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Real-World Experience With CPX-351 Treatment for Acute Myeloid Leukemia in England: Updated Analysis of the Cancer Analysis System Database

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Background

- As of 2018, the National Institute for Health Care Excellence (NICE) and European Medicines Agency (EMA) have recommended the use of CPX-351, a dual-drug liposomal encapsulation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio, for adults with newly diagnosed, therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC)[1,2]
- The recommendation from the NICE and EMA was based on the primary analysis of the pivotal phase 3 trial conducted in adults aged 60-75 years with newly diagnosed, high-risk/secondary AML[1,3,4]
  - After a median follow-up of 20.7 months, CPX-351 significantly improved overall survival (OS) vs conventional 7+3 chemotherapy; Kaplan-Meier (KM) estimates of 1-year and 2-year OS were 41.5% vs 27.6% and 31.1% vs 12.3%, respectively[3]
  - At a median follow-up of 60.9 months, improved OS with CPX-351 vs 7+3 was maintained, with higher 3-year (21% vs 9%) and 5-year (18% vs 8%) KM estimates of OS with CPX-351 vs 7+3[4]
  - The overall safety profile of CPX-351 was consistent with the known safety profile of 7+3[3]
- As the pivotal trial only included patients aged 60-75 years, we previously conducted a retrospective population-based cohort study in England (data cutoff date of March 31, 2022) to characterize clinical outcomes with CPX-351 outside of a clinical trial setting and in a broader patient population, including younger adult patients (aged <60 years), who were treated in everyday clinical practice[5]
  - This study provided real-world evidence of the effectiveness of CPX-351 in both younger (<60 years) and older adults (≥60 years) with AML

Objective

- This analysis reports updated data (up to ~4 years) on longer-term real-world survival outcomes in adult patients with AML who received CPX-351 in routine clinical practice in England

Methods

- This study included adults (aged ≥18 years) with AML who were treated with CPX-351 in a real-world setting in England between January 1, 2013, and June 30, 2023
  - Patients receiving CPX-351 as part of a clinical trial were excluded from the study
- Patient records were sourced from England's Cancer Analysis System (CAS) database, available through the National Cancer Registration and Analysis Service
  - Electronic medical records from the Cancer Outcomes and Services Dataset (COSD) and COSD-linked Hospital Episode Statistics (HES) inpatient secondary care were used to identify patient diagnoses
  - HES inpatient and outpatient care data were used to identify hematopoietic cell transplantation (HCT)
  - Systemic anticancer treatment (SACT) and radiotherapy information were provided via the SACT dataset and radiotherapy dataset
- OS was estimated from the diagnosis date and landmarked from the HCT date
  - Patients were censored on the last day of disease assessment or hematology assessment
  - Survival probabilities were estimated using the KM method

Results

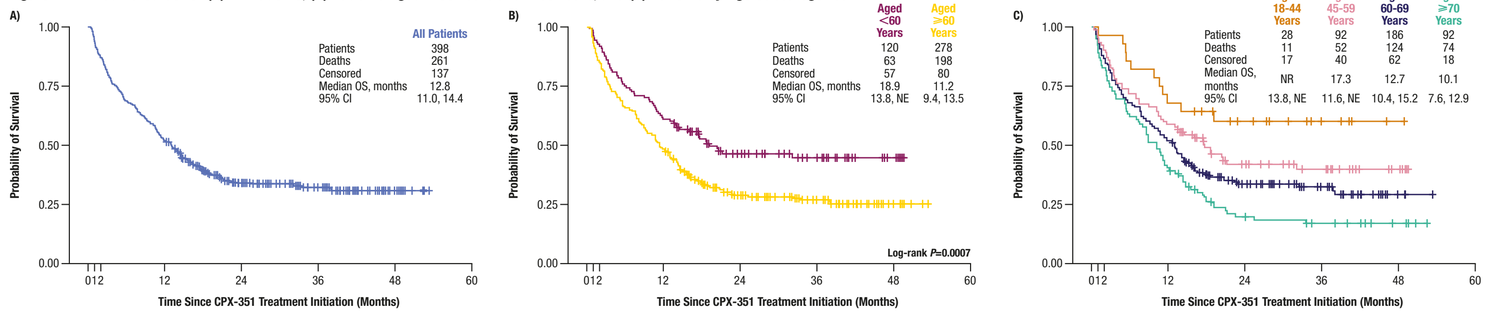
Table 1. Patient Demographic and Clinical Characteristics

