Penn Medicine

Advances in Acute Leukemias

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2024 Hematology Highlights: A Post ASH Review Conference – University of Nebraska, Omaha February 3rd 2024

Disclosures

- Grant support to institution for clinical trials from : Astellas, Agios, Abbvie, Daiichi Sankyo, Millennium
- Scientific Advisory Boards: Astellas, Abbvie, Agios, Astra Zeneca, Boston Biomedical, BMS Celgene, Hoffman La Roche, Immunogen, Jazz Pharmaceuticals, Servier
- Off label usage: Enasidinib, Venetoclax, Gilteritinib for AML

Topics of talk

- AML High intensity frontline
  - 7&3 + Quizartinib : FLT3 Like molecular signature
- AML Venetoclax Doublet and Triplet therapy
  - AZA/VEN/QUIZ for FLT3 mut disease
  - ENA/VEN for IDH2 mut disease
  - ASTX/VEN/IDHi for IDH mut disease
- AML relapsed disease
  - Revumenib for 11q23 relapsed leukemia
  - HAM-Ven
- ALL
  - B-cell ALL ECOG 1910 Age and Number of Blinatumomab cycles
  - T-cell ALL molecular risk score via NGS

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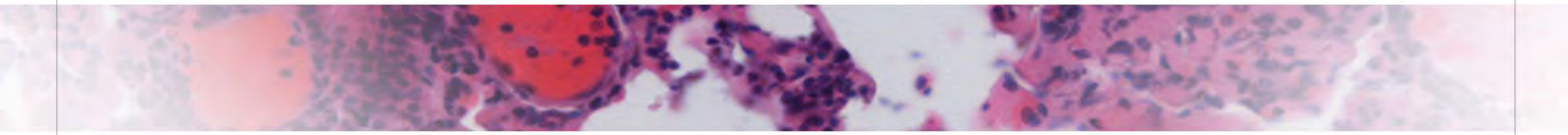


The FLT3-Like Gene Expression Signature Predicts Response to Quizartinib in FLT3 ITD-negative Acute Myeloid Leukemia: an analysis of the PETHEMA QUIWI trial

Adrian Mosquera, Manuel Perez, Jose A. Diaz, Rebeca Rodriguez, Juan M. Bergua, Jesús Lorenzo, Carmen Botella, Jose A. Perez, Teresa Bernal, Mar Tormo, Maria Calbacho, Olga Salamero, Josefina Serrano, Victor Noriega, Juan A. Lopez, Susana Vives, Mercedes Colorado, Jose L. Lopez, Maria Vidriales, Raimundo Garcia, Maria T. Olave, Pilar Herrera, Olga Arce, Manuel Barrios, Maria J. Sayas, Marta Polo, Maria I. Gomez, Eva Barragan, Rosa Ayala, Carmen Chillon, Maria J. Calasanz, Blanca Boluda, Andres Peleteiro, Raquel Amigo, David Martinez, Jorge Labrador & Pau Montesinos

The Quiwi Trial: design and interim results

Study Overview & Results

Aims: the trial compared Quiz vs PBO + standard chemo in newly diagnosed FLT3-ITD WT AML patients.

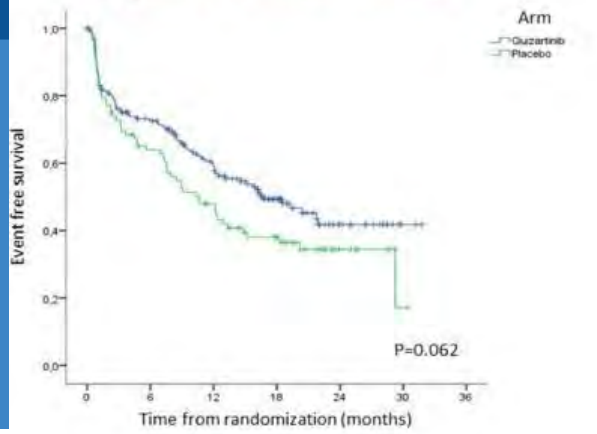
Methods: Multicenter, double-blinded, randomized phase II clinical trial (N=284).

Summary & Conclusion

The study suggests that the addition of Quiz to 3+7 chemotherapy may extend both EFS and OS in newly diagnosed FLT3-ITD WT AML patients.

Final results of the trial planned for 2024.

Figure 1A.- Event free survival



Results

Median EFS was 16.6 months with Quiz vs. 10.6 months with PBO.

Median OS was N.R. with Quiz vs. 15 months with PBO.

2-year OS rate was higher in the Quiz group.

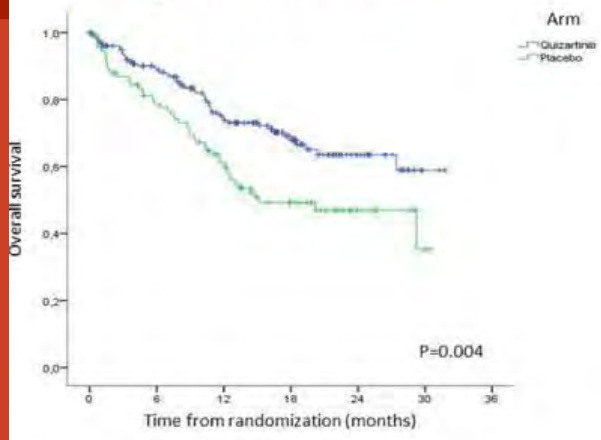
Other Significant Outcomes

OS was superior in the Quiz arm (2-year OS of 63.5% vs 47%, p<0.001).

Outcomes were improved in ELN-17 low and intermediate risk.

No new adverse safety signals were identified.

Figure 1B.- Overall survival



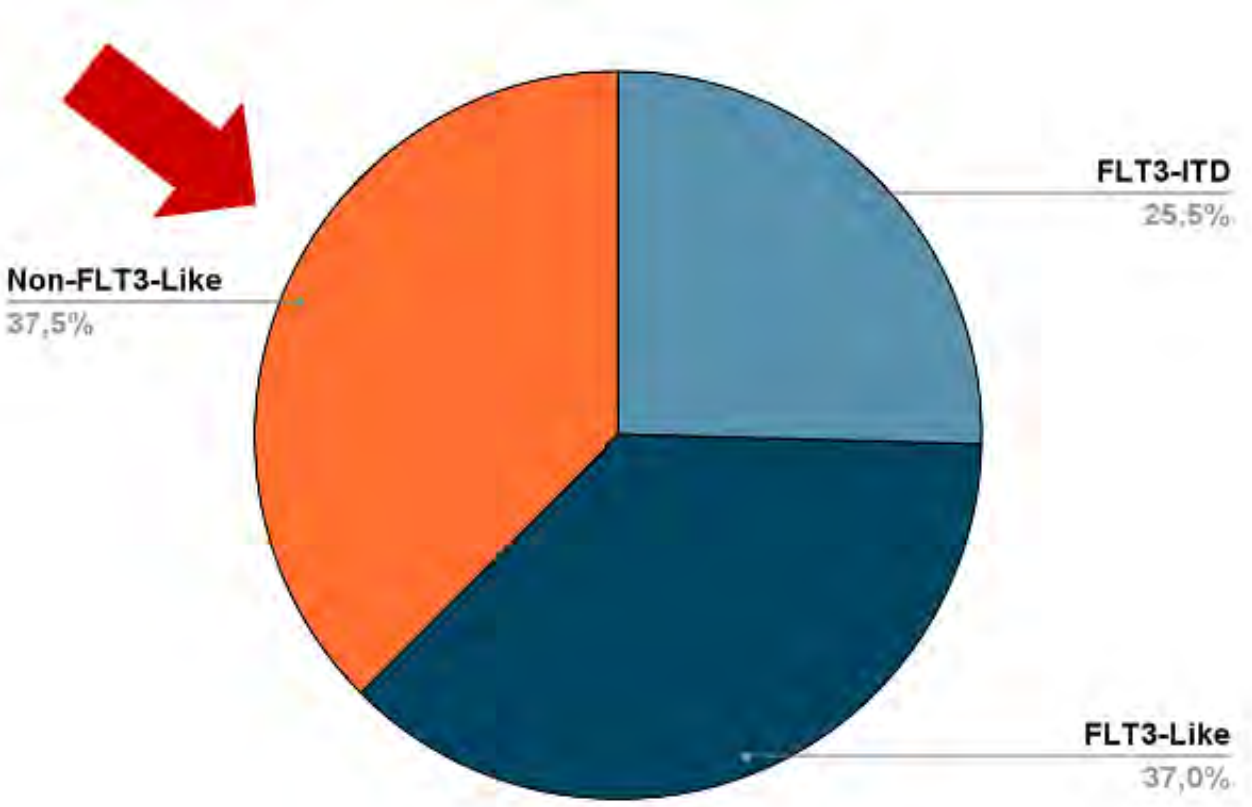
Outcome analysis of Non-FLT3-like AML patients

Overview of the Non-FLT3-Like Cluster

Non-FLT3-Like Patients: 50.33% of FLT3-ITD negative patients (N=81)

ELN-17 Classification:

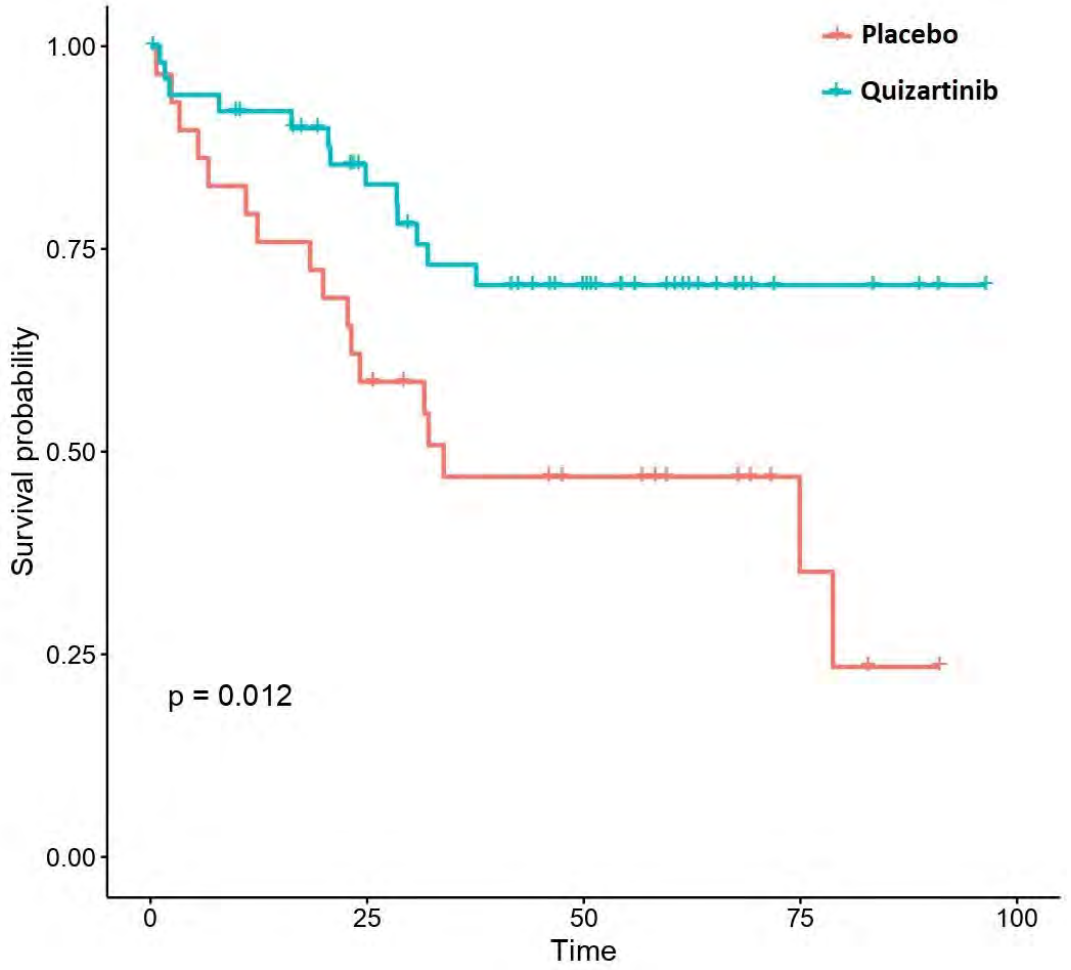
- Low Risk: 18.2%
- Intermediate Risk: 39.5%
- High Risk: 42.0%



Outcome analysis of FLT3-like AML patients

Results Among FLT3-Like Patients

- Total Deaths: Significant difference (p=0.004)
- EFS: Significant difference (p=0.009; HR 0.45)
- RFS: Significant difference (p=0.01; HR 0.37)
- OS: Significant difference (p=0.01; HR 0.41)



Phase I/II Study of Quizartinib, Venetoclax, and Decitabine Triple Combination in FLT3-ITD Mutated AML

