Aptose Biosciences

Precision oncology company developing tuspetinib to treat hematologic malignancies

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TSX: **APS**
OTC: **APTOF**

Tuspetinib in Frontline Triple Drug Therapy to Treat Newly Diagnosed AML

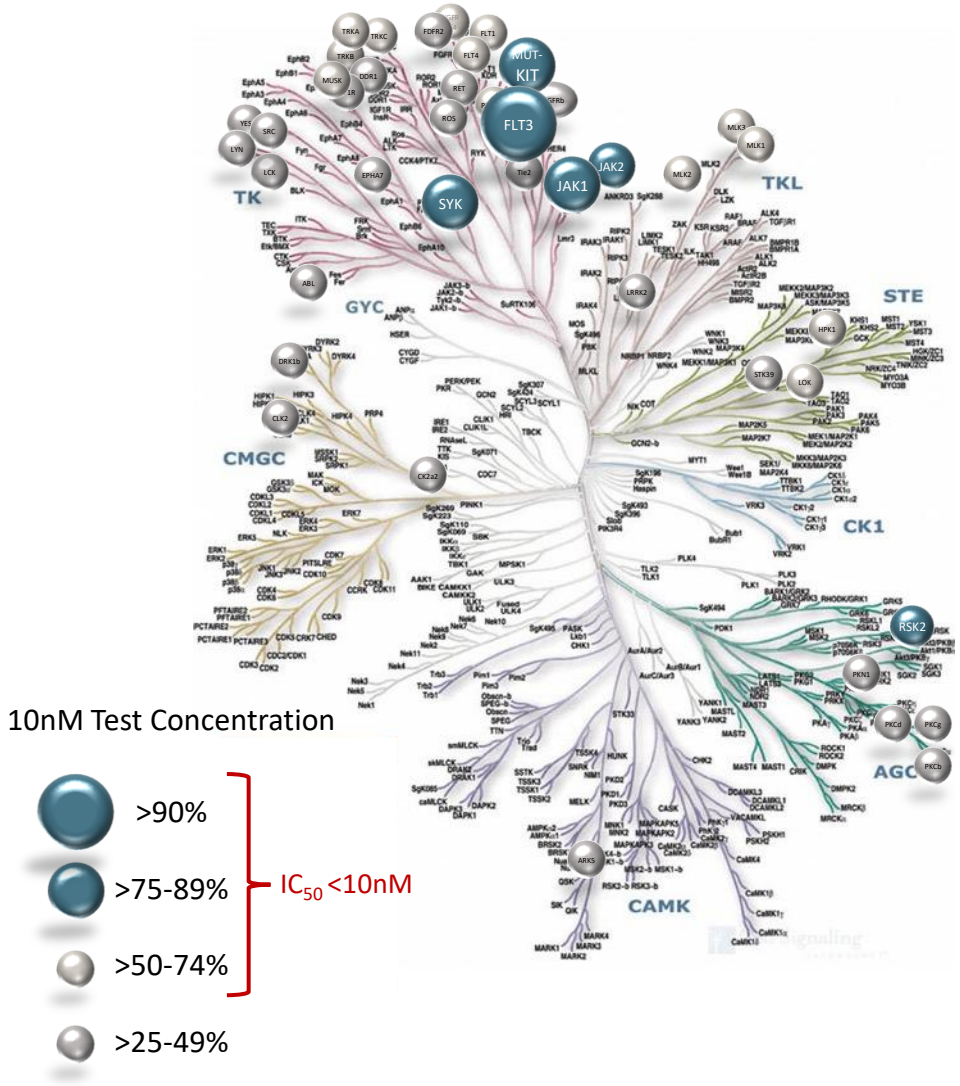
Creating a Safe and Mutation Agnostic Frontline Therapy for Newly Diagnosed AML

TUSCANY Trial Update

August 2025

Tuspetinib Kinase Inhibition Profile

Directly suppresses oncogenic signaling pathways: FLT3, SYK, KIT, JAK/STAT, RAS/MAPK/ERK
Leads to indirect inhibition of MCL-1 expression



Assay Methodology	Kinase	Mutation Status	Activity
Binding Affinity (K_D, nM)	FLT3	WT	0.58
		ITD	0.37
		D835Y	0.29
		D835H	0.4
		ITD/D835V	0.48
		ITD/F691L	1.3
Inhibition of Kinase Enzyme Activity (IC_{50}, nM)	FLT3	WT	1.1
		ITD	1.8
		D835Y	1.0
	SYK	WT	2.9
	JAK	JAK-1	2.8
		JAK-2	6.3
		JAK-2 (V617F)	9.9
	c-KIT	WT	> 500
		D816H	3.6
		D816V	3.5
	RSK	RSK-2	9.7
	TAK1-TAB1	TAK1-TAB1	7.0

