REGIONE DEL VENETO
ULSS8 BERICA

GIORNATE EMATOLOGICHE VICENTINE

XI edizione

9-10 ottobre 2025
Palazzo Bonin Longare - Vicenza

XI edizione

GIORNATE EMATOLOGICHE VICENTINE

Venerdì 10 ottobre 2025

SESSIONE 5
Leucemia acuta/trapianto

Moderatore: *M. Gottardi*

9:00 **DLI e terapie cellulari nel post-trapianto allogenico**
B. Rambaldi

09:30 **Il ruolo del trapianto di midollo nella LAL**
C. Skert

10:00 **L'induzione nella AML: quando preferisco l'inibitore di BCL2 alla chemioterapia standard**
G. Marconi

10:30 **Approccio terapeutico alle AML ad alto rischio citogenetico**
A. Candoni

AML AD ALTO RISCHIO CITOGENETICO-APPROCCIO TERAPEUTICO

AGENDA

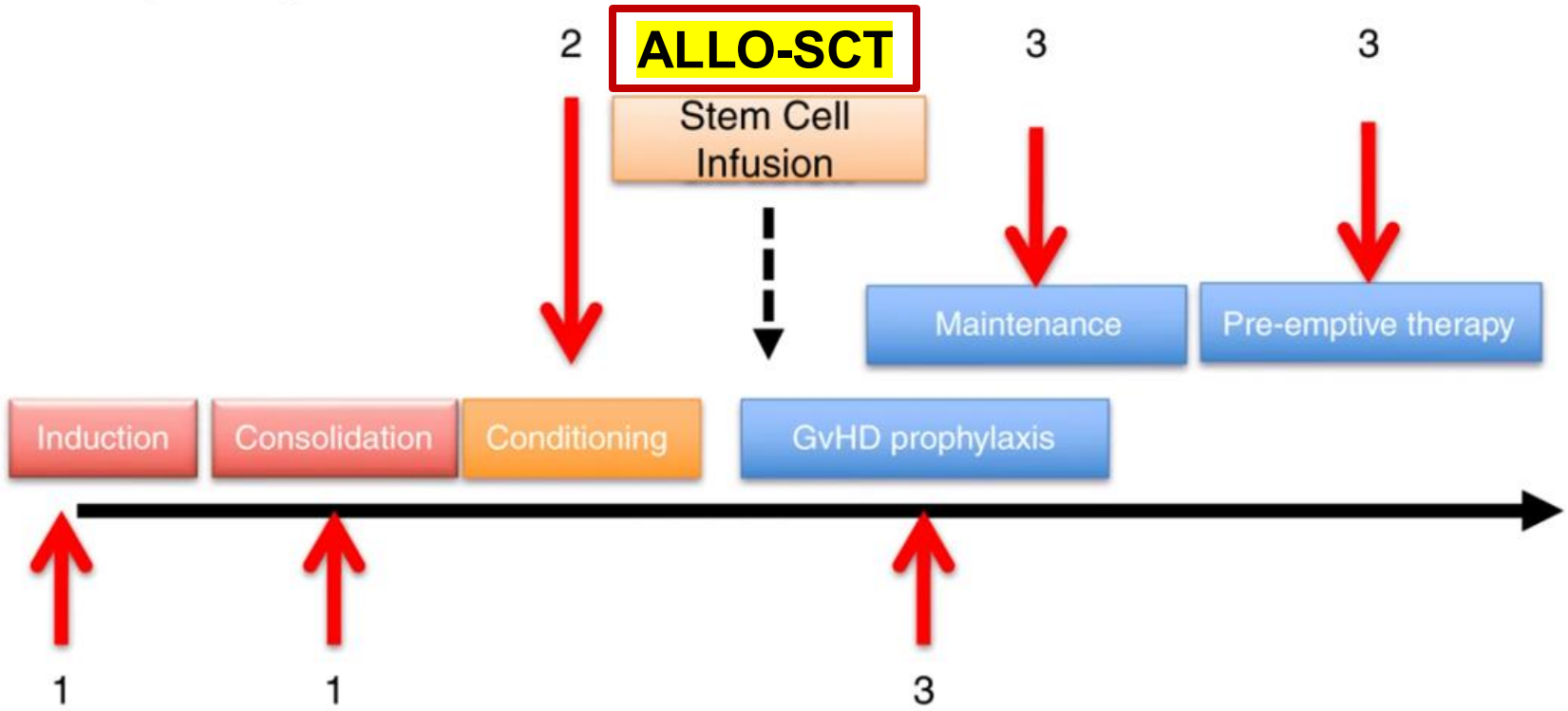
- ***INTRODUZIONE***
- ***APPROCCI TERAPEUTICI***

CLASSIFICAZIONE CITOGENETICO-MOLECOLARE ELN-2022

Favorable	• *t(8;21)(q22;q22.1)/RUNX1::RUNX1T1* • *inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/CBFB-MYH11* • *Mutated NPM1 without FLT3-ITD* • *bZIP in-frame mutated CEBPA*	Patients with non-adverse risk AML with MRD persistence should be considered for SCT
Intermediate	• Mutated NPM1 with FLT3-ITD • Wild-type NPM1 with FLT3-ITD • t(9;11)(p21.3;q23.3)/MLLT3::KMT2A • Cytogenetic and/or molecular abnormalities not classified as favorable or adverse	
Adverse	• t(6;9)(p23;q34.1)/DEK::NUP214 • t(v;11q23.3)/KMT2A-rearranged • t(9;22)(q34.1;q11.2)/BCR::ABL1 • t(8;16)(p11;p13)/KAT6A::CREBBP • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/GATA2, MECOM(EVI1) • t(3q26.2;v)/MECOM(EVI1)-rearranged • -5 or del(5q); -7; -17/abn(17p) • Complex karyotype, monosomal karyotype • Mutated ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, or ZRSR2 • Mutated TP53	Early intensification in CR1

Pharmacologic opportunities to optimize leukemia stem cell targeting in patients receiving allogeneic hematopoietic cell transplants for acute myeloid leukemia

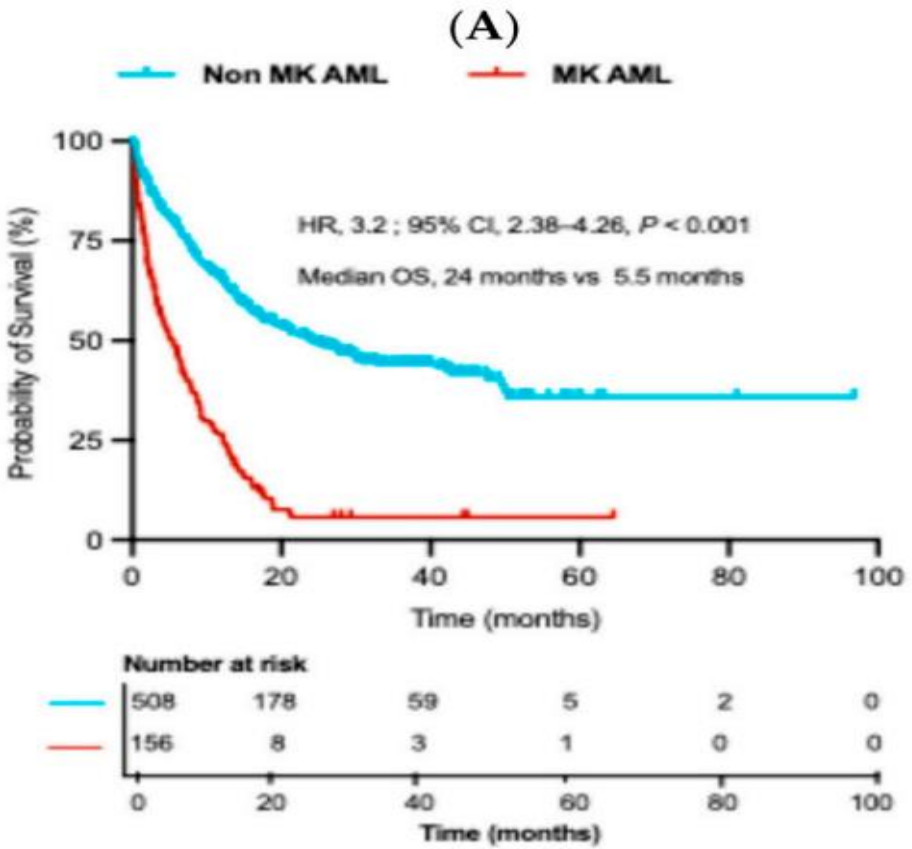
1) Minimize pre-transplant disease burden
2) Optimize cytotoxic properties of the conditioning regimen
3) Target leukemia specific antigens post-transplant:
   - adjunctive biological therapies with direct anti-tumor effect
   - optimizing a GVL effect

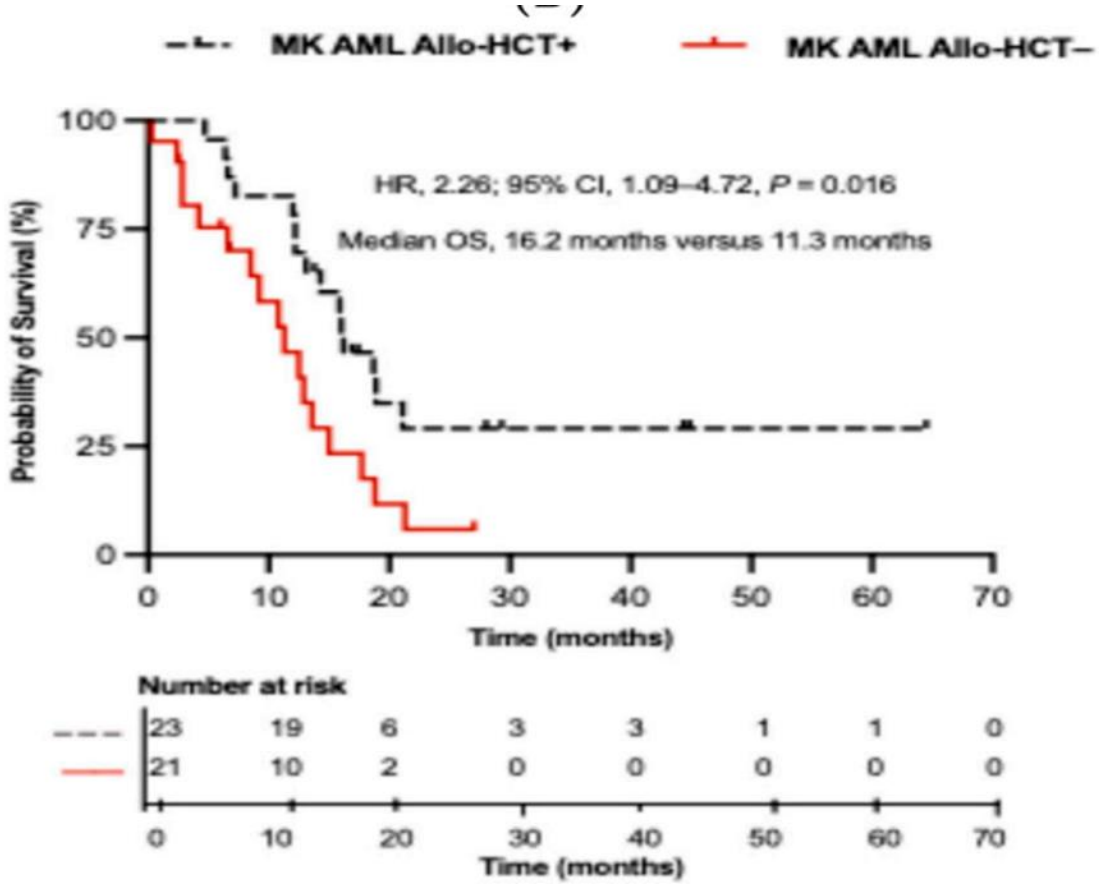


Bone Marrow Transplant **54**, 6–16 (2019).

