KURA ONCOLOGY

DEVELOPING PRECISION MEDICINES FOR THE TREATMENT OF CANCER

ASH Investor Event – December 9, 2024

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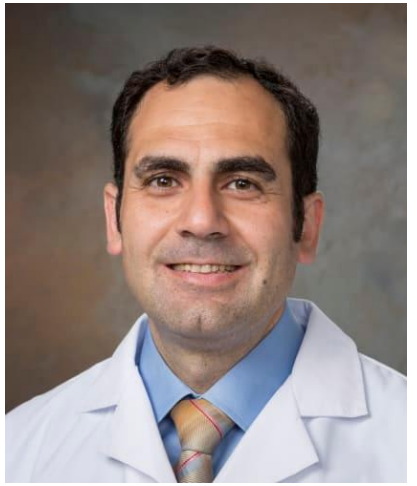
KOMET-007 Investigators

Amir Fathi, M.D.

- Program Director, Center for Leukemia, Massachusetts General Hospital Cancer Center
- Associate Professor of Medicine, Harvard Medical School



Amer Zeidan, MBBS

- Chief, Division of Hematologic Malignancies, Director of Hematology Early Therapeutics Research, Yale Cancer Center
- Associate Professor of Medicine (Hematology), Yale University

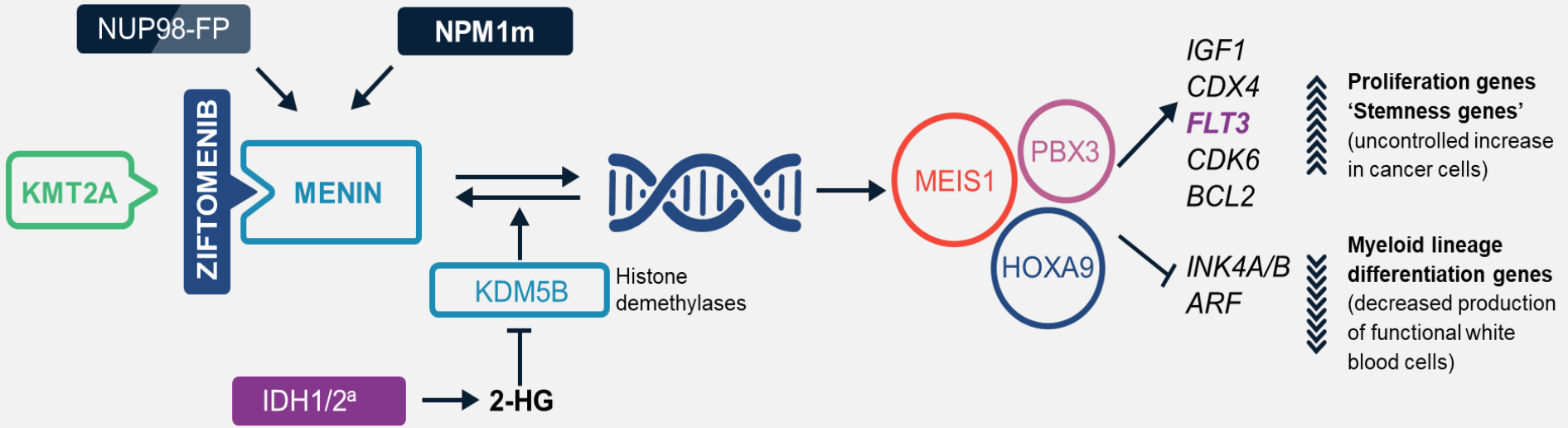
ZIFTOMENIB IN RELAPSED/REFRACTORY AML

Amir Fathi, M.D. – Massachusetts General Hospital

Ziftomenib Targets the Menin Pathway, a Foundational Target in AML

- In ~35–40% of AML, leukemogenesis is driven by either *NPM1* mutations or *KMT2A* rearrangements,[1,2] which are upstream regulators of key genes critical for AML (eg, *HOXA9/MEIS1*)[3]
- KMT2A (MLL) and NPM1 sit upstream from major AML targets (ie, FLT3, BCL2 and IDH1/2)[4]
- Inhibiting the menin-KMT2A complex downregulates *HOXA9/MEIS1*, leading to differentiation of leukemic blasts[5]
- Ziftomenib – a potent, highly selective, oral investigational menin inhibitor – has shown clinical activity (35% CR/CRh) as monotherapy in adults with relapsed/refractory *NPM1*-m AML[6]

Ziftomenib Mechanism of Action[3, 7-14]



[a]Mutations in AML are loss of function. 1. Papaemmanuil et al. *N Engl J Med* 2016; 375: 900-1; 2. Issa GC et al. *Leukemia* 2021;3:2482-95; 3. Collins and Hess. *Curr Opin Hematol* 2016;23(4)354-61; 4. Matthews AH et al. *Cancers* (Basel) 2022 Nov 29;14(23):5906. 5. Thomas. *Oncol Ther* 2024;12(1):57-72; 6. Wang ES et al. *Lancet Oncol* 2024; 25(10):1310-24; 7. Lu et al. *Cancer Cell* 2016;30(1):92–107; 8. Ferreira et al. *Oncogene* 2016;35(23):3079-82; 9. Jeong et al. *Nat Genet* 2014;46(1):17-23; 10. Wang et al. *Blood* 2005;106(1):254–64; 11. Chowdhury et al. *EMBO Rep* 2011;12(5):463-9; 12. Schmidt et al. *Leukemia* 2019;33(7):1608-19; 13. Xu et al. *Cancer Cell* 2016;30(6):863-78; 14. Brunetti et al. *Cancer Cell* 2018; 34(3):499–512.

KOMET-001: Phase 1/2 Study of Ziftomenib in R/R AML

komet-001
ACUTE LEUKEMIAS
KURA KO-MEN-001

Phase 1a Dose Escalation	Phase 1b Validation Cohorts	Phase 1b Expansion	Phase 2 Registration-Enabling
Completed	*Completed*	*Completed*	*Enrollment Completed*
50 mg QD — 100 mg QD — 1000 mg QD	Cohort 1: 200 mg QD Cohort 2: 600 mg QD	Expansion of 600 mg QD	600 mg QD
NPM1-m, *KMT2A*-r, Other	*NPM1*-m or *KMT2A*-r	*NPM1*-m	*NPM1*-m

OBJECTIVES

- Safety and tolerability
- Pharmacokinetics
- Early evidence of antitumor activity

- Safety and tolerability
- Pharmacokinetics
- Clinical activity

Continue enrollment of Phase 1b validation cohort(s) consistent with FDA's Project Optimus

