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**REVUMENIB + CHEMIOTERAPIA INTENSIVA IN PAZIENTI CON LEUCEMIA MIELOIDE ACUTA
DI NUOVA DIAGNOSI CON ALTERAZIONI GENETICHE DI *KMT2A*, *NPM1* O *NUP98*:
RISULTATI AGGIORNATI DELLO STUDIO DI FASE 1 SNDX-5613-0708**

**REVUMENIB + INTENSIVE CHEMOTHERAPY FOR NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA HARBORING
GENETIC ALTERATIONS IN *KMT2A*, *NPM1*, OR *NUP98*: UPDATED PHASE 1 RESULTS FROM SNDX-5613-0708**

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Disclosures of Cristina Papayannidis

Consultancy

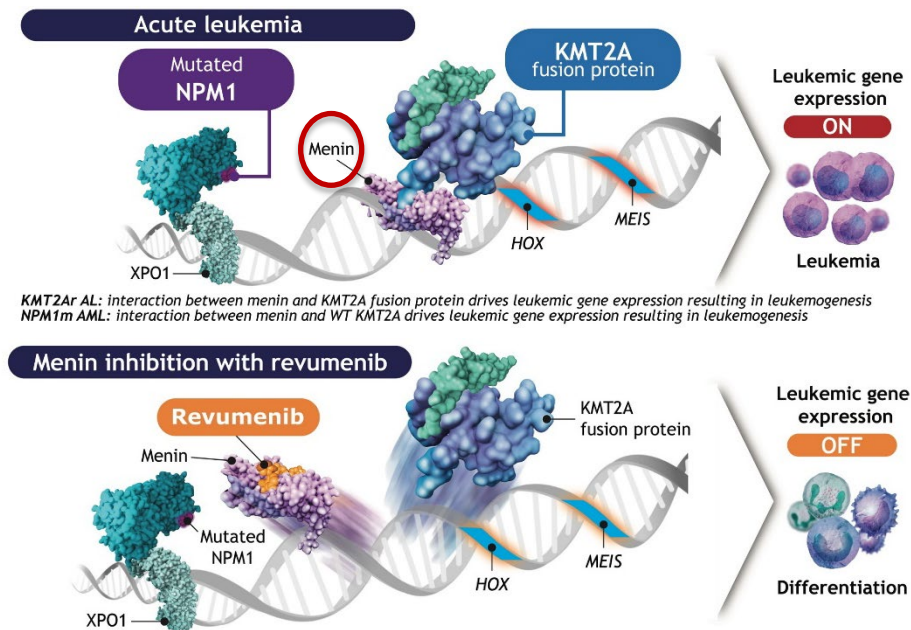
Pfizer, GSK, AbbVie, Delbert Laboratoires, Astellas, Blueprint,
Jazz Pharmaceuticals, Novartis, Janssen

Honoraria

BMS, Menarini/Stemline, Pfizer, AbbVie, Astellas, Amgen,
Novartis, Janssen, Servier

Targeting menin-KMT2A in newly diagnosed AML

- Genetic alterations such as *KMT2Ar* and *NUP98r* promote leukemogenesis and are associated with poor clinical outcomes in acute leukemia¹⁻⁴
- Revumenib, a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction, is used for the treatment of R/R AML harboring an ***NPM1* mutation** or R/R AL with a ***KMT2A* translocation** in adult and pediatric patients ≥1 year^{5,6}
- Adding revumenib to IC may further decrease leukemic cell proliferation and enhance differentiation, improving overall response to treatment



Here we report updated findings from the dose level 1 and 2 cohorts of the dose-escalation portion of the phase 1 study of revumenib + IC in newly diagnosed AML with *NPM1m*, *KMT2Ar*, or *NUP98r*

Study design (NCT06226571)

- Multicenter, open-label, nonrandomized, dose-escalation and -expansion study of revumenib + IC

Phase 1: Revumenib + IC induction, IC and/or HSCT consolidation, and post-consolidation maintenance

