PF474

Long-Term Real-World Experience With CPX-351 Treatment for Acute Myeloid Leukemia in England

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Background

- Since 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 (AML) or AML with myelodysplasia-related changes[1,2]
- The recommendation from the NICE and EMA was based on the primary analysis of the pivotal phase 3 trial in adults aged 60-75 years with newly diagnosed, high-risk/secondary AML, conducted in the United States and Canada[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]
  - A 5-year follow-up (median follow-up of 60.9 months) of the pivotal trial showed a maintained survival benefit with CPX-351 vs 7+3, with higher 3-year (21% vs 9%) and 5-year (18% vs 8%) KM estimates of OS[4]
  - The overall safety profile of CPX-351 was consistent with the known safety profile of 7+3[3]
- We previously conducted a retrospective population-based cohort study in England to characterize clinical outcomes with CPX-351 outside of a clinical trial setting and in a broader patient population, including younger adults (aged <60 years) who were excluded from the pivotal trial[3,5,6]
- This analysis provides longer-term real-world evidence of the effectiveness of CPX-351 in both younger (aged <60 years) and older adults (aged ⩾60 years) with AML

Objective

- In this analysis of England's Cancer Analysis System (CAS) database, we report updated real-world outcomes (up to 5 years) in patients with AML who received CPX-351 in routine clinical practice in England

Methods

- This study included adults (aged ⩾18 years) who were diagnosed with AML between January 1, 2013, and December 31, 2023, and treated with CPX-351 in a real-world setting in England
  - Patients receiving CPX-351 as part of a clinical trial were excluded from the study
- Patient records were sourced from England's 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
  - Survival probabilities were estimated using the KM method
  - Patients were censored on the last day of disease assessment or hematology assessment

Results

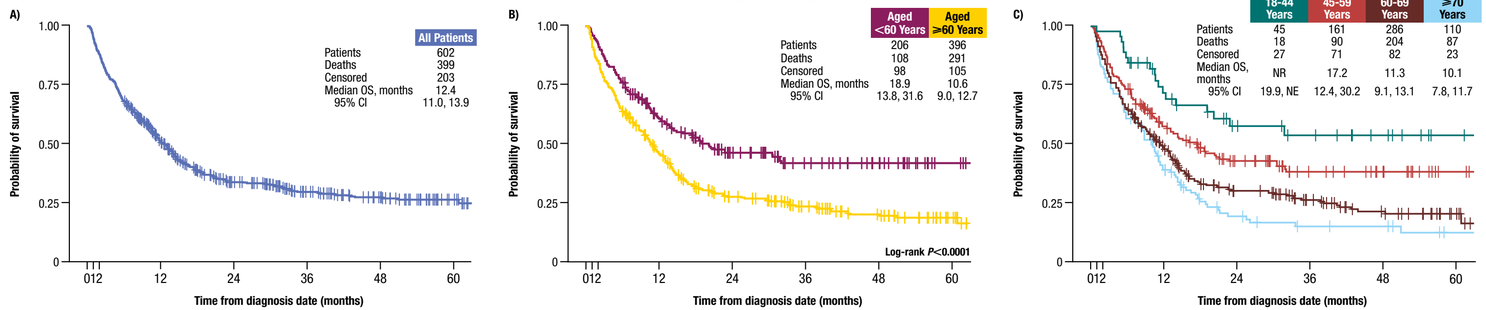
Table 1. Patient Demographic and Clinical Characteristics

	All Patients (N=602)	Aged <60 Years (n=206)	Aged ⩾60 Years (n=396)
Age at diagnosis, years			
Mean (SD)	61 (10)	50 (10)	67 (4)
Median (IQR)	63 (57, 68)	54 (46, 58)	67 (63, 70)
Age categories at diagnosis (years), n (%)			
18-44	45 (7)	45 (22)	-
45-59	161 (27)	161 (78)	-
60-69	286 (48)	-	286 (72)
70-74	98 (16)	-	98 (25)
⩾75	12 (2)	-	12 (3)
Sex, n (%)			
Female	226 (38)	100 (49)	126 (32)
Male	376 (62)	106 (51)	270 (68)
Ethnicity, n (%)			
White	512 (85)	163 (79)	349 (88)
Asian	40 (7)	24 (12)	16 (4)
Other[a]	50 (8)	19 (9)	31 (8)
AML subtype, n (%)			
t-AML	165 (27)	56 (27)	109 (28)
AML with a prior MDS or CMML diagnosis	156 (26)	49 (24)	107 (27)
AML-MRC (by ICD-O-3)	77 (13)	27 (13)	50 (13)
Unspecified AML only	204 (34)	74 (36)	130 (33)

