Optimising CPX-351 (liposomal cytarabine-daunorubicin) treatment for t-AML/AML-MRC patients in the outpatient setting: a modified Delphi consensus

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BACKGROUND

- Acute myeloid leukaemia (AML) is commonly treated with intensive chemotherapy regimes, including regimens of cytarabine and anthracycline.[1]
- Vyxeos® liposomal (CPX-351, liposomal cytarabine-daunorubicine) is recommended for patients with treatment-related AML (t-AML) and AML with myelodysplasia-related changes (AML-MRC), including the US, Europe and Australia.[2-4]
- Unlike conventional chemotherapy, CPX-351 is delivered as 90-minute infusions over 3 days, enabling delivery in outpatient settings.[5]
- Increasing adoption of outpatient treatment is being reported in clinical practice.[6] Real-world evidence from CREST-UK, indicates that outpatient CPX-351 can improve patient quality of life, lower the risk of infection, reduce healthcare costs, and maintain survival benefits.[5] These advantages, together with demonstrated survival benefits, highlight the importance of developing clear guidance to optimise CPX-351 use in outpatient settings.
- A well-established Delphi method provides a structured approach to obtaining expert opinion and reaching consensus, guided by established standards of good practice.

OBJECTIVE

- To gain clinical consensus on recommendations for the optimisation of CPX-351 treatment in the outpatient setting.

METHOD

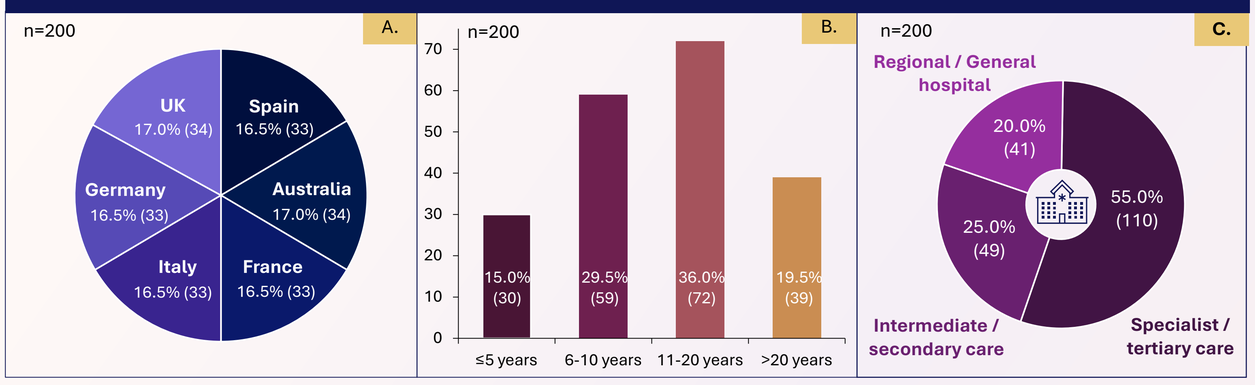
- A modified Delphi method was used to convene a steering committee of 9 haematologists across Europe and Australia, with experience in outpatient treatment in AML with CPX-351.
- The steering committee generated 43 consensus statements, classified into 6 key domains:

A	Determining patients suitable for CPX-351 treatment
B	The different settings for administering CPX-351 treatment
C	The benefits of administering CPX-351 treatment in an outpatient setting
D	Key requirements for administering CPX-351 treatment in an outpatient setting
E	Barriers to administering CPX-351 treatment in an outpatient setting
F	Optimising CPX-351 treatment in the outpatient setting

- An electronic survey containing these statements was developed and distributed by a third party (M3 Global) to be validated by a wider panel of 200 haematologists (Australia, UK, France, Germany, Italy and Spain) with experience in intensive chemotherapy and outpatient care for AML patients with CPX-351.
- Respondents rated their level of agreement with each statement using a 4-point Likert scale. Following this, the results were analysed to determine level of agreement for each statement.
- The consensus threshold was set a priori at ≥75% agreement (i.e., strongly agree and tend to agree).

RESULTS

Figure 1. Delphi Survey Respondents by (A) Country; (B) Years of experience; and (C) Hospital setting



- At the end of the survey round, 42 of 43 statements (98%) achieved consensus of ≥75% agreement, with 31 achieving ≥90% agreement (Figure 2). As the stopping criteria (sufficient consensus) was satisfied, no additional rounds of survey were conducted.

