

What Actually Changes Practice in 2026: Myeloid Updates

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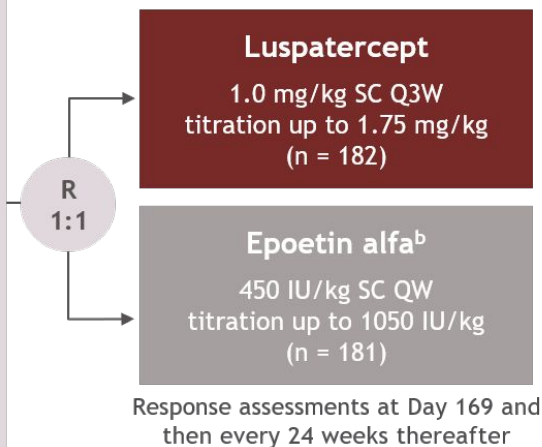
COMMANDS: Study Design

Key patient eligibility criteria

- ≥ 18 years of age
- IPSS-R very low-, low-, or intermediate-risk MDS (with or without RS) by WHO 2016 classification, with $< 5\%$ BM blasts^a
- Required RBC transfusions (2-6 pRBC U/8 weeks, minimum of 8 weeks prior to randomization)
- ESA-naïve
- Endogenous sEPO < 500 U/L

Patients stratified by

- Baseline RBC transfusion burden (< 4 or ≥ 4 pRBC U/8 weeks)
- Baseline endogenous sEPO level (≤ 200 or > 200 U/L)
- RS status (RS+ or RS-)



End of treatment

- Due to lack of clinical benefit^c or disease progression per IWG 2006 criteria

Post-treatment safety follow-up

- Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, and survival for 5 years from first dose

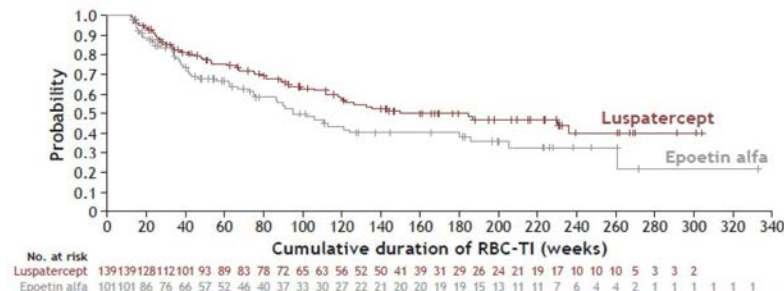
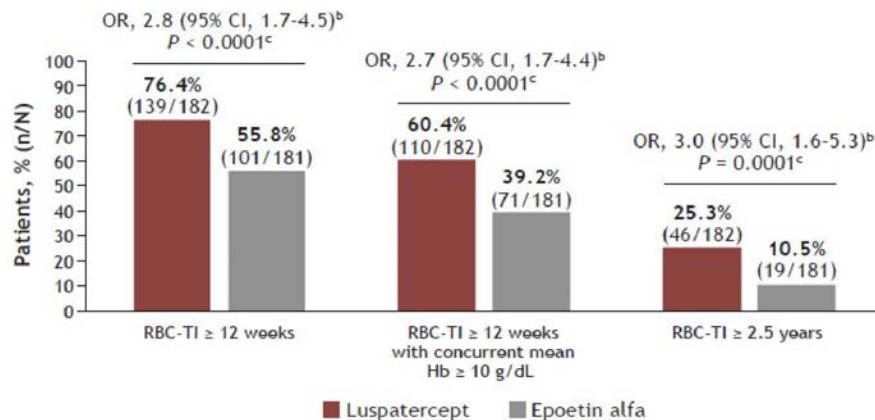
Primary endpoint

- RBC-TI for ≥ 12 weeks (Weeks 1-24) with concurrent mean Hb increase ≥ 1.5 g/dL

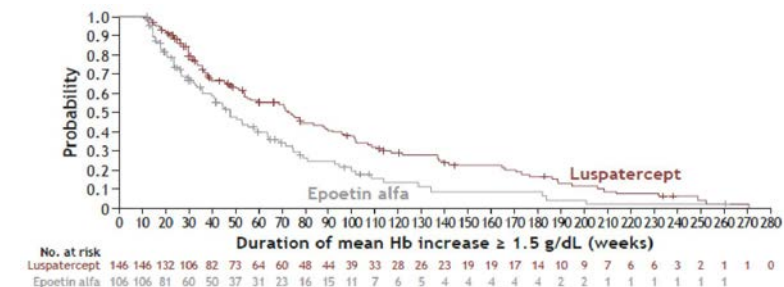
Secondary endpoints

- RBC-TI for ≥ 12 weeks (Weeks 1-24)
- Duration of RBC-TI ≥ 12 weeks
- OS
- Progression to AML
- Safety