Percentages may not add to 100% due to rounding.
[a]Other ethnicity groups were Mixed, Black, and Chinese/Other.
AML, acute myeloid leukemia; AML-MRC, acute myeloid leukemia with myelodysplasia-related changes; CMML, chronic myelomonocytic leukemia; ICD-O-3, International Classification of Diseases for Oncology, 3rd Edition; IQR, interquartile range; MDS, myelodysplastic syndrome; SD, standard deviation; t-AML, therapy-related acute myeloid leukemia.

- A total of 602 patients who received CPX-351 in England were identified in the CAS database
- Overall, 206 (34%) patients were aged <60 years and 396 (66%) were ⩾60 years
- Twenty-four (4%) patients received azacitidine for prior malignancy, 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

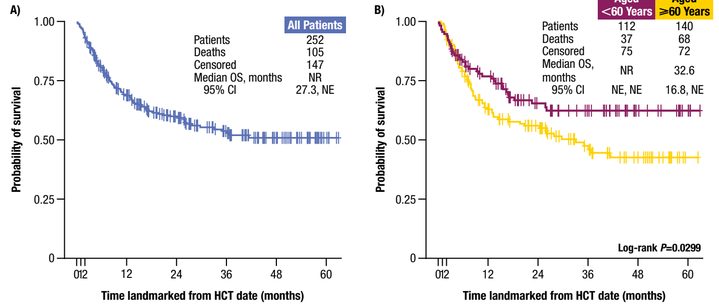


Time Point	All Patients n at Risk	All Patients Probability of Survival (95% CI)	Aged <60 Years n at Risk	Aged <60 Years Probability of Survival (95% CI)	Aged ⩾60 Years n at Risk	Aged ⩾60 Years Probability of Survival (95% CI)	Aged 18-44 Years n at Risk	Aged 18-44 Years Probability of Survival (95% CI)	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	574	0.95 (0.93, 0.97)	200	0.97 (0.95, 0.99)	374	0.94 (0.92, 0.96)	44	0.98 (0.94, 1.00)	156	0.97 (0.94, 1.00)	271	0.94 (0.92, 0.97)	103	0.93 (0.88, 0.98)
2 months	530	0.88 (0.85, 0.91)	192	0.93 (0.90, 0.97)	338	0.85 (0.82, 0.89)	44	0.98 (0.94, 1.00)	148	0.92 (0.88, 0.96)	247	0.86 (0.82, 0.90)	91	0.83 (0.76, 0.90)
12 months (1 year)	274	0.51 (0.47, 0.55)	109	0.61 (0.55, 0.68)	165	0.46 (0.41, 0.51)	28	0.72 (0.59, 0.87)	81	0.58 (0.51, 0.66)	125	0.48 (0.43, 0.54)	40	0.39 (0.31, 0.50)
24 months (2 years)	141	0.34 (0.30, 0.38)	64	0.46 (0.39, 0.54)	77	0.27 (0.23, 0.32)	17	0.58 (0.44, 0.76)	47	0.43 (0.35, 0.52)	62	0.30 (0.25, 0.36)	15	0.19 (0.13, 0.30)
36 months (3 years)	89	0.30 (0.26, 0.34)	41	0.42 (0.35, 0.50)	48	0.23 (0.19, 0.28)	13	0.54 (0.40, 0.73)	28	0.38 (0.31, 0.48)	39	0.26 (0.21, 0.33)	9	0.15 (0.09, 0.25)
48 months (4 years)	58	0.27 (0.23, 0.32)	28	0.42 (0.35, 0.50)	30	0.20 (0.16, 0.25)	8	0.54 (0.40, 0.73)	20	0.38 (0.31, 0.48)	22	0.22 (0.16, 0.28)	8	0.15 (0.09, 0.25)
60 months (5 years)	20	0.26 (0.22, 0.31)	9	0.42 (0.35, 0.50)	11	0.18 (0.14, 0.24)	*	0.54 (0.40, 0.73)	7	0.38 (0.31, 0.48)	8	0.21 (0.15, 0.27)	*	0.13 (0.07, 0.23)

*<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; NHS, National Health Service; NR, not reached; OS, overall survival.

