haematologica
Journal of the Ferrata Storti Foundation

Dexamethasone added to induction and post-remission therapy in older patients with newly diagnosed acute myeloid leukemia: a multicenter, phase II trial (DEXAML-02)

by Sarah Bertoli, Emilie Bérard, Pierre Peterlin, Romain Guieze, Yohan Desbrosses, Yosr Hicheri, Omar Benbrahim, Martin Carre, Corentin Orvain, Anne Banos, Marc Bernard, Emmanuel Gyan, Alain Saad, Safia Chebrek, Gabrielle Roth Guepin, Veronique Dorvaux, Laurence Sanhes, Maria Pilar Gallego-Hernanz, Carole Exbrayat, Laure Vincent, Chantal Himberlin, Célestine Simand, Norbert Vey, Cindy Fenoll, Ariane Mineur, Anne Huynh, Francois Vergez, Isabelle Luquet, Laetitia Largeaud, Eric Delabesse, Arnaud Pigneux, and Christian Recher.
Collaborative Groups: French Innovative Leukemia Organization (FILO).

Received: December 13, 2024.
Accepted: January 28, 2025.

Citation: Sarah Bertoli, Emilie Bérard, Pierre Peterlin, Romain Guieze, Yohan Desbrosses, Yosr Hicheri, Omar Benbrahim, Martin Carre, Corentin Orvain, Anne Banos, Marc Bernard, Emmanuel Gyan, Alain Saad, Safia Chebrek, Gabrielle Roth Guepin, Veronique Dorvaux, Laurence Sanhes, Maria Pilar Gallego-Hernanz, Carole Exbrayat, Laure Vincent, Chantal Himberlin, Célestine Simand, Norbert Vey, Cindy Fenoll, Ariane Mineur, Anne Huynh, Francois Vergez, Isabelle Luquet, Laetitia Largeaud, Eric Delabesse, Arnaud Pigneux, and Christian Recher.
Collaborative Groups: French Innovative Leukemia Organization (FILO).
Dexamethasone added to induction and post-remission therapy in older patients with newly diagnosed acute myeloid leukemia: a multicenter, phase II trial (DEXAML-02).
Haematologica. 2025 Feb 6. doi: 10.3324/haematol.2024.286807 [Epub ahead of print]

Dexamethasone added to induction and post-remission therapy in older patients with newly diagnosed acute myeloid leukemia: a multicenter, phase II trial (DEXAML-02)

Sarah Bertoli,[1] Emilie Bérard,[2] Pierre Peterlin,[3] Romain Guieze,[4] Yohan Desbrosses,[5] Yosr Hicheri,[6] Omar Benbrahim,[7] Martin Carre,[8] Corentin Orvain,[9] Anne Banos,[10] Marc Bernard,[11] Emmanuel Gyan,[12] Alain Saad,[13] Safia Chebrek,[14] Gabrielle Roth Guepin,[15] Veronique Dorvaux,[16] Laurence Sanhes,[17] Maria Pilar Gallego-Hernanz,[18] Carole Exbrayat,[19] Laure Vincent,[20] Chantal Himberlin,[21] Célestine Simand,[22] Norbert Vey,[6] Cindy Fenoll,[23] Ariane Mineur,[23] Anne Huynh,[1] Francois Vergez,[24] Isabelle Luquet,[24] Laetitia Largeaud,[24] Eric Delabesse,[24] Arnaud Pigneux[25] and Christian Récher,[1] on behalf of the French Innovative Leukemia Organization (FILO)

Collaborative Groups: French Innovative Leukemia Organization (FILO)

[1] Service d'Hématologie, Centre Hospitalier Universitaire de Toulouse, Institut Universitaire du Cancer de Toulouse Oncopole, Toulouse, France

[2] Service d'Epidémiologie, Centre Hospitalier Universitaire de Toulouse, CERPOP, Inserm, Université Toulouse III Paul Sabatier, Toulouse, France

[3] Service d'Hématologie, Centre Hospitalier Universitaire de Nantes, France

[4] Service d'Hématologie clinique et de thérapie cellulaire, Centre Hospitalier Universitaire de Clermont-Ferrand, France

[5] Département d'Hématologie, Aix-Marseille Univ, Inserm, CNRS, Institut Paoli-Calmettes, CRCM, Marseille, France

[6] Service d'Hématologie, Centre Hospitalier Universitaire de Besançon, France

[7] Service d'Hématologie, Centre Hospitalier d'Orléans, France

[8] Service d'Hématologie, Centre Hospitalier Universitaire de Grenoble, France

[9] Maladies du Sang, CHU d'Angers, Fédération Hospitalo-Universitaire Grand-Ouest Acute Leukemia, FHU-GOAL, Université d'Angers, Inserm UMR 1307, CNRS UMR 6075, Nantes Université, CRCI2NA, Angers, France

