POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

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Bologna
Palazzo Re Enzo
13-15 Febbraio 2025

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Terapia delle sindromi mielodisplastiche ad alto rischio

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Disclosures of Valeria Santini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
abbvie						X	
ascentage						x	
bms	x					x	
geron						x	
keros						x	
novartis						x	
servier						x	
syros						x	
janssen							x

Oral communications dedicated to higher risk MDS: 10

Posters dedicated to higher risk MDS: 41

Educational : NO

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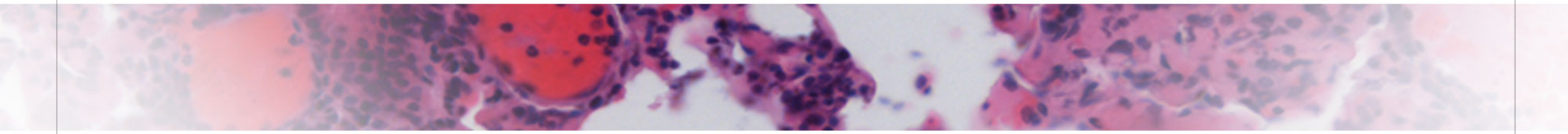

Results From a Phase 1 Open-Label Dose Escalation and Expansion Trial of Oral Azacitidine + Cedazuridine (ASTX030) in Patients With Myelodysplastic Syndromes (MDS) and MDS/Myeloproliferative Neoplasm (MPN)

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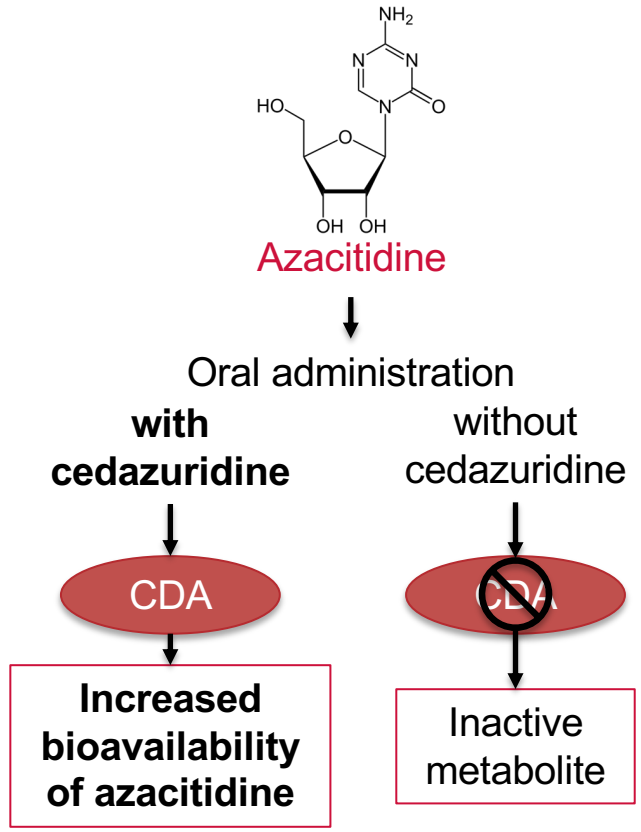
Oral presentation at the 66th ASH Annual Meeting and Exposition, December 7–10, 2024

Publication number: 662

ASTX030-01: Introduction

- Azacitidine and decitabine are parenteral DNMTis approved for the treatment of patients with MDS and AML[1–3]
- When administered orally, azacitidine is rapidly degraded by cytidine deaminase (CDA), resulting in poor bioavailability and variable systemic exposures
- Combining the DNMTi decitabine with the CDA inhibitor cedazuridine has previously demonstrated oral availability, leading to the approval of oral decitabine plus cedazuridine (DEC-C) based on PK AUC exposure equivalence vs IV decitabine[4,5]
- ASTX030-01 (NCT04256317) is a phase 1–3 trial of oral azacitidine plus cedazuridine (ASTX030) vs SC azacitidine in patients with MDS and MDS/MPN, including CMML[6]



AML, acute myeloid leukemia; AUC, area under the concentration-time curve; CMML, chronic myelomonocytic leukemia; DNMTi, DNA methyltransferase inhibitor; IV, intravenous; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; PK, pharmacokinetic; SC, subcutaneous. **1.** VIDAZA [prescribing information]. Summit, NJ: Celgene Corporation; 5/2022. **2.** DACOGEN® [prescribing information]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; 6/2020. **3.** VENCLEXTA® [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 6/2022. **4.** Garcia-Manero G et al. *Lancet Haematol.* 2024;11:e15–26. **5.** INQOVI® [prescribing information]. Princeton, NJ: Taiho Oncology, Inc.; 3/2022. **6.** Garcia-Manero G et al. Poster presented at the 65th ASH Annual Meeting and Exposition; San Diego, CA: December 9–11, 2023. Abstract #3245.

ASTX030-01: Objectives

- The aim of the phase 1 trial was to determine the optimal dose and formulation to achieve oral azacitidine PK AUC comparable to SC azacitidine
- **Primary objective:** RP2D of ASTX030
- **Secondary objectives:** PK, efficacy, safety and tolerability, change in DNA methylation

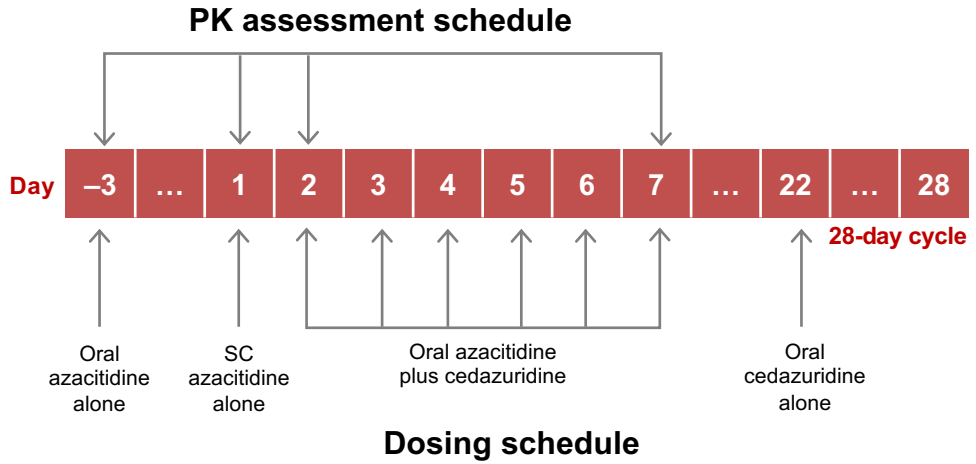
AUC, area under the concentration-time curve; PK, pharmacokinetic; RP2D, recommended phase 2 dose; SC, subcutaneous.

ASTX030-01: Methods

Oral azacitidine and cedazuridine dose level combinations

Phase	Cohort (N=88)	Azacitidine dose, mg	Cedazuridine dose, mg
IR cohorts			
1a (dose escalation)	**1** (n=6)	100	100
	2a (n=7)	100	80
	2b (n=5)	80	100
1b (dose expansion)	**101** (n=8)	100	100
	102 (n=7)	80	100
DR cohorts			
1a (dose escalation)	**3** (n=7)	60	100
	4 (n=6)	60	60
	5 (n=7)	60	40
	6 (n=6)	100	20
	7 (n=7)	136	20
1b (dose expansion)	**103** (n=15)	144	20
	104 (n=7)	136	20

- This open-label phase 1 trial enrolled adult patients with confirmed MDS and MDS/MPN overlap syndromes who may benefit from single-agent azacitidine
- Immediate-release (IR) and delayed-release (DR) azacitidine formulations at several dose combinations were explored



DR, delayed-release capsule; IR, immediate-release tablet; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; PK, pharmacokinetic; SC, subcutaneous.

ASTX030-01: Results

PK data for the DR azacitidine formulation

Cohort	Azacitidine dose, mg	Cedazuridine dose, mg	Bioavailability, F	Oral/SC AUC, %
3 (n=7)	60	100	3.77	129
4 (n=6)	60	60	2.44	86
5 (n=7)	60	40	1.78	58
6 (n=6)	100	20	~1.0	73[a]
7 and 104 (n=14)	136	20	~1.0	100 and 91[b]
103 (n=14)	144	20	~1.0	111

[a]Body-weight adjusted ratio for representative population range.
[b]Excluded one patient with an atypical (low and incomplete) SC profile.

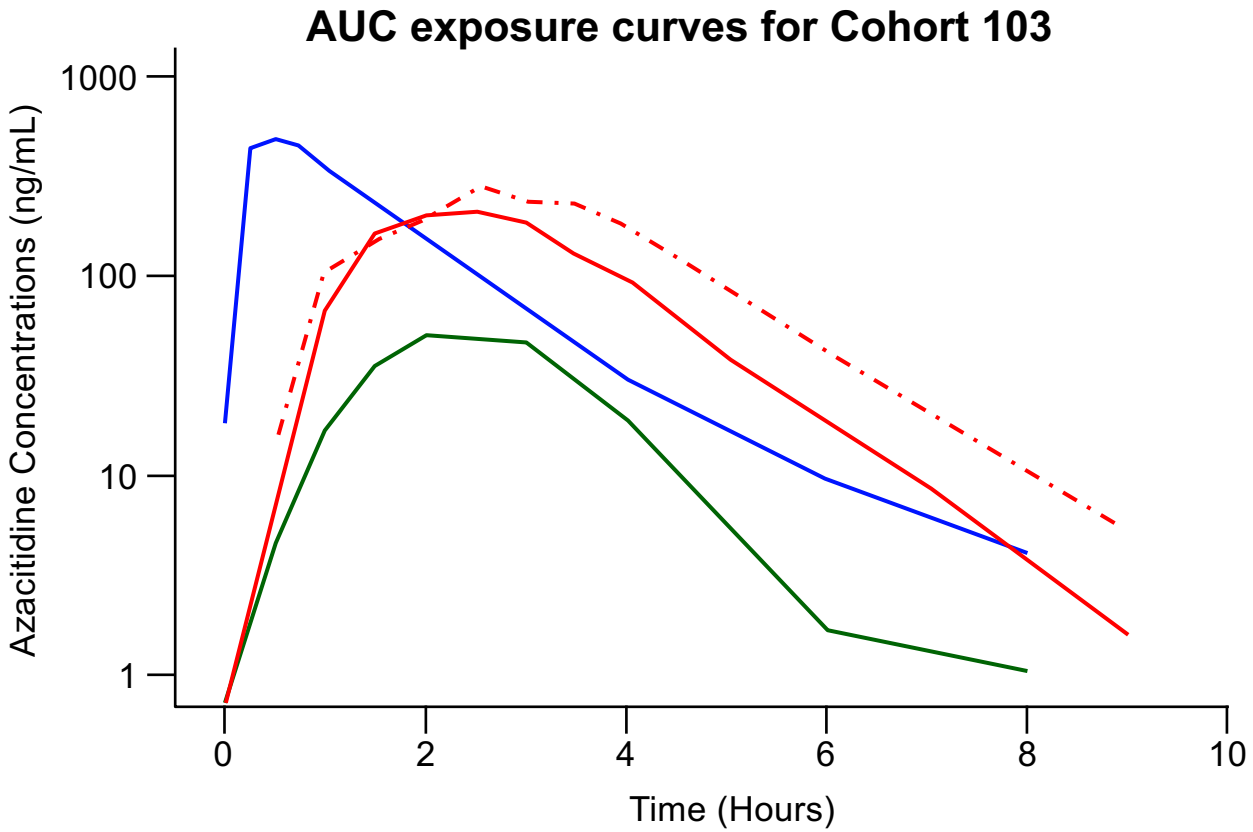
- The DR azacitidine formulation allowed for an optimized interaction with cedazuridine, with ~100% azacitidine bioavailability with cedazuridine 20 mg
- Two dose combinations were evaluated in the phase 1b (dose expansion) cohorts: 136/20 and 144/20 mg azacitidine/cedazuridine

140/20 mg azacitidine/cedazuridine was selected as the RP2D

AUC, area under the concentration-time curve; DR, delayed-release capsule; PK, pharmacokinetic; RP2D, recommended phase 2 dose; SC, subcutaneous.