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

Department of Leukemia, MD Anderson Cancer Center
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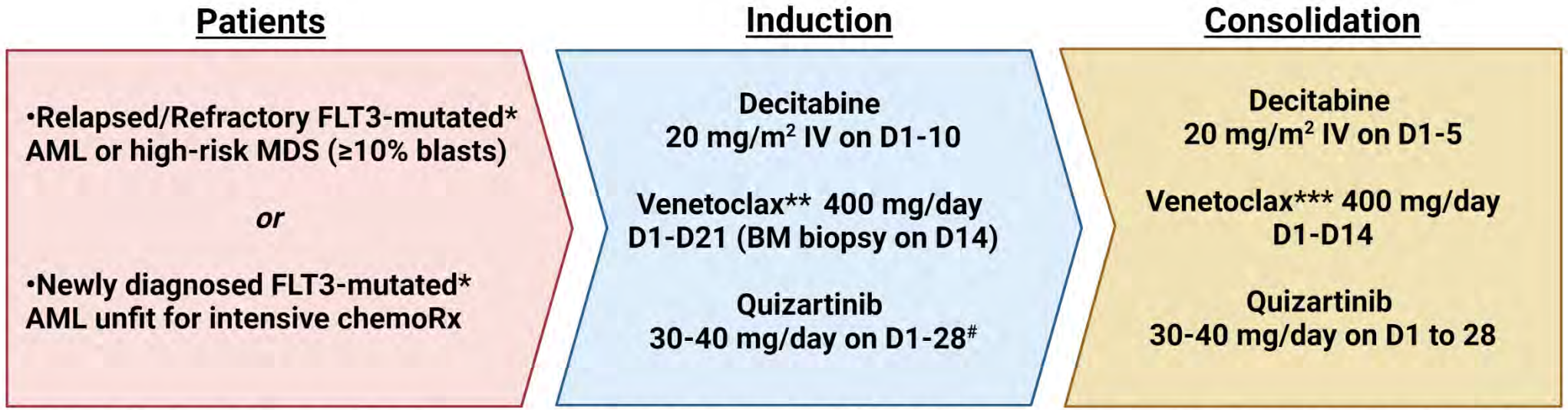
DAC + VEN + Quizartinib in FLT-ITD mutated AML

Primary Objective:

- To establish RP2D of quizartinib in combination with DAC + VEN in pts with FLT3m AML

Secondary Objective:

- To determine complete remission (CR), CR with incomplete count recovery (CRi), minimal residual disease (MRD), and overall survival (OS)



*FLT3-ITD with/without TKD mutations allowed

**Venetoclax discontinued on D14 in pts with BM blasts ≤5% or hypoplastic BM
#Amendment - reduced quizartinib to 14 days in C1

Up to 12 cycles. ***Venetoclax duration reduced to 14 > 10 >7 days in subsequent cycles for pts in CR based on count recovery durations. Quizartinib dose reduced to 14 days in pts with prolonged count recovery

Baseline Clinical Characteristics

Characteristics	Relapse/Refractory (N=43)	Frontline (N=14)
	N (%), Median [Range]	N (%), Median [Range]
Age-years	59 [19-86]	70 [62-85]
Gender- Male	26 (60)	7 (50)
Diagnosis, AML		
De novo	31 (72)	6 (43)
Secondary	9 (21)	6 (43)
Therapy related	3 (7)	2 (14)
Prior therapies, median	3 [1-5]	n/a
HMA + VEN	24 (56)	n/a
≥1 prior FLT3i	36 (83)	n/a
≥ 2 prior FLT3i	9 (23)	n/a
Prior Gilteritinib	21 (74)	n/a
ASCT, yes	16 (37)	n/a
Karyotype		
Diploid	17 (40)	8 (56)
Adverse	13 (30)	3 (22)
Other	13 (30)	3 (22)

Frontline Cohort - Response Rates

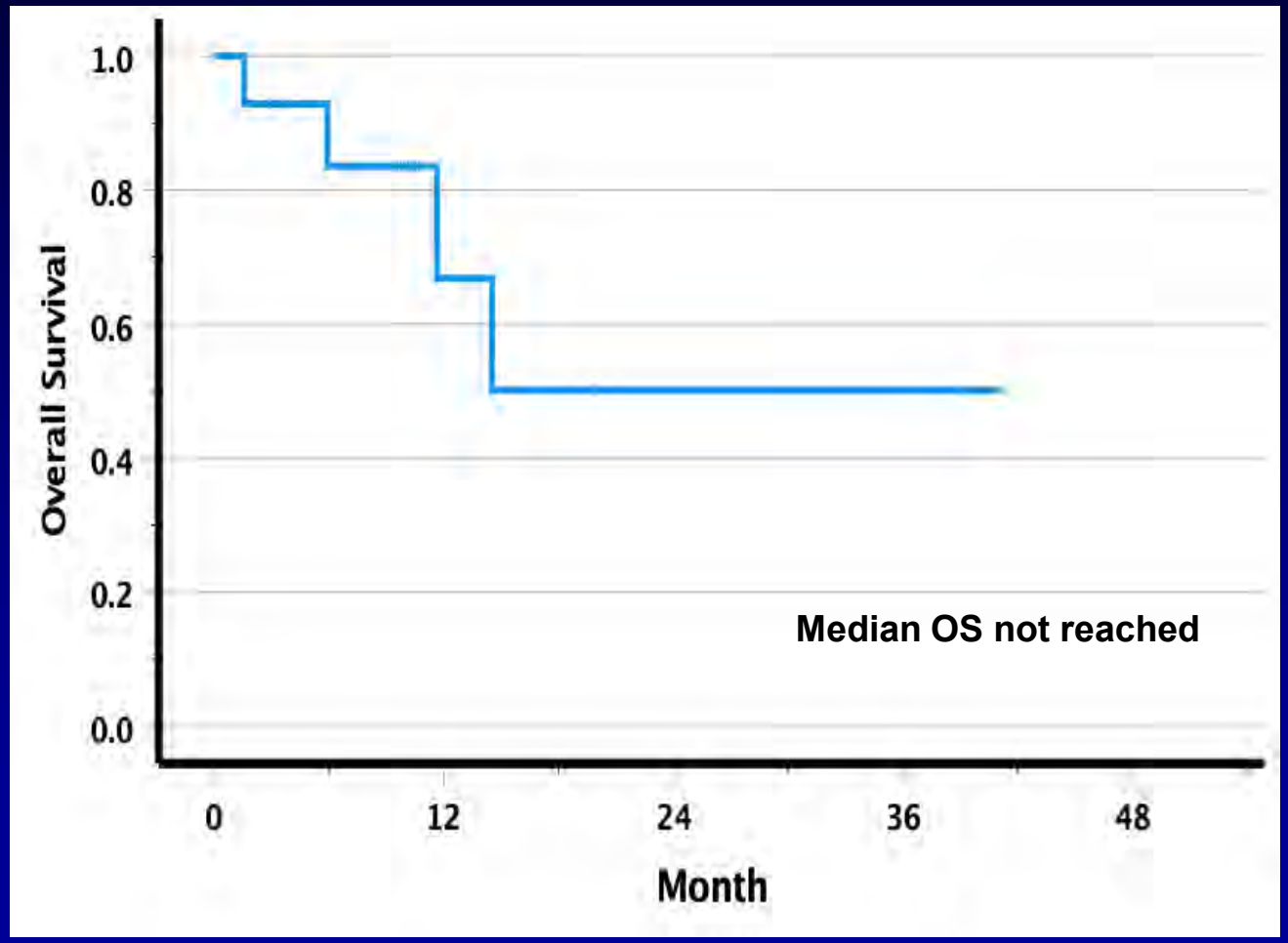
Response*, N (%)	All Patients (N=14)
CRc	**14 (100)**
CR	11 (79)
CRi	3 (21)
MLFS	0 (0)
Day 14 BM blasts ≤5%¥	**14 (100)**

Response*, N (%)	All Patients (N=14)
Best MRD, anytime	
Flow Cytometry (-)	9/12 (75)
FLT3 PCR (-)	12/14 (86)
30-day mortality	0 (0)
60-day mortality	**1 (7)**
Bridge to ASCT	**4 (19)**

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

Frontline Cohort

Overall Survival



Median follow-up: 11 months

Last follow-up

2 relapses:

- 1 TP53, complex (FLT3-)
- 1 MECOM (FLT3-)

4 deaths:

- 2 deaths in CR (1 post-SCT)
- 2 deaths after relapse

10 alive:

- All in CR
  - 2 post-SCT
  - 8 no SCT, on Rx

Adverse Events (all patients)

Non-hematological	Grade 3-5	Grade 1-2
Febrile Neutropenia	26 (42)	1 (2)
Lung infection	22 (35)	0 (0)
Infection - other	10 (16)	6 (10)
Sepsis	6 (10)	0 (0)
Hypermagnesemia	2 (3)	8 (13)
Syncope	2 (3)	0 (0)
Hyperbilirubinemia	2 (3)	18 (29)
Hypocalcemia	1 (2)	33 (53)
Hypokalemia	0 (0)	37 (60)
Hyponatremia	0 (0)	34 (55)
Dyspnea	0 (0)	26 (42)
Diarrhea	0 (0)	26 (42)
Hypophosphatemia	0 (0)	26 (42)
Hypoalbuminemia	0 (0)	25 (40)
Hypomagnesemia	0 (0)	19 (31)
QTcF Prolongation	1 (2)	6 (10)

A total of 62 patients were evaluated for toxicity (including 5 patients who were not evaluable for response). Only grade 3-5 (=/>5%) and grade 1-2 (=/ >30%) frequencies are shown (except QTcF, and overlapping toxicities between groups).

Prolonged Myelosuppression

Frontline Cohort (N=14)

Quizartinib D1-D28 in C1
6 patients: 3CR, 3CRi

Median time to ANC >500: 43 days [36-56 d]
Median time to PLT >50K: 42 days [21-46 d]

⇩

Reduced Quizartinib to D1-D14 in C1
8 patients: 8CR

Median time to ANC >500: 36 days [28-41 d]
Median time to PLT >50K: 35 days [27-71 d]

Final Results of the Phase Ib/II Study Evaluating Enasidenib in Combination With Venetoclax in Patients With *IDH2*-Mutated Relapsed/Refractory Myeloid Malignancies

Guillaume Richard-Carpentier, Gopila Gupta, Charina Cameron, Severine Cathelin, Aniket Bankar, Marta Davidson, Vikas Gupta, Dawn Maze, Mark D. Minden, Tracy Murphy, Aaron D. Schimmer, Andre C. Schuh, Hassan Sibai, Karen Yee, Courtney D. DiNardo, Joseph Brandwein, Caroline J. McNamara, Steven M. Chan

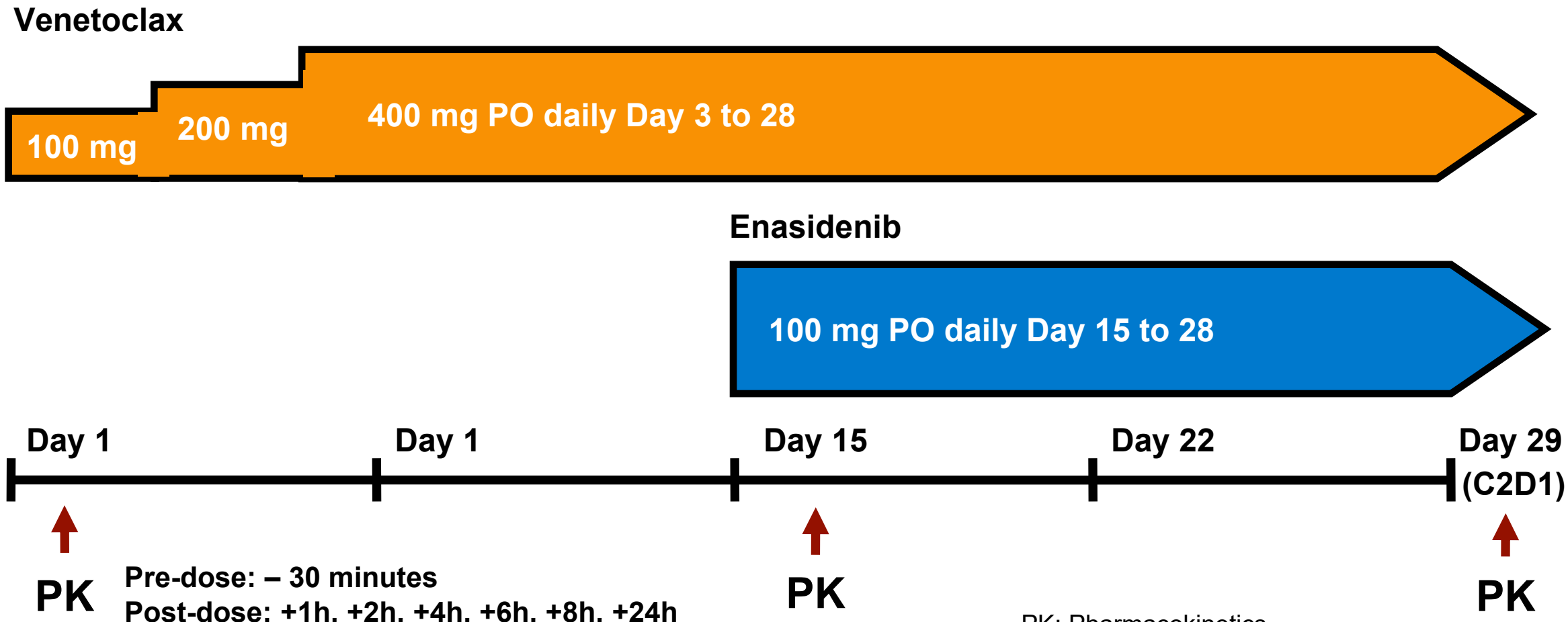
Medicine
UNIVERSITY OF TORONTO

Abstract number 159
American Society of Hematology Annual Meeting
San Diego, December 9th 2023