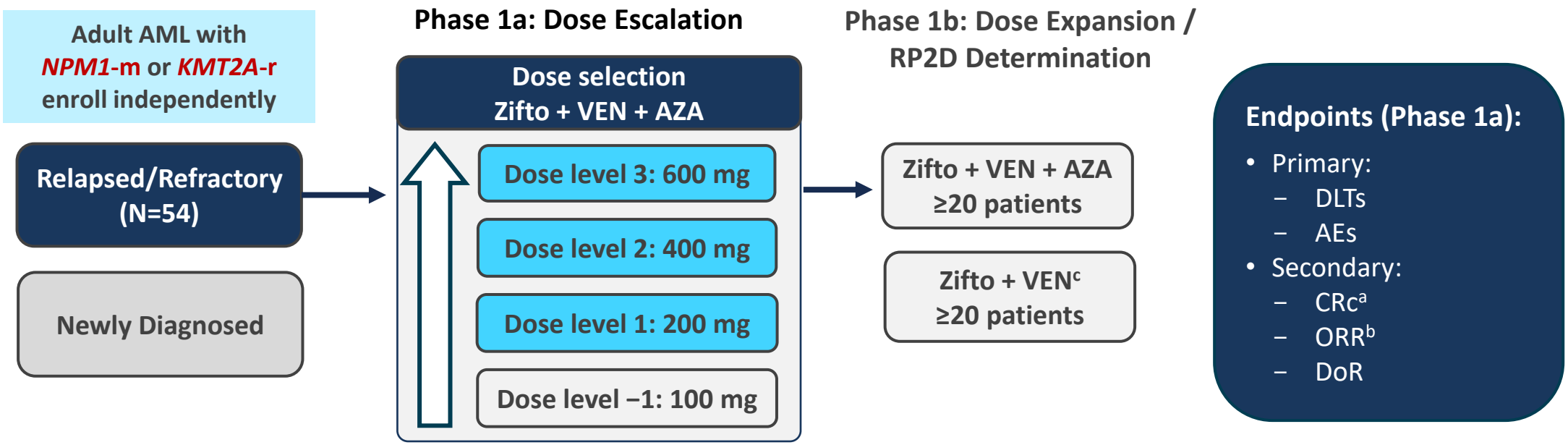
- Safety and tolerability
- Pharmacokinetics
- Clinical activity

- Primary endpoint:
  - CR/CRh
- Secondary endpoints:
  - Duration of CR/CRh
  - Transfusion independence
  - CR/CRh MRD negativity
  - Adverse events

CR, complete remission; CRh, complete remission with partial hematological recovery; FDA, United States Food and Drug Administration; MRD, measurable residual disease; R/R, relapsed/refractory; RP2D, recommended phase 2 dose.

KOMET-007: Phase 1 Combination Study of Ziftomenib in R/R AML

Ziftomenib / Venetoclax / Azacitidine Combination (NCT05735184)



- Ziftomenib started on Cycle 1 Day 8 and was administered continuously thereafter
- Venetoclax administered per label in 28-day cycles; adjustments to cycle length based on Cycle 1 bone marrow biopsy results
- Azacitidine administered per label on Cycle 1 Days 1–7; additional cycles based on bone marrow biopsy results

[a]CR, CRh, or CRi; [b]CRc or MLFS; [c]Zifto + VEN only for *NPM1*-m patients

Baseline Patient Characteristics: R/R AML

	All Patients N=54[a]	*NPM1*-m				*KMT2A*-r			
		200 mg n=7	400 mg n=7	600 mg n=12	Total n=26	200 mg n=11	400 mg n=9	600 mg n=7	Total n=28[a]
Median age, years (range)	59 (22–86)	55 (41–77)	71 (45–86)	68 (34–76)	69 (34–86)	53 (23–71)	45 (32–69)	65 (22–72)	53 (22–72)
Female, n (%)	30 (56)	4 (57)	3 (43)	8 (67)	15 (58)	6 (55)	4 (44)	4 (57)	15 (54)
Race, n (%)									
White	27 (50)	5 (71)	5 (71)	4 (33)	14 (54)	5 (45)	4 (44)	4 (57)	13 (46)
Black/African American	10 (19)	0	0	3 (25)	3 (12)	2 (18)	4 (44)	0	7 (25)
Other/not recorded	17 (31)	2 (29)	2 (29)	5 (42)	9 (35)	4 (36)	5 (56)	3 (43)	8 (29)
ECOG PS, n (%)									
1	30 (56)	5 (71)	4 (57)	5 (42)	14 (54)	7 (64)	5 (56)	4 (57)	16 (57)
2	11 (20)	1 (14)	0	4 (33)	5 (19)	2 (18)	1 (11)	2 (29)	6 (21)
Co-mutations, n (%)	37 (69)	5 (71)	5 (71)	9 (75)	19 (73)	6 (55)	3 (33)	3 (43)	12 (43)
FLT3	19 (35)	2 (29)	2 (29)	7 (58)	11 (42)	1 (9)	0	1 (14)	2 (7)
IDH1/2	8 (15)	3 (43)	2 (29)	3 (25)	8 (31)	0	0	0	0
Both *FLT3* and *IDH1/2*	4 (7)	1 (14)	1 (14)	2 (17)	4 (15)	0	0	0	0
Median prior therapies, n (range)	2 (1–8)	2 (1–8)	1 (1–3)	2 (1–4)	2 (1–8)	1 (1–7)	3 (1–6)	2 (1–4)	2 (1–7)
Prior therapy, n (%)									
HSCT	16 (30)	4 (57)	0	2 (17)	6 (23)	3 (27)	5 (56)	1 (14)	10 (36)
Venetoclax	37 (69)	5 (71)	5 (71)	6 (50)	16 (62)	8 (73)	7 (78)	5 (71)	21 (75)
Menin Inhibitors	10 (19)	2 (29)	1 (14)	0	3 (12)	4 (36)	2 (22)	1 (14)	7 (25)

a Includes one patient who did not receive a dose of ziftomenib
Data cutoff: Oct 1, 2024

Safety and Tolerability of Ziftomenib in R/R AML

Treatment-Emergent Adverse Events in ≥20% of All Patients

TEAEs, n (%)	All Patients N=54[a]	*NPM1*-m				*KMT2A*-r			
		200 mg n=7	400 mg n=7	600 mg n=12	Total n=26	200 mg n=11	400 mg n=9	600 mg n=7	Total n=28[a]
Any Grade	53 (98)	6 (86)	7 (100)	12 (100)	25 (96)	11 (100)	9 (100)	7 (100)	28 (100)
Nausea	21 (39)	5 (71)	1 (14)	4 (33)	10 (38)	2 (18)	5 (56)	4 (57)	11 (39)
Constipation	18 (33)	3 (43)	2 (29)	3 (25)	8 (31)	4 (36)	4 (44)	2 (29)	10 (36)
Platelet count decreased	18 (33)	3 (43)	1 (14)	0	4 (15)	6 (55)	5 (56)	3 (43)	14 (50)
Diarrhea	17 (31)	3 (43)	2 (29)	2 (17)	7 (27)	4 (36)	4 (44)	2 (29)	10 (36)
Anemia	16 (30)	1 (14)	2 (29)	0	3 (12)	4 (36)	6 (67)	3 (43)	13 (46)
Febrile neutropenia	15 (28)	1 (14)	2 (29)	2 (17)	5 (19)	3 (27)	5 (56)	2 (29)	10 (36)
Vomiting	15 (28)	2 (29)	1 (14)	2 (17)	5 (19)	3 (27)	4 (44)	3 (43)	10 (36)
Fatigue	13 (24)	3 (43)	2 (29)	4 (33)	9 (35)	0	3 (33)	1 (14)	4 (14)
Decreased appetite	12 (22)	2 (29)	1 (14)	0	3 (12)	4 (36)	4 (44)	1 (14)	9 (32)
Hypokalemia	12 (22)	3 (43)	2 (29)	1 (8)	6 (23)	2 (18)	2 (22)	2 (29)	6 (21)
Hypophosphatemia	12 (22)	2 (29)	2 (29)	1 (8)	5 (19)	5 (45)	2 (22)	0	7 (25)
Hyperphosphatemia	11 (20)	2 (29)	1 (14)	1 (8)	4 (15)	3 (27)	2 (22)	2 (29)	7 (25)
Neutrophil count decreased	11 (20)	1 (14)	1 (14)	0	2 (8)	4 (36)	3 (33)	2 (29)	9 (32)
Grade ≥3	49 (91)	6 (86)	7 (100)	9 (75)	22 (85)	11 (100)	9 (100)	6 (86)	27 (96)
Platelet count decreased	17 (31)	2 (29)	1 (14)	0	3 (12)	6 (55)	5 (56)	3 (43)	14 (50)
Anemia	14 (26)	1 (14)	1 (14)	0	2 (8)	4 (36)	5 (56)	3 (43)	12 (43)
Febrile neutropenia	14 (26)	1 (14)	2 (29)	2 (17)	5 (19)	3 (27)	5 (56)	1 (14)	9 (32)

a Includes one patient who did not receive a dose of ziftomenib
Data cutoff: Oct 1, 2024. AEs were graded according to CTCAE v5.0.