- Over a median follow-up of 10.6 months (interquartile range [IQR]: 4.6, 22.5; 5- to 95-percentile range: 1.0, 55.3), 399 (66%) patients died and estimated 5-year OS was 26% (95% confidence interval [CI]: 22, 31)
- When stratified by age, estimated 5-year OS was higher for patients aged <60 years (42% [95% CI: 35, 50]) than those aged ⩾60 years (18% [95% CI: 14, 24])
  - Notably, OS stabilized at 42% at 3 years for patients aged <60 years

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

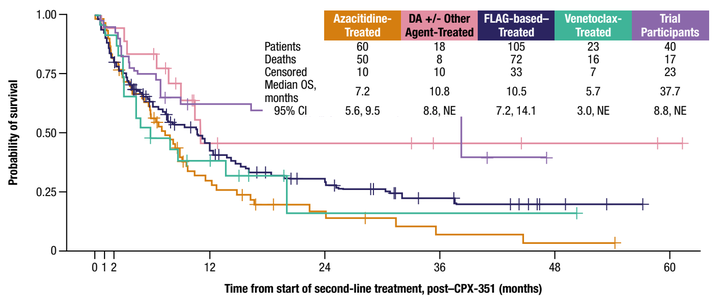


Time Point	All HCT Patients n at Risk	All HCT Patients Probability of Survival (95% CI)	HCT Patients Aged <60 Years n at Risk	HCT Patients Aged <60 Years Probability of Survival (95% CI)	HCT Patients Aged ⩾60 Years n at Risk	HCT Patients Aged ⩾60 Years Probability of Survival (95% CI)
1 month	246	0.98 (0.96, 1.00)	107	0.96 (0.92, 0.99)	139	0.99 (0.98, 1.00)
2 months	236	0.94 (0.91, 0.97)	106	0.95 (0.91, 0.99)	130	0.93 (0.89, 0.97)
12 months (1 year)	153	0.69 (0.63, 0.75)	74	0.77 (0.69, 0.85)	79	0.63 (0.55, 0.72)
24 months (2 years)	100	0.60 (0.54, 0.67)	44	0.65 (0.56, 0.76)	56	0.56 (0.48, 0.65)
36 months (3 years)	64	0.54 (0.47, 0.61)	31	0.62 (0.53, 0.73)	33	0.47 (0.39, 0.58)
48 months (4 years)	32	0.51 (0.44, 0.59)	13	0.62 (0.53, 0.73)	19	0.43 (0.34, 0.54)
60 months (5 years)	*	0.51 (0.44, 0.59)	*	0.62 (0.53, 0.73)	*	0.43 (0.34, 0.54)

*<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; HCT, hematopoietic cell transplantation; KM, Kaplan-Meier; n, number; NCRAS, National Cancer Registration and Analysis Service; NE, not estimable; NHS, National Health Service; NR, not reached; OS, overall survival.

- In total, 42% (252/602) of patients received HCT
  - In patients aged <60 years vs ⩾60 years, HCT rate was 54% (112/206) vs 35% (140/396)
- Median age at diagnosis of patients undergoing HCT was 61 years (IQR: 53, 66)
- In the overall population who underwent HCT, estimated 4-year OS landmarked from HCT date was 51% (95% CI: 44, 59) and was higher for patients aged <60 years (62% [95% CI: 53, 73]) vs ⩾60 years (43% [95% CI: 34, 54])

