Activity, tolerability and resistance profile of the menin inhibitor ziftomenib in adults with relapsed or refractory NPM1-mutated AML

Harry P. Erba[1], Eunice S. Wang[2], Ghayas C. Issa[3], Jessica K. Altman[4], Pau Montesinos[5], Stephane DeBotton[6], Roland Walter[7], Kristen Pettit[8], Stephen Strickland[9], Mrinal Patnaik[10], Marina Kremyanskaya[11], Maria R. Baer[12], James Foran[13], Gary Schiller[14], Lionel Ades[15], Mael Heiblig[16], Celine Berthon[17], Jolanta Grembecka[8], Tomasz Cierpicki[8], Bradley Clegg[8], Pierre Peterlin[18], Eduardo Rodriguez Arboli[19], Olga Salamero Garcia[20], Cristina Papayannidis[21], Kun Nie[22], Julie Mackey[22], Marilyn Tabachri[22], Daniel Corum[22], Mollie Leoni[22], Stephen Dale[22], Amir T. Fath[23]

[1]Duke Cancer Institute, Durham, NC; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [3]MD Anderson Cancer Center, Houston, TX; [4]Northwestern University-Robert H. Lurie Comprehensive Cancer Center, Chicago IL; [5]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [6]Institut Gustave Roussy Service d'Hématologie Clinique, Paris, France; [7]Fred Hutchinson Cancer Research Center, Seattle, WA; [8]University of Michigan, Ann Arbor, MI; [9]Sarah Cannon Research Institute, Nashville, TN; [10]Mayo Clinic-Minnesota, Rochester, MN; [11]Mount Sinai-PRIME, New York, NY; [12]University of Maryland-Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD; [13]Mayo Clinic-Florida, Jacksonville, FL; [14]UCLA Medical Center, Los Angeles, CA; [15]Hospital Saint-Louis, Paris, France; [16]Centre Hospitalier Lyon Sud, Lyon, France; [17]Centre Hospitalo-Universitaire Lille, Lille, France; [18]CHU de Nantes-Hôtel-Dieu, Nantes, France; [19]Hospitales Universitarios Virgen del Rocío, Sevilla, Spain; [20]Hospital Universitari Vall d'Hebron-Institut de Recerca (VHIR), Barcelona, Spain; [21]IRCCS Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy; [22]Kura Oncology, Inc., San Diego, CA; [23]Massachusetts General Hospital, Boston, MA

komet-001
ACUTE LEUKEMIAS KURA KO-MEN-001

INTRODUCTION

- The menin and histone-lysine-N-methyltransferase 2A (KMT2A) protein complex is an essential epigenetic regulator of genes (eg, MEIS1 and the homeobox [Hox] gene family) critical for maintenance of multiple genetic subtypes of leukemia[1]
- This protein complex is implicated in acute myeloid leukemia (AML) with nucleophosmin 1-mutation (NPM1-m; approximately 25%-30% of AML) as well as AML with lysine[K]-specific methyltransferase 2A-rearrangement (KMT2A-r; 5%-10% of AMLs) (Figure 1)[2,3]
- The presence of co-mutations, and relapsed/refractory (R/R) disease in general, portend a poor prognosis[3]
- R/R AML with NPM1-m or KMT2A-r represent a high unmet need, as no United States Food and Drug Administration-approved targeted therapies exist today[4-6]
- Here, we report updated data on the Phase 1 NPM1-m patients dosed at the 600 mg recommended Phase 2 dose (RP2D)

FIGURE 1. *NPM1*-m AND *KMT2A*-r AML REPRESENT A SIGNIFICANT UNMET NEED

NPM1-mutant AML

~ 6,000 new cases annually in the U.S.[7]



Adult patients with *NPM1*-mutant AML and select co-mutations and/or relapsed/refractory disease are associated with poor prognosis[8]

5-year Overall Survival ~50%[9]