ASTX030-01: Results

PK data from the phase 1 (dose escalation/optimization) part



- Cedazuridine 20 mg resulted in sufficient inhibition of CDA to increase absolute bioavailability of oral azacitidine to ~100% and achieve similar AUC exposures vs SC azacitidine[1]

AUC, area under the concentration-time curve; C, cycle; D, day; CDA, cytidine deaminase; PK, pharmacokinetic; SC, subcutaneous.

1. Garcia-Manero G et al. Poster presented at the 65th ASH Annual Meeting and Exposition; San Diego, CA: December 9–11, 2023. Abstract #3245.

ASTX030-01: Results

Safety and tolerability in the overall population

TEAEs in ≥20% of patients (N=88)		
AE,[a] n (%)	Any Grade	Grade ≥3
TOTAL	88 (100)	76 (86)
Nausea	65 (74)	2 (2)
Vomiting	51 (58)	1 (1)
Diarrhea	49 (56)	0
Constipation	48 (55)	1 (1)
Fatigue	39 (44)	3 (3)
Decreased appetite	37 (42)	4 (5)
Leukopenia	31 (35)	24 (27)
Anemia	30 (34)	22 (25)
Dizziness	27 (31)	0
Thrombocytopenia	26 (30)	22 (25)
Arthralgia	24 (27)	1 (1)
Dyspnea	24 (27)	1 (1)
Headache	24 (27)	2 (2)
Neutropenia	24 (27)	23 (26)
Neutrophil count decreased	24 (27)	22 (25)
Hyponatremia	23 (26)	2 (2)
Contusion	21 (24)	0
Edema peripheral	21 (24)	0
Abdominal pain	19 (22)	1 (1)

- The most common Grade ≥3 TEAEs were related to myelosuppression
  - Incidence of GI toxicity was comparable to previous reports for SC azacitidine,[1] and was manageable at Grade 1/2
  - Serious TEAEs (all Grade ≥3) were reported in 43 (49%) patients
  - 8 (9%) patients discontinued treatment due to an AE
- Oral azacitidine up to 144 mg was well tolerated with cedazuridine 20 mg
- The safety profile of oral azacitidine plus cedazuridine was consistent with previous reports for SC azacitidine[1]

[a]Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term. AE, adverse event; GI, gastrointestinal; SC, subcutaneous; TEAE, treatment-emergent adverse event.

ASTX030-01: Results

Best response in the overall population

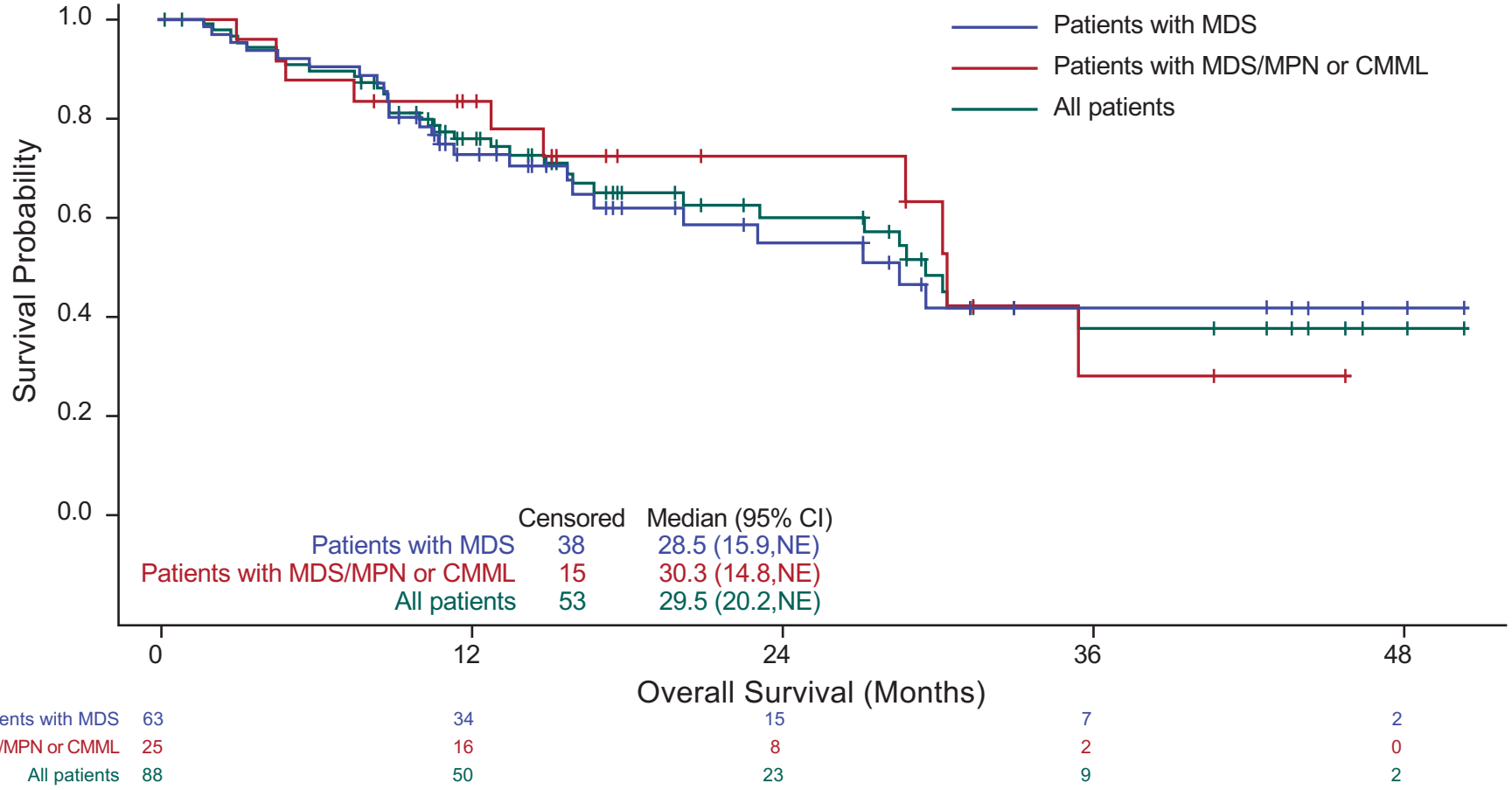
Best response, n (%)	Patients with MDS[a] (n=63)	Patients with MDS/MPN or CMML[b] (n=25)	All patients (N=88)
Complete response (CR)	5 (8)	5 (20)	10 (11)
Partial response (PR)	0	0	0
Marrow complete response (mCR)	24 (38)	6 (24)	30 (34)
mCR with hematologic improvement	11 (18)	1 (4)	12 (14)
Hematologic improvement (HI)	8 (13)	1 (4)	9 (10)
Erythroid response	6 (10)	0	6 (7)
Neutrophil response	1 (2)	0	1 (1)
Platelet response	4 (6)	1 (4)	5 (6)
Overall response (CR + PR + mCR + HI)	37 (59)	12 (48)	49 (56)
Stable disease	15 (24)	9 (36)	24 (27)
Progressive disease	2 (3)	0	2 (2)
Not evaluable	9 (14)	4 (16)	13 (15)

- Of patients who were transfusion dependent at baseline, 38% (8/21) and 14% (1/7) became transfusion independent for ≥56 days for RBCs and platelets, respectively
- Of the 20 patients who proceeded to transplant as an alternative therapy (after a median 4 [range, 2–11] cycles), 19 proceeded to transplant before achieving a best response of CR

[a]Per IWG 2006 response criteria. [b]Per IWG 2015 response criteria.
CMML, chronic myelomonocytic leukemia; IWG, International Working Group; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; RBC, red blood cell.

ASTX030-01: Results

OS in the overall population



- Data cutoff: October 8, 2024
- Median cycles: 7 (range, 1–32)
- Median follow-up: 17.7 months

CI, confidence interval; CMML, chronic myelomonocytic leukemia; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; NE, not estimable; OS, overall survival.

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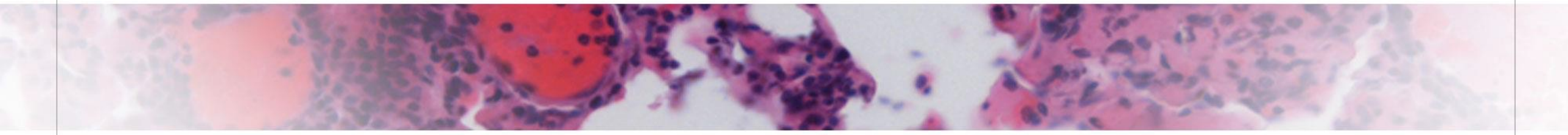
Abstract #661



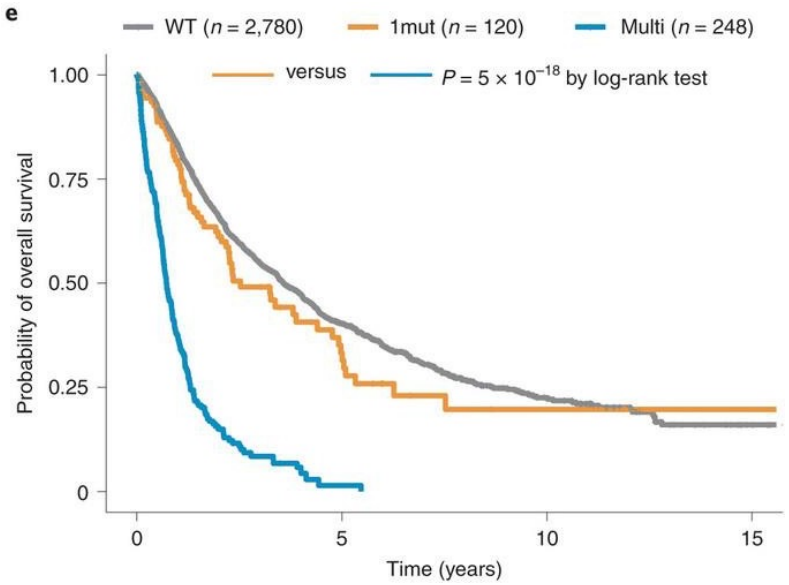
Oral Decitabine-Cedazuridine in Patients with MDS and *TP53* Mutations: A Propensity Score Matching Analysis from the Phase II and III Trials