Responses



	Luspatercept	Epoetin alfa	HR (95% CI) ^a
Median cumulative duration of RBC-TI ≥ 12 weeks, ^b weeks	184.4	95.1	0.537 (0.362-0.796); P = 0.0017 ^d

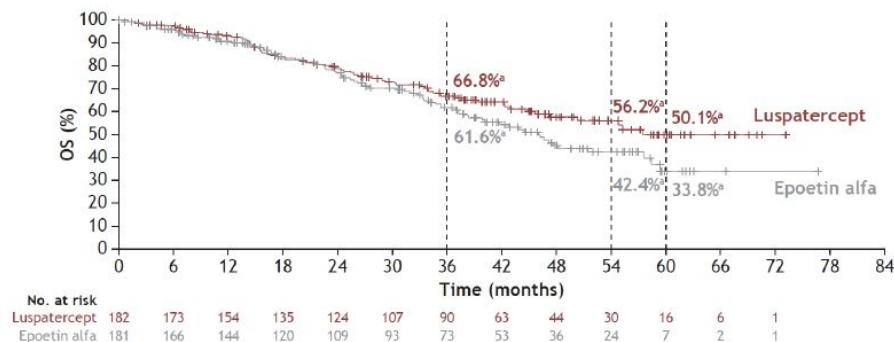


	Luspatercept	Epoetin alfa	HR (95% CI) ^a
Median duration of mean Hb increase ≥ 1.5 g/dL, ^b weeks	72.9	47.9	0.611 (0.441-0.845); P = 0.0027 ^d

OS in the ITT Population and Among Subgroups

- In the ITT population, the median OS was not reached in the luspatercept arm and 46.0 months in the epoetin alfa arm (HR, 0.781; 95% CI, 0.559-1.092; $P = 0.1485$)
- An exploratory subgroup analysis showed similar OS trends across baseline stratification subgroups

