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CPX-351 Versus Standard of Care as Bridging to AlloHCT in Patients With Higher-Risk Myelodysplastic Neoplasms or Oligoblastic Acute Myeloid Leukemia: Results of the Randomized Phase 2 PALOMA Study

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Objective

- To compare the efficacy and safety of CPX-351 and CCR before alloHCT as first-line treatment in patients with HR-MDS or oligoblastic AML

Conclusions

- PALOMA is the first trial comparing CPX-351 versus standard of care as bridge to alloHCT in patients with HR-MDS/oligoblastic AML
- Included were patients with HR-MDS and oligoblastic AML (bone marrow blast counts ≥5% and ≤29%) scheduled for alloHCT
  - Blast counts were assessed by central morphology
  - Patients with mutations associated with *de novo* AML, including *NPM1*, and favorable cytogenetic alterations such as t(15;17), inv(16), and t(8;21) were excluded at screening
- AlloHCT rate was high and comparable in both treatment arms
- The final analysis for the primary endpoint of the PALOMA study shows that CPX-351 significantly improves EFS compared with CCR in patients with HR-MDS or oligoblastic AML scheduled for alloHCT
  - Likely caused by a higher proportion of patients achieving morphologic blast clearance prior to planned alloHCT
- At interim analysis median OS was not reached for the CPX-351 arm compared with 35.4 months for the CCR arm
  - Final analysis will be available in September 2026
- No new safety signals were observed for CPX-351
- Measurable residual disease (MRD) data are not yet available
  - Prior data suggest that treatment with CPX-351 is associated with achievement of MRD negativity among older patients with high-risk AML and that MRD negativity may contribute to improved OS in patients treated with CPX-351 compared to CCR[7,8]
- These findings support the use of CPX-351 as a bridge to alloHCT in patients with HR-MDS or oligoblastic AML

Background

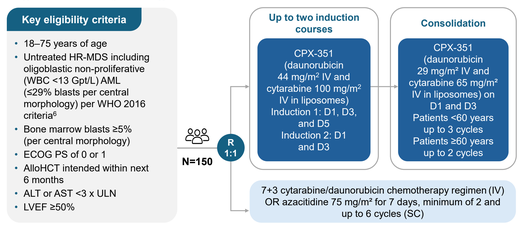
- AlloHCT remains the only potentially curative treatment option for patients with higher risk myelodysplastic neoplasms (HR-MDS) or oligoblastic acute myeloid leukemia (AML)[1,2]
- Hypomethylating agents, such as azacitidine, or conventional induction chemotherapy are commonly used as a bridge from diagnosis to alloHCT[3]
- There is a need for alternative bridging strategies that result in higher response rates and more durable responses, with manageable toxicity, thus enabling more patients to proceed to alloHCT with more favorable longer-term outcomes[3,4]
- CPX-351 is a liposomal formulation of daunorubicin and cytarabine at a fixed ratio, and has previously demonstrated benefits in patients with MDS-related mutations compared with conventional induction chemotherapy regimens[4]

Methods

PALOMA (**P**rimary comp**A**rison of **L**ipos**O**mal anthracycline based treatment versus conventional care strategies prior to allogeneic stem cell transplantation in patients with higher risk **M**DS or oligoblastic **A**ML)

A phase 2, multicenter, randomized open-label, study of CPX-351 versus CCR as first-line treatment before alloHCT (NCT04061239)[5]

Figure 1. Study Design



Key exclusion criteria

- History of MPN* or combined MDS/MPN
- WHO-2016 defined AML entities: t(15;17), *PML-RARA*; t(8;21), *RUNX1-RUNX1T1*; inv(16)/t(16;16), *CBFB-MYH11*; biallelic *CEBPA* mutation; or mut *FLT3* or *NPM1*
- Active CNS leukemia
- Currently active† secondary malignancy (except NMSC)

Endpoints

- **Primary endpoint:** Data cutoff for final analysis Sept 30, 2025
  - EFS defined as time from randomization to primary refractory disease, relapse, death from any cause, or treatment change
- **Secondary endpoints:** Data cutoff for pre-planned interim analysis Sept 30, 2025; final Sept 2026
  - OS (key secondary)
  - Best and overall response rate, proportion of patients proceeding to alloHCT, MRD, QoL, and safety

*Defined as a history of essential thrombocytosis, polycythemia vera, or idiopathic myelofibrosis prior to the diagnosis of AML. †Patients who have completed therapy and are considered by their physician to be at ≥30% risk of relapse within 1 year.

alloHCT, allogeneic hematopoietic cell transplantation; ALT, alanine aminotransferase; AML, acute myeloid leukemia; AST, aspartate aminotransferase; CPX-351, liposomal daunorubicin and cytarabine; CNS, central nervous system; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; HR-MDS, higher-risk myelodysplastic neoplasms; inv, inversion; IV, intravenous; LVEF, left ventricular ejection fraction; MDS, myelodysplastic neoplasms; MPN, myeloproliferative neoplasms; MRD, minimal residual disease; NMSC, non-melanoma skin cancer; OS, overall survival; QoL, quality of life; R, randomized; SC, subcutaneous; t, translocation; ULN, upper limit of normal; WBC, white blood cell; WHO, World Health Organization.