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TUS+VEN+AZA Triplet in Newly Diagnosed AML Patients | TUSCANY Trial

TUSCANY Ph 1/2 study purpose is to select the optimal dose for Ph 2/3 pivotal studies

TUS Dose Level Selection for Triplet

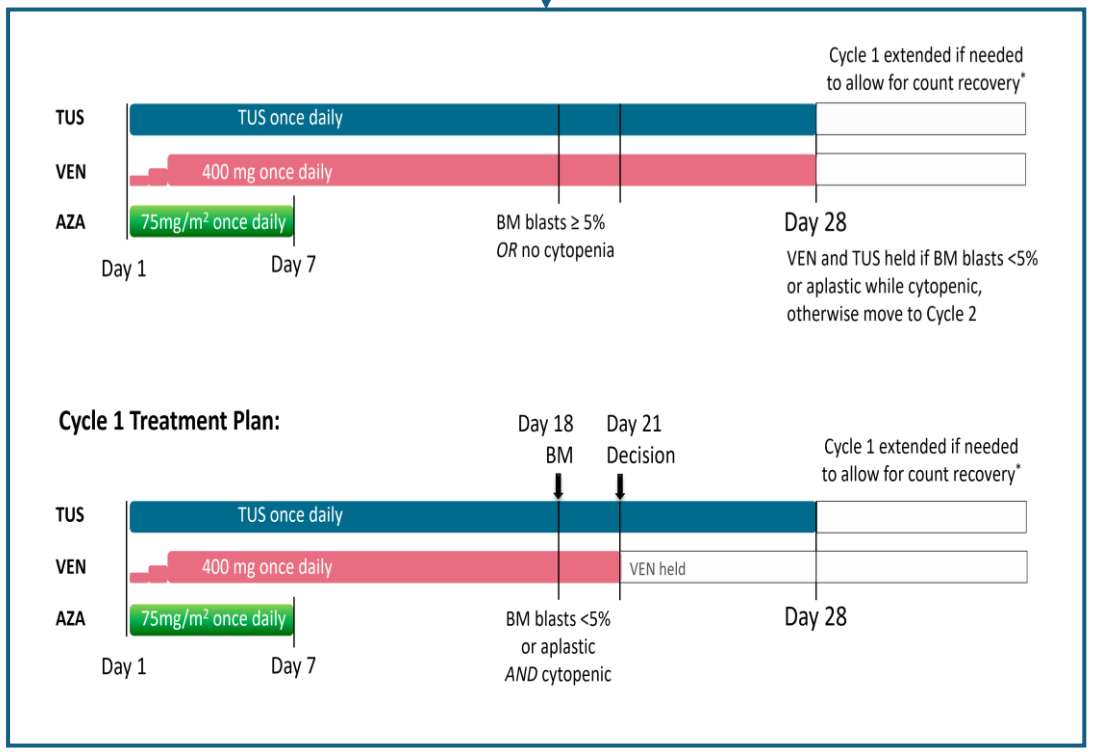
- 40mg = Initial Dose | Many/not all patients reach therapeutic exposure
- 80mg = Second Dose | Consistent therapeutic exposure
- 120mg = Third Dose | Increased therapeutic exposure
- 160mg = Fourth Dose | Increased therapeutic exposure

Study is Active at 10 Leading U.S. Clinical Sites

- Clinical Investigators are leading KOLs in AML
- Stanford, Yale, Univ. Miami, Moffitt, MDACC, others

Findings to Date with 40 mg, 80 mg, 120 mg TUS

- **No DLTs** (dose limiting toxicities) or safety concerns
- **CRs** (Complete Remissions) consistently achieved
  - Across patients from diverse genetic subpopulations
- **MRD-negativity*** consistently achieved
  - Across patients from diverse genetic subpopulations
  - **CR / MRD-** correlates with durability and longer survival



* MRD refers to the amount of Measurable Residual Disease by central flow cytometry to measure the number of leukemic cells of bone marrow or blood < 0.1%

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Developing VEN+AZA+TUS Triplet in Newly Diagnosed AML

FDA requires **CR/CRh** complete responses and **overall survival** for approval of AML drug