ITT population



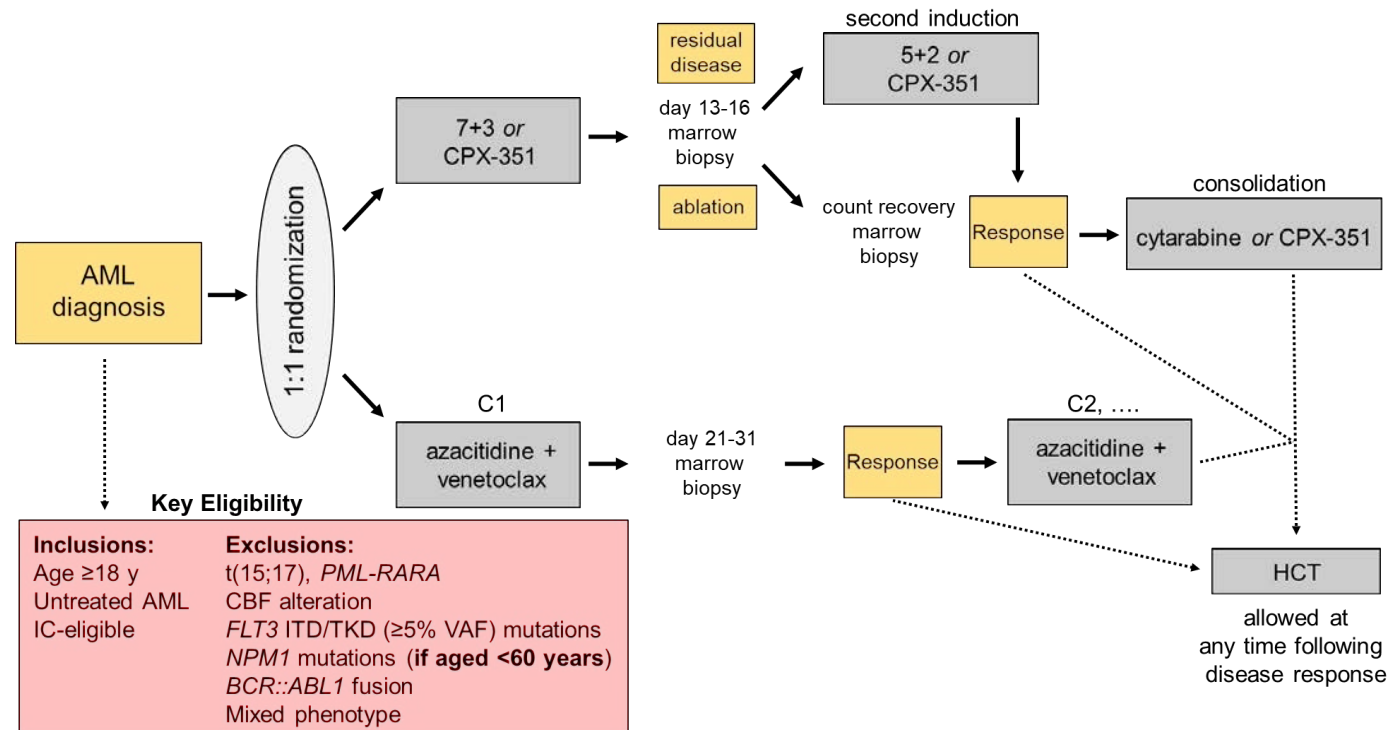
Subgroup analysis

	Luspatercept		Epoetin alfa		HR (95% CI) ^c
	Median OS, months ^b	Deaths, n/N (%)	Median OS, months ^b	Deaths, n/N (%)	
Overall (ITT)	NR	66/182 (36.3)	46.0	77/181 (42.5)	0.781 (0.559-1.092)
Baseline sEPO, U/L					
≤ 200	NR	51/145 (35.2)	51.4	53/144 (36.8)	0.814 (0.554-1.196)
> 200	43.0	15/37 (40.5)	35.4	24/37 (64.9)	0.669 (0.350-1.278)
Baseline TB, pRBC U/8 weeks					
< 4	57.5	43/118 (36.4)	47.2	41/111 (36.9)	0.870 (0.567-1.334)
≥ 4	NR	23/64 (35.9)	39.9	36/70 (51.4)	0.623 (0.369-1.054)
RS status					
Positive	NR	45/133 (33.8)	47.2	52/130 (40.0)	0.698 (0.468-1.040)
Negative	54.8	21/49 (42.9)	46.2	24/50 (48.0)	0.956 (0.531-1.723)

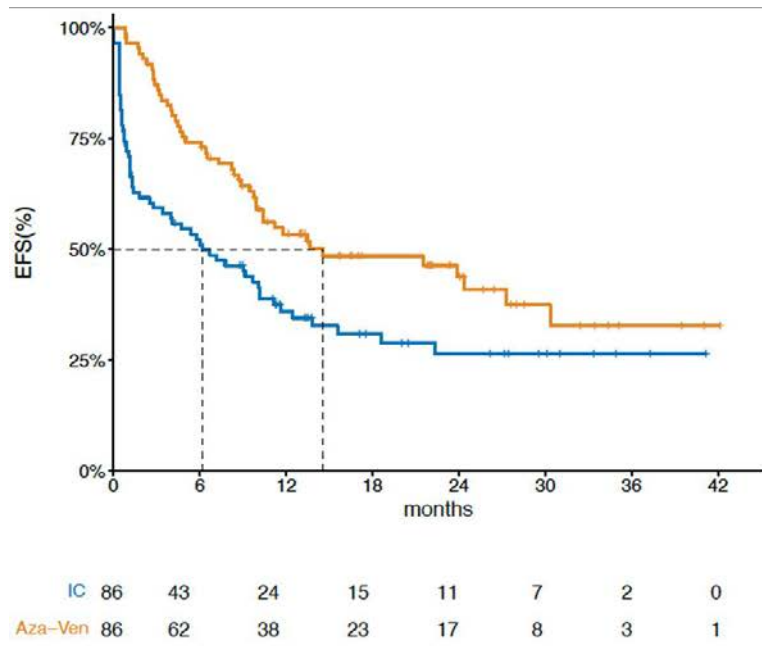
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Favors luspatercept Favors epoetin alfa

The PARADIGM Trial: Intensive Induction vs HMA/Venetoclax



The PARADIGM Trial: Intensive Induction vs HMA/Venetoclax



Moving Towards All-Oral Induction for AML: Decitabine-Cedazuridine + Venetoclax

C1
28-D cycle

Dosing

- Day 1: DEC-C + VEN 100 mg (ramp up)
- Day 2: DEC-C + VEN 200 mg (ramp up)
- Days 3–5: DEC-C + VEN 400 mg
- Days 6–28: VEN 400 mg

