Role of BCL-2 Inhibitors in the Management of AML

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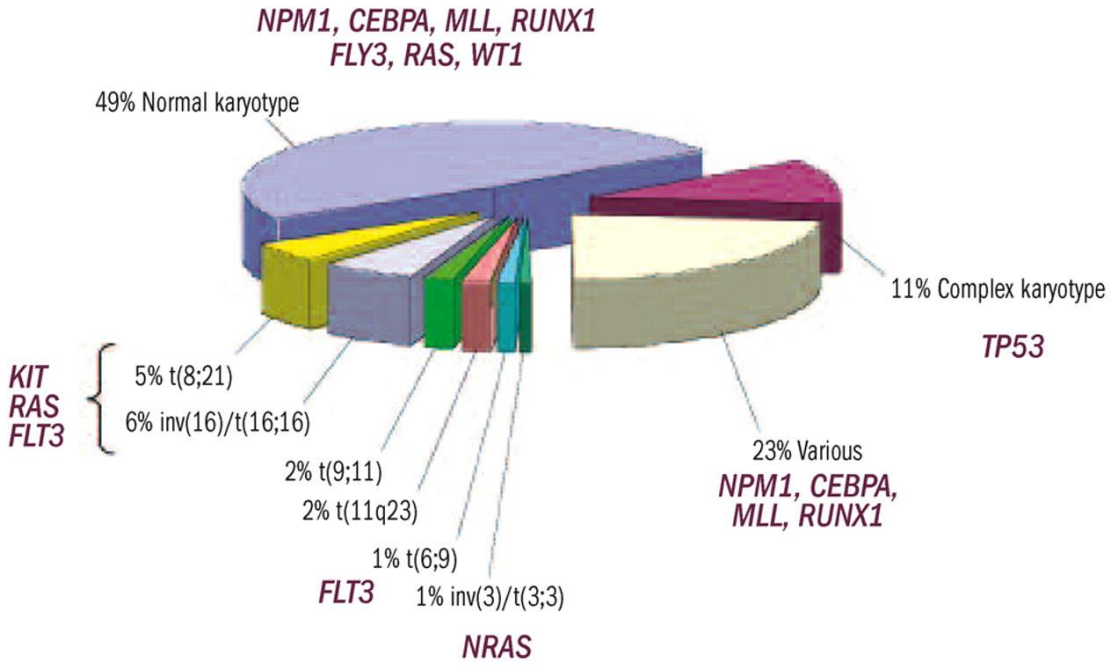
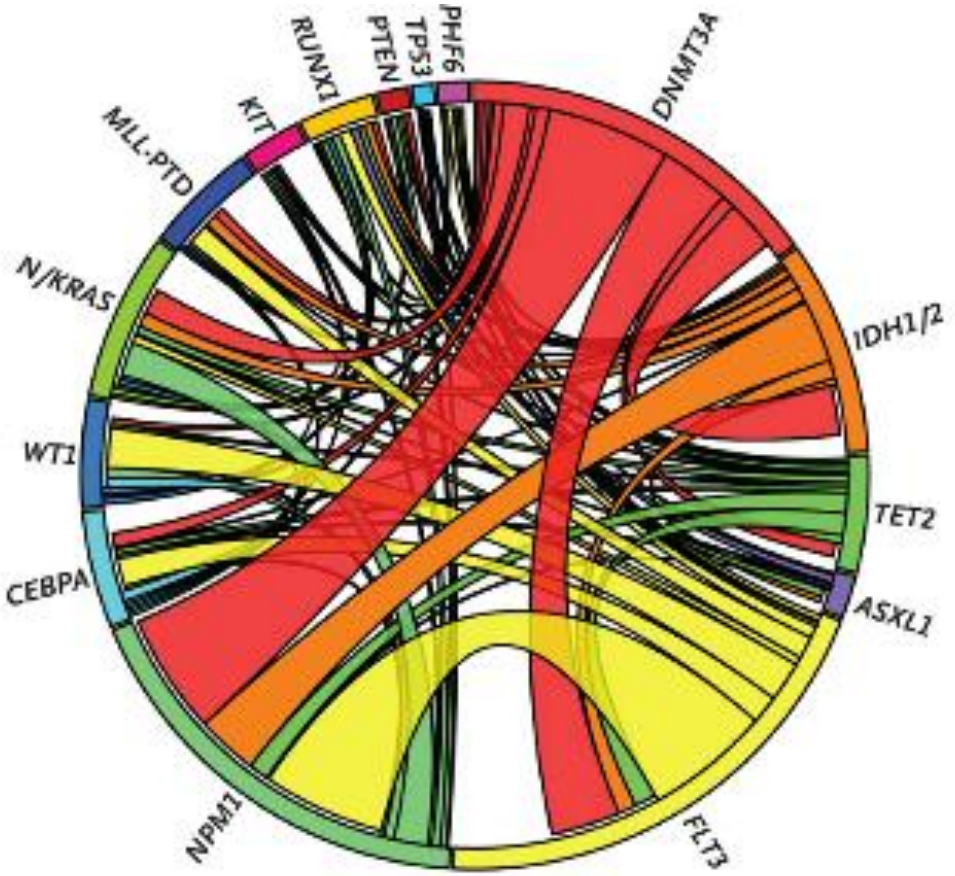
Topics to cover – Meant to be interactive discussion

- General approach to treatment for patients not eligible for stem cell transplant
  - Mutation agnostic
  - IDH mutated
  - FLT3 mutated
- Impact of mutations on treatment decisions
- Dose modifications for venetoclax
- Referral patterns: BMT vs treatment?
- Measurable residual disease – what is it and how do we measure? (If time)

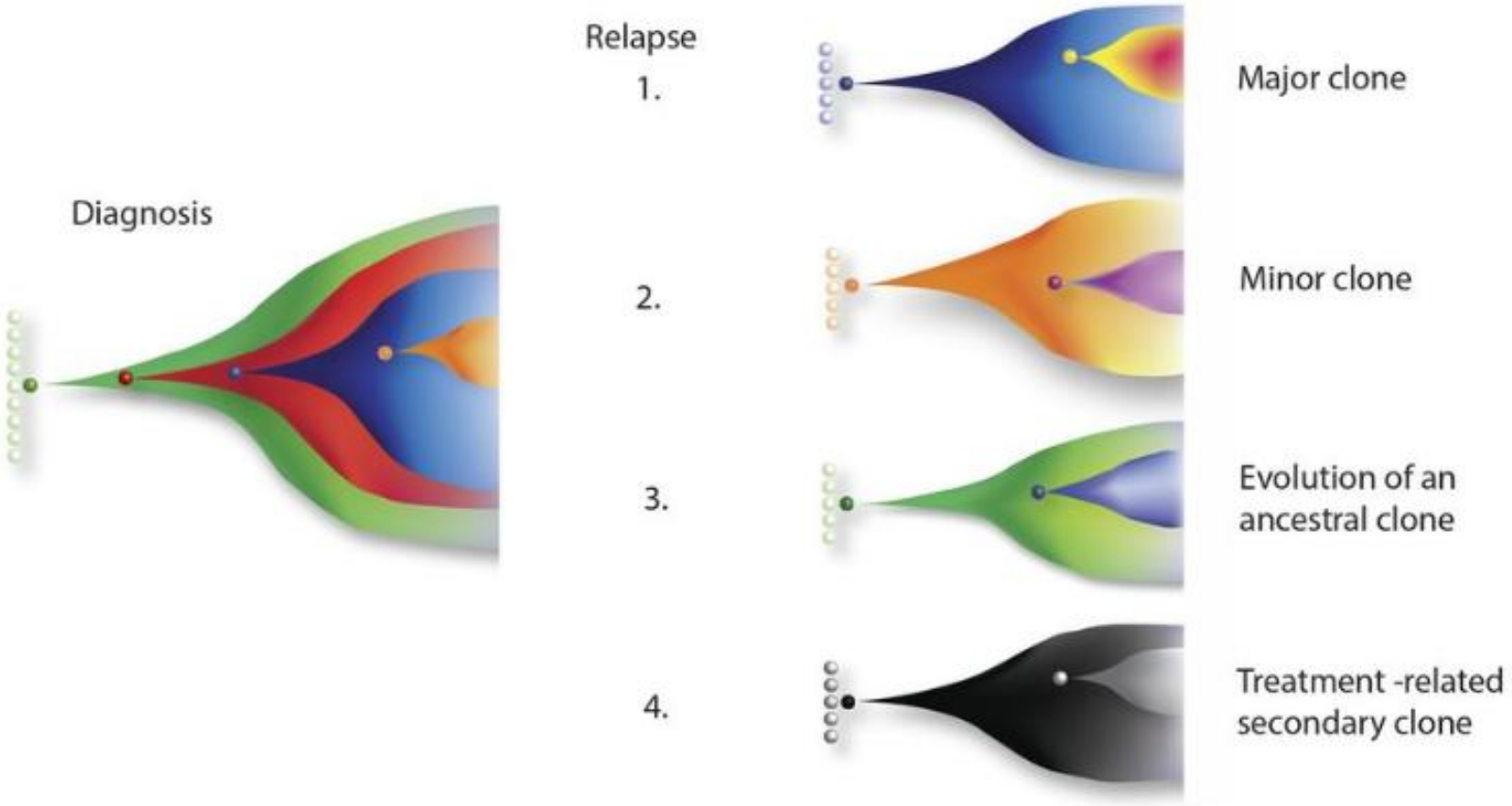
AML is Not One Disease





Patel et al. N Engl J Med 2012
Papaemmanuil et al. NEJM 2016

Clonal Evolution Makes Treatment Challenging

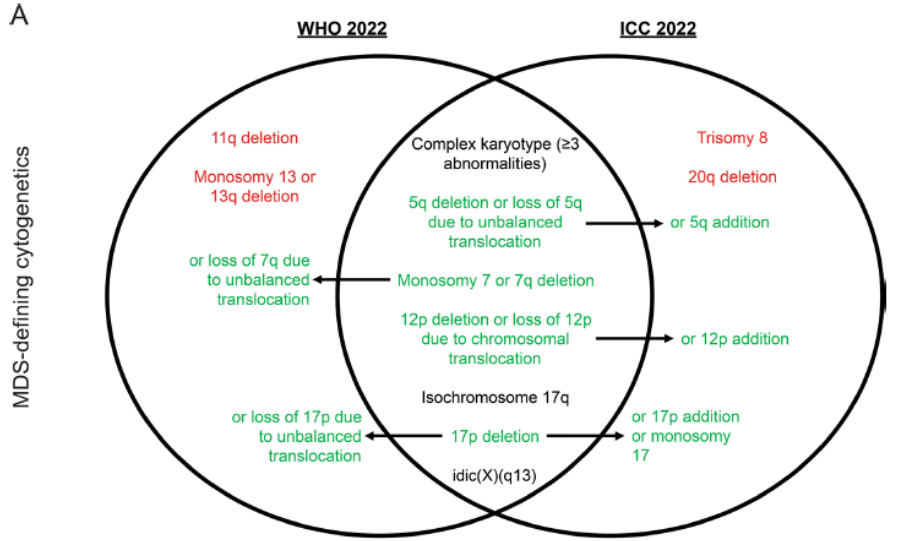


Grimwade et al. Blood 2016 127:29-41

World Health Organization (WHO) and International Consensus Classification Guidelines (ICC) 2022