[10] Service d'Hématologie, Centre Hospitalier de la Côte Basque, Bayonne, France

[11] Service d'Hématologie, Centre Hospitalier Universitaire de Rennes, France

[12] Service d'Hématologie, Centre Hospitalier Universitaire de Tours, France

[13] Service d'Hématologie, Centre Hospitalier de Béziers, France

[14] Service d'Onco-Hématologie, Centre Hospitalier d'Avignon, France

[15] Service d'Hématologie, Centre Hospitalier Universitaire de Nancy, France

[16] Service d'Hématologie, Centre Hospitalier de Metz, France

[17] Service d'Hématologie, Centre Hospitalier de Perpignan, France

[18] Service d'Hématologie, Centre Hospitalier Universitaire de Poitiers, France

[19] Service d'Hématologie, Clinique du Parc, Castelnau-le-Lez, France.

[20] Service d'Hématologie, Centre Hospitalier Universitaire de Montpellier, France

[21] Service d'Hématologie, Centre Hospitalier Universitaire de Reims, France

[22] Service d'Hématologie, Centre Hospitalier Universitaire de Strasbourg, France

[23] French Innovative Leukemia Organisation, Hôpital Bretonneau, Tours, France

[24] Laboratoire d'Hématologie, Centre Hospitalier Universitaire de Toulouse, Institut Universitaire du Cancer de Toulouse Oncopole, Toulouse, France

[25] Service d'Hématologie Clinique et de Thérapie Cellulaire, Centre Hospitalier Universitaire de Bordeaux, France

Running head: Dexamethasone in AML

Corresponding author : Prof. Christian Récher, Service d'Hématologie, Institut Universitaire du Cancer de Toulouse Oncopole, 1 avenue Irène Joliot-Curie, 31059 Toulouse cedex 9, France. Tel: +33531156355; fax: +33561777541; email: recher.christian@iuct-oncopole.fr

Trial registration: ClinicalTrialsRegistry.eu (Eudra-CT 2017-004860-36) and ClinicalTrials.gov (NCT03609060).

Contributions

CR, SB and EB contributed to the study conception and design. SB, PP, RG, YD, YH, OB, MC, MH, AB, MB, EG, AS, SC, GRG, VD, LS, MPGH, CE, LV, CH, CS NV, AP and CR treated patients and participated in clinical data collection and assembly. CR, SB, FV, IL, LL, ED and EB analysed the data. IL reviewed all cytogenetic results. LL and ED performed next-generation sequencing. FV carried out flow cytometry analyses. EB conducted statistical analyses. CR wrote the first draft of the manuscript. CR and EB wrote the manuscript. All authors had full access to all the data in the study, contributed to writing the manuscript and provided final approval of the submitted version.

Disclosures

SB declares a consulting or advisory role with Abbvie, Astellas, BMS-Celgene, Jazz Pharmaceuticals as well as Servier and received travel grants from Abbvie and Pfizer. CR declares a consulting or advisory role with Abbvie, Amgen, Astellas, BMS, Boehringer, Jazz Pharmaceuticals, J&J as well as Servier, received research funding from Abbvie, Amgen, Astellas, BMS, Iqvia and Jazz Pharmaceuticals, and support for attending meetings and/or travel from Abbvie, Novartis and Servier. PP declares a consulting or advisory role with Abbvie, BMS, as well as Servier, and received research funding from Astellas and Jazz Pharmaceuticals. NV declares a consulting or advisory role with Abbvie, Amgen, BMS, Boehringer, Janssen, Jazz Pharmaceuticals, Novartis as well as Servier, and received research funding from Novartis and Jazz Pharmaceuticals. AP declares a consulting or advisory role with Astellas, BMS, Servier, Abbvie, Gilead, Jazz Pharmaceuticals, Novartis, Pfizer, received research funding from Astellas, BMS, Roche, Servier and support for attending meetings and/or travel from Servier, Abbvie. All other authors declare no competing interests.

Acknowledgements

The authors thank the patients who participated in this trial and their families, the trial investigators, nurses, clinical research associates and other support staff at the clinical centers. A list of FILO institutions and investigators are presented in the appendix. The authors also wish to thank Prof. Marie Christine Béné, Lamya Haddaoui and Alexandra Fayault for their assistance in data management, patient sample processing (FILOtheque) and general organisation.

