



POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting
della Società Americana
di Ematologia

Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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ALGORITMI TERAPEUTICI 2026

LEUCEMIE MIELOIDI



ANNA CANDONI

UOC EMATOLOGIA-TREVISO



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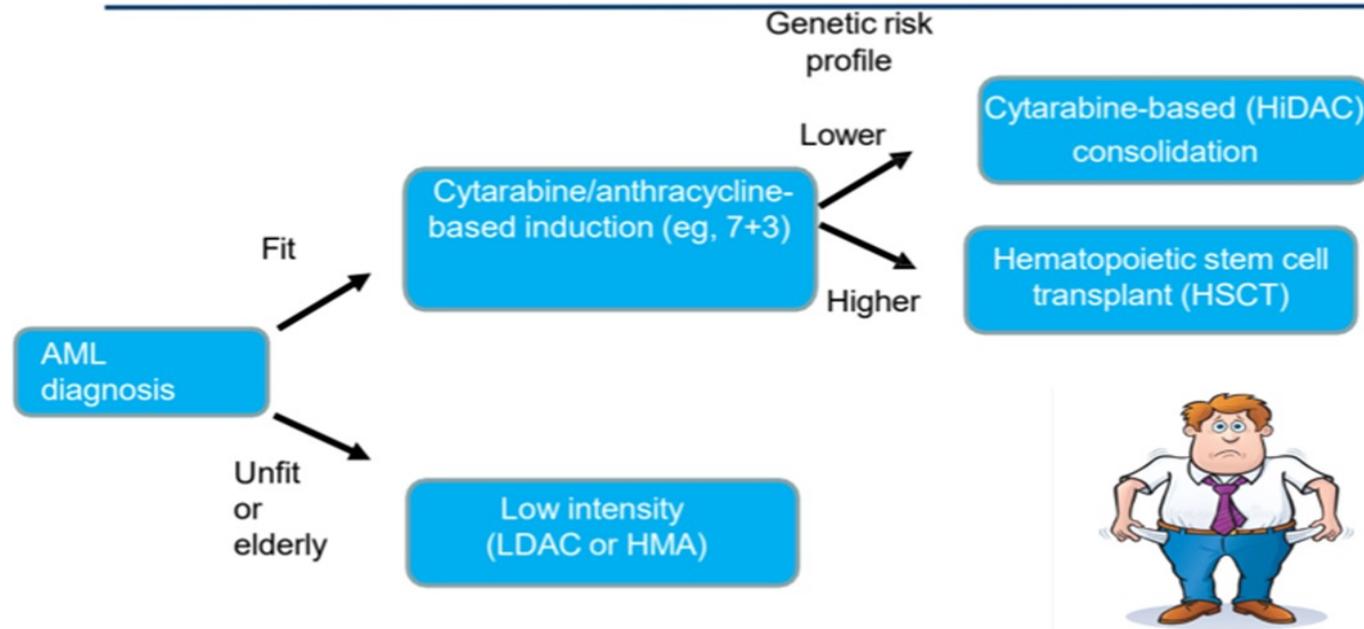
Torino, 19-21 Febbraio 2026

DICHIARAZIONE ANNA CANDONI

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Astellas			X			X	
Abbvie			X			X	
Beigene							X
Jazz			X			X	
Servier			X			X	
Pfizer			X			X	
Otsuka							X
Daiichi S						X	
Incyte						X	X



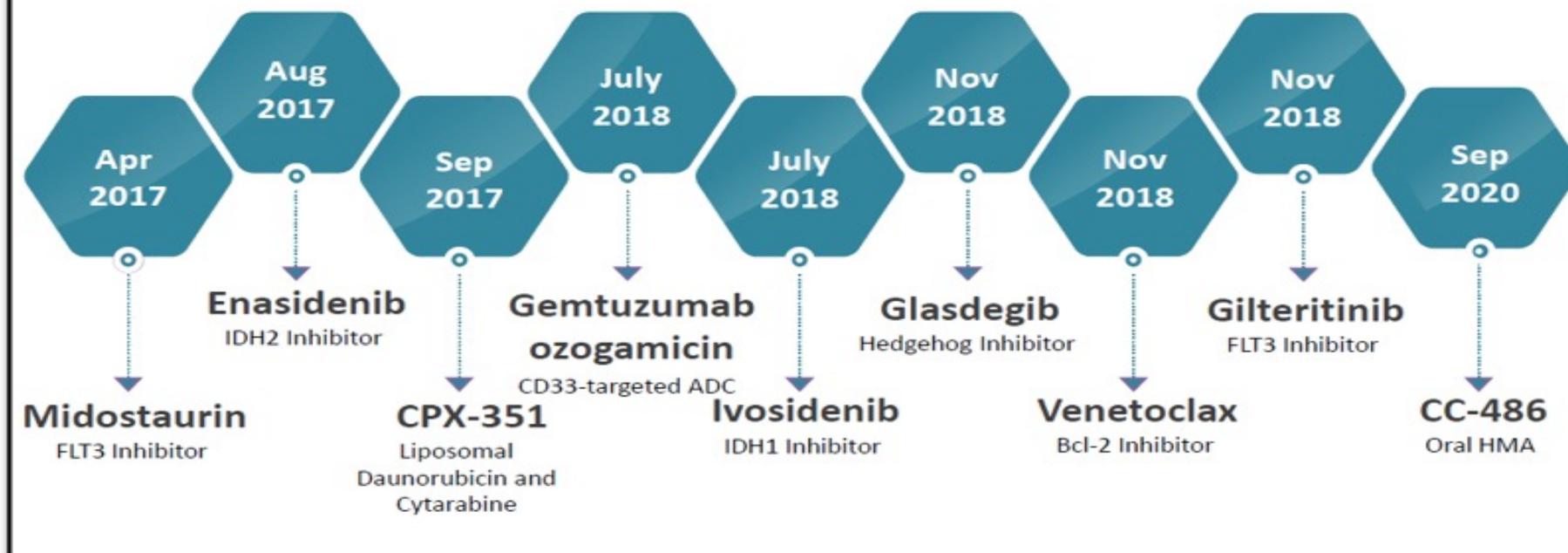
The Pre-2017 Paradigm (Dark Ages...Scientific Revolution)





2026

Personalizing AML Treatment: Recent Approvals



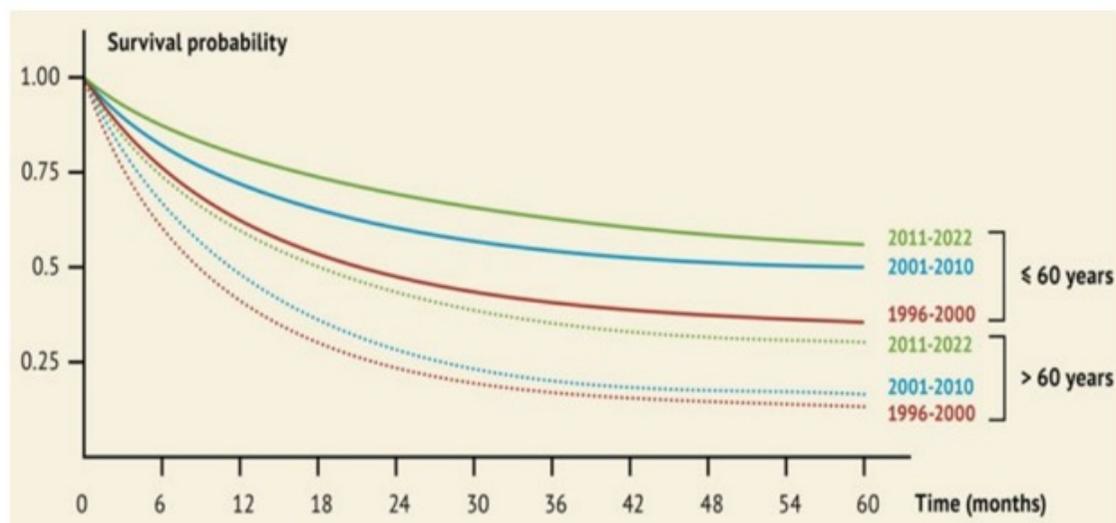


Improving long-term outcomes with intensive induction chemotherapy for patients with AML

