 9; 17%), differentiation syndrome (n = 8; 15%) and diarrhea (n = 6;11%)

CRc = composite complete response (CR); CRh = CR with partial hematologic recovery; CRp = CR with incomplete platelet recovery; CRi = CR with incomplete hematologic recovery; MLFS = morphologic leukemia-free state; MTD = maximum tolerated dose; DLT = dose-limiting toxicity; AE = adverse event

Stein EM et al. ASH 2021;Abstract 699.

Select Additional Ongoing Trials of Menin Inhibitors in AML

Trial identifier	Estimated enrollment	Description	Estimated primary completion date
KOMET-001 (NCT04067336)	60	A Phase I/IIa study of ziftomenib (KO-539) for R/R AML	June 2022
NCT04752163	122	A Phase I/II study of DS-1594b with or without azacitidine, venetoclax or mini-HCVD for R/R AML or ALL	Nov 2022
NCT04811560	110	A Phase I study of JNJ-75276617 in R/R acute leukemias harboring KMT2A or MPM1 gene mutations	Dec 2023

www.clinicaltrials.gov. Accessed May 2022.

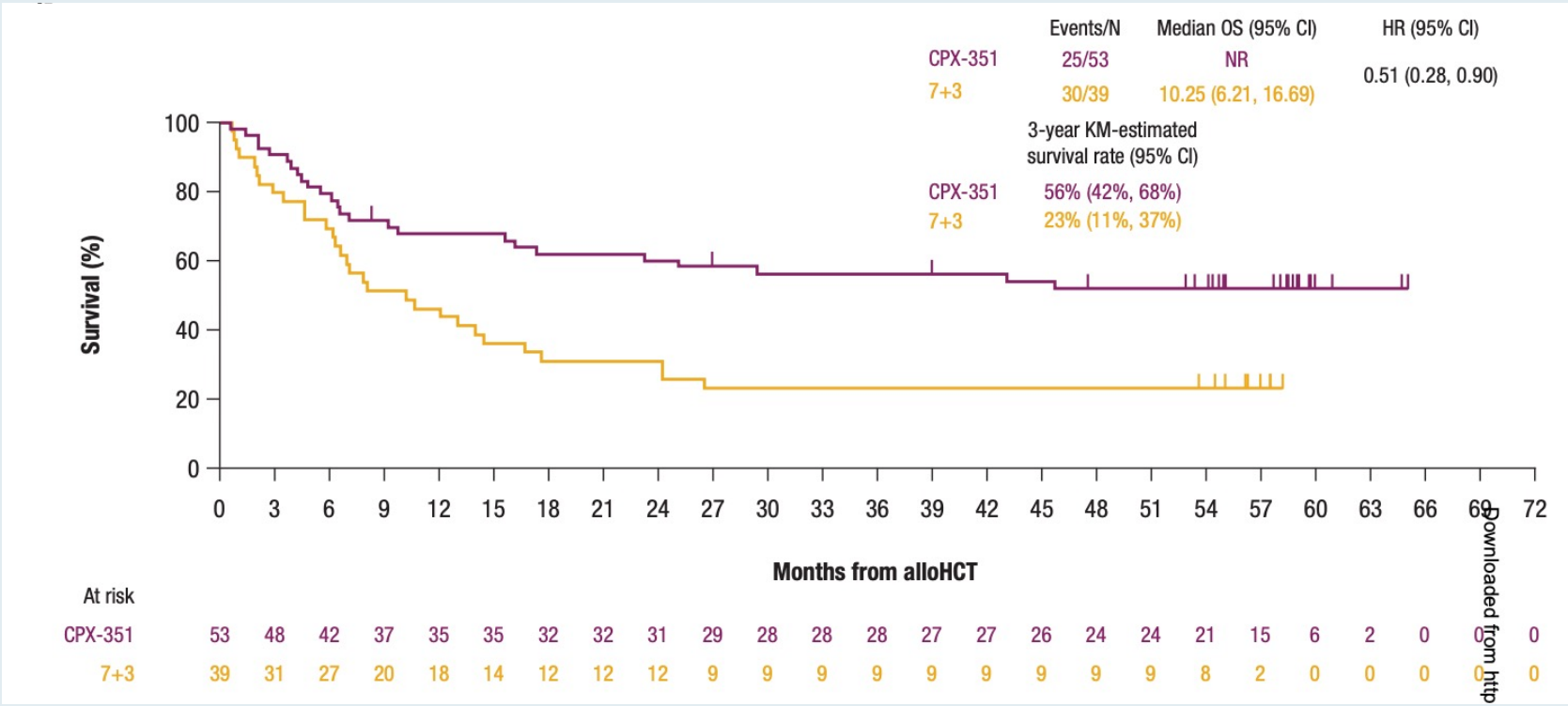
Case 1 — Michael R Savona, MD

- **68yo F**
  - **Stage IIa TNBC treated with surgery, XRT and AC+T at age 61 yo**
  - **History of HTN, HLP**
  - **Retired, non smoker, long distance runner**
  - **Sister 63 yo with chronic thrombocytopenia; grandmother with AML**
  - **ECOG PS 0 – recurrent UTIs new led to CBC which revealed neutropenia**
  - **Referred to hematology for CBC results performed by PCP:**
    - **WBC 1.9K, Hgb 11.2 g/dL, Plts 54K. ANC 400**
    - **Bone marrow demonstrates myelomonocytic/monocytic AML with morphologic dysplasia, monosomy 7 on metaphase spread and *RUNX1 Y260X* (VAF 49%), *RUNX1 A142S* (VAF 12%), *SRSF2 P95A* (VAF 42%), *WT1 A170V* (VAF 31%)**

Case 1 — Michael R Savona, MD

What are the treatment paradigms and key nuances?

- **ELN - Unfavorable risk AML**
- **Induction options**
  - **CPX-351 vs 7 + 3**

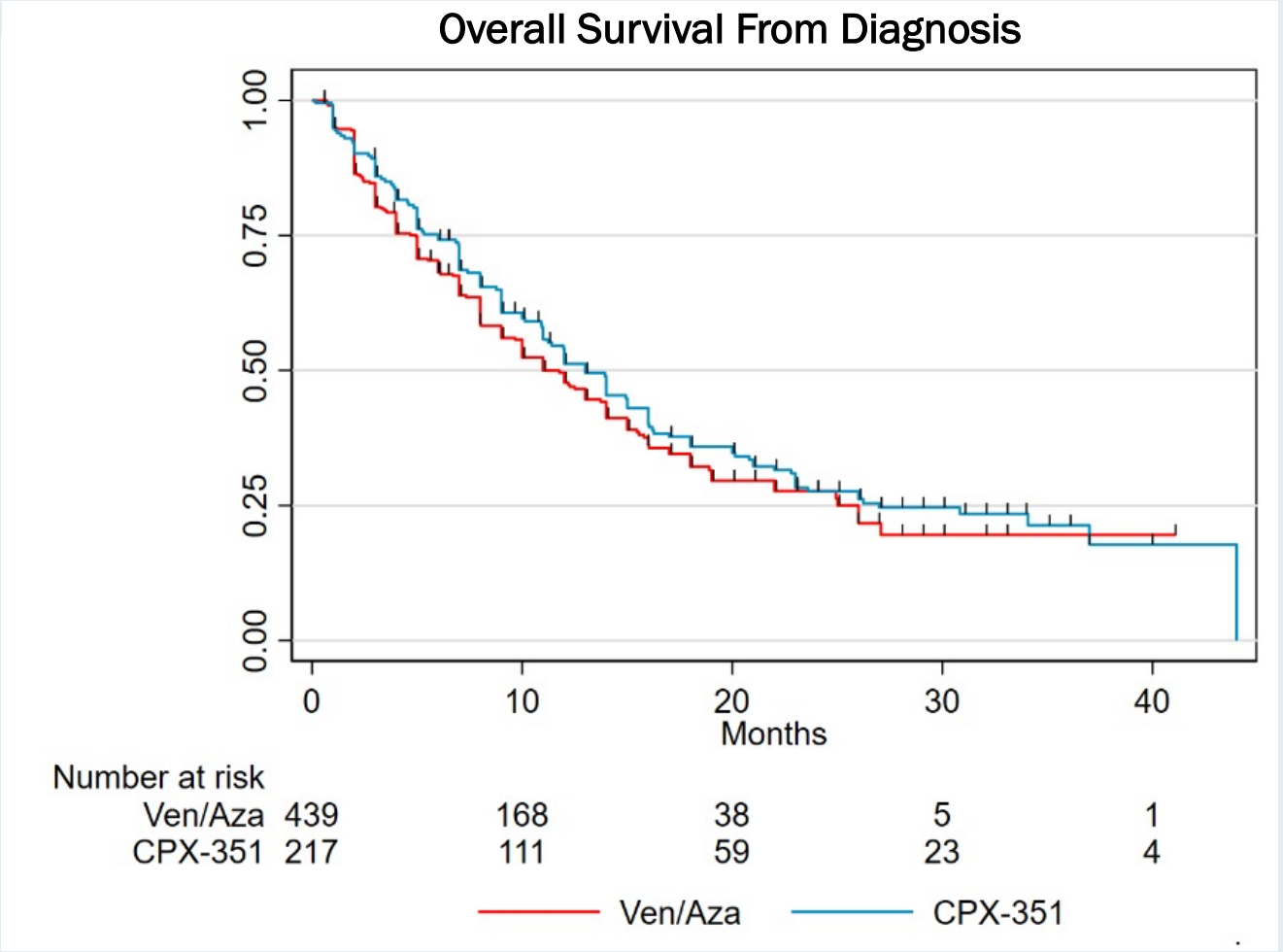


Uy et al. *Blood Adv* 2022.

Case 1 — Michael R Savona, MD

What are the treatment paradigms and key nuances?

- **ELN - Unfavorable risk AML**
- **Induction options**
  - **Ven + DNMTi**



Uy et al. *Blood Adv* 2022.

Matthews A, et al. Blood Advances. 2022.

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Case 1 — Michael R Savona, MD

What are the treatment paradigms and key nuances?

- **Transplant eligibility and donor selection**

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Case 1 — Michael R Savona, MD

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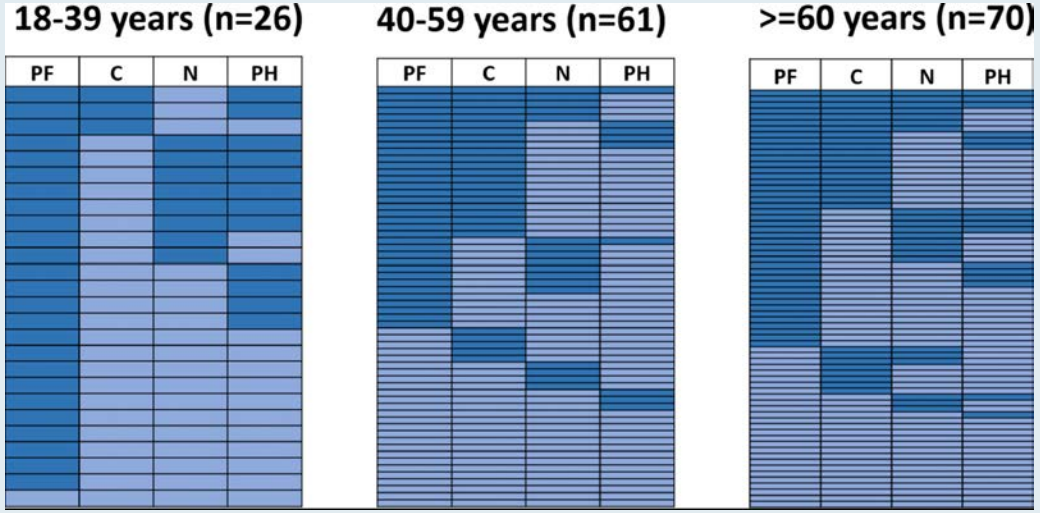

RTP RESEARCH TO PRACTICE

Case 1 — Michael R Savona, MD

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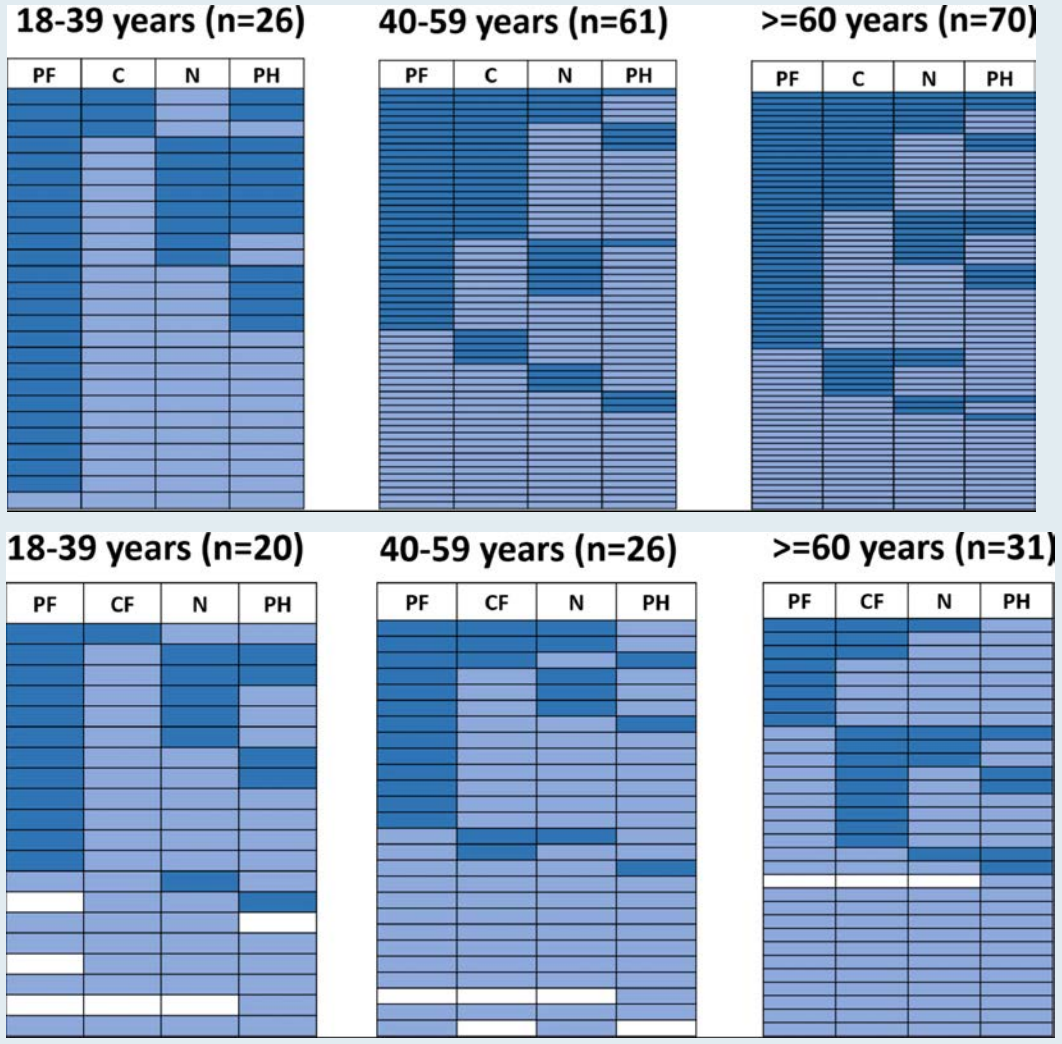

RTP RESEARCH TO PRACTICE

Case 1 — Michael R Savona, MD

What are the treatment paradigms and key nuances?

- **Transplant donor selection**

Bone marrow demonstrates myelomonocytic/monocytic AML with morphologic dysplasia, monosomy 7 on metaphase spread and RUNX1 Y260X (VAF 49%), RUNX1 A142S (VAF 12%), SRSF2 P95A (VAF 42%), WT1 A170V (VAF 31%)

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Case 1 — Michael R Savona, MD

What are the treatment paradigms and key nuances?

- **Transplant donor selection**

Bone marrow demonstrates … … RUNX1 Y260X (VAF 49%), RUNX1 A142S (VAF 12%), SRSF2 P95A (VAF 42%), WT1 A170V (VAF 31%)

Sister 63 yo with chronic thrombocytopenia; grandmother with AML

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Case 1 — Michael R Savona, MD

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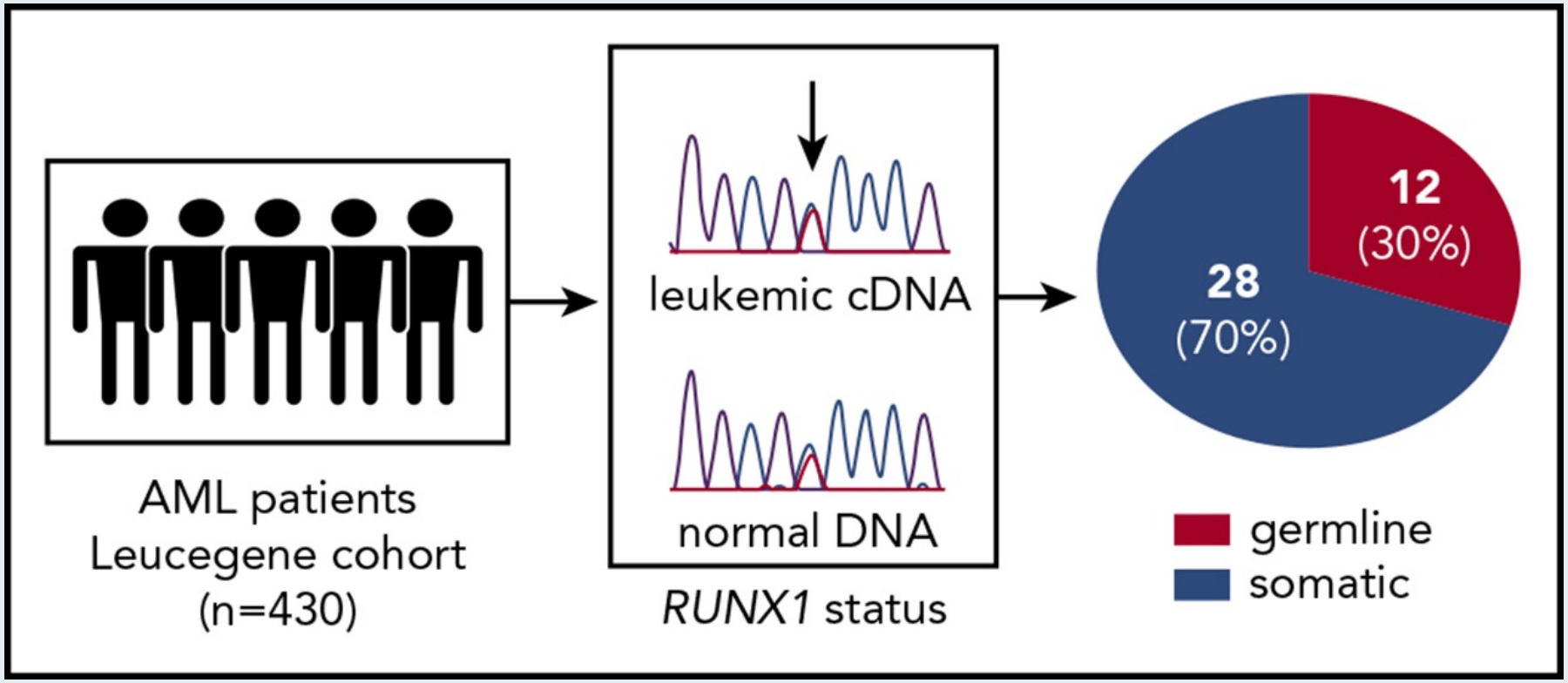

Simon et al. Blood, 2020.

Case 1 — Michael R Savona, MD

- **Patient receives CPX-351 on D1,4**
- **D14 BMBx reveals 15% cellularity and 20% blasts**
- **CPX-351 reinduction is chosen**
- **Pt develops grade 3 typhlitis on D31 (D17 reinduction) and E. coli bacteremia treated successfully with carbapenem-based antibiotic therapy**
- **BMBx on D49 (D35 of reinduction) reveals 10% cellular marrow and no increase in blasts, 46, XX, with resolution of normal blood counts**
- **Consolidation with cytarabine was continued for 2 cycles prior to allogeneic stem cell transplant with RIC from 12/12 URD match**

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

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Case 1 — Eunice S Wang, MD

- **The patient is a 60 yo African American man who presented to local ER with several days of fevers and lower abdominal pain. Mild productive cough.**
- **Exam unremarkable. Vital signs stable.**
- **Labs: WBC 35K, hgb 7.9 g/dL, plts 50K, 60% blasts, 10% monocytes**
- **BMBx: Hypercellular marrow (99%) with 62% myeloblasts**
- **Cytogenetics: Normal karyotype (XY) in all 20 cells**
- **NGS: *DNMT3A, FLT3-ITD, TET2, NPM1* mutations**
- **Received induction therapy with 7 + 3/midostaurin followed by 4 cycles of HIDAC/ midostaurin consolidation (1.5 g/m^2).**

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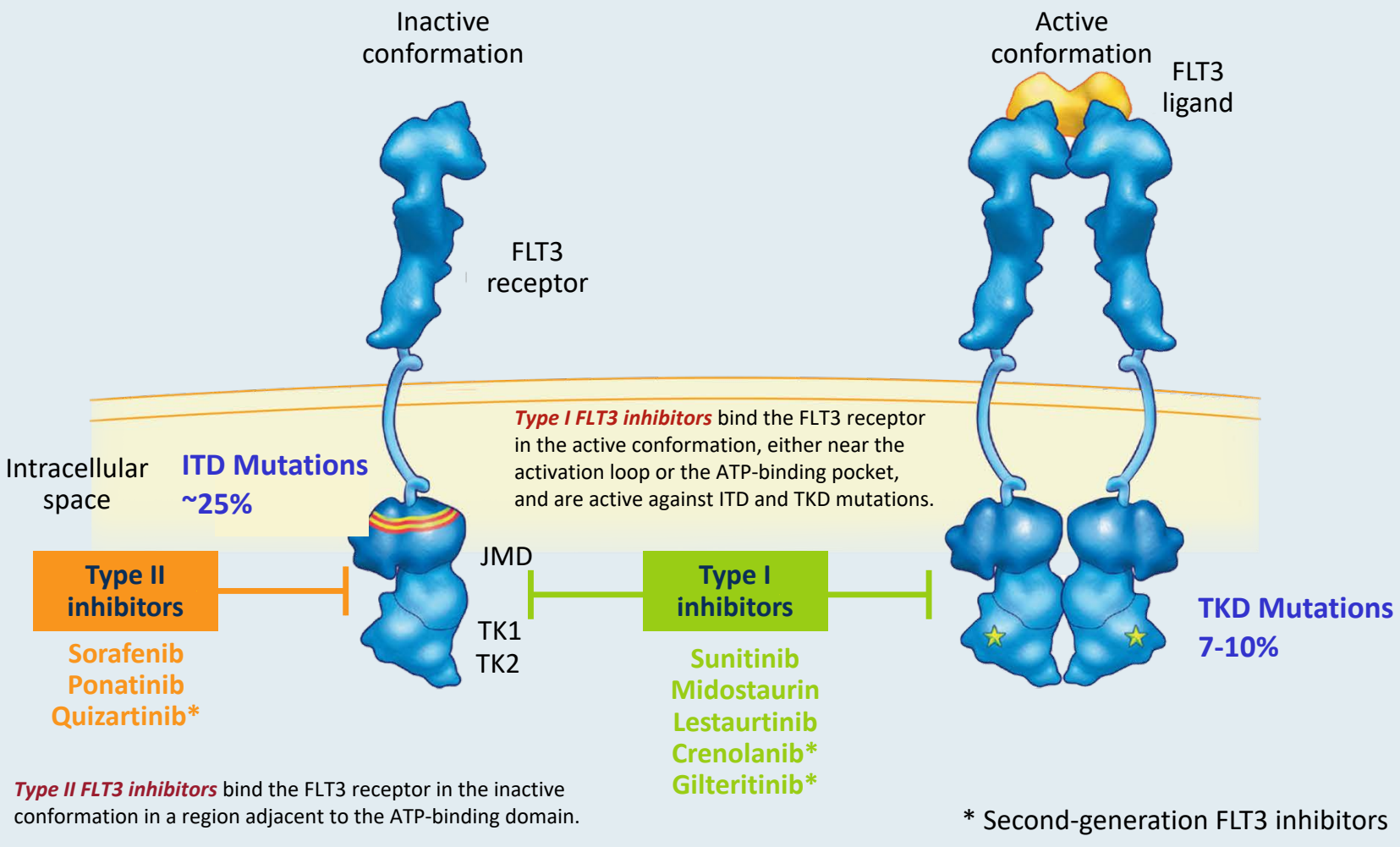
Case 1 — Eunice S Wang, MD

- **BMBX after C4 demonstrated AML in remission.**
- **Unfortunately, he was not able to receive midostaurin maintenance due to insurance coverage issues. Two months later, he presented to clinic with new pancytopenia.**
- **Repeat BMBx: Relapsed AML with 70% blasts**
- **NGS: *DNMT3A, FLT3-ITD, TET2, NPM1* mutations**
- **Started on gilteritinib 120 mg daily**
- **Repeat BMBX after 1 month demonstrated MLFS; his counts gradually recover and he achieves a MRD-negative (by flow) CR after 3 months.**

FLT3 Mutations (ITD and TKD) Occur in Approximately 30% to 35% of Patients with AML



Daver N et al. *Leukemia* 2019;33:299-312.