Median Overall Survival in patients with R/R *NPM1*-m AML is ~ 6.1 mo.[10]

KMT2A-rearranged AML

~ 1,000-2,000 new cases annually in U.S.[7]



Adult patients with *KMT2A*-rearranged AML have poor prognosis with high rates of resistance and relapse following current standard of care[11,12]

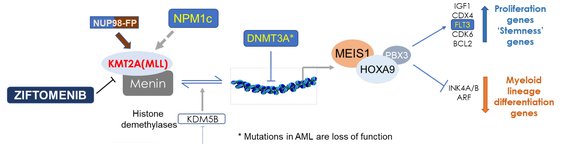
5-year Overall Survival <20%[11]

Median Overall Survival in patients with R/R *KMT2A*-r AML is 6 mo. following 2L treatment and 2.4 mo. following 3L treatment[11]

AML, acute myeloid leukemia; *KMT2A*-r, lysine[K]-specific methyltransferase 2A-rearrangment; mo, month; *NPM1*-m, nucleophosmin 1-mutation; R/R, relapsed or refractory; SOC, standard of care; US, United States; 2L, second line; 3L, third line.

FIGURE 2. ZIFTOMENIB TARGETS THE MENIN-KMT2A PATHWAY, A FOUNDATIONAL TARGET IN AML[13-20]

- *NPM1*-m and *KMT2A-r* drive overexpression of *HOXA9*/*MEIS1* genes, which are critical for transformation to AML
- KMT2A(MLL) sits upstream from major AML targets (*i.e., FLT3, IDH1/2, DNMT3A*)
- KMT2A(MLL)-dependent genes contribute to therapeutic resistance and relapse to current therapies
- Menin inhibition downregulates *HOXA9*/*MEIS1*, leading to differentiation of leukemic blasts

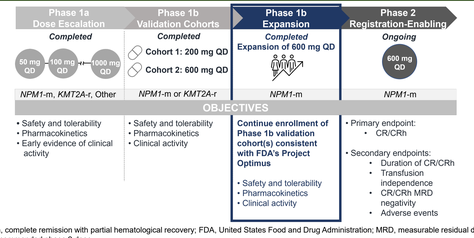


KMT2A = lysine[K]-specific methyltransferase 2; MEIS1 = meis homeobox 1; MLL-mixed lineage leukemia; NPM1-c = cytoplasmic localization of nucleophosmin-1

OBJECTIVE

- The purpose of the Phase 1 portion of KO-MEN-001 (NCT04067336) is to establish the safety, tolerability, and the RP2D for ziftomenib monotherapy in *NPM1*-m and *KMT2A*-r R/R AML

FIGURE 3. STUDY DESIGN



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.

METHODS

- KO-MEN-001 is a global, open-label Phase 1/2 study of ziftomenib in adult patients (≥18 years) with R/R AML (**Figure 3**)
- The dose escalation (Phase 1a) and randomized, multi-dose expansion (Phase 1b) study in patients with *KMT2A*-r or *NPM1*-m R/R AML is fully enrolled
- Ziftomenib is dosed orally, once daily, in 28-day cycles until relapse, progression, or unacceptable toxicity

KURA ONCOLOGY
Corresponding author: medicalaffairs@kuraoncology.com

RESULTS

- As of April 12, 2023, 20 patients with *NPM1*-m were dosed with ziftomenib 600 mg in Phase 1b (**Table 1**)
- *FLT3* and *IDH1/2* co-mutations were common, for the *NPM1*-m group (n=6 [30%] with *FLT3*, n=8 [40%] with *IDH1/2*); 20% (4 of 20 patients) have co-mutations in both *FLT3* and *IDH1/2*
- Patients were heavily pre-treated; median number of prior therapies was 3 (range: 1-10)
  - 20% had ≥1 prior stem cell transplant and 65% had prior venetoclax treatment