	All Patients (N=398)	Aged <60 Years (n=120)	Aged ≥60 Years (n=278)
Age at Diagnosis, Years			
Mean (SD)	62 (10)	50 (10)	67 (4)
Median (IQR)	64 (58-69)	54 (45-57)	67 (64-70)
Age Categories at Diagnosis (Years), n (%)			
18-44	28 (7)	28 (23)	-
45-59	92 (23)	92 (77)	-
60-69	186 (47)	-	186 (67)
70-74	78 (20)	-	78 (28)
≥75	14 (4)	-	14 (5)
Sex, n (%)			
Female	148 (37)	58 (48)	90 (32)
Male	250 (63)	62 (52)	188 (68)
Ethnicity, n (%)			
White	346 (87)	96 (80)	250 (90)
Asian	24 (6)	13 (11)	11 (4)
Other	28 (7)	11 (9)	17 (6)
AML Subtype, n (%)			
t-AML	117 (29)	30 (25)	87 (31)
AML with a prior MDS or CMML diagnosis	106 (27)	29 (24)	77 (28)
AML-MRC (by ICD-O-3)	54 (14)	19 (16)	35 (13)
Unspecified AML only	121 (30)	42 (35)	79 (28)

AML, acute myeloid leukemia; AML-MRC, acute myeloid leukemia with myelodysplasia-related changes; CMML, chronic myelomonocytic leukemia; ICD, International Classification of Diseases; IQR, interquartile range; MDS, myelodysplastic syndrome; SD, standard deviation; t-AML, therapy-related acute myeloid leukemia.

- A total of 398 patients with AML who were treated with CPX-351 in England were identified in the CAS database; more than half of the patients (56%) had secondary AML
- Overall, 120 (30%) patients were aged <60 years and 278 (70%) were aged ≥60 years
- Twenty (5%) patients received azacitidine prior to their AML diagnosis and no patients received midostaurin in combination with CPX-351

Figure 1. KM-Estimated OS for (A) All Patients, (B) Patients Aged <60 Years and ≥60 Years, and (C) Patients by Age Subcategories

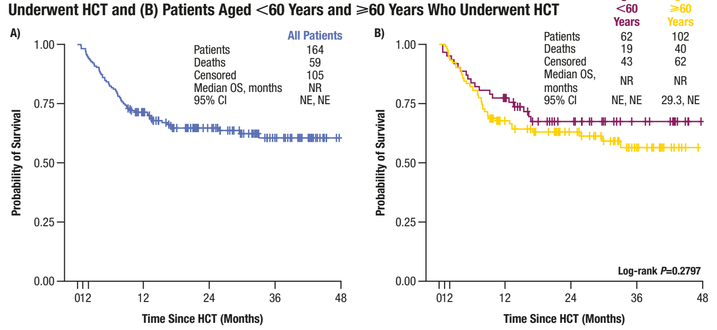


Time Point	All Patients N at Risk	All Patients Probability of Survival (95% CI)	Aged <60 Years N at Risk	Aged <60 Years Probability of Survival (95% CI)	Aged ≥60 Years N at Risk	Aged ≥60 Years Probability of Survival (95% CI)	Aged 18-44 Years N at Risk	Aged 18-44 Years Probability of Survival (95% CI)	Aged 45-59 Years N at Risk	Aged 45-59 Years Probability of Survival (95% CI)	Aged 60-69 Years N at Risk	Aged 60-69 Years Probability of Survival (95% CI)	Aged ≥70 Years N at Risk	Aged ≥70 Years Probability of Survival (95% CI)
1 month	377	0.94 (0.92, 0.96)	115	0.96 (0.92, 0.99)	262	0.93 (0.90, 0.96)	27	0.96 (0.90, 1.00)	88	0.96 (0.92, 1.00)	177	0.95 (0.91, 0.98)	85	0.90 (0.84, 0.96)
2 months	346	0.87 (0.84, 0.90)	110	0.92 (0.87, 0.97)	236	0.85 (0.81, 0.89)	27	0.96 (0.90, 1.00)	83	0.90 (0.84, 0.96)	160	0.86 (0.81, 0.91)	76	0.83 (0.75, 0.91)
12 months (1 year)	207	0.52 (0.47, 0.57)	73	0.61 (0.53, 0.70)	134	0.48 (0.42, 0.54)	19	0.68 (0.53, 0.88)	54	0.59 (0.49, 0.70)	97	0.52 (0.45,0.59)	37	0.40 (0.31, 0.52)
24 months (2 years)	96	0.34 (0.30, 0.39)	38	0.46 (0.38, 0.57)	58	0.29 (0.24, 0.35)	12	0.60 (0.44, 0.82)	26	0.42 (0.32, 0.54)	43	0.33 (0.27, 0.41)	15	0.20 (0.13, 0.30)
36 months (3 years)	55	0.32 (0.28, 0.37)	22	0.45 (0.36, 0.55)	33	0.27 (0.22, 0.33)	*	0.60 (0.44, 0.82)	17	0.40 (0.30, 0.52)	23	0.32 (0.26, 0.40)	10	0.17 (0.10, 0.27)
48 months (4 years)	13	0.31 (0.26, 0.36)	6	0.45 (0.36, 0.55)	7	0.25 (0.20, 0.32)	*	0.60 (0.44, 0.82)	*	0.40 (0.30, 0.52)	*	0.29 (0.22, 0.38)	*	0.17 (0.10, 0.27)