Samuel Urrutia[1], Koji Sasaki[2], Alex Bataller[2], Hagop Kantarjian[2], Guillermo Montalban-Bravo[2], James McCloskey[3], Elizabeth Griffiths[4], Karen Yee[5], Amer Zeidan[6], Michael Savona[7], Aram Oganesian[8], Yuri Sano[8], Harold N Keer[8], Guillermo Garcia-Manero[2]

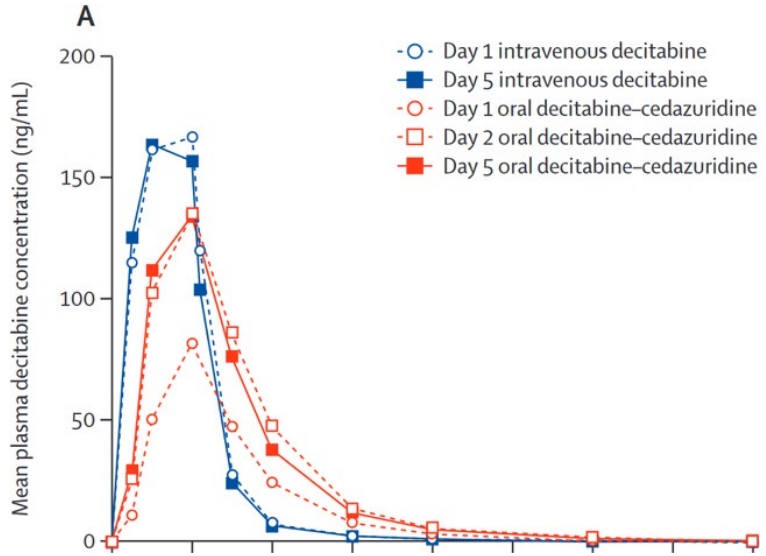
1. Div. of Oncology, Washington University School of Medicine, St. Louis MO 2. Dept of Leukemia, MD Anderson Cancer Center, Houston, TX. 3. Hackensack University Medical Center, Hackensack, NJ. 4. Roswell Park Comprehensive Cancer Center, Buffalo, NY. 5. Princess Margaret Cancer Centre, Toronto,

Patients with *TP53mut* MDS have a poor prognosis

- In MDS, the allelic **burden** of ***TP53*** alterations is closely tied to survival.[1]



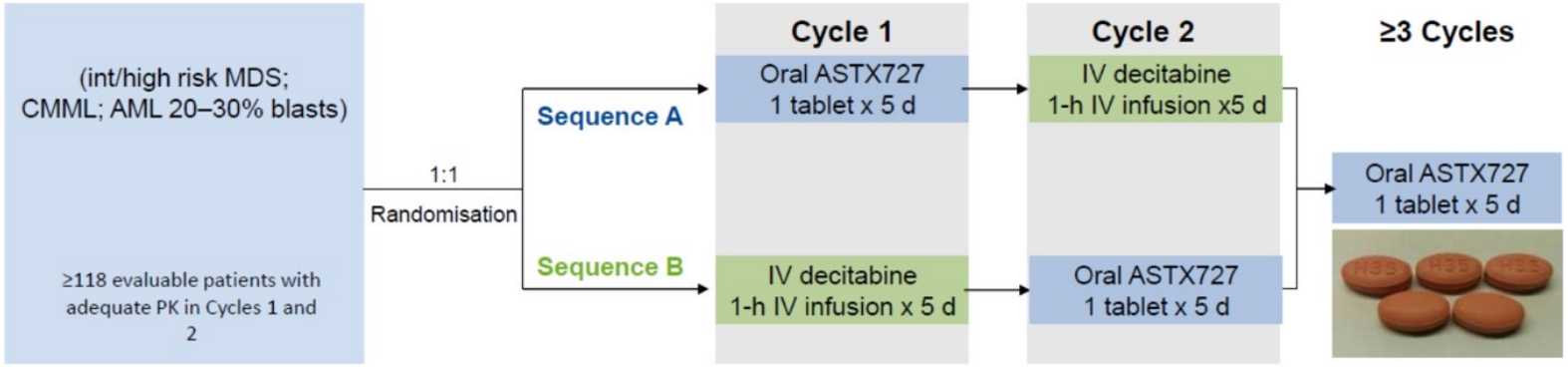
Oral decitabine-cedazuridine (DEC-C) was approved in intermediate and high-risk MDS based on AUC equivalence.[2]

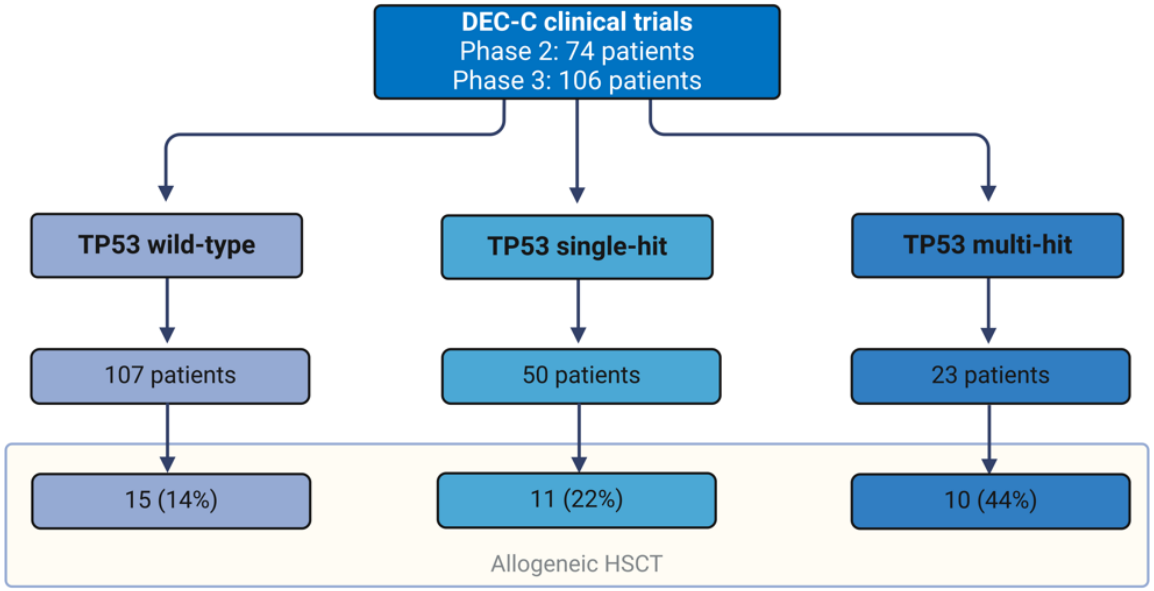


In this study, we report the characteristics **and outcomes of patients with MDS and *TP53mut*** who were treated in **the phase II and III DEC-C trials**.

1. Bernard, Nat Med 2020.
2) Garcia-Manero, Blood 2020; Lancet, 2024.

ASCERTAIN trial design, *TP53* study design and definitions





Definition of *TP53* mut burden states

TP53^{wt}:

Absence of mutations in the *TP53* gene

TP53$^{single\text{-}hit}$:

One gene mutation with VAF <50%

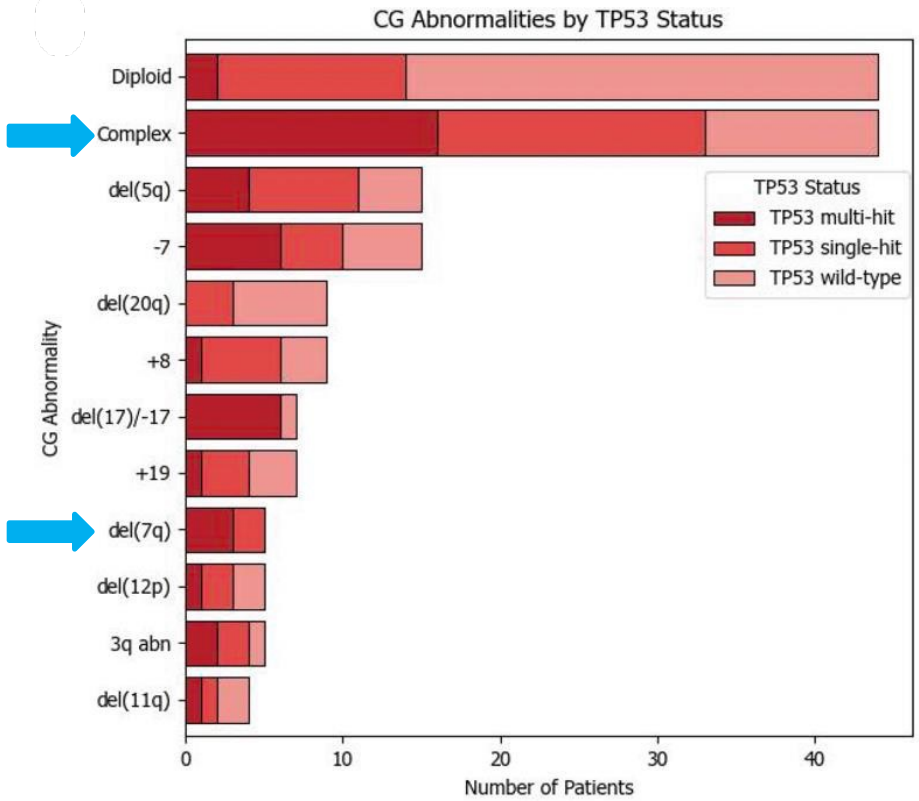
TP53$^{multi\text{-}hit}$:

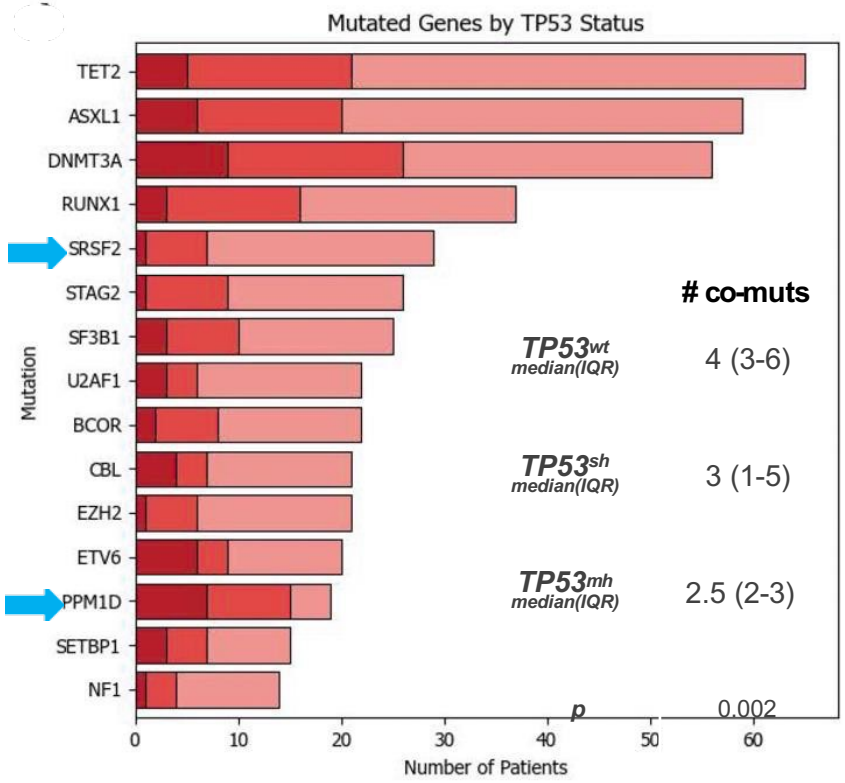
-*TP53* mutation with VAF ≥ 50%
-Two or more *TP53* mutations
-*TP53* mutation + del17p **or** -17