C_{≥2}
28-D cycle

Dosing

- Days 1–5: DEC-C + VEN 400 mg
- Days 6–28: VEN 400 mg

PK Studies (Cycle 2 only)

- Serial: Days 1, 2, 5, 15
- Pre-dose: Days 3, 6, 8, 12, 16

Continue treatment until disease progression, unacceptable toxicity, or patient is withdrawn from study

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

Characteristic	Phase 1 (N = 30)	Phase 2a (N = 58)	Phase 2b (N = 101)
Median age (range) — yr	78.0 (66–87)	75.0 (56–91)	78.0 (63–88)
Sex — no. (%)			
Male	16 (53)	33 (57)	61 (60)
Female	14 (47)	25 (43)	40 (40)
ECOG performance-status score — no. (%)†			
0	1 (3)	3 (5)	27 (27)
1	18 (60)	24 (41)	52 (51)
2	11 (37)	28 (48)	18 (18)
>2	0	3 (5)	3 (3)
Missing	0	0	1 (1)
Cytogenetic classification according to ELN 2017 criteria — no. (%)			
Favorable	0	2 (3)	1 (1)
Intermediate	23 (77)	40 (69)	66 (65)
Adverse	5 (17)	13 (22)	24 (24)
Test failed or missing	2 (7)	3 (5)	10 (10)
Mutation profiling according to sequencing — no. (%)‡			
TP53	NA	3 (5)	17 (17)
IDH1	NA	6 (10)	6 (6)
IDH2	NA	6 (10)	12 (12)
FLT3-ITD	NA	NA	11 (11)
KMT2A fusions	NA	2 (3)	0
NPM1	NA	8 (14)	13 (13)
KRAS	NA	3 (5)	12 (12)
NRAS	NA	6 (10)	11 (11)
NPM1/FLT3	NA	2 (3)	4 (4)
≥2 Reasons for ineligibility to receive intensive chemotherapy — no. (%)	NA	10 (17)	19 (19)

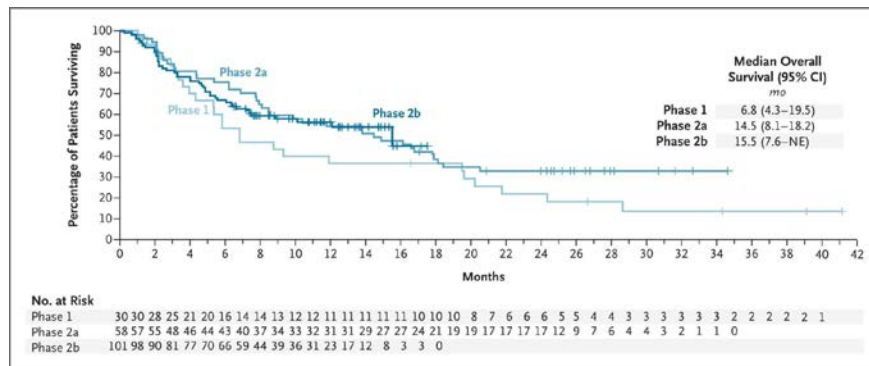
* Percentages may not total 100 owing to rounding. ELN denotes European LeukemiaNet, and NA not available.

† Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 5, with higher scores indicating greater disability.

‡ Sequencing was performed for 50 patients in phase 2a and 96 patients in phase 2b.

