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Quality of life and symptoms in acute myeloid leukaemia with early palliative care: real-world observational study

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ABSTRACT

Objectives To describe longitudinal changes in quality of life (QOL) and symptoms among patients with acute myeloid leukaemia (AML) receiving real-world early palliative care (EPC) during the first year after diagnosis.

Methods This prospective observational study enrolled consecutive adults with AML followed in an outpatient EPC clinic. QOL and symptoms were assessed monthly using the Functional Assessment of Cancer Therapy–Leukemia (FACT-Leu), the Edmonton Symptom Assessment Scale (ESAS) and the Hospital Anxiety and Depression Scale (HADS). Scores were analysed through joint modelling, integrating longitudinal and survival data, and sensitivity analyses.

Results Thirty-eight patients contributed 169 FACT-Leu, 151 ESAS and 111 HADS questionnaires. From baseline, median FACT-Leu scores improved from 108.7 to 135.7 at 4 months and remained stable through 8 and 12 months ($p \leq 0.011$), while ESAS scores decreased from 25.2 to 5.7 by 4 months and remained low through 12 months ($p < 0.001$), indicating sustained symptom improvement. HADS scores showed no statistically significant changes, although a modest anxiety improvement was noted. Trajectories remained consistent across all sensitivity analyses.

Conclusions In AML patients receiving EPC in a real-world outpatient setting, QOL and symptom burden showed sustained improvement over time. These descriptive findings highlight the potential effectiveness and clinical relevance of EPC in routine AML care and provide real-world reference data for future controlled studies.

INTRODUCTION

Patients with acute myeloid leukaemia (AML) experience a heavy symptom burden, profound psychological distress and reduced quality of life (QOL), often comparable to patients with advanced solid tumours.[1 2] The disease abrupt onset, intensive treatment and unpredictable prognosis can result in marked suffering and uncertainty.[3]

Early integration of palliative care (EPC) has shown multiple benefits in patients with metastatic solid tumours, including improved QOL and, in some cases, prolonged survival.[4] In AML, one phase 2 and two phase 3 trials conducted during hospitalisation have similarly demonstrated the feasibility and clinical value of EPC.[1 5 6]

However, evidence from real-world outpatient settings remains limited.[7 8] Previous studies from our group have shown that integrating EPC into routine AML care is feasible, with high adherence to quality-of-care indicators and low rates of aggressive end-of-life interventions.[7 8] Building on this work, this study aimed to describe longitudinal changes in QOL and symptoms among patients with AML receiving real-world outpatient EPC, providing empirical

evidence on its potential effectiveness and clinical relevance in routine haematologic practice.

MATERIALS AND METHODS

Study design and population

This prospective, observational study was conducted at the EPC outpatient clinic of the Hematology Section of the University Hospital of Modena (Italy) between January 2022 and December 2023. Consecutive adults (≥18 years) with de novo or relapsed AML, diagnosed or reclassified within the preceding 12 months, ineligible for allogeneic transplantation and referred to EPC were included. Exclusion criteria were cognitive impairment or language barriers preventing questionnaire completion. A 1-year observation period was selected because this interval typically encompasses multiple clinically meaningful events that may substantially influence patient-reported outcomes (PROs). A more detailed description of inclusion criteria and definitions is provided in the online supplemental materials. The study was approved by the local Ethics Committee (protocol CE 833/2018), and all participants provided written informed consent.

PRO measures

Patients' QOL and symptoms were assessed at baseline and at scheduled EPC visits using three validated PRO instruments:

- Functional Assessment of Cancer Therapy–Leukaemia (FACT-Leu),
- Edmonton Symptom Assessment Scale (ESAS).
- Hospital Anxiety and Depression Scale (HADS).

FACT-Leu assesses overall health-related QOL, including physical, emotional, social, functional and leukaemia-specific domains; ESAS evaluates the severity of common physical and psychological symptoms; and HADS measures anxiety and depressive symptoms. Each scale was used according to standard scoring procedures, with higher FACT-Leu scores, indicating better QOL and higher ESAS and HADS scores, indicating greater symptom burden.[9–11] Full descriptions of scoring methods, items and minimal clinically important differences (MCIDs) are provided in the online supplemental materials.