	WHO 2022	ICC 2022*
AML with defining genetic abnormalities**	APL with *PML::RARA* fusion	APL with t (15;17) (q24.1;q21.2)/*PML::RARA*§
		APL with other *RARA* rearrangements§
	AML with *RUNX1::RUNX1T1* fusion	AML with t (8;21) (q22;q22.1)/*RUNX1::RUNX1T1*§
	AML with *CBFB::MYH11* fusion	AML with inv (16) (p13.1q22) or t (16;16) (p13.1;q22)/*CBFB::MYH11*§
	AML with *DEK::NUP214* fusion	AML with t (6;9) (p22.3;q34.1)/*DEK::NUP214*§
	AML with *RBM15::MRTFA* fusion	*Not recognized*
	AML with *BCR::ABL1* fusion	AML with t (9;22) (q34.1;q11.2)/*BCR::ABL1*#
	AML with *KMT2A* rearrangement	AML with t (9;11) (p21.3;q23.3)/*MLLT3::KMT2A*§
		AML with other *KMT2A* rearrangements§
	AML with *MECOM* rearrangement	AML with inv (3) (q21.3q26.2) or t (3;3) (q21.3;q26.2)/*GATA2; MECOM (EVI1)*§
		AML with other *MECOM* rearrangements§
	AML with *NUP98* rearrangement	*Not recognized*
	AML with *NPM1* mutation	AML with mutated *NPM1*§
	AML with *CEBPA* mutation	AML with in-frame bZIP *CEBPA* mutations§
	AML, myelodysplasia-related†	AML# and MDS/AML§ with mutated *TP53*
		AML# and MDS/AML§ with myelodysplasia-related gene mutations
		AML# and MDS/AML§ with myelodysplasia-related cytogenetic abnormalities
		MDS/AML NOS§
	AML with other defined genetic alterations	AML with other rare recurring translocations#
		Myeloid proliferations associated with Down syndrome
AML, defined by differentiation	AML with minimal differentiation	AML NOS#
	AML without maturation	
	AML with maturation	
	Acute basophilic leukemia	
	Acute myelomonocytic leukemia	
	Acute monocytic leukemia	
	Acute erythroid leukemia	
	Acute megakaryoblastic leukemia	
	Myeloid sarcoma	Myeloid sarcoma
	Blastic plasmacytoid dendritic cell neoplasm	Blastic plasmacytoid dendritic cell neoplasm

A



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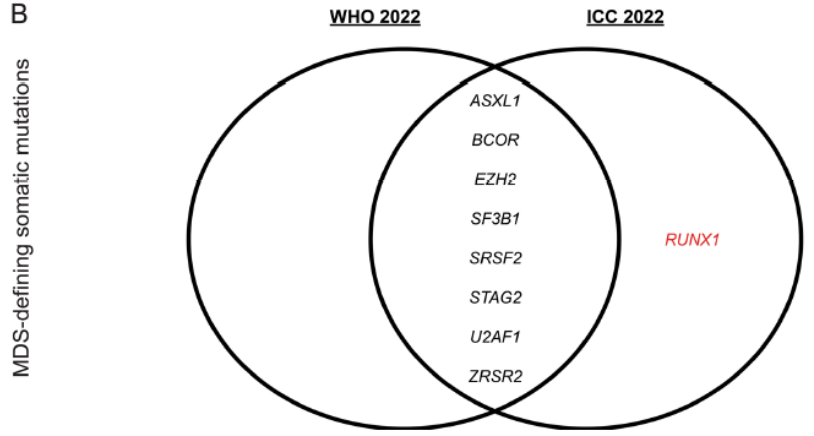
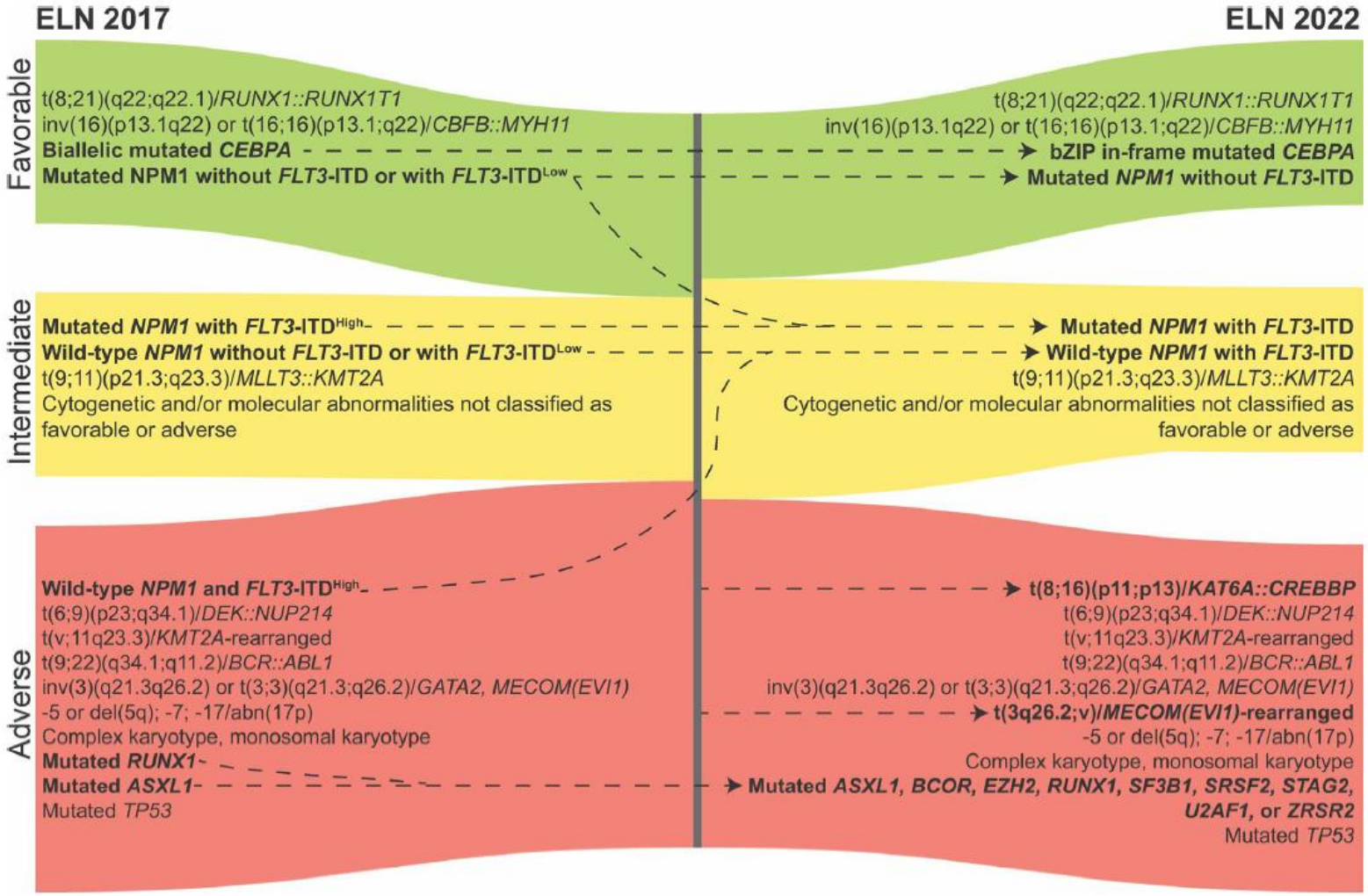


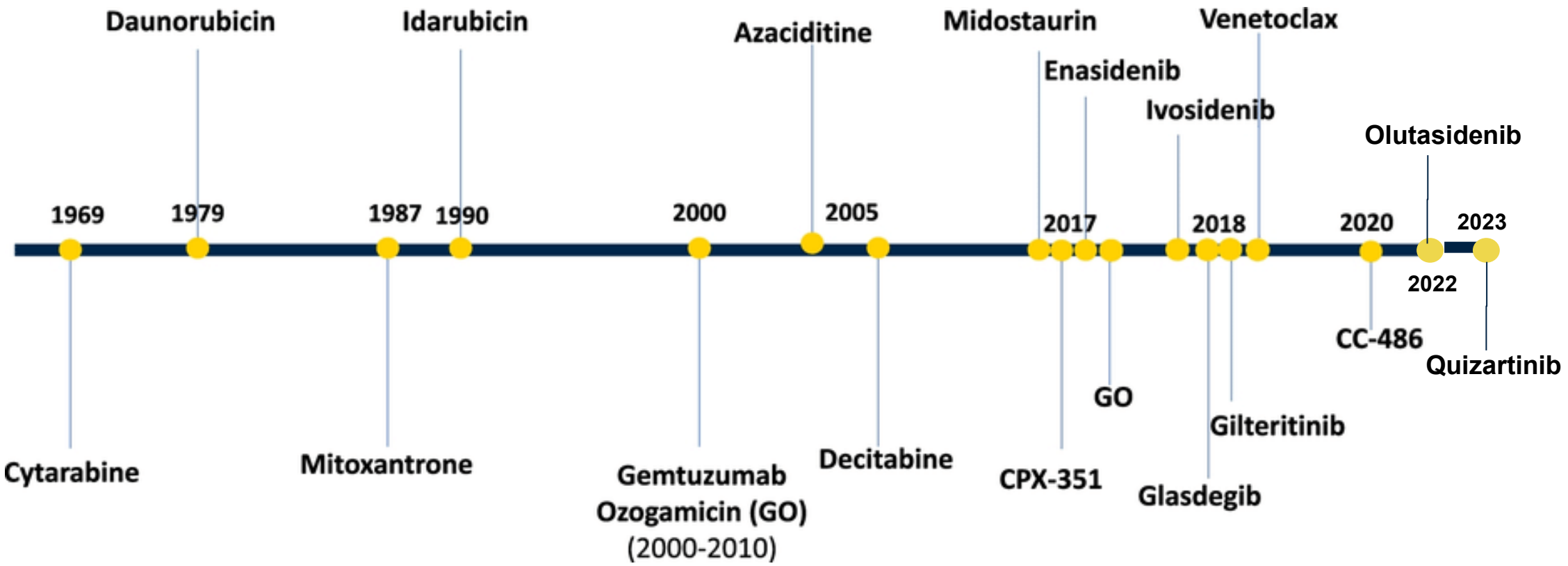
Bhansali, Lai et al. Journal of Hematology & Oncology 2023

European Leukemia Network Updated in 2022



Bhansali, Lai et al. Journal of Hematology & Oncology 2023

What has been accomplished in AML treatment?



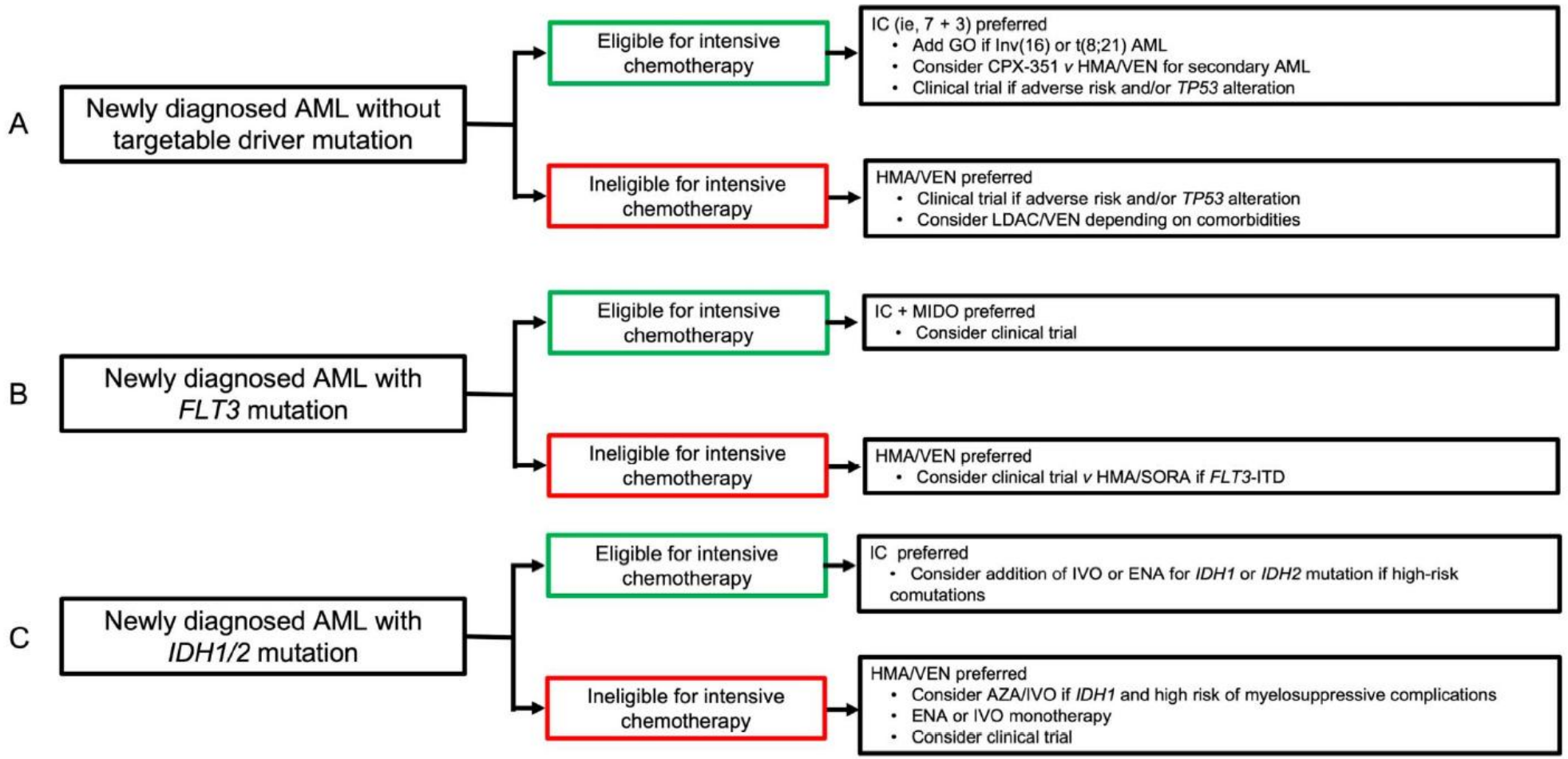
Adapted from Ochs et al. Annals of Hematology 2022