- **VEN+AZA** achieves a **65% CR/CRh** response rate — ***Triplet target | 75-80% for new approval @ optimal dose***
  - Among CR/CRh pts, 41% become MRD-negative*
- **VEN+AZA** achieves survival of **14.7 months** — ***Triplet target | Improved survival @ optimal dose***
- **VEN+AZA** has **multiple safety issues** — ***Triplet target | Well tolerated @ optimal dose***
- **VEN+AZA** fails **TP53-mutated patients** — ***Triplet target | Treat TP53-mutated patients***
  - Among $TP53^{MUT}$ CR/CRh pts, 30% become MRD-negative

The Bar to Beat for VEN+AZA+TUS in the TUSCANY Trial

- Relative to **VEN+AZA** SOC, **VEN+AZA+TUS** seeks to improve CR/CRh rates, improve MRD-negativity* rates, improve mOS survival, and show acceptable safety across the spectrum of AML
- Improvement of CR/CRh rates and survival in TP53-mutated AML would be a remarkable achievement

* MRD refers to the amount of Measurable Residual Disease by central flow cytometry to measure the number of leukemic cells of bone marrow or blood < 0.1%

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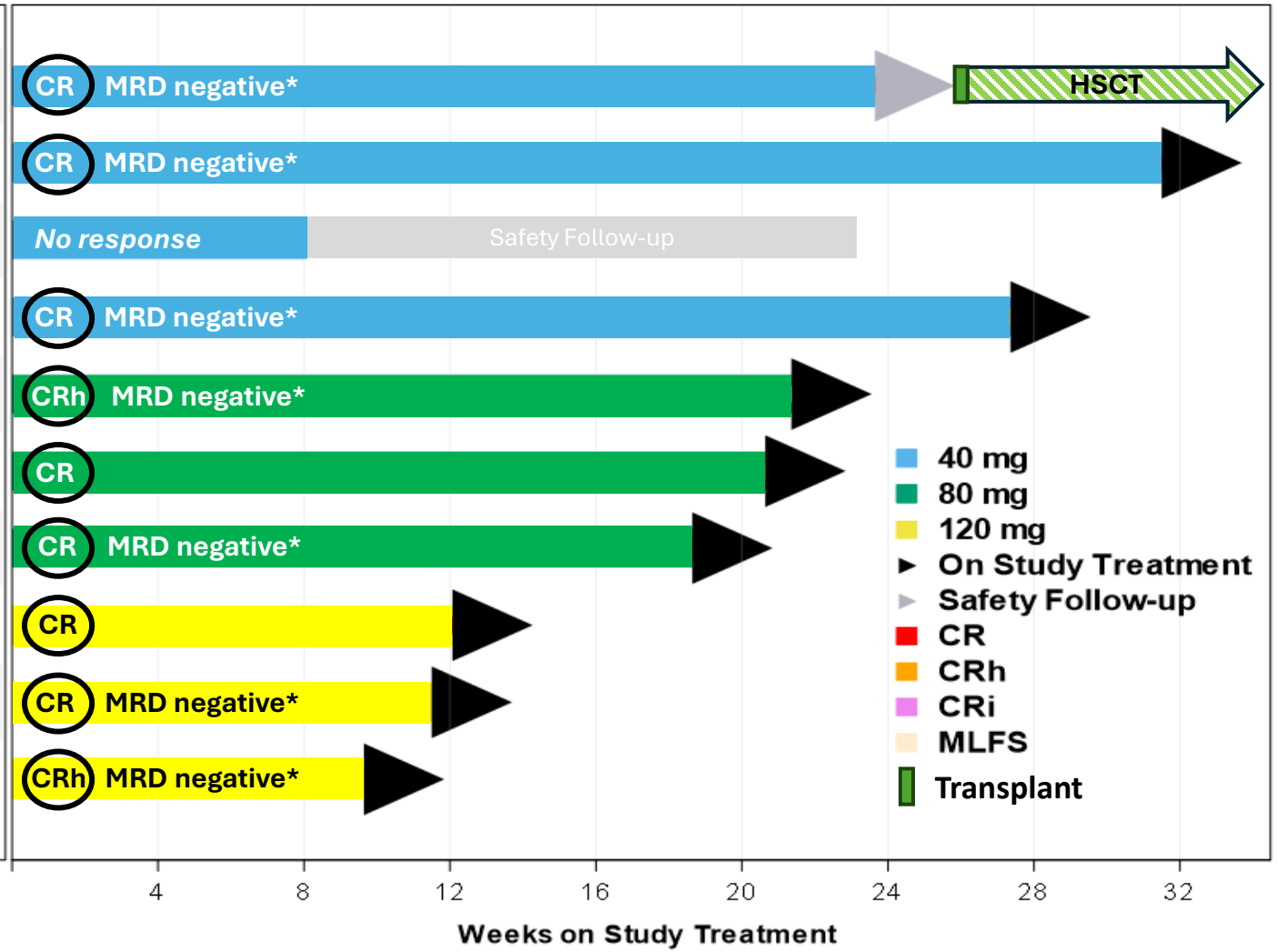
Study Status by Weeks on Treatment