Christoph Röllig

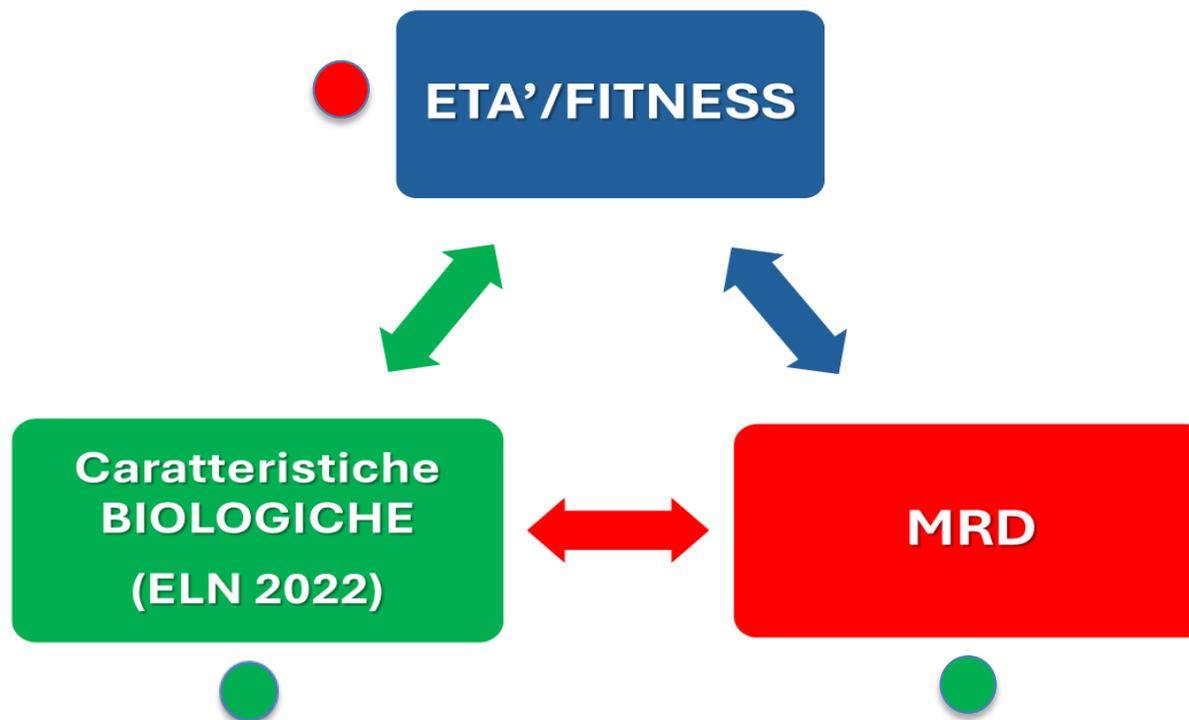
Department of Internal Medicine I, University Hospital TU Dresden, Dresden, Germany

Overall survival in relation to age and period of treatment. Data based on clinical trials of the Study Alliance Leukemia Group (SAL) and the SAL AML registry.





AML: FATTORI PRINCIPALI CONDIZIONANTI LA SCELTA DEL TRATTAMENTO E LA PROGNOSI





Definitions of ELN 2022 Risk Categories¹

Risk Category	Genetic Abnormality
Favorable	<ul style="list-style-type: none"> t(8;21)(q22;q22.1)/RUNX1::RUNX1T1 inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/CBFB::MYH11 } CBF AML Mutated <i>NPM1</i> without <i>FLT3</i>-ITD bZIP in-frame mutated <i>CEBPA</i>
Intermediate	<ul style="list-style-type: none"> Mutated <i>NPM1</i> with <i>FLT3</i>-ITD Wild-type <i>NPM1</i> with <i>FLT3</i>-ITD (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3)/MLLT3::KMT2A Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	<ul style="list-style-type: none"> t(6;9)(p23.3;q34.1)/DEK::NUP214 t(v;11q23.3)/KMT2A-rearranged t(9;22)(q34.1;q11.2)/BCR::ABL1 t(8;16)(p11.2;p13.3)/KAT6A::CREBBP inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/GATA2, MECOM(<i>EVI1</i>) t(3q26.2;v)/MECOM(<i>EVI1</i>)-rearranged -5 or del(5q); -7; -17/abn(17p) Complex karyotype, monosomal karyotype Mutated <i>ASXL1</i>, <i>BCOR</i>, <i>EZH2</i>, <i>RUNX1</i>, <i>SF3B1</i>, <i>SRSF2</i>, <i>STAG2</i>, <i>U2AF1</i>, and/or <i>ZRSR2</i> Mutated <i>TP53</i>

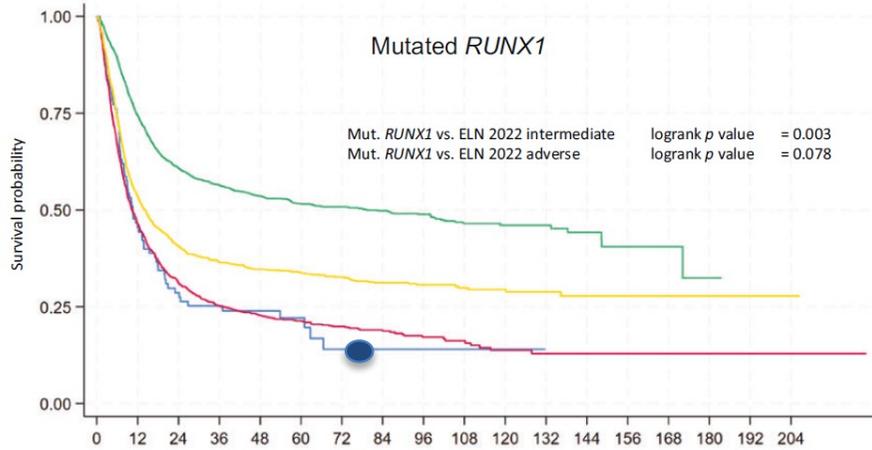
1. Döhner H et al. *Blood*. 2022;140:1345-1377.

Acute Myeloid Leukemia

Differential prognostic impact of myelodysplasia-related gene mutations in a European cohort of 4978 intensively treated AML patients

Marius Bill ^{1,2,3,4,34}, Jan-Niklas Eckardt ^{1,34}, Konstanze Döhner ⁵, Maximilian-Alexander Röhner ¹, Christian Rausch ⁶, Klaus H. Metzeler ⁷, Karsten Spiekermann ⁶, Sebastian Stasik ¹, Alexander A. Wurm ^{1,2,3,4}, Tim Sauer ⁸, Sebastian Scholl ⁹, Ulf Schnetzke ⁹, Andreas Hochhaus ⁹, Martina Crysandt ¹⁰, Tim H. Brümmendorf ¹⁰, Utz Krug ¹¹, Bernhard Wörmann ¹², Hermann Einsele ¹³, Wolfgang Hiddemann ⁶, Dennis Görlich ¹⁴, Cristina Sauerland ¹⁴, Björn Steffen ¹⁵, Andreas Neubauer ¹⁶, Andreas Burchert ¹⁶, Kerstin Schäfer-Eckart ¹⁷, Wolfgang E. Berdel ¹⁸, Christoph Schliemann ¹⁸, Stefan W. Krause ¹⁹, Mathias Hänel ²⁰, Maher Hanoun ²¹, Martin Kaufmann ²², Lars Fransecky ²³, Jan Braess ²⁴, Johannes Schetelig ¹, Jan Moritz Middeke ¹, Lars Bullinger ¹², Michael Heuser ^{25,26}, Felicitas Thol ²⁶, Hubert Serve ¹⁵, Claudia D. Baldus ²³, Uwe Platzbecker ⁷, Carsten Müller-Tidow ⁶, Jan Válka ²⁷, Jiří Šrámek ^{28,29}, Barbora Weinbergerova ³⁰, Jiri Mayer ³⁰, Pierre-Yves Dumas ³¹, Sarah Bertoli ³², Eric Delabesse ³², Christian Récher ³², Arnaud Pigneux ³¹, Tobias Herold ^{6,33}, Arnold Ganser ²⁶, Hartmut Döhner ⁵, Martin Bornhäuser ^{1,2,3,4}, Christian Thiede ¹ and Christoph Röllig ^{1,34}