EPC intervention

All patients received EPC as implemented in our routine outpatient clinical practice.[7 8 12] The intervention was initiated at, or within 4 weeks from, AML diagnosis and delivered by a dedicated interdisciplinary palliative care team, including physicians with specific training in haematologic malignancies, communication skills and strategies to support patients' coping, as previously described.[7 8 12] The EPC intervention focused on five core domains—rapport building, symptom management, support with coping, cultivation of prognostic awareness and facilitation of end-of-life planning—consistent with established models of EPC reported in the literature.[13–16] The frequency and duration of visits were individualised according to clinical needs, typically ranging from one to two visits per month, with flexibility to increase contacts during periods of clinical deterioration or major care transitions. To ensure continuity of care, the EPC team coordinated with local home-care services and conducted regular telephone follow-ups for patients unable to attend scheduled visits or receiving exclusive home-based care.[7 8 12]

Statistical analysis

Descriptive statistics summarised sociodemographic and clinical characteristics. Longitudinal changes in PRO scores were examined using joint models that integrated a linear mixed-effects model for repeated measures with a Cox proportional hazards model for survival. This approach allowed us to account for informative dropout due to death, irregular follow-up times and differences in observation windows across patients. All models were adjusted for age and sex. The analysis was conducted at four distinct time points, commencing from diagnosis: t0 (baseline), T1 (1 month), T2 (4 months), T3 (8 months) and T4 (12 months). These intervals were selected based on evidence from randomised clinical trials in both haematologic and solid tumours, suggesting that a minimum of two to four EPC visits is required to detect clinically meaningful improvements in QOL.[4]

Analyses were descriptive and hypothesis-generating. Sensitivity analyses explored the robustness of findings across alternative time-interval configurations (models A–C). Detailed model specifications, rationale for the analytic approach, and full sensitivity results are reported in the online supplemental materials.

RESULTS

Baseline characteristics

Of the 40 patients screened, 38 met the inclusion criteria and were enrolled in the study. All referred patients accepted the EPC referral and attended at least one EPC clinic visit. Participants attended a median of six EPC visits (range 3–11). Most patients (71%) received non-intensive therapy—predominantly hypomethylating agents with or without venetoclax—and 61% had adverse-risk disease. Attrition during follow-up was mainly due to disease progression or death. A detailed patient flow diagram and complete baseline characteristics are provided in online supplemental figure 1 and online supplemental table 1.

Quality of life (FACT-Leu)

A total of 169 FACT-Leu questionnaires were analysed. The mean FACT-Leu scores increased progressively from 108.68 (95% CI 99.50 to 117.87) at T0 to 113.28 (102.50 to 124.06) at T1, 127.14 (117.07 to 137.22) at T2, 134.28 (125.74 to 142.83) at T3, and 135.73 (127.55 to 143.91) at T4. Compared

with baseline, the mean time variations (MTV) indicated an improvement already at T1 (MTV=4.60 ± 6.61; 95% CI −8.36 to 17.55; p=0.487), which became both clinically and statistically significant at T2 (MTV=4.62±1.82; 95% CI −1.05 to 8.18; p=0.011), T3 (MTV=3.38 ± 0.76; 95% CI 1.89 to 4.87; p<0.001) and T4 (MTV=2.13 ± 0.50; 95% CI 1.15 to 3.11; p<0.001) (figure 1A). These improvements exceeded the MCID for FACT-Leu (13–17 points), indicating a meaningful enhancement in patients' perceived QOL.

Symptom burden (ESAS)

A total of 151 ESAS questionnaires were collected. The mean ESAS scores decreased from 25.20 (95% CI 18.77 to 31.62) at T0 to 20.50 (10.79 to 30.21) at T1, 5.65 (0 to 12.42) at T2, 5.49 (0.03 to 10.96) at T3 and 9.40 (3.79 to 15.01) at T4. Compared with baseline, the MTV demonstrated a clinically relevant reduction already at T1 (MTV=−4.70±6.18; 95% CI −16.81 to 7.41; p=0.447), which became statistically significant at T2 (MTV=−4.89±1.28; 95% CI −7.40 to −2.38; p<0.001), T3 (MTV=−2.46±0.54; 95% CI −3.52 to −1.41; p<0.001), and T4 (MTV=−1.32±0.34; 95% CI −1.98 to −0.66; p<0.001). This consistent decline in symptom severity suggests sustained improvement in both physical and psychological symptom domains over time.