UHN
Toronto General
Toronto Western
Princess Margaret
Toronto Rehab
Michener Institute

Treatment protocol — Cycle 1

Dose level 0



PK: Pharmacokinetics

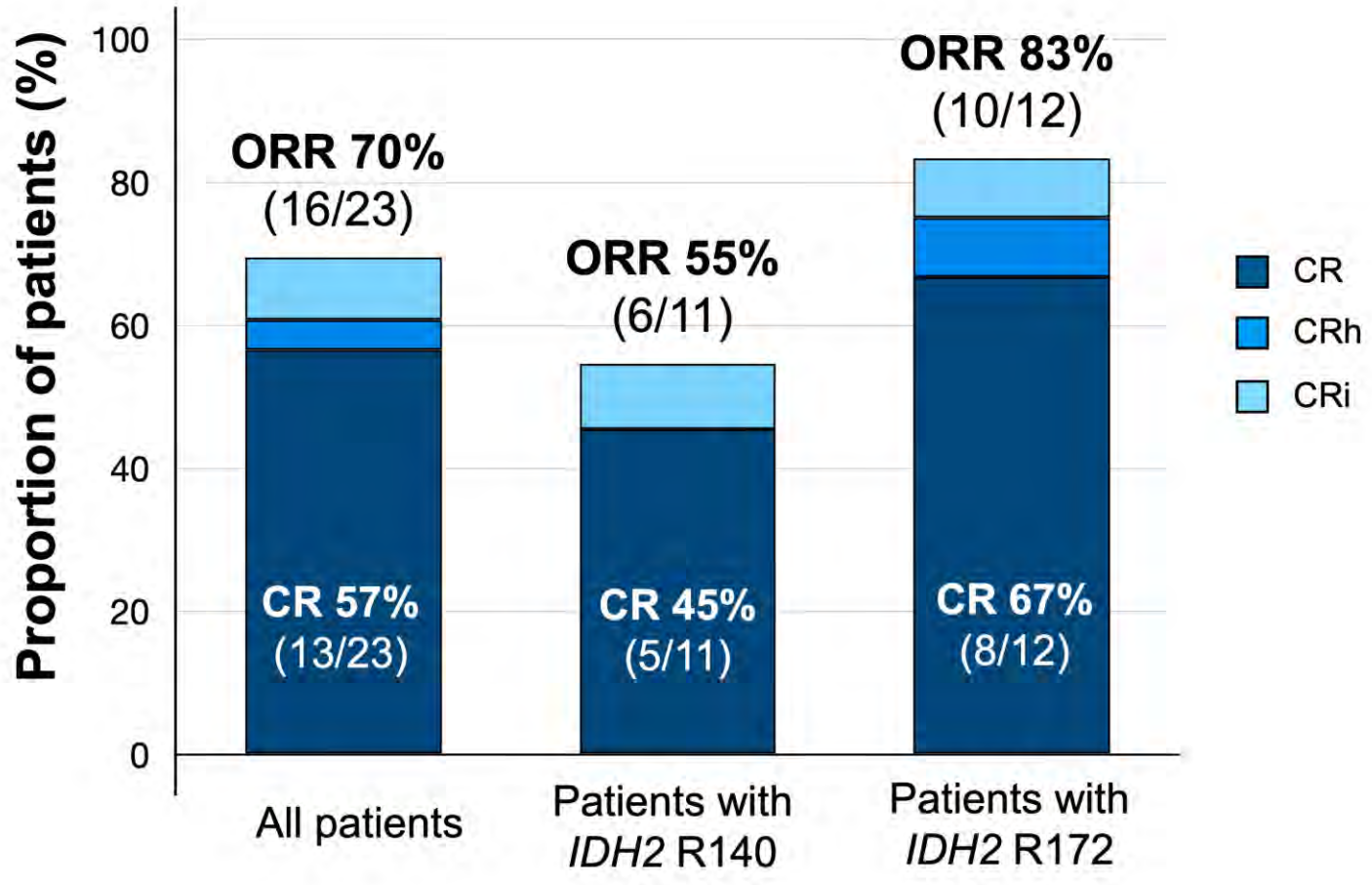
Baseline Patient Characteristics

Characteristics	Total (N = 27)
Age (years), median [range]	70 [23 – 84]
Sex (male), n (%)	16 (59)
WBC count (x 10^9/L), median [range]	1.3 [0.4 - 14.3]
BM blasts (%), median [range]	25 [5 - 94]
PB blasts (%), median [range]	7 [0 -100]
Diagnosis, n (%)	
Relapsed MDS-IB2	1 (4)
Relapsed AML	17 (63)
Refractory AML	9 (33)

Characteristics	Total (N = 27)
Number of prior lines of treatment, n (%)	
1 line of treatment	17 (63)
2 lines of treatment	10 (37)
Prior therapy, n (%)	
Chemotherapy	23 (85)
HMA	9 (33)
Allogeneic SCT	5 (19)
***IDH2* mutant allele**, n (%)	
R140Q	15 (56)
R172K/W	12 (44)
***IDH2* mutant VAF**, median [range]	23.4 [2.3 – 49.9]

Abbreviations: WBC, white blood cells; BM, bone marrow; PB, peripheral blood; MDS-IB2, myelodysplastic syndrome with increased blasts 2; AML, acute myeloid leukemia.

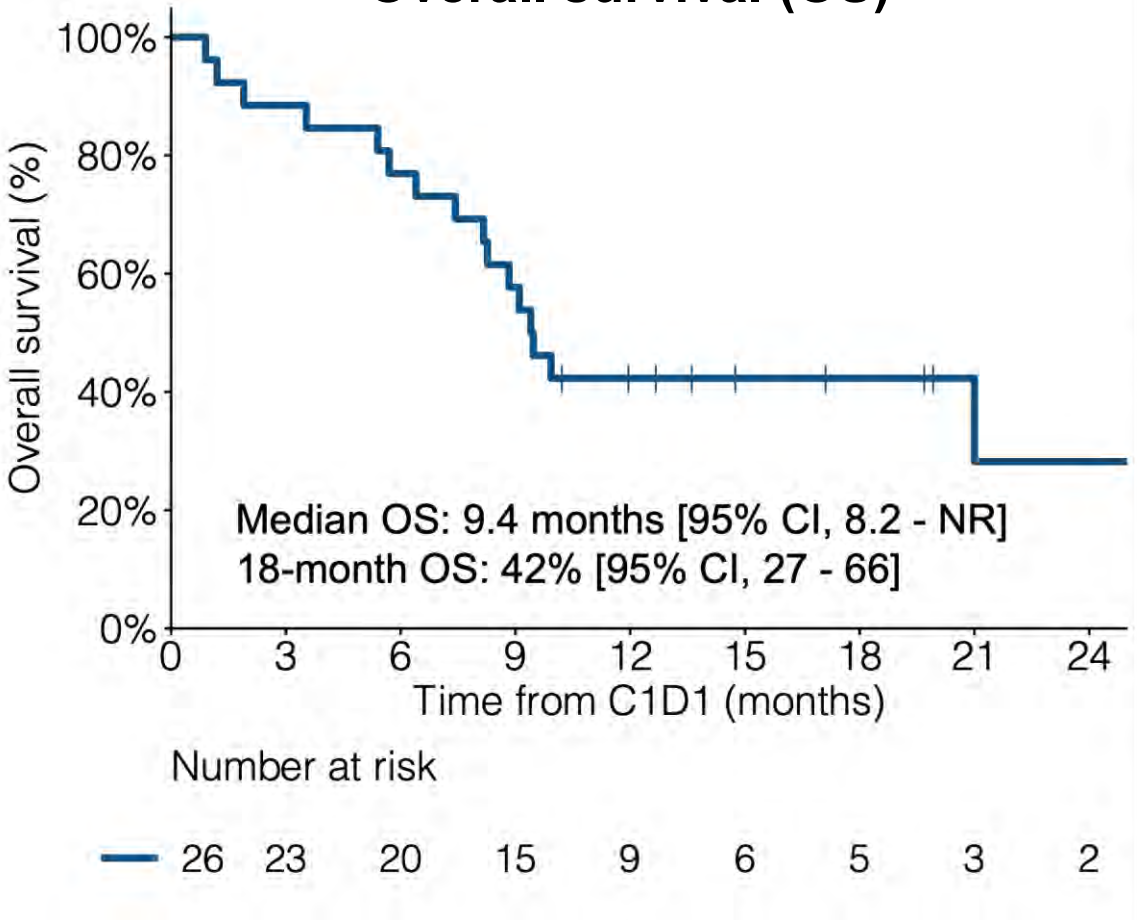
Response rates in patients with *IDH2*-mutated R/R AML



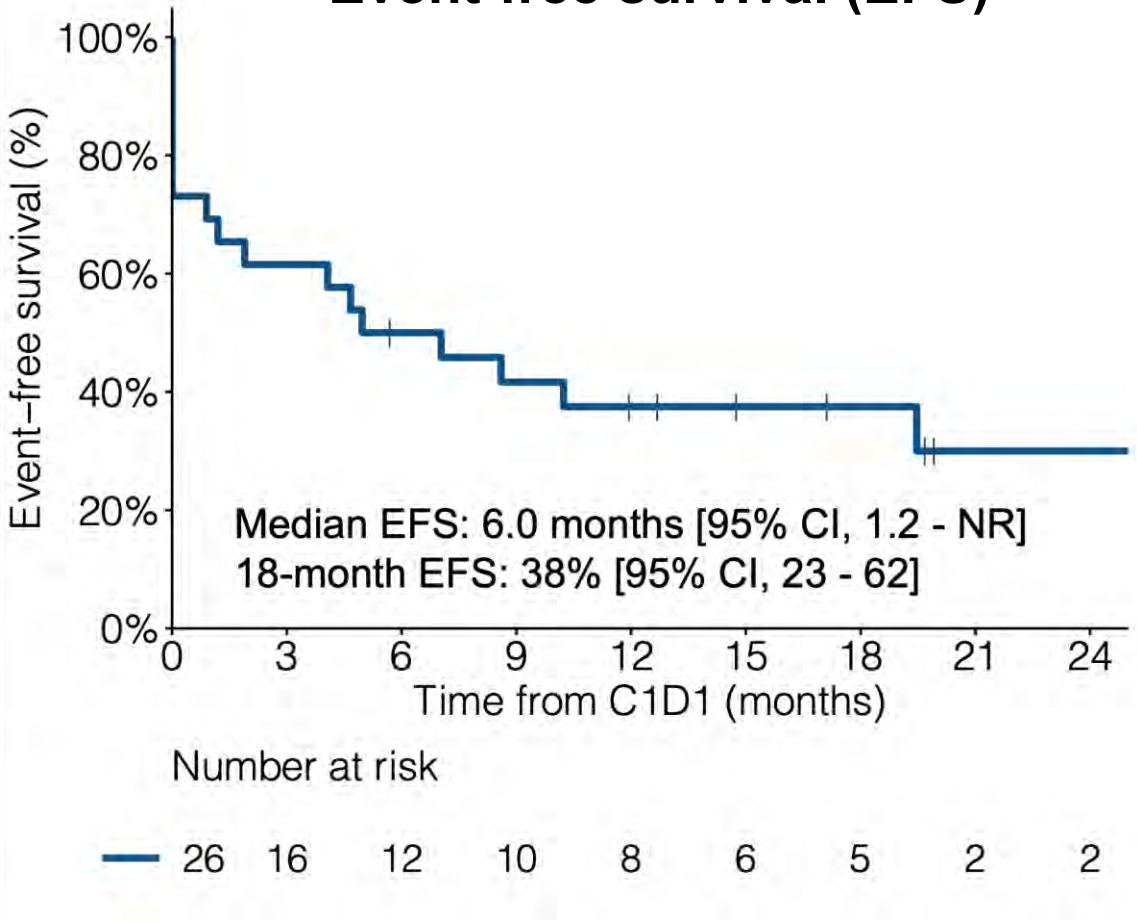
★ The patient with R/R MDS received less than 1 cycle of treatment and was not evaluable for response

Survival analyses in patients with *IDH2*-mutated R/R AML

Overall survival (OS)



Event-free survival (EFS)



Median Follow-up: 17.1 months [range, 0.9 — 31.4 months]