Characteristics of Select FLT3 Inhibitors

FLT3 inhibitor	Inhibitory type	FLT3 kinase inhibition IC50 (nmol/L)	Non-FLT3 targets	FLT3-TKD mutation activity	Major toxicities
Midostaurin 50 mg BID	I	6.3	c-KIT PDGFR PKC VEGFR	Yes	GI toxicity Myelosuppression
Gilteritinib 120 mg qd	I	0.29	AXL LTK ALK	Yes	Elevated transaminases Diarrhea
Quizartinib 30 – 60 mg qd	II	1.6	c-KIT	No	QTc prolongation Myelosuppression
Crenolanib 100 mg TID	I	1.3	PDGFR	Yes	GI toxicity

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

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

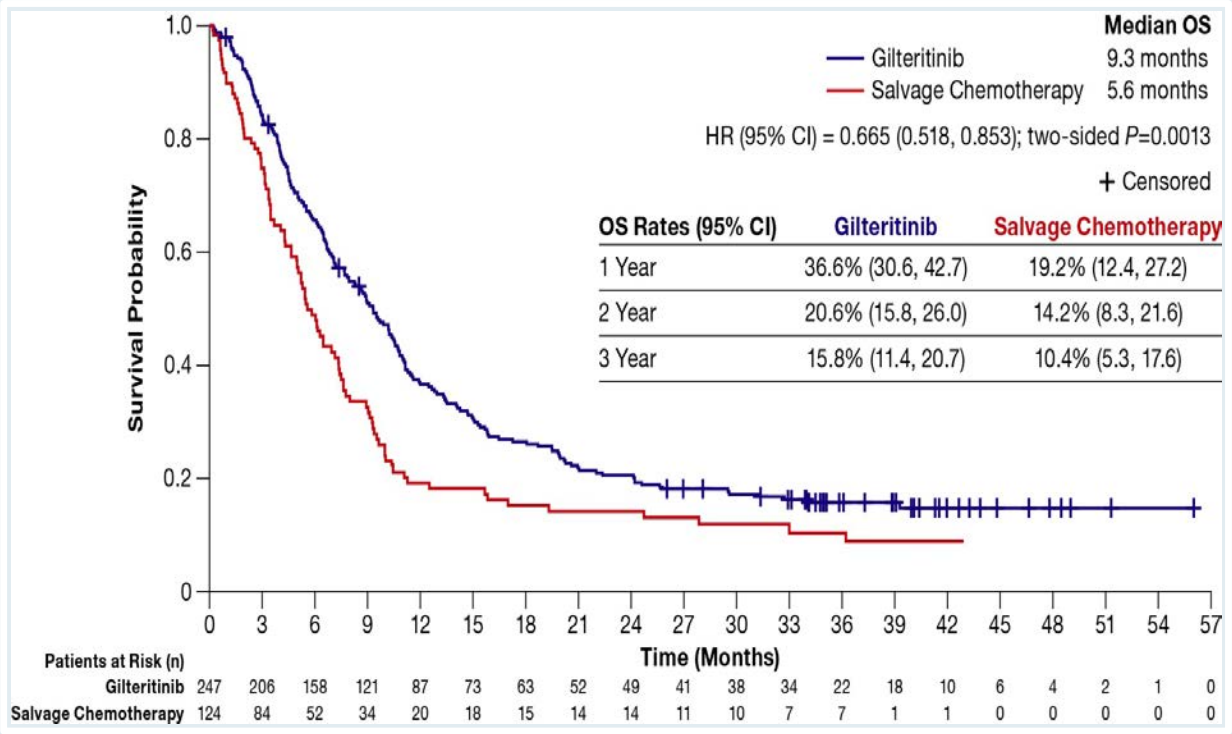
Alexander E. Perl[1]; Richard A. Larson[2]; Nikolai A. Podoltsev[3]; Stephen Strickland[4] ; Eunice S. Wang[5] ; Ehab Atallah[6]; Gary J. Schiller[7]; Giovanni Martinelli[8]; Andreas Neubauer[9]; Jorge Sierra[10]; Pau Montesinos[11]; Christian Recher[12]; Sung-Soo Yoon[13]; Naoko Hosono[14]; Masahiro 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

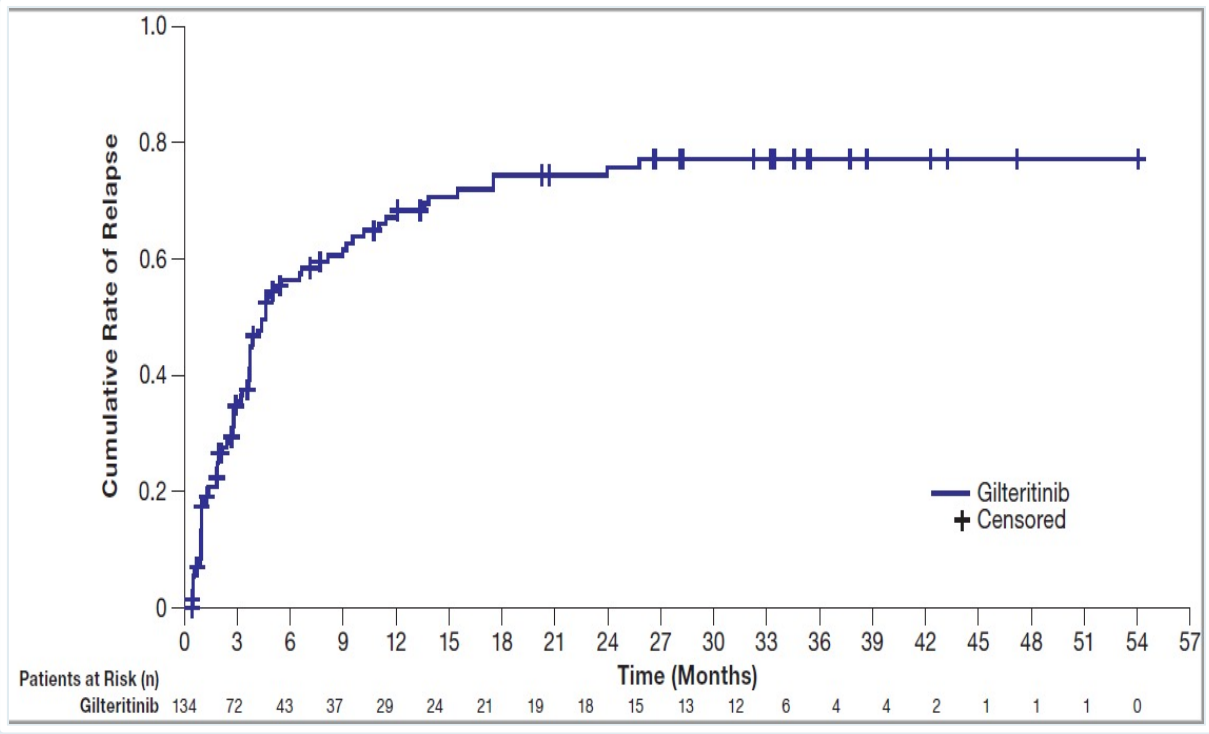
Blood 2022;[Online ahead of print].

ADMIRAL: Updated Overall Survival and Cumulative Relapse Rate

Overall Survival for Patients with RR AML with FLT3 mutations (ITT Population; N = 371)



Cumulative Incidence of Relapse in Patients Experiencing CRc with Gilteritinib

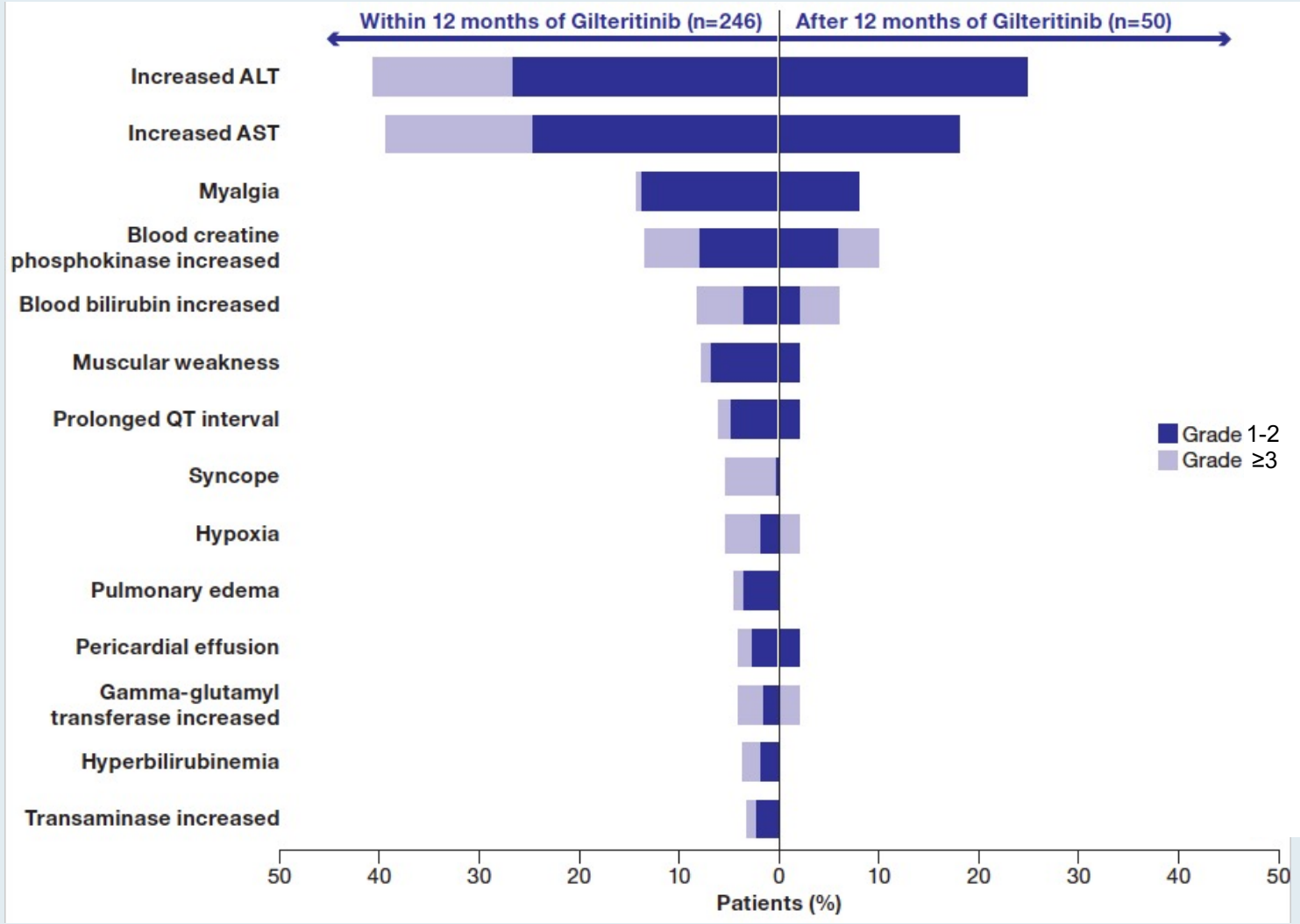


- With a median follow-up of 37.1 months, the median OS remained longer with gilteritinib than with salvage chemotherapy
- Most relapses after CRc occurred within 12 months and rarely occurred after 18 months

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

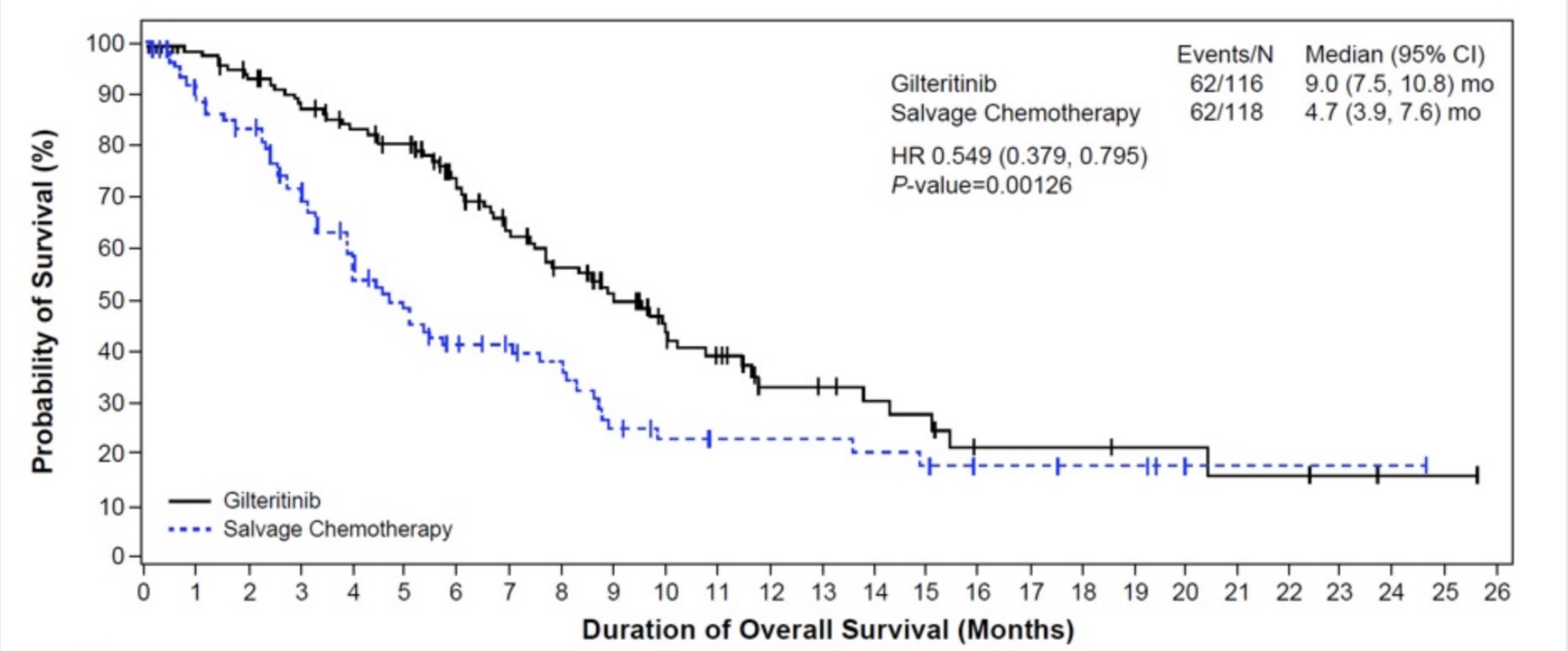
RTP RESEARCH TO PRACTICE

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



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

COMMODORE: Overall Survival with Gilteritinib in Asian Patients with R/R FLT3-Mutated AML



Wag J et al. ASH 2021;Abstract 695.

RTP RESEARCH TO PRACTICE

A Phase I Study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Patients with Newly Diagnosed AML: Final Results Update

Pratz KW et al.

EHA 2021;Abstract EP437.

Final Phase I Study Results with Gilteritinib in Combination with Induction and Consolidation Chemotherapy for Newly Diagnosed AML

Clinical endpoint	N = 38 patients who received MTD of 120 mg/d
Composite complete response	89.5%
Complete response (CR)	71.1%
CR with incomplete hematologic recovery	18.4%
Median overall survival	Not reached
Median disease-free survival	13.3 months

- In the safety analysis set of patients (n = 79), Grade ≥3 nonhematologic AEs were increased alanine aminotransferase (13.9%), pneumonia (13.9%), sepsis (11.4%) and bacteremia (11.4%).

Pratz KW et al. EHA 2021;Abstract EP437.

Impact of FLT3 Mutation Clearance After Front-Line Treatment with Gilteritinib plus Azacitidine, or Gilteritinib or Azacitidine Alone in Patients with Newly Diagnosed AML: Results from the Phase 2/3 LACEWING Trial

Wang ES et al.

ASH 2021;Abstract 3445.

Author Conclusions: *Regardless of MRD threshold, rates of MRD negativity were not substantially different between newly diagnosed FLT3^{mut+} AML patients ineligible for intensive induction chemotherapy who received gilteritinib alone, gilteritinib plus AZA, or AZA alone. Advanced age coupled with a worse baseline ECOG performance score at baseline may have compromised treatment response and achievement of FLT3 mutation clearance in patients treated with gilteritinib. The mutation clearance thresholds used in this analysis showed similar median OS in patients who received gilteritinib.*

Quizartinib Added to Chemotherapy Demonstrates Superior Overall Survival in Comparison to Chemotherapy Alone for Adult Patients with Newly Diagnosed AML with FLT3 Mutations

Press Release: November 18, 2021

"Positive topline results [were announced] from the global pivotal QuANTUM-First phase 3 trial evaluating quizartinib, a highly potent and selective FLT3 inhibitor, in patients with newly diagnosed *FLT3*-ITD positive acute myeloid leukemia (AML).

QuANTUM-First met its primary endpoint, demonstrating that patients who received quizartinib in combination with standard induction and consolidation chemotherapy and then continued with single agent quizartinib had a statistically significant and clinically meaningful improvement in overall survival (OS) compared to those who received standard treatment alone. The safety of quizartinib was shown to be manageable and consistent with the known safety profile."

https://www.businesswire.com/news/home/20211118006328/en/Quizartinib-Added-to-Chemotherapy-Demonstrates-Superior-Overall-Survival-Compared-to-Chemotherapy-Alone-in-Adult-Patients-with-Newly-Diagnosed-FLT3-ITD-Positive-AML

RTP RESEARCH TO PRACTICE

Quizartinib Prolonged Survival vs Placebo plus Intensive Induction and Consolidation Therapy Followed by Single-Agent Continuation in Patients Aged 18-75 Years with Newly Diagnosed FLT3-ITD+ AML

Erba H et al.

EHA 2022;Abstract S100 (Presidential Symposium).

June 11, 2022

Quizartinib with Decitabine and Venetoclax (Triplet) Is Active in Patients with FLT3-ITD Mutated Acute Myeloid Leukemia – A Phase I/II Study

Yilmaz M et al.

EHA 2022;Abstract S127 (Oral).

June 11, 2022

Case 2 — Courtney D DiNardo, MD, MSCE

- **72yo F**
  - **History of rate-controlled atrial fibrillation on anticoagulation**
  - **Obesity and severe osteoarthritis of b/l knees**
  - **Recurrent sinus infections and bronchitis**
  - **ECOG PS 2 – fatigue, dyspnea on exertion and decreased mobility**
  - **Was referred by orthopedic surgeon based on the preoperative lab work prior to knee replacement**
    - **WBC 2.3K, Hgb 7.8 g/dL, Plts 180K. ANC 200 with 18% circulating blasts.**
    - **Bone marrow demonstrates AML, with DNMT3A and IDH1 mutations and +8 cytogenetics.**

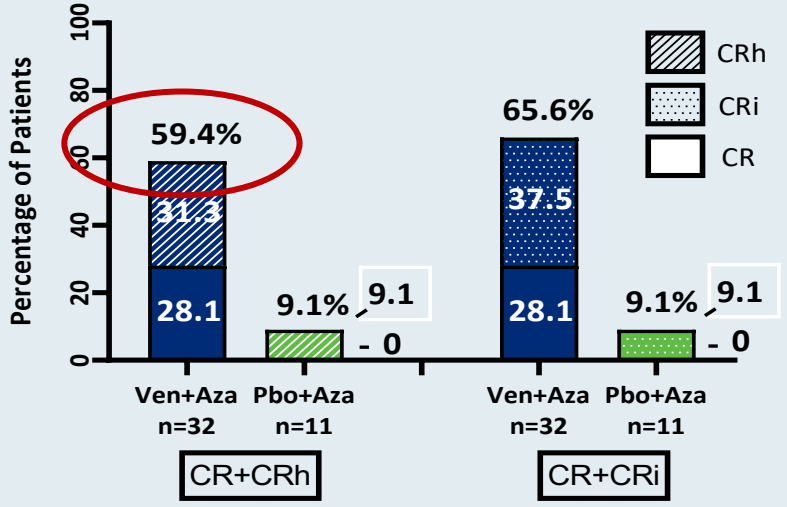
Case 2 — Courtney D DiNardo, MD, MSCE

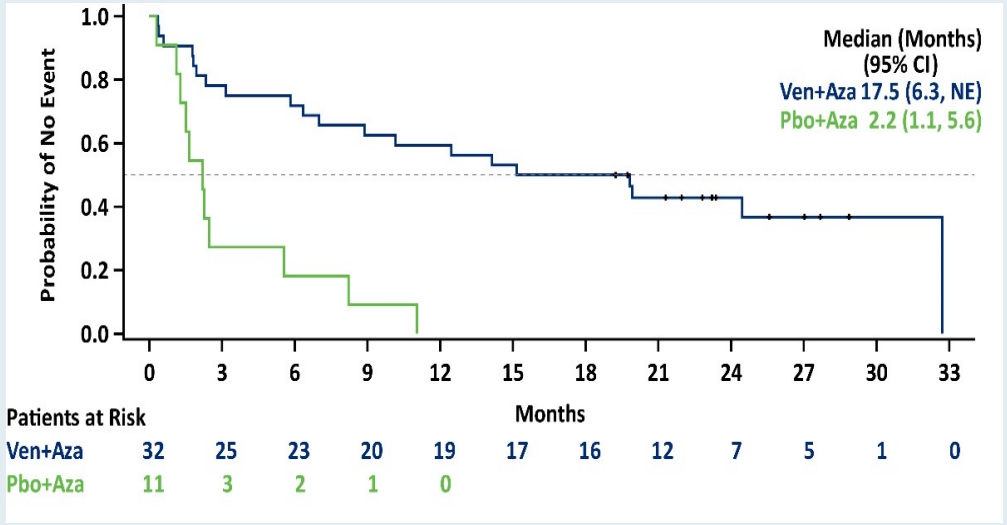
- **AZA + VEN vs AZA + IVO?**
- **Both good options – how do you choose?**
  - **How long does it take to get IDH sequencing results back?**
    - **The case I presented is not realistic for all because often treatment starts prior to NGS panel results**
  - **The AE profile is different:**
    - **Neutropenia and neutropenic infections with AZA + VEN**
    - **QTC prolongation and differentiation syndrome with AZA + IVO**
- **AZA + VEN + IVO, update to be presented at ASCO (poster discussion session on Sat)**

Case 2 — Courtney D DiNardo, MD, MSCE

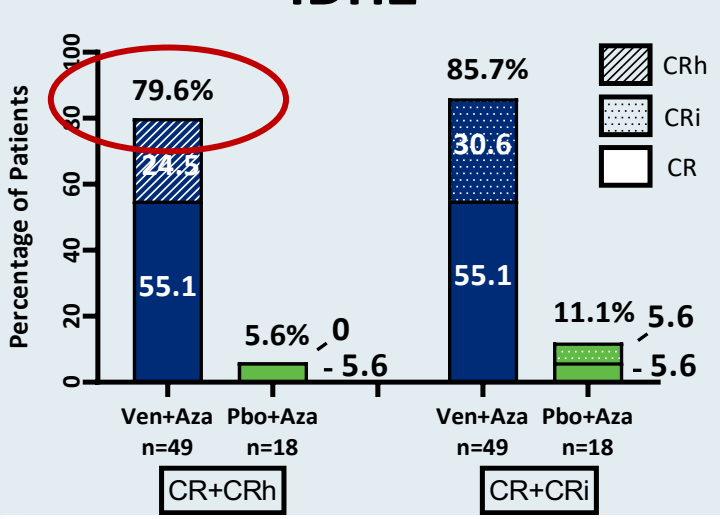
Response rates and OS with *IDH1* or *IDH2* mutations