Patient eligibility

- 18–75 y of age
- Newly diagnosed *NPM1*m, *KMT2A*r, or *NUP98*r^a AML by WHO 2022 criteria
- ECOG PS score of 0–2 (0 or 1 if >65 y of age)
- Candidate for IC
- <3% *FLT3*-ITD or *FLT3*-TKDm or no plan to receive *FLT3*i

Study schema

Dose escalation^b

DL2^c

Revumenib q12h
160 mg/270 mg
± strong CYP3A4i

DL1

Revumenib q12h
110 mg/220 mg
± strong CYP3A4i

DL (-1)^d

Revumenib q12h
75 mg/160 mg
± strong CYP3A4i

Dose expansion

20 patients each at RP2D

HR *NPM1*m

*KMT2A*r

Treatment overview

Induction
(up to 2 cycles)
Revumenib
(D8–D28) + 7 + 3^e

HiDAC consolidation
(up to 4 cycles)
Revumenib (D6–D26) + HiDAC^f

Eligible^g patients who
achieve remission may
initiate HSCT at any
point after induction
and before completing
4 cycles of HiDAC

HSCT

Revumenib
maintenance
(D1–D28)^h

Until disease
progression
or toxicityⁱ

Endpoints^j

Primary

- Occurrence of DLTs^k
- Frequency and severity of TEAEs, TRAEs, and SAEs^l

Secondary

- PK parameters

Exploratory^m

- CR rate
- CRc rateⁿ
- ORR^o
- TTR
- MRD–negativity rate^p

^aWhile *NUP98* patients were eligible, none had enrolled at time of analysis. ^bStudy uses a “rolling 6” design with a backlog of approximately 6 patients at tolerated doses for a total of 12 evaluable patients per DL. Alternate dosing schedules (eg, 14 days) may be explored. ^cHighest dose not to exceed the RP2D from AUGMENT-101. ^dFor dose escalation only. ^e5 + 2 schedule used in Cycle 2. Chemotherapy doses: cytarabine 100–200 mg/m², idarubicin 12 mg/m², or daunorubicin 60 mg/m². ^fChemotherapy doses: cytarabine 1.5 g/m² (≥60 years of age; Days 1, 3, and 5) or 3.0 g/m² (<60 years of age; Days 1–3 or 1, 3, and 5). ^gPatient must have achieved CR or CRi. ^hPatient must have achieved CR or CRi after ≥3 cycles. Treatment can continue for up to 2 years. ⁱRelevant to the current analysis. ^jDLTs were predefined in the protocol and assessed by investigator per NCI CTCAE v5.0¹; all were reviewed and confirmed by the safety review committee. ^kAEs (differentiation syndrome, grade ≥2 QTcF prolongation, and potential Hy’s Law cases) will also be assessed, though not as a per-protocol primary endpoint. ^lFor response and MRD assessments, bone marrow aspirate was collected following evidence of progressive disease in peripheral blood. ^mCRc = CR + CRi. ⁿORR = CRc + MLFS. ^oAssessed locally. ^pAEs, adverse event of special interest; CR, complete remission; CRc, composite CR; CRi, CR with incomplete hematologic recovery; CTCAE v5.0, Common Terminology Criteria for Adverse Events v5.0; CYP3A4i, cytochrome P450 3A4 inhibitor; D, day; DL, dose level; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; FLT3i, FLT3 inhibitor; HiDAC, high-dose cytarabine; HR, high-risk; IC, intensive chemotherapy; ITD, internal tandem duplication; MLFS, morphologic leukemia-free state; MRD, measurable residual disease; NCI, National Cancer Institute; ORR, overall response rate; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TKDm, tyrosine kinase domain mutation; TRAE, treatment-related adverse event; TTR, time to response; WHO, World Health Organization.