Dose (mg)	FLT3 Status	Other Mutations	Sex/ Age
40/400/75	WT	IDH2/ASXL1/SRSF2/STAG2	M/74
40/400/75	WT	TP53/CK	F/80
40/400/75	WT	IDH2/RUNX1/BCOR/SRSF2	M/78
40/400/75	ITD	NPM1	F/69
80/400/75	WT	TP53/CK	F/78
80/400/75	WT	ASXL1/DDX41/CBFA2T3/IL2RB	F/81
80/400/75	ITD	NPM1/TET2	F/69
120/400/75	WT	ASXL1	M/77
120/400/75	WT	RUNX1/SRSF2/TET2	M/70
120/400/75	WT	RAS/KIT	F/79



Data from TUSCANY Trial as of August 14, 2025

* MRD by central flow cytometry of bone marrow or blood < 0.1%

CK – complex karyotype; WT – wild type; ITD – internal tandem duplication

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Excellent Early Data from the First 10 Pts to Receive VEN+AZA+TUS

- **Doses of TUS to be Administered with VEN+AZA (current SOC therapy) in the TUSCANY Trial**
  - 80 mg, 120 mg, and 160 mg TUS consistently deliver the required blood levels of TUS for responses
  - FDA requires testing begin with lower dose of 40 mg before escalating to 80 mg, 120 mg, and 160 mg
- **TUSCANY Trial of VEN+AZA+TUS** As of August 14, 2025
  - 40 mg : Initial Dose Level Set by FDA
    - 4 pts dosed | 3 CR | 3 MRD-negative | 1 advanced to HSCT
    - 1 pt did not achieve required TUS exposure levels of TUS and did not respond to therapy
  - **80 mg Dose Level**
    - 3 pts dosed | 2 CR &1 CRh | 2 MRD-negative | 100% CR/CRh rate
  - **120 mg Dose Level**
    - 3 pts dosed | 2 CR & 1 CRh | 2 MRD-negative | 100% CR/CRh rate
- ***Broad-Spectrum Efficacy* and *Excellent Safety* with No DLT to Date**
  - CR/CRh achieved across diverse genetic populations | FLT3-mut/WT, NPM1-mut, NRAS-mut, TP53-mut, others

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Addition of TUS to VEN+AZA Increases Activity Across AML Mutation Subgroups

TUSCANY **VEN+AZA+TUS** Data of **CR/CRh** Complete Responses to Date in 10 Patients Dosed at 40 mg, 80 mg or 120 mg TUS

Patient Population	Response Rates	
	CR/CRi of VEN+AZA[1]	CR/CRh of VEN+AZA+TUS[2]
All subjects	66% (n = 587 pts)	90% (9/10)
NPM1-mut	78%	100% (2/2)
FLT3-ITD	61%	100% (2/2)
TP53-mut or CK	52%	100% (2/2)
All Responders	-	100% (9/9)

100% (6/6) **CR/CRh at Optimal Dose Levels** (80mg & 120mg)

70% (7/10) **MRD-Negative[3] Among All Patients Dosed**

100% (5/5) **CR/CRh & MRD-Negative of $TP53^{MUT}$, $FLT3^{MUT}$, RAS^{MUT}**

78% (7/9) **MRD-Negative Among All CR/CRh Responders**

[1] DiNardo et al. *New England Journal of Medicine*, August 2020; Volume 383(7):617-629.
Pratz et al. *Journal of Clinical Oncology*, December 2021; Volume 40 (8):855-865.
Othman et. al. *Blood Neoplasia*; September 2024; Volume 1 (3):1-11.
Döhner *Blood*. 2024 Nov 21;144(21):2211-2222.