Results

- Baseline characteristics were generally well balanced between the treatment arms
- The CCR arm included 52 patients (69.3%) treated with 7+3 cytarabine/daunorubicin and 23 patients (30.7%) treated with azacitidine

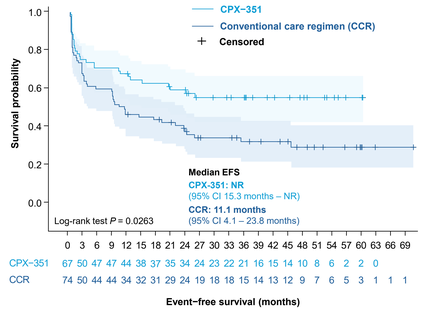
Table 1. Baseline Characteristics

	Total (n = 150)	CPX-351 (n = 75)	CCR (n = 75)
Sex, n (%)			
Male	92 (61.3)	41 (54.7)	51 (68.0)
Female	58 (38.7)	34 (45.3)	24 (32.0)
Age, median (range) years	63 (31–75)	64 (41–75)	63 (31–73)
Age ≥60 years, n (%)	**97 (64.7)**	48 (64.0)	49 (65.3)
WHO classification, n (%)			
AML/myeloid sarcoma	31 (20.7)	16 (21.3)	15 (20.0)
MDS	**117 (78.0)**	59 (78.7)	58 (77.3)
Missing	2 (1.3)	0	2 (2.7)
BM blast counts, n (%)			
<20%	116 (77.3)	58 (77.3)	58 (77.3)
20%–30%	34 (22.7)	17 (22.7)	17 (22.7)
ECOG PS, n (%)			
0	78 (52.0)	40 (53.3)	38 (50.7)
1	72 (48.0)	35 (46.7)	37 (49.3)
Cytogenetics, n (%)			
Complex	**42 (28.0)**	20 (26.7)	22 (29.3)
Non-complex	100 (66.7)	54 (72.0)	46 (61.3)
Missing/not performed	8 (5.3)	1 (1.3)	7 (9.3)
IPSS score, n (%)			
Intermediate-1	6 (4.0)	3 (4.0)	3 (4.0)
Intermediate-2	**77 (51.3)**	38 (50.7)	39 (52.0)
High	**59 (39.3)**	30 (40.0)	29 (38.7)
Missing	8 (5.3)	4 (5.3)	4 (5.3)
Sorror score, median (range)	1 (0–9)	1 (0–9)	0.5 (0–6)

AML, acute myeloid leukemia; BM, bone marrow; CCR, conventional care regimen; CPX-351, liposomal daunorubicin and cytarabine; ECOG PS, Eastern Cooperative Oncology Group performance status; IPSS, International Prognostic Scoring System; MDS, myelodysplastic neoplasms; WHO, World Health Organization.

Figure 2. Event-Free Survival

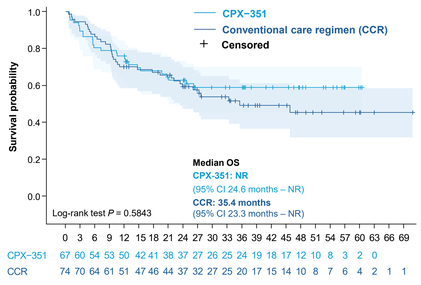
Median EFS was significantly longer with CPX-351 compared to CCR



CCR, conventional care regimen; CI, confidence interval; CPX-351, liposomal daunorubicin and cytarabine; EFS, event-free survival; NR, not reached.

Figure 3. Overall Survival

In the Interim analysis, median OS did not differ significantly between the CPX-351 and CCR treatment arms



CCR, conventional care regimen; CI, confidence interval; CPX-351, liposomal daunorubicin and cytarabine; NR, not reached; OS, overall survival.

Table 2. Event-Free Survival by Event Type

Less events were observed in the CPX-351 (n = 29, 43.3%) than in the CCR arm (n = 50, 67.6%)

Disease refractory to study treatment was less frequent with CPX-351 (n = 8, 11.9%) than with CCR (n = 17, 23.0%)

	Total (n = 141)	CPX-351 (n = 67)	CCR (n = 74)
Patients with an event, n (%)	79 (56.0)	**29 (43.3)**	**50 (67.6)**
Discontinued treatment, n (%)	7 (5.0)	3 (4.5)	4 (5.4)
Refractory disease to study treatment, n (%)	25 (17.7)	**8 (11.9)**	**17 (23.0)**
Relapse after alloHCT, n (%)	16 (11.3)	6 (9.0)	**10 (13.5)**
Death, n (%)	31 (22.0)	12 (17.9)	**19 (25.7)**

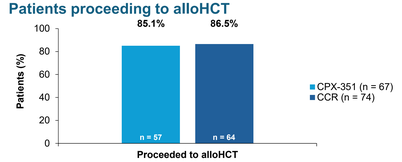
alloHCT, allogeneic hematopoietic cell transplantation; CCR, conventional care regimen; CPX-351, liposomal daunorubicin and cytarabine.