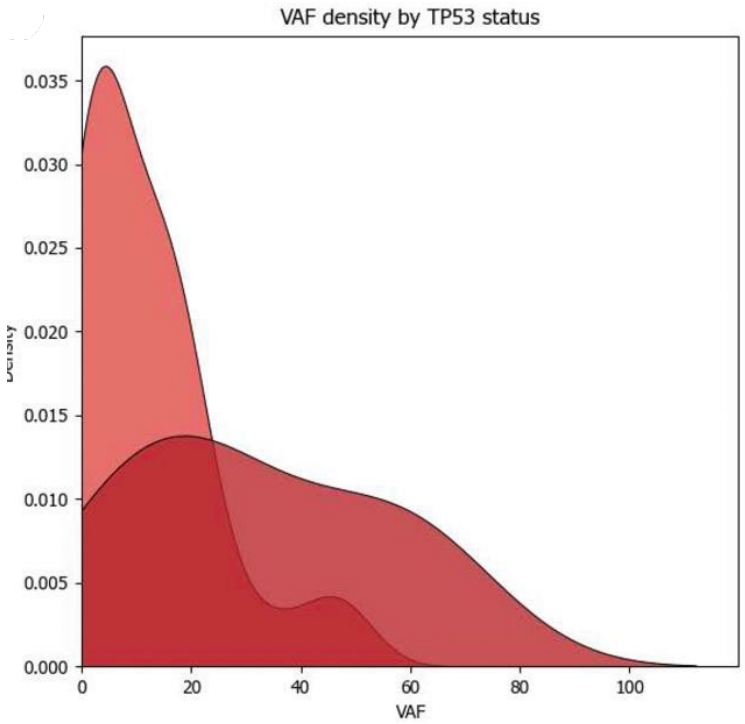
VAF: variant allele fraction

Key characteristics at enrollment

	TP53$^{wild\text{-}type}$	*TP53*$^{single\text{-}hit}$	*TP53*$^{multi\text{-}hit}$	*P*
Characteristic	**(N=107)**	**(N=50)**	**(N=23)**	
Male - no.(%)	75 (70.1)	31 (62.0)	16 (69.6)	0.588
Age - yr.	71.0 [64.0,76.5]	70.0 [66.2,76.8]	69.0 [57.5,74.0]	0.230



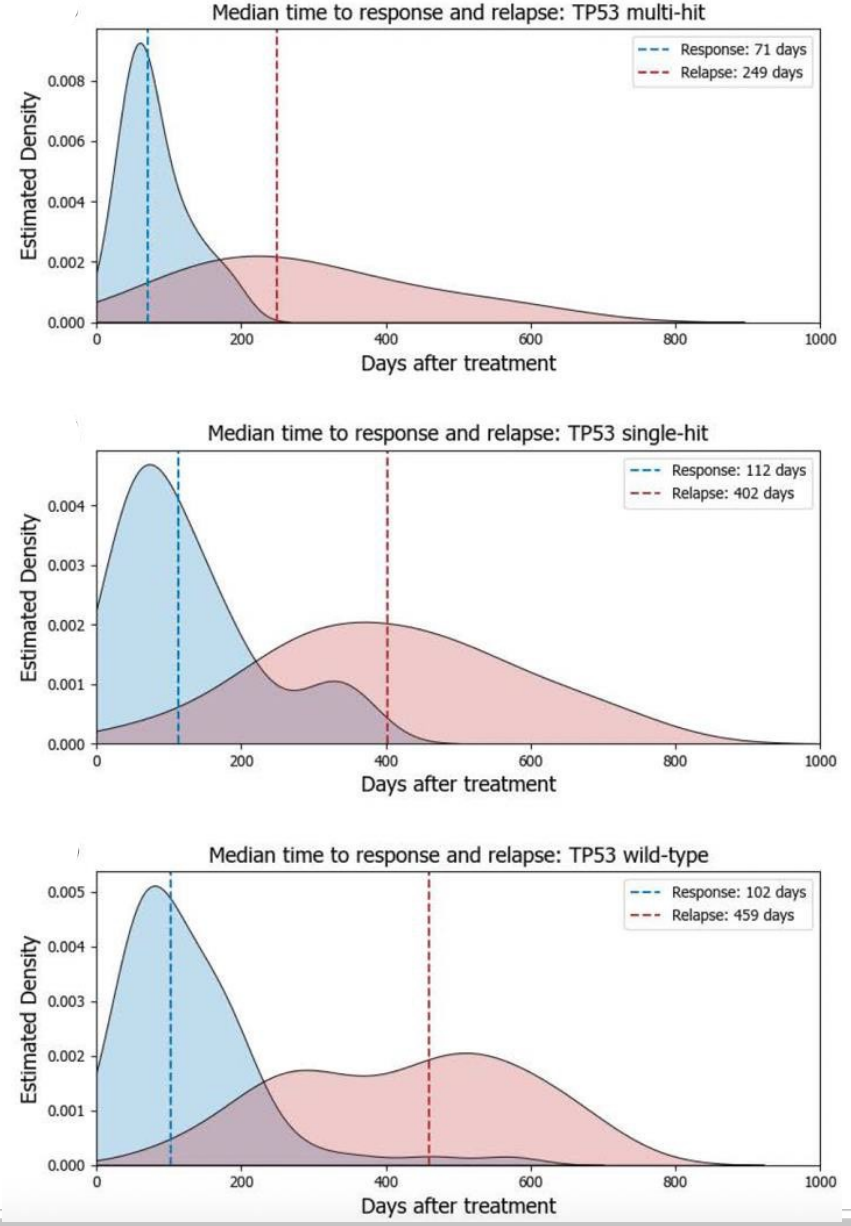




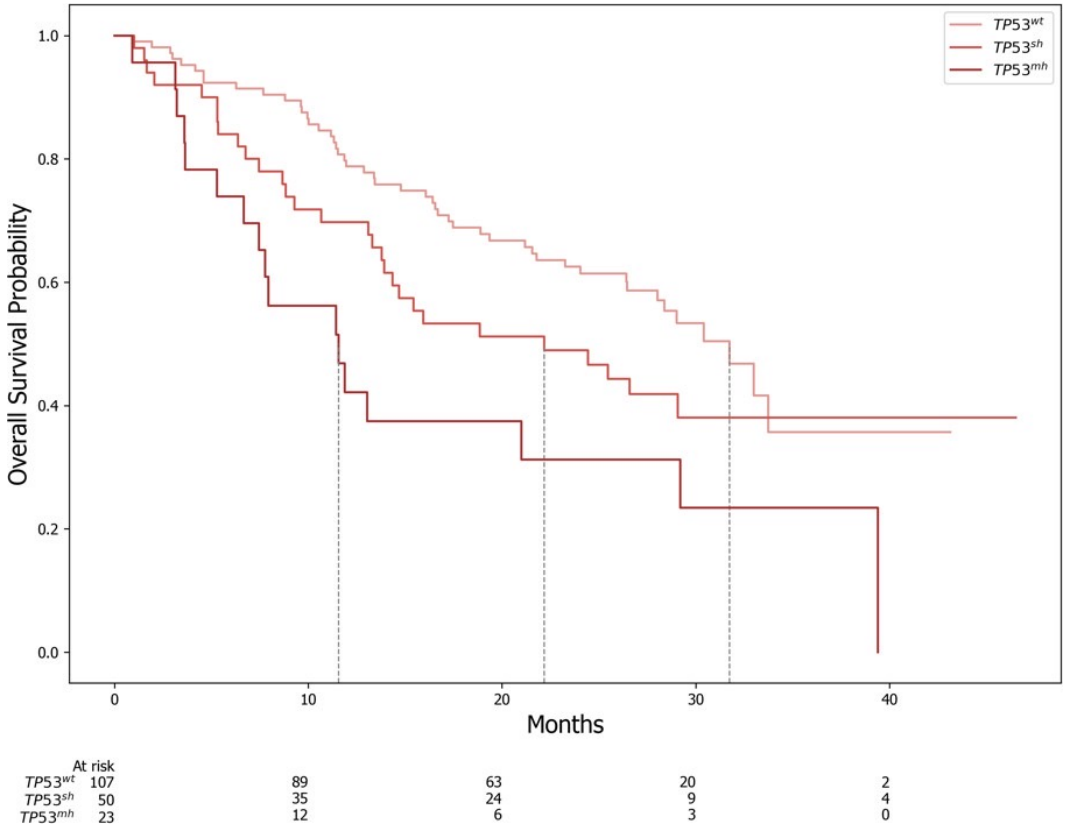
Complex cytogenetics co-occur in *TP53*^{sh} state and spliceosome mutations are rare in *TP53*^{mh} state.