[2] Including 40 mg, 80 mg, and 120 mg dose levels of TUS as of August 14, 2025
[3] MRD by central flow cytometry of bone marrow or blood < 0.1%

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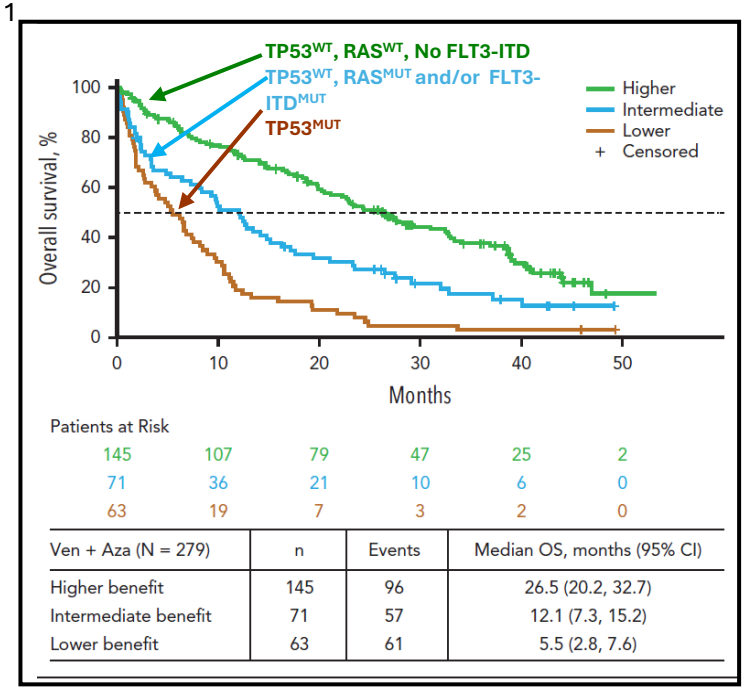
Addition of TUS to VEN+AZA Improves CR Rates Across AML Subgroups

Addition of TUS to VEN+AZA improves CR rates across Higher, Intermediate, and Lower Benefit subgroups

Patient Benefit Subgroup	[1] VEN+AZA CR rate	[2] VEN+AZA+TUS CR rate
Higher Benefit	48.3%	80% (4/5)
Intermediate Benefit	38.0%	67% (2/3)
Lower Benefit	22.2%	50% (1/2)

[1]