FDA Approved Drugs Since 2017

- **Newly diagnosed**
  - Midostaurin – April 2017
  - CPX-351 – August 2017
  - Venetoclax – November 2018
  - Glasdegib – November 2018
  - Quizartinib – July 2023
- **Relapsed/refractory**
  - Enasidenib – August 2017
  - Gilteritinib – November 2018
  - Olutasidenib – December 2022
- **Newly diagnosed and Relapsed/Refractory**
  - Gemtuzumab ozogamicin – September 2017
  - Ivosidenib – July 2018, May 2019
- **Maintenance**
  - CC-486 – September 2020

What is your general approach to treatment for newly diagnosed AML patients unfit for allogenic bone marrow transplant?

New Standard Approach to Newly Diagnosed AML



Lai et al. ASCO Education Book 2023

NCCN Guidelines Version 1.2024
Acute Myeloid Leukemia (Age ≥18 years)

NCCN Guidelines Index
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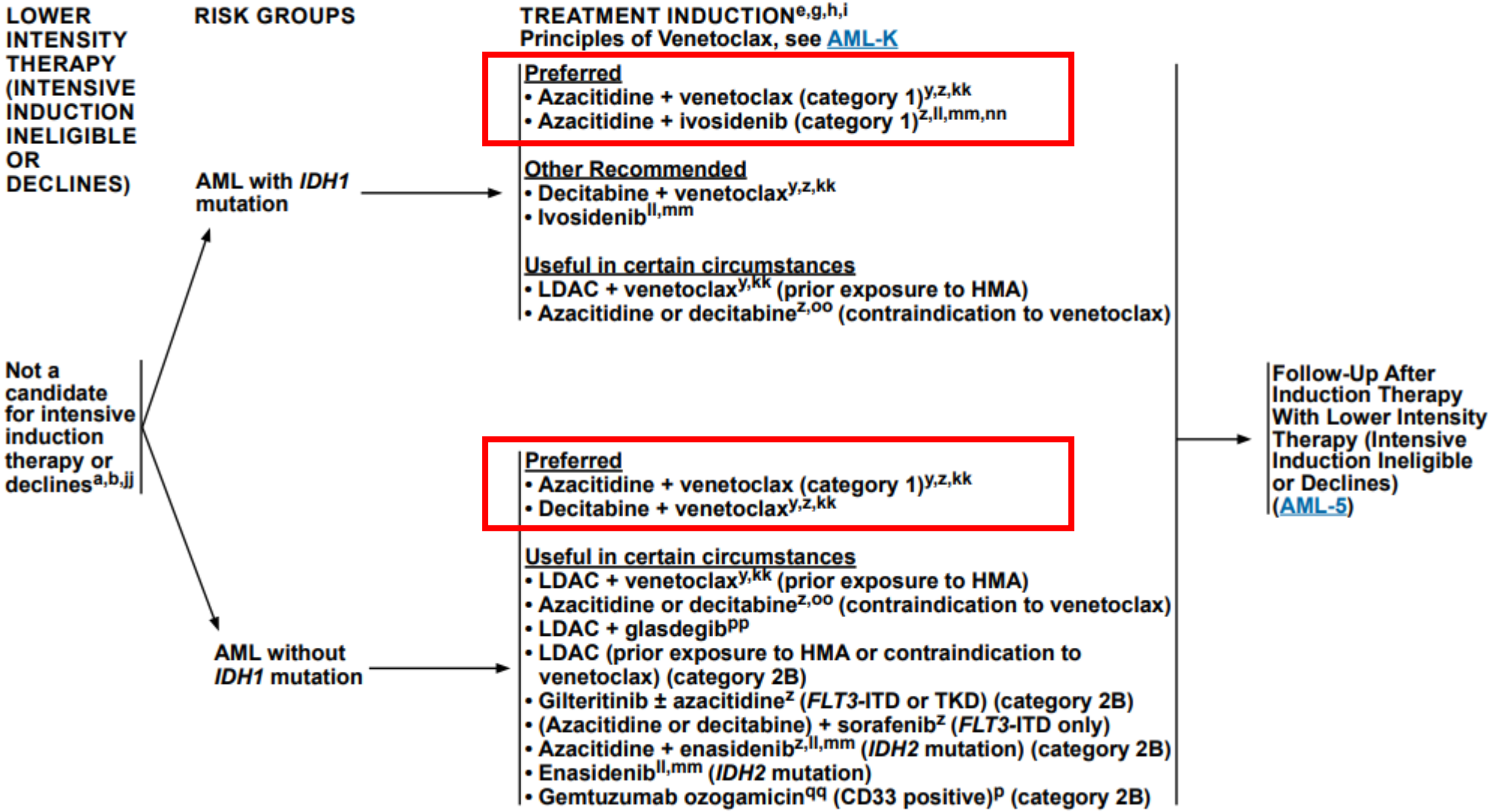
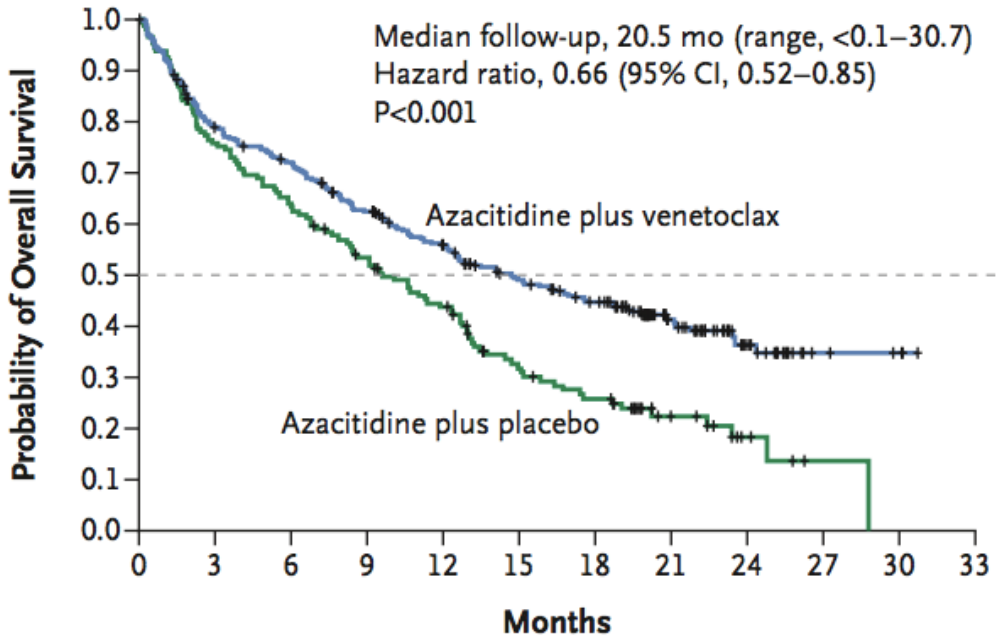
Discussion



Are you aware of the updated guidelines?

How do you use NCCN?

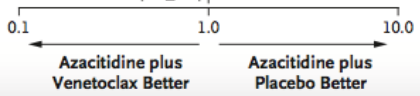
VIALE-A: Azaciditine + Venetoclax Superior to AZA Alone



No. at Risk

Azacitidine plus venetoclax	286	219	198	168	143	117	101	54	23	5	3	0
Azacitidine plus placebo	145	109	92	74	59	38	30	14	5	1	0	0

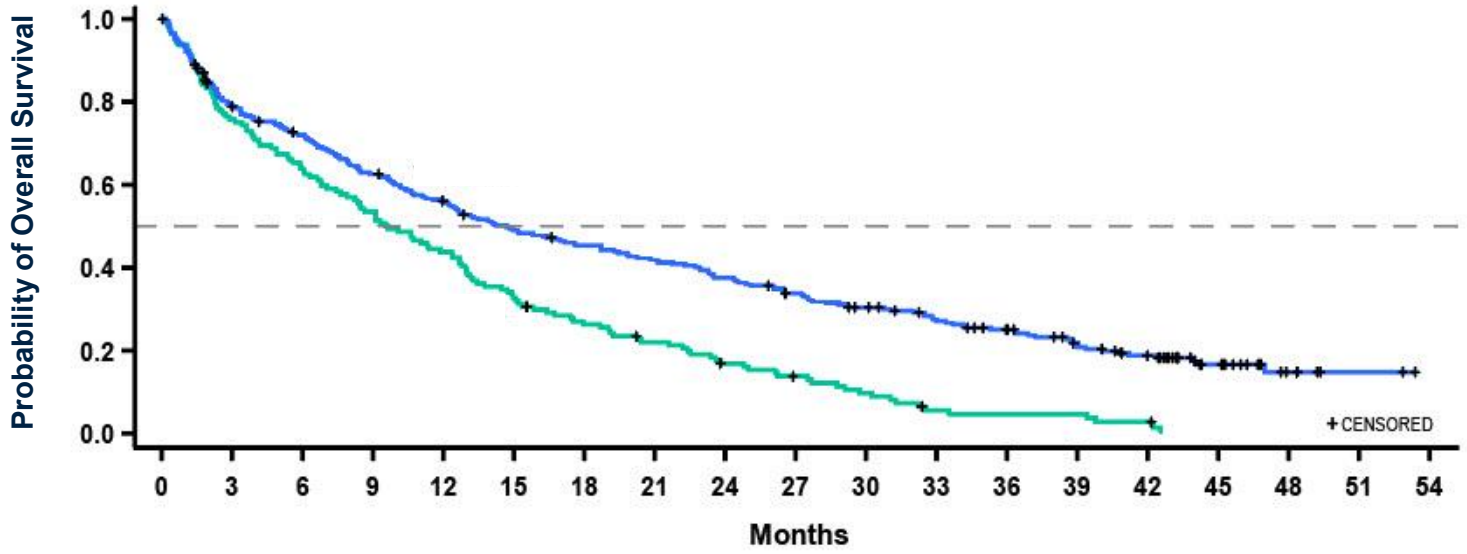
Subgroup	Azacitidine plus Venetoclax	Azacitidine plus Placebo	Hazard Ratio for Death (95% CI)
	no. of events/total no. (%)		
All patients	161/286 (56.3)	109/145 (75.2)	0.64 (0.50–0.82)
Sex			
Male	61/114 (53.5)	41/58 (70.7)	0.68 (0.46–1.02)
Female	100/172 (58.1)	68/87 (78.2)	0.62 (0.46–0.85)
Age			
<75 yr	66/112 (58.9)	36/58 (62.1)	0.89 (0.59–1.33)
≥75 yr	95/174 (54.6)	73/87 (83.9)	0.54 (0.39–0.73)
Geographic region			
United States	27/50 (54.0)	21/24 (87.5)	0.47 (0.26–0.83)
Europe	70/116 (60.3)	46/59 (78.0)	0.67 (0.46–0.97)
China	9/24 (37.5)	5/13 (38.5)	1.05 (0.35–3.13)
Japan	10/24 (41.7)	9/13 (69.2)	0.52 (0.20–1.33)
Rest of world	45/72 (62.5)	28/36 (77.8)	0.73 (0.45–1.17)
Baseline ECOG score			
Grade <2	89/157 (56.7)	65/81 (80.2)	0.61 (0.44–0.84)
Grade ≥2	72/129 (55.8)	44/64 (68.8)	0.70 (0.48–1.03)
Type of AML			
De novo	120/214 (56.1)	80/110 (72.7)	0.67 (0.51–0.90)
Secondary	41/72 (56.9)	29/35 (82.9)	0.56 (0.35–0.91)
Cytogenetic risk			
Intermediate	84/182 (46.2)	62/89 (69.7)	0.57 (0.41–0.79)
Poor	77/104 (74.0)	47/56 (83.9)	0.78 (0.54–1.12)
Molecular marker			
FLT3	19/29 (65.5)	19/22 (86.4)	0.66 (0.35–1.26)
IDH1	15/23 (65.2)	11/11 (100.0)	0.28 (0.12–0.65)
IDH2	15/40 (37.5)	14/18 (77.8)	0.34 (0.16–0.71)
IDH1 or *IDH2*	29/61 (47.5)	24/28 (85.7)	0.34 (0.20–0.60)
TP53	34/38 (89.5)	13/14 (92.9)	0.76 (0.40–1.45)
NPM1	16/27 (59.3)	14/17 (82.4)	0.73 (0.36–1.51)
AML with myelodysplasia-related changes			
Yes	56/92 (60.9)	38/49 (77.6)	0.73 (0.48–1.11)
No	105/194 (54.1)	71/96 (74.0)	0.62 (0.46–0.83)
Bone marrow blast count			
<30%	46/85 (54.1)	28/41 (68.3)	0.72 (0.45–1.15)
30 to <50%	36/61 (59.0)	26/33 (78.8)	0.57 (0.34–0.95)
≥50%	79/140 (56.4)	55/71 (77.5)	0.63 (0.45–0.89)