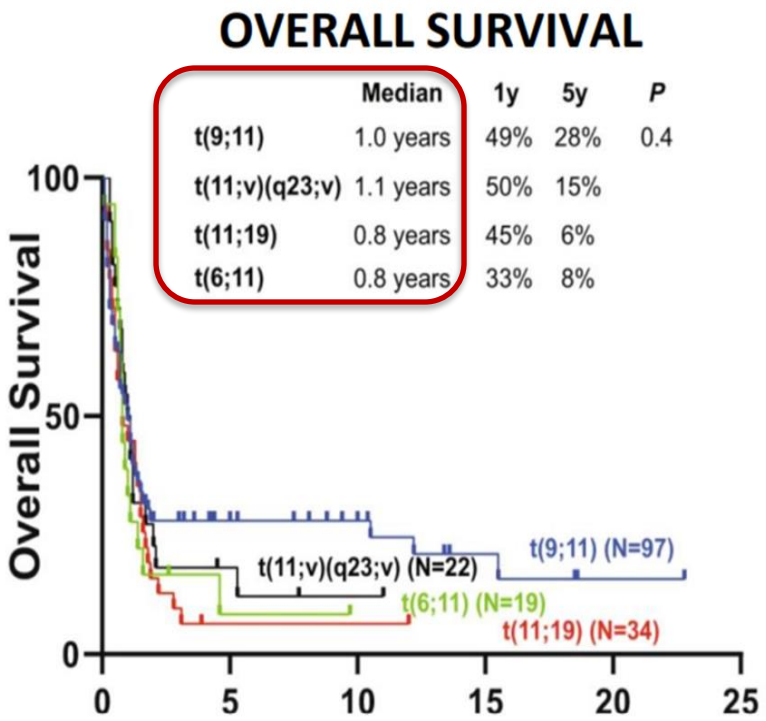
Article

Genomic Profile and Clinical Outcomes in Acute Myeloid Leukemia with Monosomal Karyotype



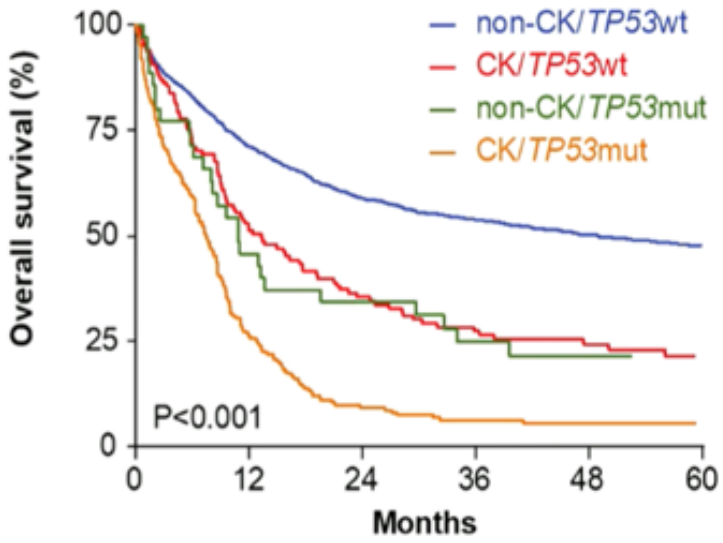


r-*KMT2A* AML outcome



Issa G C et al, Blood Cancer Jour 2021

Poor Outcome in *TP53* in relation to complex karyotype



TP53-mutated patients with complex karyotypes
→ "very adverse"

Grob et al. Blood, 2022

AML-MRC → AML-MR

The terminology of AML with myelodysplasia related changes (AML-MRC) is replaced by AML, myelodysplasia-related (AML-MR) in WHO-HAEM5, representing a single entity defined by the presence of at least one of the following: history of MDS or MDS/MPN, MR cytogenetic abnormalities and/ or MR gene mutations

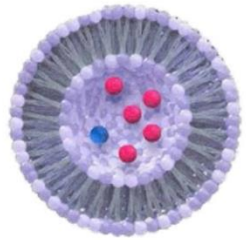
alterazioni correlate a mielodisplasia (AML-MRC)

WHO 2016	WHO 2022	ICC 2022
AML-MRC	**AML-MR**	**AML with**
• complex karyotype • cytogenetic abnormalities: • unbalanced abnormalities • -7/del(7q) • del(5q)/t(5q) • i(17q)/t(17p) • -13/del(13q) • del(11q) • del(12p)/t(12p) • idic(X)(q13) • balanced abnormalities	**Defining cytogenetic abnormalities:** • complex karyotype • del5q or 5q loss • -7, del7q or 7q loss • del11q • del12p or 12p loss • -13 or del13q • del17p or 17p loss or i17q • idic(X)(q13) **Defining somatic mutations:** *ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2*	**MDS-related genetic abnormalities:** • complex karyotype • del(5q)/t(5q)/add(5q), • -7/del(7q), • +8 • del(12p)/t(12p)/add(12p), i(17q), -17/add(17p) or del(17p) • del(20q), • idic(X)(q13) **MDS-related gene mutations:** *ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2, RUNX1*

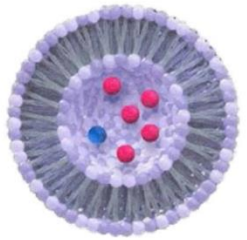
Indicazione autorizzata: CPX-351 è indicato per il trattamento di adulti con nuova diagnosi di leucemia mieloide acuta correlata a terapia (t-AML) o AML con alterazioni correlate a mielodisplasia (AML-MRC).

Tabella 1: Dose e schema per CPX-351

Terapia	Schema posologico
Prima induzione	Daunorubicina 44 mg/m² e citarabina 100 mg/m² nei giorni 1, 3 e 5
Seconda induzione	Daunorubicina 44 mg/m² e citarabina 100 mg/m² nei giorni 1 e 3
Consolidamento	Daunorubicina 29 mg/m² e citarabina 65 mg/m² nei giorni 1 e 3



CPX-351 phase III study



- Randomised, open-label, parallel-arm, standard therapy-controlled study
  - 1:1 randomisation, enrolled from December 2012 to November 2014

Primary endpoint: OS

Secondary endpoints: response rates and duration, EFS, and safety

ETA' > 60 aa

MEDIA = 67,7 (DS 4)

Key eligibility criteria

- Aged 60–75 years
- Newly diagnosed
- t-AML
- AML with antecedent MDS or CMML*
- *De novo* AML with MDS-related cytogenetic abnormalities

CPX-351 (n=153)

Stratifications:

- Age
- t-AML
- History of MDS with and without prior HMA
- History of CMML
- *De novo* AML HR

7+3 (n=156)

CPX-351

Induction (1–2 cycles)

7+3

Patients in CR or CRi:

Consolidation (1–2 cycles)

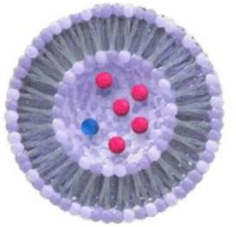
- **T-AML 20%**
- **AML prior MDS 47%**
- **AML prior CMML 7%**
- **De novo AML but with MDS K 26%**

NCT01696084

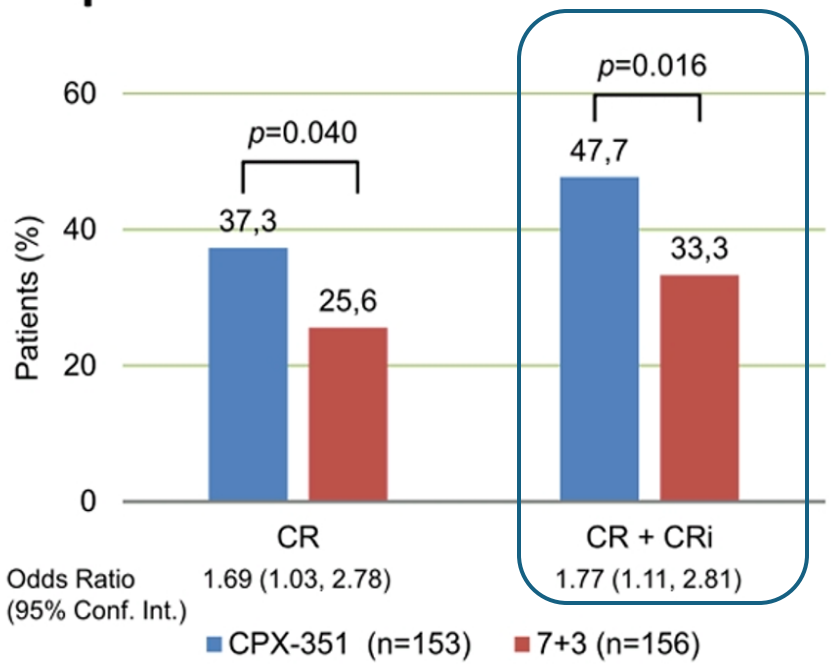
Prior HMA exposure 45% !!

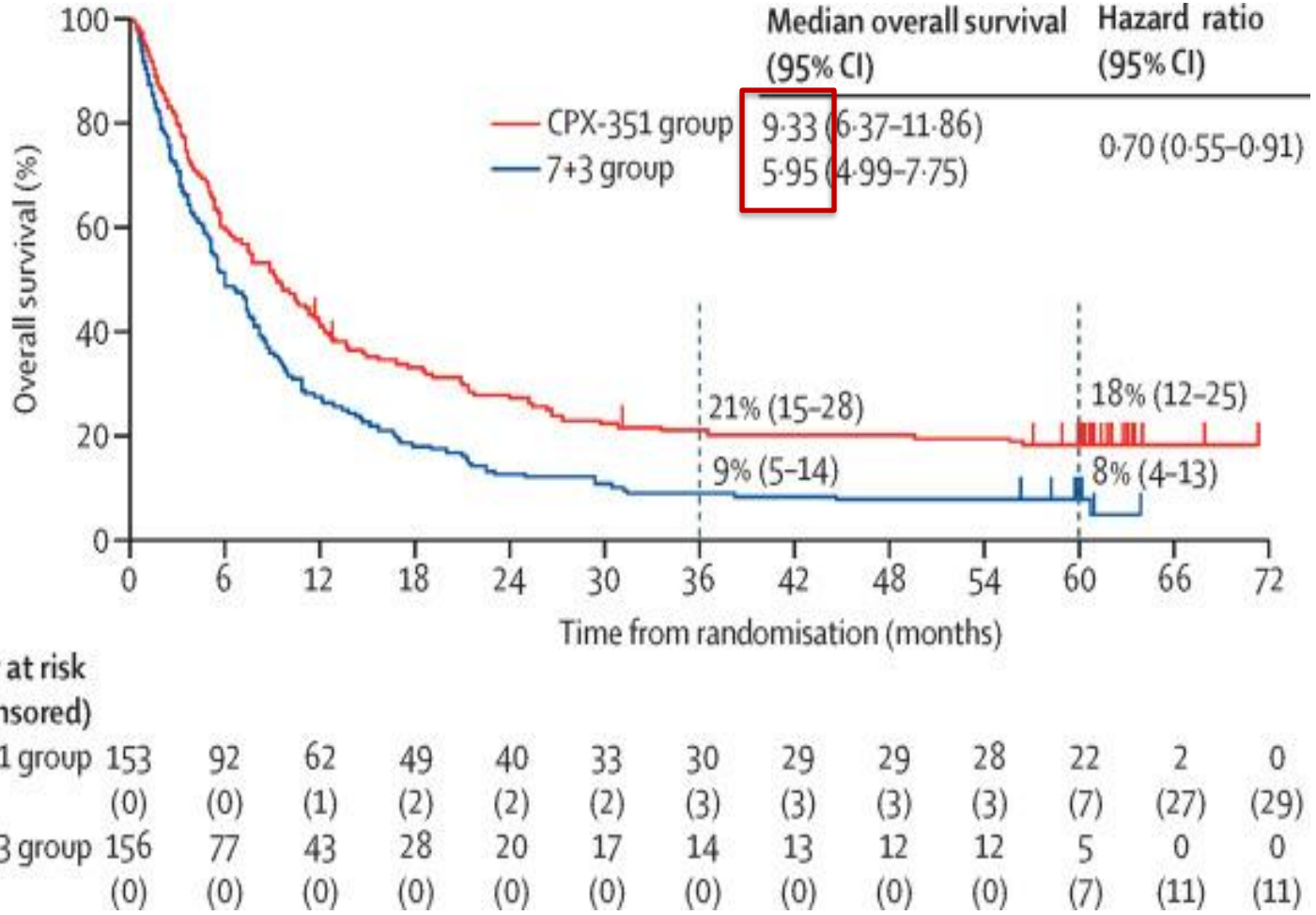
Lancet JE et al. J Clin Oncol 2018;36:2684–2692