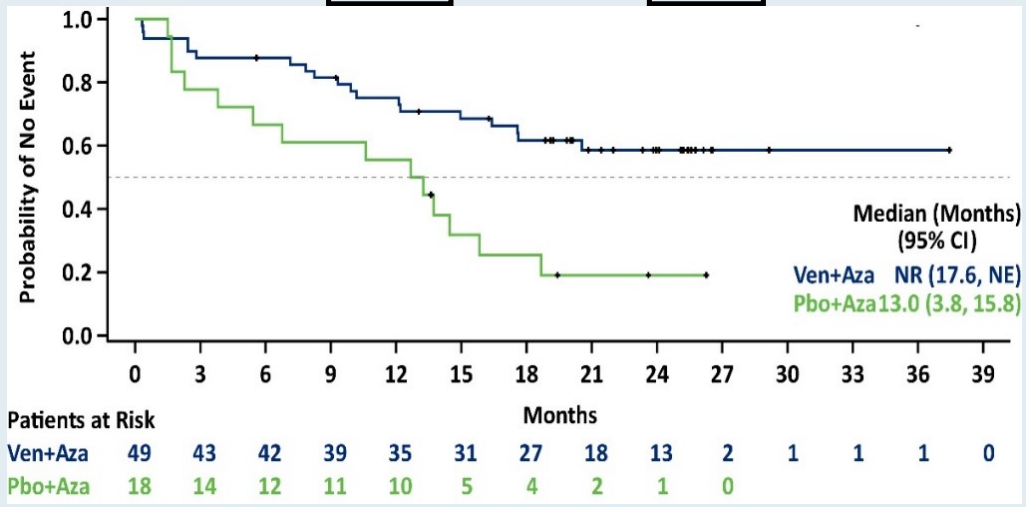
IDH1





IDH2





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Case 2 — Courtney D DiNardo, MD, MSCE

VIALE-A data: Summary of adverse events

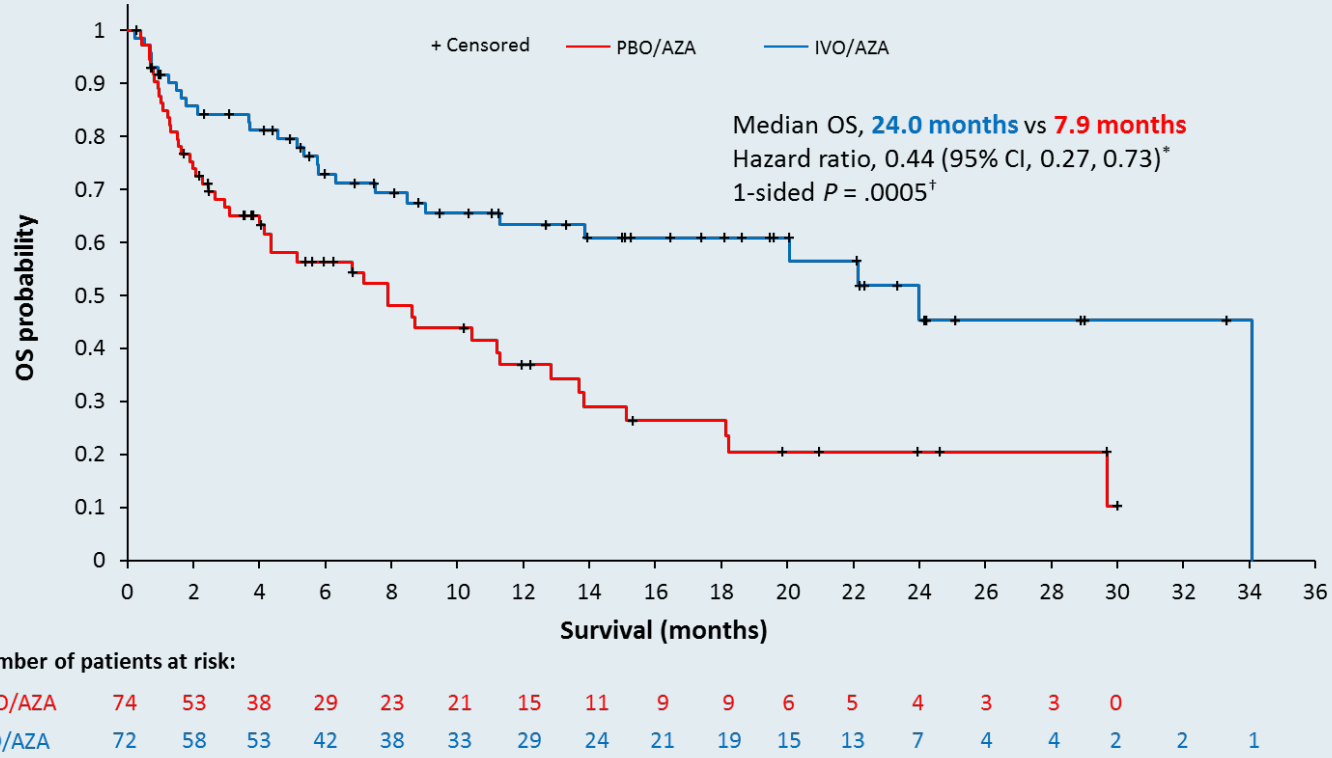
Serious AEs in ≥5% of patients, n (%)	Aza + Ven N = 283	Aza + Pbo N = 144
All serious AEs	**235 (83)**	**105 (73)**
Febrile neutropenia	84 (30)	15 (10)
Anemia	14 (5)	6 (4)
Neutropenia	13 (5)	3 (2)
Atrial fibrillation	13 (5)	2 (1)
Pneumonia	47 (17)	32 (22)
Sepsis	16 (6)	12 (8)
Any AE leading to		
Dose discontinuation	69 (24)	29 (20)
Dose interruption*	204 (72)	82 (57)
Dose reduction†	7 (3)	6 (4)
Deaths, n (%)		
≤30 days after first dose of study drug	21 (7)	9 (6)
≤60 days after first dose of study drug	43 (15)	24 (17)
Other, n (%)		
Tumor lysis syndrome	3 (1)	0

*Dose interruptions commonly due to neutropenia (19%/10%), febrile neutropenia (20%/4%), and thrombocytopenia (10%/4%); interruptions include delays between cycles and reduced duration from 28 to 21 days per cycle for count recovery after marrow leukemia clearance; †Dose reduction for AEs or other medications

Case 2 — Courtney D DiNardo, MD, MSCE

AGILE: IVO/AZA vs PBO/AZA

Response Rates		IVO/AZA (n=72)	PBO/AZA (n=74)
CR	**Rate, n (%) [95% CI]**	**34 (47.2) [35.3 to 59.3]**	**11 (14.9) [7.7 to 25.0]**
	Median DOR (95% CI), months	NE (13.0 to NE)	11.2 (3.2 to NE)
	Median time to CR (range), months	4.3 (1.7 to 9.2)	3.8 (1.9 to 8.5)
CR+ CRh	**Rate, n (%) [95% CI]**	**38 (52.8) [40.7 to 64.7]**	**13 (17.6) [9.7 to 28.2]**
	Median DOR (95% CI), months	NE (13.0 to NE)	9.2 (5.8 to NE)
ORR	**n (%) [95% CI]**	**45 (62.5) [50.3 to 73.6]**	**14 (18.9) [10.7 to 29.7]**
	Median DOR (95% CI), months	22.1 (13.0 to NE)	9.2 (6.6 to 14.1)
	Median TTFR (range), months	2.1 (1.7 to 7.5)	3.7 (1.9 to 9.4)



Additionally, clinically meaningful improvements were observed in global health status/QoL and fatigue subscales in the IVO/AZA arm vs PBO/AZA

Hazard ratio was estimated using a Cox's proportional hazards model stratified by the randomization stratification factors. †P value was calculated from the one-sided log-rank test stratified by the randomization stratification factors

Montesinos P, et al. Blood. 2021;138: Abstract 697.

RTP RESEARCH TO PRACTICE

Case 2 — Courtney D DiNardo, MD, MSCE

Treatment-emergent adverse events (TEAEs)

	IVO+AZA (n=71)		PBO+AZA (n=73)	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any TEAE, n (%)	70 (98.6)	66 (93.0)	73 (100)	69 (94.5)
Any hematologic TEAEs, n (%)	55 (77.5)	50 (70.4)	48 (65.8)	47 (64.4)
Most common hematologic TEAEs (>20%[a]), n (%)				
Anemia	22 (31.0)	18 (25.4)	21 (28.8)	19 (26.0)
Febrile neutropenia	20 (28.2)	20 (28.2)	25 (34.2)	25 (34.2)
Neutropenia	20 (28.2)	19 (26.8)	12 (16.4)	12 (16.4)
Thrombocytopenia	20 (28.2)	17 (23.9)	15 (20.5)	15 (20.5)
Most common TEAEs (>20%[a]), n (%)				
Nausea	30 (42.3)	2 (2.8)	28 (38.4)	3 (4.1)
Vomiting	29 (40.8)	0	19 (26.0)	1 (1.4)
Diarrhea	25 (35.2)	1 (1.4)	26 (35.6)	5 (6.8)
Pyrexia	24 (33.8)	1 (1.4)	29 (39.7)	2 (2.7)
Constipation	19 (26.8)	0	38 (52.1)	1 (1.4)
Pneumonia	17 (23.9)	16 (22.5)	23 (31.5)	21 (28.8)
Bleeding, n (%)	29 (40.8)	4 (5.6)	21 (28.8)	5 (6.8)
Infections, n (%)	20 (28.2)	15 (21.1)	36 (49.3)	22 (30.1)

[a]>20% cutoff used for any-grade TEAEs based on IVO+AZA
[b]QT prolongation with PBO+AZA includes electrocardiogram QT prolonged (2.7%) and syncope (1.4%)

- **TEAEs of special interest with IVO+AZA vs PBO+AZA included grade ≥2 differentiation syndrome (14.1% vs 8.2%) and grade ≥3 QT prolongation (9.9% vs 4.1%[b]).**
- **Infections were less common with IVO+AZA (28.2%) compared with PBO+AZA (49.3%).**
- **There were no deaths deemed related to treatment.**

RTP RESEARCH TO PRACTICE

A Phase Ib/II Study of Ivosidenib with Venetoclax +/- Azacitidine in IDH1-Mutated Hematologic Malignancies

Lachowiez CA et al.

ASCO 2022;Abstract 7018.

Pivotal Studies of IDH Inhibitor Monotherapy for AML with IDH Mutations

IDH inhibitor	Enasidenib	Ivosidenib	
FDA approval	Aug 1, 2017	July 20, 2018	May 2, 2019
Setting	Relapsed/refractory	Relapsed/refractory	Newly diagnosed
Trial	AG221-C-001	AG120-C-001	AG120-C-001
IDH mutation	IDH2	IDH1	IDH1
N	109	179	28
Dose	100 mg qd	500 mg qd	500 mg qd
CR + CRh	23%	30.4%	42.9%
Median duration of response	8.2 mo	8.2 mo	Not estimable
Median OS, ITT	9.3 mo	8.8 mo	12.6 mo
Median OS, complete remission	19.7 mo	Not reached	Not reported

CRh = CR with partial hematologic recovery

Stein EM et al. *Blood* 2017;130(6):722-731; Enasidenib PI, rev 11/2020; DiNardo CD et al. *N Engl J Med* 2018;378(25):2386; Roboz GJ et al. *Blood* 2020;135(7)463-71; Ivosidenib PI, rev 8/2021.

FDA Approves Ivosidenib in Combination with Azacitidine for Newly Diagnosed Acute Myeloid Leukemia

Press Release: May 25, 2022

"On May 25, 2022, the Food and Drug Administration approved ivosidenib in combination with azacitidine for newly diagnosed acute myeloid leukemia (AML) with a susceptible IDH1 mutation, as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

Approval was based on a randomized, multicenter, double-blind, placebo-controlled study (AG120-C-009, NCT03173248). Patients were randomized 1:1 to receive ivosidenib, 500 mg daily (N = 72), or matched placebo orally once daily (N = 74), on Days 1-28 in combination with azacitidine 75 mg/m^2/day on Days 1-7 or Days 1-5 and 8-9 of each 28-day cycle until disease progression, unacceptable toxicity, or hematopoietic stem cell transplantation."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ivosidenib-combination-azacitidine-newly-diagnosed-acute-myeloid-leukemia

A Phase Ib/II Study of Ivosidenib with Venetoclax +/- Azacitidine in IDH1-Mutated Hematologic Malignancies

Lachowiez CA et al.

ASCO 2022;Abstract 7018 (Poster Discussion).

Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant
June 4, 2022
2:15 PM – 3:45 PM EDT

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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

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Case 2 — Eunice S Wang, MD

- **The patient is a 75 yo man hx rheumatoid arthritis who fell and broke his hip after slipping on ice. He was admitted emergently and underwent R hip replacement; however, he was noted to have persistent anemia (requiring 7u RBCs during surgery) and was referred to hematology for further workup.**
- **Exam: Older gentleman with walker, no acute distress**
- **Labs: WBC 4.08, hgb 7.1, plts 264K, 4% monocytes, no blasts**
- **BMBx: Hypercellular marrow (80%) with dysplastic trilineage hematopoiesis and left-shifted myeloid series with 9% blasts**
- **Cytogenetics: XY, trisomy 8**
- **NGS: *IDH2, NRAS, ASXL1, SRSF2, STAG2* mutations**

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Case 2 — Eunice S Wang, MD

- **Patient consented to treatment on clinical trial:**
- ***A randomized double-blind multicenter study comparing magrolimab + azacitidine vs placebo + azacitidine in treatment-naïve pts with higher risk MDS***
- **Tolerates therapy well with no significant issues**
- **Repeat BMBX after 4 months: Hypercellular marrow (80%) with trilineage hematopoiesis and left-shifted myeloid series together with 3% blasts**
- **Now cycle 12 of placebo/magrolimab + Aza with stable counts**

Case 2 — Michael R Savona, MD

- **77yo F**
  - **History of DM, CABG 3v @ age 75, Afib**
  - **Retired, smoker**
  - **Benign family history**
  - **Followed for 5 years (age 71-76) in CHIP clinic for *SF3B1 K700E* (VAF 14%)**
  - **At regular annual follow up, found to have asymptomatic anemia, Hgb 10.0g/dL**
  - **LDH, bilirubin, DAT nl/neg; no evidence of bleeding, retic inappropriately low and BMBx reveals no dysplasia, but some atypia**
  - **Follow up in CHIP clinic is moved to q6mo for diagnosis of CCUS**

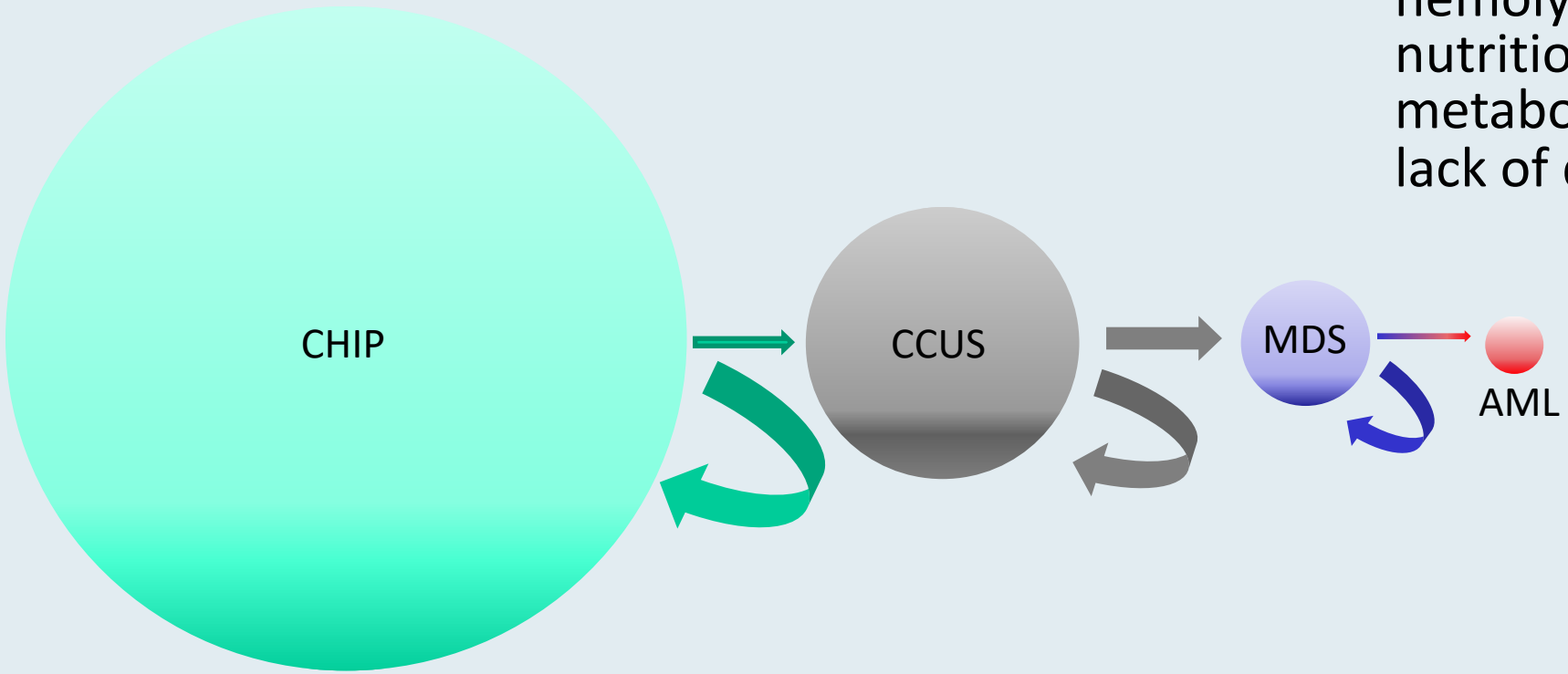
Case 2 — Michael R Savona, MD

CH+ cytopenias = CCUS

Clonal cytopenias of unknown significance = CCUS

CCUS implies:

Absence of other cause of cytopenias (eg, hemolysis, bleeding, nutritional, infectious or metabolic disorder) and lack of dyplasia on BMBx



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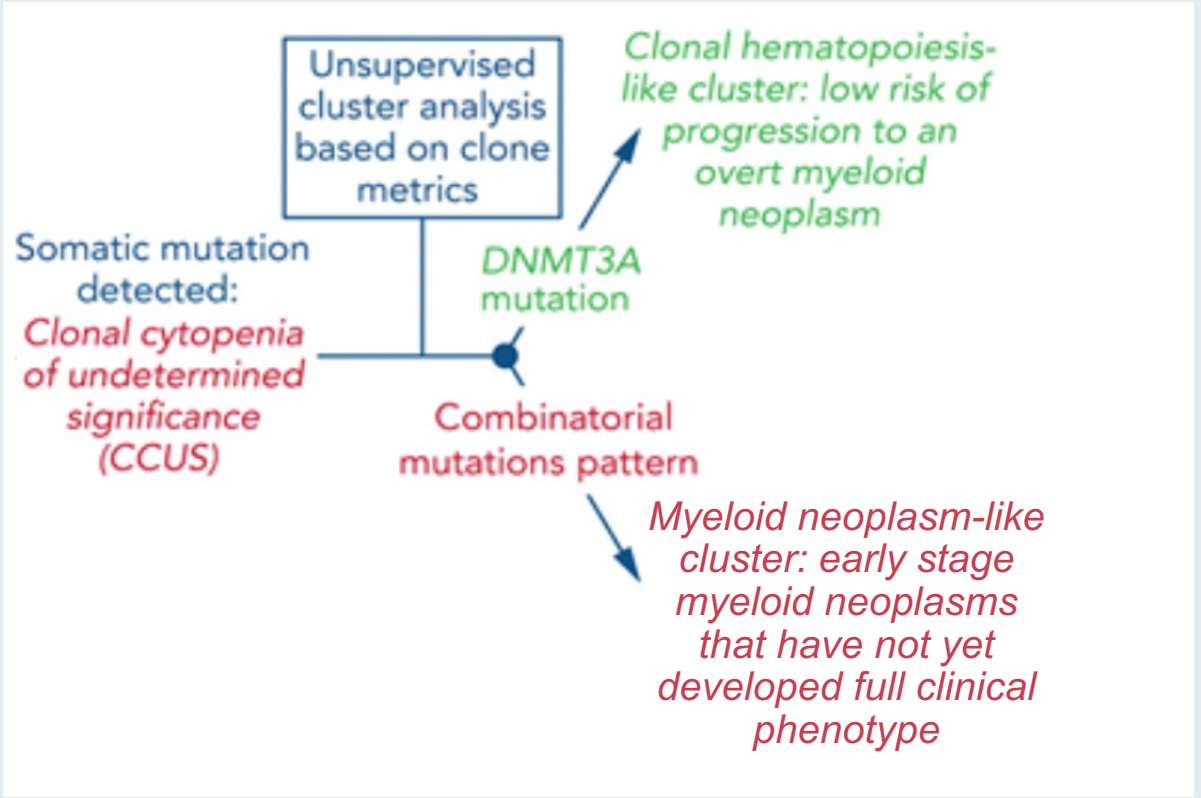
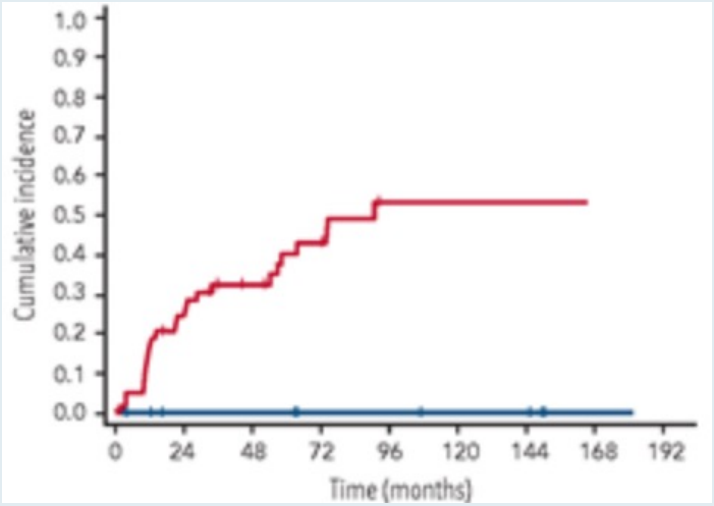
Case 2 — Michael R Savona, MD

Risk of CCUS transforming to MDS is…

1. Specific *mutation* dependent
2. *VAF* dependent
3. Combination/*signature* dependent
4. **Probably *variant* dependent**





Red – mutations in MDS-like genes (SRSF2, etc), high allele burden, compound mutations
Blue – DTA mutations, lower allele fractions, and single mutations

Galli et al, Blood, 2021.