Efficacy of DEC-C + Venetoclax

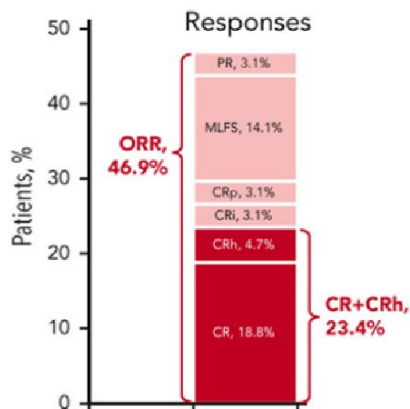
Variable	Phase 1 (N=30)	Phase 2a (N=58)	Phase 2b (N=101)
Complete response — % (95% CI)	40 (23–59)	38 (26–52)	47 (36–57)
Complete response with incomplete hematologic recovery — % (95% CI)	23 (10–42)	28 (17–41)	17 (10–26)
Complete response with partial hematologic recovery — % (95% CI)	17 (6–35)	21 (11–33)	5 (2–11)
Complete response or complete response with incomplete hematologic recovery — % (95% CI)	63 (44–80)	66 (52–78)	63 (53–73)
Complete response or complete response with partial hematologic recovery — % (95% CI)	57 (37–74)	59 (45–71)	51 (41–62)
Complete response, complete response with incomplete hematologic recovery, or complete response with partial hematologic recovery — % (95% CI)	63 (44–80)	66 (52–78)	63 (53–73)
Complete response that was sustained at 12 mo — % (95% CI)	75 (41–91)	71 (47–86)	75 (57–87)
Median time to complete response (range) — mo	1.9 (0.9–9.6)	2.4 (0.8–12.2)	2.4 (0.7–15.3)



Revumenib in NPM1m AML (R/R)

Adult Efficacy Results (n = 64)

- Almost half of all patients experienced a clinically meaningful response (ORR 47%), with 23% achieving a complete response (CR or CRh) across various subgroups.

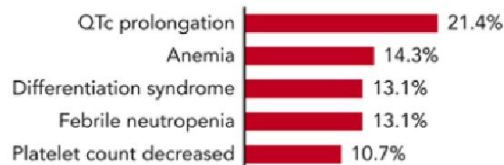


Selected subgroup	Patients, %	CR+CRh rate (95% CI), %
Overall	100.0	
Prior HSCT		
Yes	21.9	
No	78.1	
Number of prior lines of therapy		
1	25.0	
2	39.1	
≥3	35.9	
Prior venetoclax		
Yes	75.0	
No	25.0	
IDH1 status		
Wild type	62.5	
Mutant	12.5	
Not available	25.0	
IDH2 status		
Wild type	62.5	
Mutant	12.5	
Not available	25.0	
FLT3 status		
Wild type	48.4	
ITD	34.4	
TKD	6.3	
Not available	10.9	

Safety Results (N = 84)

- Fewer than 5% of treated patients discontinued due to a treatment-related adverse event

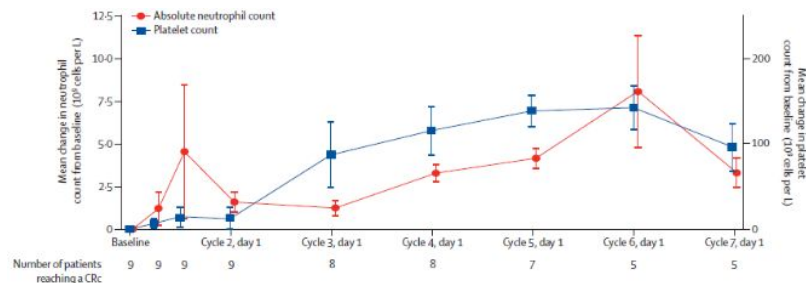
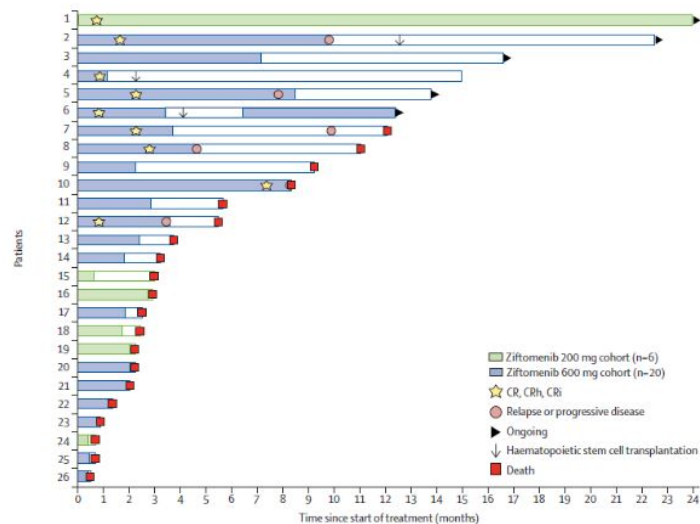
Most Common Grade ≥3 Treatment-Related AEs, %