CPX-351 RESPONSE AND OVERALL SURVIVAL



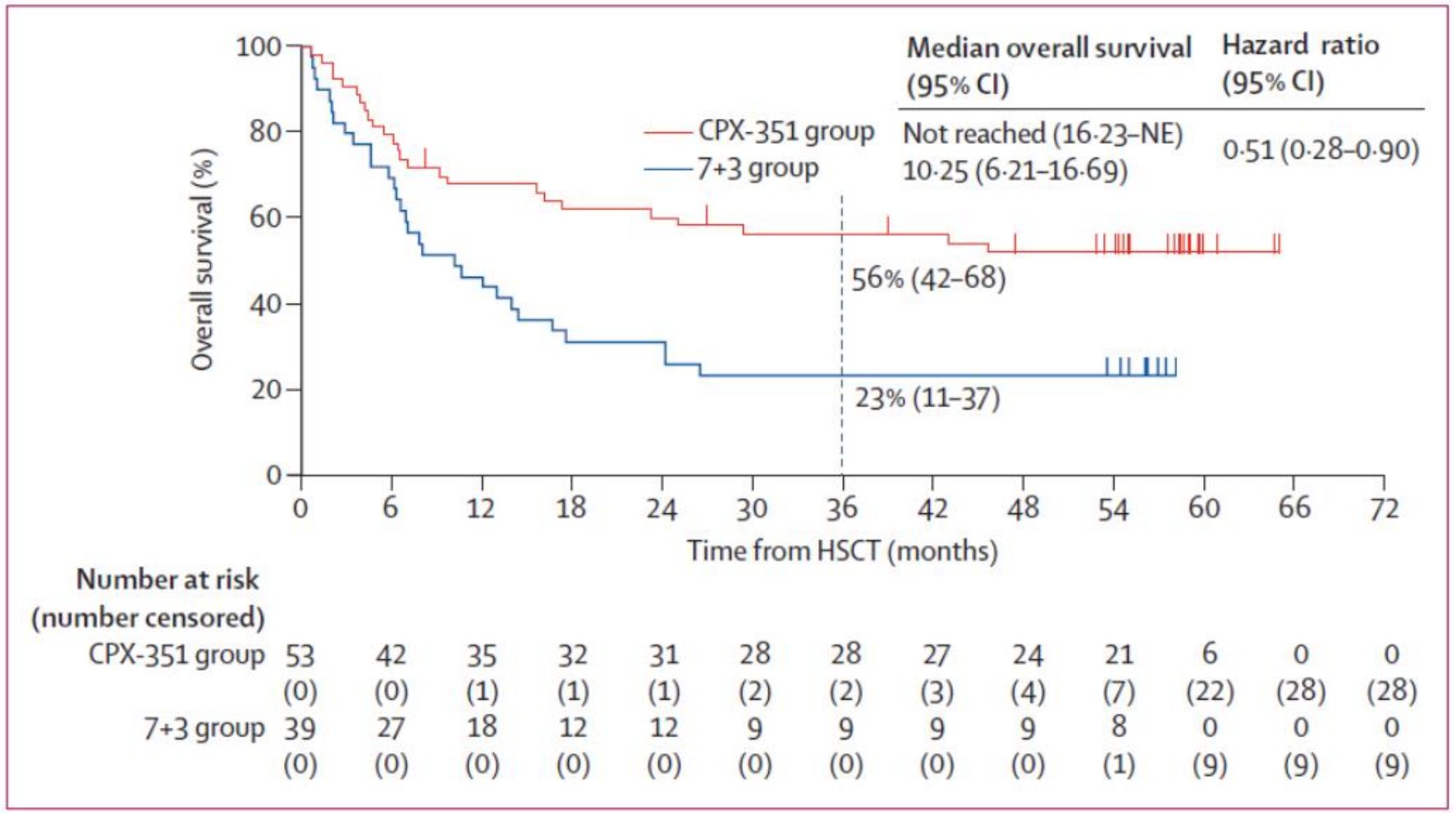
Response Rate





1. Lancet JE, et al. *Lancet Hematol* 2021;8:e481–91. **2.** Lancet JE, et al. *J Clin Oncol* 2018;36(26):2684-2692.

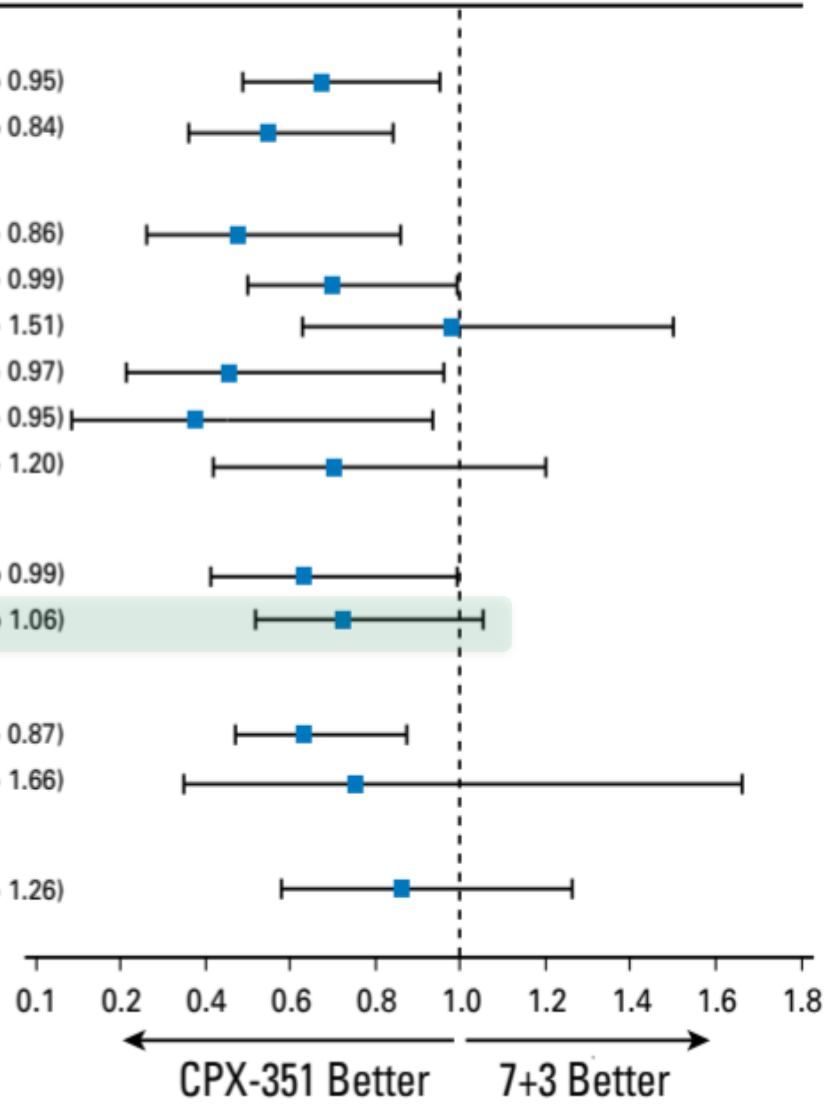
Overall survival from date of HSCT: 5-year results[1]



1. Lancet JE, et al. *Lancet Hematol* 2021;8:e481–91. **2.** Lancet JE, et al. *J Clin Oncol* 2018;36(26):2684-2692.

B

Subgroup	CPX-351 No.	CPX-351 Median OS, months	7+3 No.	7+3 Median OS, months	HR (95% CI) for Death
Age					
60-69 years	96	9.63	102	6.87	0.68 (0.49 to 0.95)
70-75 years	57	8.87	54	5.62	0.55 (0.36 to 0.84)
Type of AML					
Therapy-related AML	30	12.17	33	5.95	0.48 (0.26 to 0.86)
AML with antecedent MDS or CMML	82	7.38	86	5.95	0.70 (0.50 to 0.99)
MDS with prior HMA exposure	50	5.65	55	7.43	0.98 (0.64 to 1.51)
MDS without prior HMA exposure	21	15.74	19	5.13	0.46 (0.21 to 0.97)
CMML	11	9.33	12	2.28	0.37 (0.14 to 0.95)
De novo AML with MDS karyotype	41	10.09	37	7.36	0.71 (0.42 to 1.20)
Cytogenetic risk at screening					
Favorable/intermediate	71	14.72	63	8.41	0.64 (0.41 to 0.99)
Unfavorable	72	6.60	83	5.16	0.73 (0.51 to 1.06)
Baseline *FLT3* mutation status					
FLT3 wild type	116	9.33	120	5.98	0.64 (0.47 to 0.87)
FLT3 mutation	22	10.25	21	4.60	0.76 (0.34 to 1.66)
Overall HMA experience					
All patients with prior HMA exposure*	62	5.65	71	5.90	0.86 (0.59 to 1.26)



1. Lancet JE, et al. *Lancet Hematol* 2021;8:e481–91. **2.** Lancet JE, et al. *J Clin Oncol* 2018;36(26):2684-2692.

A randomized comparison of CPX-351 and FLAG-Ida in adverse karyotype AML and high-risk MDS: the UK NCRI AML19 trial

Jad Othman,[1,2] Charlotte Wilhelm-Benartzi,[3] Richard Dillon,[1,2] Steve Knapper,[4] Sylvie D. Freeman,[5] Leona M. Batten,[3] Joanna Canham,[3] Emily L. Hinson,[3] Julie Wych,[3] Sophie Betteridge,[3] William Villiers,[1] Michelle Kleeman,[6] Amanda Gilkes,[4] Nicola Potter,[1] Ulrik Malthe Overgaard,[7] Priyanka Mehta,[8] Panagiotis Kottaridis,[9] Jamie Cavenagh,[10] Claire Hemmaway,[11] Claire Arnold,[12] Mike Dennis,[13] and Nigel H. Russell,[2] on behalf of the UK National Cancer Research Institute Acute Myeloid Leukaemia Working Group

[1]Department of Medical and Molecular Genetics, Kings College London, London, United Kingdom; [2]Department of Haematology, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [3]Centre for Trials Research, Cardiff University, Cardiff, United Kingdom; [4]School of Medicine, Cardiff University, Cardiff, United Kingdom; [5]Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom; [6]Genomics Facility, NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London, London, United Kingdom; [7]Copenhagen University Hospital, Copenhagen, Denmark; [8]Bristol Haematology and Oncology Centre, University Hospitals of Bristol and Weston NHS Trust, Bristol, United Kingdom; [9]Department of Haematology, University College Hospital, London, United Kingdom; [10]Department of Haemato-Oncology, Barts Health NHS Trust, St Bartholomew's Hospital, London, United Kingdom; [11]Department of Haematology, Auckland Hospital, Auckland, New Zealand; [12]Clinical Haematology, Belfast City Hospital, Belfast, Northern Ireland; and [13]The Christie NHS Foundation Trust, Manchester, United Kingdom

- **The high-risk cohort of the UK NCRI AML19 trial (ISRCTN78449203) compared CPX-351 with FLAG-Ida in younger adults with newly diagnosed adverse cytogenetic AML or high-risk myelodysplastic syndromes (MDS).**
- **A total of 189 patients were randomized (median age, 56 years).**

	FLAG-IDA (n = 82)	CPX-351 (n = 105)
Cytogenetics + FISH*		
Complex ≥3 abnormalities	43 (54%)	51 (50%)
Complex ≥4 abnormalities	40 (51%)	49 (48%)
–5 / del5q / add5q	32 (40%)	45 (43%)
–7 / del7q / add7q	36 (45%)	46 (44%)
–17 / abn17p	12 (15%)	25 (24%)
11q23	6 (8%)	8 (7.7%)
3q21	3 (4%)	6 (5.8%)
MDS-related cytogenetics (WHO 2016)	60 (75%)	74 (71%)
Cytogenetic risk group (MRC 2010)		
Adverse	69 (84%)	87 (83%)
Intermediate	11 (13%)	17 (16%)

Key Points

- In high-risk AML and MDS, CPX-351 did not improve response or survival compared with FLAG-Ida but produced better relapse-free survival.
- In the exploratory subgroup of patients defined by the presence of mutations in MDS-related genes, CPX-351 improved OS.

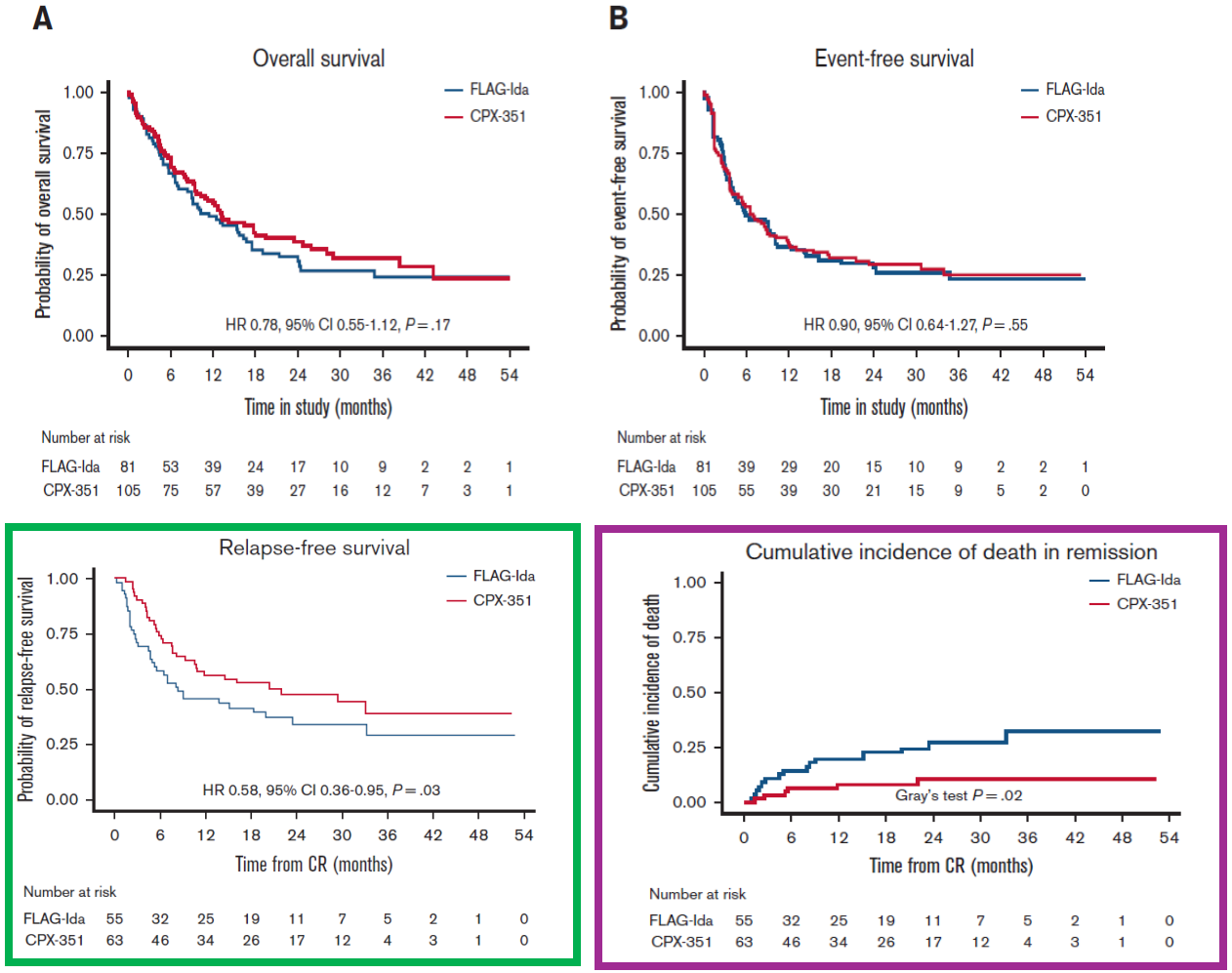
blood advances

22 AUGUST 2023 • VOLUME 7, NUMBER 16

ELN 2022 risk group		
Adverse	78 (95%)	99 (94%)
Intermediate	3 (4%)	5 (5%)
Missing	1 (1%)	1 (1%)