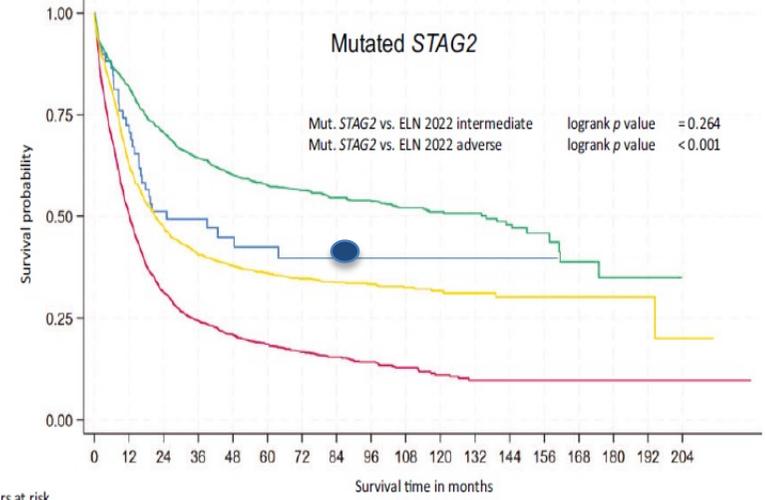
I



Numbers at risk

Survival time in months	0	12	24	36	48	60	72	84	96	108	120	132	144	156	168	180	192	204
Mut. <i>RUNX1</i>	92	41	25	21	16	9	4	3	2	1	1	0	0	0	0	0	0	0
ELN 2022 fav	1411	1030	800	680	554	462	381	295	222	141	92	57	34	11	6	1	0	0
ELN 2022 int	1072	571	418	335	279	238	192	136	102	74	48	34	16	6	4	2	1	1
ELN 2022 adv	1144	519	328	228	174	126	99	69	48	29	20	11	6	6	2	2	1	1

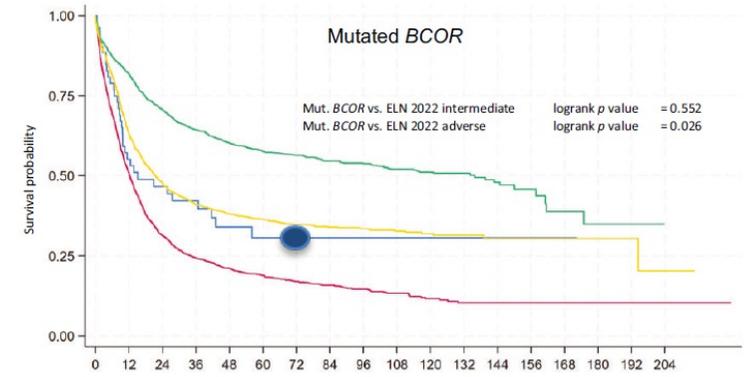
F



Numbers at risk

Survival time in months	0	12	24	36	48	60	72	84	96	108	120	132	144	156	168	180	192	204
Mut. <i>STAG2</i>	56	41	28	26	18	17	13	13	11	9	5	4	2	2	0	0	0	0
ELN 2022 fav	1650	1307	1076	906	731	606	500	399	299	205	140	88	51	24	13	4	1	0
ELN 2022 int	1357	843	617	494	394	326	255	189	138	98	62	45	21	9	8	6	3	2
ELN 2022 adv	1995	989	580	413	299	206	157	109	71	44	29	18	11	8	5	4	3	1

B



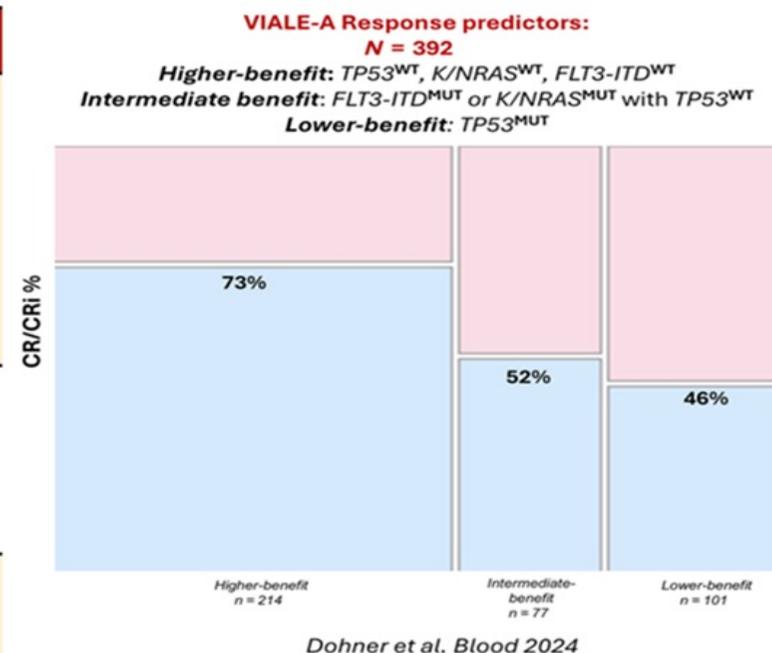
Numbers at risk

Survival time in months	0	12	24	36	48	60	72	84	96	108	120	132	144	156	168	180	192	204
Mut. <i>BCOR</i>	52	27	21	18	12	9	6	3	2	2	2	2	2	1	1	0	0	0
ELN 2022 fav	1630	1307	1076	906	731	606	500	388	299	205	140	88	51	24	13	4	1	0
ELN 2022 int	1360	849	622	499	368	330	258	192	141	100	63	46	22	10	6	6	3	2
ELN 2022 adv	1998	997	582	416	301	210	161	116	77	49	31	19	10	6	4	4	3	1