Demographics

Characteristic	DL1 (n = 15)	DL2 (n = 20)	Total (N = 35)
Age, median (range), y	43.0 (20.0–73.0)	57.5 (19.0–68.0)	50.0 (19.0–73.0)
Female, n (%)	10 (67)	16 (80)	26 (74)
Race, n (%)			
White	10 (67)	17 (85)	27 (77)
Black or African American	1 (7)	0	1 (3)
Asian	2 (13)	1 (5)	3 (9)
Not reported	2 (13)	1 (5)	3 (9)
Other	0	1 (5)	1 (3)
Ethnicity, not Hispanic, n (%)	11 (73)	19 (95)	30 (86)

Characteristic	DL1 (n = 15)	DL2 (n = 20)	Total (N = 35)
ECOG PS score, n (%)			
0	8 (53)	8 (40)	16 (46)
1	4 (27)	12 (60)	16 (46)
2	3 (20)	0	3 (9)
Genetic aberration, n (%)			
<i>NPM1</i> m	2 (13)	12 (60)	14 (40)
<i>KMT2A</i> r	13 (87)	8 (40)	21 (60)
Co-occurring mutations, n (%) ^a			
<i>FLT3</i> -ITD (allelic ratio of <3% <i>FLT3</i> -ITD/total <i>FLT3</i>)	0	3 (15)	3 (9)
<i>FLT3</i> -TKDm (no plan for <i>FLT3</i> -targeted therapy)	1 (7)	0	1 (3)

- As of 30 November 2025, 15 patients were dosed at DL1 and 20 were dosed at DL2

^aNo *NUP98*r patients were enrolled. No other co-occurring mutations were planned for detection.

DL, dose level; ECOG PS, Eastern Cooperative Oncology Group performance status; ITD, internal tandem duplication; *KMT2A*r, *KMT2A* rearranged; *NPM1*m, *NPM1* mutated; TKDm, tyrosine kinase domain mutation.

Safety: treatment-emergent AEs

Parameter, n (%)	DL1 (n = 15)		DL2 (n = 20)		Total (N = 35)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TEAE^a	14 (93)	13 (87)	20 (100)	19 (95)	34 (97)	32 (91)
Thrombocytopenia/platelet count decreased ^b	8 (53)	7 (47)	13 (65)	13 (65)	21 (60)	20 (57)
Febrile neutropenia	8 (53)	8 (53)	13 (65)	11 (55)	21 (60)	19 (54)
Diarrhea	6 (40)	0	13 (65)	1 (5)	19 (54)	1 (3)
Neutropenia/neutrophil count decreased ^b	8 (53)	7 (47)	9 (45)	9 (45)	17 (49)	16 (46)
Nausea	6 (40)	0	7 (35)	0	13 (37)	0
Anemia	4 (27)	4 (27)	7 (35)	7 (35)	11 (31)	11 (31)
Hypokalemia	3 (20)	0	8 (40)	4 (20)	11 (31)	4 (11)
Vomiting	4 (27)	1 (7)	6 (30)	0	10 (29)	1 (3)
Hypophosphatemia	4 (27)	0	5 (25)	0	9 (26)	0
White blood cell count decreased	4 (27)	4 (27)	4 (20)	4 (20)	8 (23)	8 (23)

- Rates of thrombocytopenia were not unexpected for a population receiving IC

Safety: revumenib-related treatment-emergent AEs

Parameter, n (%)	DL1 (n = 15)		DL2 (n = 20)		Total (N = 35)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Revumenib-related TEAEs^a	10 (67)	5 (33)	13 (65)	12 (60)	23 (66)	17 (49)
Anemia	3 (20)	3 (20)	3 (15)	3 (15)	6 (17)	6 (17)
Thrombocytopenia ^b	2 (13)	1 (7)	3 (15)	3 (15)	5 (14)	4 (11)
Platelet count decreased ^b	2 (13)	2 (13)	2 (10)	1 (5)	4 (11)	3 (9)
Neutropenia ^b	1 (7)	1 (7)	3 (15)	2 (10)	4 (11)	3 (9)
Neutrophil count decreased ^b	4 (27)	3 (20)	2 (10)	2 (10)	6 (17)	5 (14)
QTcF prolongation ^c	3 (20)	1 (7)	5 (25)	2 (10)	8 (23)	3 (9)

- 1 DLT of grade 3 QTcF prolongation was reported in DL1; the patient discontinued revumenib during Cycle 1 and achieved MRD–negative CR at the end of Cycle 1 and proceeded to HSCT