Table 2. Response and outcomes in each group (FLAG IDA/CPX)

	FLAG-IDA (n = 82)	CPX-351 (n = 105)
Response after cycle 1		
CR	42 (51%)	42 (40%)
CRi	11 (13%)	12 (11%)
ORR (CR + CRi)	53 (65%)	54 (51%)
Best response after 2 cycles		
CR	55 (68%)	63 (60%)
CRi	7 (9%)	4 (4%)
ORR (CR+CRi)	62 (77%)	67 (64%)
Allogeneic transplant		
Allogeneic transplant at any time	36 (44%)	53 (50%)
Allogeneic transplant in first response*	30 (48%)	43 (64%)



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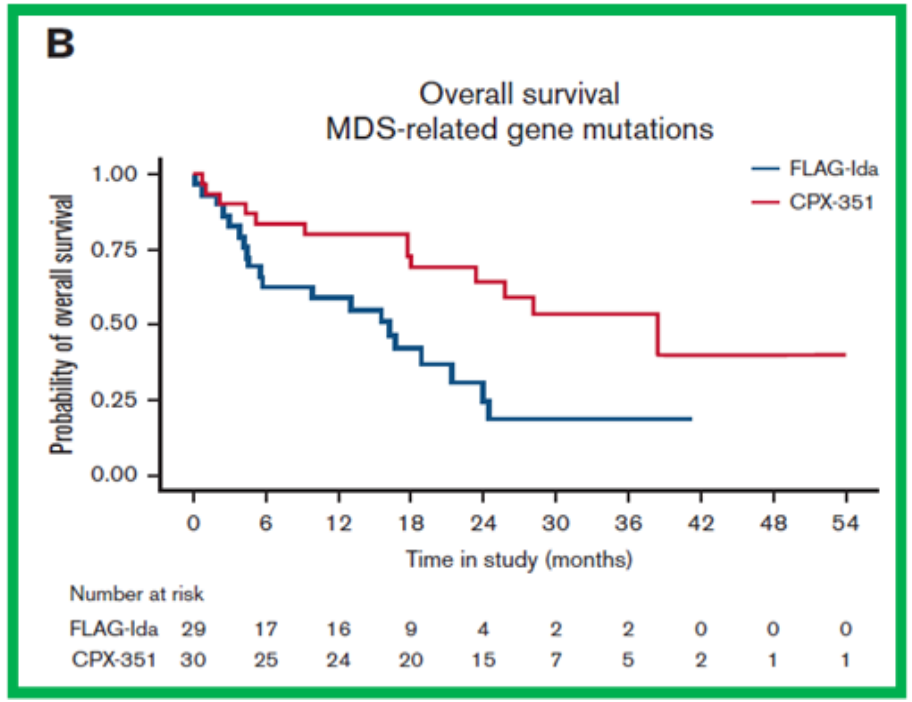
A Randomised Comparison of CPX-351 and FLAG-Ida in Adverse Karyotype AML and High-Risk MDS: The UK NCRI AML19 Trial

1. In high-risk AML and MDS CPX-351 did not improve response or survival compared to FLAG-Ida but produced better relapse-free survival

2. In the exploratory sub-group of patients defined by the presence of mutations in MDS-related genes CPX-351 improved overall survival

Othman J et al, Blood Adv 2023



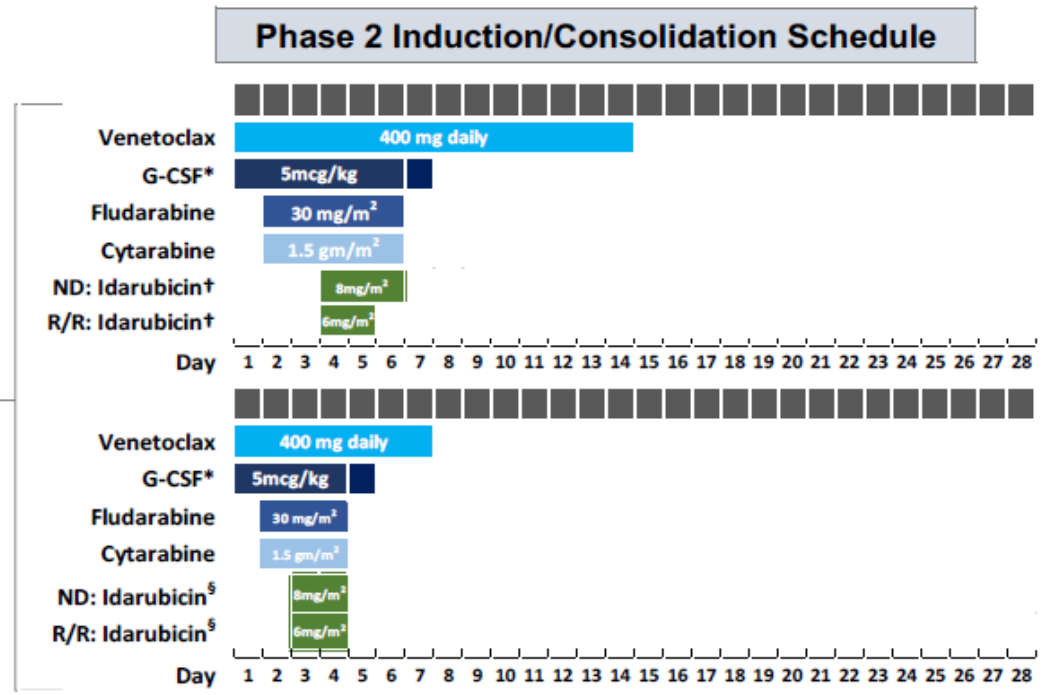
FLAG-IDA-VEN: Study Cohorts and Treatment Schedule, DiNardo et al, Am J Hematol, 2022. ?Alternative to '3=7"

Phase 1b	Phase 2A	Phase 2B
R/R-AML	ND-AML	R/R-AML
N=16	N=29	N=23

Induction	Consolidation
Venetoclax 400 mg D1-14	Venetoclax 400 D1-7
G-CSF D1-6	G-CSF D1-4
Pegfilgrastim or biosimilar D7	Pegfilgrastim or biosimilar D5
Fludarabine 30 mg/m^2 D2-6	Fludarabine 30 mg/m^2 D2-4
Cytarabine 1.5 gm/m^2 D2-6	Cytarabine 1.5 gm/m^2 D2-4
ND: Idarubicin 8 mg/m^2 D4-6	ND: Idarubicin 8 mg/m^2 D3-4
R/R: Idarubicin 6 mg/m^2 D4-5	R/R: Idarubicin 6 mg/m^2 D3-4

Phase 1b		Phase 2
Cytarabine 2 gm/m^2	RP2D*	**Cytarabine 1.5 gm/m^2**
Venetoclax D1-21		**Venetoclax D1-14**

* 5/6 initially enrolled P1b patients developed bacteremia/sepsis with P1b dosing



*G-CSF: 5 mcg/kg the day prior to and days of IV chemotherapy followed by 1 dose of pegfilgrastim or biosimilar each 28 D cycle
† Induction: ND-AML: Idarubicin 8 mg/m^2 days 4-6, R/R-AML Idarubicin 6 mg/m^2 days 4 and 5
§ Consolidation: Idarubicin permitted on days 3 and 4 in 2 post-remission cycles (ie. C2 or C3 and C5 or C6) at physician discretion

RESEARCH ARTICLE

Courtney D. DiNardo

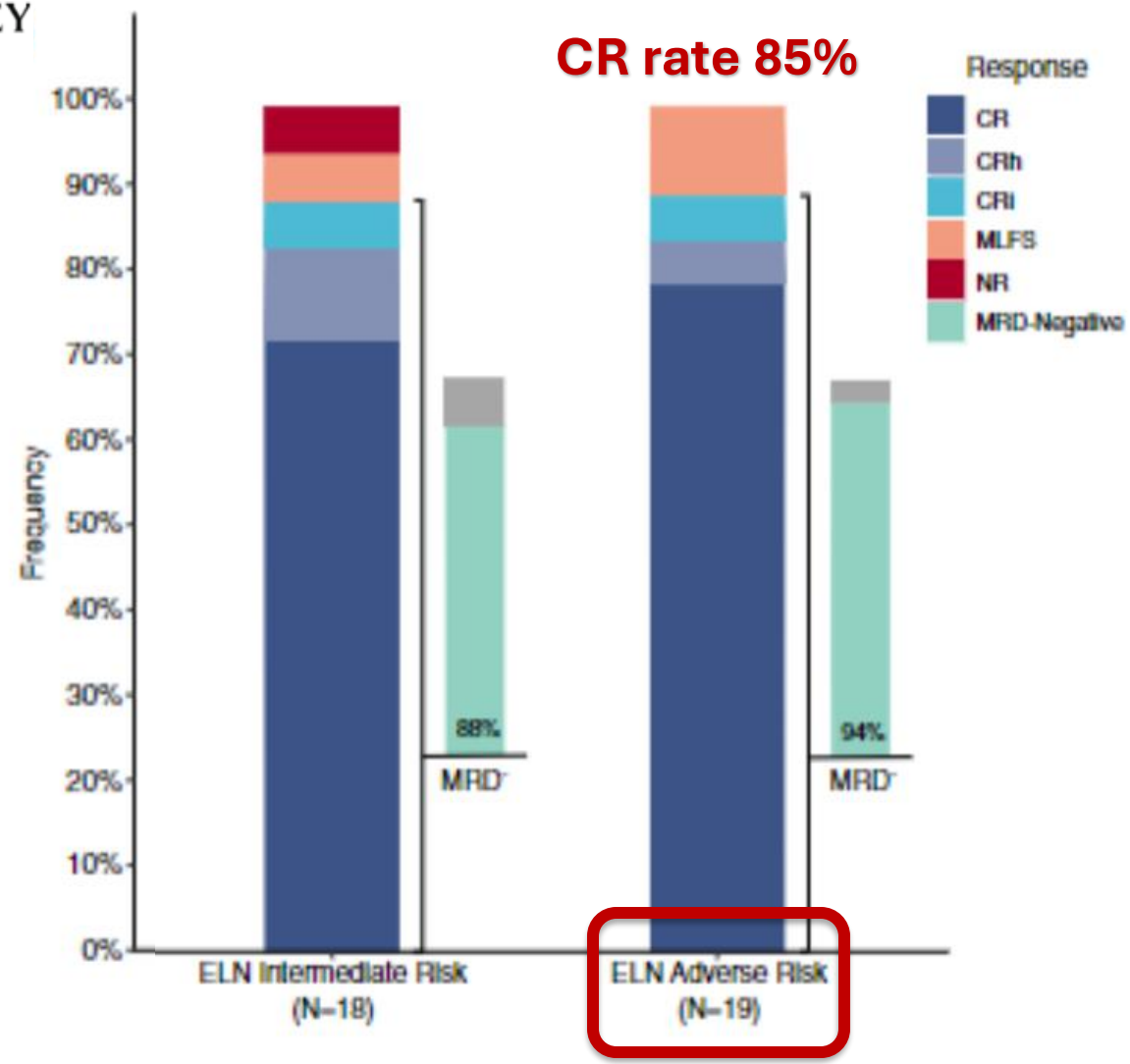
AJH WILEY

Venetoclax combined with FLAG-IDA induction and consolidation in newly diagnosed acute myeloid leukemia