Ziftomenib/Backbone-Related Adverse Events of Interest in R/R/ AML

- Four cases (8%) of differentiation syndrome (DS) were manageable; no discontinuations due to DS:
  - 1 Gr3 *NPM1*-m 400 mg
  - 1 Gr3 *KMT2A*-r 200 mg
  - 1 Gr3 *KMT2A*-r 400 mg
  - 1 Gr2 *KMT2A*-r 400 mg
- No ziftomenib-associated QTc prolongation
- No dose-limiting toxicities (DLTs) at any dose level

Data cutoff: Oct 1, 2024

Clinical Activity in Response-Evaluable[a] R/R Patients

Response, n (%)	*NPM1*-m 200 mg n=7	*NPM1*-m 400 mg n=6	*NPM1*-m 600 mg n=9	*NPM1*-m Total n=22	*KMT2A*-r 200 mg n=11	*KMT2A*-r 400 mg n=9	*KMT2A*-r 600 mg n=6	*KMT2A*-r Total n=27[b]
CRc	4 (57)	3 (50)	4 (44)	11 (50)	2 (18)	1 (11)	1 (17)	4 (15)
ORR	5 (71)	4 (67)	6 (67)	**15 (68)**	4 (36)	4 (44)	1 (17)	**9 (33)**
CR	1 (14)	2 (33)	2 (22)	5 (23)	2 (18)	0	1 (17)	3 (11)
CRh	2 (29)	1 (17)	0	3 (14)	0	1 (11)	0	1 (4)
CRi	1 (14)	0	2 (22)	3 (14)	0	0	0	0
MLFS	1 (14)	1 (17)	2 (22)	4 (18)	2 (18)	3 (33)	0	5 (19)

Response, n (%)	NO Prior VEN *NPM1*-m n=8	NO Prior VEN *KMT2A*-r n=7	Prior VEN *NPM1*-m n=14	Prior VEN *KMT2A*-r n=20
CRc	6 (75)	1 (14)	5 (36)	3 (15)
ORR	**8 (100)**	**3 (43)**	**7 (50)**	**6 (30)**
CR	4 (50)	1 (14)	1 (7)	2 (10)
CRh	1 (13)	0	2 (14)	1 (5)
CRi	1 (13)	0	2 (14)	0
MLFS	2 (25)	2 (29)	2 (14)	3 (15)

a Defined as patients who have ≥1 response assessment or who had died; bIncludes 1 patient who did not receive a dose of ziftomenib
Data cutoff: Oct 1, 2024

ANC and Platelet Recovery in CRc Responders in R/R Patients

Median (range)	*NPM1*-m and *KMT2A*-r		
	200 mg n=6	400 mg n=4	600 mg n=5
Days to ANC ≥0.5 x 10^9, Cycle 1	34 (28–66)	38 (35–50)	35 (29–42)
Days to ANC ≥1.0 x 10^9, Cycle 1	46 (28–137)	46 (37–54)	42 (34–43)
Days to Platelets ≥50 x 10^9, Cycle 1[a]	20 (0–76)	38 (0–84)	14 (0–29)
Days to Platelets ≥100 x 10^9, Cycle 1[a]	46 (0–61)	37 (22–84)	13 (0–35)

a Includes 4 NPM1-m patients (200 mg n=1, 400 mg n=1, 600 mg n=2) with platelet counts that were never below 50 x 10^9/L.
Data cutoff: Oct 1, 2024

Conclusions

- **In the ongoing KOMET-007 study, ziftomenib combined with venetoclax/azacitidine was well tolerated at all dose levels tested and continued to demonstrate promising clinical activity in relapsed/refractory *NPM1*-m and *KMT2A*-r AML**
- **Ziftomenib combination therapy was well tolerated**
  - No dose-limiting toxicities or ziftomenib-induced QTc prolongation were reported
  - On-target DS occurred in 8% (4/53) of patients receiving ziftomenib (all Grade 2 or 3), including in 3 *KMT2A-r* patients and 1 *NPM1*-m patient; all patients had resolution of DS with appropriate management and continued on treatment
- **Clinical activity was demonstrated in *NPM1-m* and *KMT2A-r* R/R AML, including VEN-experienced patients**
  - In the *NPM1*-m response-evaluable population: ORR 68%, CRc 50%
  - In *NPM1-m* patients with VEN exposure: ORR 50%, CRc 36%
  - In *KMT2A*-r patients, approximately one-third of patients responded, including those with prior VEN exposure
- **Based on these encouraging initial results, a dose expansion phase evaluating this triplet combination is underway in R/R *NPM1-m* and *KMT2A-r* AML patients**

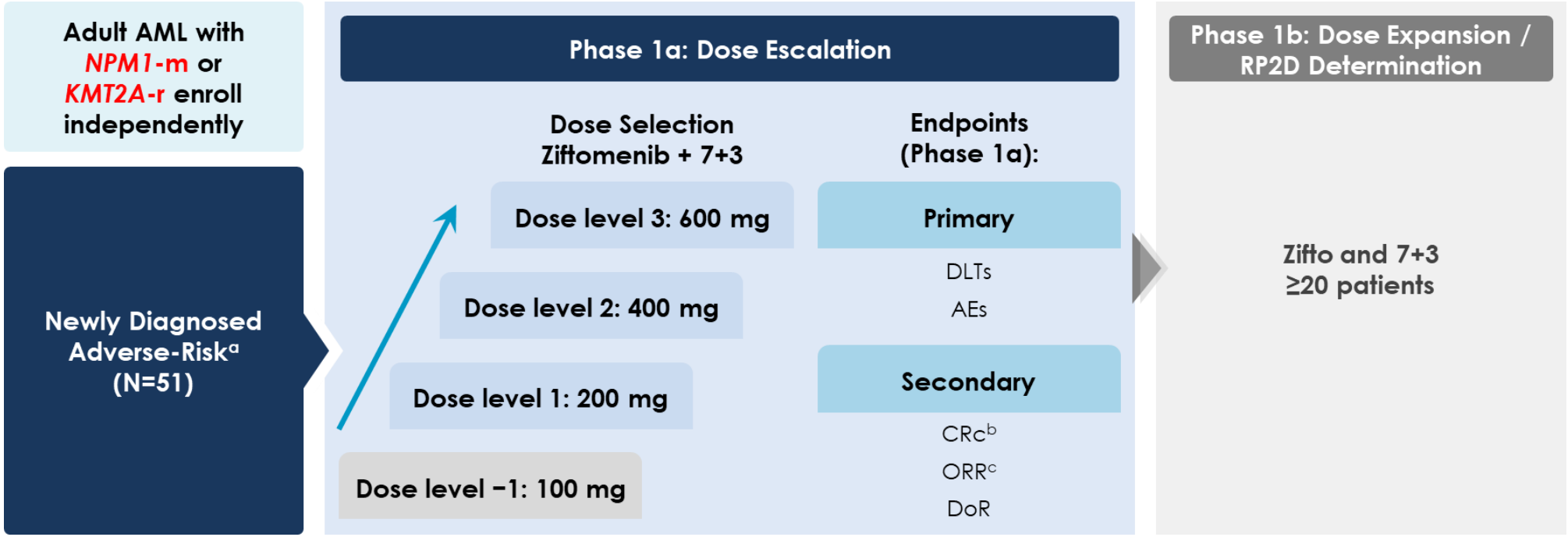
ZIFTOMENIB IN NEWLY DIAGNOSED ADVERSE-RISK AML

Amer Zeidan, MBBS – Yale Cancer Center

Disclosure: Honoraria or consultation fees provided by Kura Oncology

KOMET-007: Ongoing Phase 1 Combination Trial of Ziftomenib in Patients with Newly Diagnosed Adverse-Risk[a] AML