Figure 4. Treatment Cycles and Patients Proceeding to AlloHCT

The proportion of patients proceeding to alloHCT did not differ significantly between the CPX-351 and CCR treatment arms

	Total (n = 141)	CPX-351 (n = 67)	CCR (n = 74)
Number of started cycles, median (range)	1 (1–4)	1 (1–2)	1.5 (1–4)
Days from randomization to alloHCT, median (range)	81 (39–222)	77 (43–157)	89 (39–222)

Patients proceeding to alloHCT



alloHCT, allogeneic hematopoietic cell transplantation; CCR, conventional care regimen; CPX-351, liposomal daunorubicin and cytarabine.

Table 3. Overall and Best Response

74 patients (52.5%) achieved a blast clearance, which was more frequent with CPX-351 (n = 47, 70.1%) versus CCR (n = 27, 36.5%)

	Total (n = 141)	CPX-351 (n = 67)	CCR (n = 74)
Overall response rate, n (%) (CR + CRi + PR + HI)	**16 (11.3)**	5 (7.5)	11 (14.9)
Blast clearance (CR+ CRi + MLFS)	**74 (52.5)**	**47 (70.1)**	**27 (36.5)**
Best response, n (%)			
Complete remission	6 (4.3)	2 (3.0)	4 (5.4)
Complete remission with incomplete hematologic recovery	6 (4.3)	3 (4.5)	3 (4.1)
Partial remission	2 (1.4)	0	2 (2.7)
Hematologic improvement	2 (1.4)	0	2 (2.7)
Morphologic leukemia-free state	**62 (44.0)**	**42 (62.7)**	20 (27.0)
Stable disease	**40 (28.4)**	13 (19.4)	**27 (36.5)**
Primary refractory disease/progressive disease/relapse	19 (13.5)	6 (9.0)	13 (17.6)
Missing	4 (2.8)	1 (1.5)	3 (4.1)

Response was assessed per protocol:

- For CPX-351 and IC (CCR) on D21 after C1 and - in case of a second induction - on D57
- For AZA (CCR) on D57 (after C2) and – in case of additional cycles – D113 (after C4) and D169 (after C6)

AZA, azacitidine; C, cycle; CCR, conventional care regimen; CPX-351, liposomal daunorubicin and cytarabine; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; D, day; HI, hematologic improvement; IC, induction chemotherapy; MLFS, morphologic leukemia-free state; PR, partial remission.

Table 4. Safety

No new safety signals for CPX-351 were seen

	CPX-351 (n = 75)	CCR (n = 75)
AE (grade ≥3), n (%)	**71 (94.7)**	**67 (89.3)**
SAE, n (%)	**20 (26.7)**	**21 (28.0)**
Most common grade ≥3 AEs,* n (%)		
Thrombocytopenia	65 (86.7)	55 (73.3)
Leukopenia	55 (73.3)	46 (61.3)
Febrile neutropenia	44 (58.7)	35 (46.7)
Anemia	29 (38.7)	31 (41.3)
Neutropenia	7 (9.3)	10 (13.3)
Pneumonia	**20 (26.7)**	9 (12.0)
Sepsis	**15 (20.0)**	9 (12.0)
Pyrexia	12 (16.0)	9 (12.0)
Bacteriaemia	**8 (10.7)**	5 (6.7)
AEs leading to death, n (%)†	**6 (8.0)**	**6 (8.0)**

*Affecting >10% of patients in either treatment arm. †Grade 5 severe adverse events.
AE, adverse event; CCR, conventional care regimen; CPX-351, liposomal daunorubicin and cytarabine; SAE, serious adverse event.

Median follow-up time at data cutoff: 38 months. While the analysis of the primary endpoint is final, all other results are interim and therefore may still be subject to change. Efficacy endpoints were evaluated in the full analysis set (FAS) = all randomized patients excluding patients without informative data for EFS assessment, n = 141.

Abbreviations: alloHCT, allogeneic hematopoietic cell transplantation; **AML**, acute myeloid leukemia; **CCR**, conventional care regimen; **CPX-351**, liposomal daunorubicin and cytarabine; **EFS**, event-free survival; **HR-MDS**, higher-risk myelodysplastic neoplasms; **MDS**, myelodysplastic neoplasms; **MRD**, measurable residual disease; **OS**, overall survival.

References: 1. Hellström-Lindberg ES, Kröger N. *Blood*. 2023;142:2268–2281; **2**. Greco R, et al. *Bone Marrow Transplant*. 2025;60(11):1499-1525; **3**. Stempel J, et al. *Cancers*. 2025;17:2469; **4**. Othman J, et al. *Blood Adv*. 2023;7:4539–4549; **5**. ClinicalTrials.gov ID NCT04061239. https://clinicaltrials.gov/study/NCT04061239. Accessed May 8, 2026; **6**. Arber DA, et al. *Blood*. 2016;127:2391–2405; **7**. Plesa A, et al. *Leuk Res*. 2021;111:106673; **8**. Cluzeau T, et al. *Blood Adv*. 2021;9(4):752–758.

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