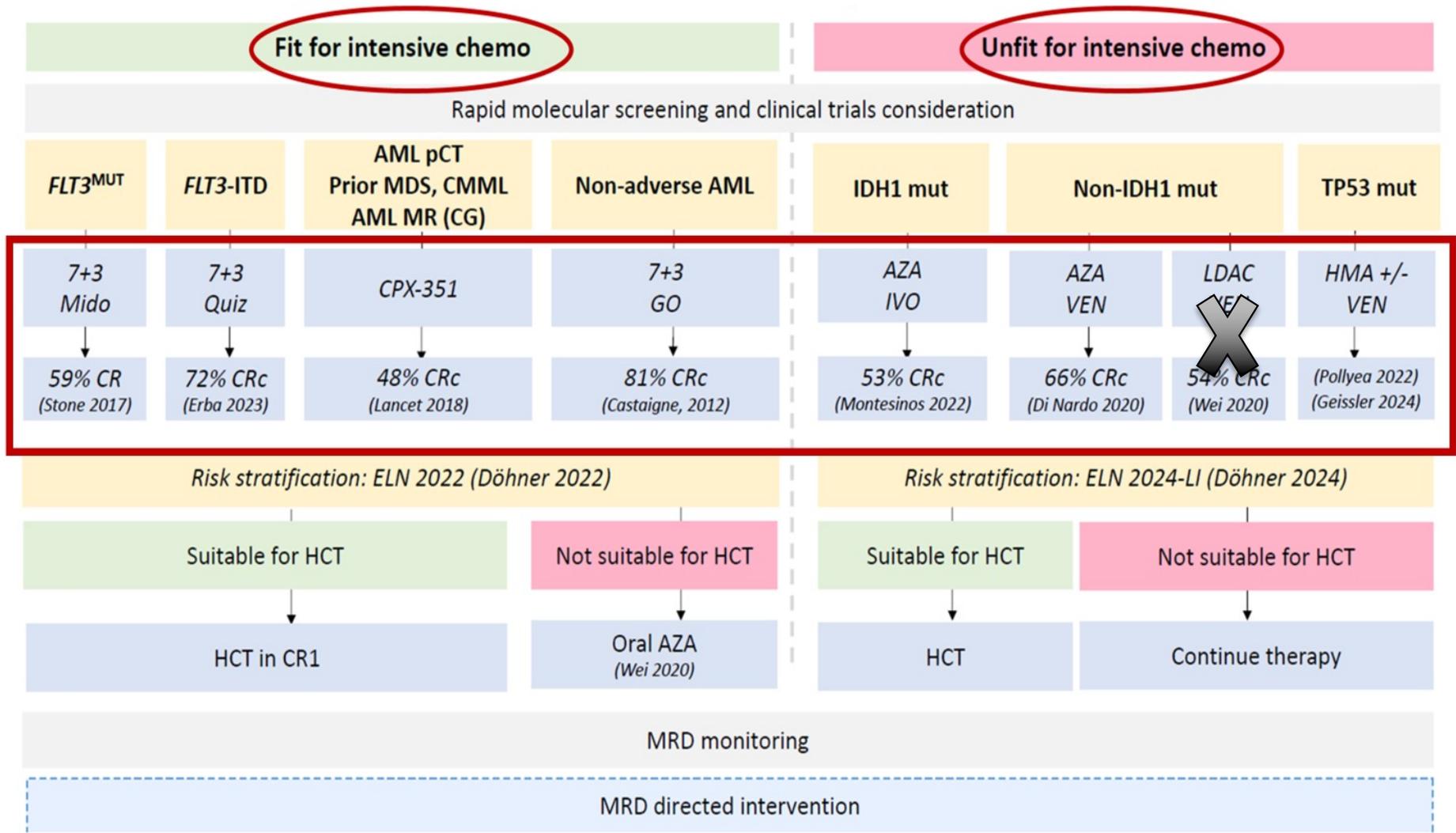


Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations

Genetic marker	Median OS, mo
Favorable-risk group	
Mutated <i>NPM1</i> (<i>FLT3-ITD</i> ^{neg} , <i>NRAS</i> ^{wt} , <i>KRAS</i> ^{wt} , <i>TP53</i> ^{wt})	39
Mutated <i>IDH2</i> (<i>FLT3-ITD</i> ^{neg} , <i>NRAS</i> ^{wt} , <i>KRAS</i> ^{wt} , <i>TP53</i> ^{wt})	37
Mutated <i>IDH1*</i> (<i>TP53</i> ^{wt})	29
Mutated <i>DDX41</i>	>24
AML with MR gene mutations (<i>FLT3-ITD</i> ^{neg} , <i>NRAS</i> ^{wt} , <i>KRAS</i> ^{wt} , <i>TP53</i> ^{wt})	23
Intermediate-risk group	
AML with MR gene mutations (<i>FLT3-ITD</i> ^{pos} and/or <i>NRAS</i> ^{mut} and/or <i>KRAS</i> ^{mut} ; <i>TP53</i> ^{wt})	13
Other cytogenetic and molecular abnormalities (<i>FLT3-ITD</i> ^{pos} and/or <i>NRAS</i> ^{mut} and/or <i>KRAS</i> ^{mut} ; <i>TP53</i> ^{wt})	12
Adverse-risk group	
Mutated <i>TP53</i>	5-8

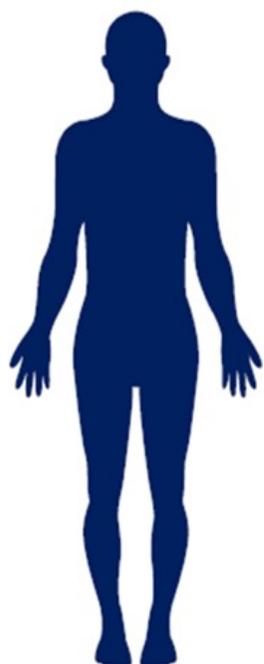


AML ALGORITMO TERAPEUTICO 2026



Phase III CALGB 10603 RATIFY Trial

Patients with FLT3-mutated AML received standard induction/consolidation chemotherapy plus either midostaurin or placebo. Patients in remission after consolidation entered a maintenance phase (midostaurin or placebo).



N = 717

Midostaurin Group



74.7 Months

Median OS

Placebo Group



25.6 Months

Median OS

Hazard ratio for death, 0.78; one-sided $P = .009$



8.2 Months

Median EFS



3.0 Months

Median EFS

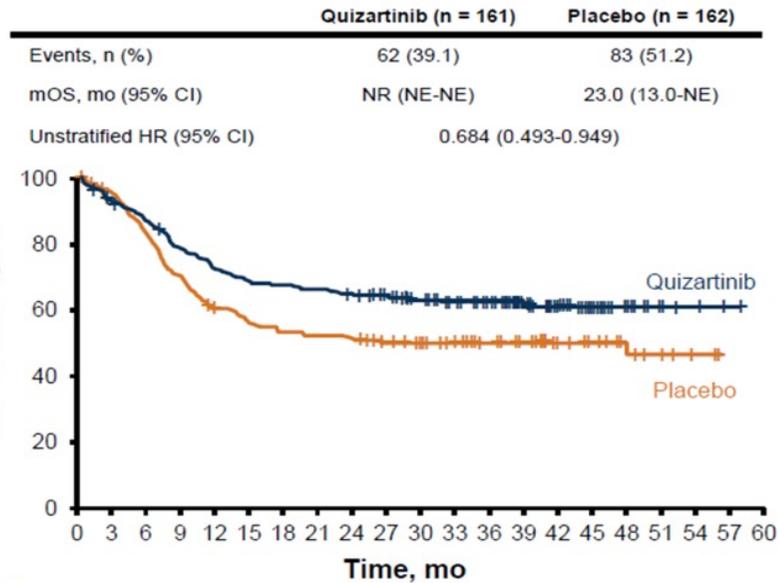
Hazard ratio for event or death, 0.78; one-sided $P = .002$

- Benefit of midostaurin consistent across FLT3 subtypes
- Rate of SAEs similar in the two groups

Midostaurin added to standard chemotherapy significantly prolonged overall and event-free survival

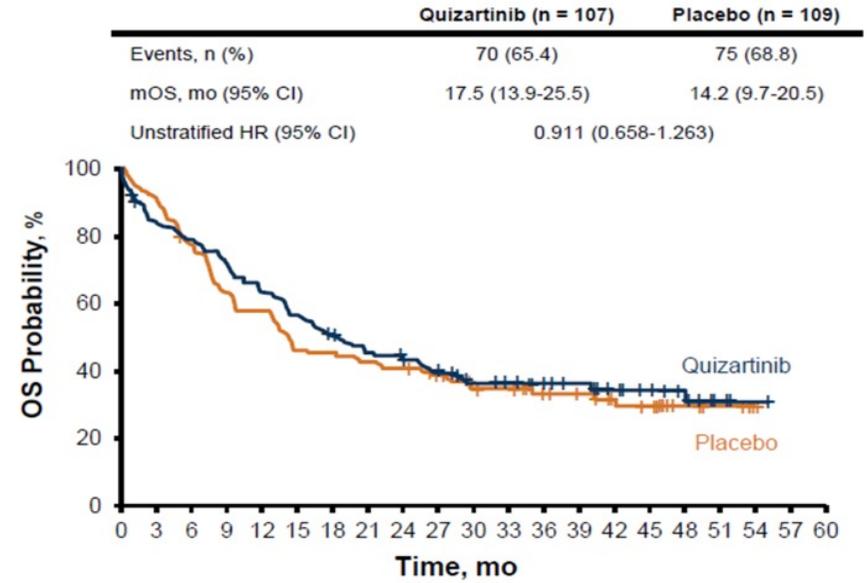
QuANTUM-First: Overall Survival by Age¹

OS of Patients <60 Years of Age



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
Quizartinib	161	145	134	120	111	104	103	101	97	90	81	69	60	48	37	24	15	4	3	1	0
Placebo	162	150	128	108	90	83	79	77	75	65	58	53	48	37	25	20	11	4	2	0	0

OS of Patients ≥60 Years of Age



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
Quizartinib	107	88	82	75	65	58	50	44	42	36	29	27	23	20	16	12	9	4	1	0	0
Placebo	109	99	83	67	61	48	47	44	42	38	33	28	22	19	14	11	6	4	3	0	0

1. Erba H et al. *Lancet*. 2023;401:1571-1583.



Elimination of MRD by *FLT3* ITD NGS MRD Assay in QuANTUM-First Trial by Treatment Course

	<u>CRc After Induction</u>		<u>After 2 Cycles of CTx</u>		<u>After Last Consolidation Cycle</u>	
	QUIZ	PLAC	QUIZ	PLAC	QUIZ	PLAC
Patients with non-detectable MRD, %	22.8	11.9	31.7	21.7	55.8	41.2
Nominal <i>P</i> value	0.0122		0.0609		0.0089	