Ziftomenib / 7+3 combination (NCT05735184)



- Ziftomenib started on Cycle 1 Day 8 and administered continuously thereafter. Cytarabine administered on Cycle 1 Days 1–7; daunorubicin on Cycle 1 Days 1–3; re-induction cycles allowed based on bone marrow biopsy results
- Here, we present data from the dose escalation (Phase 1a) in patients with Adverse-Risk[a] AML (data cutoff: Oct 1, 2024)
- Dose expansion (Phase 1b) is ongoing and includes all newly diagnosed *NPM1*-m and *KMT2A*-r AML patients, with or without adverse-risk

[a]Adverse-risk *NPM1*-m AML defined as having high-risk cytogenetics per ELN criteria, age ≥60 yrs and/or treatment-related *NPM1*-m/*KMT2A*-r AML regardless of age. [b]CR, CRh, or CRi. [c]CRc or MLFS.
AE, adverse event; CRc, composite complete remission; CRh, complete remission with partial hematological recovery; CRi, complete remission with incomplete hematological recovery; DLT, dose limiting toxicity; DoR, duration of response; MLFS, morphologic leukemia-free state; RP2D, recommended phase 2 dose.

Baseline Characteristics & Disposition: 1L AML (N=51)

		NPM1-m				*KMT2A*-r			
	All Patients (N=51)	**200 mg (n=8)**	**400 mg (n=7)**	**600 mg (n=9)**	**Total (n=24)**	**200 mg (n=10)**	**400 mg (n=9)**	**600 mg (n=8)**	**Total (n=27)**
Median age, years (range)	**60 (18–74)**	65 (43–74)	66 (55–68)	66 (60–68)	**66 (43–74)**	53 (31–73)	51 (28–60)	40 (18–67)	**50 (18–73)**
Female, n (%)	31 (61)	4 (50)	4 (57)	4 (44)	12 (50)	7 (70)	6 (67)	6 (75)	19 (70)
Race, n (%)									
White	33 (65)	7 (88)	6 (86)	4 (44)	17 (71)	8 (80)	4 (44)	4 (50)	16 (59)
Non-White	18 (35)	1 (13)	1 (14)	5 (56)	7 (29)	2 (20)	5 (56)	4 (50)	11 (41)
ECOG PS 0, n (%)	16 (31)	4 (50)	4 (57)	4 (44)	12 (50)	0	2 (22)	2 (25)	4 (15)
1	18 (35)	3 (38)	1 (14)	4 (44)	8 (33)	3 (30)	2 (22)	5 (63)	10 (37)
2	7 (14)	1 (13)	1 (14)	1 (11)	3 (13)	3 (30)	1 (11)	0	4 (15)
Co-mutations, n (%)	17 (33)	2 (25)	1 (14)	5 (56)	8 (33)	4 (40)	2 (22)	3 (38)	9 (33)
FLT3	3 (6)	0	0	0	0	1 (10)	0	2 (25)	3 (11)
IDH1/2	7 (13)	2 (25)	0	5 (56)	7 (29)	0	0	0	0
Therapy-related AML, n (%)	11 (22)	1 (13)	1 (14)	1 (11)	3 (13)	3 (30)	2 (22)	3 (38)	8 (30)
Patients on study[a], n (%)	**45 (88)**	8 (100)	7 (100)	9 (100)	**24 (100)**	6 (60)	8 (89)	7 (88)	**21 (78)**
Median follow-up, weeks (range)	25 (2–66)	46 (35–66)	31 (29–34)	21 (17–24)	31 (17–63)	33 (2–43)	25 (15–31)	10 (4–17)	19 (2–43)

[a]Patients on-treatment or in long-term follow-up.

Data cutoff: Oct 1, 2024. ECOG PS, Eastern Cooperative Oncology Group performance status

Safety and Tolerability of Ziftomenib in Combination with 7+3 in 1L AML (N=51)

TEAEs in ≥30% of All Patients

TEAEs, n (%)	All Patients (N=51)	*NPM1*-m 200 mg (n=8)	*NPM1*-m 400 mg (n=7)	*NPM1*-m 600 mg (n=9)	*NPM1*-m Total (n=24)	*KMT2A*-r 200 mg (n=10)	*KMT2A*-r 400 mg (n=9)	*KMT2A*-r 600 mg (n=8)	*KMT2A*-r Total (n=27)
Any Grade	**48 (94)**	8 (100)	6 (86)	8 (89)	22 (92)	10 (100)	9 (100)	7 (88)	26 (96)
Febrile neutropenia	**34 (67)**	5 (63)	4 (57)	8 (89)	17 (71)	8 (80)	4 (44)	5 (63)	17 (63)
Diarrhea	**27 (53)**	4 (50)	4 (57)	4 (44)	12 (50)	6 (60)	7 (78)	2 (25)	15 (56)
Platelet count decreased	**22 (43)**	7 (88)	4 (57)	4 (44)	15 (63)	3 (30)	2 (22)	2 (25)	7 (26)
Anemia	**19 (37)**	4 (50)	2 (29)	4 (44)	10 (42)	4 (40)	3 (33)	2 (25)	9 (33)
Nausea	**19 (37)**	4 (50)	3 (43)	3 (33)	10 (42)	4 (40)	2 (22)	3 (38)	9 (33)
Neutrophil count decreased	**18 (35)**	6 (75)	3 (43)	3 (33)	12 (50)	3 (30)	2 (22)	1 (13)	6 (22)
Constipation	**18 (35)**	5 (63)	2 (29)	2 (22)	9 (38)	5 (50)	2 (22)	2 (25)	9 (33)

- Safety profile of ziftomenib in combination with intensive chemotherapy was similar to that reported for newly diagnosed AML patients treated with 7+3 alone[1]
- Rate of TEAEs was consistent across escalating doses of ziftomenib

[1]Lin et al. *Blood Adv* 2021 Mar 23;5(6):1719-1728 (NCT01696084).
Data cutoff: Oct 1, 2024. TEAE, treatment-emergent adverse event.