Figure 2. Scatterplot illustrating aggregated agreement across all statements by geographical setting; The green line signifies the ≥75% threshold for consensus

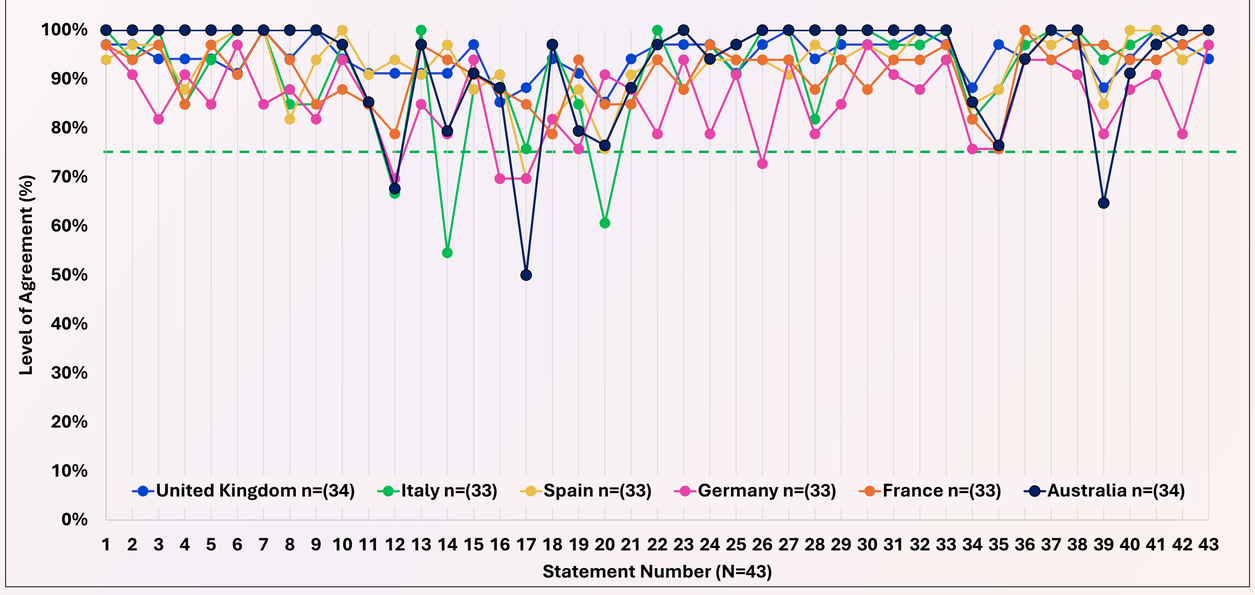


Table 1. Selected consensus statements and corresponding levels of agreement

No.	Statement	Agreement		
	Level of agreement (%)	<75%	75 - 89%	≥90%
Domain A: Determining patients suitable for CPX-351 treatment				
1	In patients with high-risk t-AML or AML-MRC (according to ELN 2022 risk classification), who are eligible for intensive treatment, induction chemotherapy followed by a consolidating allogeneic HSCT is the treatment of choice			97.5%
2	All t-AML and AML-MRC patients must be assessed to determine whether they are fit for intensive chemotherapy before receiving CPX-351 treatment (e.g., for performance status, active comorbidities causing instability, etc.)			95.5%
3	Treatment decisions for CPX-351 and other intensive chemotherapies for stable patients with t-AML and AML-MRC should be made based on as much prognostic information as possible, in line with the latest ELN, ICC and WHO guidelines			90.5%
4	Once complete genetic information has been obtained, CPX-351 treatment should commence without delay where indicated, unless a patient has life-threatening hyperleukocytosis and chemotherapy should be initiated immediately			90.5%
5	Cytogenetics is a key investigation in the management of t-AML and AML-MRC, and a full karyotype result should be available within 5-7 working days of receipt in lab			94.5%
6	Next-generation sequencing (NGS) is important in the prognostication of t-AML and AML-MRC, and can add value if available in a timely fashion (i.e., 4-15 days), but should not excessively delay starting CPX-351 treatment			96.5%
Domain B: The different settings for administering CPX-351 treatment				
7	"Inpatient treatment" can be defined as the delivery of chemotherapy and management in a hospital stay, until count recovery is achieved			97.5%
8	"Outpatient treatment" can be defined as the delivery of chemotherapy in an outpatient or at-home setting, until count recovery is achieved			90.5%
9	"Ambulatory treatment" can be defined as the delivery of chemotherapy and management in an ambulatory setting or a hybrid of ambulatory/at-home and inpatient setting, until count recovery is achieved			91.0%
10	"Home therapy" can be defined as the delivery of chemotherapy at home, and subsequent management at home, until count recovery is achieved, although this is a rare, innovative approach only offered in select centres			95.0%
Domain C: The benefits of administering CPX-351 treatment in an outpatient setting				
11	Administering CPX-351 treatment in an outpatient setting can enable improved mobility compared with prolonged hospital stays			87.0%
12	Administering CPX-351 treatment in an outpatient setting can support better nutritional intake and minimises the risk of unwanted weight loss associated with prolonged hospital stays			78.0%
13	Administering CPX-351 treatment in an outpatient setting can enhance psychological well-being, and reduces feelings of isolation and anxiety associated with prolonged hospital stays			93.5%
14	Administering CPX-351 treatment in an outpatient setting can promote independent living and empowers patients to practice self-care			82.5%
15	Administering CPX-351 treatment in an outpatient setting can improve overall patient quality of life, by reducing the time spent in hospital, and helping to maintain normal routines and social connections			91.5%
16	Administering CPX-351 treatment in an outpatient setting can improve a patient's physical and psychological condition pre-HSCT			85.5%
17	Administering CPX-351 treatment in an outpatient setting can accelerate the start of treatment and ensure treatment is initiated on-time, particularly in centres where patients must wait for a hospital bed to become available		73.0%	
18	Administering CPX-351 treatment in an outpatient setting reduces hospital bed occupancy, offering significant cost and resourcing advantages			88.5%
19	Administering CPX-351 treatment in an outpatient setting reduces the risk of hospital-acquired infections and mitigates complications that can arise from prolonged hospital stays, and associated costs			85.5%
Domain D: Key requirements for administering CPX-351 treatment in an outpatient setting				
20	t-AML and AML-MRC patients can be treated with CPX-351 in an outpatient setting for induction and/or consolidation therapy, if deemed appropriate considering the patient's status, social circumstances, and hospital safety requirements for outpatient management			79.0%
21	t-AML and AML-MRC patients can be discharged after CPX-351 inpatient treatment and treated and/or managed in an outpatient setting going forward, if deemed appropriate considering the patient's status, social circumstances, and hospital safety requirements for outpatient management			88.5%