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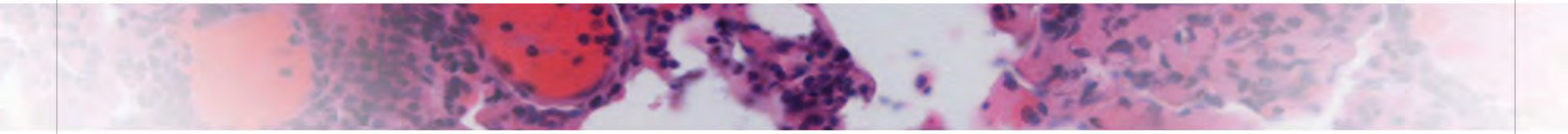
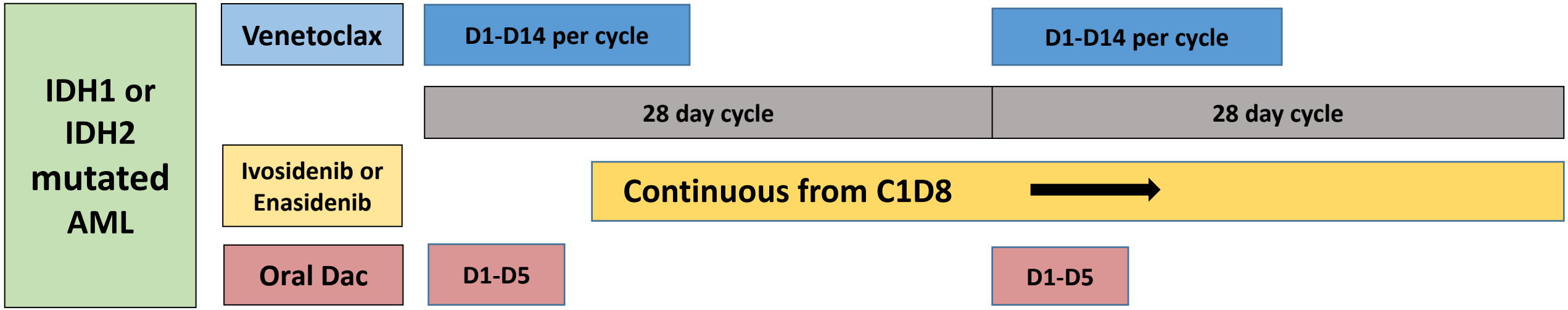


Phase Ib/2 Study of Oral Decitabine/Cedazuridine (ASTX727) and Venetoclax in Combination with the Targeted Mutant *IDH1* Inhibitor Ivosidenib or the Targeted Mutant *IDH2* Inhibitor Enasidenib: 2023 Update

Himachandana Atluri, MD[1], Jillian Mullin, MS[2], Koichi Takahashi, MD, PhD[3], Sanam Loghavi, MD[4] Abhishek Maiti, MD[3], Koji Sasaki, MD[3], Naval G. Daver, MD[3], Yesid Alvarado,MD[3], Naveen Pemmaraju, MD[3], Gautam Borthakur, MD[3], Danielle Hammond,MD[3], Kelly Chien,MD[3], Alessandra Ferrajoli, MD[3], Nicholas J. Short, MD[3], Hussein A. Abbas, MD, PhD[3], Elias Jabbour,MD[3], Michael Andreeff, MD, PhD[3], Farhad Ravandi, MD[3], Rebecca S. S. Tidwell, MS[5], Xuemei Wang, MS[5], Marina Konopleva, MD[6] , Guillermo Garcia-Manero, MD[3], Hagop M. Kantarjian[3], Courtney D. DiNardo, MD[3]

Treatment Schema



Selected RP2D Combination Doses
Arm A: **ASTX727 (D1-5) + VEN 600 mg (D1-14) + Ivosidenib 500 mg daily (D8 onwards)**
Arm B: **ASTX727 (D1-5) + VEN 400 mg (D1-14) + Enasidenib 100 mg daily (D8 onwards)**

Friese et al. J Clin Pharmacology. 2017
Lachowiez et al. Blood Advances. 2022

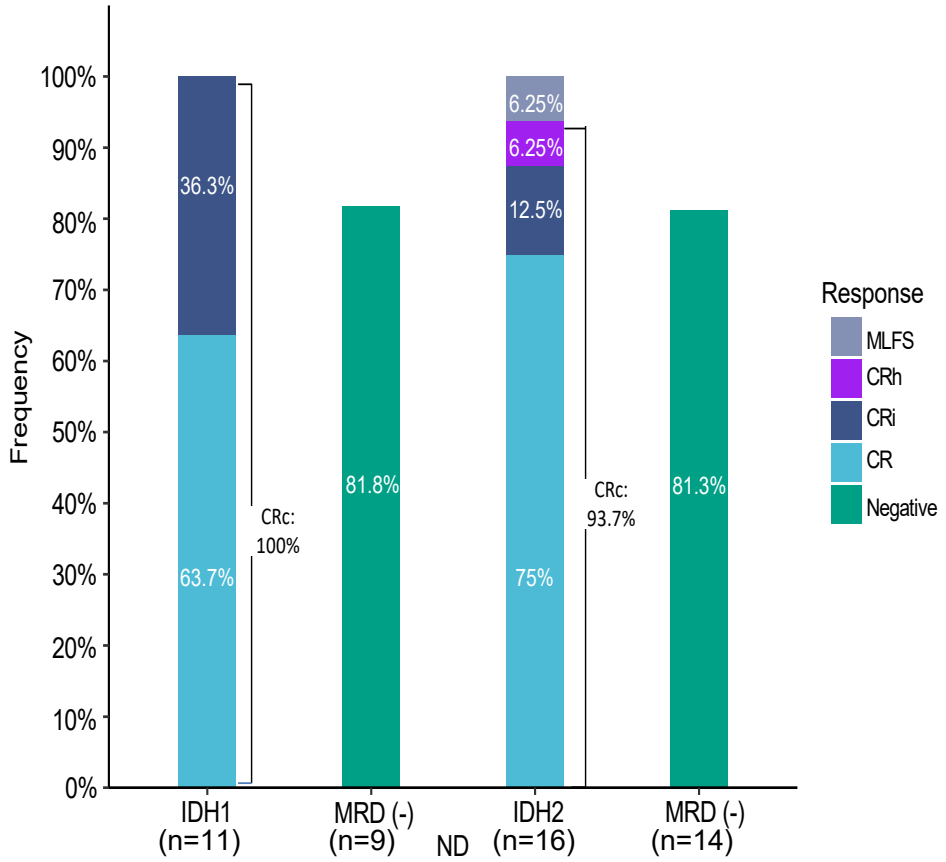
Demographics

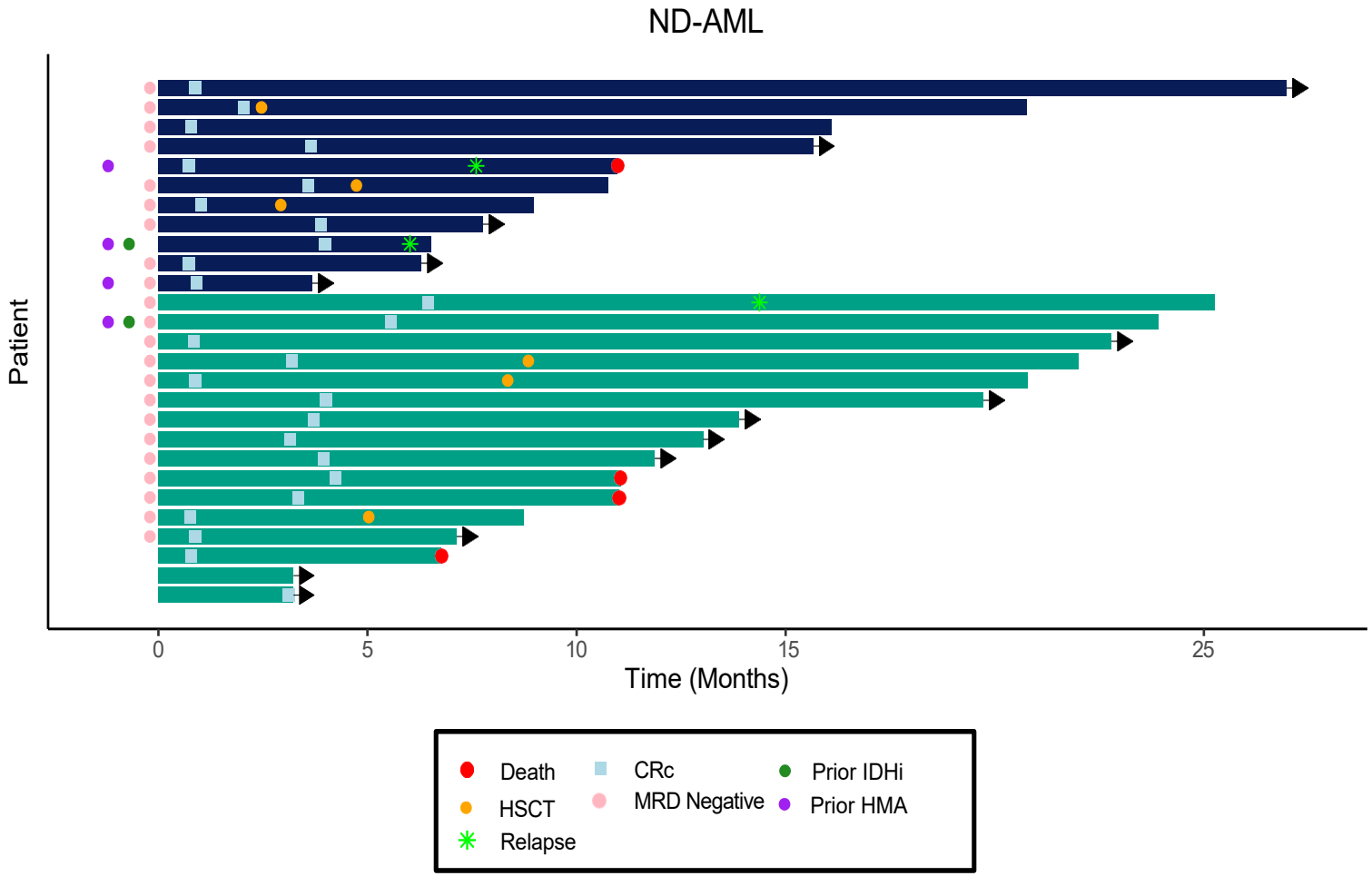
Baseline Characteristics					
Variable	All (n=57)	Newly Diagnosed (n=27)		Relapsed Refractory (n=30)	
		IDH1 (n=11)	IDH2 (n=16)	IDH1 (n=11)	IDH2 (n=19)
Age (years)	72 (41-86)	74 (70-80)	71 (62-83)	73 (41-86)	70 (56-84)
Male	35 (61)	4 (36)	12 (75)	8 (72)	11 (58)
ECOG	1 (1-2)	2 (1-2)	2 (1-2)	1 (1-2)	1(1-2)
ELN Risk (2022)					
ELN Favorable	7 (12)	3 (27)	2 (13)	1 (9)	1 (5)
ELN Intermediate	2 (4)	-	1 (6)	-	2 (10)
ELN Adverse	47 (82)	8 (72)	13 (81)	10 (91)	16 (85)
Cytogenetic Risk					
Intermediate Risk	37 (65)	8 (73)	14 (88)	4 (36)	11 (58)
Adverse Risk	20 (35)	3 (27)	2 (12)	7 (64)	8 (42)
Co-Occurring Mutations					
NPM1	9 (16)	3 (27)	3 (19)	2 (18)	1 (5)
KRAS/NRAS	6 (14)	1 (9)	3 (19)	1 (9)	1 (5)
FLT3	1 (2)	-	-	1 (9)	-
TP53	12 (21)	-	2 (12)	6 (55)	4 (21)

Most are ELN Adverse due to presence of splicing mutations

Prior Treatments (R/R Only)		
	IDH1 (n=11)	IDH2 (n=19)
Prior HMA + VEN	6 (55)	13 (68)
No Prior VEN	3 (27)	6 (32)
Prior IDHi	4 (36)	3 (16)
HMA/VEN/IDHi naïve	1 (9)	4 (21)