Safety and Tolerability of Ziftomenib in Combination with 7+3 in 1L AML (N=51)

Grade ≥3 TEAEs in ≥10% of All Patients

TEAEs, n (%)	All Patients (N=51)	*NPM1*-m 200 mg (n=8)	*NPM1*-m 400 mg (n=7)	*NPM1*-m 600 mg (n=9)	*NPM1*-m Total (n=24)	*KMT2A*-r 200 mg (n=10)	*KMT2A*-r 400 mg (n=9)	*KMT2A*-r 600 mg (n=8)	*KMT2A*-r Total (n=27)
Grade ≥3	**46 (90)**	8 (100)	6 (86)	8 (89)	**22 (92)**	10 (100)	8 (89)	6 (75)	**24 (89)**
Febrile neutropenia	**30 (59)**	5 (63)	4 (57)	8 (89)	**17 (71)**	7 (70)	3 (33)	3 (38)	**13 (48)**
Platelet count decreased	**21 (41)**	7 (88)	4 (57)	3 (33)	**14 (58)**	3 (30)	2 (22)	2 (25)	**7 (26)**
Anemia	**18 (35)**	4 (50)	2 (29)	3 (33)	**9 (38)**	4 (40)	3 (33)	2 (25)	**9 (33)**
Neutrophil count decreased	**18 (35)**	6 (75)	3 (43)	3 (33)	**12 (50)**	3 (30)	2 (22)	1 (13)	**6 (22)**
White blood cell count decreased	**13 (26)**	3 (38)	2 (29)	2 (22)	**7 (29)**	2 (20)	3 (33)	1 (13)	**6 (22)**
Sepsis	**7 (14)**	2 (25)	0	2 (22)	**4 (17)**	1 (10)	1 (11)	1 (13)	**3 (11)**
Pneumonia	**6 (12)**	1 (13)	2 (29)	0	**3 (13)**	2 (20)	0	1 (13)	**3 (11)**

Ziftomenib in Combination with 7+3-related Adverse Events of Interest

- One case of Gr3 differentiation syndrome (*NPM1*-m 600 mg); successfully managed and patient remained on treatment
- No ziftomenib-associated QTc prolongation
- No dose-limiting toxicities (DLTs) at any dose level

Data cutoff: Oct 1, 2024. TEAE, treatment-emergent adverse event.

Clinical Activity in All Response-Evaluable[a] 1L Patients (N=46)

- Historically, only 33% of 7+3 treated newly diagnosed Adverse-Risk AML patients achieve CRc, with a median overall survival of ~6 months[1-2]

Response, n (%)	All Patients (N=46)	*NPM1*-m 200 mg (n=8)	*NPM1*-m 400 mg (n=7)	*NPM1*-m 600 mg (n=8)	*NPM1*-m Total (n=23)	*KMT2A*-r 200 mg (n=10)	*KMT2A*-r 400 mg (n=9)	*KMT2A*-r 600 mg (n=4)	*KMT2A*-r Total (n=23)
CRc	**42 (91)**	8 (100)	7 (100)	8 (100)	**23 (100)**	9 (90)	6 (67)	4 (100)	**19 (83)**
ORR	**42 (91)**	8 (100)	7 (100)	8 (100)	**23 (100)**	9 (90)	6 (67)	4 (100)	**19 (83)**
CR	**42 (91)**	8 (100)	7 (100)	8 (100)	**23 (100)**	9 (90)	6 (67)	4 (100)	**19 (83)**
CRh	0	0	0	0	0	0	0	0	0
CRi	0	0	0	0	0	0	0	0	0
MLFS	0	0	0	0	0	0	0	0	0
PR	0	0	0	0	0	0	0	0	0
NR	3 (7)	0	0	0	0	0	3 (33)	0	3 (13)
NE	1 (2)	0	0	0	0	1 (10)	0	0	1 (4)
MRD negativity, n/N[b]	**28/37 (76)**	8/8 (100)	4/6 (67)	4/7 (57)	**16/21 (76)**	5/8 (63)	5/6 (83)	2/2 (100)	**12/16 (75)**

[a]Patients who have ≥1 response assessment or who had died.
[b]Among CRc responders tested for MRD per local assay (NGS, RT-qPCR, FISH, flow cytometry).

1. Lin et al. *Blood Adv* 2021 Mar 23;5(6):1719-1728. 2. Lancet et al. *Blood* 2014 May 22;123(21):3239-46.
Data cutoff: Oct 1, 2024. Per ELN 2022: CR, complete remission; CRc, composite complete remission; CRh, complete remission with partial hematological recovery; CRi, complete remission with incomplete hematological recovery; FISH, fluorescence in situ hybridization; MLFS, morphologic leukemia-free state; MRD, measurable residual disease; NE, not evaluable; NGS, next-generation sequencing; NR, no response; PR, partial remission; RT-qPCR, quantitative reverse transcription polymerase chain reaction.

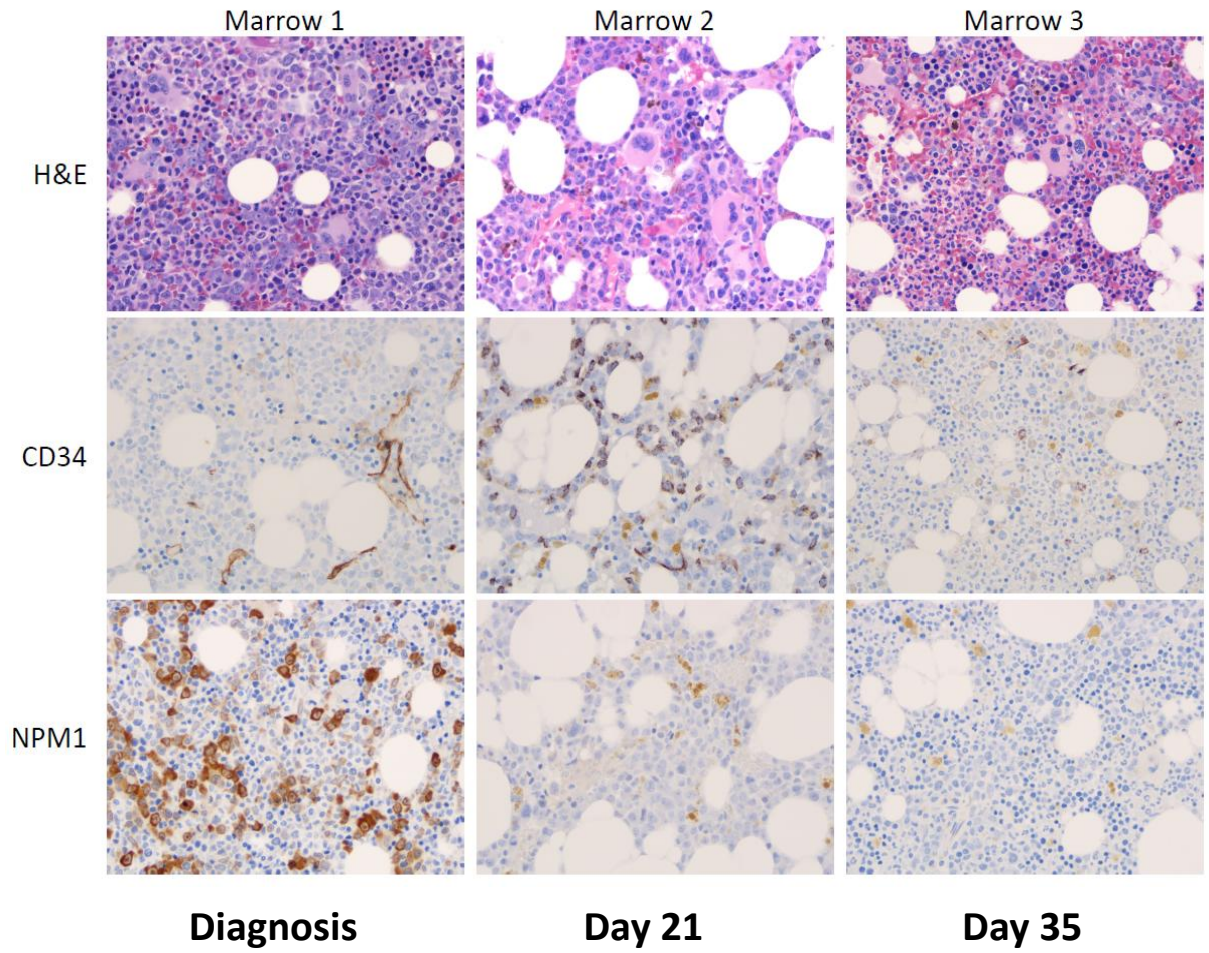
Case Study

60-yr-old Female with Newly Diagnosed *NPM1*-m AML Treated with Ziftomenib and 7+3