22	t-AML and AML-MRC patients should be considered for consolidation CPX-351 outpatient treatment if they have not had significant complications during induction treatment, in line with hospital safety and patient/caregiver requirements for outpatient management			93.5%
23	To be considered for CPX-351 outpatient treatment, a patient must be mobile and have a performance status of ≤2, as defined by the Eastern Cooperative Oncology Group (ECOG) scale			92.5%
24	To be considered for CPX-351 outpatient treatment, a patient must be able to access a hospital (or be transported by a caregiver) within 1 hour, 24 hours a day, 7 days a week, or have local accommodation provided by the healthcare institution			93.0%
25	To be considered for CPX-351 outpatient treatment, a patient (or their caregiver) must be able to communicate easily (e.g., not be hard of hearing) and understand the native language			93.0%
26	To be considered for CPX-351 outpatient treatment, a patient (or their caregiver) must have 24/7 telephone access			93.0%
27	To be considered for CPX-351 outpatient treatment, a patient (or their caregiver) must be educated (through verbal and accessible written instructions) and physically able to monitor for complications of cytopenia, and take immediate action if complications arise (e.g., neutropenic fever, sepsis, bleeding)			96.5%
28	To be considered for CPX-351 outpatient treatment, a patient must have proficient understanding (through verbal and accessible written instructions) and the physical ability to self-medicate as needed			90.0%
29	To be considered for CPX-351 outpatient treatment, a patient must not have any active uncontrolled infections			95.0%
30	To enable the administration of CPX-351 treatment in an outpatient setting, a hospital must have clear protocols and resources to assess and admit unwell patients to a haematology ward at any time, in case they develop complications of cytopenia (e.g., neutropenic fever, sepsis, bleeding)			96.5%
31	To enable the administration of CPX-351 treatment in an outpatient setting, a trained doctor and/or nurse must follow-up with outpatients at least twice a week, or more if required (e.g., for blood count monitoring or product support)			95.5%
32	To enable the administration of CPX-351 treatment in an outpatient setting, there must be effective verbal and written communication between inpatient and outpatient care settings (e.g., via standardised, detailed, easy-to-follow protocols)			96.5%
33	The prompt and effective management of neutropenic sepsis (including administering antibiotics) is fundamental in the safe delivery of CPX-351 treatment and ongoing care in an outpatient setting			98.0%
Domain E: Barriers to administering CPX-351 treatment in an outpatient setting				
34	Lack of available on-site accommodation can be addressed by partnering with local accommodation providers or patient advocacy/support organisations			83.0%
35	Lack of specialist staff suitably trained on CPX-351 outpatient care (including risks) can be addressed through targeted training programmes			83.5%
Domain F: Optimising CPX-351 treatment in the outpatient setting				
36	Patients should be routinely assessed for symptoms and well-being using a standardised, easily accessible assessment tool			96.5%
37	Patients and caregivers should be instructed and educated to immediately report any fever or illness to a 24/7 healthcare professional, and be prepared to travel to hospital at once, if required (e.g., have a pre-packed bag)			97.5%
38	Clear written instructions should be provided to the patient and caregiver to ensure they understand what side effects to monitor, what steps to take and who to speak to in the event of adverse events			97.5%
39	Prophylactic measures (e.g., broad-spectrum antibiotics) should be integral to outpatient care protocols for CPX-351 to reduce the risk of adverse events			84.5%
40	Healthcare professionals should receive ongoing training on the practical aspects of CPX-351 outpatient care			94.0%
41	The routine, systematic collection and analysis of patient feedback and outcomes is important to continuously improving the CPX-351 outpatient experience and offering tailored care			97.0%
42	Communication and coordination across the multidisciplinary team (MDT), including pharmacists, specialist nurses, psychologists, physiotherapists, nutritionists and palliative care (if appropriate), is crucial for comprehensive care and optimal outpatient outcomes during and after CPX-351 treatment			93.5%
43	Sharing best practices and experiences between centres can enhance the quality of care for patients undergoing outpatient chemotherapy, fostering innovation and consistency in treatment approaches			97.5%