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

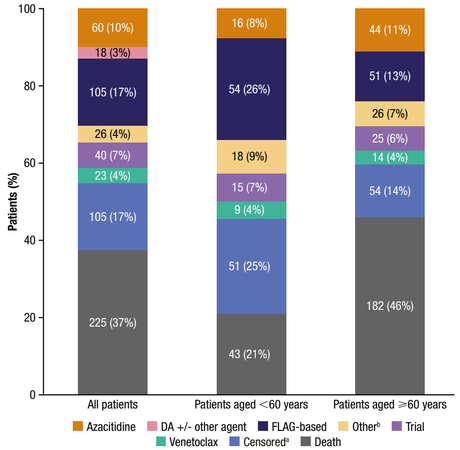


Time Point	Azacitidine-Treated n at Risk	Azacitidine-Treated Probability of Survival (95% CI)	DA +/- Other Agent-Treated n at Risk	DA +/- Other Agent-Treated Probability of Survival (95% CI)	FLAG-Based–Treated n at Risk	FLAG-Based–Treated Probability of Survival (95% CI)	Venetoclax-Treated n at Risk	Venetoclax-Treated Probability of Survival (95% CI)	Trial Participants n at Risk	Trial Participants Probability of Survival (95% CI)
1 month	58	0.97 (0.92, 1.00)	17	0.94 (0.84, 1.00)	97	0.92 (0.87, 0.98)	22	0.96 (0.88, 1.00)	38	0.95 (0.88, 1.00)
2 months	49	0.80 (0.70, 0.91)	17	0.94 (0.84, 1.00)	84	0.80 (0.73, 0.88)	21	0.91 (0.80, 1.00)	38	0.95 (0.88, 1.00)
12 months (1 year)	15	0.30 (0.20, 0.45)	*	0.94 (0.84, 1.00)	38	0.44 (0.35, 0.55)	7	0.38 (0.23, 0.65)	22	0.62 (0.49, 0.79)
24 months (2 years)	6	0.17 (0.09, 0.32)	*	0.46 (0.25, 0.83)	20	0.29 (0.21, 0.41)	*	0.16 (0.03, 0.73)	13	0.59 (0.46, 0.77)
36 months (3 years)	*	0.07 (0.02, 0.24)	*	0.46 (0.25, 0.83)	10	0.22 (0.15, 0.34)	*	0.16 (0.03, 0.73)	6	0.59 (0.46, 0.77)
48 months (4 years)	*	0.03 (0.01, 0.22)	*	0.46 (0.25, 0.83)	*	0.20 (0.12, 0.32)	*	0.16 (0.03, 0.73)	0	-
60 months (5 years)	0	-	*	0.46 (0.25, 0.83)	0	-	0	-	0	-

*<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; DA, daunorubicin + cytarabine; FLAG, fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor; KM, Kaplan-Meier; n, number; NCRAS, National Cancer Registration and Analysis Service; NE, not estimable; NHS, National Health Service; OS, overall survival.

- After CPX-351 treatment, estimated 4-year OS from the date of any second-line treatment was 24% (95% CI: 17, 32) and was 20% (95% CI: 12, 32) with fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor (FLAG)-based therapy

Figure 4. Second-Line Treatments After CPX-351 for All Patients and Patients Aged <60 Years and Aged ⩾60 Years



[a]Censored patients were those alive without receiving subsequent therapy; [b]Other second-line treatments encompassed a range of therapies including low-dose cytarabine, low-dose cytarabine + DA (in patients aged <60 and ⩾60 years), as well as cytarabine at different dose levels in combination with various drugs, including midostaurin, mitoxantrone, FLAG-Ida, gemtuzumab, doxorubicin, fludarabine, and azacitidine.
DA, daunorubicin/cytarabine; FLAG, fludarabine, high-dose cytarabine, and granulocyte-colony stimulating factor; Ida, idarubicin.

- In a treatment patterns analysis of second-line treatments after CPX-351, a total of 225/602 (37%) patients died without subsequent salvage therapy, and 105/602 (17%) were alive without receiving subsequent therapy by the end of the study period
- The two most common second-line treatments in the overall population were FLAG-based therapy (105/602 [17%]) and azacitidine (60/602 [10%])
  - When stratified by age, the most common second-line treatment used after CPX-351 was FLAG-based therapy (54/206 [26%]) in patients aged <60 years, and FLAG-based (51/396 [13%]) and azacitidine therapy (44/396 [11%]) in patients aged ⩾60 years

Conclusions

- This is the largest real-world evidence study of CPX-351 to date, complementing the 5-year follow-up data from the pivotal phase 3 trial that supported its regulatory approval[4,7]
- OS in patients aged ⩾60 years was comparable with the 5-year follow-up data from the pivotal trial, including in patients aged ⩾70 years[4]
- This dataset helps to address the gap in CPX-351 outcomes data for patients aged <60 years who were excluded from the pivotal trial.[3] Favorable OS was observed in this patient population
- 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[3,8-11]
- Patients who received second-line treatment after CPX-351 also had reasonable long-term survival, highlighting the potential for successful subsequent therapies following CPX-351
- Overall, these long-term real-world data further support that CPX-351 is an effective treatment option, with achievement of prolonged OS in both younger (aged <60 years) and older (aged ⩾60 years) adult patients with AML, particularly in those who received HCT

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Disclosures: A Lambova, **E Ralphs**, **K Keapoletswe**, and **G Wester** 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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