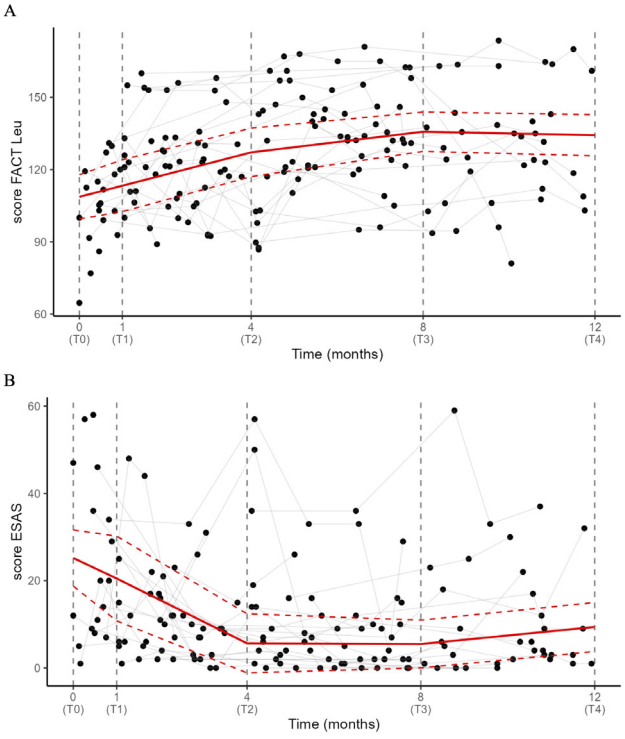

Figure 1 (A, B) Quality of life and symptom burden of patients with acute myeloid leukaemia during the delivery of early palliative care. The figure illustrates the trajectories of FACT_Leu (A) and ESAS (B) scores over time. The solid red line represents the mean trajectory estimated by the joint model, adjusted for the correlation among repeated measures and the probability of death. Dashed red lines indicate the 95% CI of the estimate. Black dots correspond to individual patient observations, while grey lines depict the observed trajectories for each patient. The score ranges are as follows: FACT-Leu (0–176) and ESAS (0–90). Higher scores indicate better quality of life in FACT-Leu and worse symptoms in ESAS. T0 corresponds to the diagnosis (baseline); T1 corresponds to one month after diagnosis; T2 corresponds to four months after diagnosis; T3 corresponds to eight months after diagnosis; and T4 corresponds to 12 months after diagnosis. ESAS, Edmonton Symptom Assessment Scale; FACT-Leu, Functional Assessment of Cancer Therapy–Leukemia.

Mood symptoms (HADS)

A total of 111 HADS questionnaires were analysed. Mean HADS-A scores were 5.30 (95% CI 3.85 to 6.75) at T0, 5.80 (4.21–7.39) at T1, 4.65 (4.00–5.31) at T2, 3.70 (2.35–5.04) at T3 and 3.99 (2.39–5.59) at T4. Mean HADS-D scores were 4.99 (2.75–7.22) at T0, 6.65 (4.40–8.89) at T1, 5.47 (3.21–7.73) at T2, 5.34 (3.42–7.25) at T3 and 6.91 (4.81–9.01) at T4 (online supplemental figure 2).

No statistically significant differences from baseline were observed for either HADS-A or HADS-D. However, small numerical improvements in anxiety approached the MCID, while depressive symptoms remained largely stable (online supplemental figure 2).

Sensitivity analyses

Sensitivity analyses performed across the three-alternative time-interval models (A–C) confirmed the robustness of the longitudinal findings. Detailed sensitivity analyses and additional trajectories (including HADS) are provided in online supplemental figure 3 and online supplemental table 2.