RECOMMENDATIONS

1. For appropriate patients with high-risk t-AML or AML-MRC, CPX-351 treatment should be promptly initiated after assessing fitness (e.g., performance status and active comorbidities) with the goal of consolidating allogenic hematopoietic stem cell transplant (allo-HSCT)
2. Outpatient CPX-351 treatment offers potential benefits to both patient experience and quality of life, and should be considered for appropriate patients
3. Patients can be considered eligible for CPX-351 outpatient treatment providing appropriate patient selection criteria and hospital safety protocols for monitoring and readmission are met
4. Optimising outpatient CPX-351 care hinges on logistical solutions, thorough patient and staff education on proactive risk management, well-coordinated multidisciplinary team communication, and continuous improvement via feedback and shared best practices

CONCLUSIONS

- Although challenges may be unique across countries and healthcare settings, this consensus reports strong levels of agreement amongst haematologists that CPX-351 can be delivered in an outpatient setting, and that this approach can realise benefits for both patient experience and quality of life and should be considered for appropriate patients.
- It is hoped that this consensus will support haematology/oncology services to consider how and in which patients CPX-351 outpatient administration should be considered.

Disclosures and acknowledgements

The study was supported by Jazz Pharmaceuticals. All authors served as consultants to Jazz Pharmaceuticals during this Delphi consensus project, no financial compensation was provided for their involvement in manuscript publication. Triducive Partners Limited was commissioned by Jazz Pharmaceuticals to facilitate the Delphi process.

Medical writing and project facilitation were provided by Emily Lassman and Ian Walker of Triducive Partners Limited.

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Presented at Blood 2025 in conjunction with the 36th Regional Congress of the ISBT, 26-29 October 2025, Perth, Australia