TABLE 1 Patient demographics

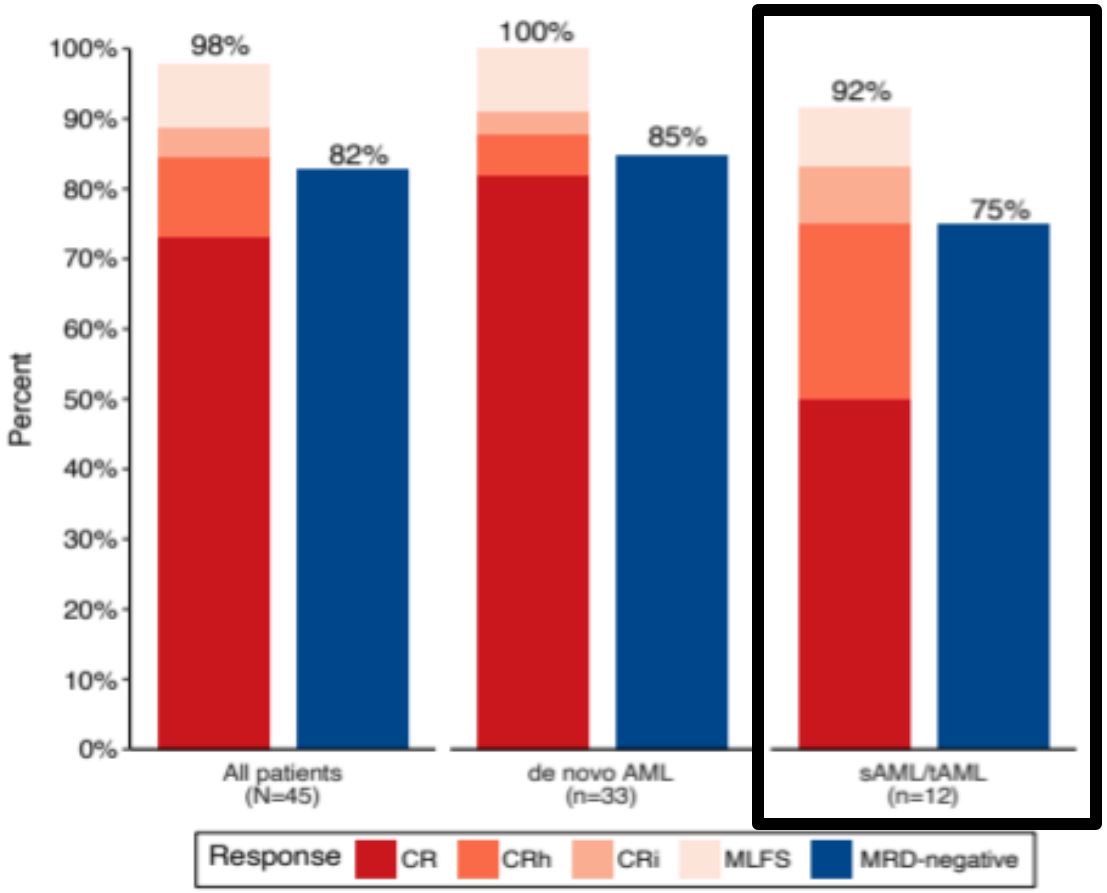
Parameter[a]	Phase 2A ND-AML (N = 45)
Age (range)	44 (20–65)
ELN 2017 risk group	
Favorable	8 (18)
Intermediate	18 (40)
Adverse	19 (42)

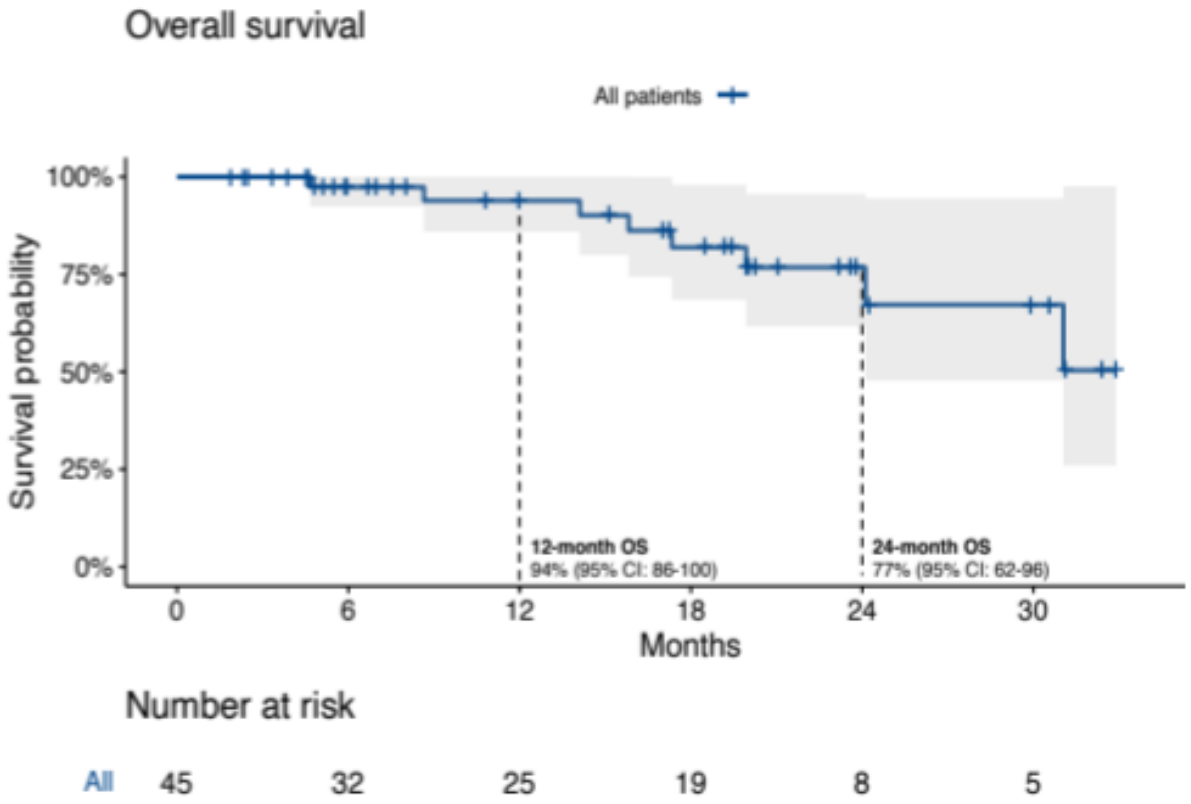
CR rate 85%



Am J Hematol. 2022;97:1035–1043.

FLAG-IDA + Venetoclax : Frontline





DiNardo et al, Am J Hematol, 2022

ALTO RISCHIO, FIT, 60-70 aa FLT3 ITD MUTATO
3/7 + FLT3i o CPX ?

RATIFY MIDOSTAURINA	QUANTUM FIRST QUIZARTINIB	CPX 351
Pz > 60 aa = 0%	Pz > 60 aa = 40%	Pz > 60 aa= 100%
HR (ELN 2017) = 7%	**HR (ELN 2017)= 7%**	HR
Secondary AML = NR	**Secondary AML= 9%**	**FLT3 POS=16% in entrambi i bracci (22 e 21 pz)**
NO DATA to DECIDE !!	**FEW DATA !!**	**CPX-351 migliore OS vs 3/7 nei pochi FLT3 +**

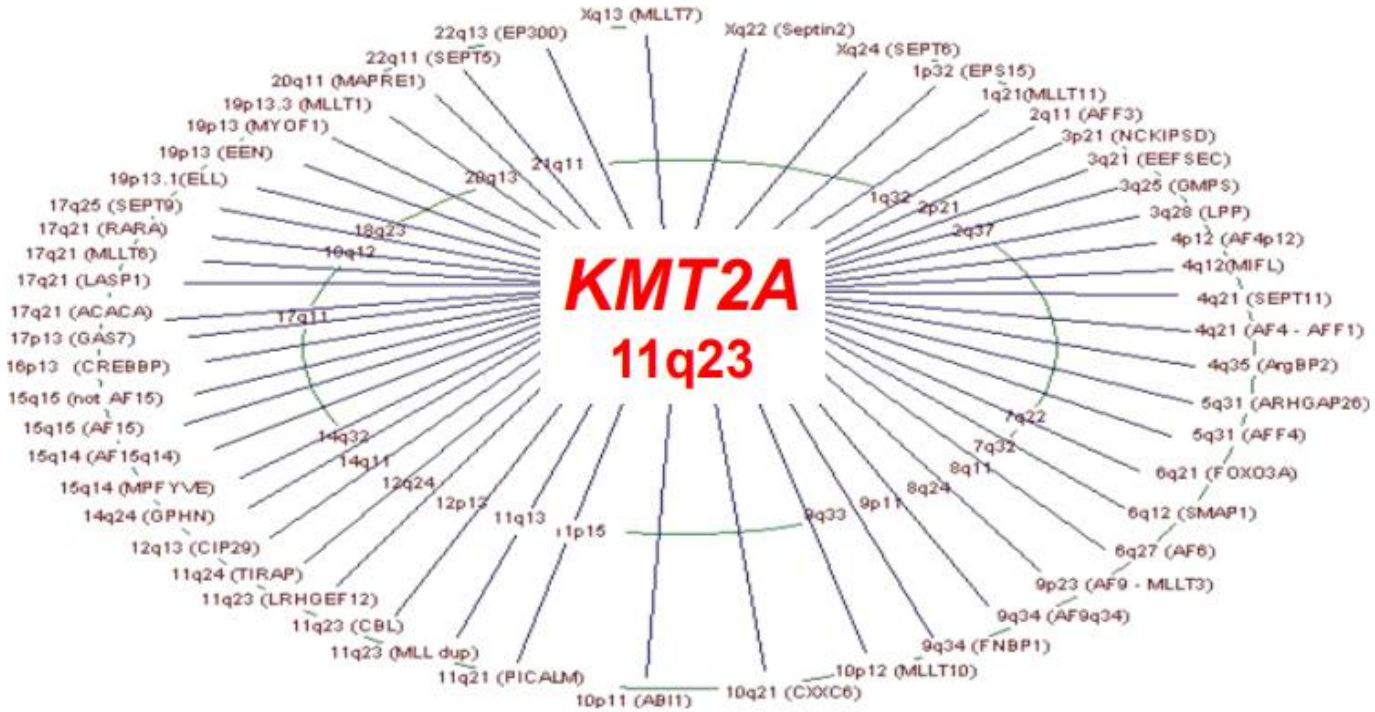
Baseline Disease Characteristics (QuANTUM-First)

Disease Characteristics	Quizartinib (N=268)[a]	Placebo (N=271)[a]
ECOG performance status, %[b]		
0	32.5	36.2
1	50.0	50.2
2	17.5	13.3
Cytogenetic risks, %		
Favorable	5.2	7.0
Intermediate	73.5	71.2
Unfavorable	7.1	10.0
Unknown	14.2	11.4
Missing	0	0.4
Mutated *NPM1*	53.0	51.7
***FLT3*-ITD/total *FLT3*, %[c,d]**		
≥3% to ≤25%	35.1	36.2
>25% to ≤50%	53.4	50.9
>50%	11.2	12.9
WBC count at diagnosis of AML, %		
<40×10^9/L	50.4	50.6
≥40×10^9/L	49.6	49.4

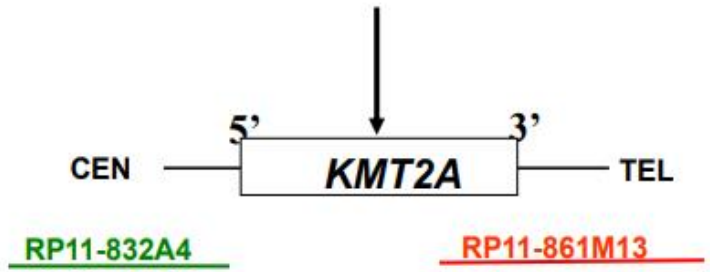
AML, acute myeloid leukemia; ECOG, Eastern Cooperative Oncology Group; FLT3, fms related receptor tyrosine kinase 3; ITD, internal tandem duplication; *NPM1*, nucleophosmin; WBC, white blood cell.
[a] Three patients in the ITT set were randomized but not treated in each arm. [b] One patient in the placebo group was missing an ECOG status. [c] Variant allele frequency was assessed by central lab testing. [d] One patient with unknown

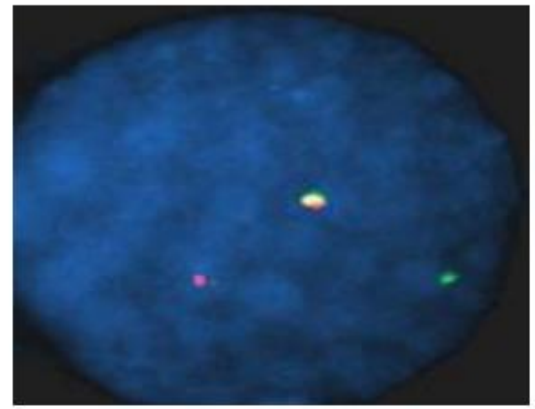
KMT2A (MLL) FUSION PARTNERS

> 80 PARTNERS



Leukemia 2006



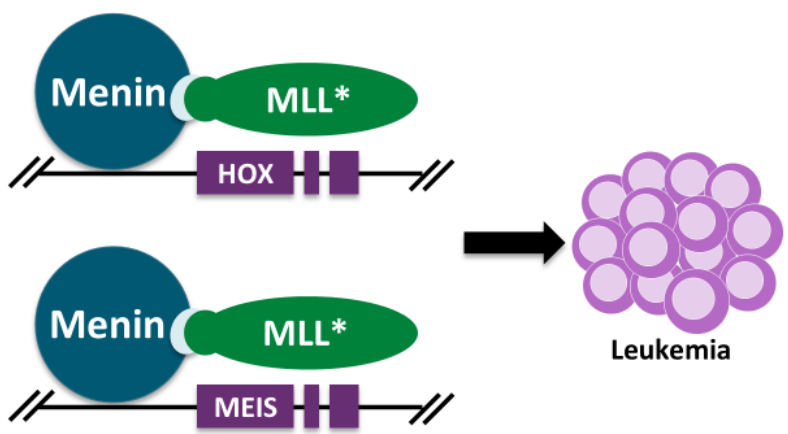


SPLIT RED/GREEN SIGNALS

PROGNOSIS may depend upon the PARTNER

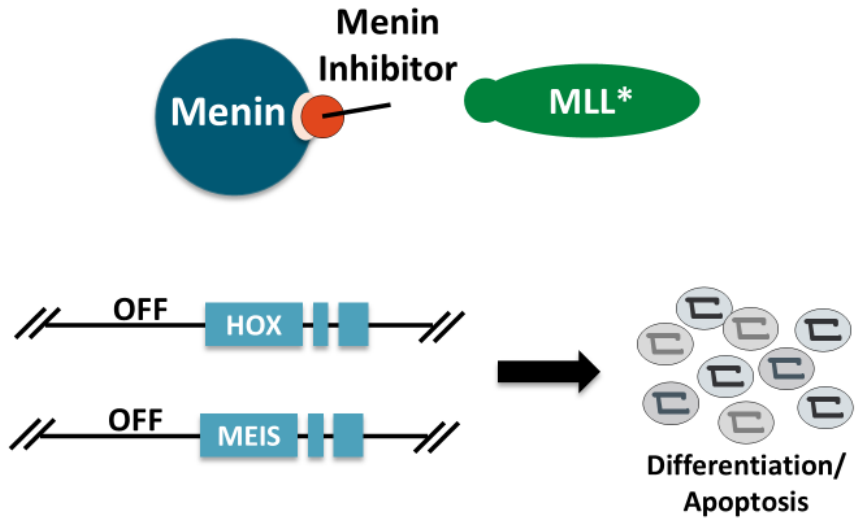
Pathogenesis of *KMT2A*-Rearranged and *NPM1*-Mutant Acute Leukemias and Menin Inhibitors