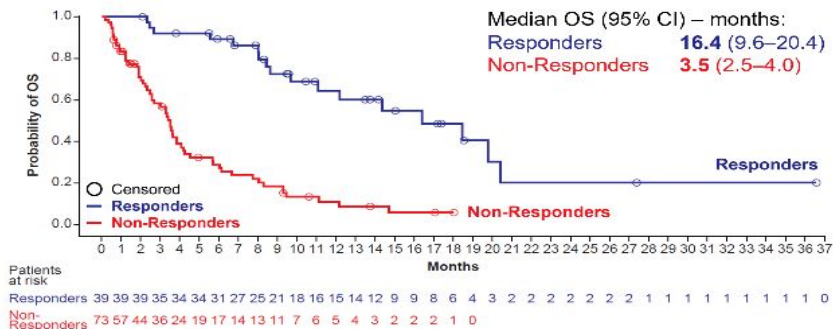
KOMET-001: Phase 1 Study of Ziftomenib in R/R *NPM1*-Mutated AML

Platelet and neutrophil counts in patients with *NPM1*-m reaching CRc response on ziftomenib

Outcomes of patients with *NPM1*-m AML treated with 200 mg or 600 mg ziftomenib across phase 1a and 1b



Overall Survival
Responders* vs. Non-Responders



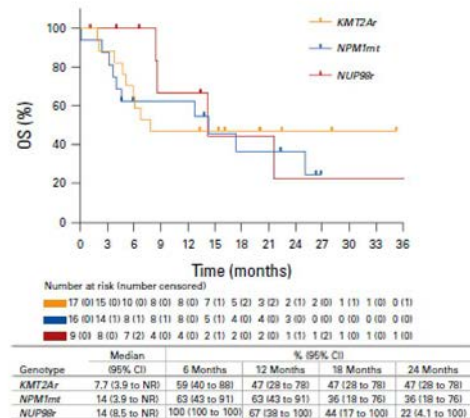
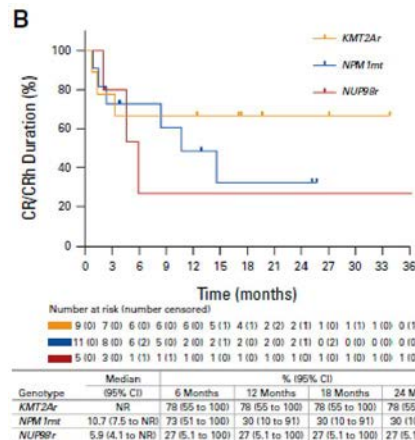
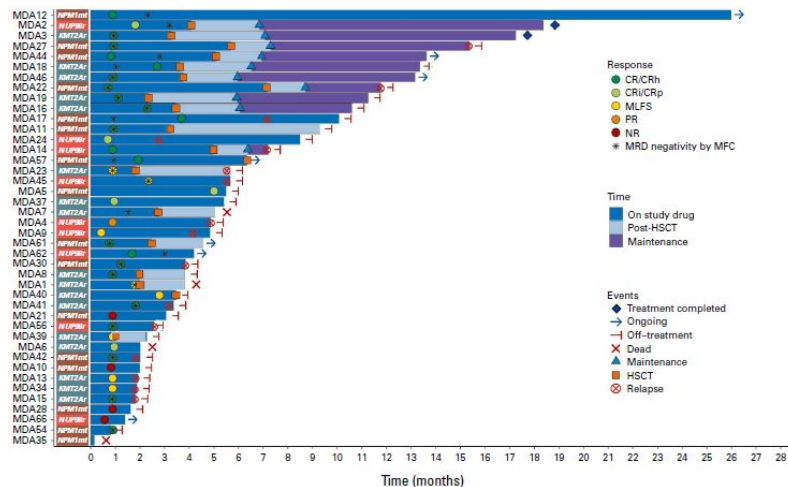
All-Oral Combination of Revumenib, Decitabine, Venetoclax (The SAVE Study)

Patients aged ≥ 12 yr with AML or myeloid MPAL and *NPM1mt*, *KMT2Ar*, or *NUP98r* AML or mixed phenotype acute leukemia;