Dinardo et al. NEJM 2020

Azacitidine + Venetoclax has Sustained Benefit Over Azacitidine Alone with Long-term Follow Up of VIALE-A

Median follow-up time: 43.2 months (range: < 0.1 - 53.4)



Patients at Risk

Ven+Aza	286	220	199	173	153	133	122	113	101	89	78	67	57	45	34	18	6	2	0
Pbo+Aza	145	109	92	77	63	47	37	30	22	17	12	6	5	5	3	0	0	0	0

	No. of events/No. of patients (%)	OS (months) median (95% CI)
Ven+Aza	222/286 (77.6)	14.7 (12.1 - 18.7)
Pbo+Aza	138/145 (95.2)	9.6 (7.4 - 12.7)

Hazard ratio: 0.58 (95% CI, 0.465 - 0.723), P < 0.001

HR reduction from 0.66 (95% CI, 0.52 - 0.85) at 75% OS analysis

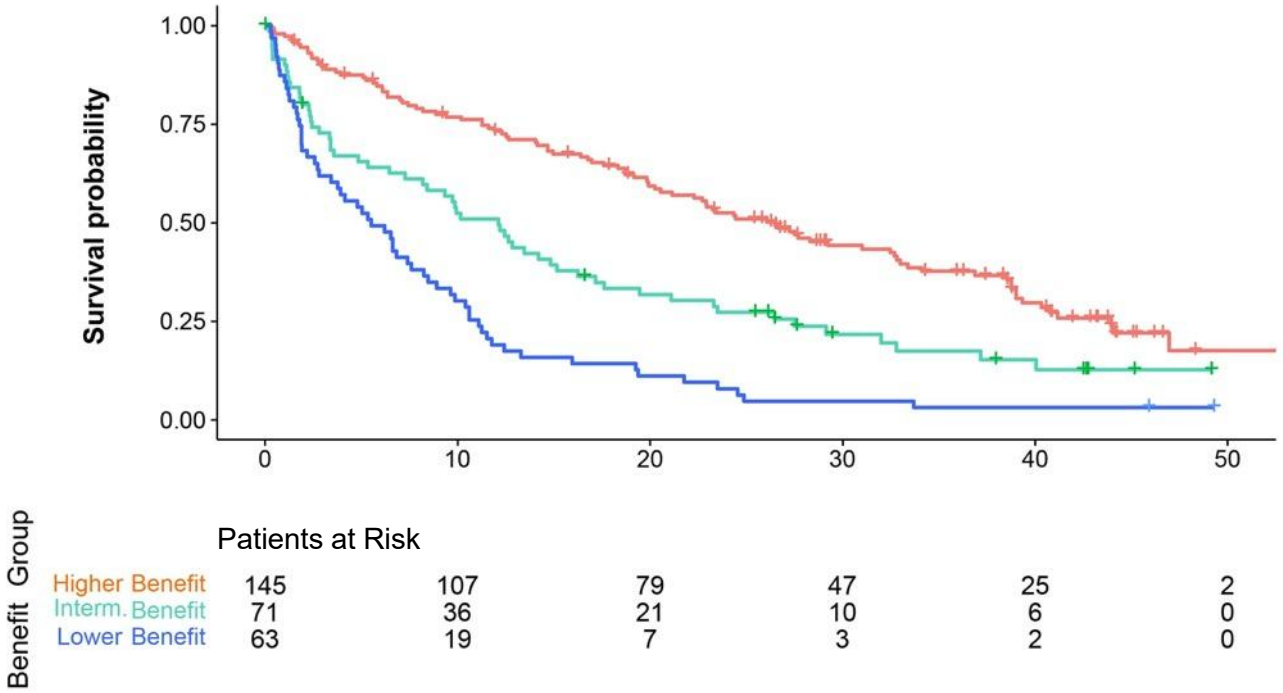
Pratz KW et al, ASH 2022, abstract #219

Patients Receiving Ven+Aza are Distinguished into Efficacy Subgroups by OS Benefit

Higher Benefit Group - *TP53*^{WT}, No *FLT3*-ITD, *K/NRAS*^{WT} (median OS >24 mo.)

Intermediate Benefit Group - *TP53*^{WT} and *FLT3*-ITD or *K/NRAS* mutated (median OS 12 mo.)

Lower Benefit Group - *TP53* mutated (median OS <6 mo.)



Ven + Aza (N = 279)	n	Events	Median OS, months (95% CI)
Higher Benefit	145	96	26.51 (20.24, 32.69)
Intermediate Benefit	71	57	12.12 (7.26 – 15.15)
Lower Benefit	63	61	5.52 (2.79 – 7.59)

- 52% (145/279) of Ven+Aza arm are in the higher benefit group
- The remainder were distributed equally between intermediate (25.4%, 71/279) and lower benefit (22.6%, 63/279) :

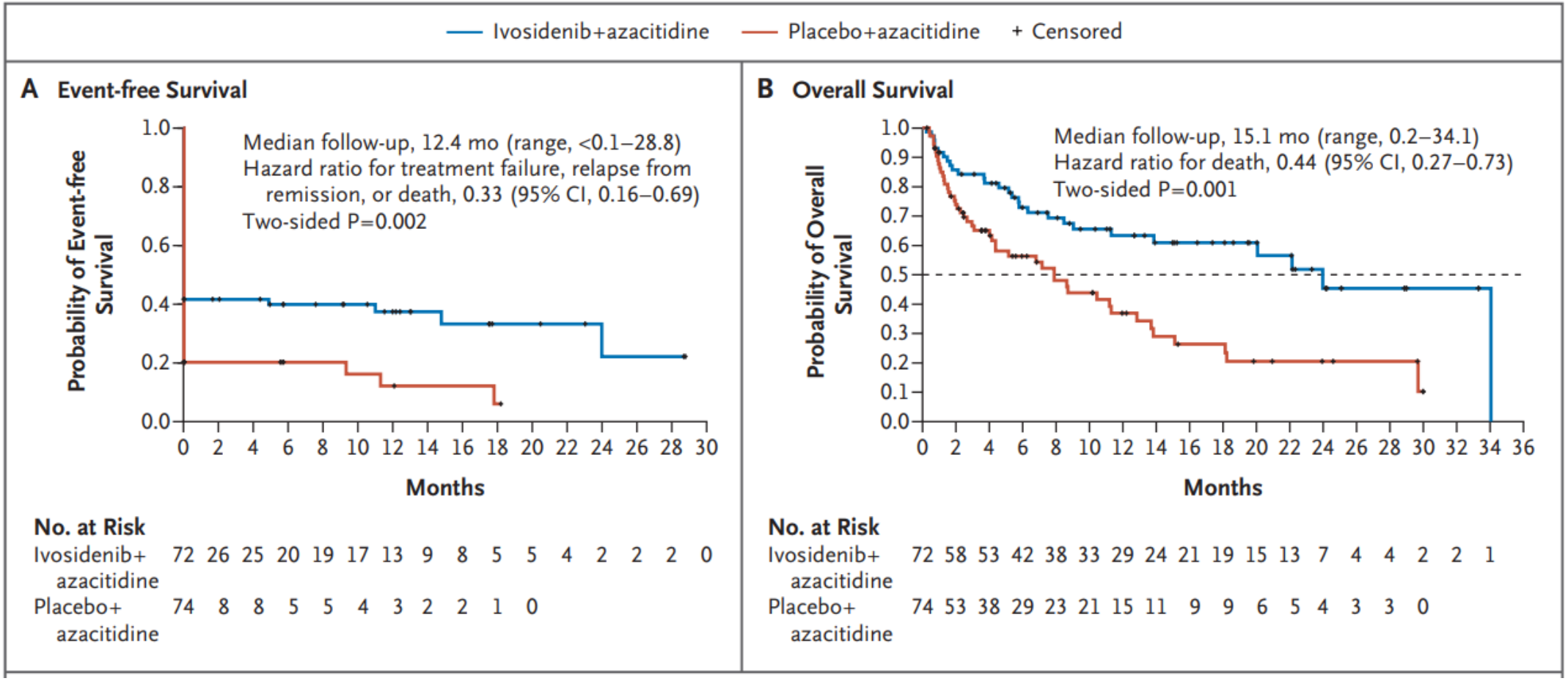
Döhner H, et al, ASH 2022, abstract #602

Ivosidenib + Azacitidine Improves Remission Rates Compared to Azacitidine Alone

Response Category	Ivosidenib + Azacitidine (N = 72)	Placebo + Azacitidine (N = 74)
Best response — no. (%)		
Complete remission	34 (47)	11 (15)
Complete remission with incomplete hematologic or platelet recovery	5 (7)	1 (1)
Partial remission	4 (6)	2 (3)
Morphologic leukemia-free state	2 (3)	0
Stable disease	7 (10)	27 (36)
Progressive disease	2 (3)	4 (5)
Could not be evaluated	1 (1)	2 (3)
Not assessed	17 (24)	27 (36)
Complete remission		
Percentage of patients (95% CI)	47 (35–59)	15 (8–25)
Odds ratio vs. placebo (95% CI); P value	4.8 (2.2–10.5); two-sided P<0.001	
Median duration of complete remission (95% CI) — mo	NE (13.0–NE)	11.2 (3.2–NE)
Median time to complete remission (range) — mo	4.3 (1.7–9.2)	3.8 (1.9–8.5)
Complete remission or complete remission with partial hematologic recovery		
No. of patients	38	13
Percentage of patients (95% CI)	53 (41–65)	18 (10–28)
Odds ratio vs. placebo (95% CI); P value	5.0 (2.3–10.8); two-sided P<0.001	
Median duration of complete remission or complete remission with partial hematologic recovery (95% CI) — mo	NE (13.0–NE)	9.2 (5.8–NE)