TABLE 1. PHASE 1B BASELINE CHARACTERISTICS OF PATIENTS WITH *NPM1*-m AML RECEIVING 600 MG ZIFTOMENIB

Demographics	600 mg, n = 20
Age, median (min, max), y	**70.5 (22, 86)**
Male, n (%)	6 (30)
ECOG PS 0, n (%)	3 (15)
PS 1	14 (70)
PS 2	3 (15)
Number of prior therapies, median (min, max)	**3 (1,10)**
Prior venetoclax, n (%)	13 (65)
Prior SCT, n (%)	4 (20)
Co-mutations, n (%)	
FLT3[1]	6 (30)
IDH1/2[1]	8 (40)
Co-mutations with both *FLT3* and *IDH1/2*	4 (20)

Disposition	600 mg, n = 20
Patients in follow-up, n (%)	**7 (35)**
Reason for treatment discontinuation, n (%)	
Adverse event (not study drug-related)[2]	5 (25)
Death	1 (5)
Disease progression (including clinical)	9 (45)
All other reasons[3]	5 (25)
Patients off study, n (%)	**13 (65)**
Reason for study discontinuation, n (%)	
Death	13 (65)

[1]Patient could have both *FLT3* and *IDH1/2* and be counted in both co-mutation categories.
[2]These adverse events leading to discontinuation were not considered study drug related.
[3]Additional reasons for treatment discontinuation include physician decision, receipt of alternative anticancer treatment, withdrawal by subject, and other.

TABLE 2. PHASE 1B SAFETY AND TOLERABILITY OF ZIFTOMENIB IN R/R *NPM1*-m AML

≥ 20% Treatment-Emergent Adverse Events (TEAEs), n (%)	*NPM1*-m, n = 20
Patients with TEAEs (All Grades)	**19 (95)**
Diarrhea	9 (45)
Hypokalemia	8 (40)
Nausea	6 (30)
Anemia	6 (30)
Back pain	6 (30)
Epistaxis	5 (25)
Patients with TEAEs (≥ Grade 3)	**17 (85)**
Anemia	5 (25)
Thrombocytopenia	4 (20)

≥ 20% Treatment-Related Adverse Events (TRAEs), n (%)	*NPM1*-m, n = 20
Patients with TRAEs (All Grades)	**12 (60)**
Nausea	4 (20)
Differentiation Syndrome	4 (20)
Patients with TRAEs (≥Grade 3)	**6 (30)**
N/A	

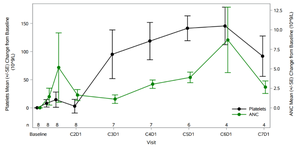
- The cumulative safety profile for the ziftomenib RP2D is consistent with prior reports, with no new signals observed; treatment-related adverse events are listed in **Table 2**
- No pattern of drug induced QT/QTc was reported
- 15% reported Grade 1 or 2 differentiation syndrome events and 5% experienced reported a Grade 3 differentiation syndrome event

TABLE 3. ZIFTOMENIB DEMONSTRATES ENCOURAGING CLINICAL ACTIVITY

Best Overall Response	n (%)
Complete remission rate (CR)	**7 (35)**
CRc rate (CR+CRh+CRi)	8 (40)
Overall response rate (CR+CRh+CRi+MLFS)	9 (45)
CR	7 (35)
CRh	0
CRi	1 (5)
MLFS	1 (5)

33% CR co-*FLT3*m (N=6)
50% CR co-*IDH*m (N=8)

Mean Change in Platelets and ANC for CRc up to C7D1



EFFICACY

- As of April 12, 2023, response rates for patients with *NPM1*-m in Phase 1b treated with 600 mg are shown in **Table 3**
- Co-mutations in FLT3 and IDH1/2 did not affect rates of response to single agent ziftomenib
- 1 patient achieved CRi, proceeded to HSCT, and achieved and remains in CR
- Median time to first response: 51 days