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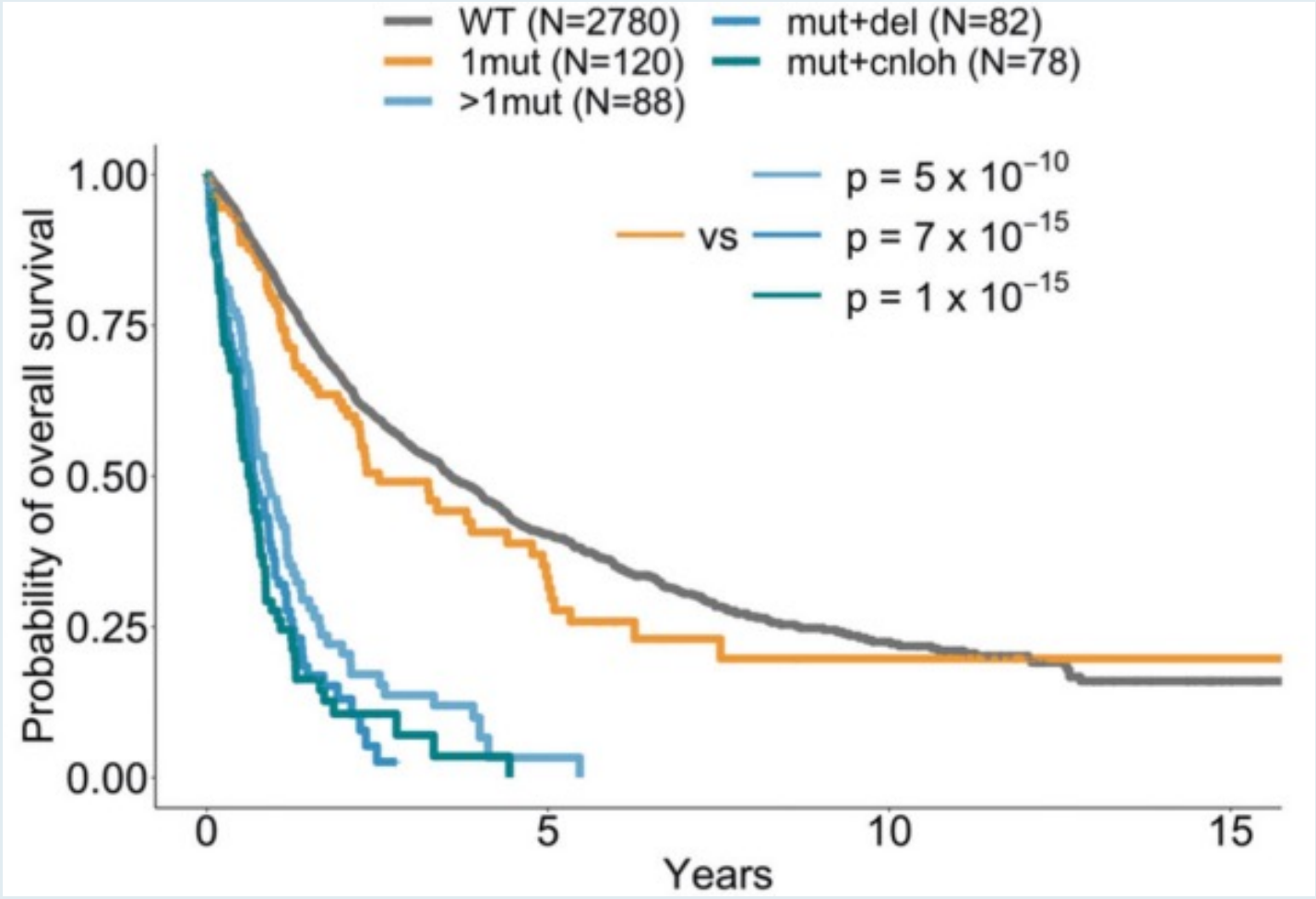
Case 2 — Michael R Savona, MD

- **77yo F**
  - **On 6mo follow up for CCUS, patient has increasing dyspnea on exertion, fatigue and new petechiae on lower extremities**
  - **Hgb 8.8g/dL, ANC 1000, plts 13k**
  - **Repeat bone marrow biopsy reveals trilineage dysplasia, increased blasts to 12%, monosomal karyotype, *SF3B1 K700E* (VAF 42%), *TP53***

Case 2 — Michael R Savona, MD

TP53 mutational status informs risk in MDS



Bernard et al, Nat Med, 2021

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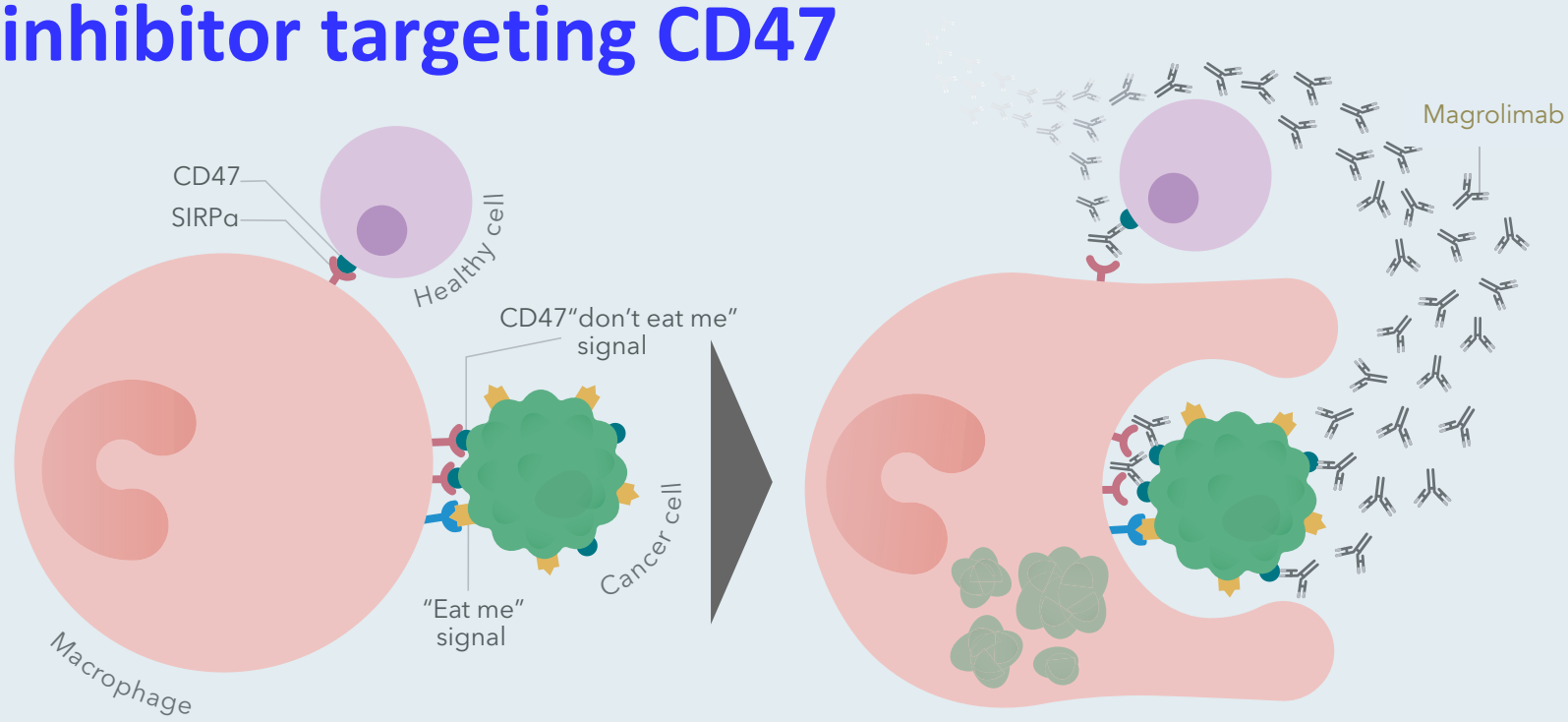
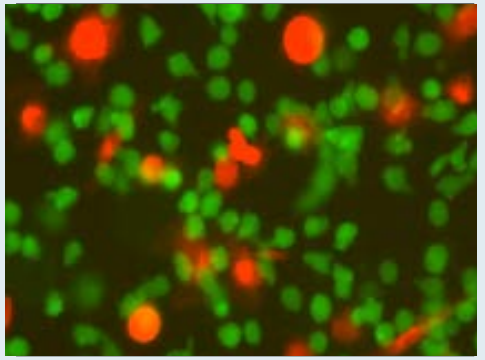
Case 2 — Michael R Savona, MD

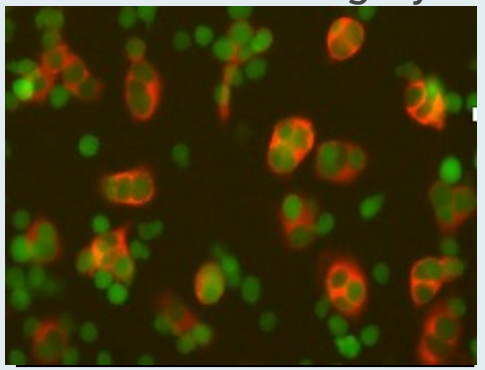
Magrolimab is a macrophage immune checkpoint inhibitor targeting CD47



Control mAb: No Phagocytosis



Anti-CD47 mAb: Phagocytosis



Macrophages Cancer cells

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

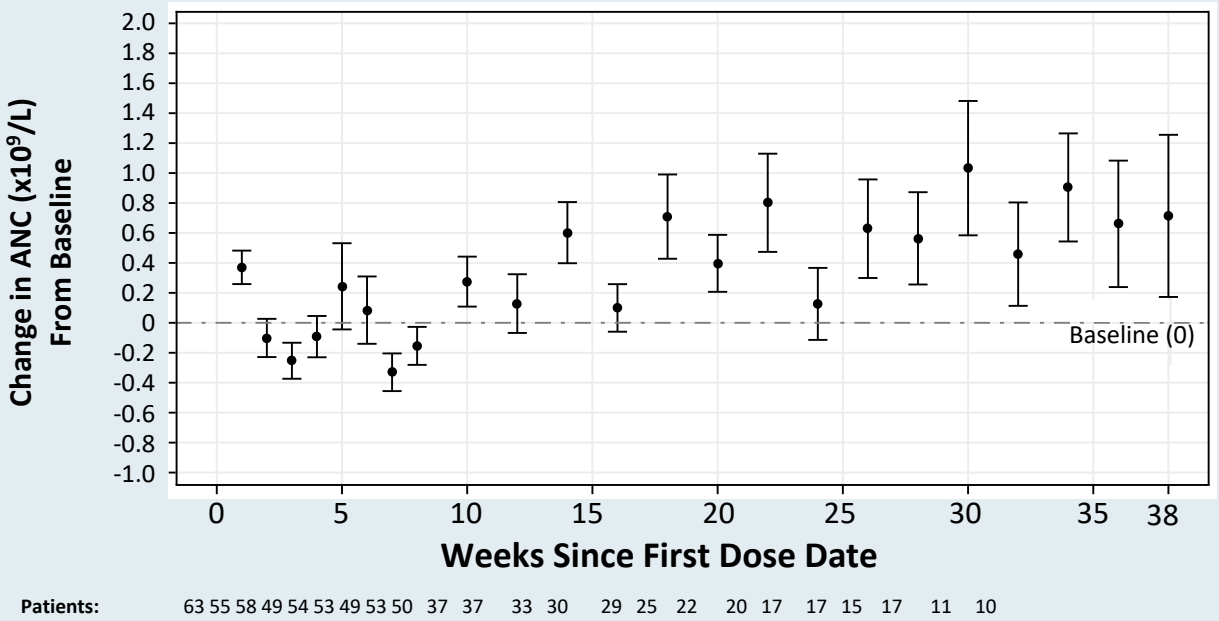
Sallman D, et al. ASCO 2020. Abstract #7507.

RTP RESEARCH TO PRACTICE

Case 2 — Michael R Savona, MD

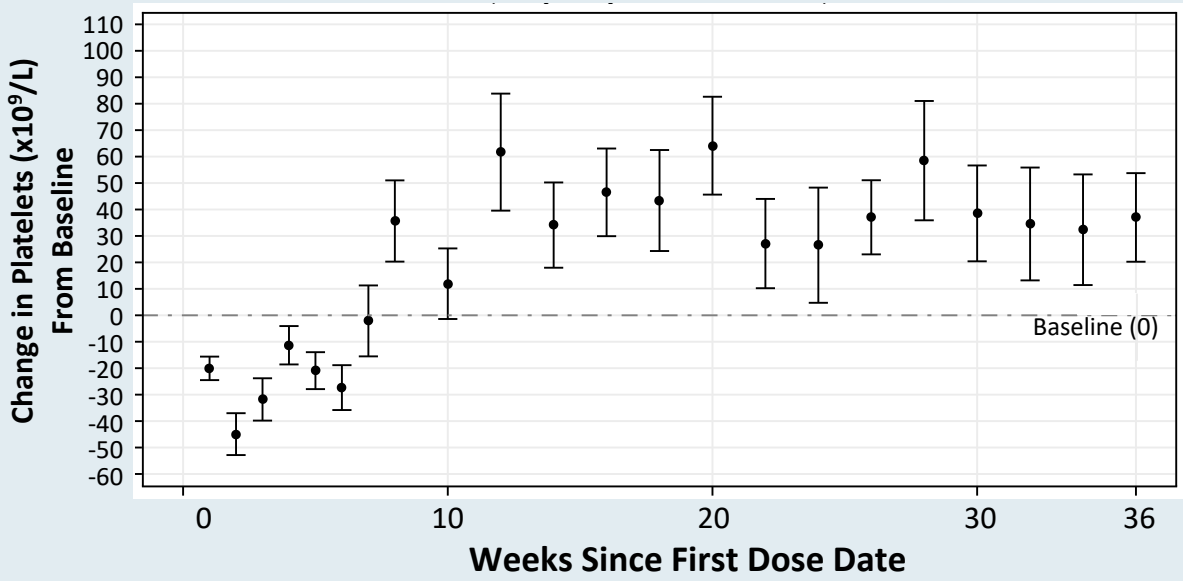
Magrolimab may lead to transient hematologic toxicities on the way to hematologic response

Neutrophil Changes on Therapy



Patients:	63	55	58	49	54	53	49	53	50	37	37	33	30	29	25	22	20	17	17	15	17	11	10

Platelet Changes on Therapy



Sallman et al, ASCO 2020 Abs 7507.

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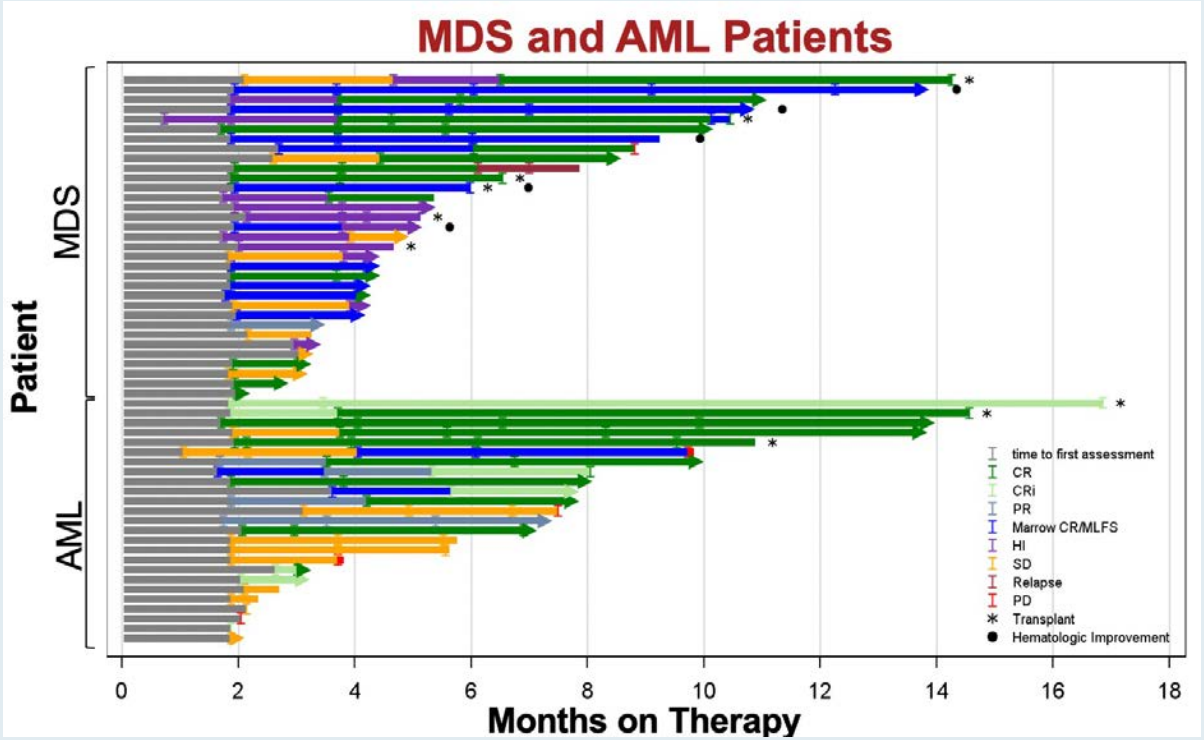
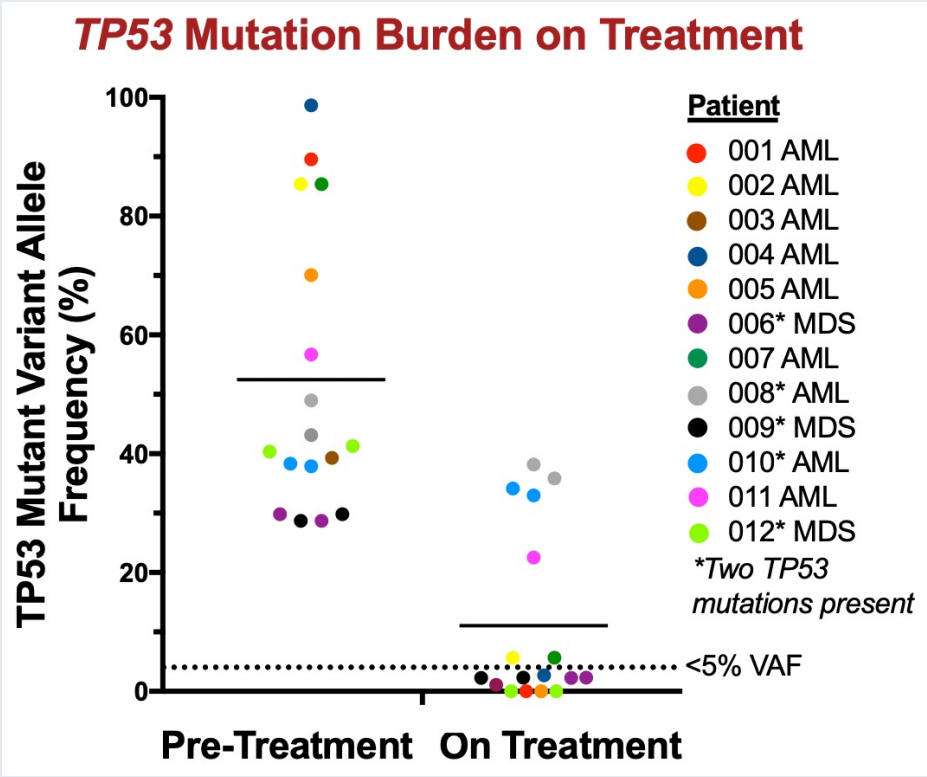
Case 2 — Michael R Savona, MD

Magrolimab leads to responses in *TP53*-mutated disease



91% ORR in MDS



75% ORR in 16 AML/MDS TP53m

Sallman et al, ASCO 2020 Abs 7507.

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N Engl J Med 2020;382:140-51.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes

P. Fenaux, U. Platzbecker, G.J. Mufti, G. Garcia-Manero, R. Buckstein, V. Santini, M. Díez-Campelo, C. Finelli, M. Cazzola, O. Ilhan, M.A. Sekeres, J.F. Falantes, B. Arrizabalaga, F. Salvi, V. Giai, P. Vyas, D. Bowen, D. Selleslag, A.E. DeZern, J.G. Jurcic, U. Germing, K.S. Götze, B. Quesnel, O. Beyne-Rauzy, T. Cluzeau, M.-T. Voso, D. Mazure, E. Vellenga, P.L. Greenberg, E. Hellström-Lindberg, A.M. Zeidan, L. Adès, A. Verma, M.R. Savona, A. Laadem, A. Benzohra, J. Zhang, A. Rampersad, D.R. Dunshee, P.G. Linde, M.L. Sherman, R.S. Komrokji, and A.F. List

Molecular Responses Are Observed Across Mutational Spectrum in Treatment-Naïve Higher-Risk Myelodysplastic Syndrome Patients Treated With Venetoclax Plus Azacitidine

Jacqueline S. Garcia[1], Andrew H. Wei[2], Meagan A. Jacoby[3], Chun Yew Fong[4], Uma Borate[5], Maria R. Baer[6], Ilona Cunningham[7], Olatoyosi Odenike[8], Joseph G. Jurcic[9], Daniel Nowak[10], Pierre Peterlin[11], Uwe Platzbecker[12], Diana Dunshee[13], Ying Zhou[14], David Hoffman[14], Yan Sun[14], Relja Popovic[14], Barrett Ainsworth[14], Kiran Naqvi[13], Steve Kye[14], Leah Hogdal[14], Guillermo Garcia-Manero[15]

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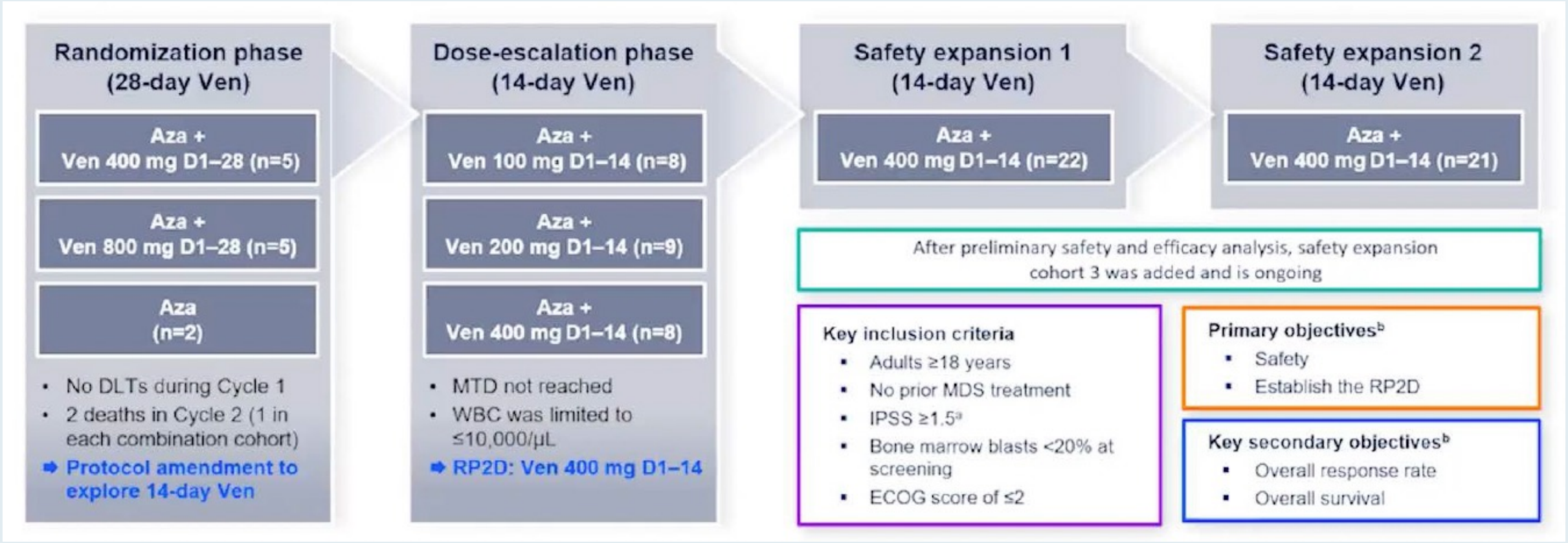
American Society of Hematology Annual Meeting, December 11–14, 2021, Atlanta, Georgia

ASH 2021;Abstract 241.