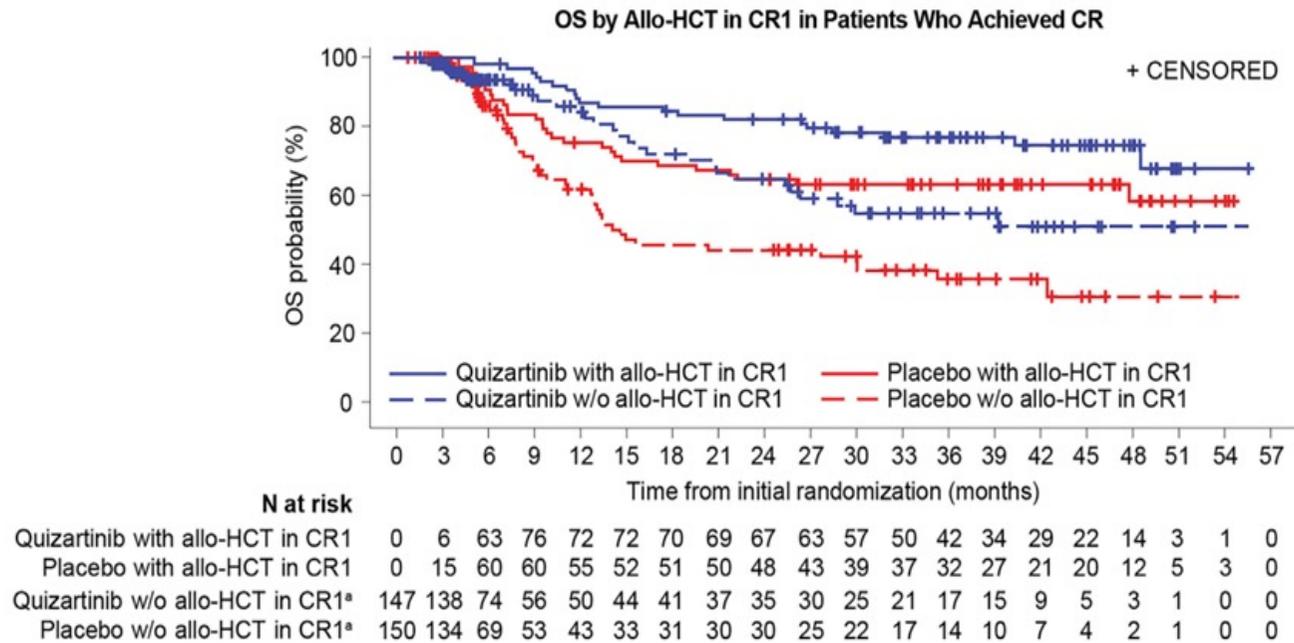
Perl A, et al. ASH 2023;Abstract 832

Impact of hematopoietic cell transplantation and quizartinib in newly diagnosed patients with acute myeloid leukemia and FMS-like tyrosine kinase 3-internal tandem duplications in the QuANTUM-First trial

Richard F. Schlenk,^{1,2} Pau Montesinos,³ Hee-Je Kim,⁴ Antonio Romero-Aguilar,⁵ Radovan Vrhovac,⁶ Elżbieta Patkowska,⁷ Pavel Žák,⁸ Po-Nan Wang,⁹ James Hanyok,¹⁰ Li Liu,¹⁰ Yasser Mostafa Kamel,^{10*} Karima Imadalou,⁹ Arnaud Lesegretain,¹⁰ Jorge Cortes,¹¹ Mikkael A. Sekeres,¹² Hervé Dombret,¹³ Sergio Amadori,¹⁴ Jianxiang Wang,¹⁵ Alexander E. Perl,¹⁶ Mark J. Levis¹⁷ and Harry P. Erba¹⁸

Correspondence: Richard F. Schlenk
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Received: September 10, 2024.

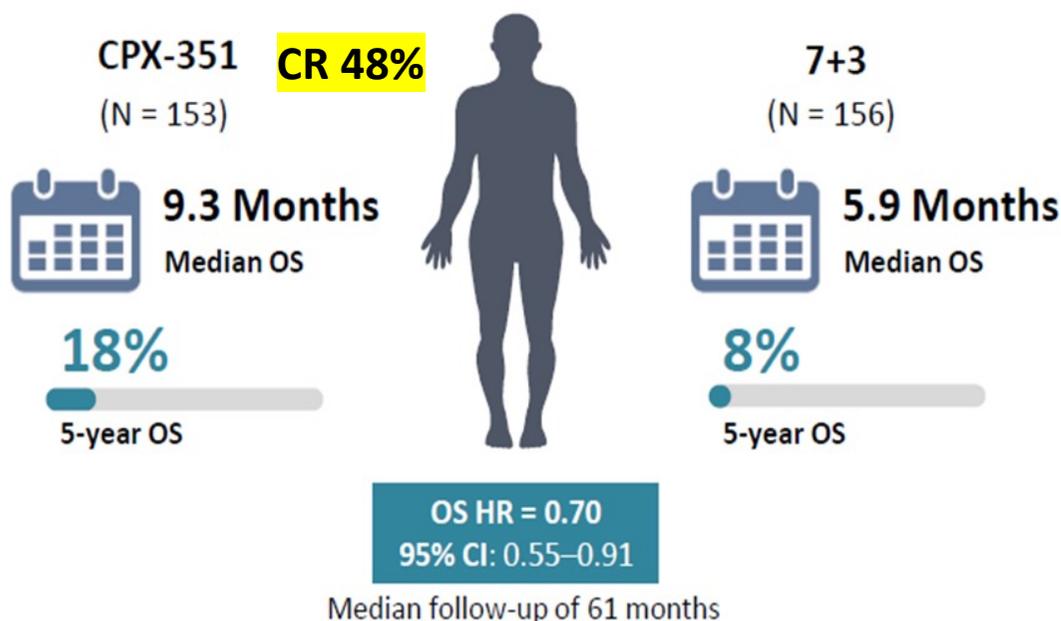


Phase III Trial; CPX-351 vs Conventional Cytarabine and Daunorubicin (7+3)



Patient Population

- ✓ 60-75 years of age
- ✓ Newly diagnosed high-risk secondary AML



Post hoc analyses

Improved median OS seen across:

- AML types (t-AML, AML-MRC)
- Age groups (60-69 yrs vs 70-75 yrs)
- After achievement of CR (w/ or w/o alloBMT)

Unclear benefit of CPX-351 in:

- **Post-HMA therapy**
- **TP53 mutations**

International real-world data corroborate clinical activity of CPX-351 in newly diagnosed AML-MRC ≥ 18 years

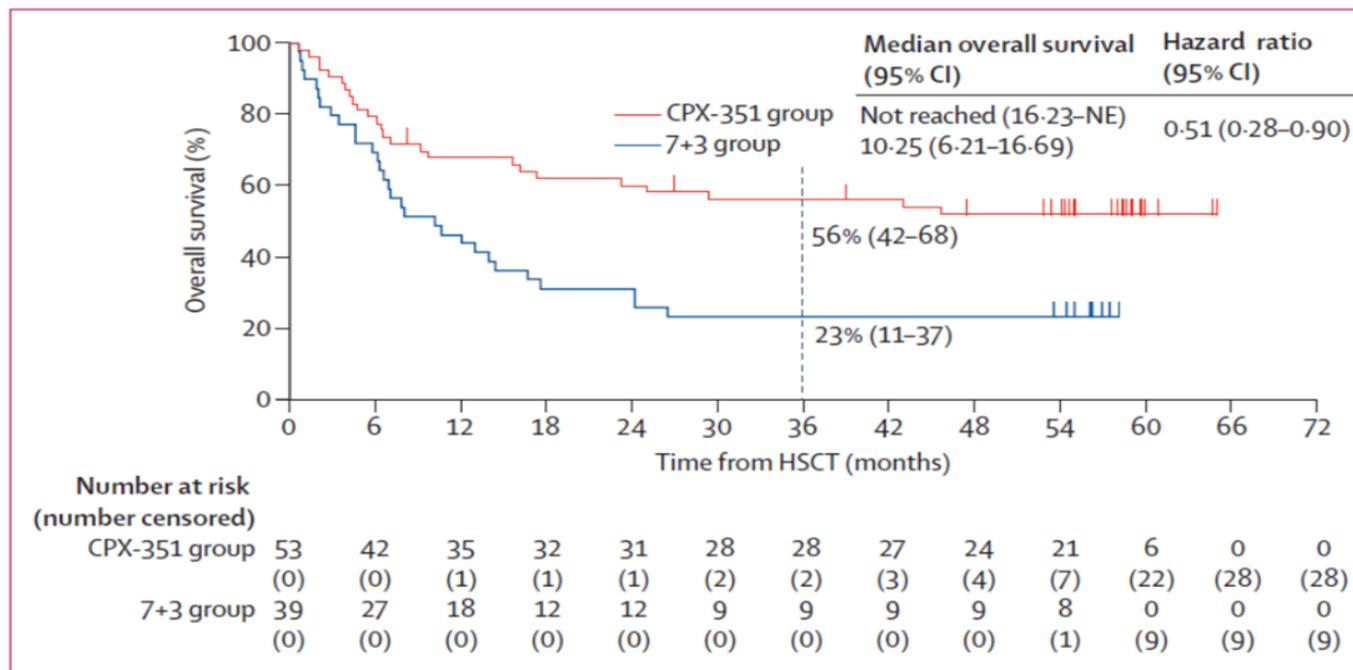
CPX-351 leads to superior outcomes compared with 7+3 in AML-MRC and represents a SOC patients aged ≥ 60 years & a treatment option for patients 18-60 years with AML-MRC

AE = Adverse Event; CI = Confidence Interval; CR = Complete Remission, CRi = Complete Remission with incomplete neutrophil or platelet recovery; LDAC = Low-Dose Cytarabine; NR = Not Reached; OS = Overall Survival; CI = Confidence Interval; HR = Hazard Ratio; SOC = Standard of Care

Cortes JE, et al. *Leukemia*. 2019; 33(2):379–389. Heuser M, et al. *Ann Hematol*. 2021;100(5):1181–1194; Chiche E, et al. *Blood Adv*. 2021;5(1):176–184; Rautenberg C, et al. *Blood Cancer J*. 2021;11(10):164.