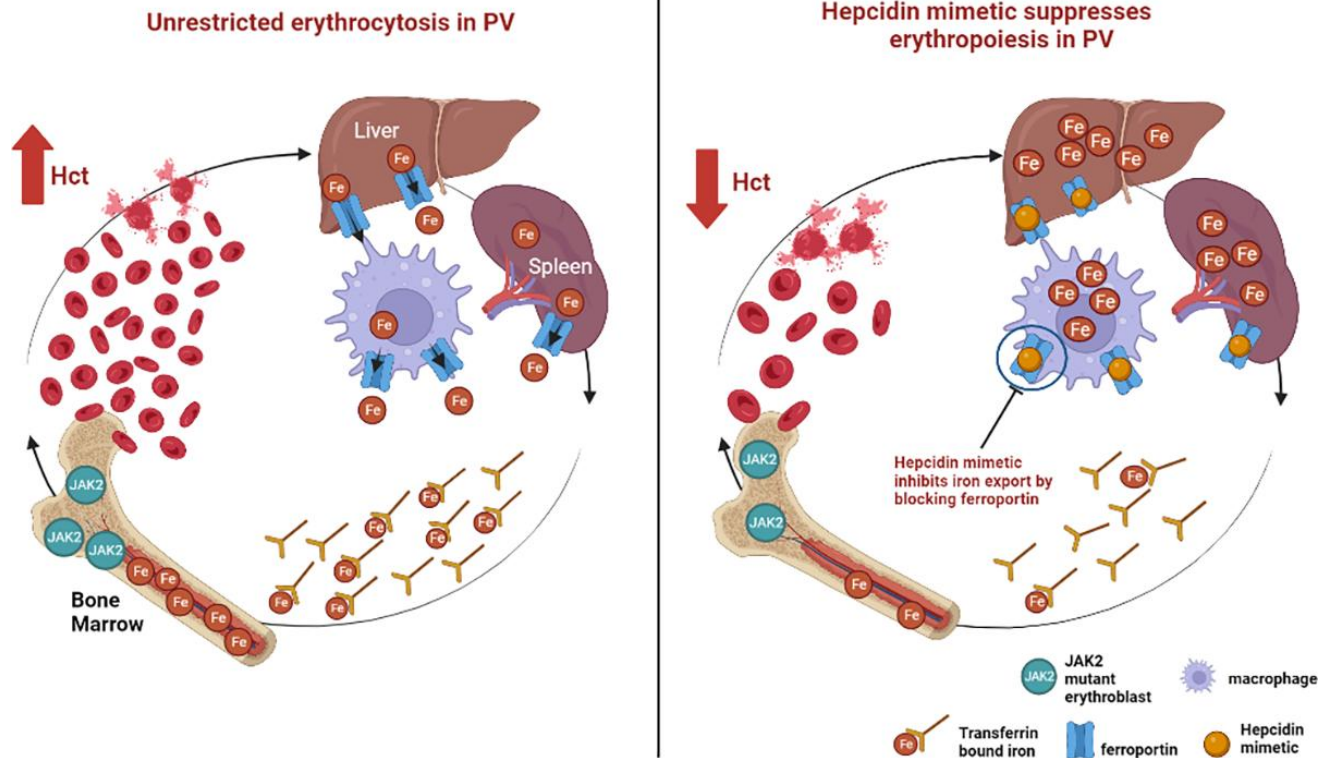
Revumenib (DL1) 270 mg without strong CYP3Ai
or 160 mg with strong CYP3Ai PO Q12h D1-28⁺

Decitabine/cedazuridine 35 mg/100 mg PO QD D1-5⁺

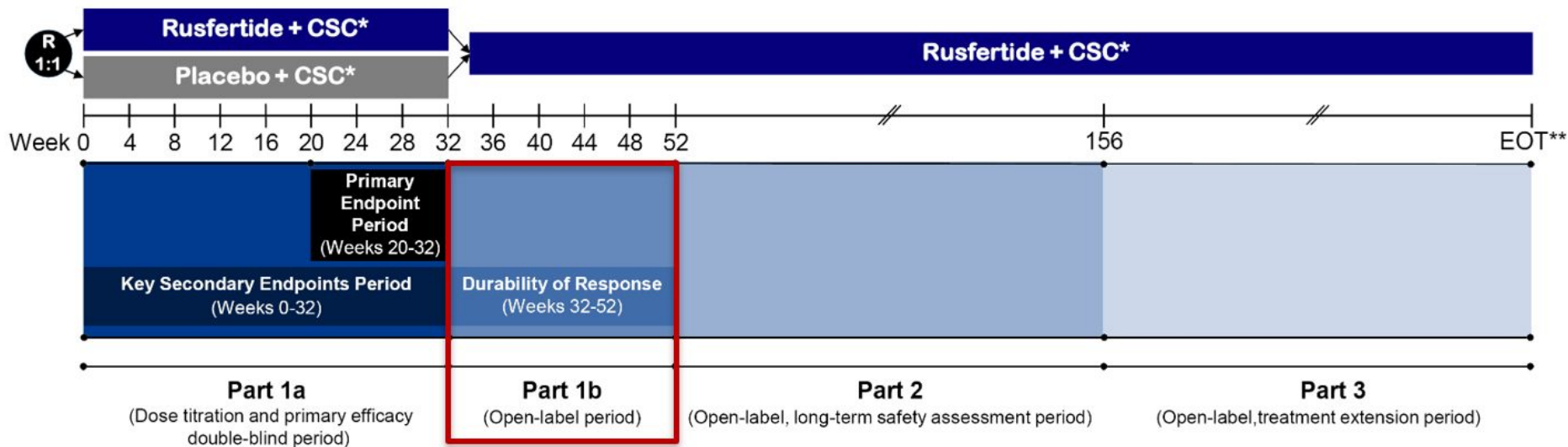
Venetoclax 400 mg (target dose with ramp up) PO QD D1-14⁺