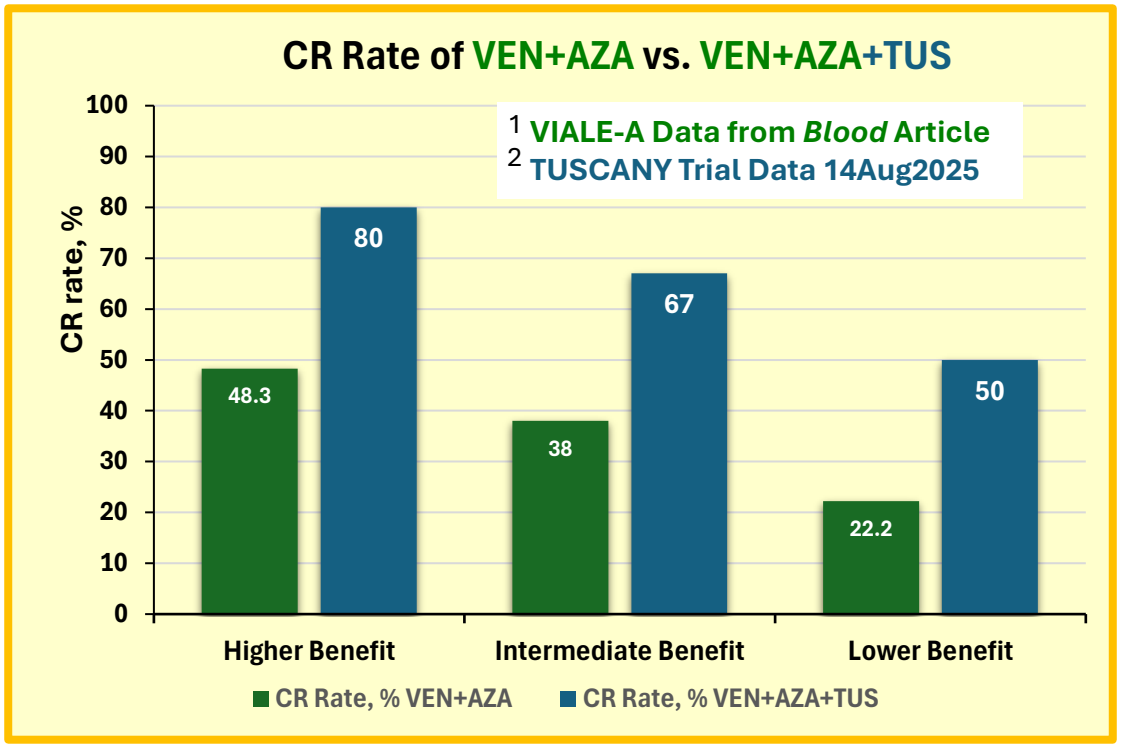


Patients at Risk

145	107	79	47	25	2
71	36	21	10	6	0
63	19	7	3	2	0

Ven + Aza (N = 279)	n	Events	Median OS, months (95% CI)
Higher benefit	145	96	26.5 (20.2, 32.7)
Intermediate benefit	71	57	12.1 (7.3, 15.2)
Lower benefit	63	61	5.5 (2.8, 7.6)

- Three benefit subgroups first based on OS and then associated with discriminating genes (TP53, N/K-RAS, FLT3-ITD)
- More NPM1, MDS-associated, RUNX1, and IDH mutation in Higher and Intermediate benefit subgroups



[1] Döhner *Blood*. 2024 Nov 21;144(21):2211-2222.

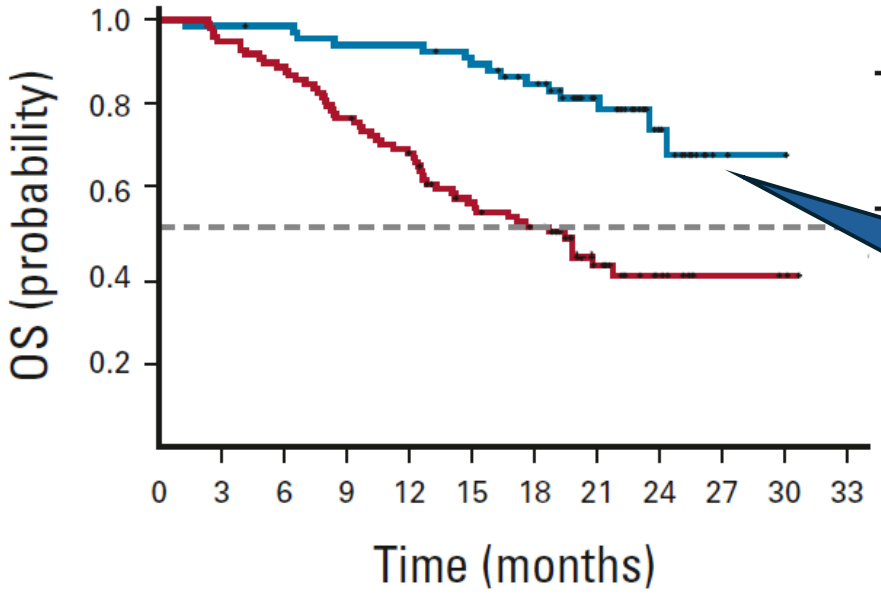
[2] Data from TUSCANY Trial as of August 14, 2025

Achieving MRD-Negativity is Critically Important

MRD-negativity correlates with extended OS, DoR and EFS

Journal of Clinical Oncology®
Volume 40, Issue 8 **855**

Measurable Residual Disease Response and Prognosis in Treatment-Naïve Acute Myeloid Leukemia With Venetoclax and Azacitidine



No. at risk:

CR + CRi + MRD < 10^{-3}	67	66	65	62	62	58	52	30	13	2	1	0
CR + CRi + MRD ≥ 10^{-3}	97	92	86	74	64	49	42	21	10	3	2	0

OS	No. of Events	12 Months, % (95% CI)	18 Months, % (95% CI)	Median OS, Months (95% CI)
CR + CRi + MRD < 10^{-3}	15	94.0 (84.7 to 97.7)	84.6 (73.3 to 91.4)	NR (24.4 to NR)
CR + CRi + MRD ≥ 10^{-3}	52	67.9 (57.6 to 76.2)	50.1 (39.6 to 59.8)	18.7 (12.9 to NR)

Achieving MRD-negativity extends Overall Survival

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Comparing MRD-Negativity of VEN+AZA+TUS to VEN+AZA (VIALE-A)

Addition of TUS to VEN+AZA improves MRD-negativity* rates – Data from TUSCANY Trial

[1] Measurable Residual Disease Response and Prognosis in Treatment-Naïve Acute Myeloid Leukemia With Venetoclax and Azacitidine