Montesinos et al. NEJM 2022

Ivosidenib + Azacitidine Improves EFS and OS Compared to Azacitidine Alone



Montesinos et al. NEJM 2022

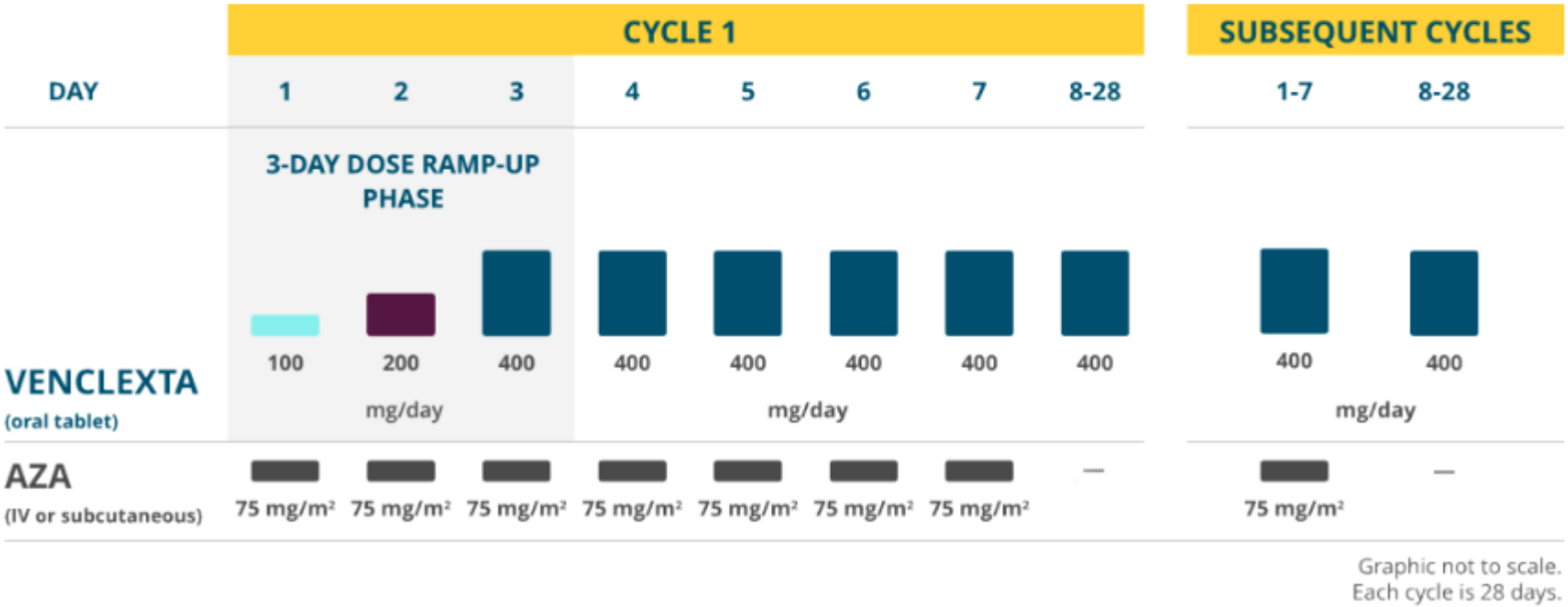
- How long does it take to get NGS results back?
- Do you wait for mutation testing to come back before starting treatment?
- Do mutations affect treatment decision?

VENCLEXTA is taken orally in combination with AZA, DEC, or LDAC[1]

In the VIALE-A trial, which evaluated the efficacy and safety of VEN+AZA:

- Azacitidine was administered in 28-day cycles, beginning on Day 1 of VENCLEXTA treatment, at a dosage of 75 mg/m^2, intravenously or subcutaneously once daily on Days 1-7 of each cycle

VENCLEXTA is taken orally in combination with AZA



Graphic not to scale.
Each cycle is 28 days.

Taken from package insert

VENCLEXTA dose should be modified for concomitant use with certain medications[1,8,9]

- VENCLEXTA is metabolized by the CYP3A enzyme; the dose should be reduced when used with P-gp inhibitors or strong or moderate CYP3A inhibitors

Dose modifications for managing potential interactions[1,3,4]

Coadministered drug	Initiation and ramp-up phase	Steady daily dose after ramp-up phase
Posaconazole	Day 1: 10 mg Day 2: 20 mg Day 3: 50 mg Day 4: 70 mg	Reduce the VENCLEXTA dose to 70 mg
Other strong CYP3A inhibitors* Clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir, ritonavir, voriconazole	Day 1: 10 mg Day 2: 20 mg Day 3: 50 mg Day 4: 100 mg	Reduce the VENCLEXTA dose to 100 mg
Moderate CYP3A inhibitors* Aprepitant, ciprofloxacin, conivaptan, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, isavuconazole, verapamil	Reduce the VENCLEXTA dose by at least 50%	
P-gp inhibitors* Amiodarone, cyclosporine, dronedarone, quinidine, ranolazine, verapamil		

Taken from package insert

- How do you dose modify venetoclax?
  - What time point?
  - What dose?
  - What duration?

Doublets versus Triplets : Is More Better?

vs.

FLT3 Mutated

Doublets

vs.

Triplets

- Venetoclax + HMA (azacitidine or decitabine)
- Azacitidine + gilteritinib

- 7+3+midostaurin
- 7+3+quizartinib
- 7+3+gilteritinib
- Venetoclax + azacitidine + gilteritinib

IDH1/2 Mutated

Doublets

- 7 + 3 (cytarabine + daunorubicin/idarubicin)
- Venetoclax + HMA (azacitidine or decitabine)
- Ivosidenib (IDH1) + azacitidine
- Enasidenib (IDH2) + azacitidine

vs.

Triplets

- 7 + 3 + ivosidenib or enasidenib
- Venetoclax + azacitidine + ivosidenib
- Venetoclax + azacitidine + enasidinib

Doublets versus Triplets :

- What triplet combination, if any, have you tried?
- In what situation do you use HMA monotherapy?

Older Patients with AML: Transplant or Not?

Question: Is there a benefit of HCT *vs.* non-HCT in less fit and/or elderly patients for mortality risks in univariate and multivariate models? Quality of life (QOL) and frailty as secondary outcomes.

Cohort: N = 692 from 13 different institutions
Patients presenting with AML or high-risk MDS for induction or re-induction therapy.

Table: Association of HCT with overall mortality, unadjusted and adjusted models with HCT modeled as a time-dependent covariate. Adjusted for AML cyto-molecular risks, disease status and response, induction treatment intensity in addition to comorbidities, frailty per walk speed, depression per PHQ-9, and activities of daily living.

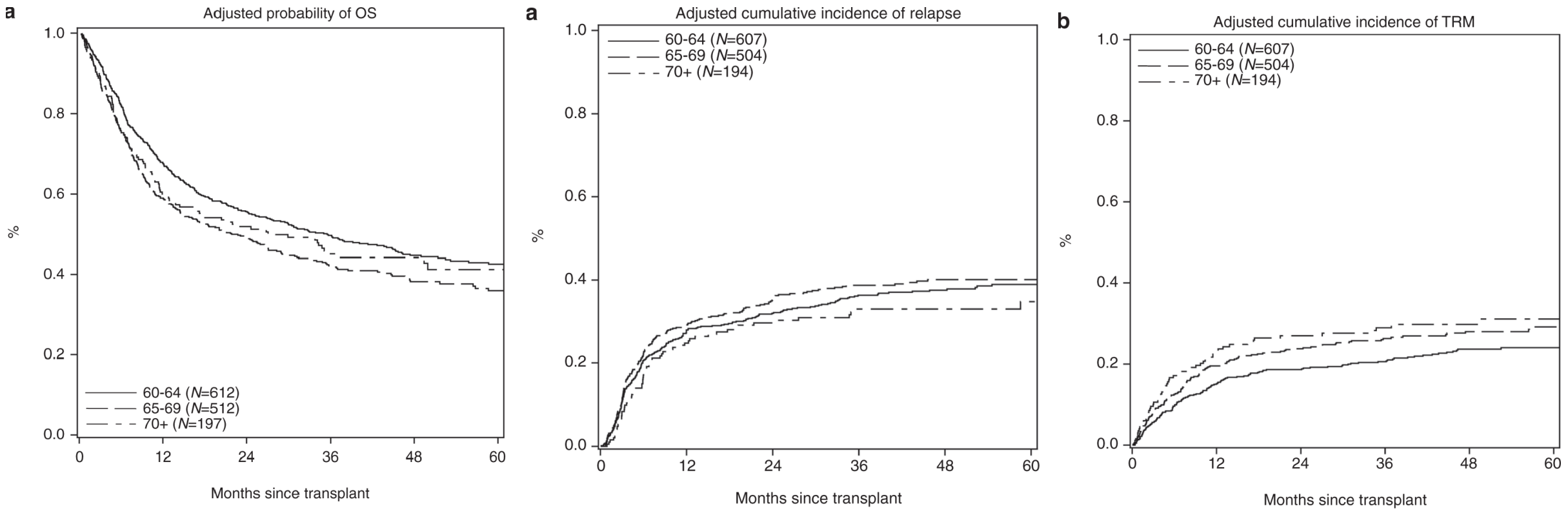
	Unadjusted		Adjusted*	
	HR (95% CI)	*P*	HR (95% CI)	*P*
All patients (n = 692)	0.71 (0.57 - 0.88)	.002	0.85 (0.66 - 1.09)	.19
Patients aged ≥65 (n = 295)	0.65 (0.46 - 0.90)	.01	0.79 (0.53 - 1.16)	.22
Patients with augmented HCT-CI scores ≥4 (n = 353)	0.63 (0.46 - 0.86)	.0004	0.84 (0.58 - 1.21)	.34
Patients with ELN intermediate risk (n = 296)	0.55 (0.40 - 0.77)	.0004	0.81 (0.55 - 1.17)	.26
Patients with ELN adverse risk (n = 248)	0.37 (0.25 - 0.54)	<.0001	0.58 (0.38 - 0.89)	.01
Patients who achieved CR1 (n = 510)	0.85 (0.67 - 1.09)	.20	0.96 (0.72 - 1.27)	.75
Patients who did not achieve CR1 (n = 182)	0.27 (0.15 - 0.51)	<.0001	0.45 (0.22 - 0.90)	.02

Conclusions:

- Health impairments negate survival benefits from HCT for AML, suggesting that the unadjusted observed benefit is due mostly to selection of the healthier candidates.
- Results strongly motivate the need for randomized trials to identify the best candidates for HCT.