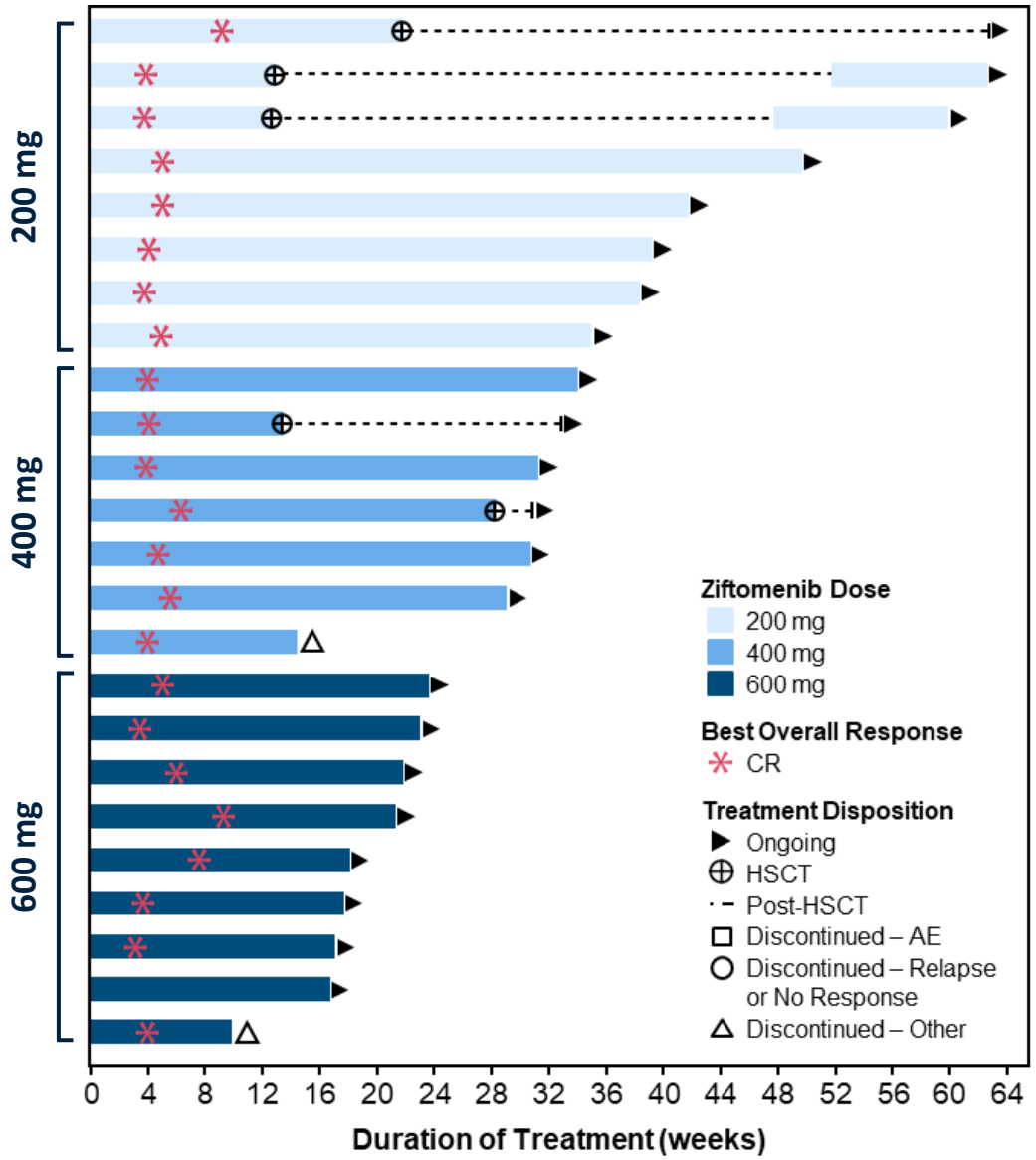
- **Screening marrow**: blasts 8%, $CD34^-$ $NPM1^+$ (IHC), NPM1 PCR 38%
- **Day 21 marrow**: 30% morphologic blasts, but now $CD34^+$ $NPM1^-$ (IHC) PCR NPM1 0.08%
- **Days 22–24**: Platelet count recovering, decision to hold off salvage therapy and repeat marrow at Day 35
- **Day 35 marrow:** 1% blasts, $NPM1^-$ (IHC), NPM1 PCR 0.05%

Key considerations:

- Distinguish refractory disease from differentiating / regenerating blasts
- Allow time for count recovery and re-assess bone marrow, especially when clinical picture suggests otherwise (eg, change in blast immunophenotype, recovering counts, high CR rate)