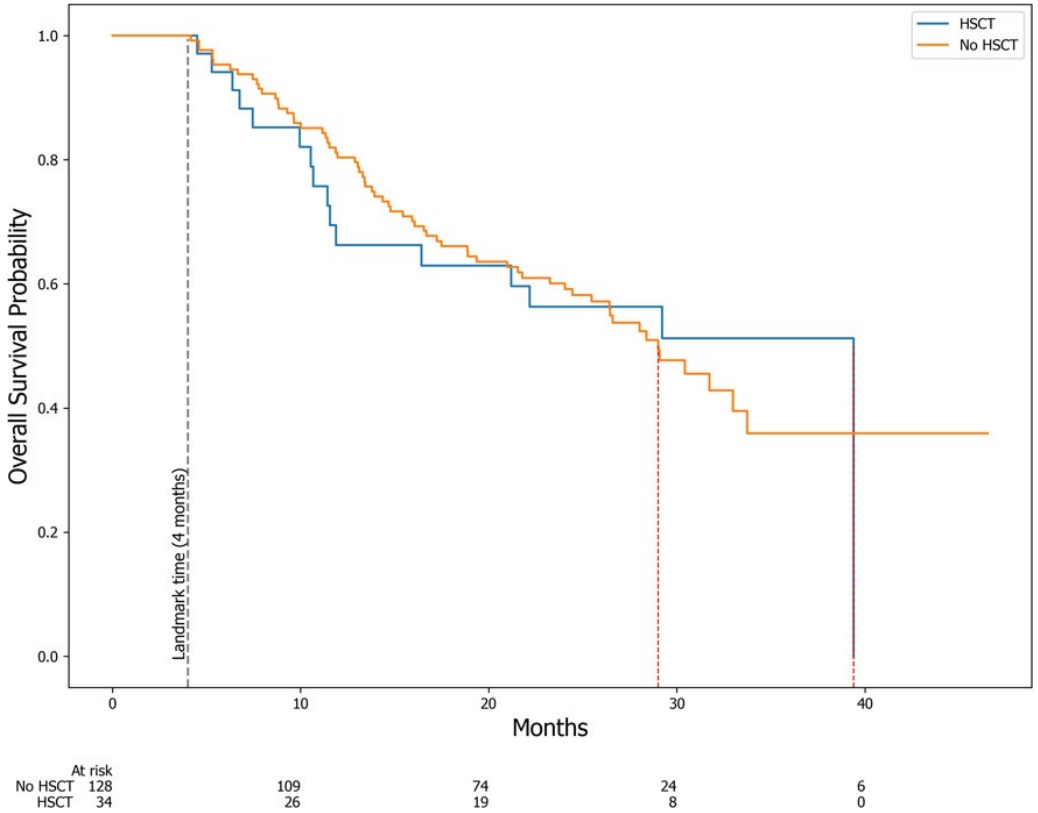
Best response and response loss kinetics

	TP53$^{wild\text{-}type}$	*TP53*$^{single\text{-}hit}$	*TP53*$^{multi\text{-}hit}$	*p*
Characteristic	**(N=107)**	**(N=50)**	**(N=23)**	
Best Response - no.(%)				0.215
Complete remission	24 (22.4)	7 (14.0)	5 (21.7)	
Marrow complete remission	24 (22.4)	19 (38.0)	5 (21.7)	
Hematologic Improvement	14 (13.1)	4 (8.0)	3 (13.0)	
No Response	29 (27.1)	14 (28.0)	9 (39.1)	
Progressive Disease	8 (7.5)			
Not Evaluable	8 (7.5)	6 (12.0)	1 (4.3)	
Number of cycles received - no.[IQR]	9.0 [4.0,16.5]	7.5 [4.2,12.8]	5.0 [3.0,7.0]	0.016



Overall survival by *TP53* burden and HSCT (4-month landmark)

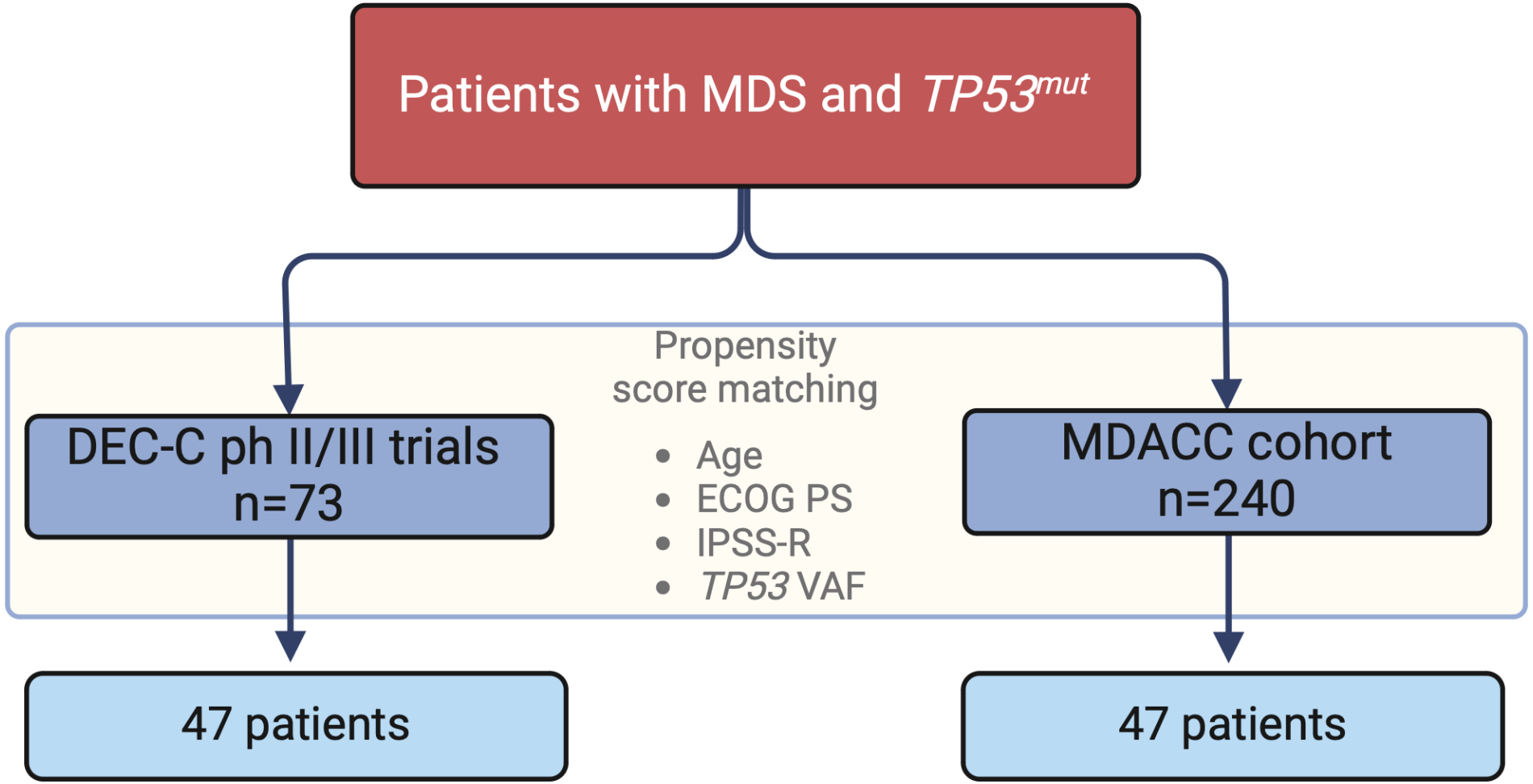




	TP53^{wt} *months (95%CI)*	*TP53*^{sh} *months (95%CI)*	*TP53*^{mh} *months (95%CI)*	*p*
mOS	31.7 (19.5-51.1)	22.1 (14.6-35.9)	11.5 (8.6-19.1)	< 0.001

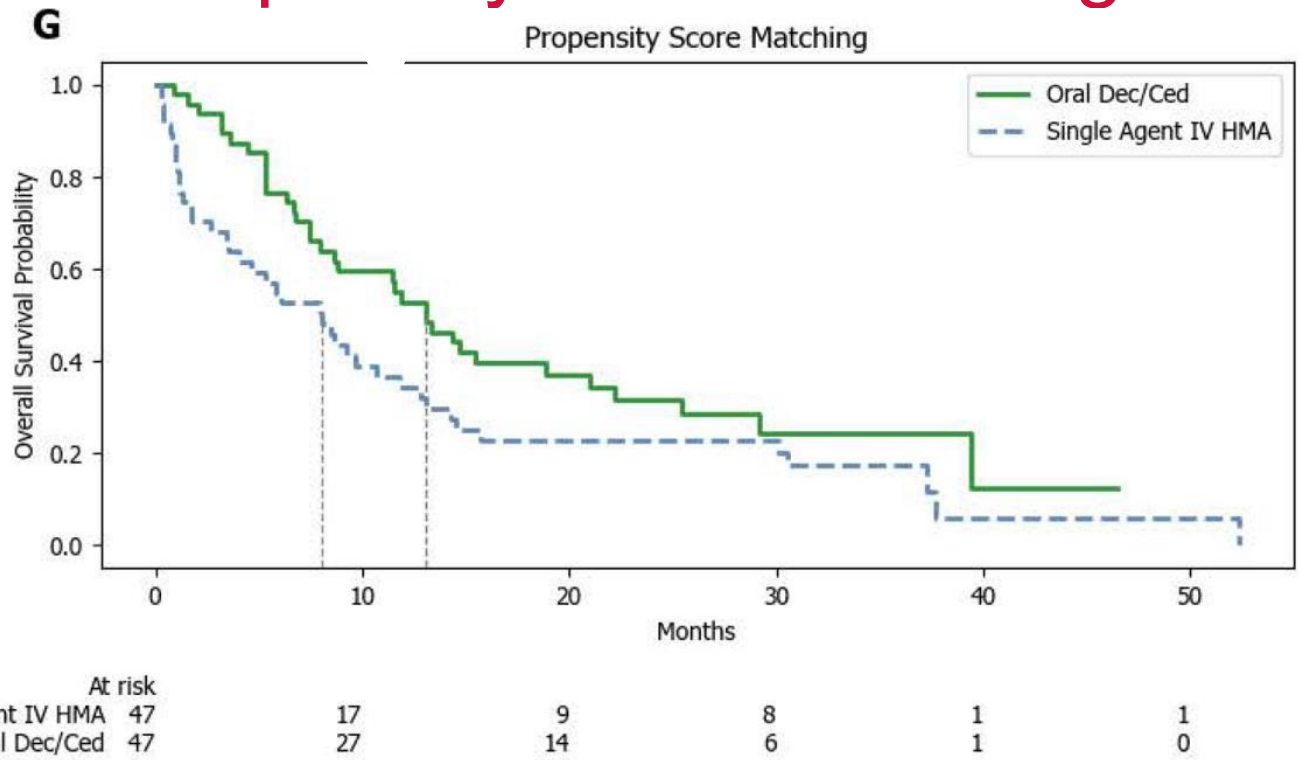
	HSCT *months (95%CI)*	*No HSCT* *months (95%CI)*	*p*
mOS	39.3 (27.3 – NE)	29.0 (17.5-45.9)	0.94