[a]Complete remission is defined as <5% bone marrow blasts with complete hematologic recovery and includes CRmrd, CRmrd-, and CR without MRD assessment. [b]CR/CRh includes complete remission and CRh. [c]CRc is defined as achieving best overall response of any of the following: CR (including CRmrd, CRmrd-, and CR without MRD assessment), CRh, CRi (including CRp). [d]Overall response is defined as achieving best overall response of any of the following: MLFS, CRi (including CRp), CRh, CR (including CRmrd, CRmrd-, and CR without MRD assessment). 95% CI is based on Clopper-Pearson method. Efficacy set contains all subjects from mITT who had at least one post-baseline response assessment, or patients who died or ended study prior to first response assessment. CI, confidence interval; CR, complete remission; CRc, composite complete remission; CRh, complete remission with partial hematological recovery; CRi, complete remission with incomplete hematologic recovery; MLFS, morphological leukemia-free state; ORR, overall response rate; *NPM1*-m, nucleophosmin 1-mutation.

DISCLOSURES

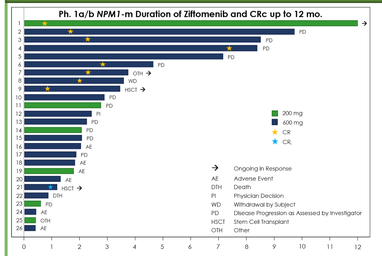
HPE: Research support, AbbVie, Agios, Astellas, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Glycomimetics, Immunogen, Incyte, Jazz, Kura Oncology, Macrogenics, Novartis, Pfizer, Servier, Syros, Takeda, and Trillium; **GCI:** Consultancy/advisory role, Novartis, Kura Oncology and NuProbe; Research funding, Celgene, Novartis, Kura Oncology, Syndax Pharmaceuticals, Merck, Cullinan Oncology and NuProbe; **ESW:** Honoraria, Stemline, Kura, Pfizer, and DAVA Oncology; Advisory boards, AbbVie, Astellas, BMS/Celgene, Genentech, Gilead, GlaxoSmithKline, Jazz, Kite Pharmaceuticals, Kura Oncology, Novartis, Pfizer, Stemline, and Takeda; Data monitoring committees, AbbVie and Rafael Pharmaceuticals; **JA:** consulting or advisory role for Gilead Sciences, Kymera, AbbVie, Amgen, Astellas, Bluebird Bio, Curio Sciences, Daiichi-Sankyo, Kura Oncology, Stemline, Syros, and Theradex; has participated in speakers' bureaus for PeerView, prIME Oncology, and the France Foundation; has served as a member of a data safety and monitoring committee for GlycoMimetics; and has received research funding from ALX Oncology, Amgen, Aptea, Astellas, Aprea, BioSight, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Fujifilm, Immunogen, Kartos, Kura Oncology, Loxo, and Takeda (as of 11/22); **PM:** Speaker's Bureau: Astellas, Novartis, Janssen: Consultancy: Celgene, Pfizer, Abbvie; Ressearch Funding: Pfizer, Abbvie, Daiichi Sankyo; **SD:** Consultancy, Servier; Daiichi Sankyo, Pfizer, , Astellas, Agios, Celgene, Novartis, Fate, Pierre, Bayer, Syros, Abbvie; Honoraria: Daiichi Sankyo Astellas, Forma, Agios, Pierre, Janssen, Seattle Genetics; Speakers Bureau: Celgene; Research funding: Forma, Agios; **RW:** Consultancy: Amgen, Argenx, Genentech, Astellas, Jazz, BioLineRx, BVictrix, Boston Biomedical, Celgene, Daiichi, Aptevo, Agios, New Link Genetics, Kite, Race Oncology, Pfizer; Research Funding: Amgen, Ang, ImmunoGen, Jazz, BioLineRx, Celgene, Aptevo, Pfizer, Macrogenics, Selvita, Seattle Genetics, StemLine, Agios; Current equity holder in publicly-traded company; Amphivena; **KP:** Other: advisory