Safety: serious TEAEs and TEAEs of special interest

Parameter, n (%)	DL1 (n = 15)	DL2 (n = 20)	Total (N = 35)
Serious TEAEs^a	7 (47)	10 (50)	17 (49)
Febrile neutropenia	3 (20)	2 (10)	5 (14)
Sepsis	1 (7)	2 (10)	3 (9)
Gastroenteritis viral	1 (7)	1 (5)	2 (6)
Pneumonia	2 (13)	0	2 (6)
TEAEs of special interest	3 (20)	5 (25)	8 (23)
QTcF prolongation ^b	2 (13)	4 (20)	6 (17)
Differentiation syndrome	0	1 (5)	1 (3)
ALT increased	1 (7)	0	1 (3)
TEAEs leading to dose modifications			
Interruption	7 (47)	12 (60)	19 (54)
Reduction	2 (13)	0	2 (6)
TEAEs leading to discontinuation^c	3 (20)	1 (5)	4 (11)
TEAEs leading to death^d	0	1 (5)	1 (3)

- Rate of patients who experienced QTcF prolongation was similar across both DLs; these AEs were manageable per protocol guidance
- Rate of patients who experienced differentiation syndrome was low, occurring only in 1 patient in DL2, and was manageable per protocol guidance
- Rate of patients who experienced ALT increased was low, occurring only in DL1
- No discontinuations were due to thrombocytopenia

Exposure and pharmacokinetics

Summary of revumenib exposure

Parameter, median (range)	DL1 (n = 15)	DL2 (n = 20)
Duration of follow-up, mo	4.8 (1.5–16.0)	2.9 (0.7–6.2)
No. of revumenib cycles received	3 (1–8)	2 (1–5)
Relative dose intensity	89.3% (56.3–104.8)	92.5% (19.1–160.7)

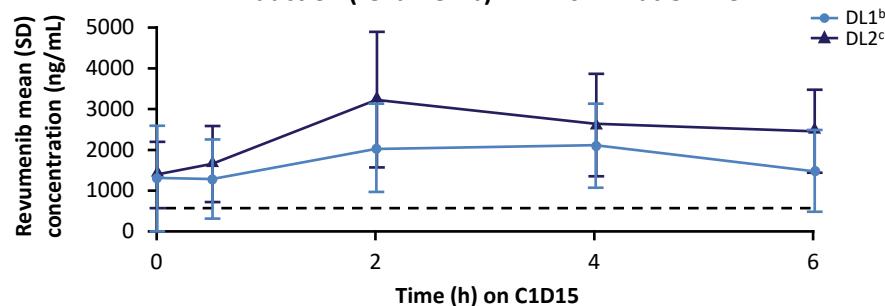
- Pharmacokinetic profiles of revumenib combination therapy in this study are consistent with those in the AUGMENT-101 monotherapy study¹
- Drug concentrations exceeded the concentration resulting in the IC₉₀ threshold at both DL1 and DL2, indicating potential for effective antileukemic activity through sustained menin inhibition

Summary of steady-state^a PK parameters of plasma revumenib

Parameter, GM (% GCV)	DL1 ^b (n = 8)	DL2 ^c (n = 13)
C _{max} , ng/mL	2710 (31)	3250 (46)
C _{avg} , ng/mL	1690 (55)	2410 (45)
AUC, ng·h/mL	10,100 (55)	14,400 (45)

Revumenib plasma concentration at steady state^a

Induction (revumenib): DL1 vs DL2 at C1D15



^aC1D15 (induction phase). ^bRevumenib was given twice daily at 110 or 220 mg with or without a strong CYP3A4i, respectively. ^cRevumenib was given twice daily at 160 or 270 mg with or without a strong CYP3A4i, respectively.