MLLr Acute Leukemias



Gene transcription ON

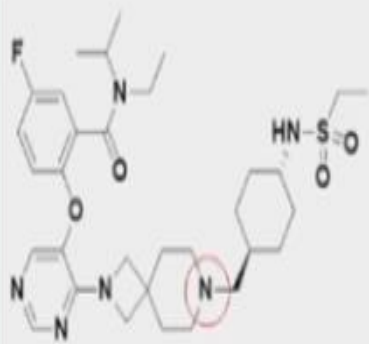
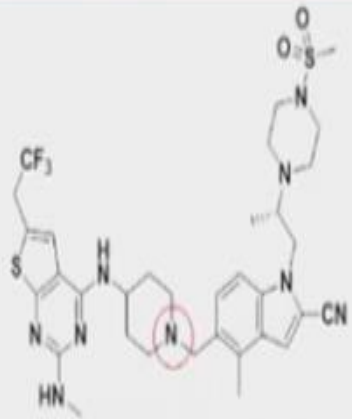
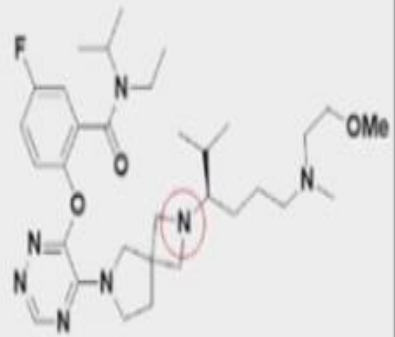
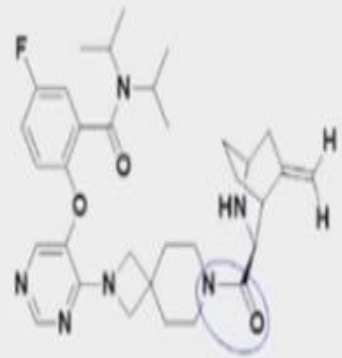
Menin Inhibitor



Gene transcription OFF

*MLL = MLLr or MLL1 wild type.

Thorsteinsdottir. Mol Cell Biol. 2001;21:224. Grembecka. Nat Chem Biol. 2012;8:277.
Uckelmann. Science. 2020;367:586. Krivtsov. Cancer Cell. 2019;36:660. Issa. Nature. 2023;615:920.

Revumenib	Ziftomenib	Bleximenib	Enzomenib
			
Tertiary amine bond	Tertiary amine bond	Tertiary amine bond	**Amide bond**

r Biotechnology Information (2024). PubChem Compound Summary for CID 132212657, 138497449, 156498110, 146430058

- **Menin inhibitors are an exciting new class of targeted therapies for *NPM1*-mutated and *KMT2Ar* AML**
  - Revumenib first menin inhibitor FDA-approved for treatment of R/R acute leukemia patients with *KMT2Ar*
- **Frontline treatment approaches and combination studies with menin inhibitors ongoing**

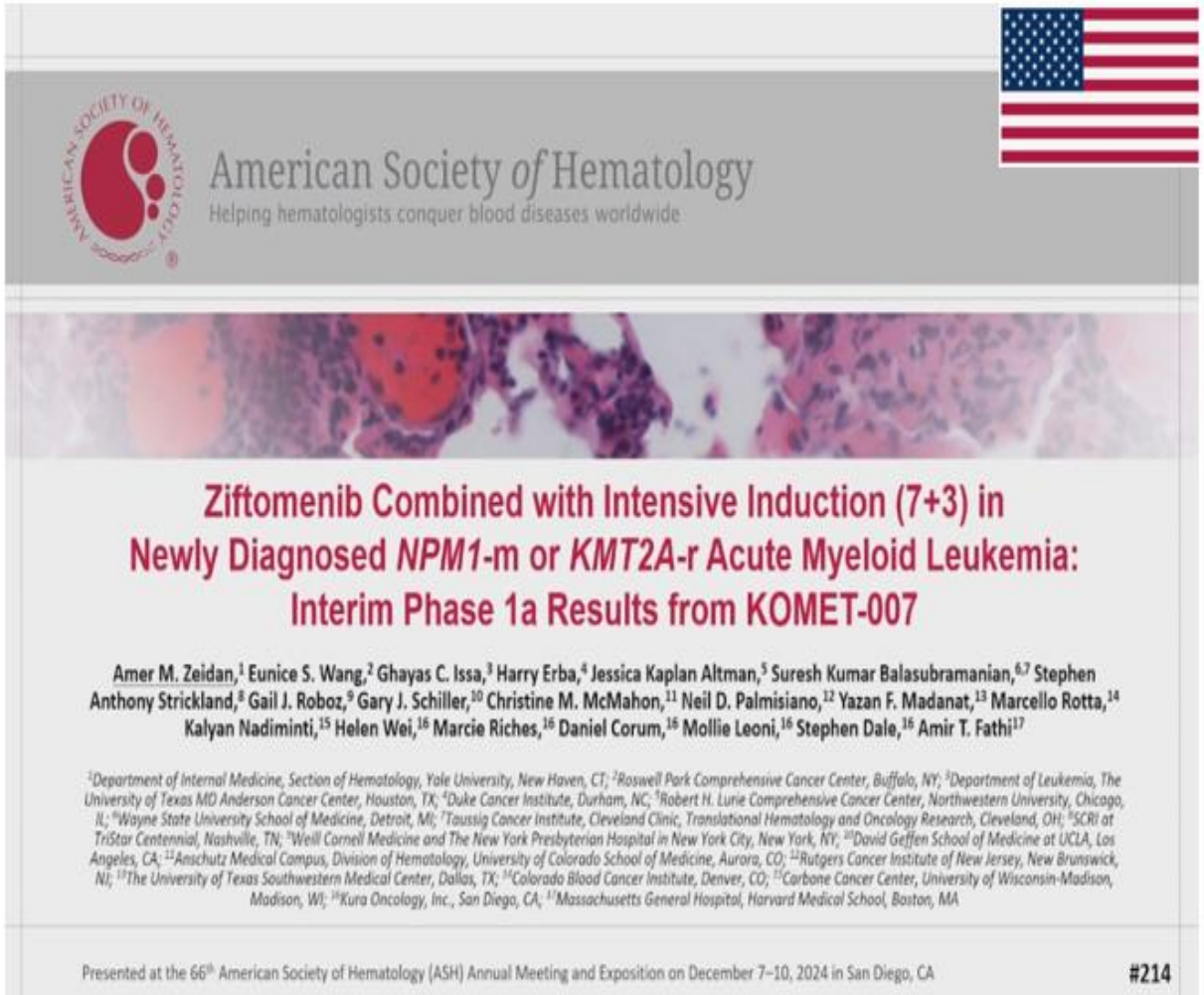
Menin Inhibitors in R/R AML: Efficacy

Parameter	Revumenib[1] (n = 97)	Ziftomenib[2] (n = 20)	Bleximenib[3] (n = 33)	Enzomenib[4] (n = 40)
Trial name	AUGMENT-101	KOMET-001	ALE1001	DSP-5336-101
Trial phase reported	II	I	I	I
Drug dose	163 mg BID with CYP450 inhibitor	600 mg QD	90-100 mg BID	200-300 mg BID
Patients with *KMT2A*r AML, n (%)	97 (100)	N/A	19 (58)	23 (57)
Patients with *NPM1*m AML, n (%)	N/A	20 (100)	14 (42)	17 (43)
Response rate, n (%)	**Revumenib[1] (n = 97)**	**Ziftomenib[2] (n = 20)**	**Bleximenib[3] (n = 33)**	**Enzomenib[4] (n = 40)**
CR, n (%)	15 (15.5)	7 (35)	6 (18)	NA
CR/CRh, n (%)	13 (22.7)	7 (35)	7 (21)	15 (37.5)
CRc (CR/CRh/CRi), n (%)	24 (24.7)	8 (40)	9 (27)	19 (42.5)
ORR (CRc +PR + MLFS), n (%)	62 (63.9)	9 (45)	15 (46)	25 (62.5)

1. Aldoss. ASH 2024. Abstr 211. 2. Wang. Lancet Oncol. 2024;25:1310.
3. Searle. ASH 2024. Abstr 212. 4. Zeidner. ASH 2024. Abstr 213.

Slide credit: clinicaloptions.com

ZIFTOMENIB + 3/7



American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Ziftomenib Combined with Intensive Induction (7+3) in Newly Diagnosed *NPM1*-m or *KMT2A*-r Acute Myeloid Leukemia: Interim Phase 1a Results from KOMET-007

Amer M. Zeidan,[1] Eunice S. Wang,[2] Ghayas C. Issa,[3] Harry Erba,[4] Jessica Kaplan Altman,[5] Suresh Kumar Balasubramanian,[6,7] Stephen Anthony Strickland,[8] Gail J. Roboz,[9] Gary J. Schiller,[10] Christine M. McMahon,[11] Neil D. Palmisiano,[12] Yazan F. Madanat,[13] Marcello Rotta,[14] Kalyan Nadiminti,[15] Helen Wei,[16] Marcie Riches,[16] Daniel Corum,[16] Mollie Leoni,[16] Stephen Dale,[16] Amir T. Fathi[17]

[1]Department of Internal Medicine, Section of Hematology, Yale University, New Haven, CT; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [3]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Duke Cancer Institute, Durham, NC; [5]Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL; [6]Wayne State University School of Medicine, Detroit, MI; [7]Taussig Cancer Institute, Cleveland Clinic, Translational Hematology and Oncology Research, Cleveland, OH; [8]SCRI at TriStar Centennial, Nashville, TN; [9]Weill Cornell Medicine and The New York Presbyterian Hospital in New York City, New York, NY; [10]David Geffen School of Medicine at UCLA, Los Angeles, CA; [11]Anschutz Medical Campus, Division of Hematology, University of Colorado School of Medicine, Aurora, CO; [12]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; [13]The University of Texas Southwestern Medical Center, Dallas, TX; [14]Colorado Blood Cancer Institute, Denver, CO; [15]Carbone Cancer Center, University of Wisconsin-Madison, Madison, WI; [16]Kura Oncology, Inc., San Diego, CA; [17]Massachusetts General Hospital, Harvard Medical School, Boston, MA

Presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition on December 7–10, 2024 in San Diego, CA #214

ABS N°214-Oral

N° CASES: 51 (Adverse Risk)

27 KMT2A, 24 NPM1

RESPONSE:

- CR RATE 92% (in both groups)
- MRD Neg 76%

SAFETY:

- 7/3 + ZIFTO = 7/3 ALONE
- NO TRM

Brief Follow-up (31 w)

- Median OS: NR
- Median duration CR: NR

BLEXIMENIB + 3/7

Phase 1b Study of Menin-KMT2A Inhibitor Bleximenib in Combination with Intensive Chemotherapy in Newly Diagnosed Acute Myeloid Leukemia with *KMT2Ar* or *NPM1* Alterations

Christian Recher, MD, PhD[1]; Jenny O'Nions, PhD, BMBCh, FRCPath[2]; Ibrahim Aldoss, MD[3]; Ana Alfonso Piérola, MD, PhD[4]; Alicia Allred[5]; Juan Manuel Alonso-Dominguez, MD, PhD[6]; Laura Barreyro, PhD[5]; Pierre Bories, MD, PhD[7]; Martin Curtis[8]; Nikki Daskalakis, MD[3]; Matteo G. Della Porta, MD[9]; Hartmut Döhner, MD[10]; Amber D'Souza, MD[5]; James Dugan, MD[11]; Jordi Esteve, MD, PhD[12]; Matthew Exum, MSN[5]; Amir T. Fathi, MD[13]; Pasquale L. Fedele, MBBS, PhD, FRACP, FRCPA[14]; Lucille Ferrante, MD, MS[5]; Stan Gaj, MS[15]; Sylvain Garciaz, MD, PhD[16]; Ana Garrido Diaz, MD[17]; Sara Garrido Paniagua, MD[18]; Christina Guttke, PhD[5]; Emmanuel Gyan, MD, PhD[19]; Brett Hiebert, MS[20]; Elias Jabbour, MD[21]; Madlen Jentzsch, MD[22]; Hagop M. Kantarjian, MD[21]; Marina Konopleva, MD, PhD[23]; Jan Krönke, MD[24]; Min Chul Kwon, PhD[15]; Christina Loefgren, MD, PhD[5]; Oliver Lomas, BMBCh, MRCP, FRCPath, DPhil[25]; Valentina Mancini, MD[26]; Ioannis Mantzaris, MD, MS[22]; Giovanni Martinelli, MD[27]; Daniel Morillo, MD[6]; Joseph Murphy, BSc[25]; Kathryn Packman, PhD[28]; Cristina Papayannidis, MD, PhD[29]; Ulrike Philippar, PhD[15]; Uwe Platzbecker, MD[22]; Sravanti Rangaraju, MD[30]; Christoph Röllig, MD, MSci[31]; Olga Salamero, MD[18]; Madhu Sanga, PhD[32]; Tim Sauer, MD[33]; Emma Searle, MD, PhD[34]; Natalia Tovar, MD, PhD[12]; Trevor Tucker, BS[5]; Nicolas Vallet, MD, PhD[19]; Lachlin Vaughan, MD[35]; Gala Vega, MD[4]; Paresh Vyas, DPhil, FRCP, FRCPath, FMedSci[36]; Andrew H. Wei, MBBS, PhD[37]