CRc Rates in ND-AML

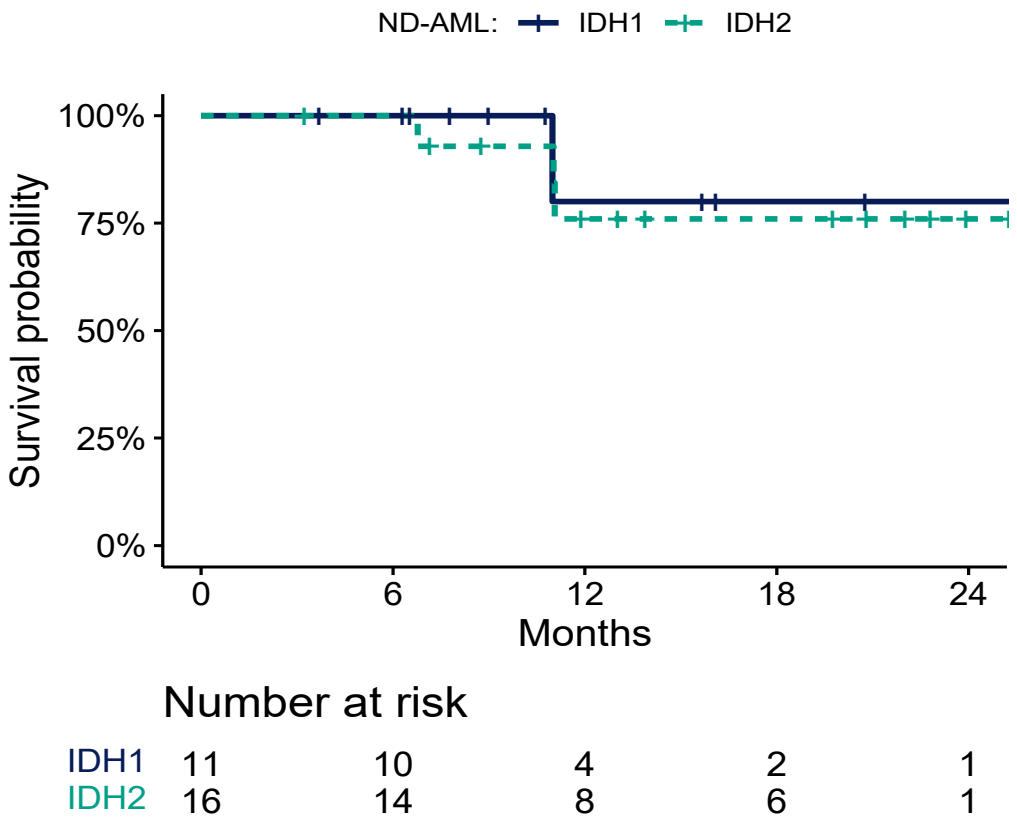




Overall CRc 96.2% with 85% MRD negative by multiparameter flow cytometry

OS and DOR in ND-AML

Overall Survival



ND-AML		
Outcome (months)	**IDH1 (n=11)**	**IDH2 (n=16)**
Median DOR	NR (6.88-NR)	NR (10.1-NR)
Median OS	NR	NR

Adverse Events

Adverse Events		
	Grade 1/2	Grade 3/4
Febrile Neutropenia	-	27 (47)
Hyperbilirubinemia*	7 (12)	3 (5)
Mucositis**	5 (9)	2 (3)
GI Toxicity	12 (21)	1 (2)
ALT/AST Elevation	17 (29)	1 (2)
Creatinine Elevation	16 (28)	-
Electrolyte abnormalities	12 (21)	-

*Related to known inhibition of UGT1A1 by enasidenib
**1 case attributed to hydroxyurea use

Adverse Events of Special Interest		
Adverse Event	IDH1 (n=22)	IDH2 (n=35)
Tumor Lysis	1 (5)	1 (3)
DS	3 (14)	2 (6)

Mortality		
Mortality	ND-AML	RR-AML
30 Day Mortality	0%	3.3%
60 Day Mortality	0%	6.6%

Cycle Lengths		
	ND-AML	R/R AML
Cycle 1	36 (23-72)	36 (23-92)
Cycle 2	35 (28-76)	48(28-88)
Cycle 3	40 (28-75)	36 (28 – 68)

*Medians reported in days (range)

Venetoclax Plus High-Dose Cytarabine and Mitoxantrone (HAM-Ven) As Salvage Treatment for Relapsed/Refractory AML: Updated Results of the Phase-I/II SAL RELAX Trial

SAL
Study Alliance Leukemia

Leo Ruhnke, Christoph Schliemann, Jan-Henrik Mikesch, Matthias Stelljes, Lars Fransecky, Björn Steffen, Martin Kaufmann, Andreas Burchert, Andreas Rank, Maher Hanoun, Alexander Höllein, Sabrina Kraus, Mathias Hänel, Kerstin Schäfer-Eckart, Annett Haake, Frank Fiebig, Sven Zukunft, Jan Moritz Middeke, Désirée Kunadt, Johannes Schetelig, Malte von Bonin, Maximilian Alexander Röhnert, Uta Oelschlägel, Friedrich Stölzel, Claudia D Baldus, Hubert Serve, Martin Wermke, Martin Bornhäuser, and Christoph Röllig

HAM+Ven in R/R AML: **RELAX trial idea / trial design**

	Drugs	d1	d2	d3	d4	d5
HAM	**Cytarabine** (1000-3000 mg/m^2 BID)	days1-3				
	Mitoxantrone (10 mg/m^2 QD)			days 3-5		

	Drugs	d1	d2	d3	d4	d5	d6	d7	d8-14
HAM + Ven	**Cytarabine** (1000 mg/m^2 BID)			days 3-5					
	Mitoxantrone (10 mg/m^2 QD)					days 5-7			
	Venetoclax (400 mg QD, initial ramp-up)	days 1-14							

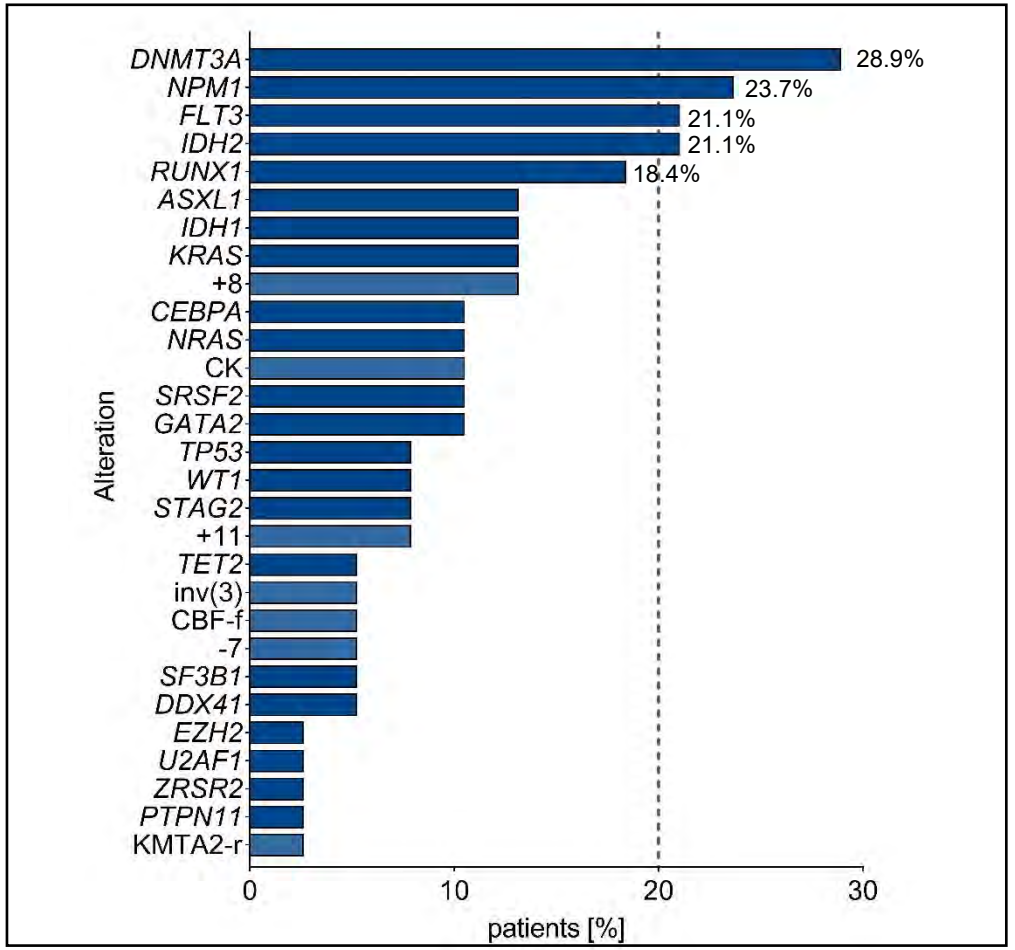
HAM+Ven in R/R AML: **Baseline characteristics**

Interim analysis: data on first 38 pts treated within RELAX trial (12 phase I, 26 phase II)

Baseline characteristics

Characteristics	All patients, n = 38 n/n (%)
Age	54 y (26-74)
Sex, female	17 (45%)
AML state	
Relapsed AML	28 (74%)
Primary refractory AML	10 (26%)
Prior therapies	
Induction therapy (DA, CPX-351)	38 (100%)
Induction plus consolidation therapy	18 (48%)
Induction plus allo-SCT	10 (26%)
ELN 2022 risk group	
Favorable	8 (21%)
Intermediate	12 (32%)
Adverse	18 (47%)

Molecular profile (initial diagnosis)



HAM+Ven in R/R AML: **Adverse Events and Early Mortality**

HAM+Ven is feasible and safe

Adverse Events	all grades, n/n (%)	≥ grade 3, n/n (%)
Febrile neutropenia	**19/36 (53%)**	**19/36 (53%)**
Nausea	9/36 (25%)	2/36 (6%)
Pneumonia	**9/36 (25%)**	**9/36 (25%)**
Mucositis oral	8/36 (22%)	4/36 (11%)
Diarrhea	6/36 (17%)	3/36 (8%)
Sepsis	**4/36 (11%)**	**4/36 (11%)**
Vomiting	4/36 (11%)	0/36 (0%)
Skin/soft tissue infections	**4/36 (11%)**	**2/36 (6%)**
Typhilitis	**3/36 (8%)**	**3/36 (8%)**
Urinary tract infections	**3/36 (8%)**	**1/36 (3%)**
Abdominal pain	3/36 (8%)	1/36 (3%)
Bacteremia	**3/36 (8%)**	**0/36 (0%)**

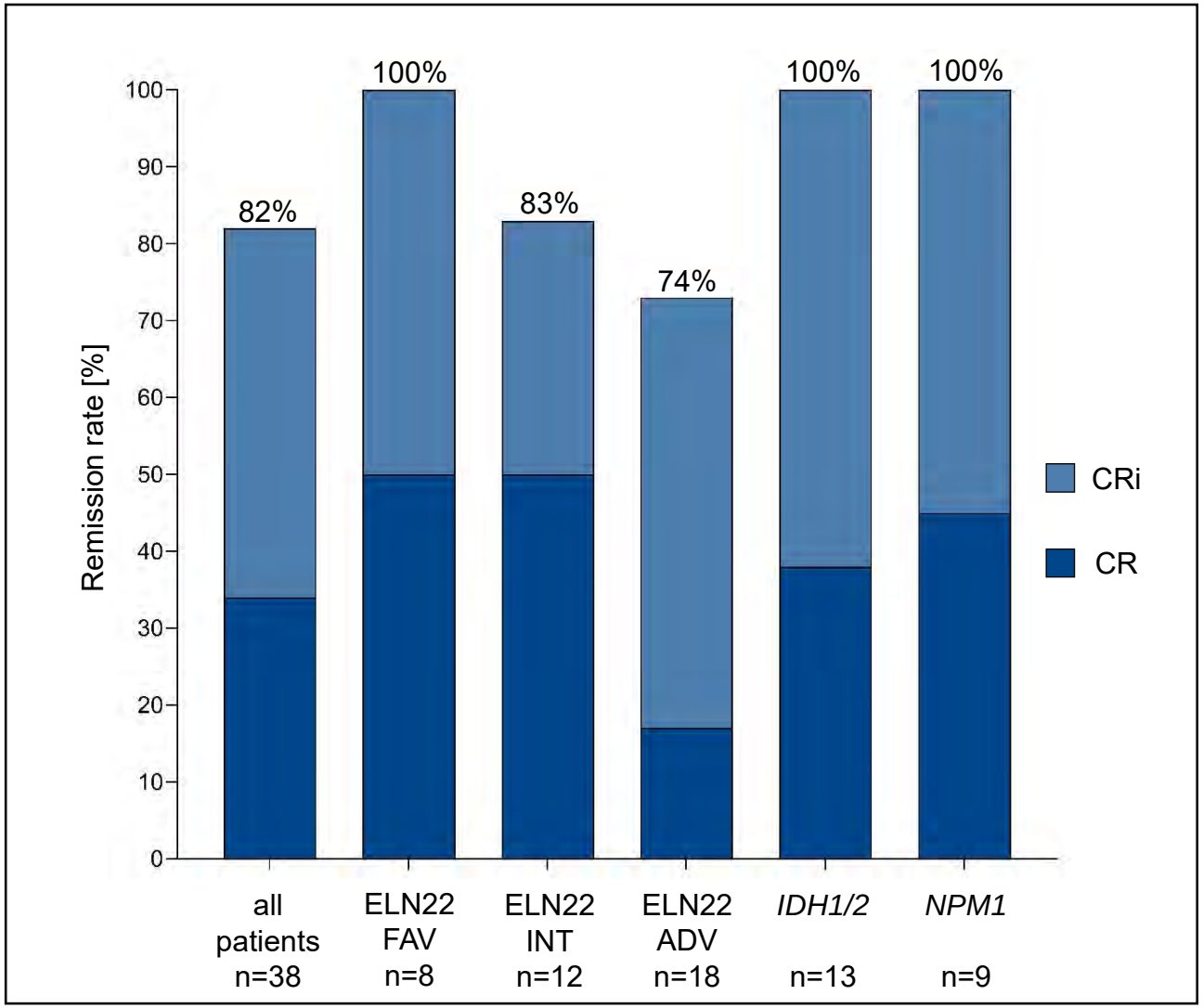
Early Mortality	n/n (%)
30-day mortality	1/38 (2.6%)
60-day mortality	2/38 (5.2%)