board, CTI Biopharma, PharmaEssentia, Kura Oncology; **SS:** Consulting or Advisory Role: Tolero Pharmaceuticals, Boehringer Ingelheim, Astellas Pharma, Novartis, Jazz Pharmaceuticals, Kite Pharma, Pfizer Research Funding: Sunesis Pharmaceuticals (Inst), Boehringer Ingelheim (Inst), Daiichi Sankyo (Inst), Astellas Pharma (Inst), Karyopharm Therapeutics (Inst), Celgene (Inst), AbbVie (Inst), Celator Pharmaceuticals/Jazz Pharmaceuticals (Inst), Novartis (Inst), Menarini (Inst); **MP:** Board of director/advisory committee: Stemline; research funding: Kura Oncology; **MK:** Honoraria: Constellation Pharmaceuticals, Protagonist Therapeutics, Incyte, AbbVie, CTI BioPharma Corp; Consulting or Advisory Role: Protagonist Therapeutics, Constellation Pharmaceuticals, Incyte, AbbVie, CTI BioPharma Corp; **MB:** Research Funding: AbbVie (Inst), Forma Therapeutics (Inst), Kite, a Gilead company (Inst), Takeda (Inst), Kura Oncology (Inst), Ascentage Pharma (Inst); **JF:** Consulting or Advisory Role: SERVIER, Bristol Myers Squibb/Celgene, Stemline Therapeutics, Taiho Pharmaceutical, Syros Pharmaceuticals, Sanofi, Certara Inc, Novartis, Pfizer, Revolution Medicines, Revolution Medicines; Research Funding: AbbVie (Inst), Actinium Pharmaceuticals (Inst), Aprea Therapeutics (Inst), Aptose Biosciences (Inst), Boehringer Ingelheim (Inst), H3 Biomedicine (Inst), Kura Oncology (Inst), Seilas Life Sciences (Inst), Takeda (Inst), Trillium Therapeutics (Inst), Xencor (Inst); **GS:** Stock and Other Ownership Interests - Amgen; Bristol-Myers Squibb, Johnson & Johnson; Consulting or Advisory Role - Agios; Celgene; Incyte; Jazz Pharmaceuticals; Novartis; Ono Pharmaceutical; Speakers' Bureau: Amgen; Astellas Pharma; Bristol-Myers Squibb; Jazz Pharmaceuticals; Kite, a Gilead company; Sanofi; Stemline Therapeutics; Research Funding - Abbvie; Actinium Pharmaceuticals; Actuate Therapeutics; Agios; Amgen; Arog; Astellas Pharma; Bristol-Myers Squibb/Celgene; Celator; Constellation Pharmaceuticals; Daiichi Sankyo; Decipherea; Delta-Fly Pharma; ElevateBio; FORMA Therapeutics; Fujifilm; Gamida Cell; Genentech/Roche; Geron; Incyte; Jazz Pharmaceuticals; Karyopharm Therapeutics; Kite, a Gilead company; Mateon Therapeutics; Novartis; Onconova Therapeutics; Ono Pharmaceutical; Pfizer; PrECOG; REGIMMUNE; Samus Therapeutics; Sangamo Bioscience; Sanofi; Seilas Life Sciences; Stemline Therapeutics; Takeda; Tolero Pharmaceuticals; Trovagene; **LA:** Consulting or Advisory Role - Celgene; Novartis; Takeda; Research Funding - Celgene (Inst); **PP:** Consulting or Advisory Role: Jazz Pharmaceuticals, Abbvie, Astellas Pharma, Daiichi Sankyo/Lilly; **JAPS:** Consultancy: Gilead, Novartis, Janssen, Jazz, Alexion; Honoraria: Novartis, Janssen, Gilead, Jazz, Alexion; Membership on an entity's Board of Directors or advisory committees: Novartis, Janssen, Gilead, Jazz, Alexion; Other, Travel, Accommodations, and Expenses, Novartis, Janssen, Gilead, Jazz, Alexion; Research Funding: AbbVie, Pfizer; **MH, CB, OSG, CP;** None; **KN, JMA, MT, DC, ML, SD:** Employees, Kura Oncology; **ATF:** Consulting, Agios, Celgne/BMS, Astellas, Daiichi Sankyo, Takeda, Kura, Amgen, Pfizer, Seattle Genetics, Abbvie, Genentech; Research support, Celgene/BMS and Agios.