Phase Ib Study of Venetoclax with Azacitidine for Patients with Treatment-Naïve High-Risk MDS

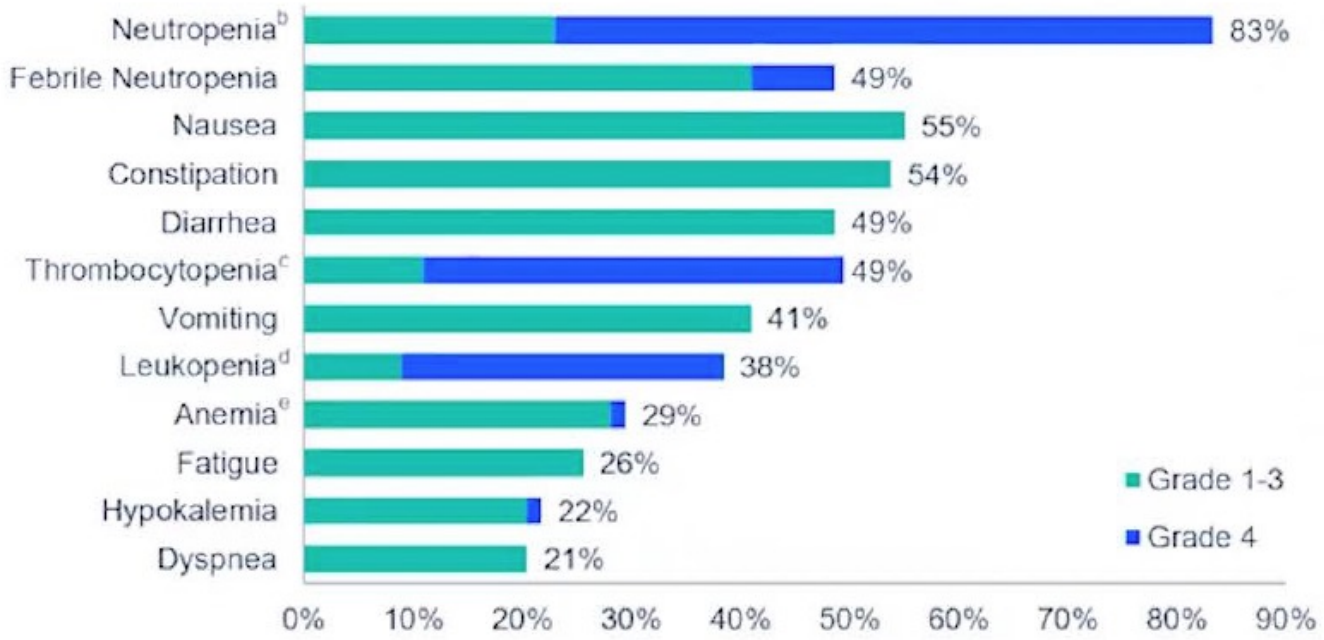


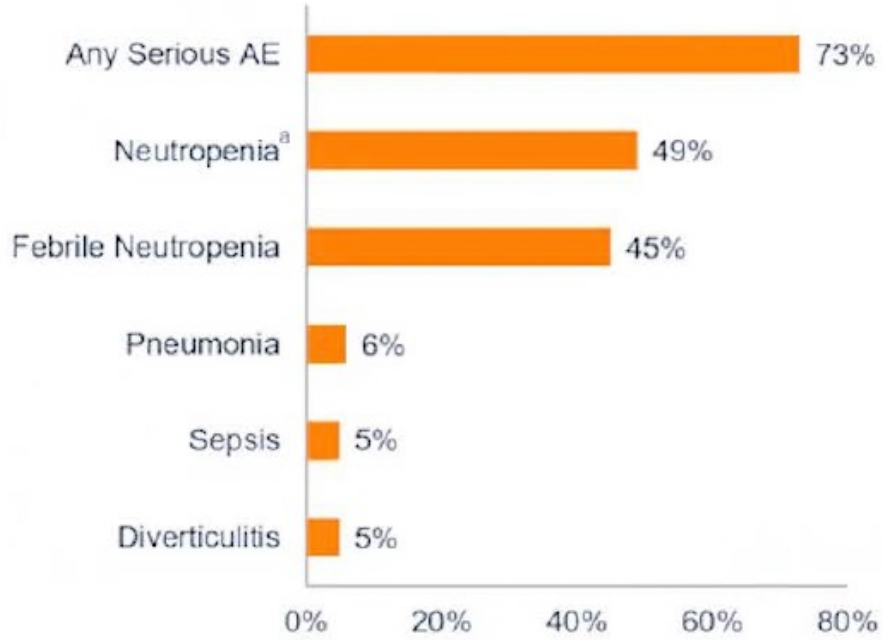
Garcia JS et al. ASH 2021;Abstract 241.

Safety of Venetoclax with Azacitidine

- Median **cycles of Aza received**: 4 (range 1-27); median **cycles of Ven received**: 4 (range 1-27)
- 30-day mortality after first dose was 1%; 7 patients (9%) experienced an AE leading to death[a]

Summary of Adverse Events in All Patients (N=78)[1]





Garcia JS et al. ASH 2021;Abstract 241.

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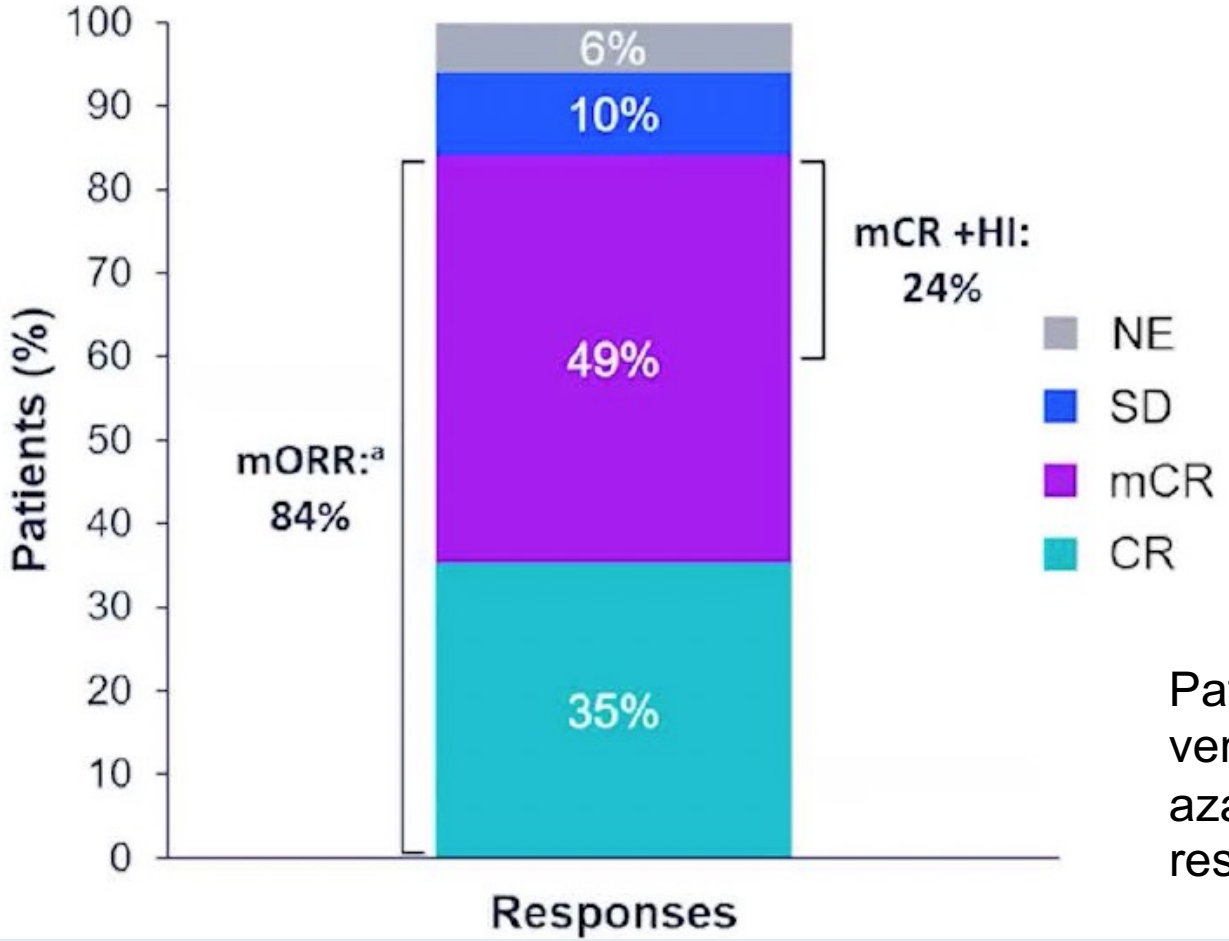
Response to Venetoclax with Azacitidine

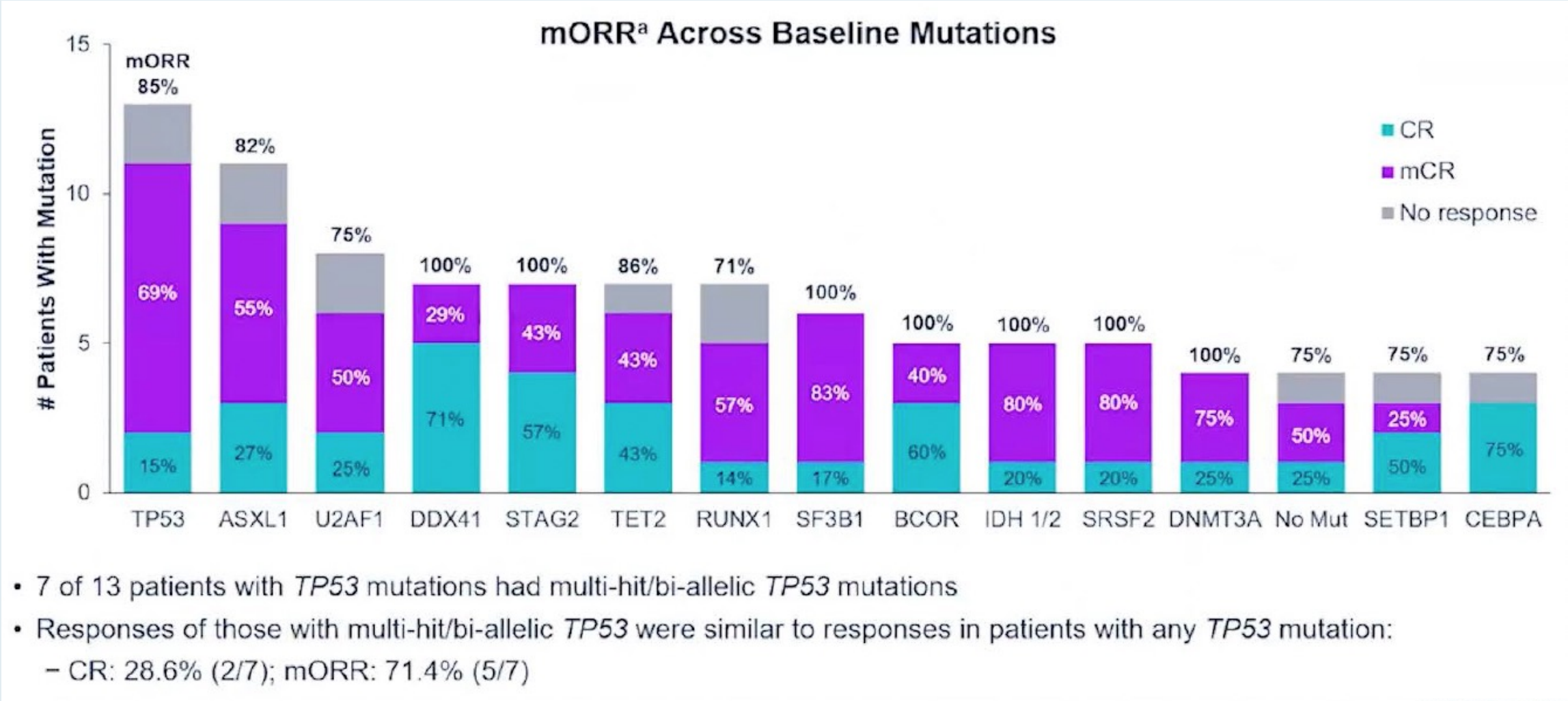


- Median time to response:
  0.9 months (95% CI, 0.7–5.8)
- Median duration of response:
  12.4 months (95% CI, 9.9–NR)

Patients with HR-MDS treated with venetoclax (400 mg D1-14) and azacitidine (75 mg/m^2) had rapid, durable responses with high remission rates

Garcia JS et al. ASH 2021;Abstract 241.

Response to Venetoclax with Azacitidine Across the Mutational Spectrum

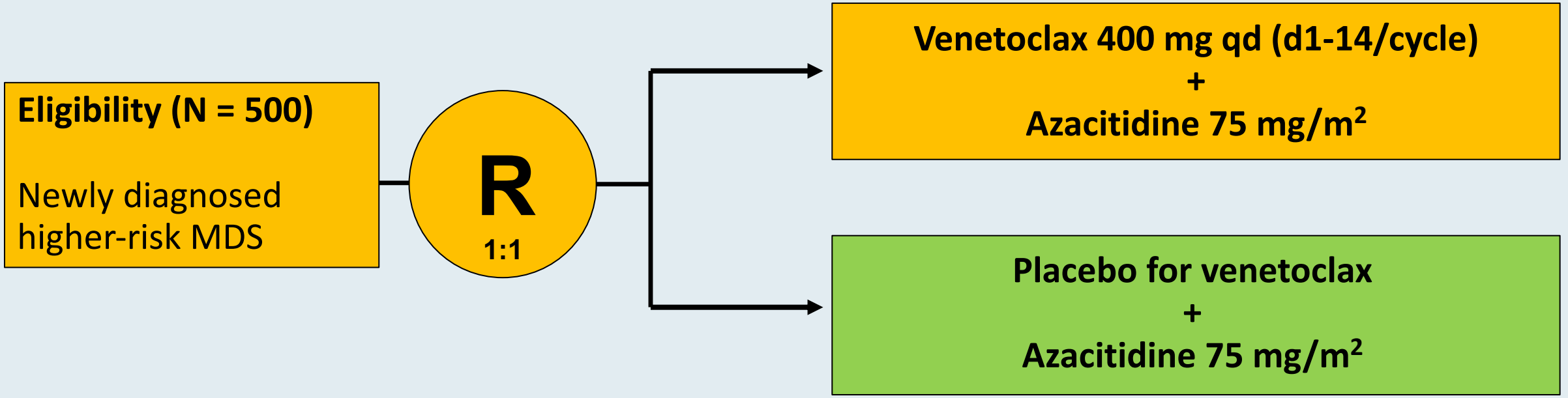


- 7 of 13 patients with *TP53* mutations had multi-hit/bi-allelic *TP53* mutations
- Responses of those with multi-hit/bi-allelic *TP53* were similar to responses in patients with any *TP53* mutation:
  - CR: 28.6% (2/7); mORR: 71.4% (5/7)

Garcia JS et al. ASH 2021;Abstract 241.

RTP RESEARCH TO PRACTICE

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

Zeidan AM et al. ASCO 2021;Abstract TPS7054.

Magrolimab in Combination with Azacitidine for Untreated Higher-Risk Myelodysplastic Syndromes (HR MDS): SF9005 Phase Ib Study Results

Sallman DA et al.

ASCO 2022;Abstract 7017 (Poster Discussion).

Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant
June 4, 2022
2:15 PM – 3:45 PM EDT

Magrolimab in Combination with Azacitidine for Patients with Untreated Higher-Risk Myelodysplastic Syndromes (HR MDS): SF9005 Phase Ib Results

Sallman DA et al.

EHA 2022;Abstract S166 (Oral).

June 12, 2022

ENHANCE Phase III Study Design

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

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

1:1 Randomization (n=520)

- Magrolimab + Azacitidine*
- Placebo + Azacitidine*

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

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

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

FDA Grants Sabatolimab Fast Track Designation for Myelodysplastic Syndromes

Press Release: May 25, 2021

"…the US Food and Drug Administration (FDA) has granted fast track designation for sabatolimab (MBG453) for the treatment of adult patients with myelodysplastic syndromes (MDS) defined with an IPSS-R risk category of high or very high risk in combination with hypomethylating agents. Fast track designation facilitates the development and expedites the review of drugs to treat serious conditions and fill unmet medical needs."

The STIMULUS clinical trial program includes multiple studies evaluating sabatolimab as part of different combination therapies in patients with MDS, including the Phase II STIMULUS-MDS1, Phase III STIMULUS-MDS2 and Phase II STIMULUS-MDS3 studies."

https://www.novartis.com/news/novartis-receives-fda-fast-track-designation-sabatolimab-mbg453-myelodysplastic-syndromes

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

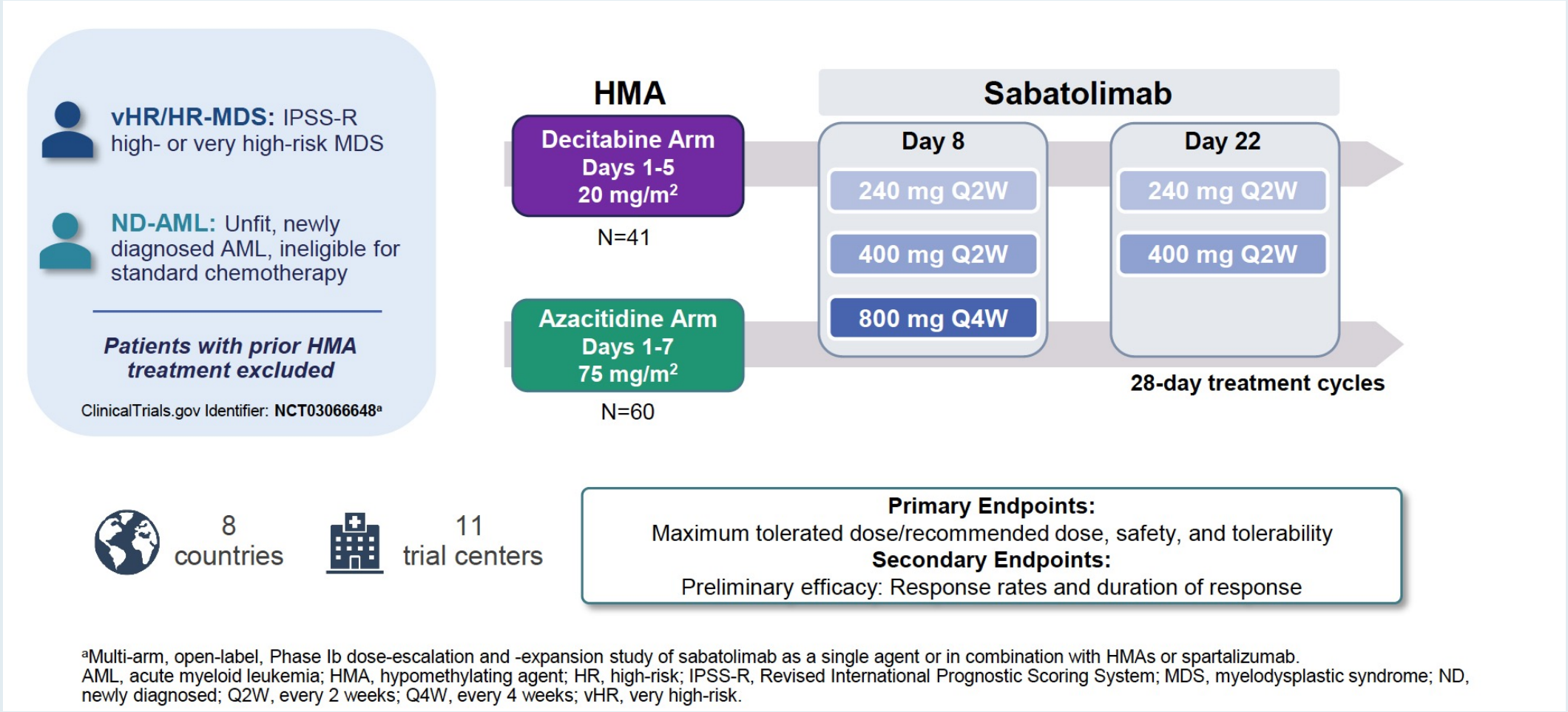
Andrew M. Brunner,[1] Jordi Esteve,[2] Kimmo Porkka,[3] Steve Knapper,[4] Elie Traer,[5] Sebastian Scholl,[6] Guillermo Garcia-Manero,[7] Norbert Vey,[8] Martin Wermke,[9] Jeroen Janssen,[10] Rupa Narayan,[1] Sun Loo,[11] Natalia Tovar,[2] Mika Kontro,[3] Oliver Ottmann,[4] Purushotham Naidu,[12] Marc 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

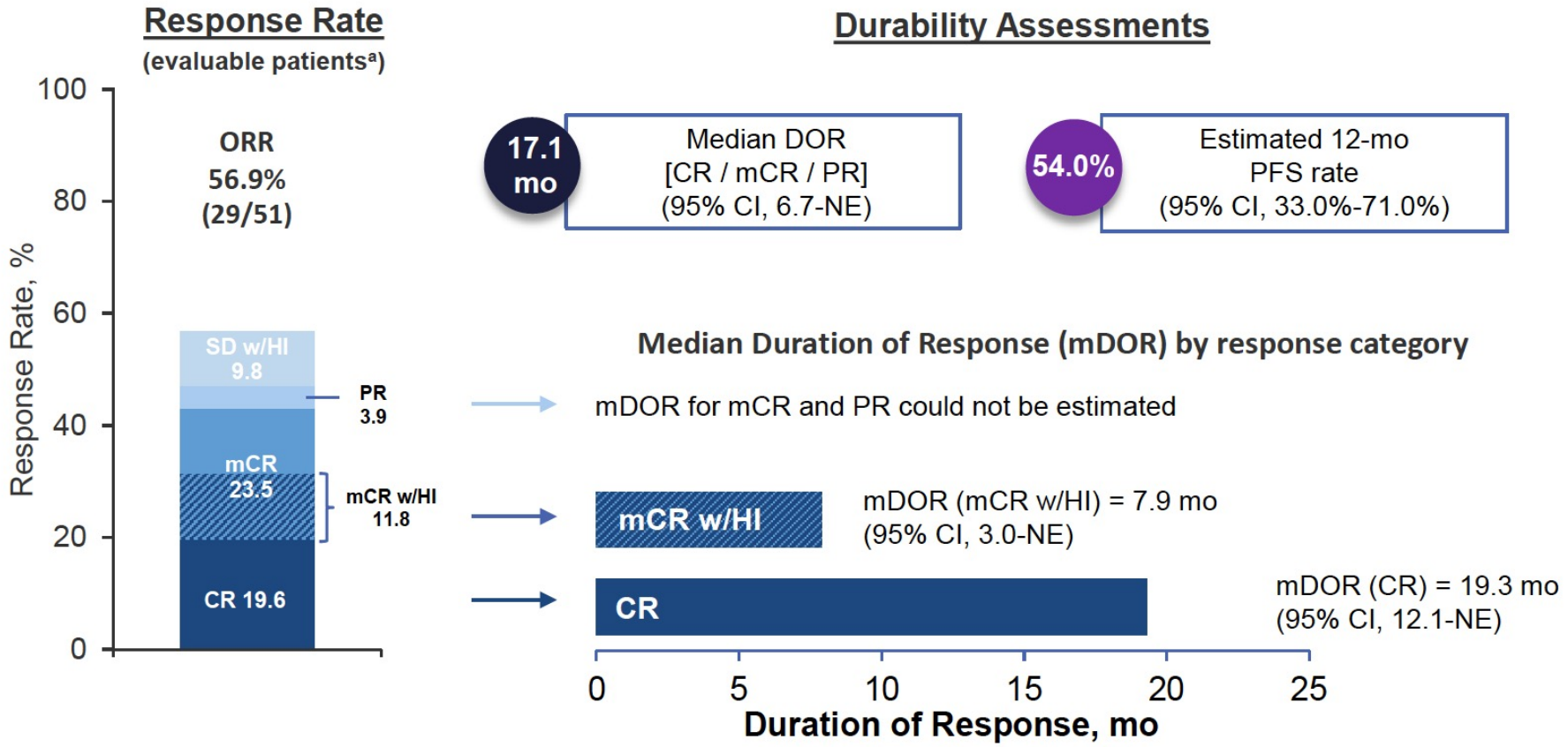


[a]Multi-arm, open-label, Phase Ib dose-escalation and -expansion study of sabatolimab as a single agent or in combination with HMAs or spartalizumab.
AML, acute myeloid leukemia; HMA, hypomethylating agent; HR, high-risk; IPSS-R, Revised International Prognostic Scoring System; MDS, myelodysplastic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

Brunner AM et al. ASH 2021;Abstract 244.