Sorror ML., et al. Blood 141:295-308, 2023

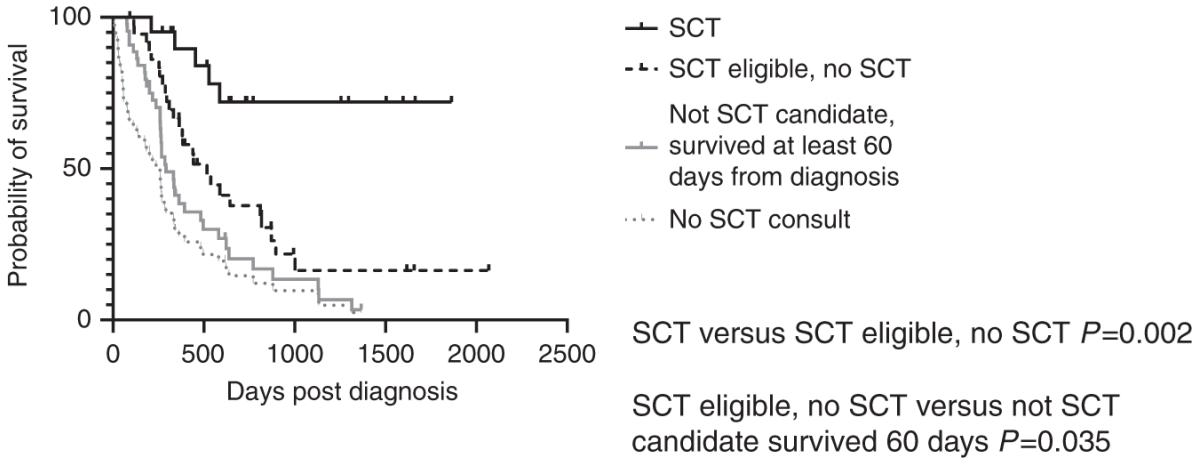
AlloHCT Outcomes for Older Patients with AML in CR1 in the Contemporary Era – a CIBMTR Analysis



Maakaron JE., et al. BMT 57:911-917, 2022

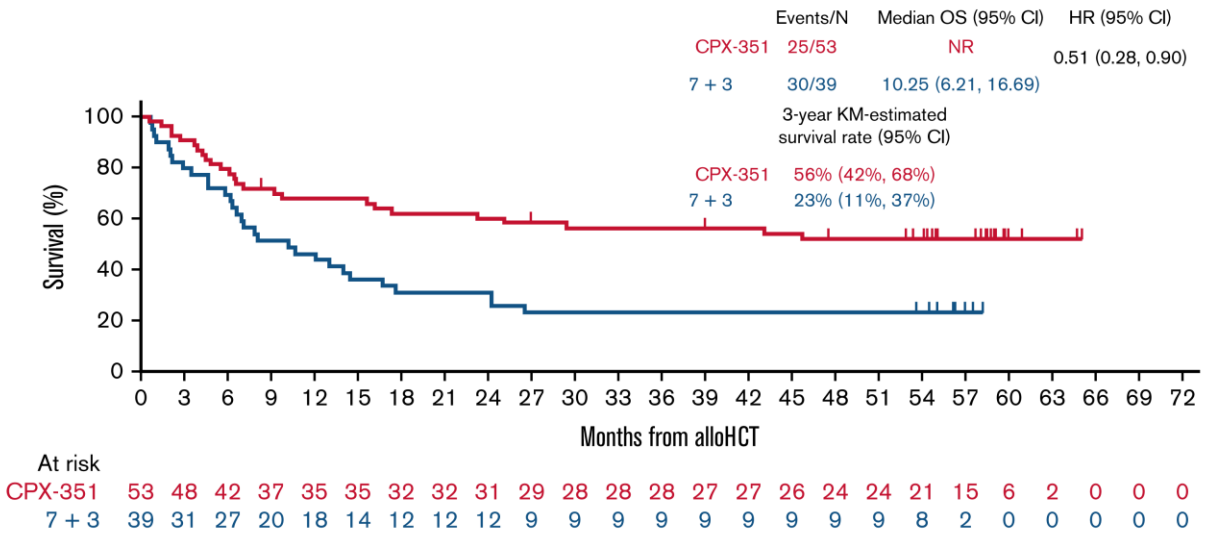
Novel AML Therapies as a Bridge to AlloHCT

Patients receiving azacitidine + venetoclax



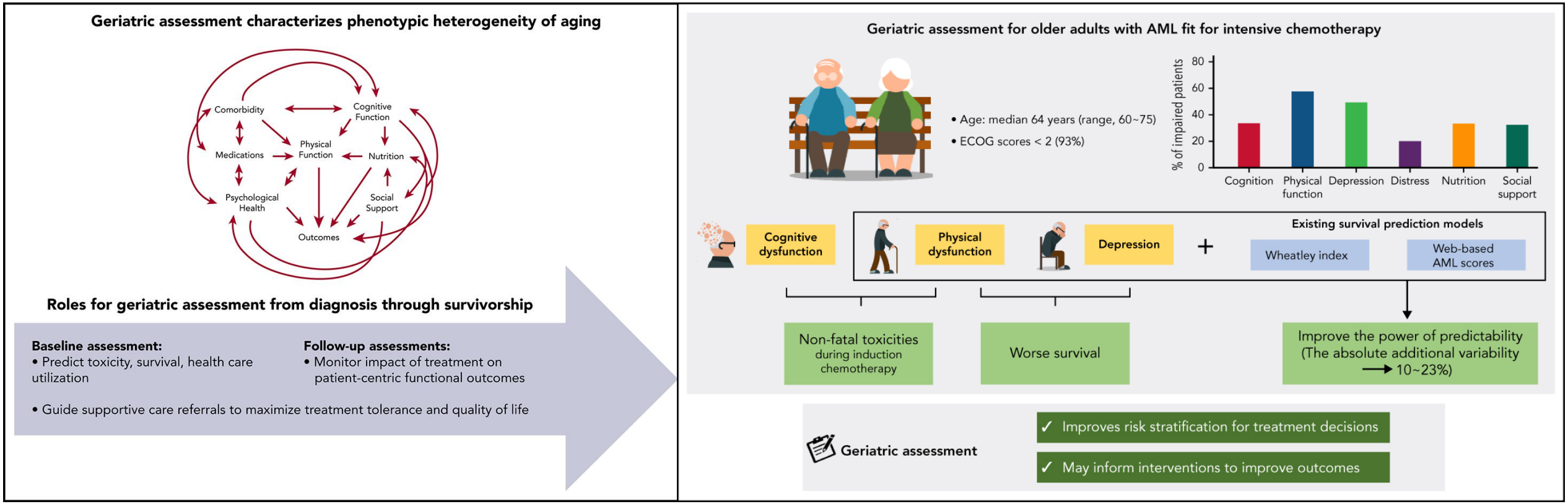
Pollyea DA., et al. BMT 57:160-166, 2022

Patients receiving Vyxeos vs 7+3



Uy GL., et al. Blood Adv 6:4898-4993, 2022

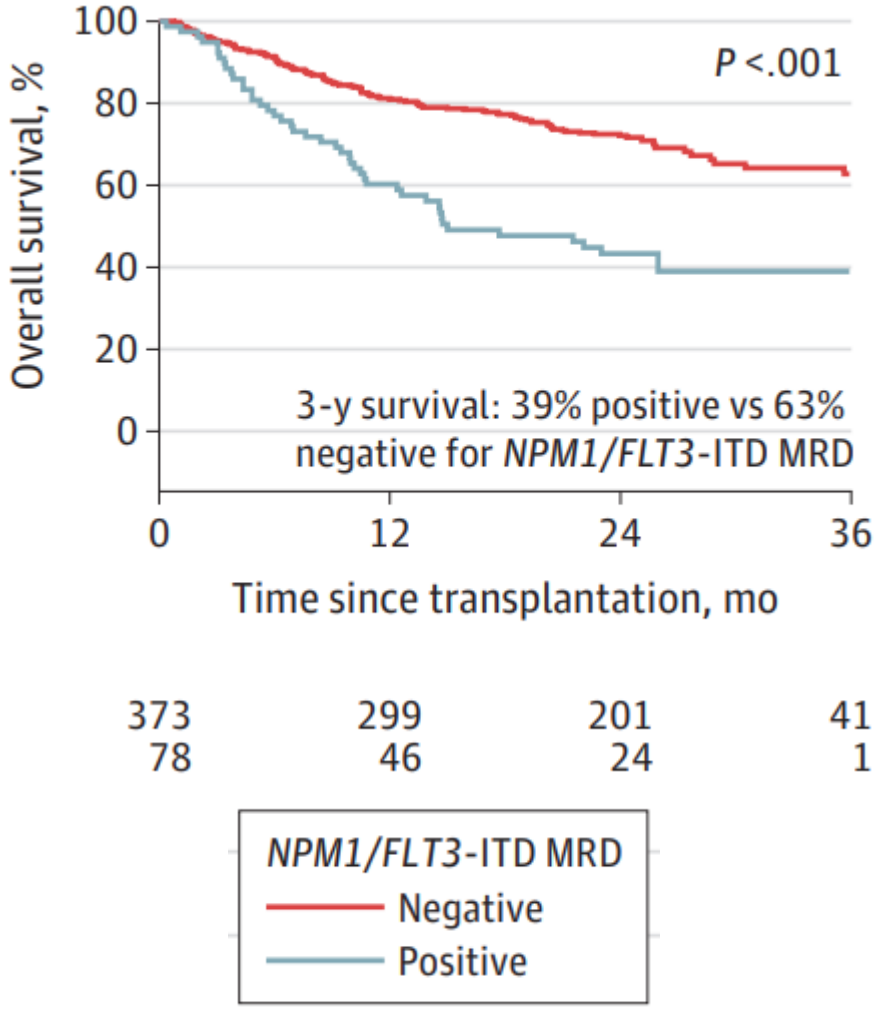
Geriatric Assessment (GA) for Older Patients with Hematologic Malignancies

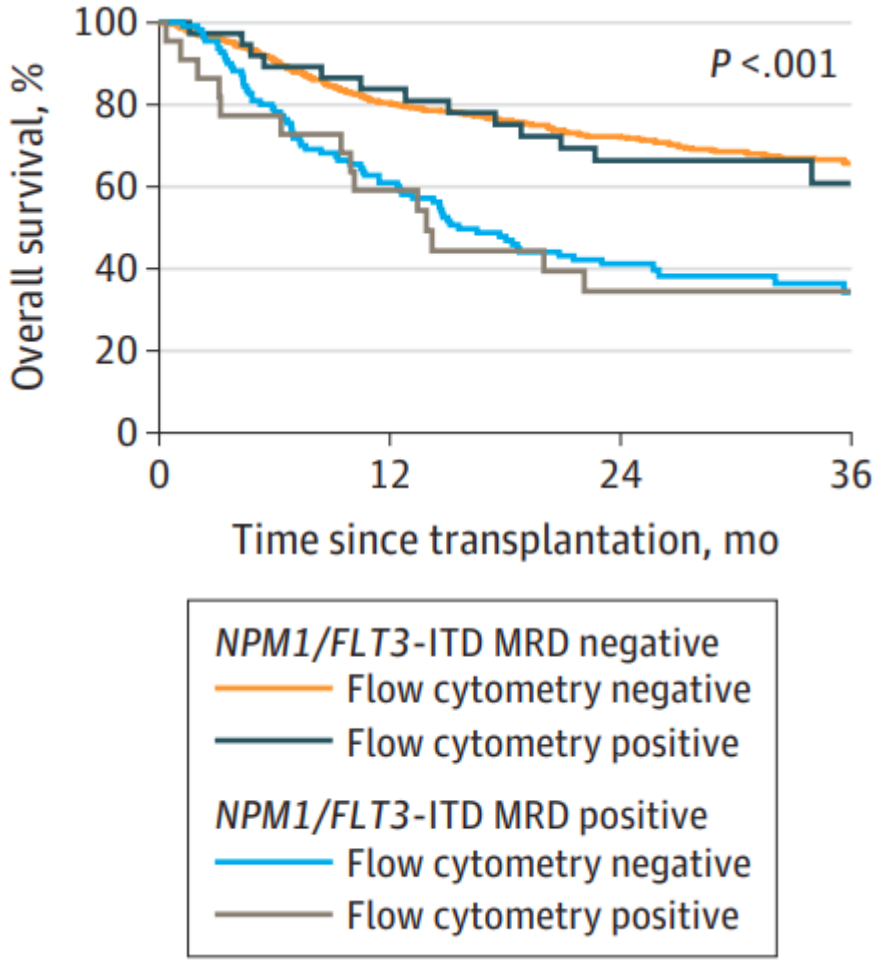


Min GJ., et al. Blood 139:1646-1658, 2022

- When do you refer patients to a tertiary care center?
  - Before starting treatment
  - After starting treatment
    - If so, at what time point?
  - If eligible for BMT
  - Clinical trial

Measurable Residual Disease (MRD) at the End of Treatment Affects Outcomes





Dillon et al. JAMA 2023

How do we define measurable residual disease (MRD)?