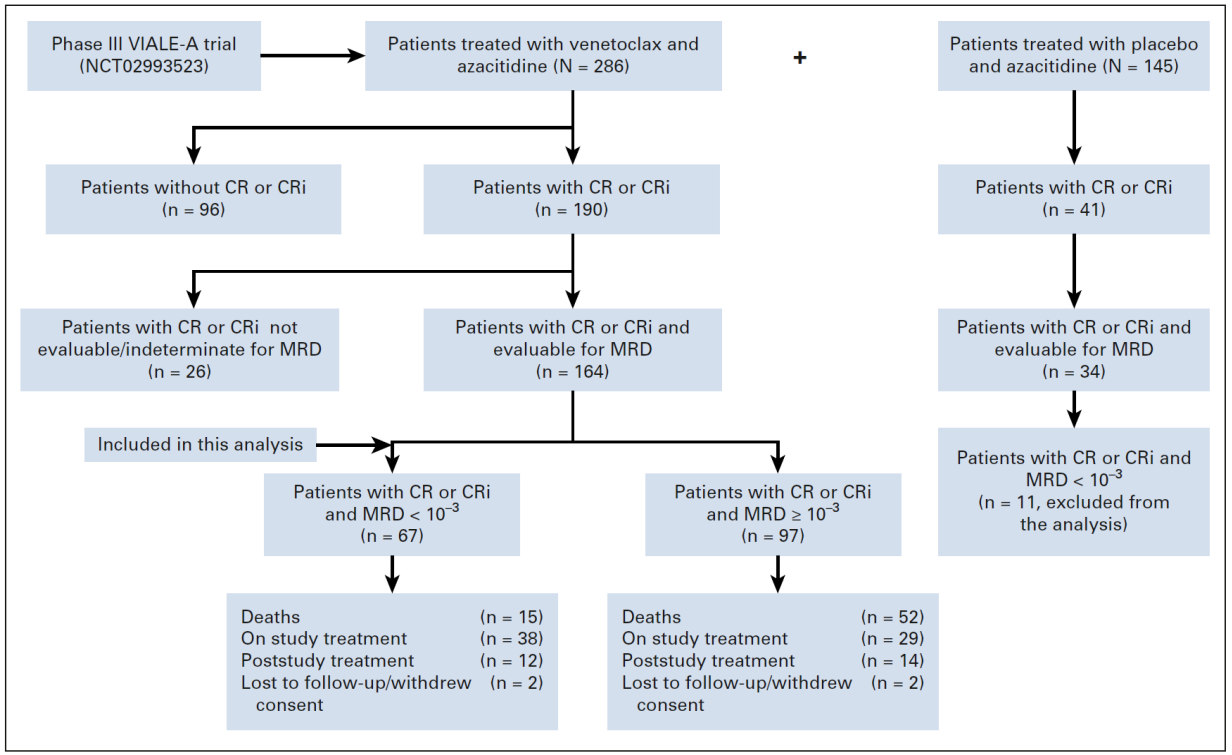
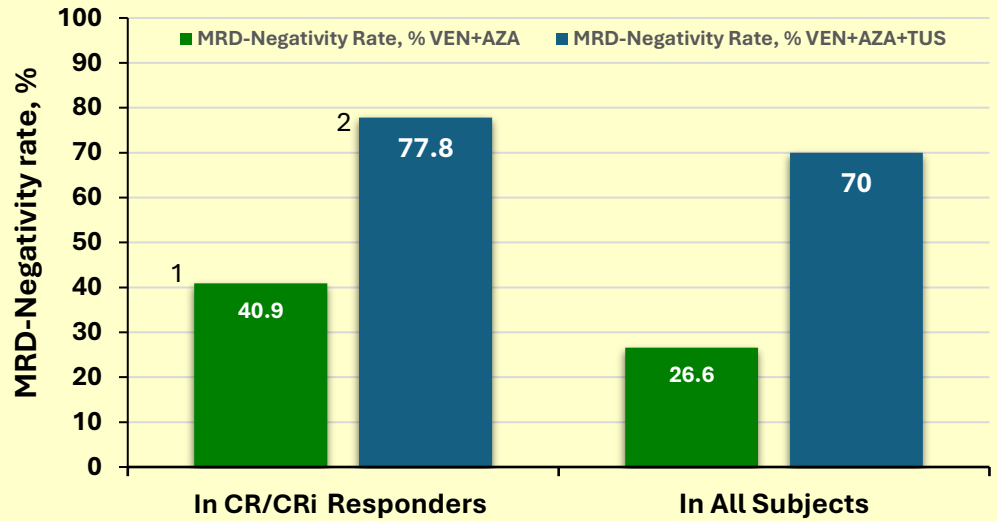


FIG 1. Profile of patients. CR, complete remission; CRi, complete remission with incomplete marrow recovery; MRD, measurable residual disease.