[1]University Cancer Institute Toulouse Oncopole, Toulouse, France; [2]University College London Hospitals NHS Foundation Trust, London, UK; [3]City of Hope National Medical Center, Duarte, CA, USA; [4]Clínica Universidad de Navarra, Navarra, Spain; [5]Janssen Research & Development, LLC, Spring House, PA, USA; [6]Hospital Universitario Fundación Jiménez Díaz, IIS-FJD, Madrid, Spain; [7]Oncopole Claudius Regaud, Institut Universitaire du Cancer Toulouse, Toulouse, France; [8]Janssen Research & Development, LLC, Durham, NC, USA; [9]IRCCS Humanitas Research Hospital and Humanitas University, Milan, Italy; [10]Ulm University Hospital, Ulm, Germany; [11]Janssen Research & Development, LLC, Raritan, NJ, USA; [12]Hospital Clínic de Barcelona, Barcelona, Spain; [13]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [14]Monash Health and School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia; [15]Janssen Research & Development, LLC, Beerse, Belgium; [16]Aix-Marseille Université, Inserm, CNRS, Institut Paoli-Calmettes, Centre de Recherche en Cancérologie de Marseille, Marseille, France; [17]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [18]University Hospital Vall d'Hebron, and Experimental Hematology, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [19]Centre Hospitalier Universitaire de Tours, Tours, France; [20]IQVIA, Whitby, ME, Canada; [21]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [22]Klinik und Poliklinik für Hämatologie, Zelltherapie und Hämostaseologie, Universitätsklinikum Leipzig, Leipzig, Germany; [23]Albert Einstein College of Medicine, Bronx, NY, USA; [24]Charité – Universitätsmedizin Berlin, Berlin, Germany; [25]Janssen Research & Development, LLC, High Wycombe, UK; [26]AOU Ospedale Niguarda Milano, Milan, Italy; [27]University of Bologna Hematological Institute, Bologna, Italy; [28]Janssen Research & Development, LLC, Cambridge, MA, USA; [29]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy; [30]University of Alabama, Birmingham, AL, USA; [31]Universitätsklinikum TU Dresden, Dresden, Germany; [32]Janssen Research & Development, LLC, Spring House, PA, USA; [33]University Hospital Heidelberg, Heidelberg, Germany; [34]The Christie NHS Foundation Trust and University of Manchester, Manchester, UK; [35]Westmead Hospital, Sydney, Australia; [36]Walter and Eliza Hall Institute of Medical Research and University of Melbourne, Melbourne, Australia

Presented by C Recher at the 66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA, USA

ABS N°215-Oral

N° CASES: 28 (13 KMT2A, 15 NPM1)

RESPONSE:

- **CR RATE 86% (in both groups)**
- **ORR 95% (in both groups)**

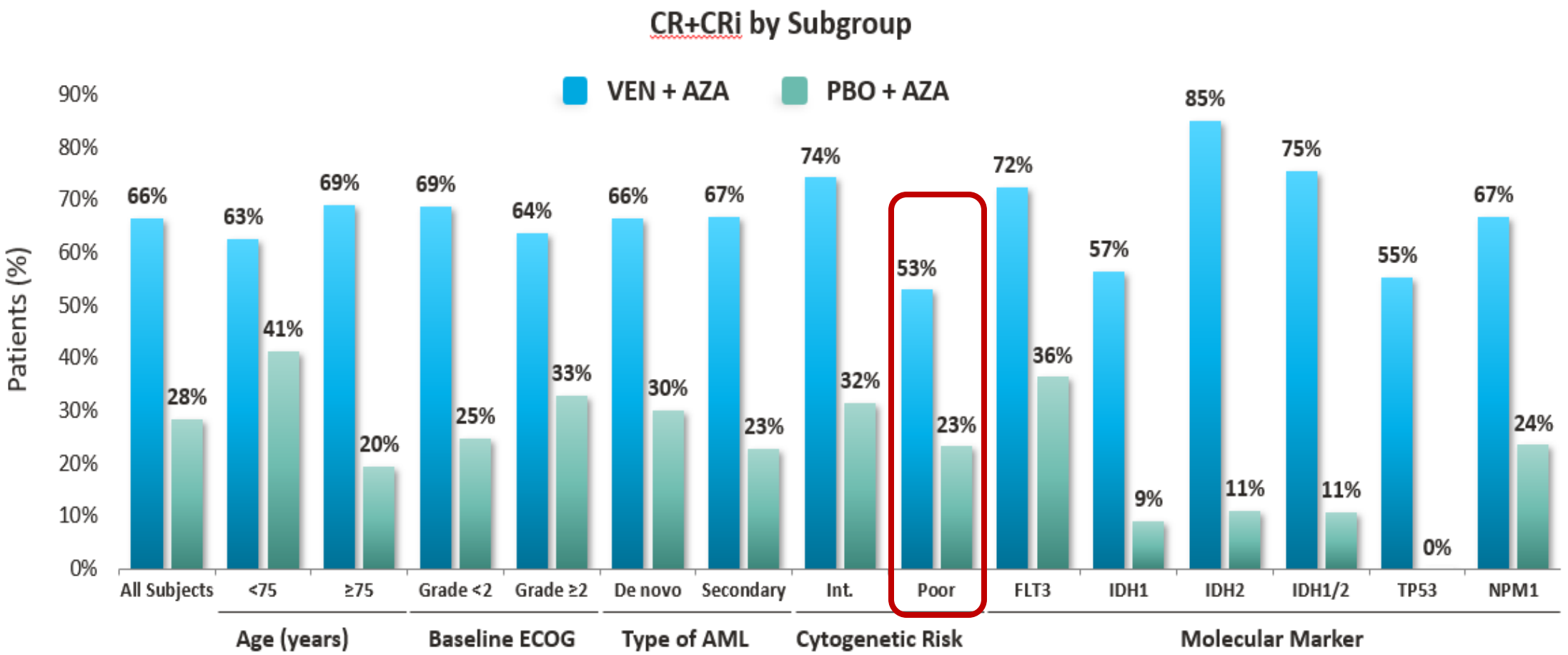
SAFETY:

- **7/3 + BLEXI = 7/3 ALONE**
- **NO TRM**

Brief Follow-up

Response by Subgroup

VIALE-A



Secondary Endpoint

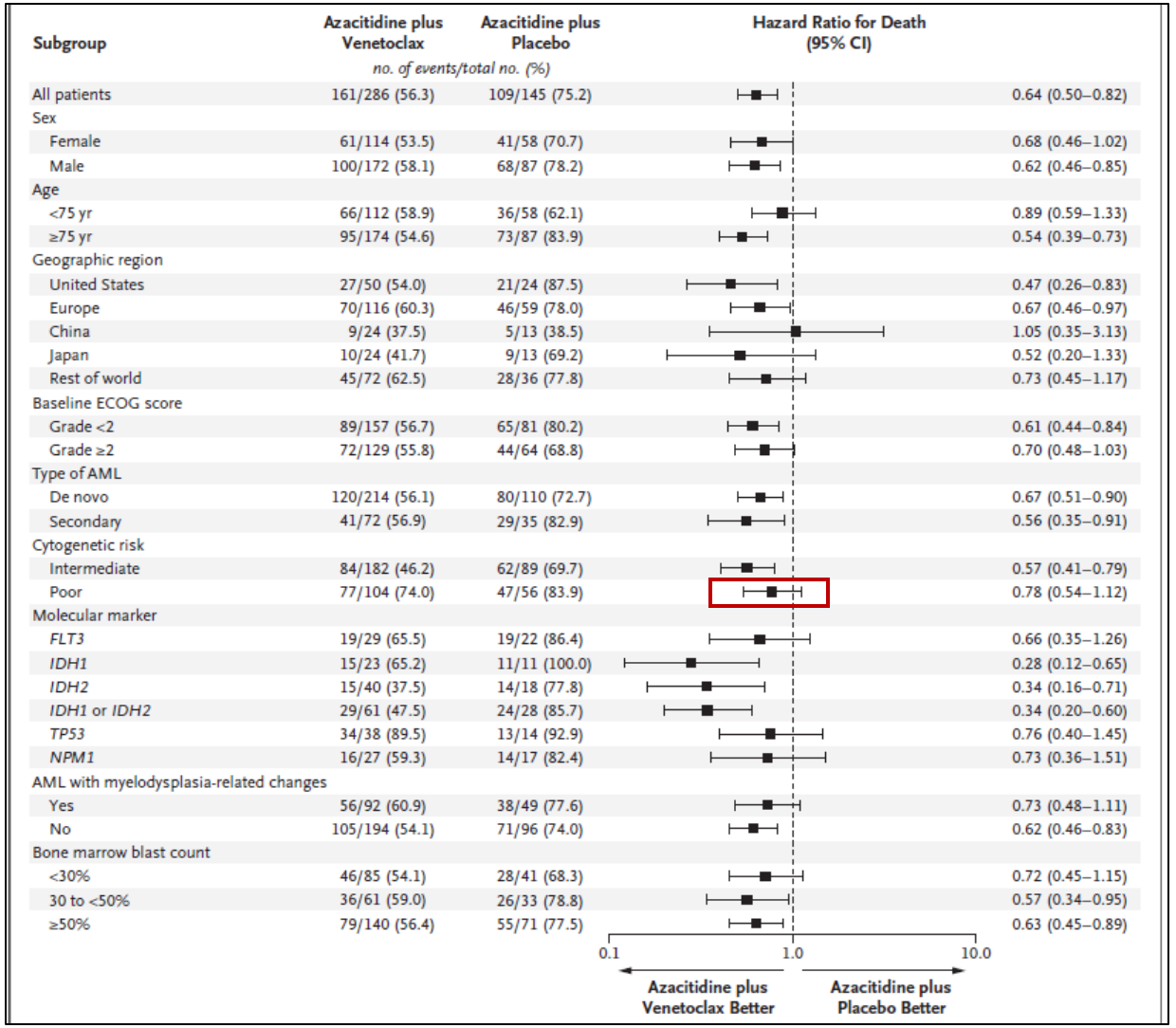
Data cutoff date: January 4, 2020.

DiNardo CD, et al. N Engl J Med. 2020;383(7):617-29 [suppl].

VIALE-A

Table 1. Baseline Demographic and Clinical Characteristics of the Patients.*

Characteristic	Azacitidine–Venetoclax Group (N=286)	Azacitidine–Placebo Group (N=145)
Age		
Median (range) — yr	76 (49–91)	76 (60–90)
≥75 yr — no. (%)	174 (61)	87 (60)
Male sex — no. (%)	172 (60)	87 (60)
AML type — no (%)		
De novo	214 (75)	110 (76)
Secondary	72 (25)	35 (24)
Secondary AML — no./total no. (%)		
History of myelodysplastic syndrome or CMML	46/72 (64)	26/35 (74)
Therapy-related AML	26/72 (36)	9/35 (26)
ECOG performance-status score — no. (%)†		
0–1	157 (55)	81 (56)
2–3	129 (45)	64 (44)
Bone marrow blast count — no. (%)		
<30%‡	85 (30)	41 (28)
≥30 to <50%	61 (21)	33 (23)
≥50%	140 (49)	71 (49)
AML with myelodysplasia-related changes — no. (%)	92 (32)	49 (34)
Cytogenetic risk category — no. (%)§		
Intermediate	182 (64)	89 (61)
Normal karyotype — no.	128	62
Trisomy 8; +8 alone — no.	13	10
Poor	104 (36)	56 (39)
7 or 7q deletion — no.	20	11
5 or 5q deletion — no.	46	22
Complex, ≥3 clonal abnormalities — no.	75	36