*<6 patients (in compliance with the NCRAS small number suppression guidelines, as outlined by NHS Digital, patient counts <6 are not presented to remove any possibility of patient re-identification).
CI, confidence interval; KM, Kaplan-Meier; N, number; NCRAS, National Cancer Registration and Analysis Service; NE, not estimable; NR, not reached; OS, overall survival.

- At data cutoff for OS (June 30, 2023), median follow-up was 12.8 months (interquartile range [IQR]: 4.4-22.5)
- Overall, 261 (66%) patients died, and estimated 4-year OS was 31% (95% confidence interval [CI]: 26, 36)
- When stratified by age, estimated 4-year OS was higher for patients aged <60 years (45% [95% CI: 36, 55]) than for those aged ≥60 years (25% [95% CI: 20, 32], log rank $P<0.001$)

Figure 2. KM-Estimated OS Landmarked From HCT Date for (A) All Patients Who Underwent HCT and (B) Patients Aged <60 Years and ≥60 Years Who Underwent HCT

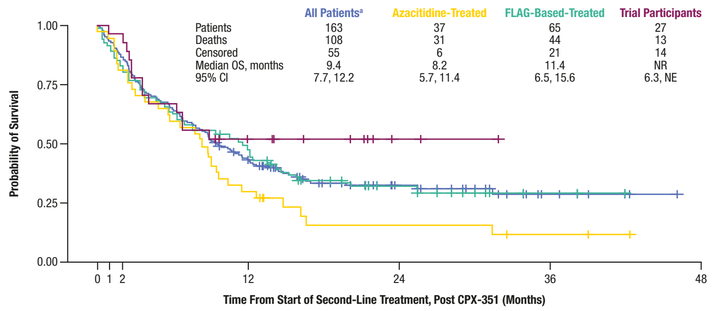


Time Point Post-HCT	All HCT Patients N at Risk	All HCT Patients Probability of Survival (95% CI)	HCT Patients Aged <60 Years N at Risk	HCT Patients Aged <60 Years Probability of Survival (95% CI)	HCT Patients Aged ≥60 Years N at Risk	HCT Patients Aged ≥60 Years Probability of Survival (95% CI)
1 month	161	0.98 (0.96, 1.00)	60	0.97 (0.92, 1.00)	101	0.99 (0.97, 1.00)
2 months	155	0.95 (0.91, 0.98)	59	0.95 (0.90, 1.00)	96	0.94 (0.90, 0.99)
12 months (1 year)	105	0.71 (0.65, 0.79)	46	0.77 (0.68, 0.89)	59	0.68 (0.59, 0.77)
24 months (2 years)	63	0.65 (0.58, 0.73)	25	0.68 (0.56, 0.81)	38	0.63 (0.54, 0.73)
36 months (3 years)	27	0.60 (0.52, 0.70)	11	0.68 (0.56, 0.81)	16	0.56 (0.46, 0.69)

CI, confidence interval; HCT, hematopoietic cell transplantation; KM, Kaplan-Meier; N, number; NE, not estimable; NR, not reached; OS, overall survival.

- HCT was reported for 164 (41%) patients; of these patients, 62 (38%) were aged <60 years and 102 (62%) were aged ≥60 years
- Median age at diagnosis of patients undergoing HCT was 62 years (IQR: 55-67 years)
- In the overall population who underwent HCT, estimated 3-year OS landmarked from HCT date was 60% (95% CI: 52, 70)
- When stratified by age, estimated 3-year OS landmarked from HCT date was higher for patients aged <60 years (68% [95% CI: 56, 81]) than for those aged ≥60 years (56% [95% CI: 46, 69])

Figure 3. KM-Estimated OS Landmarked From Post-CPX-351 Second-Line Treatment Start Date by Second-Line Treatment