RTP RESEARCH TO PRACTICE

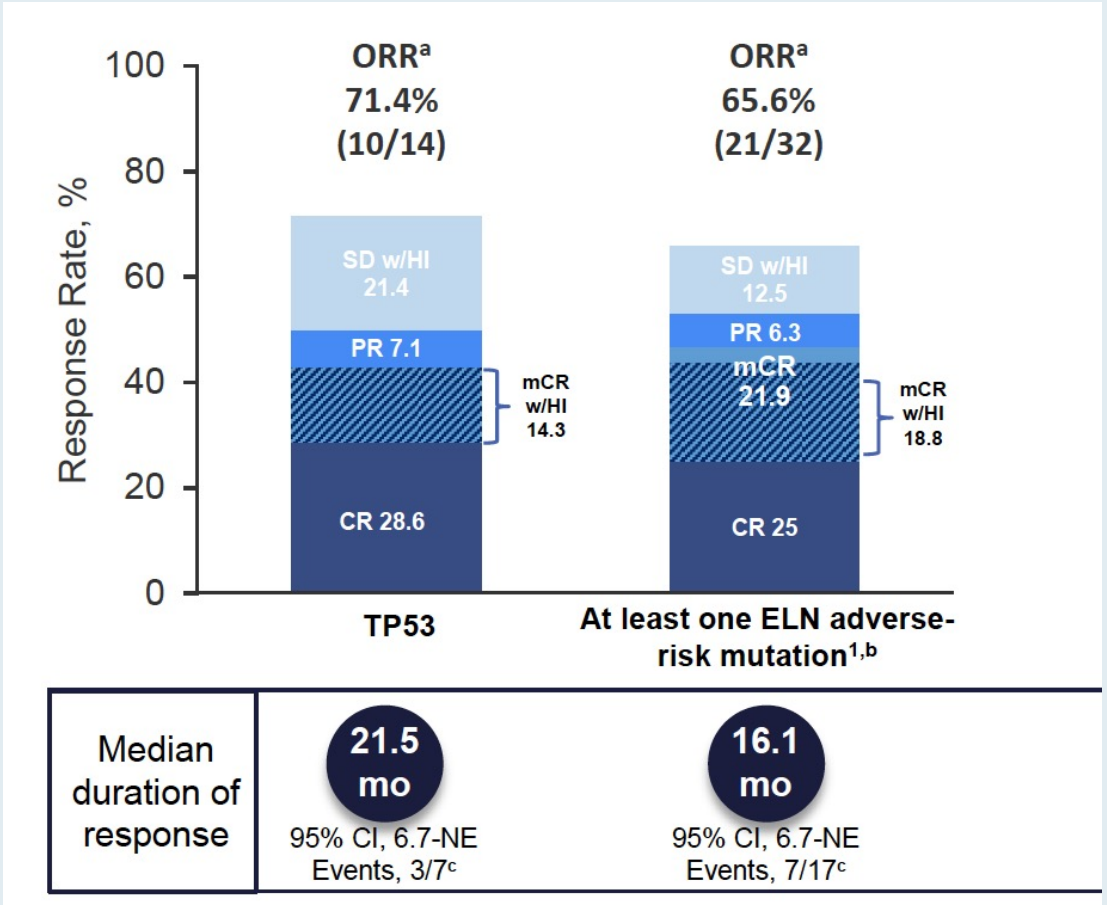
Clinical Responses Associated with Sabatolimab Combined with HMA for Very High-Risk or High-Risk MDS (vHR/HR MDS)



[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.

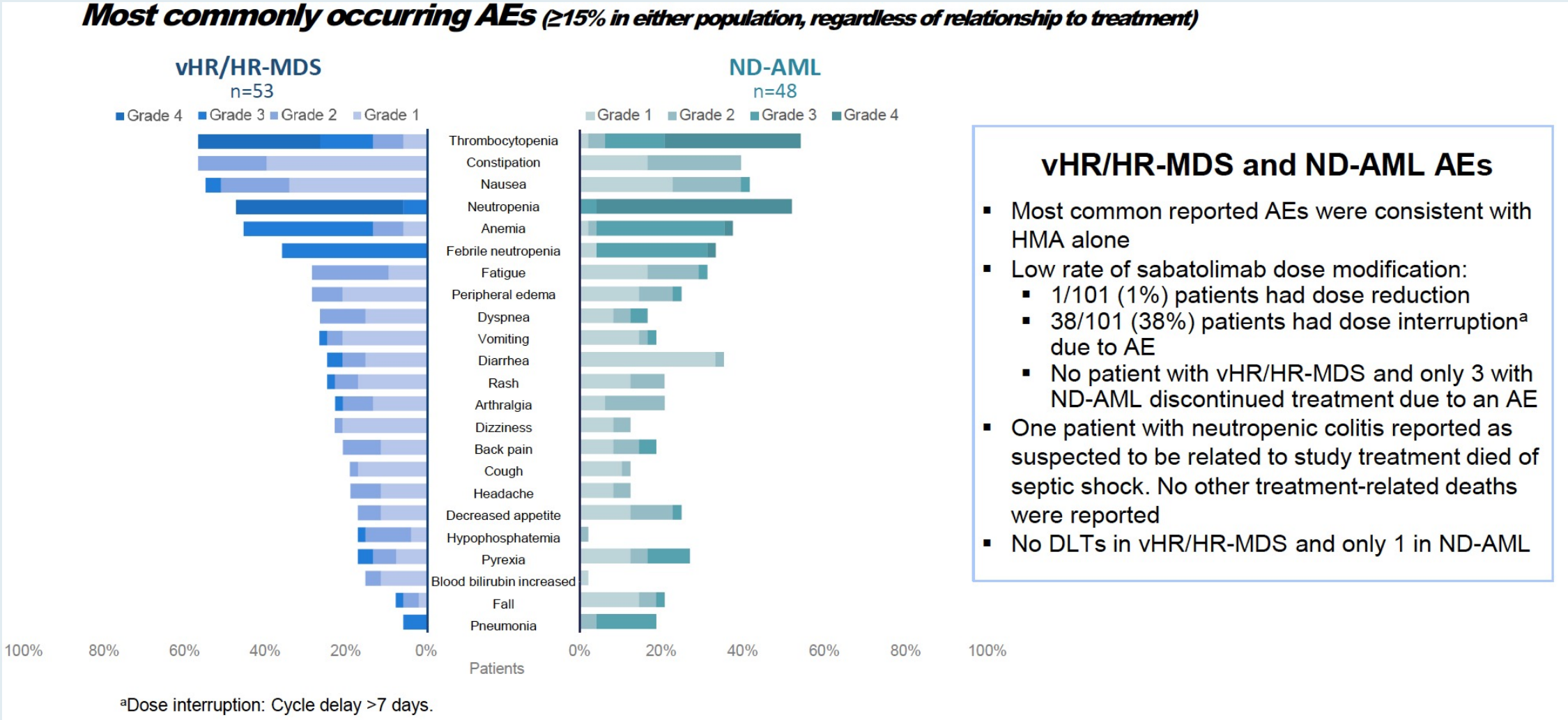
Durability of Responses Associated with Sabatolimab Combined with HMA for vHR/HR MDS



[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



[a]Dose interruption: Cycle delay >7 days.

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

Brunner AM et al. ASH 2021;Abstract 244.

STIMULUS: Clinical Trial Program for Sabatolimab in MDS

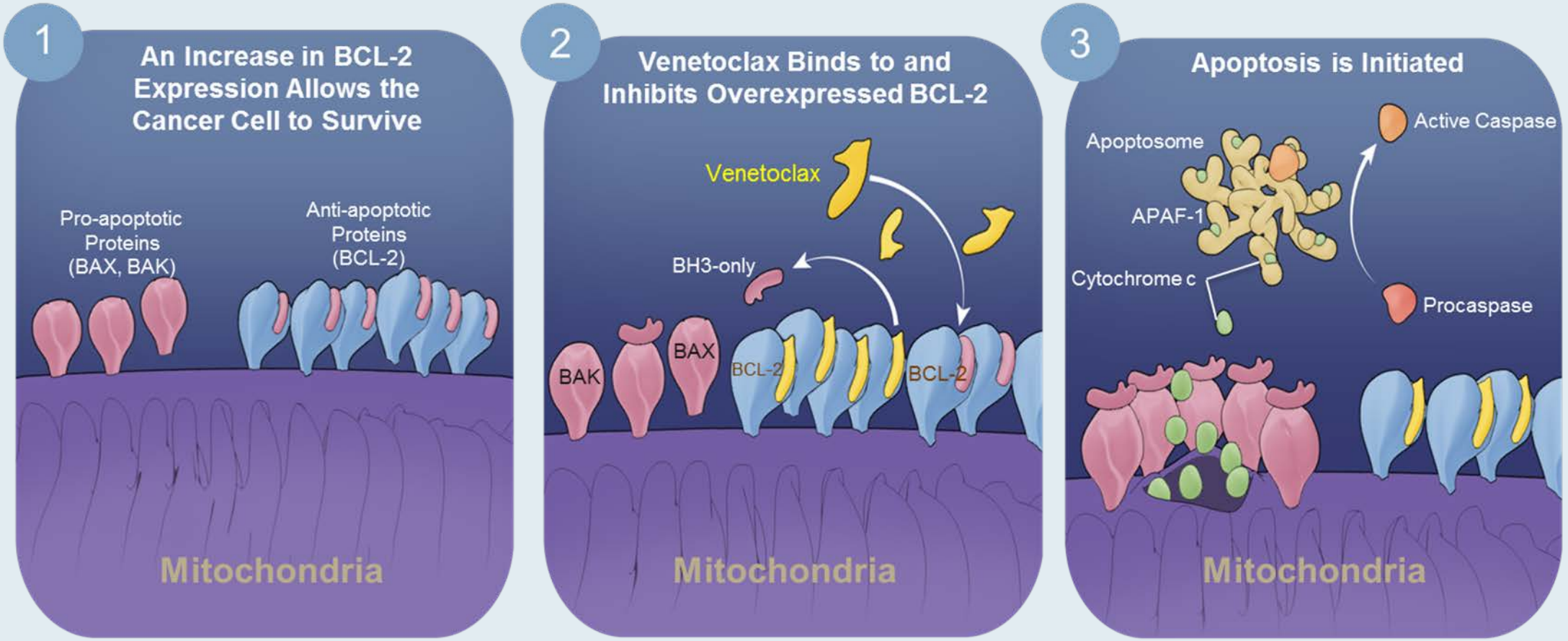
Trial identifier	Phase	Setting	Study arms
STIMULUS-MDS1 (NCT03946670)	II	IPSS-R Intermediate-, High- or Very High-risk MDS	• Sabatolimab + HMA • Placebo + HMA
STIMULUS-MDS2 (NCT04266301)	III	High- or Very High-risk MDS	• Sabatolimab + azacitidine • Placebo + azacitidine
STIMULUS-MDS3 (NCT04812548)	II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

www.clinicaltrials.gov, Accessed March 8, 2022

RTP RESEARCH TO PRACTICE

Appendix

Venetoclax Mechanism of Action



- Cancer cells increase the expression of anti-apoptotic proteins to offset the increase in pro-apoptotic proteins, tipping the balance toward cell survival
- The large # of pro-apoptotic proteins bound and sequestered by Bcl-2 in AML make them “primed” for death

Kumar et al. ASCO 2015;Abstract 8576.

V-FAST: Safety Profile

	Arm A CPX-351 + venetoclax (N = 21)	Arm B CPX-351 + midostaurin (N = 3)	Arm C CPX-351 + enasidenib (N = 2)	Overall (N = 26)
Any TEAE (all grades), n (%)[a]	21 (100)	3 (100)	2 (100)	26 (100)
Febrile neutropenia	13 (62)	2 (67)	2 (100)	17 (65)
Neutropenia	11 (52)	2 (67)	1 (50)	14 (54)
Thrombocytopenia	11 (52)	2 (67)	1 (50)	14 (54)
Nausea	9 (43)	2 (67)	2 (100)	13 (50)
Constipation	10 (48)	1 (33)	0	11 (42)
Headache	7 (33)	3 (100)	1 (50)	11 (42)
Diarrhea	6 (29)	2 (67)	2 (100)	10 (38)
Fatigue	7 (33)	0	2 (100)	9 (35)
Hypokalemia	7 (33)	1 (33)	1 (50)	9 (35)
Maculopapular rash	6 (29)	1 (33)	2 (100)	9 (35)
Leukopenia	8 (38)	0	0	8 (31)
Pyrexia	6 (29)	1 (33)	1 (50)	8 (31)
Pain in extremity	5 (24)	2 (67)	0	7 (27)
Chills	3 (14)	2 (67)	1 (50)	6 (23)
Peripheral edema	5 (24)	1 (33)	0	6 (23)
Vomiting	4 (19)	2 (67)	0	6 (23)
Any grade ≥3 TEAE, n (%)[b]	19 (90)	3 (100)	2 (100)	24 (92)
Febrile neutropenia	13 (62)	2 (67)	2 (100)	17 (65)
Neutropenia	11 (52)	2 (67)	1 (50)	14 (54)
Thrombocytopenia	11 (52)	2 (67)	1 (50)	14 (54)
Leukopenia	8 (38)	0	0	8 (31)
Anemia	3 (14)	0	0	3 (12)
Lymphopenia	3 (14)	0	0	3 (12)
Hypoxia	3 (14)	0	0	3 (12)

N – number of patients who received ≥1 dose of study drug and had sufficient data to be included in the analysis.
[a]Individual TEAEs occurring in >20% of the population.
[b]Individual grade ≥3 TEAEs occurring in >10% of the population.

- Across treatment arms, 13 serious adverse events were reported; events in >1 patient included febrile neutropenia (n = 5) and sepsis (n = 2)
- Median hematologic recovery times for Arm A
  - To platelets ≥50,000/µL: 36.0 days (range: 33, 40)
  - To neutrophils ≥500/µL: 35.5 days (range: 33, 37)
- Early mortality
  - Arm A: 5% at Day 30 and 14% at Day 60
  - Arms B and C: no early mortality has been observed

- As of this interim analysis, the drug combinations have exhibited manageable safety profiles

TEAE = treatment-emergent adverse event

Pullarkat V et al. ASCO 2021;Abstract 7026.

Liposomal Cytarabine and Daunorubicin (CPX-351) in Combination with Gemtuzumab Ozogamicin (GO) in Relapsed Refractory (R/R) Acute Myeloid Leukemia (AML) and Post-Hypomethylating Agent (Post-HMA) Failure High-Risk Myelodysplastic Syndrome (HR-MDS)

Rivera D et al.

ASH 2021;Abstract 2323.

CPX-351 in Combination with Gemtuzumab Ozogamicin: Efficacy and Safety Summary

Responses (N = 24)

ORR	13 (55)
CR/CRi	8 (34)
PR	5 (21)
NR	9 (37)
NE	2 (8)

	All grades (%)	Grade ≥ 3 (%)
Neutropenic Fever	19 (80)	19 (80)
Bacteremia	9 (37)	8 (33)
Lung Infection	9 (37)	9 (37)
Sepsis	7 (30)	7 (30)
Mucositis	5 (21)	1 (4)
GI bleed	3 (13)	2 (8)
Sinusitis	2 (8)	2 (8)

Rivera D et al. ASH 2021;Abstract 2323.

Long-term overall survival with oral azacitidine in patients with acute myeloid leukemia in first remission after intensive chemotherapy: updated results from the phase 3 QUAZAR AML-001 trial

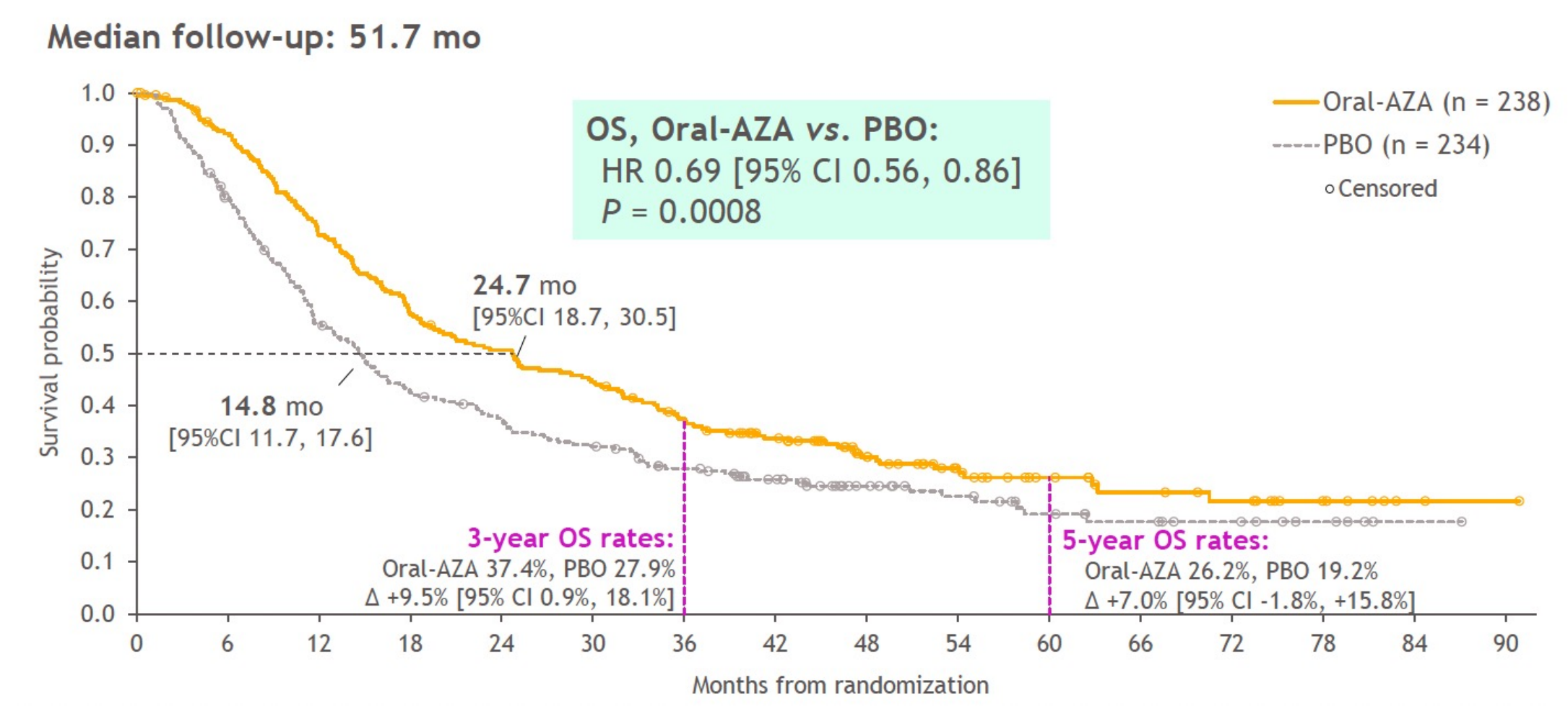
Andrew H Wei,[1,2] Hartmut Döhner,[3] Hamid Sayar,[4] Farhad Ravandi,[5] Pau Montesinos,[6] Hervé Dombret,[7,8] Dominik Selleslag,[9] Kimmo Porkka,[10,11] Jun-Ho Jang,[12] Barry Skikne,[13,14] CL Beach,[14] Olivia Yu Tian,[14] and Gail J Roboz[15,16]

[1]The Alfred Hospital, Melbourne, Australia; [2]Australian Centre for Blood Diseases, Monash University, Melbourne, Australia; [3]Ulm University Hospital, Ulm, Germany; [4]Indiana University Cancer Center, Indianapolis, IN; [5]The University of Texas MD Anderson Cancer Center, Houston, TX; [6]Hospital Universitario La Fe de Valencia, Valencia, Spain; [7]Institut de Recherche Saint Louis, Université de Paris, Paris, France; [8]Hôpital Saint-Louis, Assistance Publique - Hôpitaux de Paris (AP-HP), Paris, France; [9]AZ Sint-Jan Brugge-Oostende AV, Brugge, Belgium; [10]iCAN Digital Precision Cancer Medicine Flagship, University of Helsinki, Helsinki, Finland; [11]Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; [12]Samsung Medical Center, Seoul, Republic of Korea; [13]University of Kansas Medical Center, Kansas City, KS; [14]Bristol Myers Squibb, Princeton, NJ; [15]Weil Cornell Medical College, New York, NY; [16]New York Presbyterian Hospital, New York, NY

Presentation 871

ASH 2021

QUAZAR AML-001: Long-Term Overall Survival with Oral Azacitidine for AML in First Remission After Intensive Chemotherapy



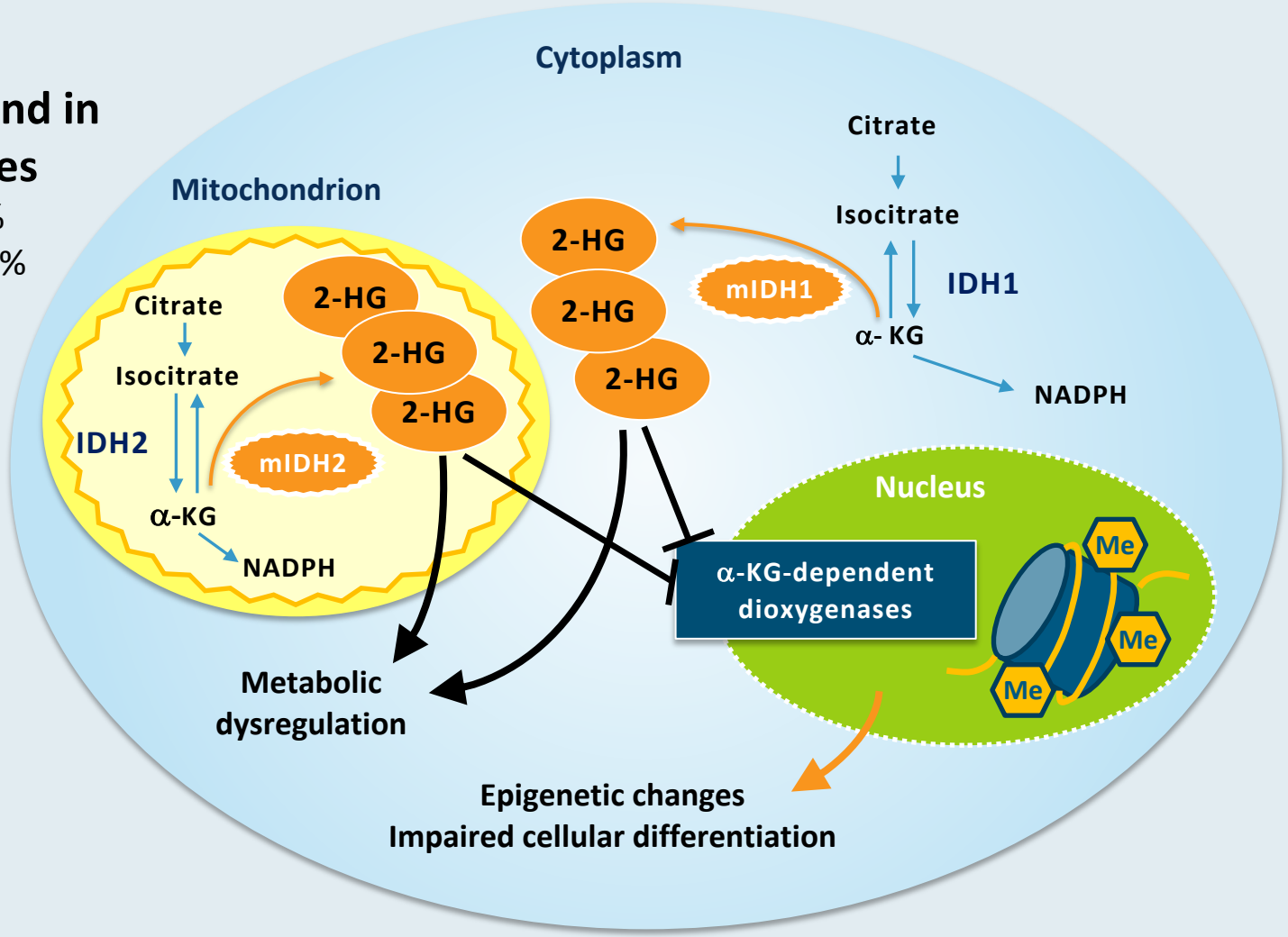
Wei AH et al. ASH 2021;Abstract 871.

RTP RESEARCH TO PRACTICE

IDH1 and IDH2 Mutations in AML

IDH mutations are found in ~16%-20% of AML cases

- IDH1 mutations in ~7.5%
- IDH2 mutations in ~8-19%



Buege MJ et al. *Cancers* 2018;10:187; Döhner H et al. *N Engl J Med* 2015;373(12):1136-52; Bullinger L et al. *J Clin Oncol* 2017;35(9):934-46.

RTP RESEARCH TO PRACTICE

Lancet Oncol 2021;22(11):1597-608.