ACKNOWLEDGEMENTS

Medical writing and editorial assistance were provided by Cynthia D. Goiello, PharmD, and Courtney Breuel, ELS, of MedVal Scientific Information Services, LLC, and were funded by Kura Oncology, Inc. Medical writing and editorial assistance were also provided by Troy A. Baudino, Ph.D. of Kura Oncology, Inc.

RESULTS

FIGURE 4. ZIFTOMENIB MONOTHERAPY DRIVES DURABLE RESPONSES



- Median DoR was **8.2 months** (95% CI: 1.0 to Not Evaluable) with a median follow up time of 8.8 months
- Patient 1 remained on ziftomenib in CR (MRD-) into Cycle 36
- Patients 9 and 21 proceeded to HSCT
  - Patient 9 remains in complete response on ziftomenib for post-HSCT maintenance
  - Patient 21 remains in complete response

TABLE 4. ZIFTOMENIB CLEARS MEASURABLE RESIDUAL DISEASE (MRD), INCLUDING SUB-CLONES

Local MRD Analysis[a]

- 67% of patients achieving CRc who were tested for MRD (4 of 6) were MRD-negative[b]

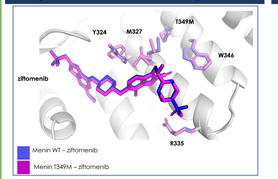
Subject 1: Prior Tx with midostaurin	*NPM1*	*FLT3*-TKD	*IDH1*
	Variant Allele Frequency (%)		
C1 D28	33	33	35
C5 D28	Not detected	Not detected	Not detected

Subject 2: Prior Tx with midostaurin and gilteritinib	*NPM1*	FLT3-ITD	*IDH2*
	Variant Allele Frequency (%)		
C1 D28	47	91	46
C4 D28	0.37	0.87	0.41

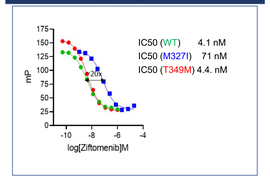
[a]4 patients by multiparameter flow cytometry (MFC), 1 patient by NGS, 1 patient RT-qPCR.
[b]6 of 8 patients who achieved CRc were tested for MRD status (local MRD test).
[c]Mutations detected in MyMRD NGS (Invivoscribe, San Diego, CA).
CRc is defined as achieving best overall response of any of the following: CR, CRh, CRi (including CRp). MRD, measurable residual disease. NGS, Next Generation Sequencing.

FIGURE 5. ZIFTOMENIB IS ACTIVE AGAINST KNOWN MENIN GATEKEEPER MUTATIONS

Crystal Structure of Ziftomenib Binding to Menin



Inhibitory Activity of Ziftomenib



- No major conformational changes observed in Menin^{T349M} vs. wild-type (WT) protein
- M327 and Y324 side chains adopt new conformations in Menin^{T349M} but do not affect ziftomenib binding
- Binding affinity of ziftomenib is reduced for Menin^{M327I} but unaffected for Menin^{T349M}
  - Per Armstrong lab[22], ziftomenib also retains activity against Menin^{G331R}
- Ziftomenib retains activity against 2 of 3 known *MEN1* mutant loci