Propensity score matching analysis methodology



MDACC: MD Anderson Cancer Center

Propensity score matching characteristics and survival



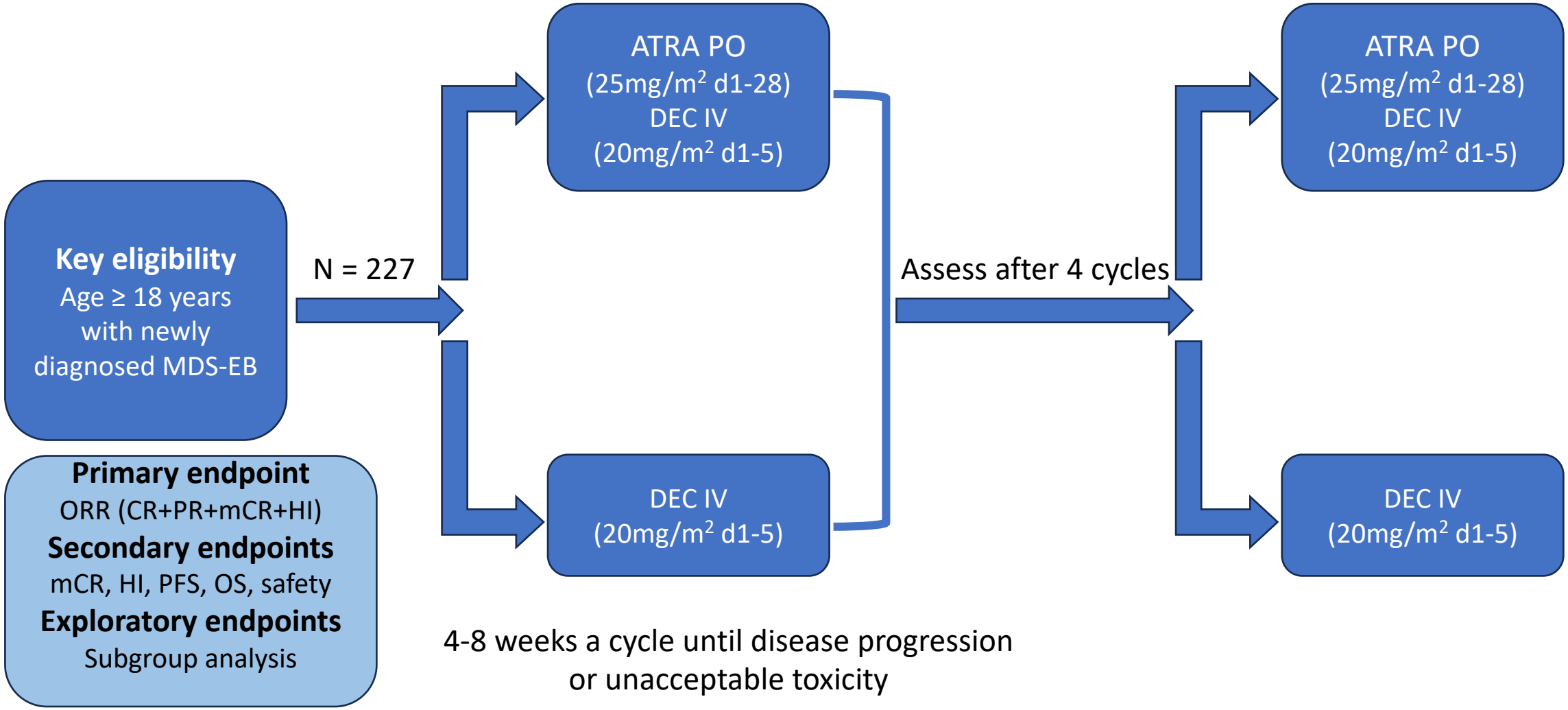
Characteristic	IV/SQ HMA	Oral Dec/Ced	p
n	47	47	
Age, median [IQR]	71 [64,77]	69.0 [63.0,75.0]	0.36
TP53 VAF, median [IQR]	20 [7,34]	10 [5,24]	0.122
BM blast, median [IQR]	4[2,7]	5 [2,8]	0.343
ECOG PS 0, n (%)	14 (29.8)	15 (31.9)	0.759
ECOG PS 1, n (%)	28 (59.6)	29 (61.7)	
ECOG PS 2, n (%)	5 (10.6)	3 (6.4)	
IPSSR, median [IQR]	6.5 [4.0,8.0]	5.8 [4.5,7.4]	0.648

	Oral Dec-C *months (95%CI)*	*IV/SQ HMA* *months (95%CI)*	*p*
mOS	13.1 (8.4-21.3)	8.0 (5.2-13.0)	0.047

Abs 663: Tong et al

DEC + ATRA vs DEC in MDS-EB:

a multicenter, randomized, open label trial



Adapted from **Tong et al. ASH 2024 abs. #663**

DEC + ATRA vs DEC in MDS-EB:

a multicenter, randomized, open label trial

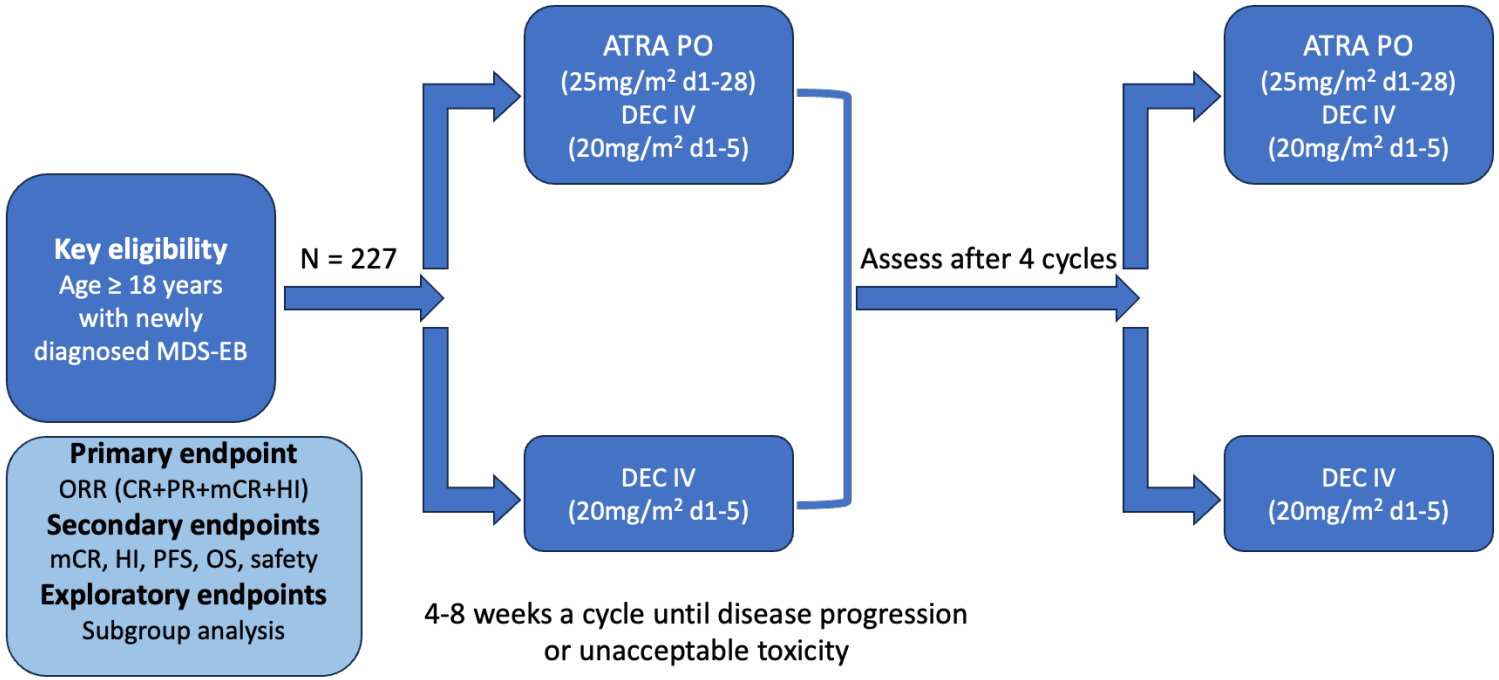
227 HR-MDS pts enrolled:
113 ATRA + DEC, 114 DEC

Median age **62**

IPSS R high/very high 82% (DEC+ATRA) vs 80% (DEC)
TP53mut was 17% in both arms

Median of cycles: 4 (DEC+ATRA) vs 3 (DEC)