Duration of Treatment & Preliminary Clinical Outcomes in *NPM1*-m 1L AML

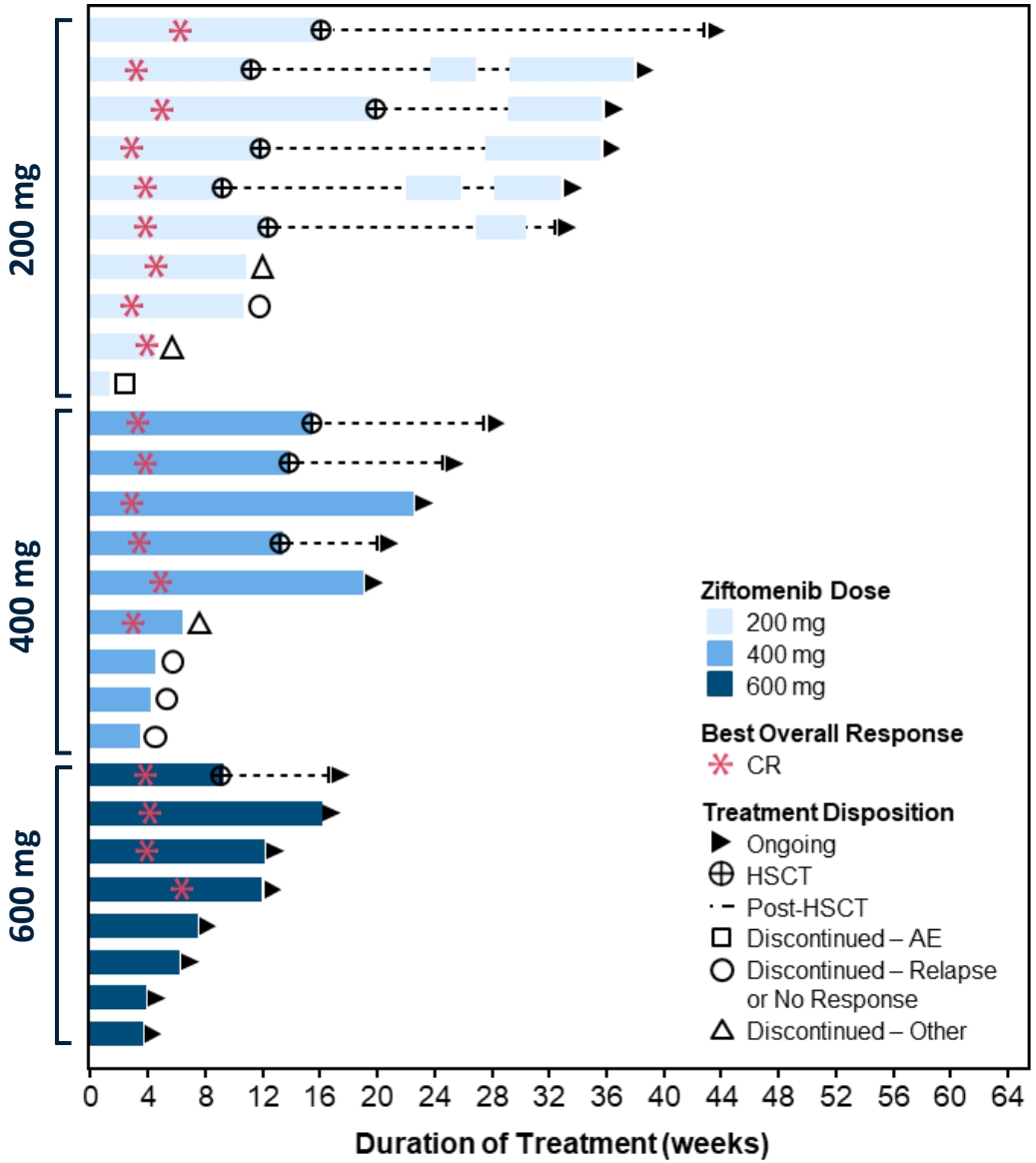


- For *NPM1*-m, after a median follow-up of 31 weeks (range 17–63):
  - Median duration of CR was **not reached**
  - Median OS was **not reached**
  - 5 *NPM1*-m patients received HSCT (200 mg n=3, 400 mg n=2). Thus far, 2 went onto ziftomenib maintenance
  - No discontinuations due to AE or relapse
  - **100% (24/24) patients remained alive**

Data cutoff: Oct 1, 2024.

AE, adverse event; CR, complete remission; HSCT, hematopoietic stem cell transplant.

Duration of Treatment & Preliminary Clinical Outcomes in KMT2A-r 1L AML



- For *KMT2A*-r, after a median follow-up of 19 weeks (range 2–43):
  - Median duration of CR was **not reached**
  - Median OS was **not reached**
  - 10 *KMT2A*-r patients received HSCT (200 mg n=6, 400 mg n=3, 600 mg n=1). Thus far, 5 went onto ziftomenib maintenance
  - **96% (26/27) patients remained alive**

Data cutoff: Oct 1, 2024.

AE, adverse event; CR, complete remission; HSCT, hematopoietic stem cell transplant.

ANC and Platelet Recovery in CRc Responders

Median (range)	*NPM1*-m + *KMT2A*-r		
	200 mg n=17	400 mg n=13	600 mg n=12
Days to ANC ≥0.5x10^9/L, Cycle 1	32 (20–40)	27 (20–40)	28 (19–38)
Days to ANC ≥1.0x10^9/L, Cycle 1	33 (21–62)	28 (20–40)	28 (20–48)
Days to Platelets ≥50x10^9/L, Cycle 1	28 (15–62)	26 (15–40)	26 (18–48)
Days to Platelets ≥100x10^9/L, Cycle 1	32 (20–62)	26 (18–40)	28 (20–48)

- Higher ziftomenib doses did not impact or delay neutrophil and platelet count recovery

Data cutoff: Oct 1, 2024. ANC, absolute neutrophil count; CRc, composite complete response.

Conclusions

- **In the ongoing KOMET-007 study, ziftomenib combined with cytarabine and daunorubicin (7+3) was well tolerated across all dose levels in patients with newly diagnosed adverse-risk *NPM1*-m and *KMT2A*-r AML**
  - No DLTs or ziftomenib-associated QTc prolongation were reported
  - On-target DS occurred in 2% (n=1, Gr3), successfully managed and patient remained on treatment
  - Higher ziftomenib doses did not impact or delay neutrophil and platelet count recovery
- **Robust clinical activity was demonstrated in newly diagnosed *NPM1*-m and *KMT2A*-r AML**
  - CR: 100% for *NPM1*-m, 83% for *KMT2A-r* patients
    - MRD negativity: 76% for *NPM1*-m, 75% for *KMT2A*-r patients
  - 100% (24/24) of *NPM1*-m and 96% (26/27) *KMT2A*-r patients remained alive (median follow-up of 31 and 19 weeks, respectively)
- **Taken together, these data support the continued advancement of ziftomenib in combination with intensive chemotherapy in all newly diagnosed *NPM1*-m and *KMT2A*-r AML patients, with or without adverse-risk**
  - Given encouraging clinical activity and the lack of impact associated with increasing ziftomenib dose and TEAEs (including DS, QTc prolongation or myelosuppression), the Phase 1b dose expansion is investigating 600 mg ziftomenib-based combinations in all newly diagnosed *NPM1*-m and *KMT2A*-r AML patients

CLINICAL DEVELOPMENT PLAN

Mollie Leoni, M.D. – Executive Vice President, Clinical Development

Maximize Value of Robust Therapeutic Pipeline

PROGRAM	CLINICAL TRIAL	STUDY STARTUP	DOSE-ESCALATION	DOSE-VALIDATION	REGISTRATION DIRECTED	ANTICIPATED MILESTONE
ZIFTOMENIB Menin Inhibitor	**KOMET-001** Monotherapy	NPM1-mutant acute myeloid leukemia (AML)				Topline data in early 2025
		KMT2A-rearranged acute lymphoblastic leukemia (ALL)				Now dosing patients
		Non-NPM1-mutant / Non-KMT2A-rearranged AML				Now dosing patients
	KOMET-007 Combinations with venetoclax/azacitidine, cytarabine + daunorubicin (7+3)	NPM1-mutant AML				Phase 1b expansion study now enrolling
		KMT2A-rearranged AML				
	KOMET-008 Combinations with gilteritinib, FLAG-IDA, LDAC	NPM1-mutant AML				Now dosing patients
		KMT2A-rearranged AML				
	KOMET-015 Combination with imatinib	Advanced GIST				Initiate proof-of-concept study in 1H 2025
KO-2806 Next-Generation Farnesyl Transferase Inhibitor (FTI)	**FIT-001** Monotherapy, combinations with cabozantinib and adagrasib	Solid tumors				Now in dose escalation as monotherapy
		Clear cell renal cell carcinoma (ccRCC)				Now dosing patients in combo with cabozantinib
		$KRAS^{G12C}$-mutant non-small cell lung cancer (NSCLC)				Now dosing patients in combo with adagrasib
TIPIFARNIB FTI	**KURRENT-HN** Combination with alpelisib	PIK3CA-dependent head and neck squamous cell carcinoma (HNSCC)				Present preliminary data in 1H 2025