FIGURE 6. ZIFTOMENIB IS ACTIVE AGAINST KNOWN MENIN GATEKEEPER MUTATIONS

- Following reports of *MEN1* resistance mutations with another menin inhibitor[23], an analysis of KOMET-001 identified 1 of 29 subjects (3.4%) with the resistance mutation (MEN1-M327I) acquired while on ziftomenib[a]



- *MEN1* mutant RNA was not detected in 13 of 13 other subjects who received ≥ 2 cycles of ziftomenib and had best response of SD or PD, suggesting that progression or lack of response in these subjects is not due to *MEN1* mutations
- Ziftomenib's ability to target MEN1 harboring G331R or T349M mutations may in part explain the low frequency of *MEN1* resistance mutations detected in KOMET-001 subjects
- Further analysis is underway to continue to characterize mechanisms of menin resistance

[a]*MEN1* mutant transcripts detected from serial analysis of bone marrow aspirate (BMA) of patients treated with at least 1 cycle of ziftomenib using RNA NGS

CONCLUSIONS

- Ziftomenib demonstrates significant clinical activity with 45% ORR (35% CR rate) and lack of myelosuppression, with maintained count recovery in heavily pretreated R/R *NPM1*-m AML
- Durable remissions with MRD clearance of foundational *NPM1*-m and other key co-mutations, including *FLT3 ITD/TKD* and *IDH1/2*, observed with ziftomenib monotherapy
- Resistance mutations have developed infrequently and ziftomenib retains activity against common menin gatekeeper mutations
- Ziftomenib is well tolerated, with no drug induced QTc and manageable DS; the lack of predicted adverse drug-drug interactions is supportive of combination approaches
- The pivotal KOMET-001 trial is currently recruiting patients with R/R *NPM1*-m AML
- KOMET-007 Phase 1 is open for enrollment (NCT05735184), studying ziftomenib in combination with existing intensive chemotherapy (IC) and non-intensive chemotherapy (NIC) standards of care (SOC) in newly diagnosed and R/R *NPM1*-m or *KMT2A-r* AML

REFERENCES

1. Krivtsov, et al. *Cancer Cell.* 2019;36(6):660-73; 2.Prata, et al. *Haematologica.* 2018;103(10):e455-e7; 3.Klossowski, et al. *J Clin Invest.* 2020;130(2):981-97; 4. Li and Song. *J Hematol Oncol.* 2021;14(1):56; 5. Kühn, et al. *Cancer Discov.* 2016;6(10):1166-81; 6.Matthews, et al. *Cancers (Basel).* 2022;14(23):5906; 7. Surveillance, Epidemiology, and End Results Program. 2023. https://seer.cancer.gov/statfacts/html/amyl.html; 8. Dohner, et al. *Blood.* 2017;129(4):424-47; 9. Angenendt, et al. *J Clin Oncol.* 2019;37(29):2632-42; 10. Venugopal, et al. ASH Abstract 2287, 2021; 11. Issa, et al. *Blood Cancer J.* 2021;11(9):162; 12. Vetro, et al. *Cancer Genet.* 2020;240:15-22; 13. Lu et al. *Cancer Cell* 2016;30(1):92-107; 14. Ferreira et al. *Oncogene* 2016;35(23):3079-82; 15. Jeong et al. *Nat Genet* 2014;46(1):17-23; 16. Wang et al. *Blood* 2005;106(1):254-64; 17. Chowdhury et al. *EMBO Rep* 2011;12(5):463-69; 18. Schmidt et al. *Leukemia* 2019;33(7):1608-19; 19. Xu et al. *Cancer Cell* 2016;30(6):863-78; 20. Collins and Hess. *Curr Opin Hematol* 2016;23(4):354-61; 21. Brunetti et al. *Cancer Cell* 2018; 34(3):499-512; 22. Perner et al. Abstract #3457 presented at AACR April 14-19, 2023, Orlando, FL; 23. Perner et al. Nature 2023; 615(7954):913-19.