Safety:
No differentiation syndromes,
only dry skin , headheache in ATRA treated

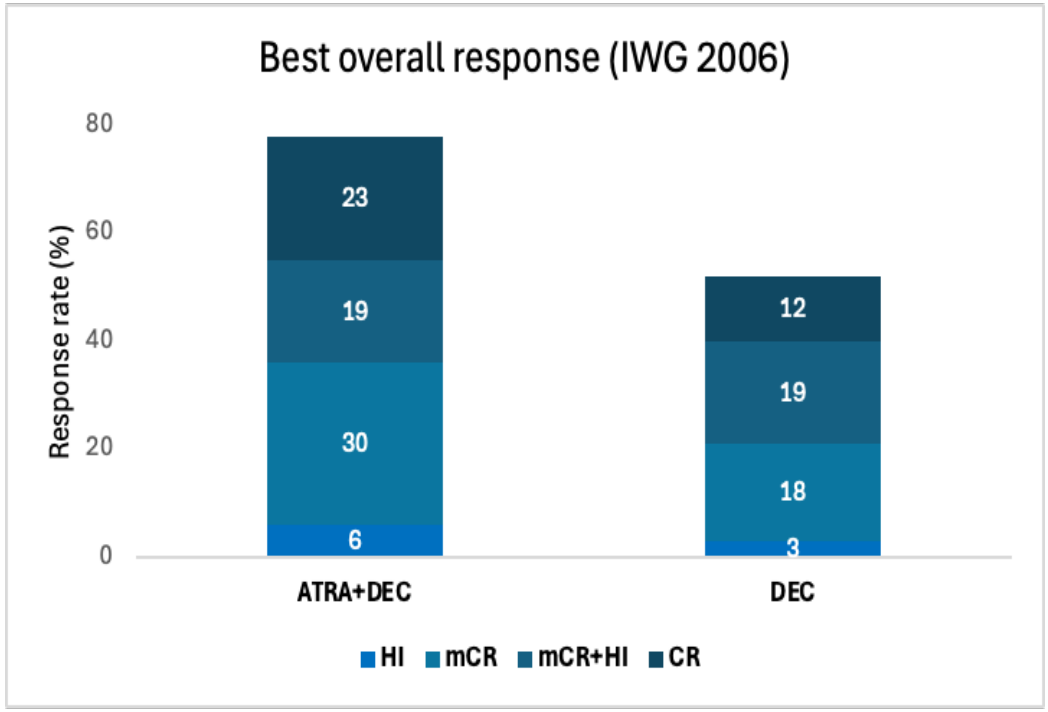


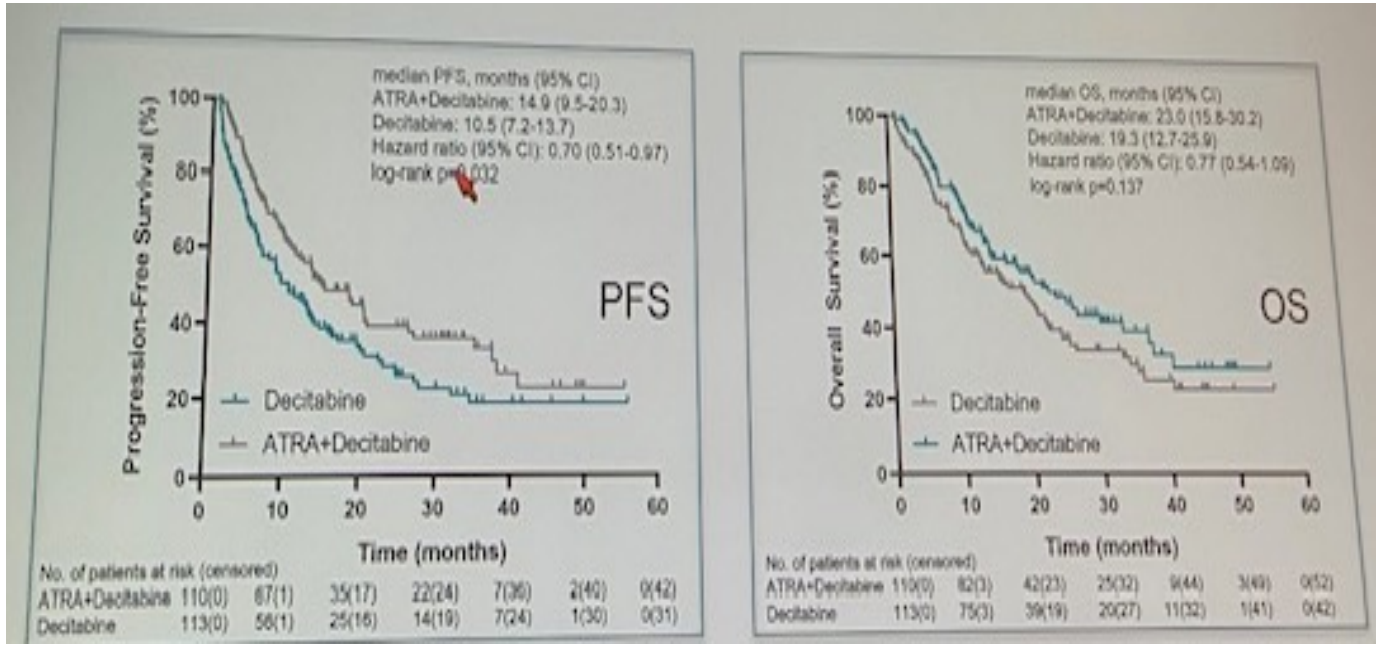
Adapted from **Tong et al. ASH 2024 abs. #663**

ATRA+DEC improved **ORR** for all subgroups (including TP53mut) compared with DEC alone

Median FU: 30 mos

20% of patients underwent **HSCT** in both arms





Median PFS (months): 14.9 (ATRA+DEC) vs 10.5 (DEC, p=0,032)

Median OS (months): 23 (ATRA+DEC) vs 19.3 (DEC, p=0,14)

Adapted from **Tong et al. ASH 2024 abs. #663**

•3206: Clinical Utilization and Outcomes of Hypomethylating Agents and Venetoclax in Patients with Myelodysplastic Syndrome – a Multicenter Retrospective Analysis. Guru Murthy et al

13 US academic centers

454 patients included, 258 patients received VEN + HMA and 196 patients HMA monotherapy. Standard doses of VEN.
Median age 66 for HMA+VEN, 69 HMA alone, 71 for 2L.
HR MDS in 1 L and 2L treatment. 49% had TP53mut in the combination arm

In the upfront setting, response rate was significantly higher with HMA-VEN than HMA monotherapy (CR: 33% vs 12%; marrow CR: 40% vs 27%, p<.001).

VEN given in the post HMA failure setting also resulted in encouraging response rates (CR 10%, marrow CR 32%). (alone? As add-on?)

The authors refers a significantly longer EFS for the combination arm after combination treatment, no OS differences

Multivariable Analysis – Event Free Survival

Variable	HR (95% CI)	P-value
Therapy		
HMA	Ref.	
HMA-Venetoclax	0.59 (0.44-0.78)	<0.001
IPSS-R		
Intermediate	Ref.	
High	1.30 (0.90-1.89)	0.2
Very high	2.33 (1.62-3.37)	<0.001
MDS type		
Denovo	Ref.	
Therapy related	1.40 (1.04-1.80)	0.02
del 17p/TP53 mutated	1.70 (1.28-2.27)	<0.001

Multivariable Analysis – Overall Survival

Variable	HR (95% CI)	P-value
Therapy		
HMA	Ref.	
HMA-Venetoclax	0.77 (0.57-1.04)	0.08
IPSS-R		
Intermediate	Ref.	
High	1.03 (0.69-1.55)	0.9
Very high	1.94 (1.32-2.85)	<0.001
MDS type		
Denovo	Ref.	
Therapy related	1.36 (0.98-1.88)	0.06
del 17p/TP53 mutated	1.77 (1.30-2.41)	<0.001

•4602: A Retrospective Cohort Study Evaluating Outcomes of Higher Risk MDS
•Treated with Hypomethylating Agents with or without Venetoclax Using International Working Group 2023 Response Criteria. Shukla et al. Multicenter NY

A total of 188 HR and LR MDS first and second line pts were treated with combination of HMA (aza and dec) + venetoclax : 35% and with HMA alone (65%). Some pts received both HMAs .
Significant difference in median age 70 (combination) vs 78 (aza alone). BM blast < 10%, but sign higher in the combination arm

Response

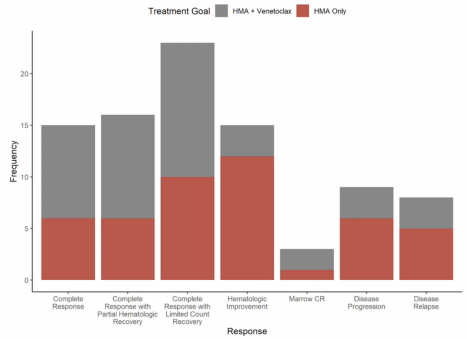
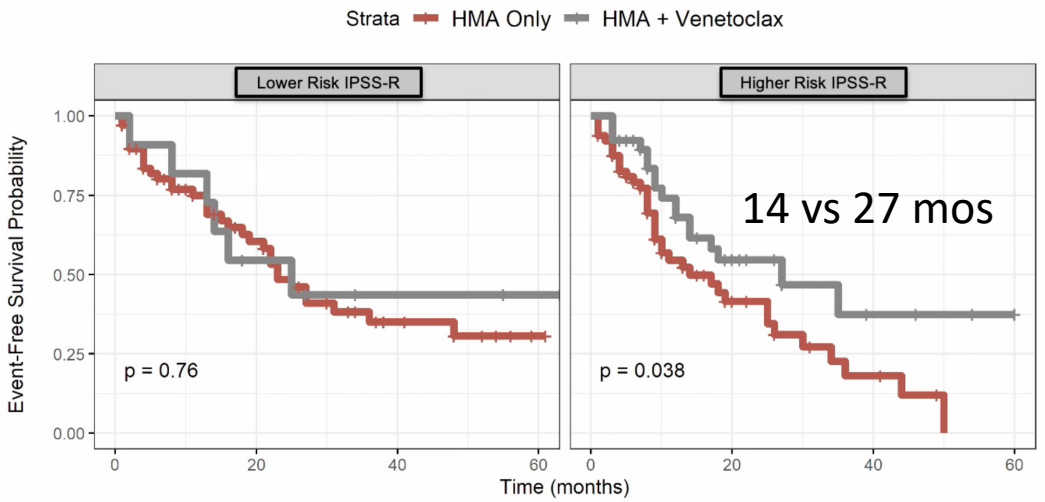


Figure 1: Response by treatment strategy, excluding patients with "no response"

Event free survival



In the HMA + VEN arm 30% of pts had TP53 mut vs 12%

In the HMA +Ven arm, only 8% of LR MDS vs 25%.

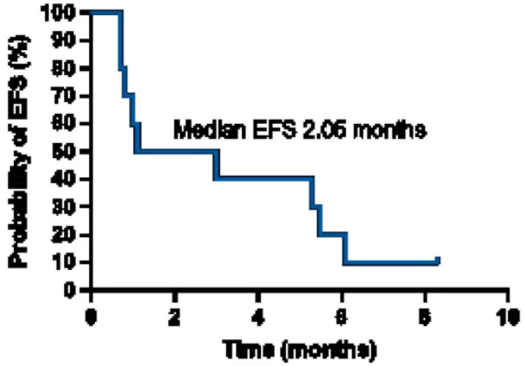
HSCT possible in 38% of combination arm versus 1.6%. (age? Not reported comorbidities.)

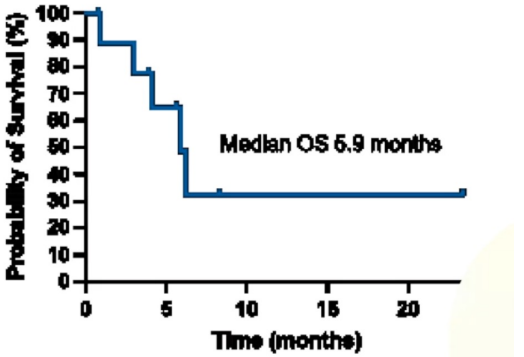
OS was 35 mos for HR MDS treated with the combination vs 26 mos HMA alone (not significant p= 0. 16)

1842 Results of a Phase I/II Study of Tagraxofusp in Combination with Decitabine for Patients with Myelodysplastic/Myeloproliferative Neoplasms and Higher Risk Myelodysplastic Syndromes
Ulianik et al.

After HMA failure, 10 pts treated: 6 HR MDS with IPSS-R > 3.5 and TP53mut (median age 72)
4 CMML 1- and CMML 2 (median age 79)

Dose Level	Decitabine dose and schedule (mg/m^2/day)	Tagraxofusp dose (µg/kg/day)
1	20mg/m^2/day days 1-5	5 µg/kg/day days 1-3*
2	20mg/m^2/day days 1-5	7 µg/kg/day days 1-3*
3	20mg/m^2/day days 1-5	9 µg/kg/day days 1-3*
4	20mg/m^2/day days 1-5	12 µg/kg/day days 1-3*

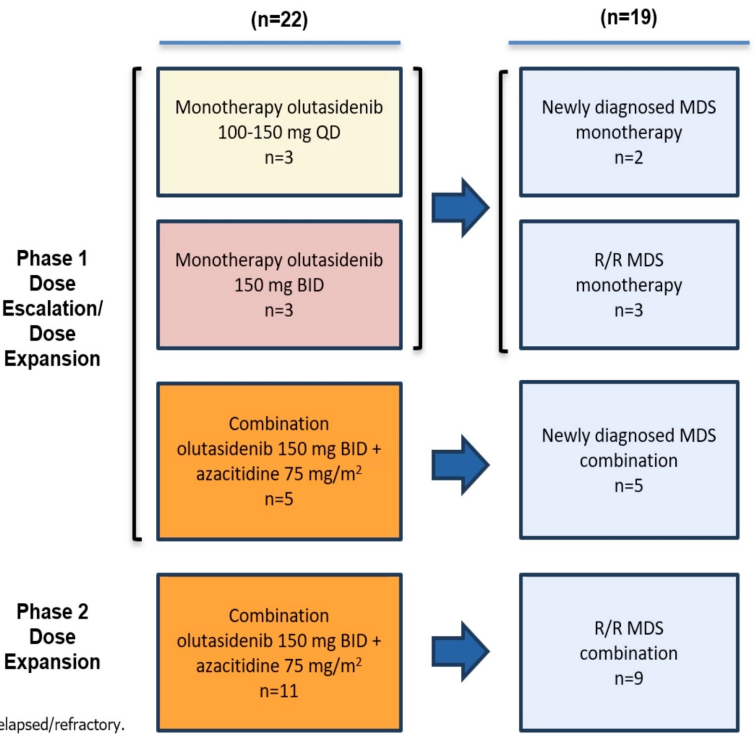




•The median number of cycles of therapy was 6 [1-7].
• All patients experienced TEAs with 5 (50%) having grade ≥3 TEAs
Dose reduction of decitabine was required in 1 pt (10%)
•Capillary leak syndrome 20% (pts > 75yr)
Out of 10 patients, 9(90%) were evaluable for response
•1 patient came off study prior to having response evaluation due to toxicity and physician choice.
•Three patients (30% overall, 33% of evaluable) had response to therapy including :
•1 CR
•1 mCR with complete neutrophil and platelet recovery
1 mCR with no hematological improvement.
•The median number of cycles to best response was 2- The median follow-up was 8.3 months