Response category	Abbreviation	Defining criteria
CR with negative MRD	$CR_{MRD}-$	1. Complete morphologic remission and 2. MRD^- in all MRD technologies that were used: a. FC-MRD^- in BM (if MFC-MRD was used). b. qPCR-MRD^- in BM (or in PB after cycle 2 for *NPM1*- and CBF-MRD) (if qPCR-MRD was used). c. NGS-MRD^- in BM (if NGS-MRD was used).
CR with positive MRD	$CR_{MRD}+$	1. Complete morphologic remission, and 2. MFC-MRD^+in PB and/or BM, or 3. NGS-MRD^+ in PB and/or BM, or 4. qPCR-MRD^+ in PB and/or BM.
CR with molecular MRD detection at low level	CR-MRD-LL	1. Morphologic CR, and 2. Molecular MRD detectable at low level in PB and/or BM (ie, qPCR for *NPM1* <2% or NGS-MRD <0.1%, but above the detection limit of the assay).
MRD relapse	—	1. Conversion of MRD negativity to MRD positivity independent of the MRD technique, or 2. increase in MRD copy numbers ≥1 $\log_{10}$ between any 2 positive samples in patients with CR-MRD-LL who are monitored by qPCR. 3. The result of (1) or (2) should be rapidly confirmed in a second consecutive sample, preferably from the BM.

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How do we measure MRD?

	Pro	Con
Morphology	Commonly used standard. Easy to perform.	Low sensitivity (~5%), many false negatives
Flow Cytometry	High sensitivity technique for determining residual AML in the right hands. Applicable to most patients.	Requires specialist expertise and equipment. Variation between centers and operators. Often requires diagnostic sample.
Cytogenetics/FISH	Clinically available.	Low sensitivity. Chromosomal abnormalities may persist from founder clone long after leukemia has been eradicated.
PCR	Extremely high sensitivity for detecting residual transcript that may be found in AML	Not inclusive of all cytogenetic or molecular abnormalities
Next-Gen Sequencing	Most AMLs have a genetic abnormality that could be tracked.	Technique not validated yet for MRD. Intrinsic error rate of NGS.

- Do you check MRD after starting therapy?
  - At what time point?
  - How do you measure?

Summary

- AML treatment landscape has improved and has become more complicated
- For older patients unable to tolerate induction, azacitidine + venetoclax remains the current standard of care for the majority of patients
- Mutation testing is an important consideration for picking optimal treatment
- Venetoclax dose and duration should be modified individually based on patients response and concomitant medications
- Many factors go into decision for BMT, not just age and newer therapies can help bridge patients that historically would not be eligible
- Measurable residual disease is important to check – especially if going to BMT

Take Home Message

Normal bone marrow

Bone marrow with AML

- Know the types of weeds in your garden = What molecular abnormalities are present? What mutations are driving the disease burden?
- Use the appropriate weed killer = Tailor treatment to individual genetic profiles and physiologic function to change survival outcomes
- Understand the optimal conditions for growth = Modify how we approach therapy in older AML based on toxicity

Thank you!

Questions?

CASE

75yo M with a history of hypertension, diabetes, and stage 2 CKD presents to primary care physician for a routine visit and is noted to have WBC 0.9k and ANC 0.28k

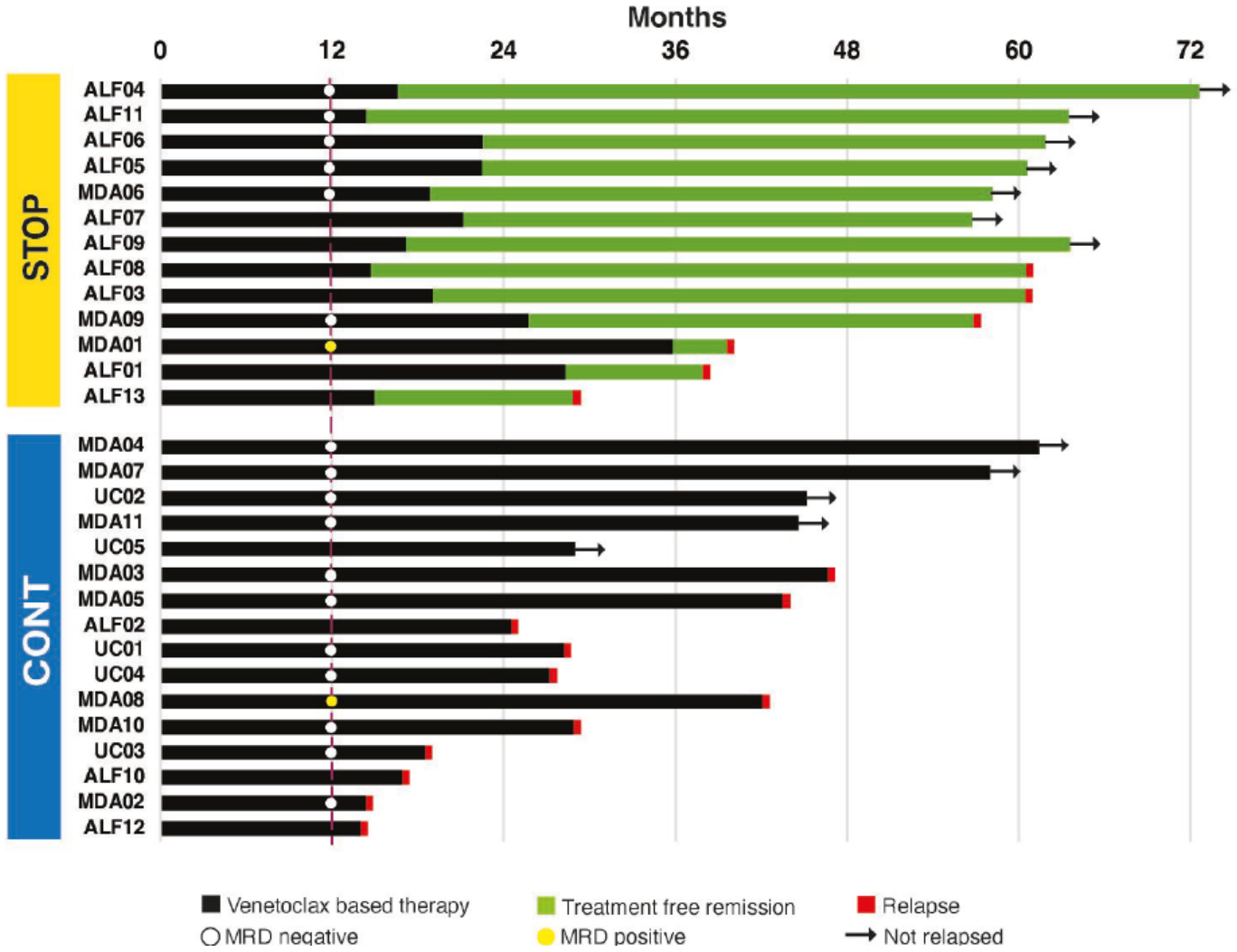
- He is referred to hematology and undergoes bone marrow aspirate/biopsy
  - The marrow is notable for 48% myeloid blasts
  - Cytogenetics are 46,XY
  - NGS myeloid panel reveals mutations in DNMT3A, BCOR, and IDH2
- Azacitidine and venetoclax are initiated with standard dosing (28-day venetoclax)
- BM aspirate/biopsy on cycle 1, day 24 reveals aplasia with no blasts; NGS myeloid panel is neg.
- Cycle 2 of azacitidine and venetoclax is held to allow for count recovery
- After a period of aplasia, counts recover approximately 8 weeks following initiation of Cycle 1
- Upon count recovery, therapy is resumed
- Cycle 2 is administered as standard dose azacitidine with 14-day venetoclax
- After a period of aplasia, counts recover 7-8 weeks following initiation of Cycle 2
- Upon full count recovery, bone marrow aspirate/biopsy reveals complete morphologic, immunophenotypic, cytogenetic, and molecular remission

After discussion, the patient is not interested in pursuing allogeneic transplantation
What is the best “maintenance” strategy for the patient?

Can we stop VEN-AZA in AML?

- AML :
  - Chua CC, Blood Adv. 2022
  - Othman J, Blood 2023

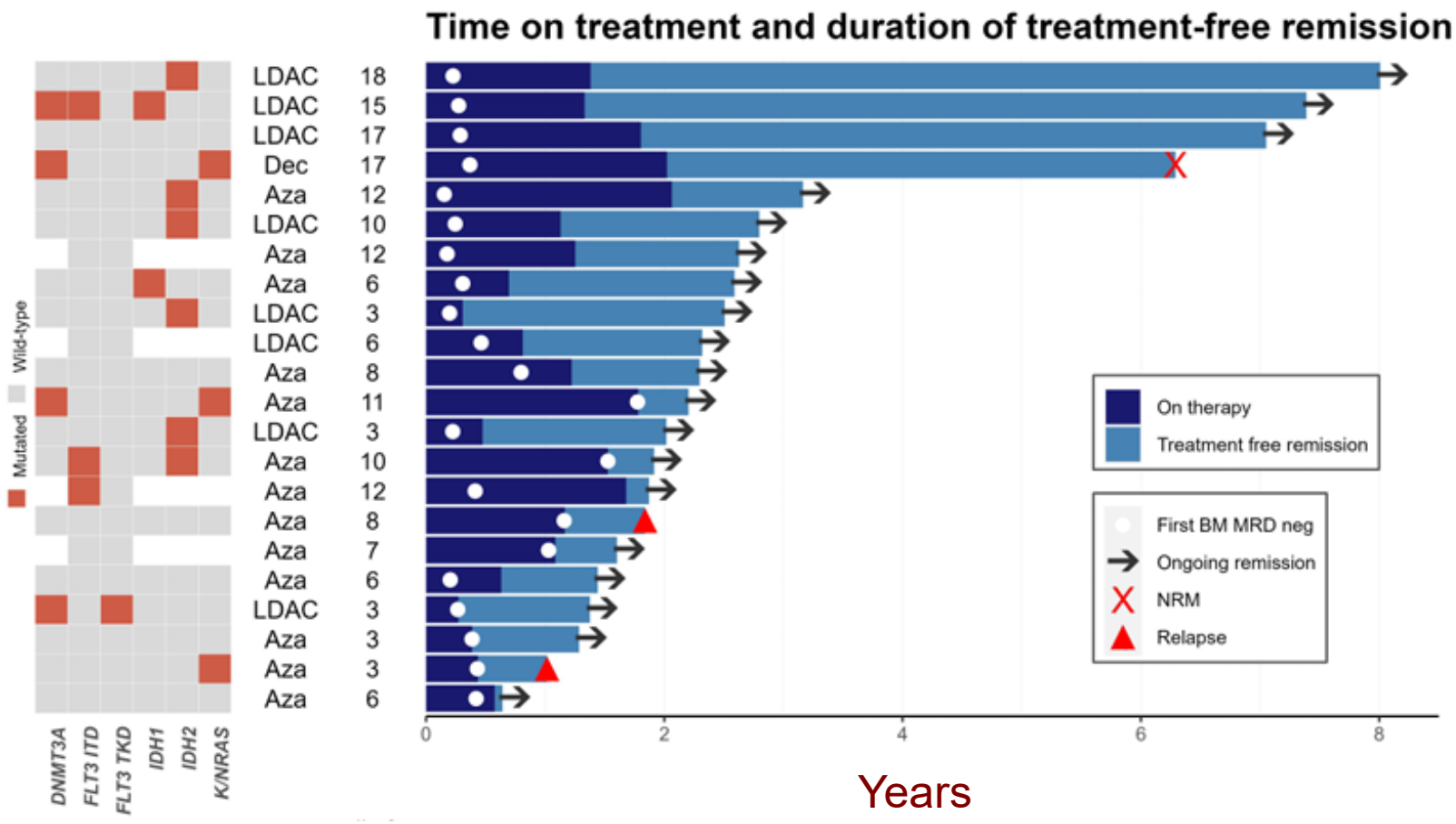
- TFR = 45.8 months among the STOP cohort



Can we stop VEN-AZA in AML?