Enasidenib plus azacitidine versus azacitidine alone in patients with newly diagnosed, mutant-*IDH2* acute myeloid leukaemia (AG221-AML-005): a single-arm, phase 1b and randomised, phase 2 trial

Courtney D DiNardo, Andre C Schuh, Eytan M Stein, Pau Montesinos, Andrew H Wei, Stéphane de Botton, Amer M Zeidan, Amir T Fathi, Hagop M Kantarjian, John M Bennett, Mark G Frattini, Patricia Martin-Regueira, Frederik Lersch, Jing Gong, Maroof Hasan, Paresh Vyas, Hartmut Döhner**

AG-221-AML-005: A Phase II Study of Enasidenib and Azacitidine for Newly Diagnosed AML with an IDH2 Mutation

Clinical endpoint	Enasidenib + azacitidine (n = 68)	Azacitidine (n = 33)
Overall response*	50 (74%)	12 (36%)
CR	37 (54%)	4 (12%)
CR + CRh	39 (57%)	6 (18%)
12-month survival estimate (%)	72%	70%
Select Grade ≥3 treatment-emergent AEs, n (%)		
Thrombocytopenia	25 (37%)	6 (19%)
Anemia	13 (19%)	7 (22%)
Febrile neutropenia	11 (16%)	5 (16%)
IDH differentiation syndrome	7 (10%)	—

* Overall response defined as proportion of patients with complete remission, complete remission with incomplete blood count or platelet recovery, partial remission or morphological leukemia-free state

DiNardo CD et al. *Lancet Oncol* 2021;22(11):1597-608.

RTP RESEARCH TO PRACTICE

Blood Cancer Journal 2022;12(1):10.

www.nature.com/bcj

ARTICLE

Efficacy and safety of enasidenib and azacitidine combination in patients with *IDH2* mutated acute myeloid leukemia and not eligible for intensive chemotherapy

Sangeetha Venugopal[1], Koichi Takahashi[1], Naval Daver[1], Abhishek Maiti[1], Gautam Borthakur[1], Sanam Loghavi[2], Nicholas. J. Short[1], Maro Ohanian[1], Lucia Masarova[1], Ghayas Issa[1], Xuemei Wang[3], Bueso-Ramos Carlos[2], Musa Yilmaz[1], Tapan Kadia[1], Michael Andreeff[1], Farhad Ravandi[1], Marina Konopleva[1], Hagop M. Kantarjian[1] and Courtney D. DiNardo[1]✉

Phase II Study of Enasidenib and Azacitidine for Patients with AML with an IDH2 Mutation Who Are Ineligible for Intensive Chemotherapy

Response	Newly diagnosed (n = 7)	Relapsed/Refractory (n = 19)
Composite complete remission*	7 (100%)	11 (58%)
Complete remission (CR)	5 (72%)	5 (26%)
CR with incomplete hematologic recovery (CRi)	2 (28%)	6 (32%)
MRD negativity by flow cytometry	7/7 (100%)	2/9 (22%)

* CR + CRi

- Seven patients with R/R AML received enasidenib + azacitidine + venetoclax triplet, median OS was not reached and 6-mo OS was 70% (median follow-up 11.2 mo)
- Adverse events of special interest included all-grade IDH differentiation syndrome (8%) and indirect hyperbilirubinemia (35%)

Venugopal S et al. *Blood Cancer J* 2022;12(1):10.

A Phase Ib/II Study of Ivosidenib with Venetoclax +/- Azacitidine in IDH1-Mutated Myeloid Malignancies

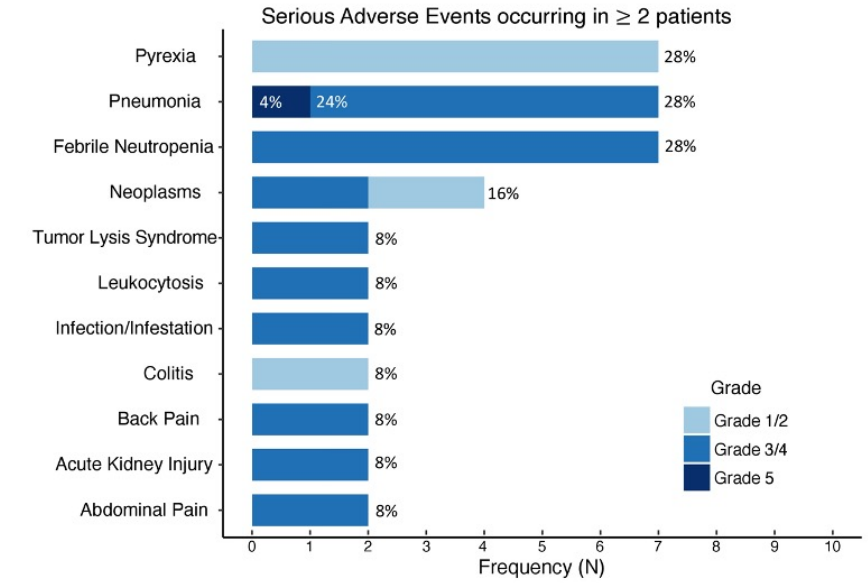
Lachowiez CA et al.

ASCO 2021;Abstract 7012.

Phase Ib/II Study of Ivosidenib with Venetoclax with or without Azacitidine for Patients with Myeloid Cancer and an IDH1 Mutation

- 3 x 3 dose escalation/de-escalation study exploring 3 dose levels in 25 patients with advanced MDS or MPN or newly diagnosed or R/R AML

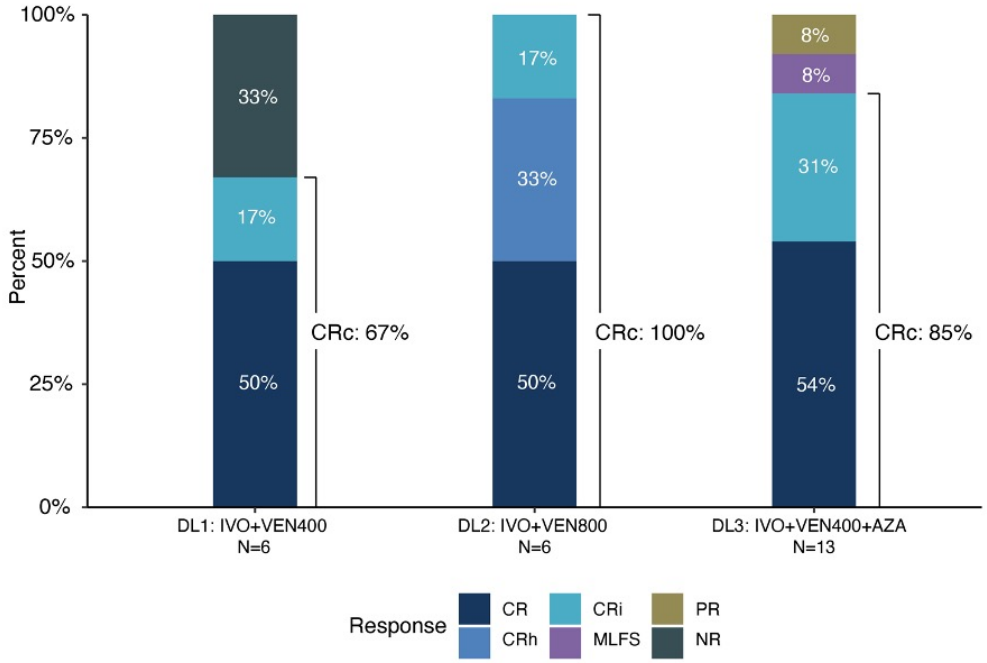
Safety



Mortality	Frequency
30-day	0%
60-day	0%
Study Deaths	1 (pneumonia)

IDH Differentiation Syndrome N (%)	
Dose Level #1	2 (33%)
Dose Level #2	1 (17%)
Dose Level #3	1 (8%)

Efficacy



	DL1 (n = 6)	DL2 (n = 6)	DL3 (n = 13)
1-year OS	50%	67%	83%

Lachowiez CA et al. ASCO 2021;Abstract 7012.

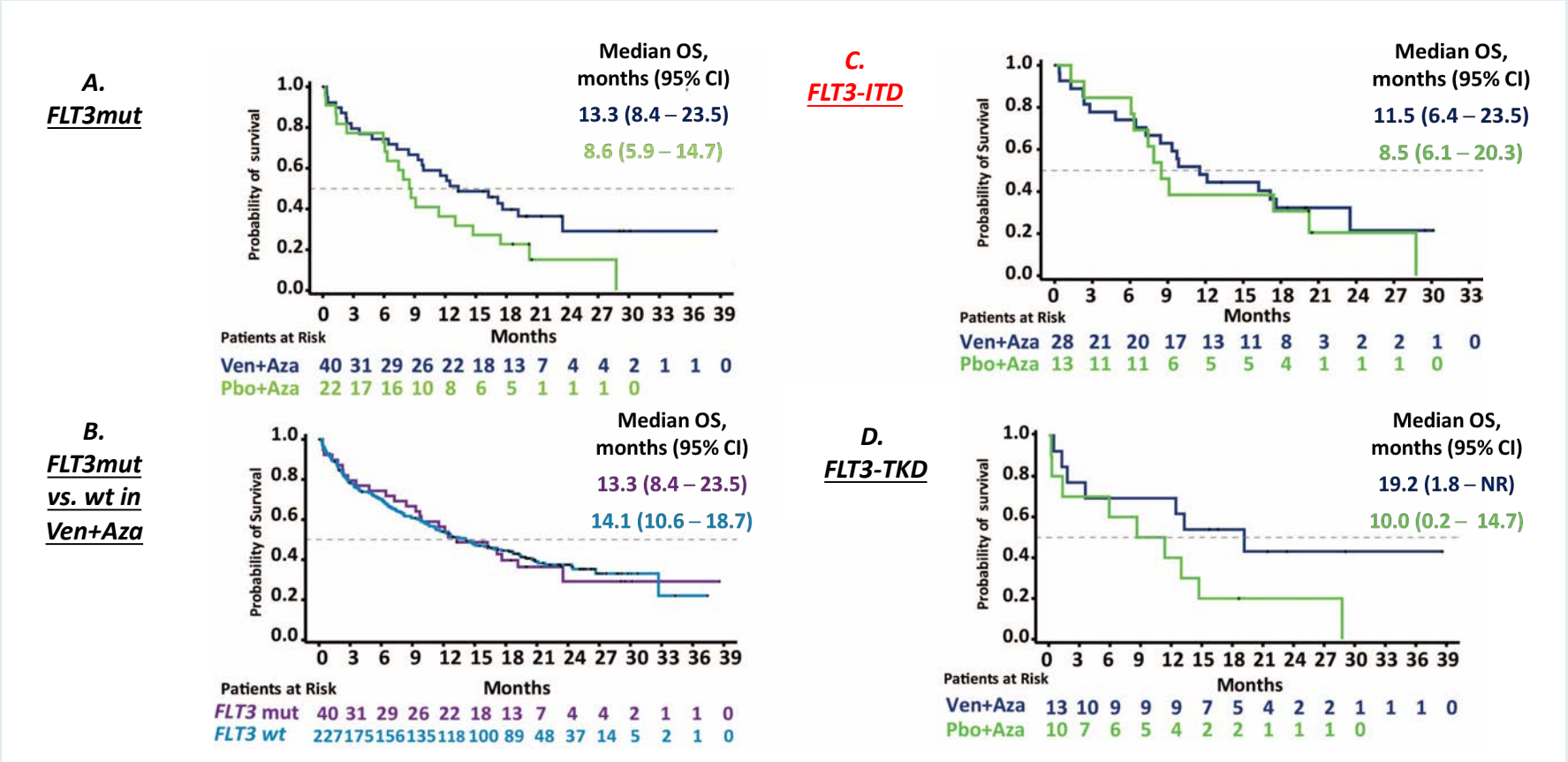
Results of Venetoclax and Azacitidine Combination in Chemotherapy Ineligible Untreated Patients with Acute Myeloid Leukemia with *FLT3* Mutations

Konopleva M et al.

ASH 2020;Abstract 1904.

Pooled Analysis of Venetoclax with Azacitidine in Patients with AML with FLT3 Mutations Who Are Ineligible for Intensive Chemotherapy

- Pooled data from Phase III trail of Ven + AZA vs Pbo + AZA and Phase Ib trial of Ven + AZA (NCT02993523/NCT02203773)



Konopleva M et al. ASH 2020;Abstract 1904.

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ASH 2021;Abstract 66.

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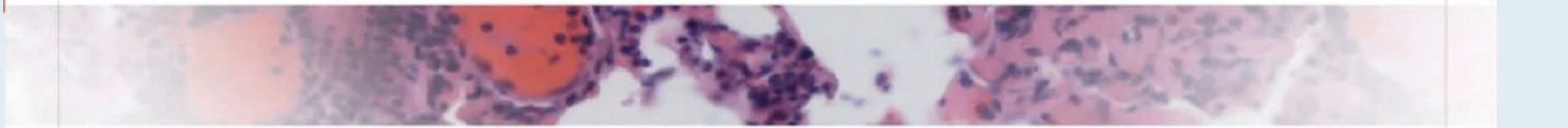

Oral Decitabine/Cedazuridine in Patients with Lower Risk Myelodysplastic Syndrome: a Longer-Term Follow-Up of from the ASCERTAIN Study

On behalf of the ASCERTAIN Investigators Team

Guillermo Garcia-Manero, MD[1], James K. McCloskey, MD[2], Elizabeth A. Griffiths, MD[3], Karen W.L. Yee, MD[4], Amer M. Zeidan, MBBS, MHS[5], Aref Al-Kali, MD[6], , H. Joachim Deeg, MD[7], Prapti A. Patel, MD[8], Mitchell Sabloff, MSc, MD, FRCPC[9], Mary-Margaret Keating, MD, FRCPC[10], Kim-Hien Dao, DO, PhD[11,26], Nancy Zhu, MD[12*], Nashat Gabrail, MD[13*], Salman Fazal, MD[14], Joseph Maly, MD[15], Olatoyosi Odenike, MD[16], Hagop M. Kantarjian, MD[17], Amy E. DeZern, MD[18], Casey L. O'Connell, MD[19], Gail J. Roboz, MD[20], Lambert Busque, MD[21], Richard A. Wells, MD, DPhil[22*], Harshad Amin, MD[23*], Jasleen K. Randhawa, MD[24], Brian Leber, MD[25], Yong Hao, MD, PhD[26*], Harold N. Keer, MD, PhD[26], Mohammad Azab, MD[26] and Michael R. Savona, MD[25]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]John Theurer Cancer Center at Hackensack Meridian Health, Hackensack, NJ; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [4]Princess Margaret Cancer Centre, Toronto, Canada; [5]Yale University and Yale Cancer Center, New Haven, CT; [6]Mayo Clinic, Rochester, MN; [7]Fred Hutchinson Cancer Research Center, Seattle, WA; [8]University of Texas Southwestern Medical Center, Dallas, TX; [9]Division of Hematology, Department of Medicine, University of Ottawa and The Ottawa Hospital Research Institute, Ottawa, ON, Canada; [10]Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; [11]Astex Pharmaceuticals, Inc., Pleasanton, CA; [12]University of Alberta, Edmonton, AB, Canada; [13]Gabrail Cancer Center Research, Canton, OH; [14]West Penn Hospital, Allegheny Health Network, Pittsburgh, PA; [15]Norton Cancer Institute, Louisville, KY; [16]University of Chicago, Chicago, IL; [17]Johns Hopkins University Hospital, Baltimore, MD; [18]USC Keck School of Medicine, University of Southern California, Los Angeles, CA; [19]Weill Cornell Medicine and The New York-Presbyterian Hospital, New York, NY; [20]Research Center, Maisonneuve-Rosemont Hospital, Montreal, QC, Canada; [21]Sunnybrook Health Sciences Centre, Toronto, Canada; [22]Boca Raton Clinical Research, Boca Raton, FL; [23]Houston Methodist Cancer Center, Houston; [24]Department of Medicine, McMaster University, Hamilton, ON, Canada; [25]Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, TN

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ASCERTAIN: Efficacy of Decitabine/Cedazuridine in Patients with Lower-Risk MDS

Response Category	Treated Patients (N=69[a]), n (%)	95% CI
Complete response (CR)	16 (23.2%)	(13.9, 34.9)
Partial response (PR)	0	
Marrow CR (mCR)	18 (26.1%)	(16.3, 38.1)
mCR with hematologic improvement	9 (13.0%)	(6.1, 23.3)
Hematologic improvement (HI)	5 (7.2%)	(2.4, 16.1)
HI-erythroid[3]	1 (1.4%)	(0.0, 7.8)
HI-neutrophils[3]	0	
HI-platelet[3]	4 (5.8%)	(1.6, 14.2)
Overall response (CR + PR + mCR + HI)	39 (56.5)	(44.0, 68.4)

[1]Responses adjudicated by independent review committee per IWG 2006
[a] Includes 3 subjects who did not receive ASTX727 (received IV decitabine cycle 1 and did not continue)

For subjects with ≥ 5% bone marrow blasts (n=26):

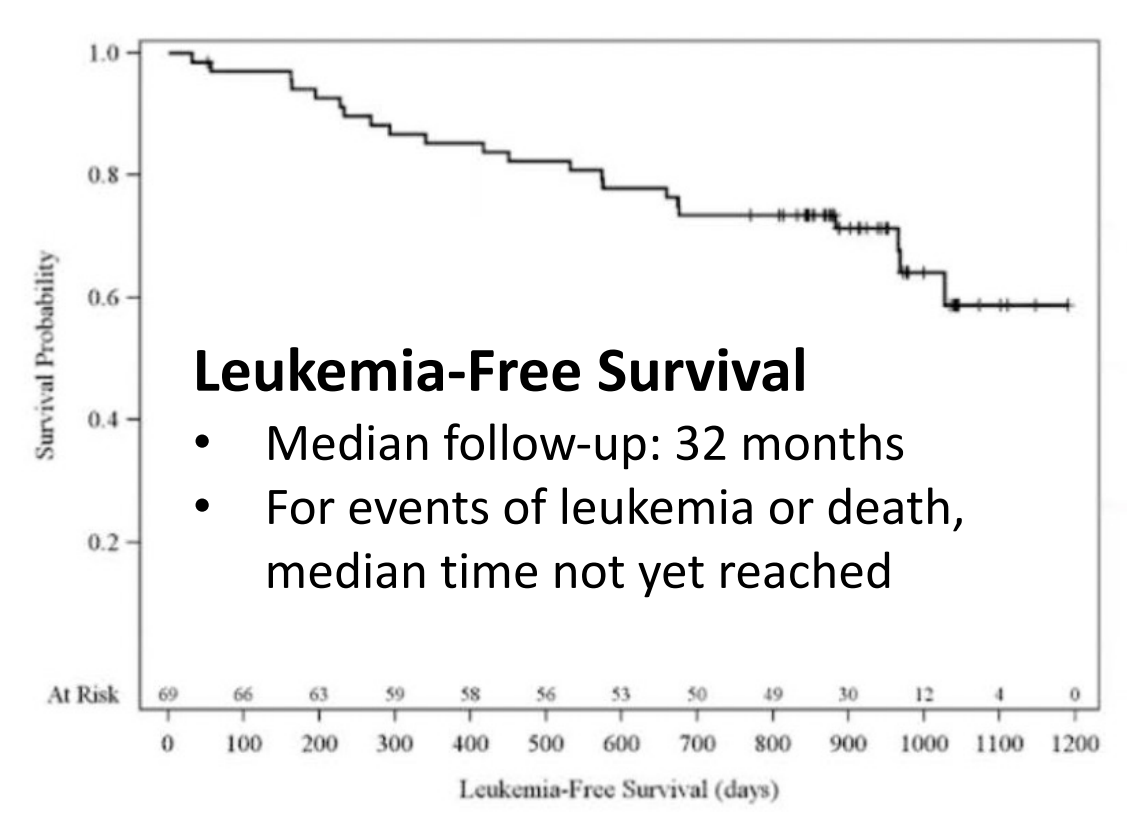
- CR 7 (26.9%)
- mCR 11 (42.3%)

For the entire group (n=69):

- Median CR duration was 15.3 months
- Median duration of best response was 13.4 months
- Median time to first and best response were 3.0 months and 4.3 months, respectively
- 18 (26.0%) subjects proceeded to HCT

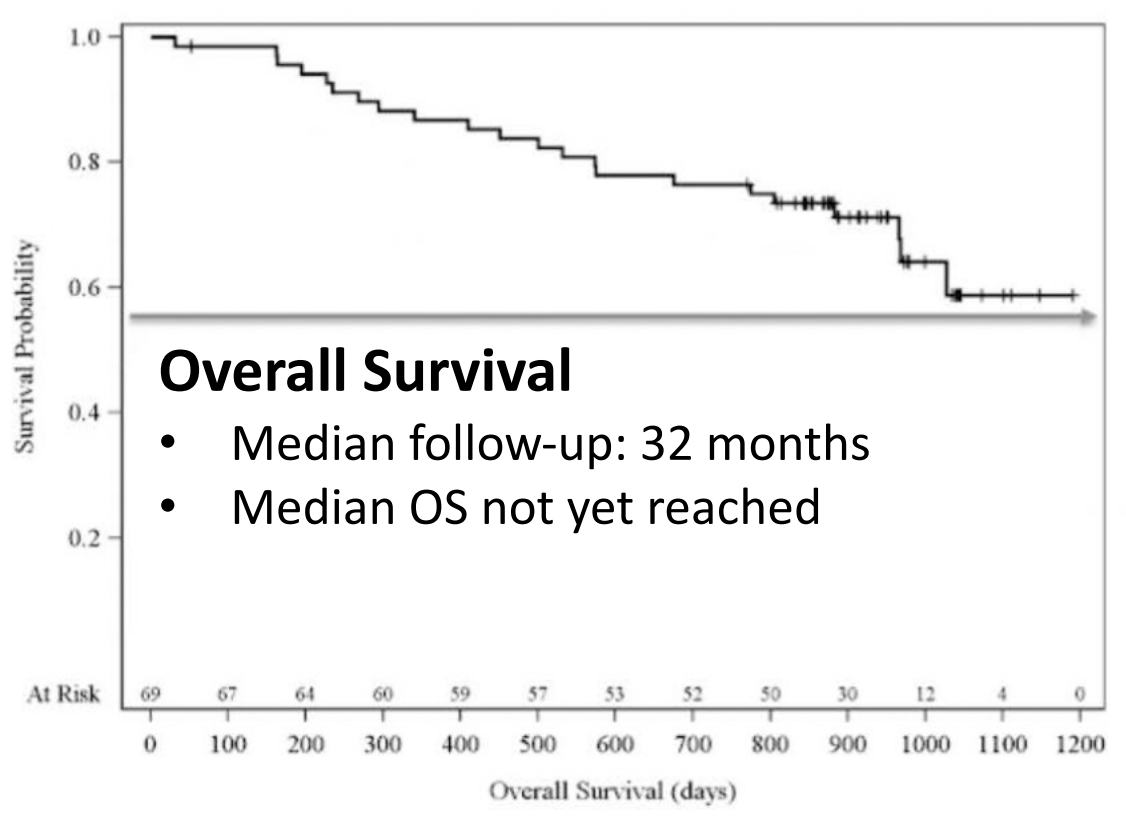
Garcia-Manero G et al. ASH 2021;Abstract 66.