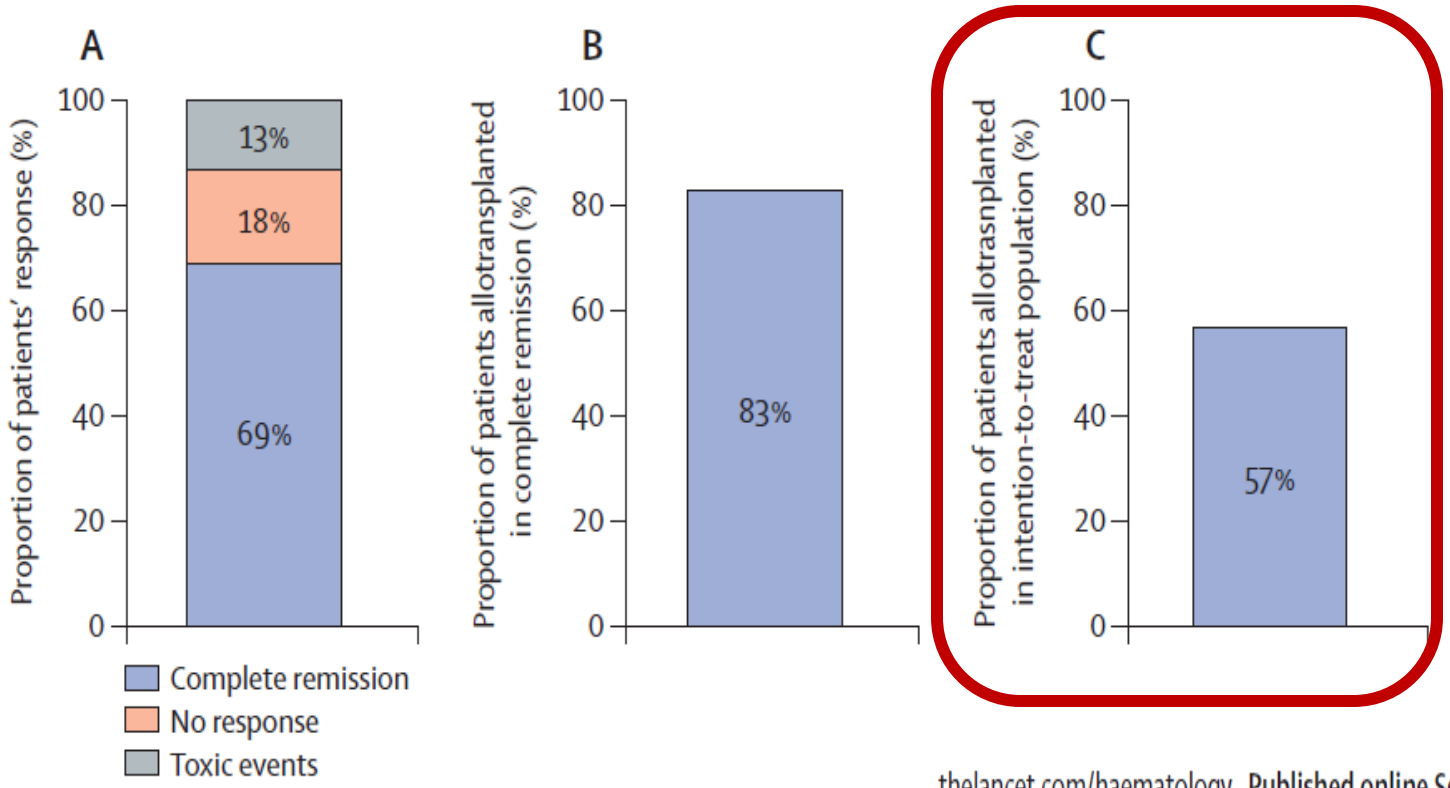
Venetoclax plus decitabine as a bridge to allogeneic haematopoietic stem-cell transplantation in older patients with acute myeloid leukaemia (VEN-DEC GITMO): final report of a multicentre, single-arm, phase 2 trial

Domenico Russo, Nicola Polverelli, Simona Bernardi, Stella Santarone, Mirko Farina, Erika Borlenghi, Francesco Onida, Luca Castagna, Stefania Bramanti, Angelo Michele Carella, Roberto Sorasio, Massimo Martino, Caterina Alati, Attilio Olivieri, Germana Beltrami, Antonio Curti, Calogero Vetro, Salvatore Leotta, Valentina Mancini, Elisabetta Terruzzi, Massimo Bernardi, Piero Galieni, Pellegrino Musto, Raffaella Cerretti, Luisa Giaccone, Cristina Skert, Vera Radici, Marika Vezzoli, Stefano Calza, Alessandro Leoni, Luca Garuffo, Cristian Bonvicini, Simone Pellizzeri, Michele Malagola, Fabio Ciceri

LIT→ BRIDGE TO SCT

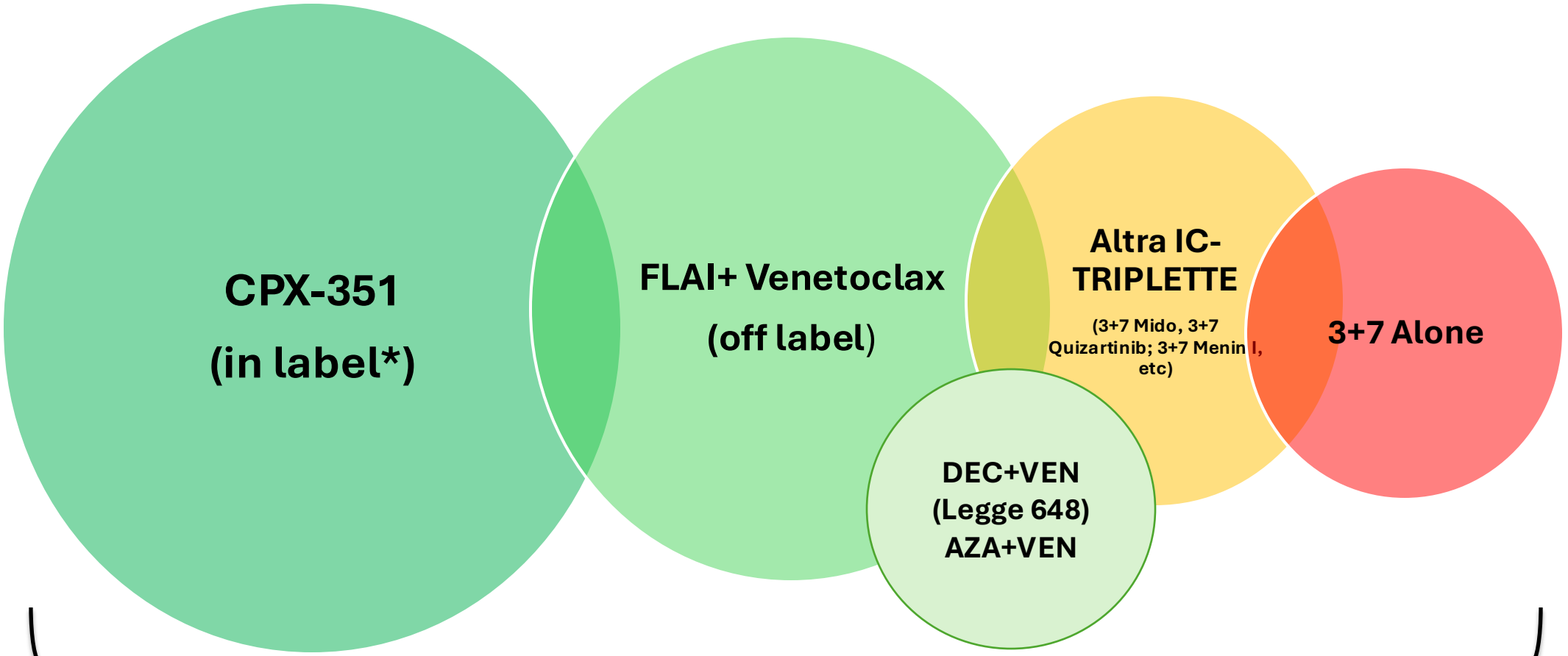
	Patients enrolled (n=93)
Age, years	68·5 (60·3–74·7)
Sex	
Male	50 (54%)
Female	43 (46%)
Race	
White	93 (100%)
Eastern Cooperative Oncology Group score	
0	54 (58%)
1	32 (34%)
2	7 (8%)
White blood cell count, ×10⁶/L	3·4 (1·8–23·9)
Platelet count, ×10⁹/L	53·0 (28·0–115·0)
Bone marrow blasts	40·0% (25·0–70·0)
Circulating blasts	8·0% (2·0–31·0)
Karyotype	
Normal	48 (52%)
Abnormal	41 (44%)
Complex	18 (19%)
Unavailable	4 (4%)
Molecular biology (RT-qPCR, nested-PCR, or HPLC)	
NPM1A	10 (11%)
FLT3-ITD	19 (20%)
FLT3-TKD (n=84)	1 (1%)

- ***primary endpoint was the proportion of patients who had allogeneic HSCT performed during first complete remission,***



thelancet.com/haematology Published online September 20, 2024

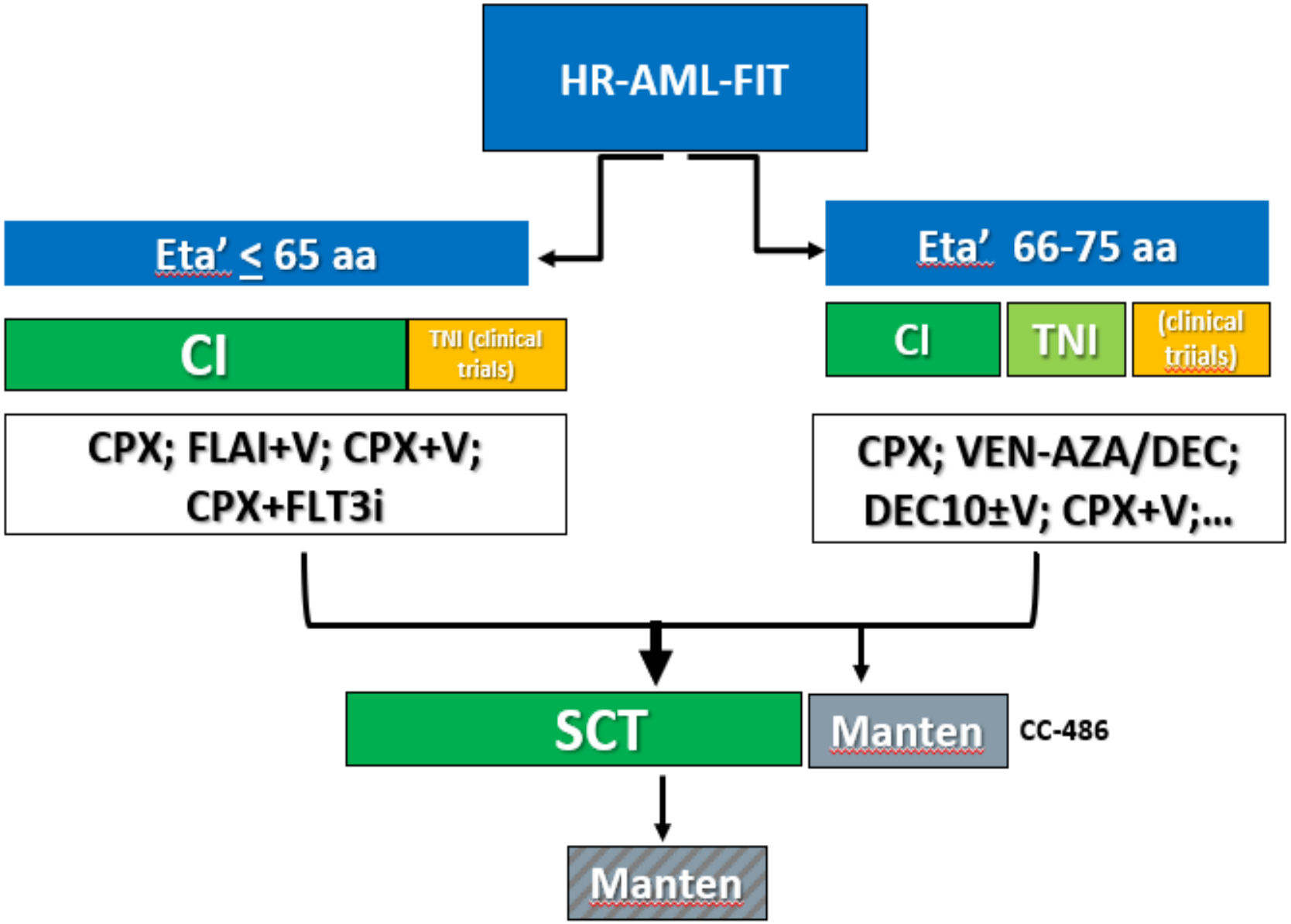
TERAPIA IN HR AML (FIT)



*è indicato per il trattamento di adulti con nuova diagnosi di leucemia mieloide acuta correlata a terapia (t-AML) o AML con alterazioni correlate a mielodisplasia (AML-MRC).

BRIDGE to Allo-SCT

ALGORITMO TERAPEUTICO
HR-AML FIT



REGIONE DEL VENETO
ULSS8 BERICA

Rete Ematologica Veneta

GIORNATE EMATOLOGICHE VICENTINE

XI edizione

9-10 ottobre 2025
Palazzo Bonin Longare - Vicenza

XI edizione

GIORNATE EMATOLOGICHE VICENTINE

Venerdì 10 ottobre 2025

SESSIONE 5
Leucemia acuta/trapianto

Moderatore: *M. Gottardi*

9:00 **DLI e terapie cellulari nel post-trapianto allogenico**
B. Rambaldi

09:30 **Il ruolo del trapianto di midollo nella LAL**
C. Skert

10:00 **L'induzione nella AML: quando preferisco l'inibitore di BCL2 alla chemioterapia standard**
G. Marconi

10:30 **Approccio terapeutico alle AML ad alto rischio citogenetico**
A. Candoni