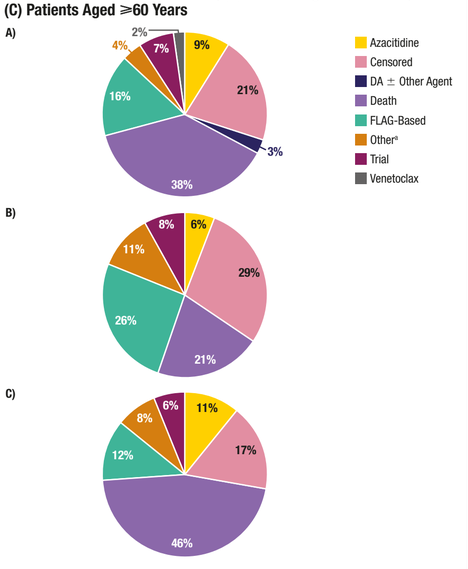


Time Point	All Patients[a] N at Risk	All Patients[a] Probability of Survival (95% CI)	Azacitidine-Treated N at Risk	Azacitidine-Treated Probability of Survival (95% CI)	FLAG-Based-Treated N at Risk	FLAG-Based-Treated Probability of Survival (95% CI)	Trial Participants N at Risk	Trial Participants Probability of Survival (95% CI)
1 month	152	0.93 (0.89, 0.97)	35	0.95 (0.88, 1.00)	59	0.91 (0.84, 0.98)	26	0.96 (0.89, 1.00)
2 months	141	0.87 (0.81, 0.92)	30	0.81 (0.69, 0.95)	53	0.82 (0.73, 0.92)	26	0.96 (0.89, 1.00)
12 months (1 year)	64	0.43 (0.36, 0.51)	11	0.30 (0.18, 0.49)	30	0.48 (0.37, 0.61)	10	0.52 (0.36, 0.75)
24 months (2 years)	23	0.32 (0.26, 0.41)	*	0.15 (0.07, 0.35)	11	0.32 (0.22, 0.46)	*	0.52 (0.36, 0.75)
36 months (3 years)	6	0.29 (0.21, 0.38)	*	0.12 (0.04, 0.32)	*	0.29 (0.19, 0.44)	0	

[a]All patients also includes DA, LDAC, other, and venetoclax-treated patients.
CI, confidence interval; DA, daunorubicin + cytarabine; FLAG, fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor; KM, Kaplan-Meier; LDAC, low-dose cytarabine; N, number; NE, not estimable; NR, not reached; OS, overall survival.

- Median OS on any second-line treatment was 9.4 months (95% CI: 7.7, 12.2)
- After CPX-351 treatment, estimated 2-year OS from the date of any second-line treatment was 32% (95% CI: 26, 41); and was 32% (95% CI: 22, 46) with FLAG-based therapy and 15% (95% CI: 7, 35) with azacitidine

Figure 4. Treatment Patterns Analysis of Second-Line Treatments After CPX-351 for (A) All Patients, (B) Patients Aged <60 Years, and (C) Patients Aged ≥60 Years



[a]Includes all other AML treatments including low-dose cytarabine for A), and includes DA and venetoclax for B) and C).
AML, acute myeloid leukemia; DA, daunorubicin/cytarabine; FLAG, fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor.

- In a treatment patterns analysis of second-line treatments after CPX-351, a total of 153/398 (38%) patients died without subsequent salvage therapy after CPX-351, and 82/398 (21%) were alive without receiving subsequent therapy by the end of the study period
  - When stratified by age, 25/120 (21%) patients aged <60 years and 128/278 (46%) patients aged ≥60 years died without subsequent salvage therapy after CPX-351, and 35/120 (29%) patients aged <60 years and 47/278 (17%) patients aged ≥60 years were alive without receiving subsequent therapy by the end of the study period
- The most common second-line treatments in the overall population were fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor (FLAG)-based therapy (n=65), and azacitidine (n=37)
  - When stratified by age, the most common second-line treatment used after CPX-351 was FLAG-based therapy (n=31) in patients aged <60 years, and FLAG-based (n=34) and azacitidine therapy (n=30) in patients aged ≥60 years

Conclusions

- This study provides updated real-world survival outcomes in adults with AML aged <60 years and ≥60 years who were treated with CPX-351 in England
- The inclusion of younger patients with AML (<60 years) who received CPX-351 treatment is noteworthy because the pivotal phase 3 trial and other real-world studies primarily included older patients[3,6-9]
- Results demonstrated improved 3- and 4-year OS compared with long-term follow-up data from the phase 3 trial that led to the approval of CPX-351[4]
- In particular, a high proportion of patients were bridged to HCT after CPX-351 treatment, which was consistent with the phase 3 trial and other real-world studies[3,6-9]
- These results suggest that, in a real-world setting, CPX-351 is an effective treatment option and may contribute to prolonged OS in both younger and older patients with AML

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Disclosures: A Lambova, **B Coles**, **K Keapoletswe**, and **K Styles** are employees of IQVIA Inc., which was contracted by Jazz Pharmaceuticals for the conduct of this analysis. **A Legg** is an employee of and holds stock in Jazz Pharmaceuticals.

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