Hepcidin Mimetics in Polycythemia Vera: The Next Frontier



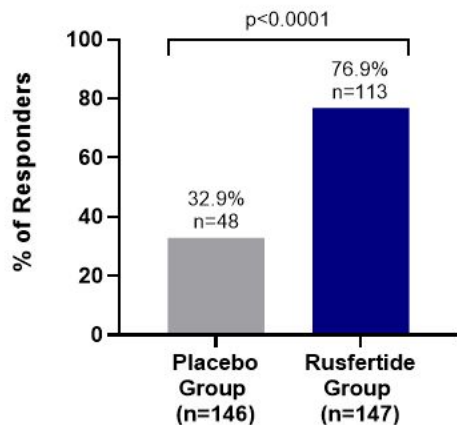
Phase 3 VERIFY Study Design



Fewer Phlebotomies, Better Quality of Life

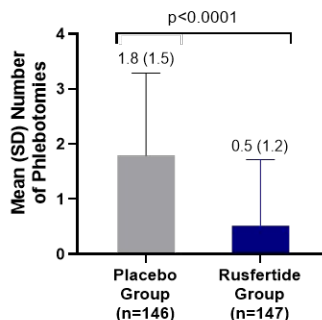
Primary Endpoint (Weeks 20-32)

More Responders With
Rusfertide vs Placebo

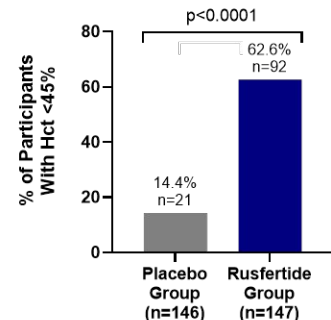


Key Secondary Endpoints 1 and 2 (Baseline to Week 32)

Fewer PHLs With
Rusfertide vs Placebo



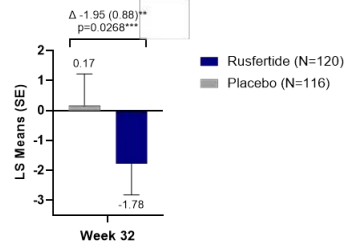
More Patients Maintained Hct
<45% With Rusfertide vs. Placebo



PRO-Focused Key Secondary Endpoints 3 and 4

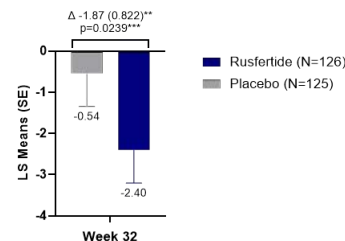
Improvement in PROMIS Fatigue SF-8a T-Score
With Rusfertide vs Placebo

LS Means Difference at Week 32:



Improvement in MFSaF TSS7
With Rusfertide vs Placebo

LS Means Difference at Week 32:



Conclusions

- Luspatercept should be considered the preferred frontline therapy for transfusion-dependent lower-risk MDS
- Lower intensity induction therapy with HMA + Venetoclax is appropriate for expanded groups of patients with AML
 - All oral HMA + Venetoclax regimens are become more standard as frontline therapy for older, less fit adults
- Combined menin inhibitor therapy appears highly efficacious in KMT2A rearranged and NPM1 mutant AML
- Hepcidin mimetics (Rusfertide) appears highly efficacious in PCV with strong potential for quality of life improvements as well