Data-sharing statement

Requests for sharing deidentified data should be directed to the corresponding author.

Fundings

The DEXAML-02 trial was funded by the FILO study group and the Force Hemato endowment funds (AO 2017).

Letter to the Editor,

The standard treatment for patients aged over 60 with newly diagnosed acute myeloid leukemia (AML) who are in good overall condition remains intensive chemotherapy.[1] With the exception of one study showing an event-free survival (EFS) benefit after addition of gemtuzumab ozogamycin (GO) to induction chemotherapy and another one demonstrating the impact of CPX-351 in therapy-related or secondary AML, there has been no recent improvement in outcome for this population.[2,3] The FILO group completed a phase 3 study showing that the addition of lomustine to intensive chemotherapy significantly increased CR rate, reduced the incidence of relapse and improved 2-year EFS.[4]

Recent retrospective studies showed that the addition of dexamethasone to intensive chemotherapy was significantly associated with lower early deaths and better outcome patients with hyperleukocytosis.[5,6] Moreover, preclinical studies demonstrated that specific oncogenic alterations or therapeutic stress (cytarabine, FLT3 inhibitors) are associated with up-regulation of the inflammatory gene response and expression of the glucocorticoid receptor which induce sensitisation to glucocorticoids in AML models.[7] Therefore, dexamethasone, used as a chemo-sensitizer, may improve treatment response and outcome regardless of leukocytosis. With this rationale, the DEXAML-02 trial evaluated the addition of dexamethasone to induction and post-remission chemotherapy in older AML patients.

This multicentre, phase 2, single-arm trial included patients aged 61 years or older, with newly diagnosed AML according to 2016 WHO classification, favorable or intermediate cytogenetic risk, Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 and hematopoietic cell transplantation-comorbidity index <3 (except history of cancer). AML arising from MDS, MPN or CMML were not included. This trial is registered at ClinicalTrialsRegistry.eu (Eudra-CT-2017-004860-36) and ClinicalTrials.gov (NCT03609060) and was approved by an Ethics Committee (CPP-IDF1-2018-ND29-cat.1) and the French National Agency for Medicines and Health Products Safety (MEDAECNAT-2018-03-00022). All patients provided written informed consent.

Induction chemotherapy was 8 mg/m² idarubicin on days (d) 1-5, 100 mg/m² cytarabine d1-7, 200 mg/m^2 lomustine d1 and 10 mg dexamethasone intravenously every 12 hours d1-3. Patients with no response after the induction cycle were off-study treatment. Patients with CR or CR with incomplete hematological recovery (CRi) were assigned to consolidation therapy consisting of 6 mini-consolidation courses every 30-45 days with 8 mg/m² idarubicin d1, 50 mg/m² cytarabine subcutaneously every 12 hours d1–5 and 20 mg dexamethasone intravenously d1. Patients with core-binding factor AML could receive 2-3 cycles of 1 cytarabine 1-1.5 g/m²/12 hours d1-3 (with the same dose of dexamethasone). Allogeneic haematopoietic stem-cell transplantation (HSCT) was recommended in patients with intermediate or adverse risk according to 2017 European LeukemiaNet (ELN) classification. The addition of midostaurin was authorised in patients with *FLT3* mutations. The primary endpoint was EFS defined according to ELN recommendations. Data analysis were performed using Stata Statistical Software (Release 17.0. Stata Corporation, College Station, Texas, USA).

120 patients were enrolled between August 2018 and February 2020. Six patients were excluded due to exclusion criteria (three with adverse karyotype, two with haematopoietic cell transplantation-comorbidity index ≥3 and one with central nervous system involvement) (Supplementary Figure 1). Characteristics of the 114 patients are shown in Table 1. Next-generation sequencing of 91 myeloid panel genes was centrally performed in 111 patients. The genetic risk according to 2022 ELN classification was favorable in 33 patients (31%), intermediate in 31 patients (29%) and adverse in 44 patients (40%).

During the induction phase, two patients prematurely discontinued dexamethasone. 23 patients with *FLT3* mutation (70%) received midostaurin. 104 patients received anti-fungal prophylaxis including 87 with an azole agent. Anti-viral and anti-pneumocystis jiroveci prophylaxes were used in 97 and 47 patients, respectively. The most common grade 3-4 adverse events were infection in 57 patients (50%), mucositis in 20 (18%) and hyperglycemia in 12 patients (11%) (Supplementary Table 1). Bacterial and fungal infections were observed in 52 and five patients, respectively. The median number of days between day 1 and an absolute neutrophil count $\geq 0.5 \times 10^9$ cells per L was 26 days

(IQR, 24-30) whereas median duration with platelet counts lower than 10 x 10^9 cells per L was 10.5 days (IQR, 1.5-19). During post-remission therapy, the frequency of grade 3-4 infections or other adverse events was low (<15%) and stable over the six chemotherapy cycles.