DISCUSSION

In this cohort of AML patients, clinically meaningful and statistically significant improvements in QOL over 1 year were observed in patients receiving a real-world outpatient EPC intervention. In addition, participants experienced a reduction in symptom burden, detectable by the third month and maintained during follow-up. No significant changes were observed in anxiety and depression. Taken together, these observations provide a first longitudinal description of QOL and symptom trajectories in AML patients receiving real-world outpatient EPC, suggesting potential benefits in symptom management and patient experience, although causality cannot be established.

Previous observational studies in patients with AML receiving standard haematologic care, with sample sizes ranging from 19 to 100 patients, have reported that QOL generally improves over the disease trajectory but tends to plateau or decline by approximately 24 weeks, particularly when assessed using the same PRO instruments employed in the present study.[17–19] In addition, QOL has been shown to

deteriorate significantly during the final 6 months of life.[20] When viewed in this context, the longitudinal changes observed in our EPC cohort appear to follow a different trajectory, with improvements in QOL and symptom burden sustained beyond 6 months. Although direct comparisons are limited by differences in study design, patient characteristics, disease stage and treatment intensity, the magnitude and durability of the observed change scores in our cohort seem at least comparable to, and potentially more prolonged than, those reported in observational cohorts receiving standard haematologic care.[17 19] Among the two available randomised controlled trials evaluating EPC in AML, only one inpatient study has been fully published, demonstrating improvements in QOL from week 2 to week 24.[1] The second, an ongoing multisite outpatient trial in patients with AML and high-risk myelodysplastic syndromes receiving non-intensive therapy, has been reported in abstract form and similarly showed improved QOL at 3 months.[5] Taken together, these findings suggest that improvements in QOL may occur in patients receiving EPC across different care settings. However, given the absence of a control group in the present study, these observations should be interpreted cautiously, and causality cannot be established. The second key finding was the reduction in symptom burden. We previously reported that EPC in AML was associated with significant pain decreases within 1 and 4 weeks from initiation.[7] In this cohort, symptom scores generally decreased over time, consistent with prior evidence in both haematologic and solid tumour populations.[4 7] In contrast, during standard haematologic care, symptoms may initially improve but often decrease by month 6.[19 20]

We did not observe statistically significant improvements in anxiety or depression. This differs from the inpatient RCT[1] but is consistent with findings from the ongoing outpatient EPC trial in AML and MDS.[5] The modest trend towards anxiety improvement observed across sensitivity analyses, together with stable depressive symptoms, may reflect the psychological adjustment period following diagnosis in patients with high-risk or non-transplant-eligible AML, given the challenging disease trajectory.

Our study has several limitations. First, the absence of a control arm limits causal inference, and causality cannot be assumed. Second, due to sample size, the joint model could not adjust for all potential confounders (eg, treatment intensity, geriatric assessment) without risking parameter instability. Third, missing data may not be completely at random, as patients with deteriorating QOL or higher symptom burden may have been less likely to complete questionnaires. However, the joint model enhances robustness by accounting for interdependence between longitudinal QOL data, survival outcomes and potential informative dropout. Finally, the single-centre design limits generalisability across diverse care settings.

Despite these limitations, this study provides valuable longitudinal observations from a real-world cohort of AML patients receiving outpatient EPC, suggesting that routine EPC may support QOL and symptom management.

In conclusion, this longitudinal prospective observational study shows that improvements in QOL and symptom burden can be observed in AML patients receiving outpatient EPC, beginning within the first months and maintained for approximately 1 year. These findings highlight the potential value of integrating EPC from diagnosis and throughout the disease trajectory in the outpatient setting. Future prospective studies with larger samples are needed to confirm these observations and clarify the long-term benefits of EPC.

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Competing interests FF: Advisory Boards for Janssen and Novartis and travel grants from Jazz Pharmaceuticals outside the submitted work. RM: honouraria from AbbVie, Roche, Janssen and Shire, outside the submitted work. FE: consultancy for AbbVie, Incyte, Novartis, Jazz Pharmaceuticals and research support (institution) from Daichi-Sankyo, outside the submitted work. EBa: Advisory Board Sandoz. ML: Advisory Board and meeting with honouraria: AbbVie, Gilead sci, Jazz Pharma, Novartis, MSD, Grifols, Sanofi, Daiichi-Sankyo, Incyte, Roche, Istituto Gentili. All the other authors have no relevant financial or non-financial interests to disclose.

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