Efficacy: response^a

Parameter, n (%)	DL1 (n = 15)	DL2 (n = 20)	Total (N = 35)
ORR,^b n (%)	15 (100)	19 (95.0)	34 (97.1)
95% CI	78.2–100.0	75.1–99.9	85.1–99.9
CRc rate,^c n (%)	15 (100)	19 (95.0)	34 (97.1)
95% CI	78.2–100.0	75.1–99.9	85.1–99.9
CR rate, n (%)	12 (80.0)	15 (75.0)	27 (77.1)
95% CI	51.9–95.7	50.9–91.3	59.9–89.6
Time to CR, median (range), d	21.0 (18.0–35.0)	26.0 (18.0–70.0)	23.0 (18.0–70.0)
MRD–negative status,^{d,e} n/N (%)			
CRc	10/12 (83.3)	15/17 (88.2)	25/29 (86.2)
CR	9/9 (100)	11/14 (78.6)	20/23 (87.0)
Time to MRD–negative status, median (range), d			
CRc	31.0 (28.0–65.0)	46.0 (28.0–77.0)	33.0 (28.0–77.0)
CR	31.0 (28.0–65.0)	34.0 (28.0–77.0)	31.5 (28.0–77.0)

HSCT and maintenance

- 9/15 (60.0%) patients in DL1 and 2/20 (10.0%) in DL2 had proceeded to HSCT
- All patients who proceeded to HSCT had *KMT2Ar* AML; of these:
 - 6/9 (66.7%) patients in DL1 resumed revumenib maintenance monotherapy following HSCT at the last tolerated dose
 - 3/6 (50.0%) were continuing treatment as of the data cutoff
- One patient in DL2 received revumenib as post-consolidation maintenance therapy without undergoing HSCT

^aAmong the response-evaluable population. ^bORR = CRc + MLFS. ^cCRc = CR + CRi. ^dFor patients who had available MRD–negativity results in the response-evaluable population. ^eMRD–negative status determined locally: DL1 (flow cytometry: n = 10; PCR: n = 1; NGS: n = 1); DL2 (flow cytometry: n = 13; PCR: n = 3; other: n = 1).



Efficacy: neutrophil and platelet recovery

Neutrophil and platelet recovery among CRc responders during induction Cycle 1

	DL1 (n = 15)	DL2 (n = 19)	Total (N = 34)
Neutrophil recovery (≥ 1000 cells/μL),^a n (%)	13 (86.7)	15 (78.9)	28 (82.4)
Time to count recovery, median (range), d	29.0 (8.0–42.0)	29.0 (22.0–55.0)	29.0 (8.0–55.0)
Platelet recovery ($\geq 100,000$ cells/μL),^a n (%)	13 (86.7)	17 (89.5)	30 (88.2)
Time to count recovery, median (range), d	28.0 (22.0–43.0)	29.0 (22.0–47.0)	29.0 (22.0–47.0)