KOMET-017: Ziftomenib Pivotal 1L Combination

Fully-funded study expected to start in mid-2025

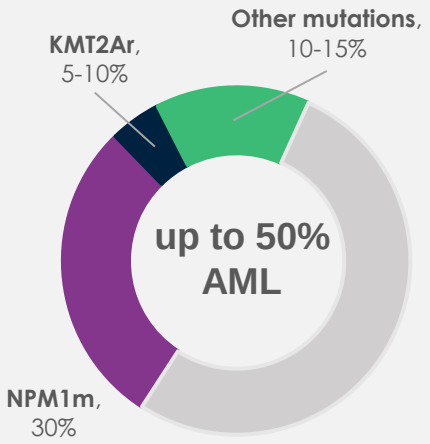
- Includes two independently powered Phase 3, randomized, double-blind, placebo-controlled studies
- Populations: Adult 1L AML with KMT2A-r or NPM1-m
  - Non-intensive therapy study
    - Ziftomenib + venetoclax + azacitidine
    - Placebo + venetoclax + azacitidine
  - Intensive therapy study
    - Ziftomenib + daunorubicin + cytarabine (7+3)
    - Placebo + daunorubicin + cytarabine (7+3)
- Approximately 150 sites in 20+ countries

MARKET OPPORTUNITY

Brian Powl – Chief Commercial Officer, Kura Oncology

Collaboration Supports Expansive Development for up to 50% of AML Patients for Whom Menin-KMT2A Pathway is a Disease Driver

Prevalence of Ziftomenib Eligible Patients



1L Treatable ~17K → **Relapsed / Refractory** ~14K

1L Treatable			Relapsed / Refractory			
FIT IC* or UNFIT NIC*	Transplant/ No Transplant	Post-Transplant Maintenance	IC or NIC Tx or tolerable therapy	Transplant/ No Transplant	Targeted Tx if FLT3m, IDH1/2m and/or NPM1m	Non-Intensive therapy / Palliative Care

komet ACUTE LEUKEMIAS
Ziftomenib Clinical Trials for Acute Leukemias

KOMET-007
- 1L zifto + ven/aza
- 1L zifto + 7+3
- 1L zifto + 7+3 + quizartinib

KOMET-017
- 1L zifto + ven/aza
- 1L zifto + 7+3

Investigator / Company Sponsored Studies
- Post-HSCT maintenance

KOMET-001
- R/R NPM1m AML

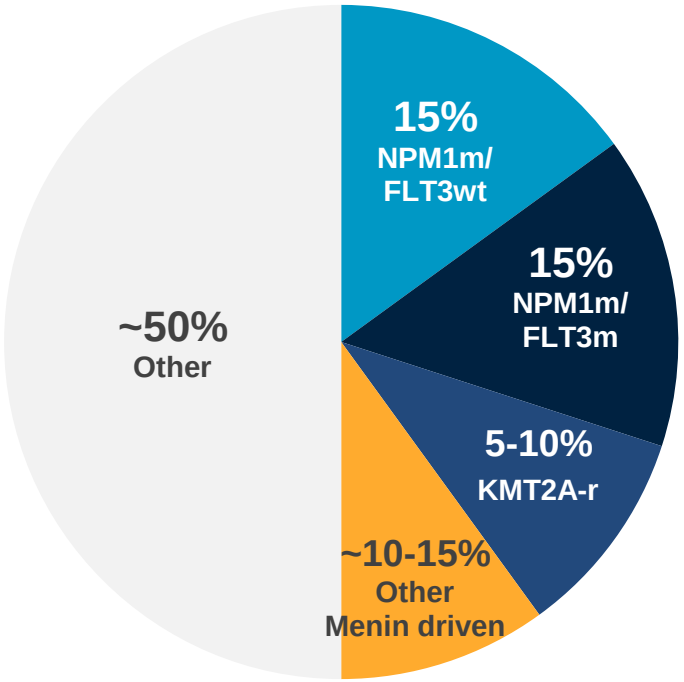
KOMET-007
- R/R zifto + ven/aza

KOMET-008
- R/R zifto + FLAG-IDA
- R/R zifto + LDAC
- R/R zifto + gilteritinib

*FIT IC = patients eligible for induction chemotherapy; UNFIT NIC = patients eligible for non-intensive chemotherapy

U.S. Market Potential in 1L AML for Patients with Menin-Driven Disease May Exceed $7B Per Year

~50% of AML patients could benefit from menin inhibitors



High unmet need exists in AML despite currently approved options, including in those patients considered to have a favorable prognosis

Opportunity to treat > 10k patients/year in U.S. across both IC and Non-IC

- *Emerging data supports durable combo with 7+3, ven/za, FLT3i*

Potential for sustained benefit / risk to support **12-24+ mo** of treatment

- *Analog pricing, including for recently approved product $36-40k/mo*

Anticipated market potential of **> $7B/year** for menin inhibitors in 1L AML

- ***Peak sales potential for ziftomenib of up to $3B/year in U.S.***

UPCOMING MILESTONES

Troy Wilson, Ph.D., J.D. – President & Chief Executive Officer, Kura Oncology

Forecasted Milestones & Financial Highlights

PROGRAM	MILESTONE	ESTIMATED TIME OF ACHIEVEMENT
ZIFTOMENIB **Menin Inhibitor**	Present updated data from KOMET-007 trial in combination with ven/aza and 7+3	✓
	Report topline results from KOMET-001 registration-directed trial in NPM1-mutant R/R AML	Early 2025
	Present preliminary data from Phase 1b expansion portion of KOMET-007	2025
	Initiate KOMET-015 study in combination with imatinib in patients with advanced GIST	1H 2025
	Nominate a next generation menin inhibitor development candidate	1H 2025
	Initiate KOMET-017 registration-directed trial in combination with ven/aza and 7+3 in 1L AML	Mid-2025
KO-2806 **Next-Generation Farnesyl Transferase Inhibitor**	Identify maximum tolerated dose as monotherapy	2H 2024
	Initiate one or more expansion cohorts in combination with cabozantinib in ccRCC	1H 2025
TIPIFARNIB **Farnesyl Transferase Inhibitor**	Identify OBAD in combination with alpelisib in PIK3CA-dependent HNSCC	End of 2024
	Present data from KURRENT-HN trial in combination with alpelisib in PIK3CA-dependent HNSCC	1H 2025

Financial Highlights Nasdaq: KURA	$785.3M in *pro forma* cash as of September 30, 2024*
	Shares outstanding as of September 30, 2024: 77.7M basic; 24.5M options, RSUs, PSUs, warrants & pre-funded warrants

OBAD = optimal biologically active dose

* Includes $455.3M in cash, cash equivalents and short-term investments as of 9/30/24 and upfront payment of $330M from strategic collaboration with Kyowa Kirin

Kura Oncology Investment Thesis

- Robust pipeline of potential blockbuster product opportunities in hematologic malignancies, solid tumors and diabetes
- Kyowa Kirin strategic collaboration accelerates expansive global development and commercialization to maximize the potential of ziftomenib for AML patients
- Kura retains program leadership in the U.S. and key strategic rights of ziftomenib to preserve strategic flexibility
- Kura anticipates collaboration plus current cash balance to fund ziftomenib AML program to commercialization in frontline combinations
- Kura retains pipeline programs, which are funded through key value inflection points in 2025-2026, including:
    - Next-gen menin inhibitors targeting oncology, diabetes and other metabolic diseases
    - Farnesyl transferase inhibitor combinations

KURA ONCOLOGY

DEVELOPING PRECISION MEDICINES FOR THE TREATMENT OF CANCER

ASH Investor Event – December 9, 2024