- AML :
  - Chua CC, Blood Adv. 2022
  - Othman J, Blood 2023

- MRDneg patients
  2-year TFR= 88%



STOP-VEN Study design

Objective:

- To study the outcome of patients who stopped AZA and/or VEN while in remission.

Key inclusion/exclusion criteria:

- Adult AML patients treated with ≥1 VEN-AZA cycle
- in response (CR, CRi or MLFS)
- VEN and/or AZA cessation >3 months
- Patients who stopped VEN for progression or lack of response or allogeneic stem cell transplantation were not included in the study.

Results newly diagnosed AML

- Patient characteristics at diagnosis

	ND (n=62)
Male gender, n (%)	33 (53.2)
Age, Median (range)	75 (26-89)
WHO 2016 classification	
De Novo, n (%)	34 (54.8)
MRC-AML, n (%)	23 (37)
Therapy-related AML, n (%)	5 (8)
Prior AZA exposure, n (%)	6 (9.7)
WBC, Median (range)	2.7 (0.6-200)
ANC, Median (range)	0.7 (0-31.6)
Platelets, Median (range)	52 (9-296)
Cytogenetics	
Favorable, n (%)	3 (4.8)
Intermediate, n (%)	47 (75.8)
Poor-risk, n (%)	12 (19.4)
Main mutations	
NPM1 (n=61), n (%)	11 (18)
IDH (n=61), n (%)	20 (32.7)
FLT3-ITD (n=60), n (%)	4 (6.6)
TP53 (n=54), n (%)	4 (7.4)

Median number of VEN-AZA cycles

- 4 (ranges, 1-17)

Response to VEN-AZA

- ORR= 57 (92%)
  - CR= 44 (79%)
  - CRi = 13 (21%).
- MLFS = 5 (8%).
- CR MRDneg 21/25 (78%)
  - 11 molecular MRD (NPM1)
  - 10 flow cytometry MRD

Reasons for VEN-AZA discontinuation

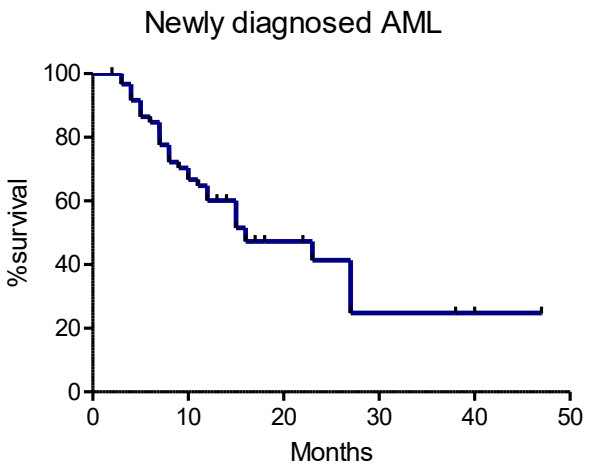
- hematological toxicities = 36 (58%),
- patient preference = 8 (13%)
- extra-hematological toxicities = 5 (8%)
- poor general status = 3 (5%)

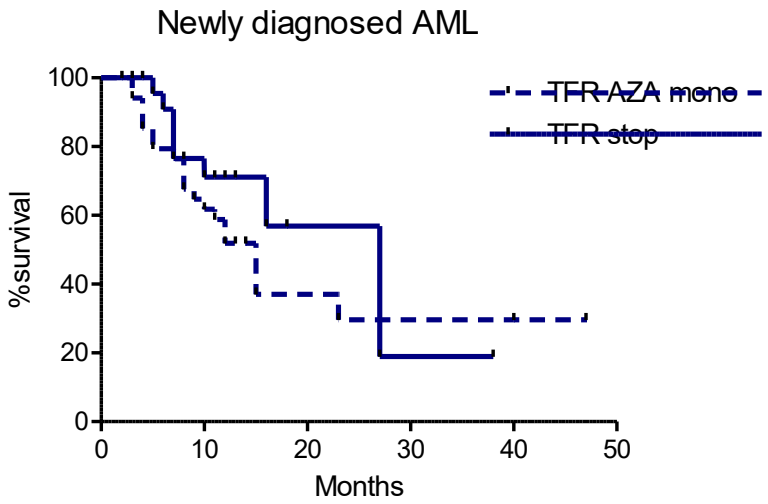
Correction of cytopenias

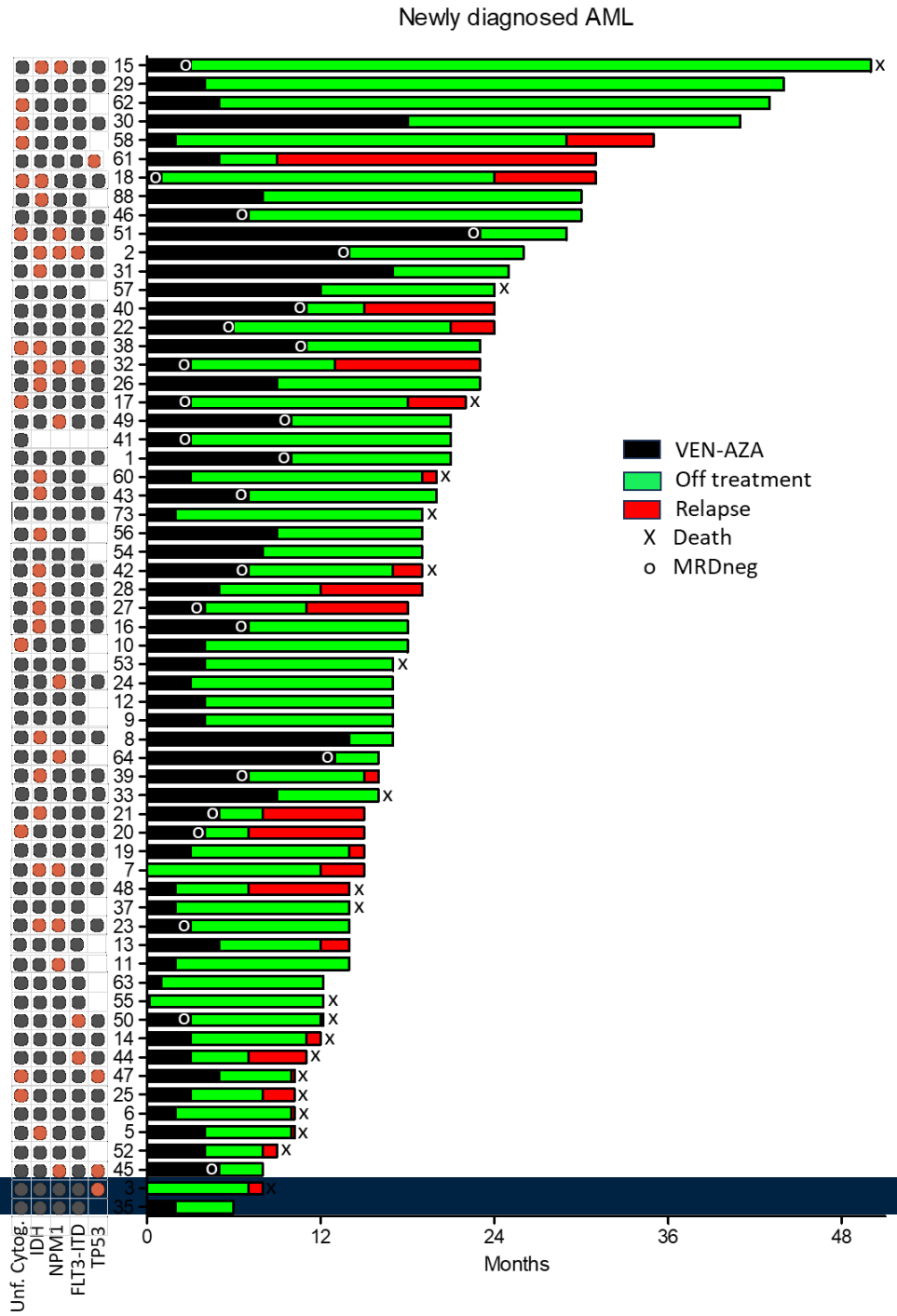
- 23/39 documented cases (59%)

Treatment-free remission

- 16 months



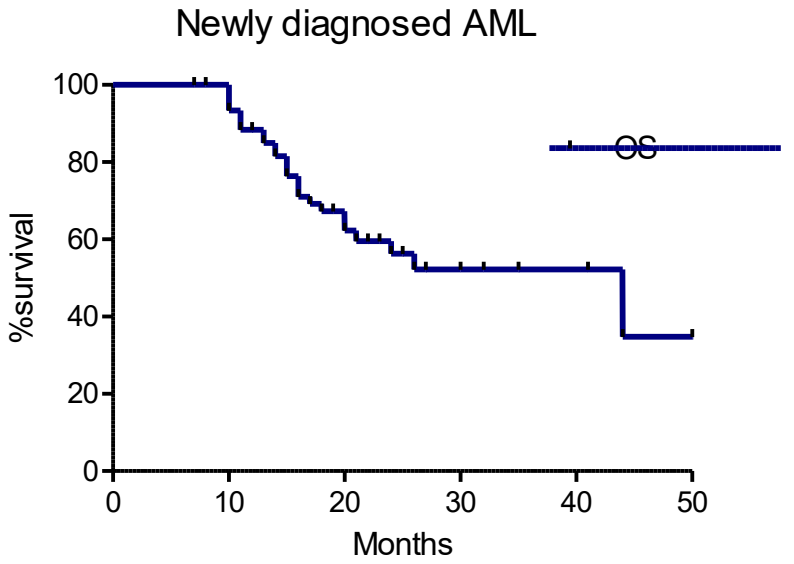


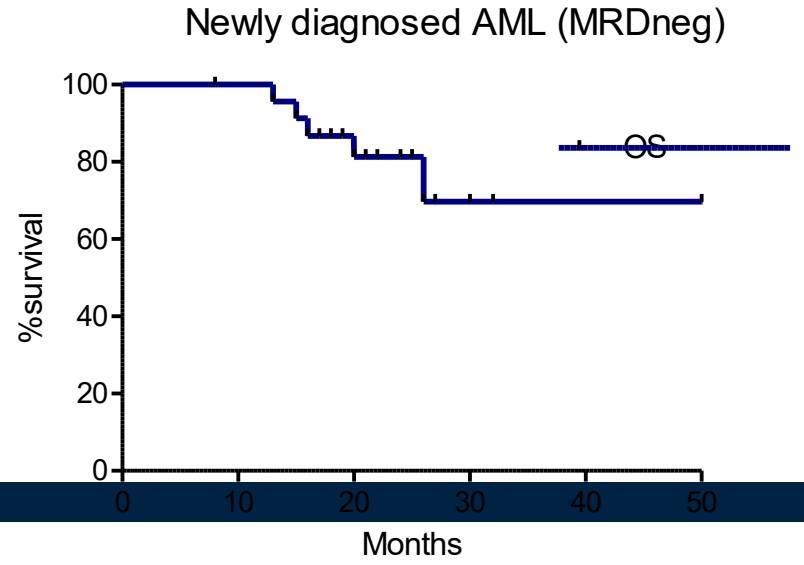


Overall survival

- All patients
  - median OS= 44 months
- MRDneg patients (n=25)
  - Median OS= NR
  - 2-y OS= 80%

- 11 patients were rechallenged with VEN-AZA. Second CR/CRi rate was 3/11 (27.3%).





CASE

- 67 y.o. woman with AML, flt3 +, s/p induction with 7+3 and midostaurin and bmt 2 yrs ago, relapsed, not interested in intensive treatment.

What is the best regimen?

- Decitabine + vent
- Decitabne +vent + gilteritinib
- Gilteritinib?

Need to gain from audience

- What is the preferred treatment approach for non-SCT patients?
- When to refer?
- Do mutations impact treatment approach?
- How do you dose venetoclax?
- When do you use HMA single agent?