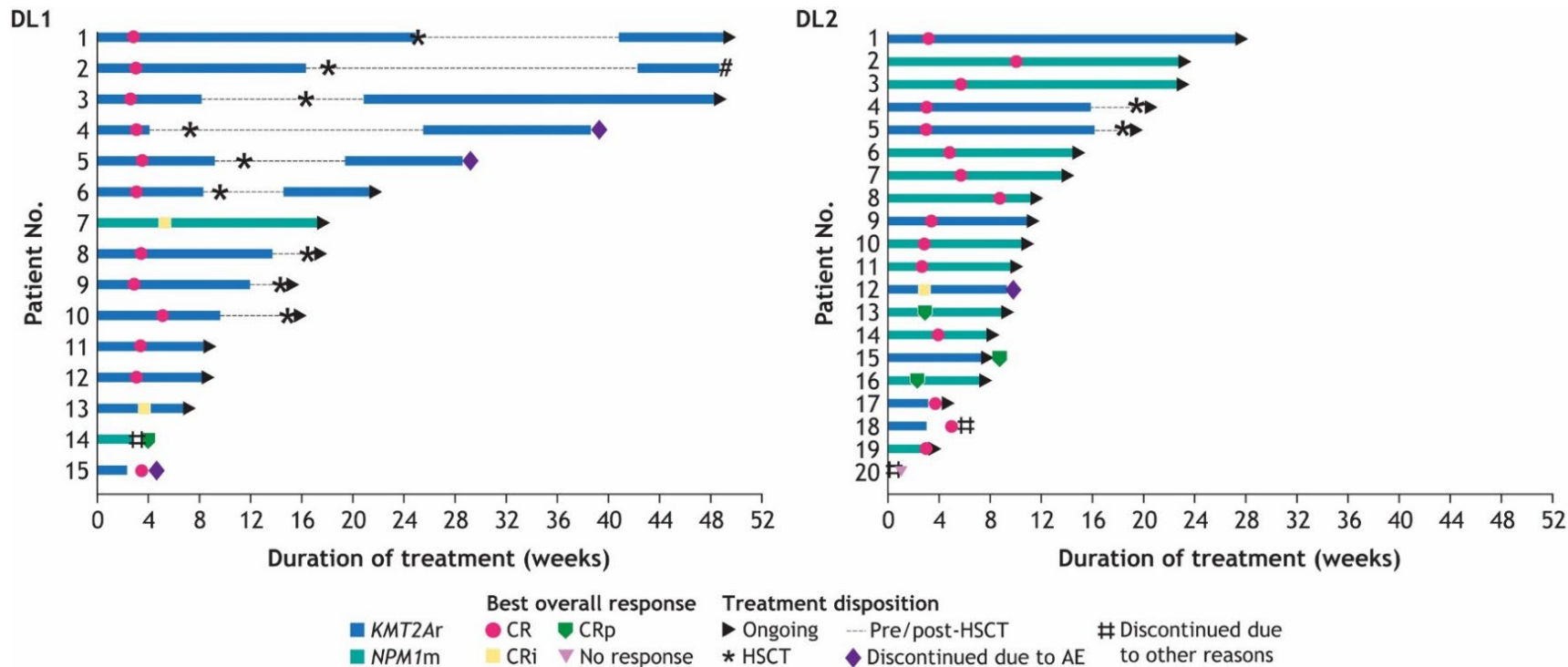
- Time to neutrophil and platelet count recovery was comparable across DLs and consistent with time to count recovery with IC alone^{1,2}

^aFrom Induction Cycle 1 Day 1.

CRc, composite complete remission; DL, dose level; IC, intensive chemotherapy.

1. Stone RM, et al. *N Engl J Med.* 2017;377(5):454–464. 2. Lancet JE, et al. *J Clin Oncol.* 2018;36(26):2684–2692.

Efficacy: duration of treatment in *NPM1*m and *KMT2A*r AML^a



^aIn the safety population.
CR, complete remission; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; DL, dose level; *KMT2A*r, *KMT2A* rearranged; *NPM1*m, *NPM1* mutated.

Conclusions



Efficacy

- These updated preliminary efficacy data as of 30 November 2025 build upon findings showing deep responses across both DLs, with high MRD–negative CR rates



Safety

- Revumenib + IC continued to demonstrate a manageable safety profile that was broadly consistent across both DLs and comparable with IC alone¹
- No new safety signals were detected for revumenib + IC, and no overlapping toxicity with combination use was observed
- Time to neutrophil and platelet recovery was comparable to that of IC alone^{2,3}



Next Steps

Overall, these safety and efficacy findings are consistent in patients with *NPM1m* and *KMT2Ar* AML and support continued evaluation of revumenib + IC at DL2 in the phase 3 REVEAL-ND NPM1 trial (NCT07211958)

REVEAL-ND NPM1: a phase 3, randomized, double-blind trial in newly diagnosed AML (open to enrollment)

REVEAL-ND NPM1

Revumenib + IC in newly diagnosed *NPM1m* AML

Patient population (N ≈ 468)

- Age ≥12 years and ≥40 kg
- Newly diagnosed, untreated AML
- *NPM1m* AML (locally determined, centrally confirmed)

Randomize 1:1

Induction (1-2 cycles)

Revumenib

+ IC

Consolidation (1-3 cycles)

Revumenib

+ cytarabine

(Double-blind treatment)

Placebo

+ IC

Placebo

+ cytarabine

HSCT
(optional)

Patients may undergo HSCT after initial induction chemo or after consolidation

Monotherapy continuation

Revumenib

Survival follow-up

Placebo

Treatment for up to 2 years (from Cycle 1, Day 1)

Primary endpoints

- EFS
- MRD– CR

Secondary endpoints

- OS
- CR
- ORR
- DoCR
- DoCRc
- DoR
- QoL

REVEAL-ND NPM1



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