HAM+Ven in R/R AML: **Outcomes (CR rate, MRD)**

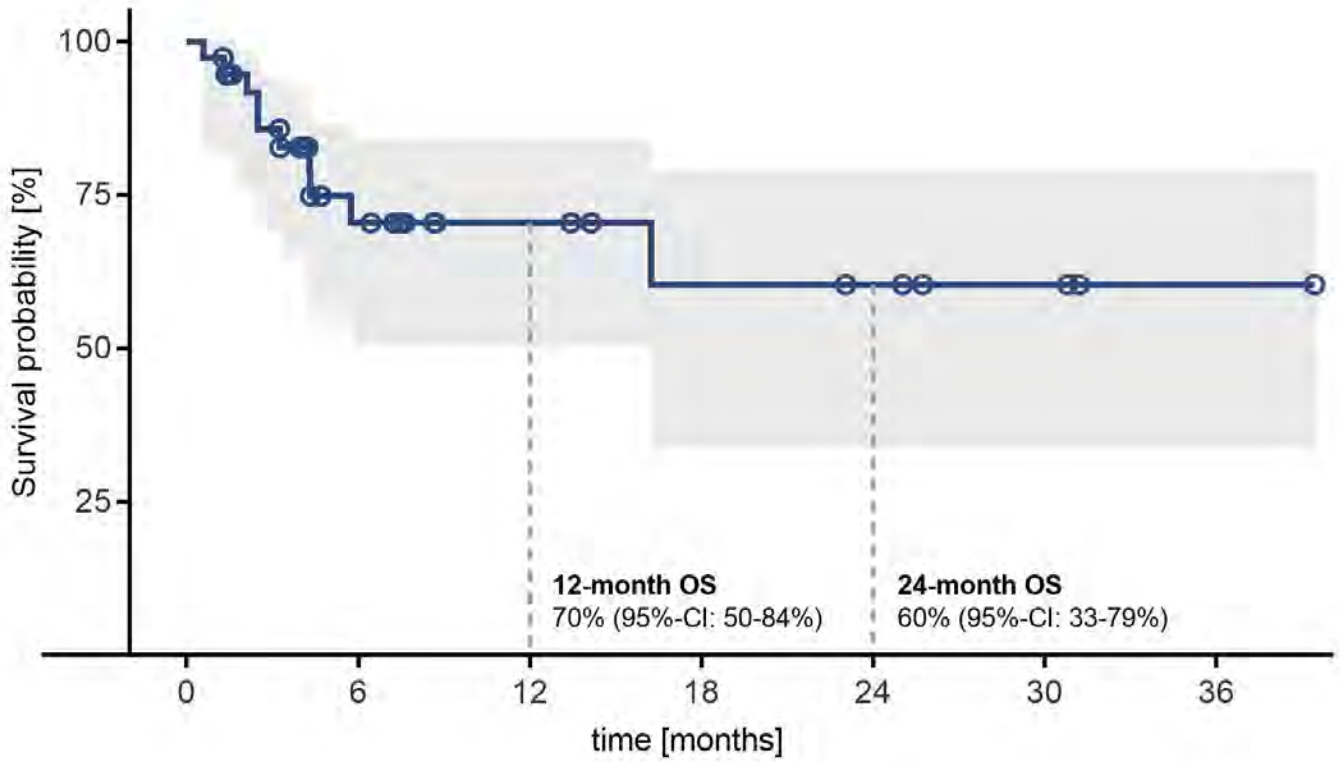
Response rates	n/n (%)
CRc	**31/38 (82%)**
CR	13/38 (34%)
CRi	18/38 (48%)
CRc ELN_{22} FAV	**8/8 (100%)**
CRc ELN_{22} INT	10/12 (83%)
CRc ELN_{22} ADV	13/18 (73%)
CRc *IDH1*/*IDH2*^{mut}	**13/13 (100%)**
CRc *NPM1*^{mut}	**9/9 (100%)**

MRD (MFC)	n/n (%)
CR_{MRD-} (MFC LAIP)	**7/22 (32%)**
CR_{MRD-} (MFC LAIP+DfN)	7/31 (23%)
CR_{MRD+} pts with MRD load <0.1%*	7/24 (29%)

*MRD events (LAIP and/or DfN)/CD45+ events



HAM+Ven in R/R AML: **Overall survival**



Demographic	All patients, (n=38)
Median follow-up, months	9
Median OS, months	NR
12-month OS	70,4%
24-month OS	60,4%

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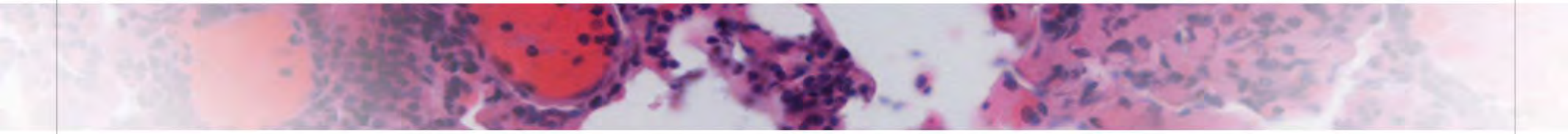


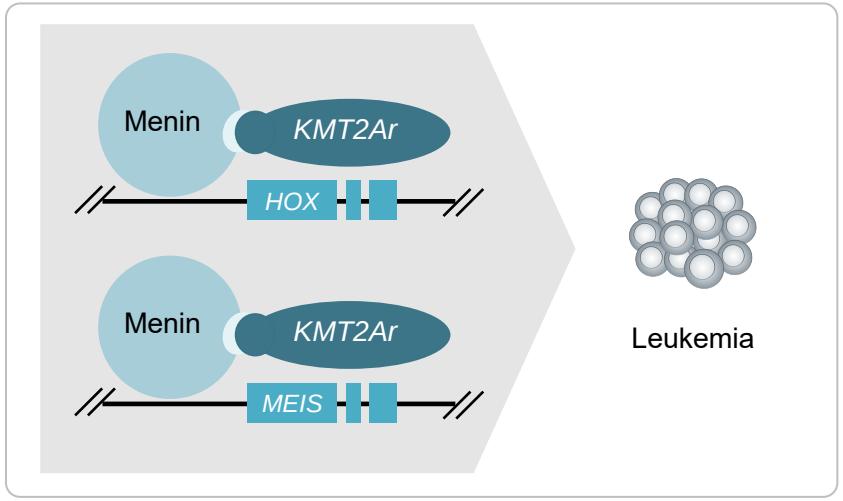
Revumenib Monotherapy in Patients with Relapsed/Refractory *KMT2Ar* Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal AUGMENT-101 Phase 2 Study

Ibrahim Aldoss, Ghayas C. Issa, Michael Thirman, John DiPersio, Martha Arellano, James S. Blachly, Gabriel N. Mannis, Alexander Perl, David S. Dickens, Christine M. McMahon, Elie Traer, C. Michel Zwaan, Carolyn Grove, Richard Stone, Paul J. Shami, Ioannis Mantzaris, Matthew Greenwood, Neerav Shukla, Branko Cuglievan, Yu Gu, Rebecca G. Bagley, Kate Madigan, Soujanya Sunkaraneni, Huy Van Nguyen, Nicole McNeer, Eytan M. Stein

Revumenib

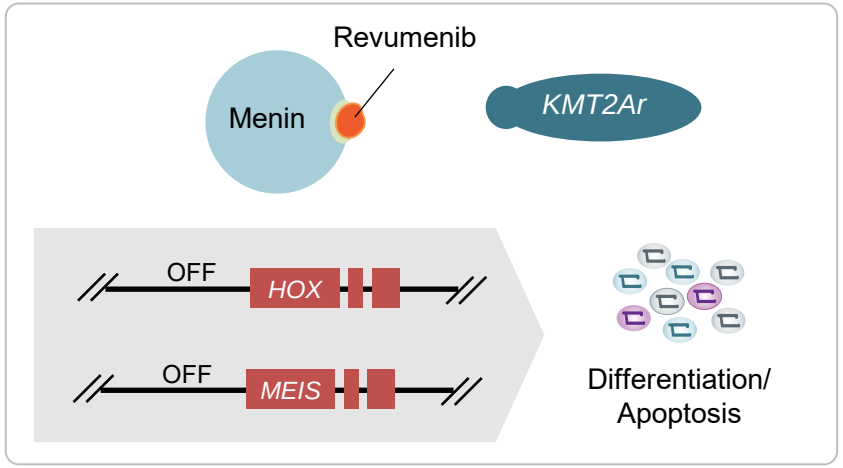
- The menin-KMT2A interaction is a key driver of leukemogenesis[1]
- In a phase 1 study of R/R *KMT2Ar* and *NPM1m* acute leukemias, revumenib demonstrated
  - Clinically meaningful responses that were consistent across subgroups[2]
  - High percentage (67%) of responders proceeding to transplant[2]
  - Manageable safety profile[2]

KMT2Ar acute leukemia



Gene transcription **ON**

Menin inhibition with revumenib



Gene transcription **OFF**

HOX, homeobox; KMT2A, histone-lysine N-methyltransferase 2A; *KMT2Ar*, KMT2A rearrangements; *MEIS*, Meis homeobox; *NPM1m*, nucleophosmin 1–mutated; R/R, relapsed/refractory.

1. Issa GC, Zarka J, Sasaki K, et al. *Blood Cancer J*. 2021;11:162. **2.** Issa GC, Aldoss I, DiPersio J, et al. *Nature*. 2023;615:920-924.

Baseline Characteristics

Parameter	Efficacy population (n=57)	Safety population (n=94)[a]
Leukemia type, n (%)		
AML	49 (86)	78 (83)
ALL	7 (12)	14 (15)
MPAL/Other	1 (2)	2 (2)
Co-mutations[b], n (%)		
FLT3	5 (9)	7 (7)
RAS	9 (16)	12 (13)
p53	4 (7)	5 (5)
Primary refractory, n (%)	14 (25)	18 (19)
Number of prior lines of therapy, median (range)	2 (1–11)	2 (1–11)
1, n (%)	17 (30)	25 (27)
2, n (%)	14 (25)	28 (30)
≥3, n (%)	26 (46)	41 (44)
Prior venetoclax, n (%)	41 (72)	61 (65)
Prior HSCT, n (%)	26 (46)	47 (50)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib. [b]In patients that had co-mutation status reported.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; *FLT3*, fms-related tyrosine kinase 3; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; MPAL, mixed phenotype acute leukemia; *RAS*, rat sarcoma virus.

Response

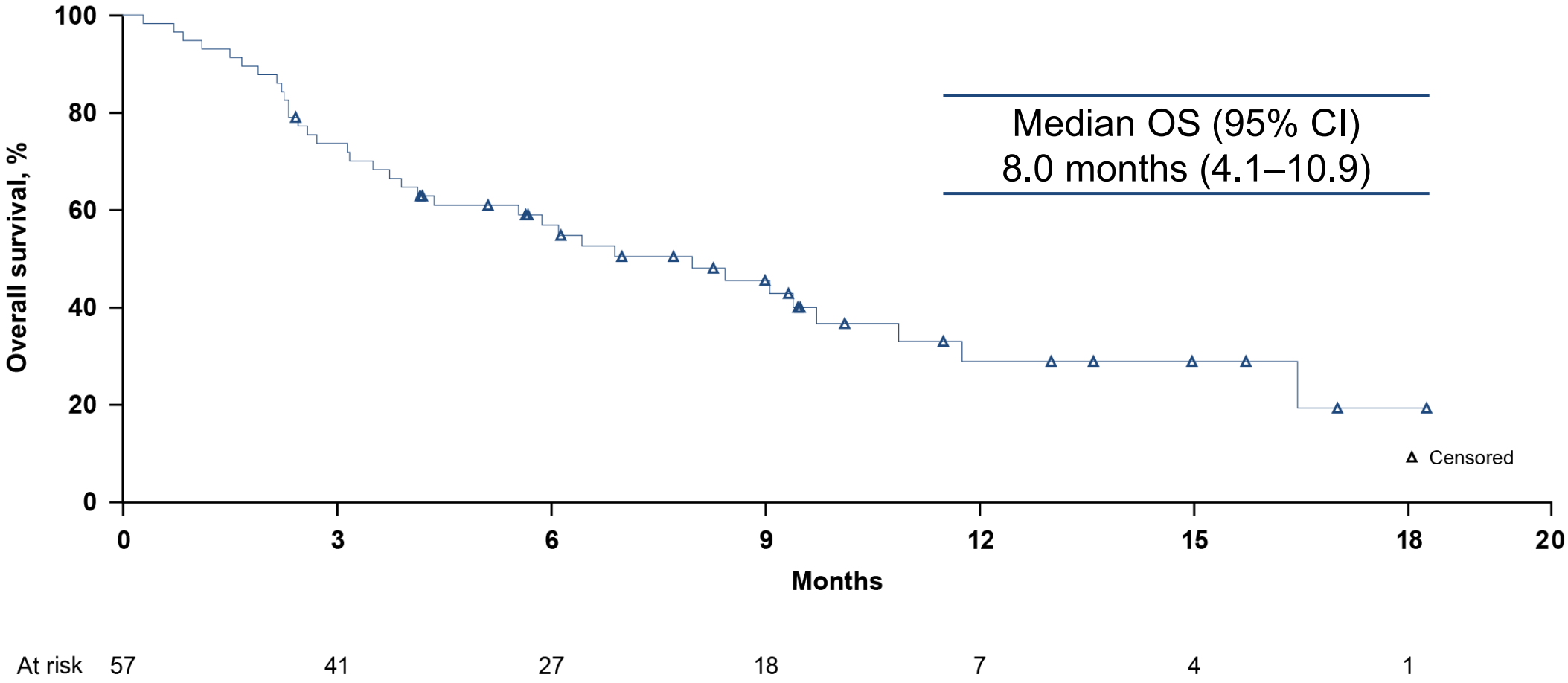
Parameter	Efficacy population (n=57)
ORR, n (%)	**36 (63)**
CR+CRh rate, n (%)	13 (23)
95% CI	12.7–35.8
P value, 1-sided	0.0036
CRc	25 (44)
95% CI	30.7–57.6
Negative MRD status[a]	
CR+CRh	7/10 (70)
CRc	15/22 (68)