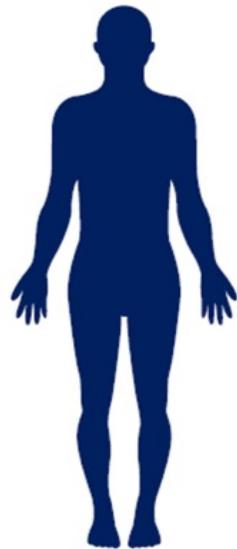
Overall survival from date of HSCT: 5-year results¹



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

Phase III ALFA-0701 Trial

Enrolled patients 50-70 years of age with previously untreated AML
Front-line induction chemotherapy +/- GO; pts in remission received consolidation +/- GO



N = 280

GO Group



17.3 months

Median EFS

(Primary Endpoint) HR: 0.56; 95%CI: 0.42–0.76; P = .0002



27.5 Months

Median OS

HR, 0.81; 95%CI: 0.60–1.09; P = .16

Control Group



9.5 Months

Median EFS



21.8 Months

Median OS

Meta-Analysis (Hills, et al)

Cytogenetic Group	Estimated OS (6+ years)		Survival Benefit
	With GO	Without GO	
Favorable	75.5%	54.8%	20.7%
Intermediate	39.6%	33.9%	5.7%
Adverse	8.9%	6.7%	2.2%

GO added to intensive chemotherapy has a favorable benefit/risk ratio in those with favorable and intermediate-risk disease

EFS = Event-Free Survival; GO = Gemtuzumab Ozogamicin; HR = Hazard Ratio; OS = Overall Survival; VOD = Veno-Occlusive Disease

Castaigne S, et al. *Lancet*. 2012;379(9825):1508-1516; Lambert J, et al. *Haematologica*. 2019;104(1):113-119; Hills RK, et al. *Lancet Oncol*. 2014;15(9):986-996.

Phase III QUAZAR AML-001 Trial



Patient Population

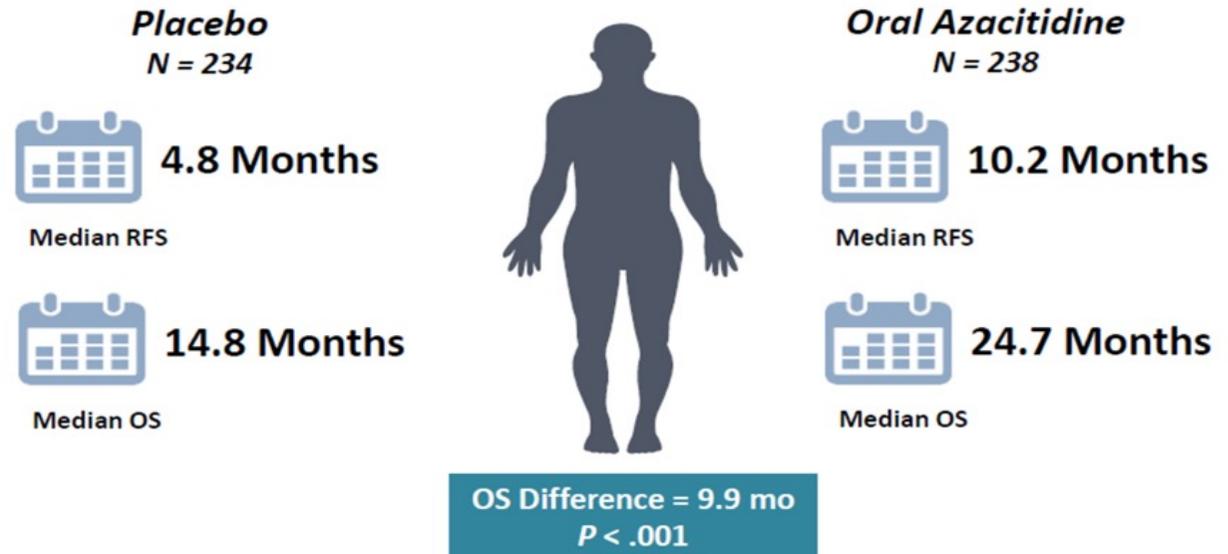
- ✓ ≥ 55 years of age
- ✓ De novo or secondary AML in first CR/CRi with IC
- ✓ Intermediate- or poor-risk genetics
- ✓ Ineligible for ASCT



Most Common Grade 3–4 AEs in Azacitidine Arm

- Neutropenia (41%)
- Thrombocytopenia (23%)
- Anemia (14%)

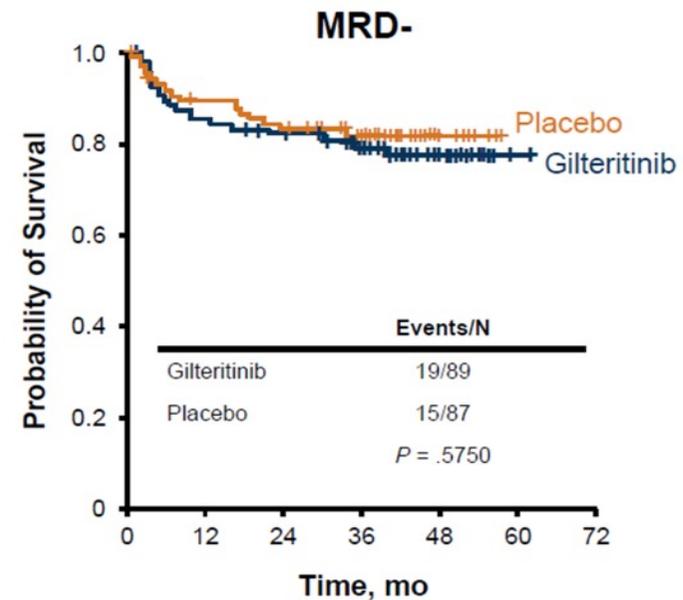
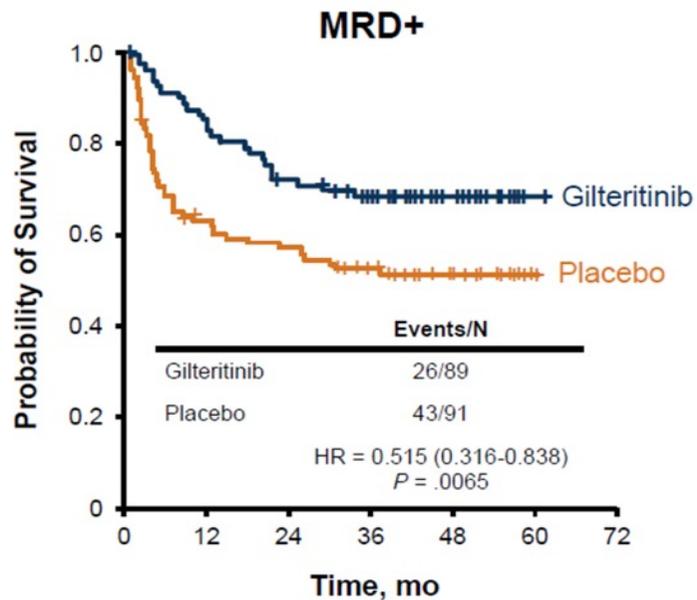
FDA Approved 09/01/20 for AML patients who achieved CR or CRi following intensive induction therapy



CI = Confidence Interval; CR = Complete Response; CRi = CR with Incomplete Blood Count; HR = Hazard Ratio; IC = Induction Chemotherapy; OS = Overall Survival; RFS = Relapse-Free Survival
Wei AH, et al. *N Engl J Med.* 2020;383(26):2526-2537.