ASCERTAIN: Survival Analyses of Patients with Lower-Risk MDS



Leukemia-Free Survival

- Median follow-up: 32 months
- For events of leukemia or death, median time not yet reached



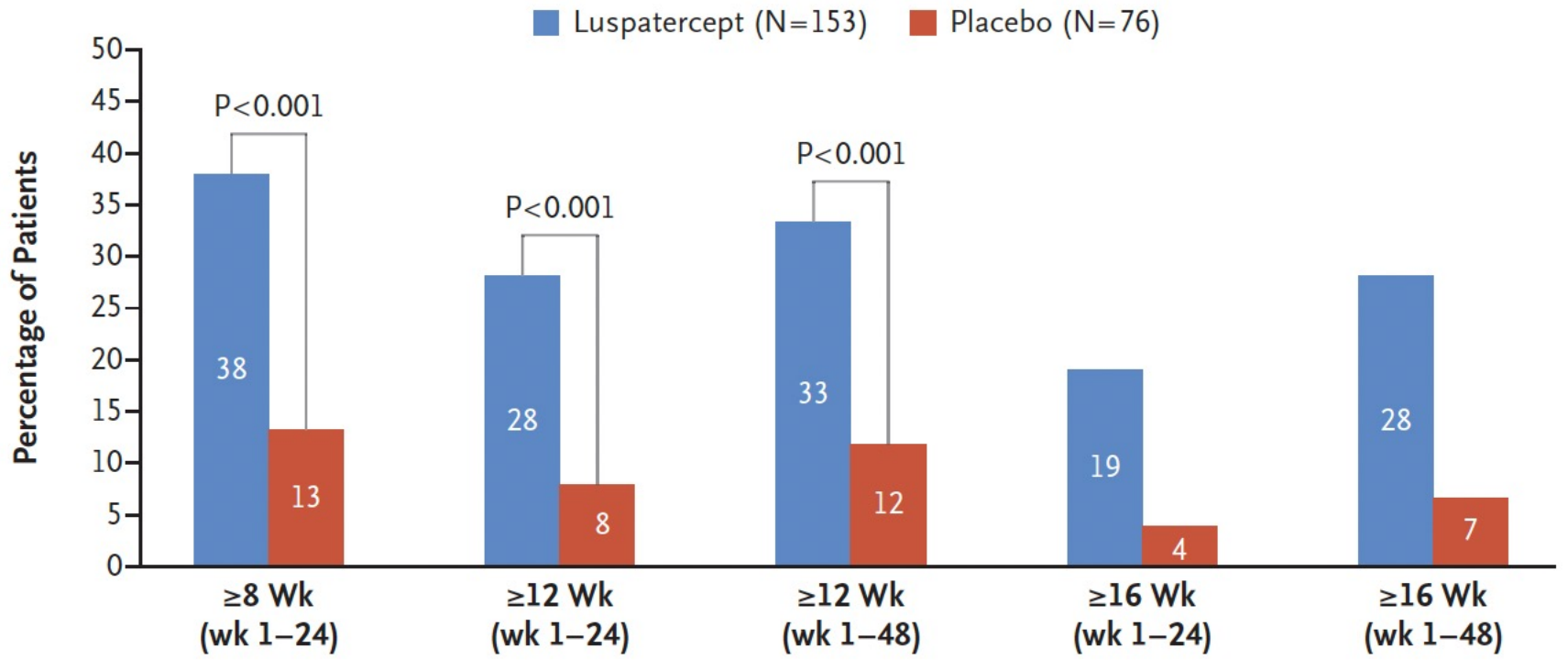
Overall Survival

- Median follow-up: 32 months
- Median OS not yet reached

Garcia-Manero G et al. ASH 2021;Abstract 66.

RTP RESEARCH TO PRACTICE

MEDALIST: Independence from Red Blood Cell Transfusion



No. of Patients with Response (% [95% CI])					
Luspatercept	58 (38 [30–46])	43 (28 [21–36])	51 (33 [26–41])	29 (19 [13–26])	43 (28 [21–36])
Placebo	10 (13 [6–23])	6 (8 [3–16])	9 (12 [6–21])	3 (4 [1–11])	5 (7 [2–15])

Fenaux P et al. *N Engl J Med* 2020;382:140-51.

Venetoclax in Combination with Azacitidine Granted FDA Breakthrough Therapy Designation for Higher-Risk MDS

Press Release: July 21, 2021

"…the US Food and Drug Administration (FDA) granted a Breakthrough Therapy Designation (BTD) to venetoclax in combination with azacitidine for the potential treatment of adult patients with previously untreated intermediate-, high- and very high-risk myelodysplastic syndromes (MDS) based on revised International Prognostic Scoring System (IPSS-R).

This designation is supported by data from the Phase 1b M15-531 study. In addition to the Phase Ib M15-531 study, venetoclax is being investigated in combination with azacitidine for the treatment of MDS in the Phase 1b M15-522 study in patients with relapsed or refractory disease, and the Phase 3 randomized VERONA study in patients with newly diagnosed higher-risk MDS."

https://www.prnewswire.com/news-releases/venetoclax-venclexta-granted-us-fda-breakthrough-therapy-designation-btd-in-higher-risk-myelodysplastic-syndrome-mds-301338030.html

Tolerability and Efficacy of the First-in-Class Anti-CD47 Antibody Magrolimab Combined With Azacitidine in MDS and AML Patients: Phase 1b Results

David A Sallman[1], Adam Asch[2], Monzr Al-Malki[3], Daniel Lee[4], Guillermo Garcia-Manero[5], William Donnellan[6], Daniel Pollyea[7], Suman Kambhampati[8], Eunice Wang[9], Deepa Jeyakumar[10], Gabe Mannis[11], Terrence Bradley[12], Richard Larson[13], Tiffany Tanaka[14], Wanxing Chai-Ho[15], Josh Zeidner[16], Guido Marcucci[3], Rami Komrokji[1], Joanna Van Elk[17], Ming Lin[17], Jens-Peter Volkmer[17], Roy Maute[17], Chris Takimoto[17], Mark Chao[17], Paresh Vyas[18], Naval Daver[5]

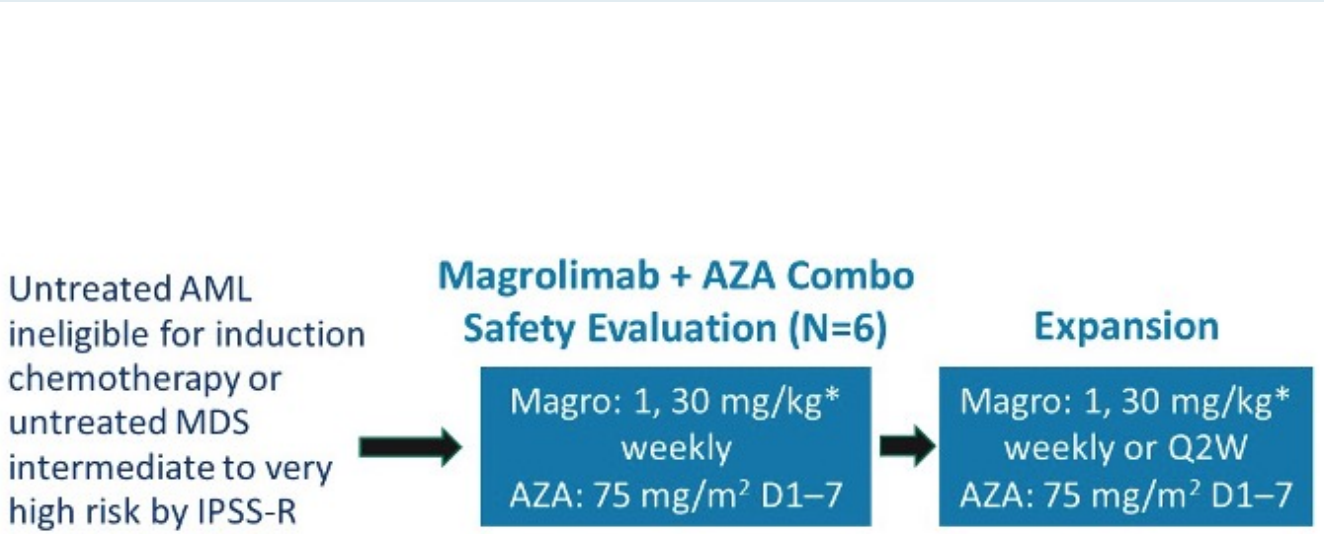
[1]Moffitt Cancer Center, Tampa, FL; [2]University of Oklahoma, Oklahoma City, OK; [3]City of Hope, Duarte, CA; [4]Columbia University, New York, NY; [5]MD Anderson Cancer Center, Houston, TX; [6]Sarah Cannon Research Institute, Nashville, TN; [7]University of Colorado, Denver, CO; [8]Healthcare Midwest, Kansas City, MO; [9]Roswell Park Cancer Center, Buffalo, NY; [10]University of California Irvine, Irvine, CA; [11]Stanford University, Stanford, CA; [12]University of Miami, Miami, FL; [13]University of Chicago, Chicago, IL; [14]University of California San Diego, San Diego, CA; [15]University of California Los Angeles, Los Angeles, CA; [16]University of North Carolina, Chapel Hill, NC; [17]Forty Seven, Inc., Menlo Park, CA; [18]University of Oxford, Oxford, UK

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: DAVID A. SALLMAN, MD

ASCO 2020;Abstract 7507.

5F9005 Study Design: Magrolimab in Combination with Azacitidine for MDS and Acute Myeloid Leukemia (AML)



Primary objectives

1. Safety of magrolimab alone or with AZA
2. Efficacy of magrolimab + AZA in untreated AML/MDS

Secondary objectives

1. Pharmacokinetics, pharmacodynamics, and immunogenicity of 5F9
2. Additional measures of efficacy (DOR, PFS, OS)

Exploratory objective

To assess CD47 receptor occupancy, markers of immune cell activity, and molecular profiling in AML/MDS

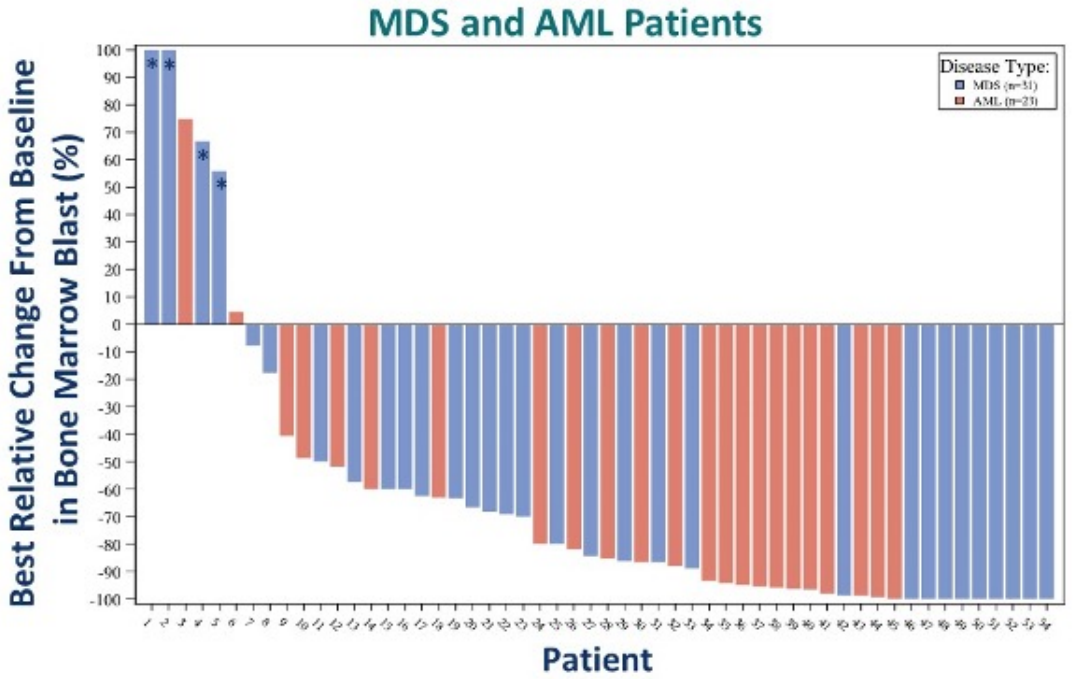
- A magrolimab priming dose (1 mg/kg) and dose ramp-up was utilized to mitigate on-target anemia

Sallman DA et al. ASCO 2020;Abstract 7507.

5F9005: Response to Magrolimab in Combination with Azacitidine for MDS and AML

Best Overall Response	1L MDS N=33	1L AML N=25
ORR	30 (91%)	16 (64%)
CR	14 (42%)	10 (40%)
CRi	NA	4 (16%)
PR	1 (3%)	1 (4%)
MLFS/marrow CR	8 (24%) 4 with marrow CR + HI	1 (4%)
Hematologic improvement (HI)	7 (21%)	NA
SD	3 (9%)	8 (32%)
PD	0	1 (4%)

Response assessments per 2006 IWG MDS criteria and 2017 AML ELN criteria. Patients with at least 1 post-treatment response assessment are shown; all other patients are on therapy and are too early for first response assessment, except for 2 MDS patients not evaluable (withdrawal of consent) and 3 AML patients (1 AE, 2 early withdrawal).



Four patients not shown due to missing values; <5% blasts imputed as 2.5%. *Baseline bone marrow blasts ≤5%.

- Magrolimab + AZA induces a 91% ORR (42% CR) in MDS and 64% ORR (56% CR/CRi) in AML
- Responses deepened over time with a 56% 6-month CR rate in MDS patients (assessed in all patients 6 months after initial treatment)
- Median time to response is 1.9 months, more rapid than AZA alone
- Magrolimab + AZA efficacy compares favorably to AZA monotherapy (CR rate 6-17%[1,2])

1. Azacitidine USPI. 2. Fenaux P, et al. *Lancet Oncol.* 2009 ;10(3):223-232.

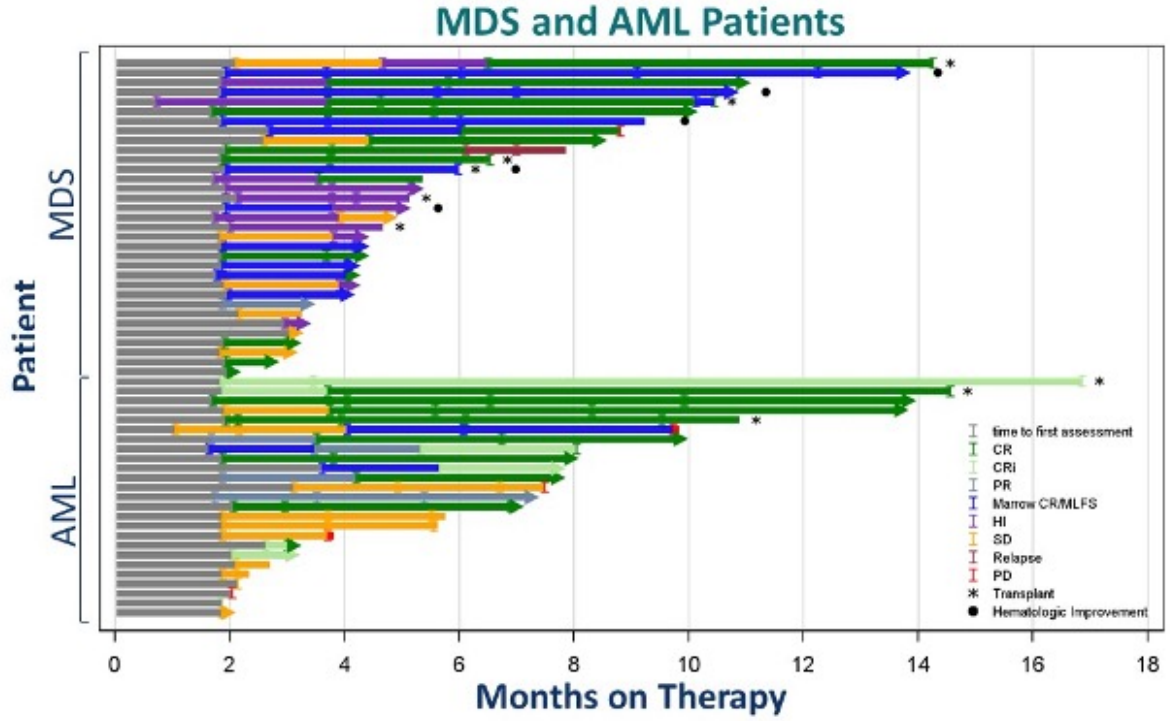
ORR = objective response rate

Sallman DA et al. ASCO 2020;Abstract 7507.

5F9005: Durability of Response to Magrolimab in Combination with Azacitidine for MDS and AML

Parameter	1L MDS N=33	1L AML N=25
RBC transfusion independence*	11/19 (58%)	9/14 (64%)
Complete cytogenetic response†	9/26 (35%)	6/12 (50%)
MRD negativity in responders	6/30 (20%)	8/16 (50%)
Median duration of response (months)	Not reached (0.03+ – 10.4+)	Not reached (0.03+ – 15.1+)
Median follow-up (range) (months)	5.8 (2.0–15.0)	9.4 (1.9–16.9)

MRD was evaluated by multiparameter flow cytometry; cytogenetic response defined per 2003 and 2006 IWG criteria.
*Patients shown for those who were RBC transfusion dependent at baseline and achieved RBC transfusion independence at any time on study.
†Responses shown for all responding patients with abnormal cytogenetics at baseline.



- Complete cytogenetic responses and MRD negativity is observed in MDS and AML patients
- No median duration of response has been reached for MDS or AML
- 16% of patients (9/58) received an allogeneic stem cell transplant
- Median OS has not been reached in either MDS or AML patients

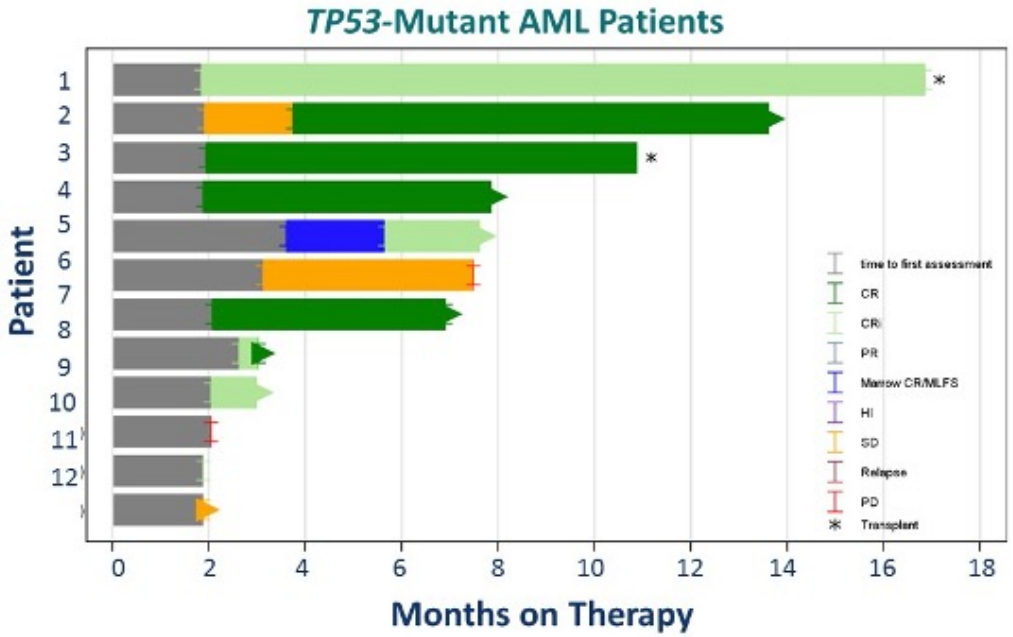
Sallman DA et al. ASCO 2020;Abstract 7507.

5F9005: Response to Magrolimab in Combination with Azacitidine for MDS and AML with TP53 Mutation

Efficacy in *TP53*-Mutant Patients

Best Overall Response	AML *TP53* Mutant (N=12)	MDS *TP53* Mutant (N=4)
ORR	9 (75%)	3 (75%)
CR	5 (42%)	2 (50%)
CRi/marrow CR	4 (33%)	1 (25%)
Complete cytogenetic response *	4/8 (50%)	3/3 (100%)
MRD negative of responders	4/9 (44%)	0
Median duration of response (months)	Not reached (0.03+ – 15.1+)	Not reached (0.03+ – 5.2+)
Survival probability at 6 months	91%	100%
Median follow-up (range) (months)	8.8 (1.9 – 16.9)	7 (4.2 – 12.2)

*Responding patients with abnormal cytogenetics at baseline.

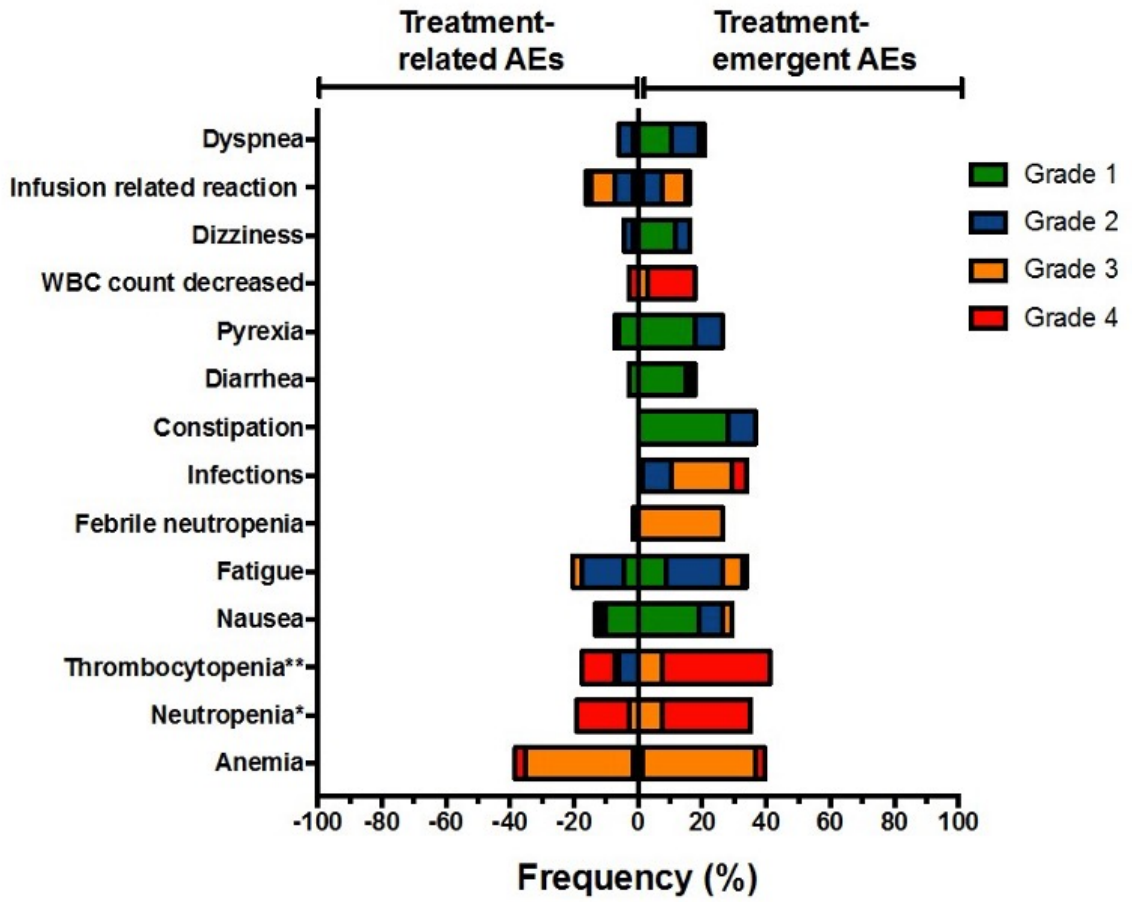


- Magrolimab + AZA has a high response rate with deep responses in *TP53*-mutant AML and MDS patients
- The estimated 6-month survival is 91% and 100% in AML and MDS patients, respectively
- Median duration and survival has not been reached, which compares favorably to current therapies
  - Venetoclax + AZA in AML: ORR 47%, DOR 5.6 mo, OS 7.2 mo[1]

1. DiNardo CD, et al. *Blood*. 2019;133(1):7-17.

Sallman DA et al. ASCO 2020;Abstract 7507.

5F9005: Safety of Magrolimab in Combination with Azacitidine for MDS and AML with TP53 Mutation



- No maximum tolerated dose was reached; magrolimab + AZA profile consistent with AZA monotherapy
- No significant cytopenias, infections, or immune-related AEs were observed (most patients were cytopenic at baseline)
- Anemia and transfusion frequency improved over time
- No deaths occurred during the first 60 days on study for either AML or MDS patients
- Treatment discontinuation due to drug-related AE occurred in only 1 of 68 (1.5%) of all patients treated with magrolimab + AZA

Sallman DA et al. ASCO 2020;Abstract 7507.

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Lung Cancer

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

Friday, June 3, 2022
6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)

Faculty

Justin F Gainor, MD
Corey J Langer, MD
Luis Paz-Ares, MD, PhD
Heather Wakelee, MD
Jared Weiss, MD
Helena Yu, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME links will be posted in the chat (Zoom participants only) and emailed to all participants within 24 hours of the program.

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