MRD-Negativity Rate < 0.1%

	[1] VEN+AZA	[2] VEN+AZA+TUS
In CR/CRi Responders:	40.9%	77.8%
In all subjects:	23.4%	70%

* MRD by central flow cytometry of bone marrow or blood < 0.1%

[1] Pratz et al. *Journal of Clinical Oncology*, December 2021; Volume 40 (8):855-865.

[2] Data from TUSCANY Trial as of August 14, 2025

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Addition of TUS to VEN+AZA Improves MRD-Negativity Rates in Lower Benefit Patients

Lower Benefit AML patients harbor mutated *TP53* gene

Lower Benefit patients have poor MRD-negativity rates with VEN+AZA [1]

Addition of TUS to VEN+AZA improves MRD-negativity rates in Lower Benefit patients

[1]

MRD response, n/N (%)	Pbo + Aza	VEN+AZA
Higher benefit	6/64 (9.4)	48/145 (33.1)
Intermediate benefit	5/27 (18.5)	19/68 (27.9)
Lower benefit	0/21 (0)	**9/62 (14.5%)**

Supplemental Table 2. MRD response rates (MRD <0.1% and CR + CRi) in patients treated with venetoclax-azacitidine or placebo-azacitidine in the higher-, intermediate-, and lower-benefit groups.

Aza, azacitidine; CR, complete remission; CRi, CR with incomplete count recovery; MRD, minimal residual disease; Pbo, placebo; Ven, venetoclax.

Bone marrow aspirate samples for MRD assessment were collected at baseline, end of cycle 1, and every 3 cycles thereafter.

- Three benefit subgroups first based on OS and then associated with discriminating genes (TP53, N/K-RAS, FLT3-ITD)
- More NPM1, MDS-associated, RUNX1, and IDH mutation in Higher and Intermediate benefit subgroups

[2]

VEN+AZA+TUS[2]
2/4 (50%)
3/3 (100%)
2/2 (100%)

[2] Data from TUSCANY Trial (CR/CRh) as of August 14, 2025

[1] Döhner *Blood*. 2024 Nov 21;144(21):2211-2222.

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[1]TUSCANY Trial Summary: VEN+AZA+TUS Triplet in Newly Diagnosed AML

Excellent Data in 10 Patients Dosed at 40 mg, 80 mg, 120 mg TUS

- **Addition of TUS improves CR/CRh rates**
  - **100% CR/CRh** response rate at 80 mg and 120 mg dose levels
  - **Appear to be achieving CR earlier with 120 mg** than with 40 mg or 80 mg
- **Addition of TUS improves MRD-negativity rates … and expected survival by correlation**
  - **MRD-negativity in 7 of 9 (78%)** already achieved in patients who responded to therapy
  - **Expect patient survival to be extended** with continued long-term treatment
- **Excellent safety** and well tolerated with no dose-limiting toxicities (No DLT)
- **Broad-spectrum activity** including two patients with highly adverse biallelic *TP53* mutations
- **Expect to maintain SOC VEN/AZA dosing** for longer periods of time

[1] Data from TUSCANY Trial as of August 14, 2025

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Next Steps: CSRC Held July 22, 2025 to Review TUSCANY Trial Findings

VEN+AZA+TUS (120 mg Tuspetinib / 400 mg Venetoclax / 75 mg/m2 Azacitidine)

- **Safety**
  - No additional safety concerns emerged with 120 mg TUS – No DLT
  - See no trend of increased safety concerns as increase dose from 40 to 80 to 120 mg
- **PK**
  - Increasing the dose of TUS increases the TUS exposure overall
  - With VEN and AZA combined dosing there is no increase in TUS exposure
  - There does not appear to be any significant interaction with TUS due to VEN and AZA
  - TUS does not appear to change the exposure of VEN in any clinically meaningful way
- **Recommendations**
  - Open Cohort for dose escalation to 160 mg TUS to enroll three (3) new subjects, THEN
  - Expand two appropriate Cohorts to 10 subject each to select doses for randomized Ph2
- **Dose Escalated to 160 mg TUS and Patients Enrollment Open**

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Thank You

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