MORPHO: Effect of Detectable MRD6 on RFS by Study Arm¹

Improvement in RFS with gilteritinib maintenance in MRD+ group



1. Levis M et al. EHA 2023. Abstract LB2711.



Unfit for intensive chemo

Phase III VIALE-A Trial

FDA Approved 10/16/20

Azacitidine + Venetoclax
N = 286



14.7
Months

Median OS



Azacitidine + Placebo
N = 145



9.6
Months

Median OS

OS HR = 0.66
95% CI: 0.52–0.85

Patient Population

- ✓ Treatment naïve
- ✓ Ineligible for standard induction due to age (≥ 75 years) and/or comorbidities

AGILE (Phase III)

FDA Approved for ≥ 75 years newly diagnosed
IDH1-mutant AML 5/25/22

Azacitidine
N = 74

19%

ORR

15%

CRR



7.9 Months
Median OS

Ivosidenib + Azacitidine
N = 72

63%

ORR

47%

CRR



24 Months
Median OS



Patient Population

- ✓ Newly diagnosed IDH1-mutant AML
- ✓ No prior treatment with hypomethylating agents
Ineligible for intensive therapy



Outcomes of genetic subgroups with VEN-based therapy

Molecular subgroup	Response (CR/CRi)	MRD-negative CR/CRi (MFC)	OS (median or 2-year)	References
<i>IDH1</i>	66.7% (n = 22/33)	42% (n = 5/12)	10.2 mo	Pollyea et al. CCR 2022; ¹⁸ Pratz et al. AJH 2024 ³⁸
<i>IDH2</i>	86% (n = 43/50)	50% (n = 16/32)	27.5 mo	Pollyea et al. CCR 2022; ¹⁸ Pratz et al. AJH 2024 ³⁸
<i>NPM1</i>	66.7% (n = 18/27)	88% (n = 15/17)	2-year OS: 71.8% ⁶⁴	DiNardo et al. Blood 2020; ¹¹ Pratz et al. AJH 2024 ³⁸
<i>FLT3-ITD</i>	63.3% (n = 19/30)	53% (n = 9/17)	9.9 mo	Konopleva et al. CCR 2022 ¹²
<i>FLT3-TKD</i>	76.9% (n = 10/13)	50% (n = 2/4)	19.2 mo	Konopleva et al. CCR 2022 ¹²
<i>N/KRAS</i>	45% (n = 13/29)	-	12 mo	Rivera et al. AJH 2022 ⁵¹
<i>TP53</i>	55% (n = 21/38)	30% (n = 6/20)	5.5-7.4 mo	DiNardo et al. Blood 2020; ¹¹ Pollyea et al. CCR 2022 ¹³

Oral bioavailability of DECITABINE has been quite poor due to rapid metabolism by Cytidine deaminase (CDA) which is highly expressed in the gut and liver.

Oral Decitabine Plus Cedazuridine (ASTX727)¹



- Cedazuridine is a novel, potent, and safe CDA inhibitor
- When given in combination with decitabine, cedazuridine enables efficient oral availability



**Agenzia Italiana
del Farmaco**

INDICAZIONI AUTORIZZATA (con Scheda monitoraggio AIFA):

DECITABINA ORALE è indicato in monoterapia per il trattamento di pazienti adulti con leucemia mieloide acuta (AML, acute myeloid leukaemia) di nuova diagnosi non idonei alla chemioterapia di induzione standard.



Received: 28 June 2024 | Accepted: 21 August 2024
DOI: 10.1111/bjh.19741

ORIGINAL PAPER

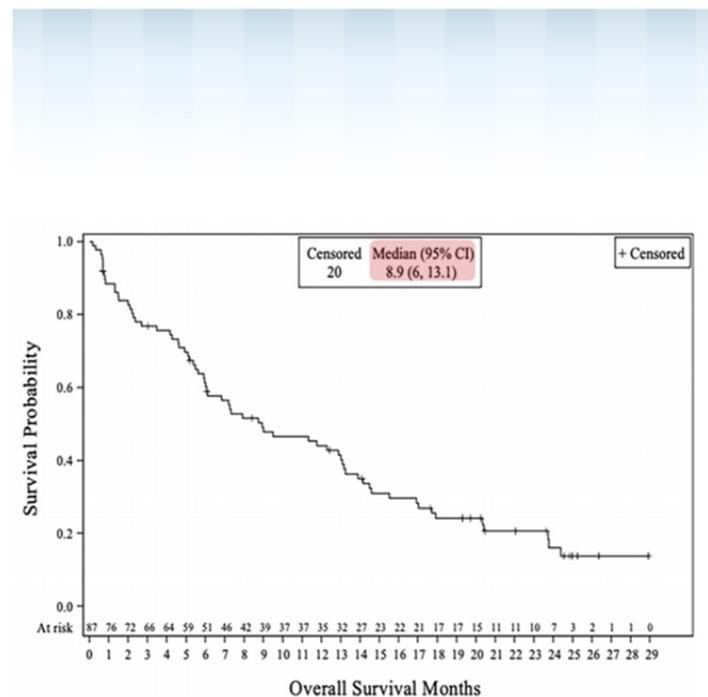
Haematological Malignancy - Clinical



Oral decitabine/cedazuridine versus intravenous decitabine for acute myeloid leukaemia: A randomised, crossover, registration, pharmacokinetics study

Klaus Geissler¹ | Zdenek Koristek² | Teresa Bernal del Castillo³ | Jan Novák⁴ | Gabriela Rodriguez-Macias⁵ | Stephan K. Metzelder⁶ | Arpad Illes⁷ | Jiří Mayer⁸ | Montserrat Arnan⁹ | Mary-Margaret Keating¹⁰ | Jürgen Krauter¹¹ | Monia Lunghi¹² | Nicola Stefano Fracchiolla¹³ | Uwe Platzbecker¹⁴ | Valeria Santini¹⁵ | Yuri Sano¹⁶ | Aram Oganessian¹⁶ | Harold Keer¹⁶ | Michael Lübbert¹⁷

Analysis	Efficacy set (n = 87)	
	n (%)	95% CI
Best response		
CR	19 (21.8)	13.7, 32.0
CRi	5 (5.7)	1.9, 12.9
CRp	2 (2.3)	0.3, 8.1
PR	4 (4.6)	1.3, 11.4
SD	33 (37.9)	27.7, 49.0
NE	26 (29.9)	20.5, 40.6
Composite response rates		
● CR + CRi + PR	28 (32.2)	22.6, 43.1
CR + CRh	21 (24.1)	15.6, 34.5
CRh	2 (2.3)	0.3, 8.1



Gilteritinib – FLT3/AXL Inhibitor
ADMIRAL, NCT02421939 (Phase III)