4600: Olutasidenib Alone or in Combination with Azacitidine in Patients with m*IDH1* Myelodysplastic Syndromes/Neoplasms: Final 5-Year Data. Cortes et al

22pts with INT and HR MDS . Median age 77 (OLU mono), 72 (OLU + AZA)



Prior HMA, n (%)	4 (67)	10 (63)	14 (64)
IDH1 mutation type			
R132C	3 (50)	4 (25)	7 (32)
R132H	2 (33)	10 (63)	12 (55)
R132L/R132G/R132S	1 (17)	1 (6)	2 (9)

	OLU Monotherapy (n=5)	Combination OLU+AZA (n=14)	Pooled (n=19)
ORR, n (%)	2 (40)	11 (79)	13 (68)
Complete remission (CR)	1 (20)	5 (36)	6 (32)
Marrow CR	1 (20)	6 (43)	7 (37)
Partial remission	0	0	0
Stable disease	1 (20)	3 (21)	4 (21)
Clinical benefit	1 (20)	0	1 (5)
Progressive disease	1 (20)	0	1 (5)

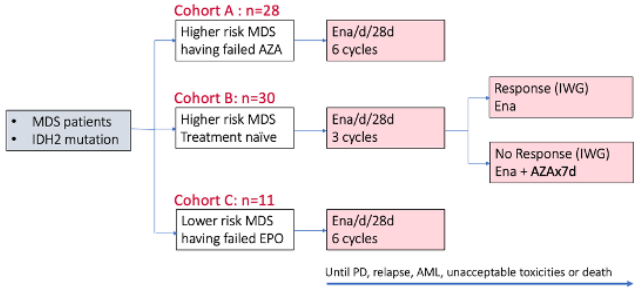
	OLU Monotherapy (n=6)	Combination OLU+AZA (n=16)	Pooled (n=22)
Time to CR, median (range)	8.3 (8.3, 8.3)	5.1 (2.5, 14.3)	5.7 (2.5, 14.3)
Duration of CR, median months (range)	NR (52, 52)	14.15 (0, 21.2)	20.5 (0, 52)
Time to CR/marrow CR, median (range)	4.65 (1, 8.3)	2 (1, 13)	2 (1, 13)
Duration of CR/marrow CR median months (range)	NR (6.7, 52)	14.6 (0, 32.8)	14.6 (0, 52)
Duration of follow-up, median (range)	60.3 (4.5, 67.2)	53.8 (1, 53.8)	53.8 (1, 67.2)
Overall survival, median (95% CI)	14 (4.5, NR)	27.5 (5, 36.6)	27.2 (6.9, 37)
12-month OS probability (95% CI)	67 (19, 90)	69 (40, 86)	68 (45, 83)

No major TAEs

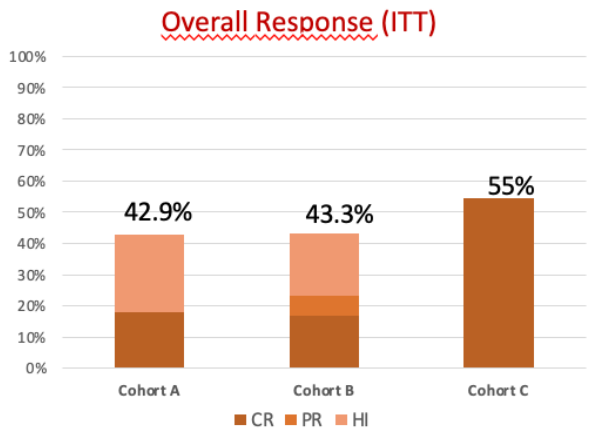
•1839: Enasidenib (ENA) Monotherapy in Patients with *IDH2* mutated Myelodysplastic Syndrome (MDS), the Ideal Phase 2 Study By the GFM and EMSCO Groups. Ades et al

A total of 69 MDS pts were treated with **28-day cycles of ENA - 100 mg PO QD**.

RESULTS



parameter	Value	n	%
Sex	Male	44	64%
	Female	25	36%
Age		69	76 (48;93)
WHO 2016	MDS-SLD	4	6%
	MDS-MLD	7	10%
	MDS-EB1	13	19%
	MDS-EB2	26	38%
	MDS-U	1	4%
	CMML	3	4%
	Low blast AML	15	22%
IPSS-R	Low	8	12%
	Int	16	23%
	High	34	49%
	Very High	11	16%
VAF IDH2	Median		36.6% (2.6-49.5)

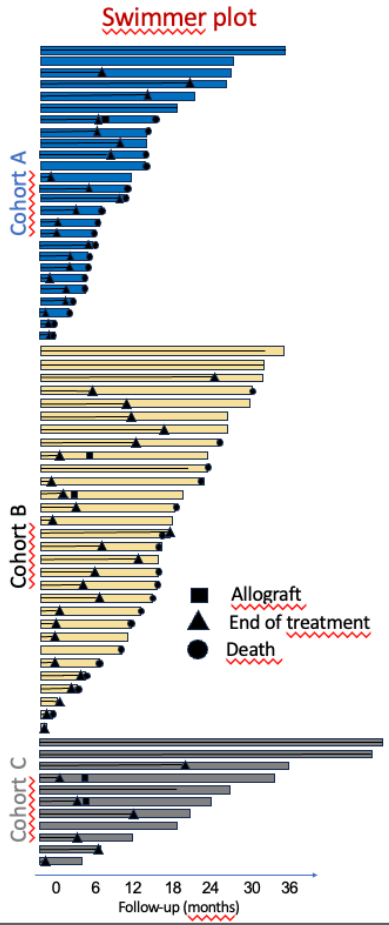


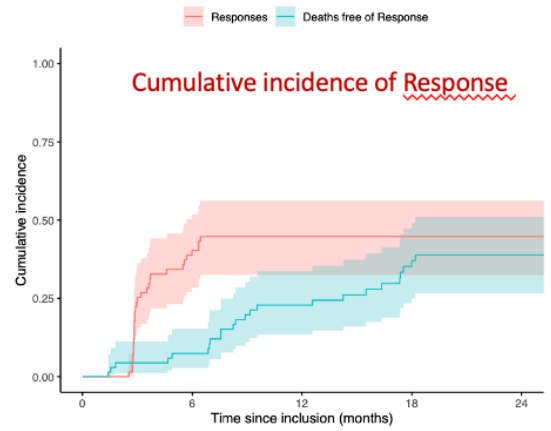
Median duration of Response

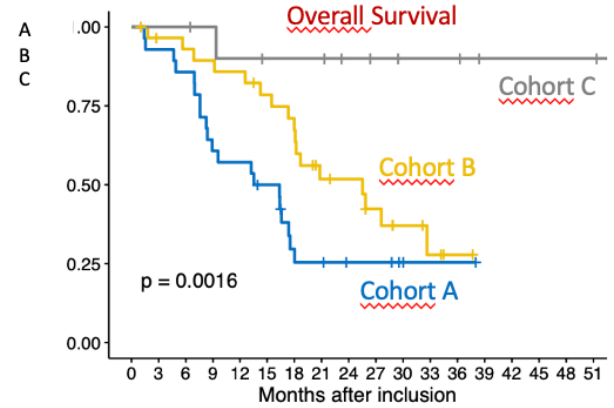
- Cohort A – 6.9 months
- Cohort B – 12.2 months (Two patients bridged to transplant)
- Cohort C – None of the responders had lost response
- In cohort B, AZA was added to ENA in 4 patients after 3 cycles leading to one additional response.

Median Overall Survival

- Cohort A –14.9 months
- Cohort B –25.5 months
- Cohort C – NR



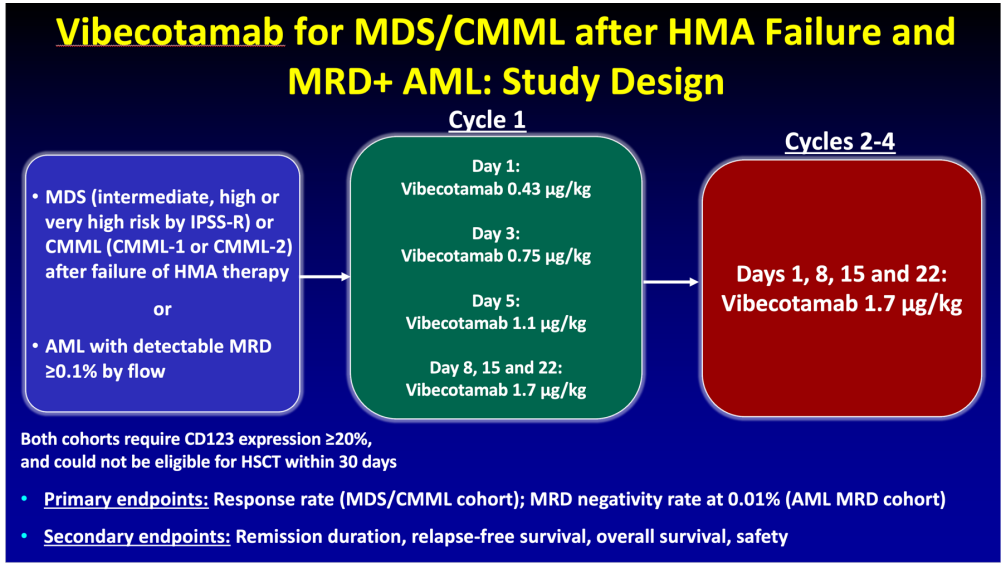




•1007: Updated Results from a Phase II Study of Vibecotamab, a CD3-CD123 Bispecific T-Cell Engaging Antibody, for MDS or CMML after Hypomethylating Failure and in MRD-Positive AML. Nguyen et al

Vibecotamab is a CD3-CD123 bispecific T-cell engaging antibody.

19 MDS pts treated with median age 74, 56% 2L,
63% VEN treated
TP53mut 42%



Overall response rate (ORR): 13/19 **(68%)**

Bone marrow blasts ≥5%: 12/17 (71%)

Prior venetoclax exposure: 9/12 (75%)

TP53-mutated: 5/8 (63%)

Prior HSCT: 2/2 (100%)

ORR in MDS cohort: 10/16 (63%)

ORR in CMML cohort: 3/3 (100%)

In AML MRD+ cohort:

MRD negativity in 5/18 (28%)

Responses in high-risk pts

Some durable MRD-negative remissions

9/10 (90%) relapsed (continuos therapy)