Parameter	Efficacy population (n=57)
Best response, n (%)	
CR	10 (18)
CRh	3 (5)
CRi	1 (1.8)
CRp	11 (19)
MLFS	10 (18)
PR	1 (1.8)
PD	4 (7)
No response	14 (25)
Other[b]	3 (5)

Data cutoff: July 24, 2023. [a]MRD done locally; not all patients had MRD status reported. [b]Includes patients without postbaseline disease assessment.

CR, complete remission; CRc, composite CR (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; MLFS, morphological leukemia-free state; MRD, minimal residual disease; ORR, overall response rate (CRc+MLFS+PR); PD, progressive disease; PR, partial remission.

Overall Survival



OS, overall survival.

Revumenib Safety Profile (cont)

Any grade TEAEs that occurred in ≥25% patients

All terms, n (%)	Safety population (n=94)[a]
Nausea	42 (45)
Febrile neutropenia	36 (38)
Diarrhea	33 (35)
Vomiting	29 (31)
Differentiation syndrome	26 (28)
Hypokalemia	26 (28)
Epistaxis	25 (27)
QTc prolongation	24 (26)

Grade ≥3 TEAEs that occurred in ≥10% patients

All terms, n (%)	Safety population (n=94)[a]
Febrile neutropenia	35 (37)
Decreased neutrophil count	15 (16)
Decreased white blood cell count	15 (16)
Decreased platelet count	14 (15)
Anemia	17 (18)
Differentiation syndrome	15 (16)
QTc prolongation	13 (14)
Sepsis	11 (12)
Hypokalemia	10 (11)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.

No patients discontinued due to differentiation syndrome, QTc prolongation, or cytopenias

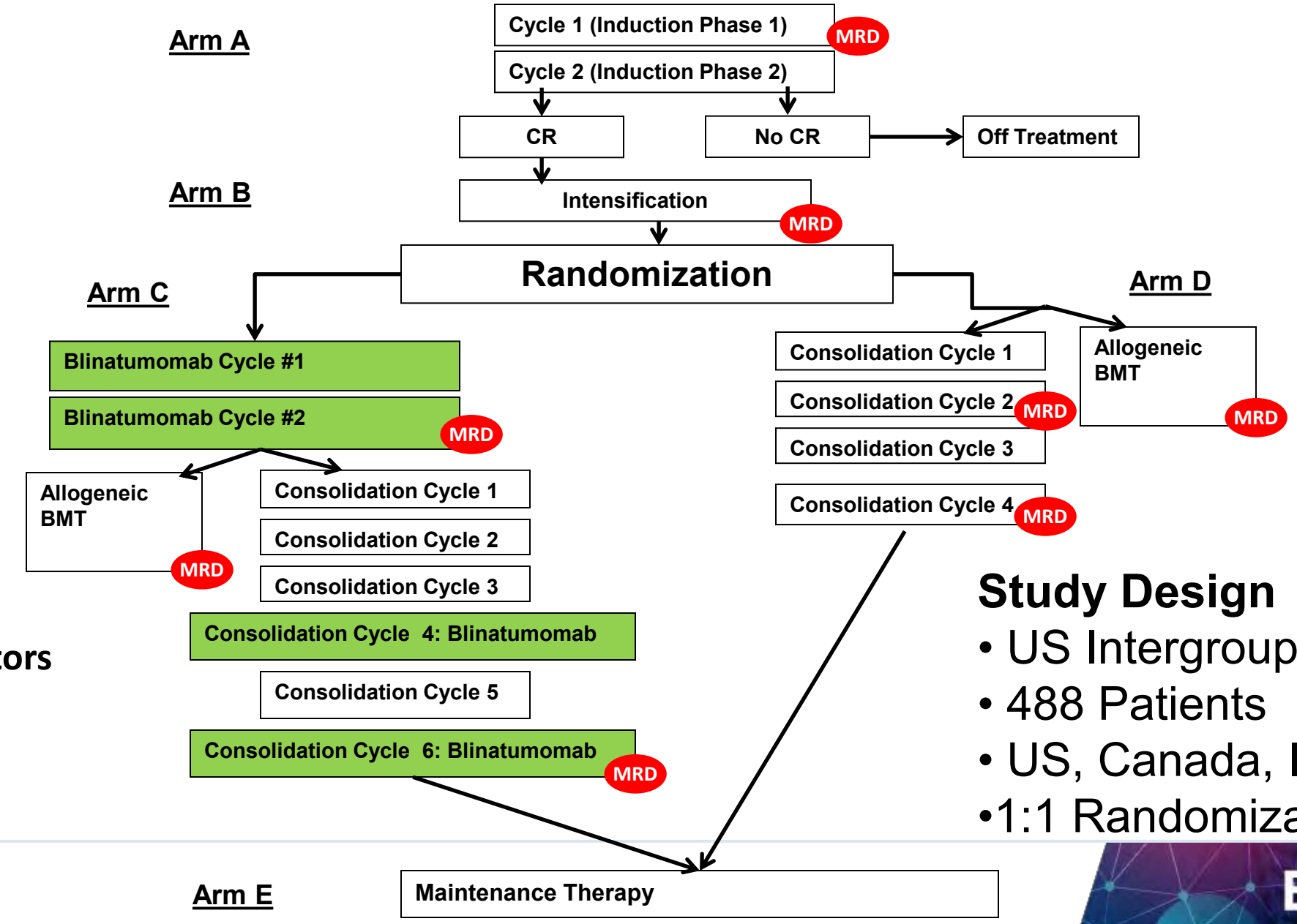
KMT2Ar, histone-lysine N-methyltransferase 2A rearrangements; TEAE, treatment-emergent adverse event.

Consolidation with Blinatumomab Improves Overall and Relapse-Free Survival in Patients with Newly Diagnosed B-Cell ALL: Impact of Age and MRD Level in ECOG-ACRIN E1910

Ryan Mattison on behalf of the E1910 Investigators
Mark Litzow, Zhuoxin Sun, Elisabeth Paietta, Charles Mullighan, Kathryn Roberts, Yanming Zhang, Janis Racevskis, Cheryl Willman, Matthew Wieduwilt, Michaela Liedtke, Julie Bergeron, Hillard Lazarus, Dan Arber, Brent Wood, Jacob Rowe, Keith Pratz, Shira Dinner, Noelle Frey, Steve Gore, Bhavana Bhatnagar, Ehab Atallah, Geoff Uy, Deepa Jeyakumar, Tara Lin, Shejal Patel, Michelle Elliott, Anjali Advani, Daniel DeAngelo, Dimitrios Tzachanis, Pankit Vachhani, Rupali Bhave, Richard Little, Harry Erba, Richard Stone, Selina Luger, Martin Tallman

June 10, 2023
Abstract S115
Session S435 Clinical Updates in ALL

E1910: Randomized Ph III Adult Frontline ALL



Stratification factors

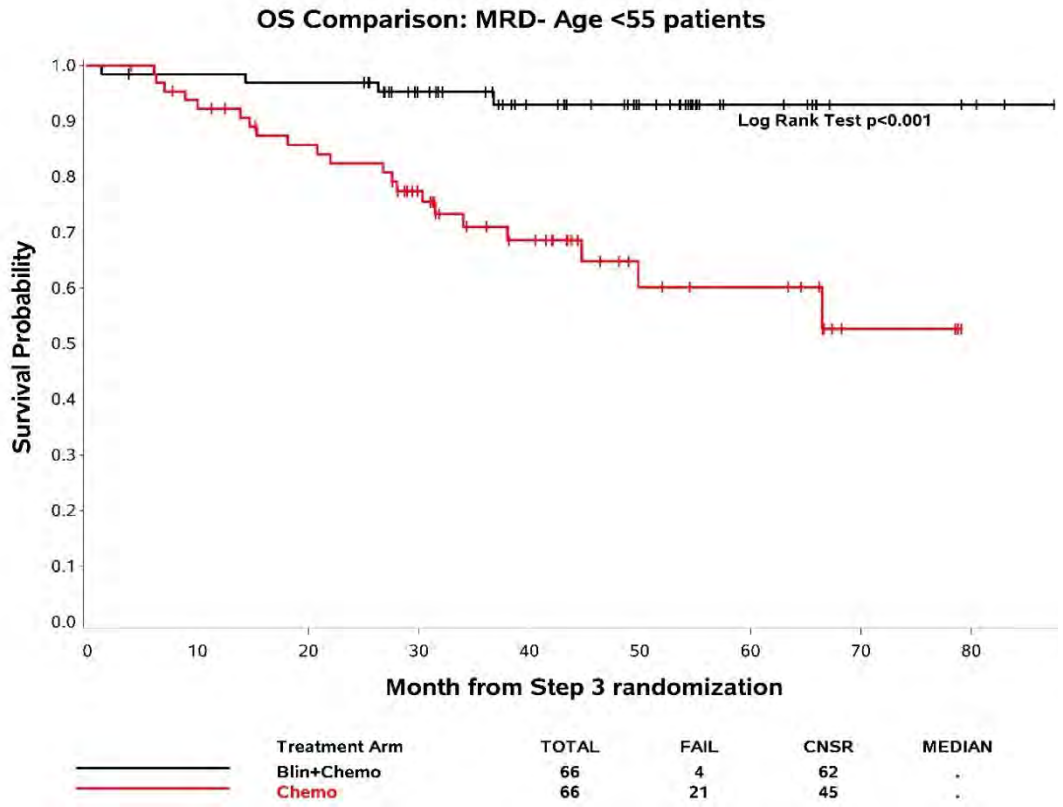
- Age < or >= 55
- CD20 status
- Rituximab use
- HSCT intent

Study Design

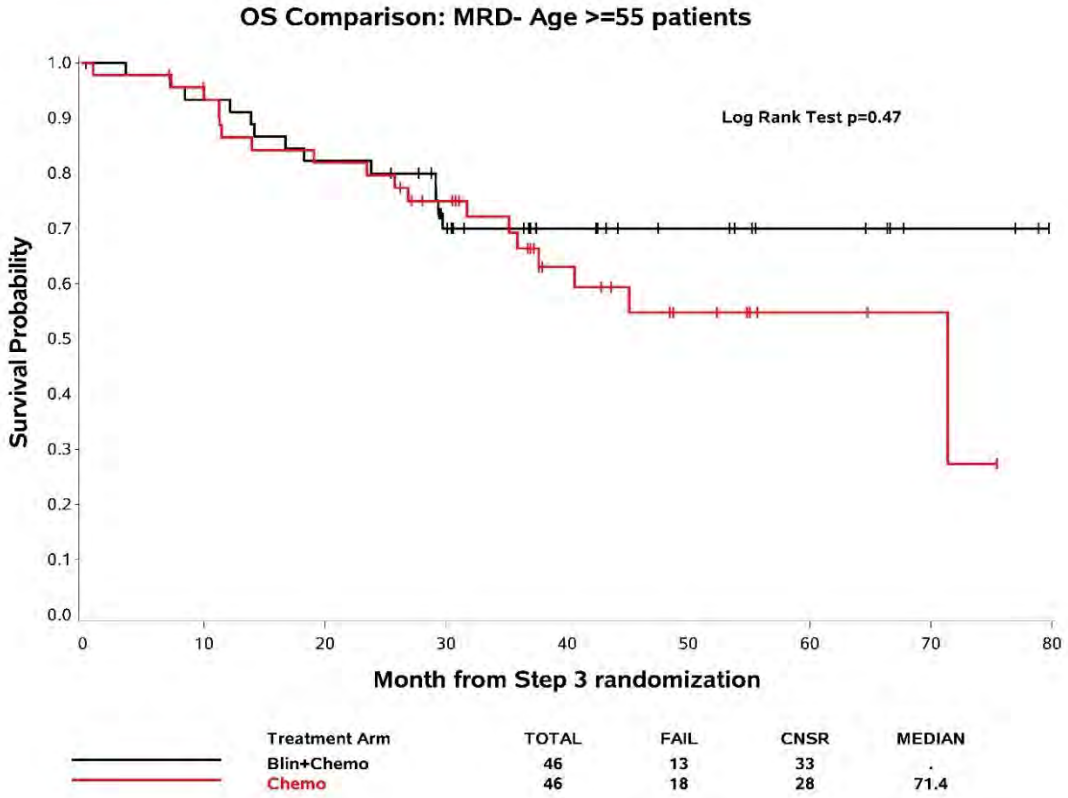
- US Intergroup study
- 488 Patients
- US, Canada, Israel
- 1:1 Randomization