Gilteritinib
N = 247

Salvage Chemotherapy
N = 124

21.1%

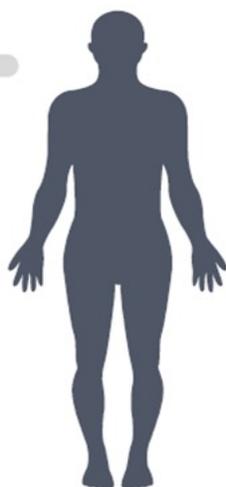
CRR

2.8 Months

mEFS

9.3 Months

mOS



10.5%

CRR

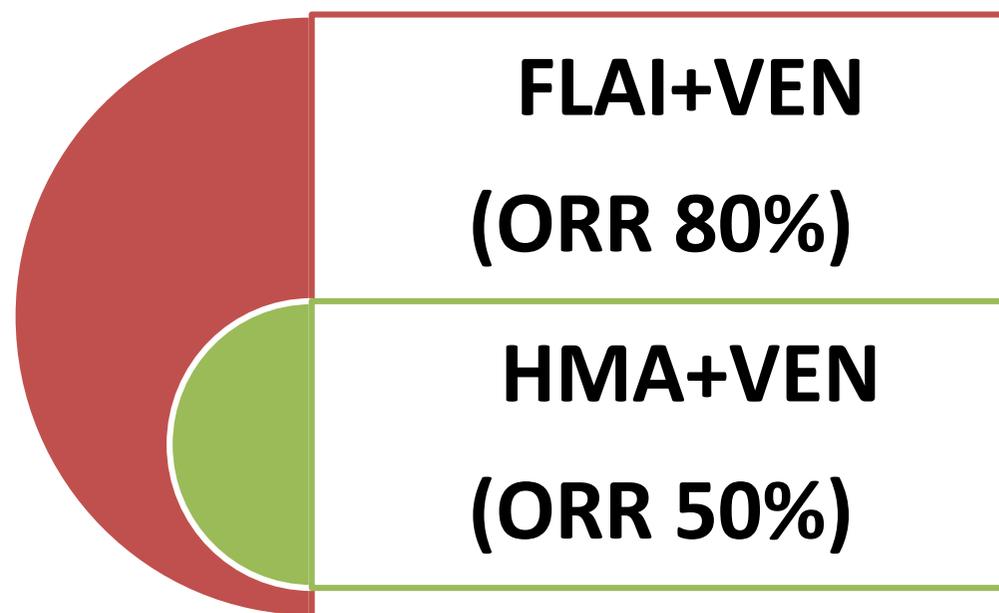
0.7 Months

mEFS

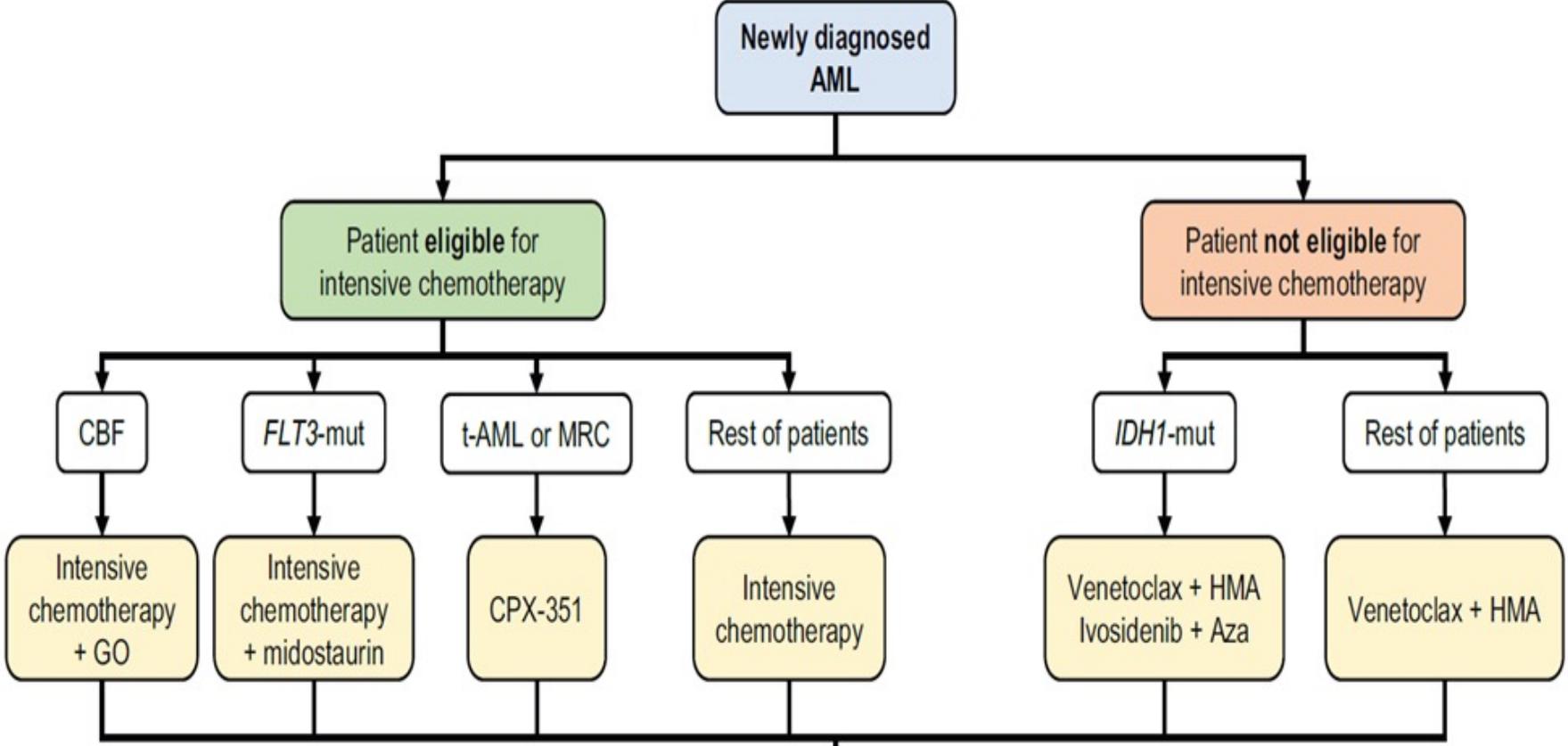
5.6 Months

mOS

OS HR = 0.64
95% CI: 0.49–0.83

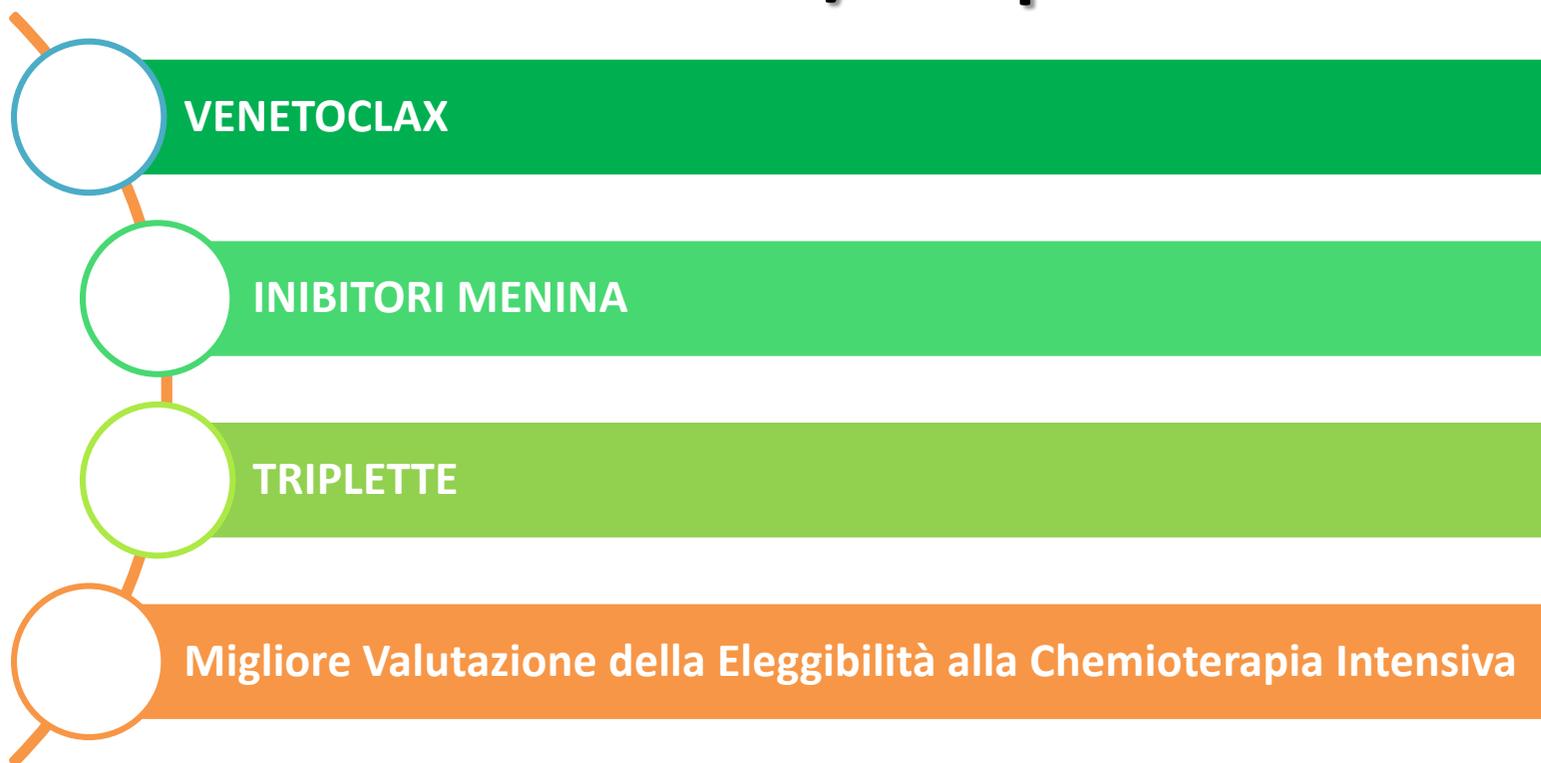


AML ALGORITMO TERAPEUTICO 2026





Considerazioni/Prospettive





POST-ORLANDO 2025

Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Torino

Centro Congressi Lingotto

19-21 febbraio 2026

COORDINATORI

Angelo Michele Carella

Pier Luigi Zinzani

BOARD SCIENTIFICO

Paolo Corradini

Mauro Krampera

Fabrizio Pane

Adriano Venditti





A patient with AML and a FLT3-ITD mutation receives 7+3 chemotherapy and a FLT3 inhibitor, and an MRD assay ordered after the completion of induction therapy is negative. Would you proceed to ASCT? What would be your most likely approach to maintenance therapy?

	Transplant	Maintenance
 Dr Erba	Yes	No maintenance therapy
 Dr Fathi	Yes	No maintenance if MRD-negative, FLT3 inhibitor if MRD-positive
 Dr Lin	Yes	No maintenance if MRD-negative, FLT3 inhibitor if MRD-positive
 Dr Perl	Yes	Gilteritinib for 2 years if peri-HSCT MRD-positive, otherwise no maintenance
 Dr Stein	Yes	No maintenance therapy
 Dr Cortes	Yes	No maintenance therapy
 Dr DiNardo	Yes	FLT3 inhibitor maintenance for 2-3 years
 Dr Wang	Yes	No maintenance therapy

HSCT = hematopoietic stem cell transplant