Results

OS for MRD-negative patients stratified by age < 55 years or >= 55 years

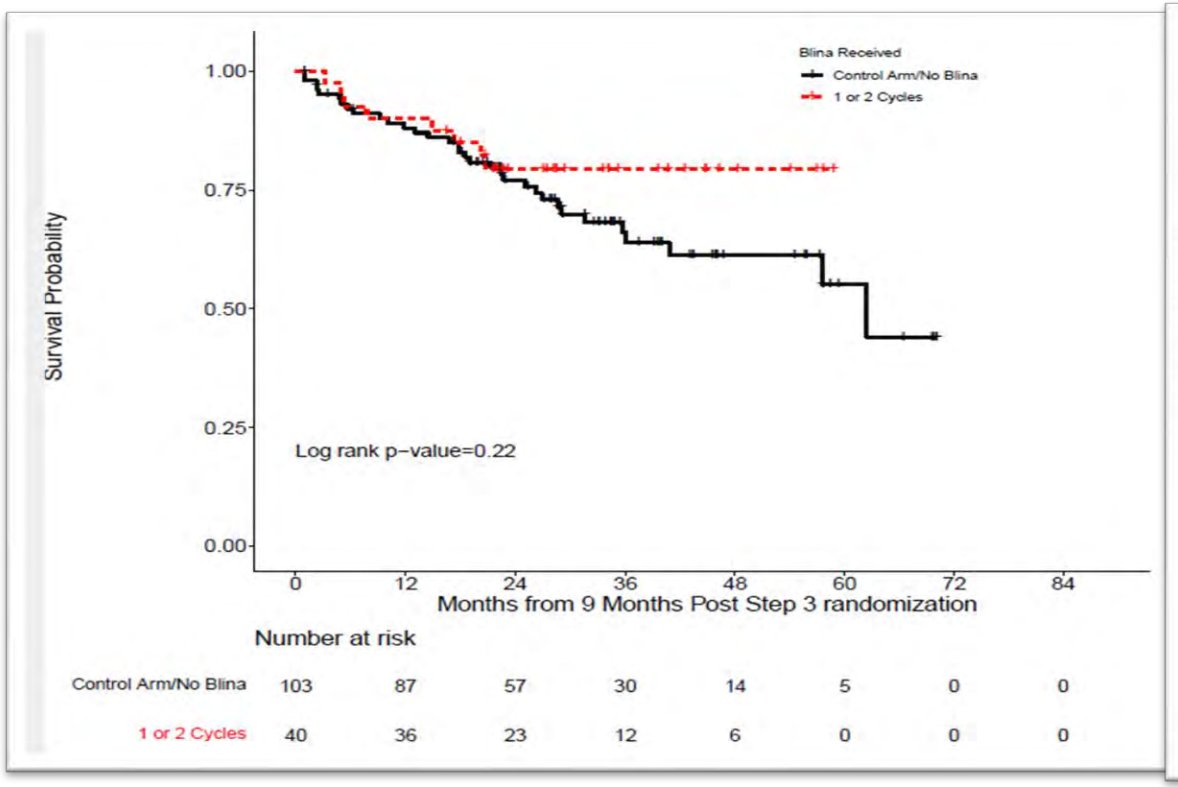


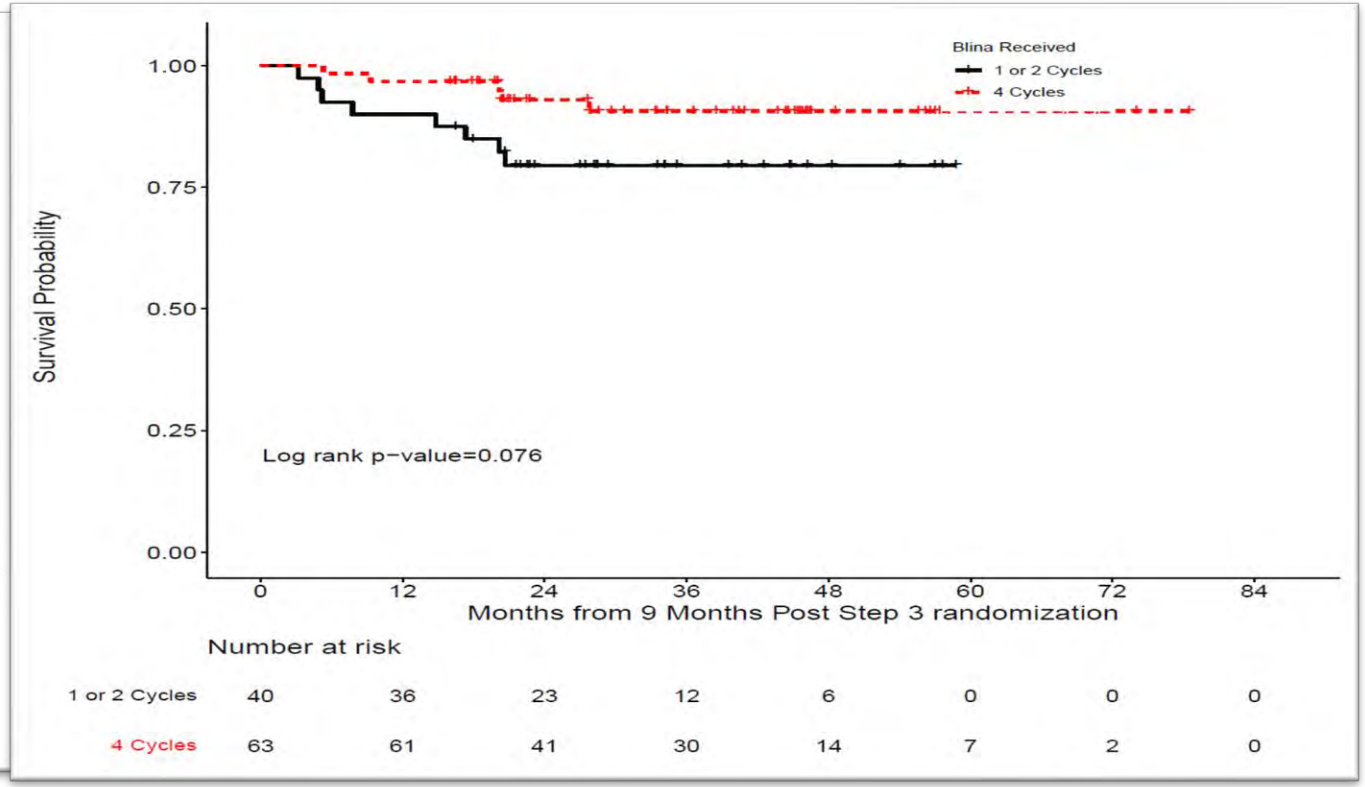
Median OS not reached both arms; HR 0.18, 95% CI: 0.06-0.52, p<0.001



Median OS NR vs 71.4 months, HR 0.77, 95% CI: 0.37-1.58, p=0.47

Assessment of Outcomes of Consolidation Therapy by Number of Cycles of Blinatumomab Received in Newly Diagnosed Measurable Residual Disease Negative Patients with B-lineage Acute Lymphoblastic Leukemia: in the ECOG-ACRIN E1910 Randomized Phase III National Clinical Trials Network Trial





Landmark analysis was used, where time 0 is 9 months post step 3 randomization (the time that patients were supposed to complete 4 cycles of blinatumomab).

Luger et al, ASH 2023

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NGS-based stratification refines the risk stratification in T-ALL and identifies a Very High-Risk subgroup of patients

M. Simonin*, **L. Vasseur***, E. Lengliné, L. Lhermitte, A. Cabannes-Hamy, M. Balsat, A. Schmidt, ME. Dourthe, A. Touzart, C. Graux, N. Grardel, JM. Cayuela, I. Arnoux, V. Gandemer, F. Huguet, S. Ducassou, V. Lhéritier, Y. Chalandon, N. Ifrah, H. Dombret, E. Macintyre, A. Petit, P. Rousselot, J. Lambert, A. Baruchel, N. Boissel, V. Asnafi

GRAALL
LALA GOELAMS SAKK

SFCE Société Française de lutte contre les Cancers et les leucémies de l'Enfant et de l'adolescent

* contributed equally

IMPACT OF NGS CLASSIFIER

GRAALL 03/05-T:

5-year CIR: p<0.0001

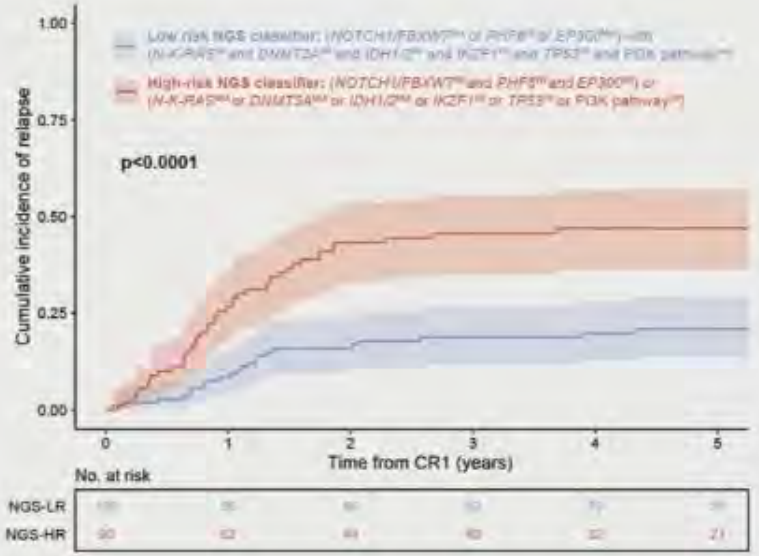
- NGS Low Risk: 21% (95%CI:14%-29%)
- NGS High Risk: 47% (95%CI:36%-57%)

5-year OS: p<0.0001

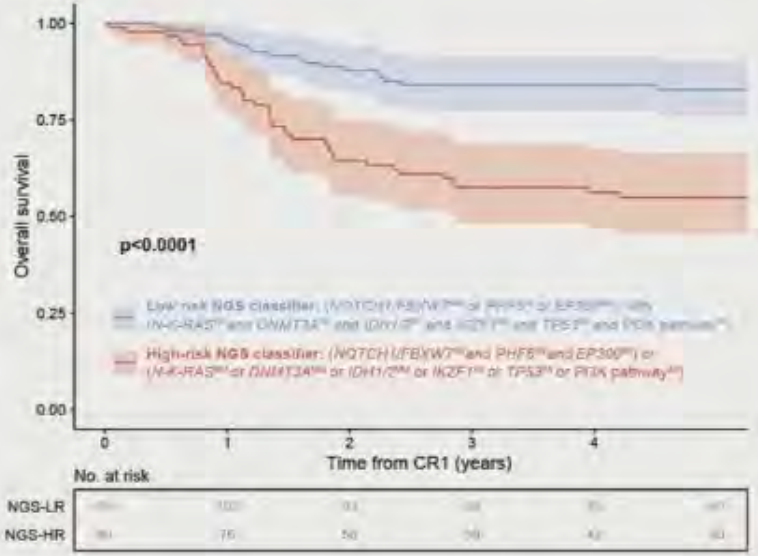
- NGS Low Risk: 83% (95%CI:76%-90%)
- NGS High Risk: 55% (95%CI:45%-66%)

		FAVORABLE GENES: - *NOTCH1, FBXW7* - *PHF6* - *EP300*	
		Mutated	*Wild-type*
ADVERSE GENES: - *PI3K pathway* - *NRAS, KRAS* - *TP53* - *IKZF1* - *DNTM3A* - *IDH1/2*	*Mutated*	High Risk	High Risk
	Wild-type	Low Risk	High Risk

Cumulative incidence of relapse in the GRAALL 03/05-T



Overall survival in the GRAALL 03/05-T



Questions?

- Email anytime : keith.pratz@pennmedicine.upenn.edu