As a marker of dexamethasone activity, CRP levels were measured at inclusion and day 8 of induction chemotherapy. Median CRP level were 17 mg/L (IQR, 5-53) and 12 mg/L (IQR, 4-27) at inclusion and day 8, respectively. 95 patients (83%) achieved CR or CRi by the end of induction (Table 2). Four patients (4%) died at day 30 and nine (8%) at day 60. 23 patients (20%) with CR/CRi were allografted after a median duration of 154 days from induction (IQR, 128-188) and after a median number of 2 consolidation cycles (IQR, 2-3). All but one patient maintained CR at time of transplant. Donor source was matched-related in four subjects, matched-unrelated in 12 patients and haplo-identical in seven patients. Other CR/CRi patients who were not transplanted in first CR/CRi received a median number of four consolidation cycles (IQR, 0-6).

After a median follow-up of 32 months (IQR, 28-35), EFS at two years was 46% (95% CI 36-54). Median EFS was 19.7 months (IQR, 6-not reached) in the whole population, not reached (IQR, 8.6-not reached) in the 2022 ELN favorable-risk group, 20.4 months (IQR, 6.6-not reached) in the intermediate group and 12.4 months (IQR, 1.8-not reached) in the adverse group (Figure 1).

In patients who experienced CR/CRi, RFS at two years was 52% (95% CI 42-62). Median RFS was 26.7 months (IQR, 9-not reached) in the whole population, not reached (IQR, 7-not reached) in the 2022 ELN favorable-risk group, 20.1 months (IQR, 7-not reached) in the intermediate group and 22.3 months (IQR, 9-not reached) in the adverse group. 48 patients (42%) received a second line therapy with intensive chemotherapy in 13 patients, hypomethylating agents in 23 patients or small molecule inhibitors including FLT3 inhibitors in seven patients or IDH inhibitors in 10 patients.

OS at two years was 63% (95% CI 54-71). Median OS was neither reached (IQR, 12-not reached) in the whole population nor in the 2022 ELN favorable (IQR, 24-not reached) or intermediate (IQR, 11-not reached) risk groups, and 27.5 months (IQR, 9-not reached) in the adverse group.

Since dexamethasone displayed anti-leukemic activity in samples with *NPM1* mutations,[5] we performed sensitivity analyses in the 43 *NPM1* mutated patients. 41 patients (95.3%) achieved CR or CRi rate by the end of induction chemotherapy and one patient died at day 30. Of the 30 CR or CRi patients who were evaluated locally using qPCR for measurable residual disease (MRD) monitoring after induction chemotherapy, nine had negative MRD and 14 had low level (<2%) MRD. Median EFS, RFS and OS were not reached. EFS at two years was 56% (95% CI 40-69). In CR/CRi patients, RFS at two years was 56% (95% CI 39-69). OS at two years was 74% (95% CI 59-85) (Supplementary Figure 2).

The DEXAML-02 trial is one of the first studies to evaluate the role of an anti-inflammatory approach combined with intensive chemotherapy in older fit patients with AML.[8] Results showed that this regimen is safe and associated with promising anti-leukemic activity.

The risk of severe sepsis and invasive fungal infections is of concern when using glucocorticoids in patients with neutropenia.[9] However, the safety profile of the three-day course of dexamethasone at the beginning of induction chemotherapy was acceptable especially regarding the risk of infection.

With 2-year EFS and OS at 46% and 63% respectively, the outcome of patients included in the DEXAML-02 study compares favorably with other studies. In the HOVON-SAKK trial evaluating high-dose daunorubicin, 2-EFS and OS rates in patients with intermediate cytogenetic risk were 21% and 34%, respectively.[10] The ALFA-0701 trial evaluating GO in 50-70 year old patients (median age, 62 years) demonstrated 2-year EFS and OS rates of 47% and 65% in the GO arm in patients with favorable or intermediate cytogenetic risk.[2] In the German inter-group trial comparing different chemotherapy strategies versus a common standard arm in patients aged over 60 (78% favorable or intermediate cytogenetic risk), 2-year EFS and OS stood at 20 and 30%.[11]

Patients with *NPM1* mutations may benefit from the addition of dexamethasone (95% CR/CRi and 74% 2-year OS). Overexpression of inflammatory gene signatures in patients with *NPM1* mutation has been revealed by transcriptomic analyses.[5,12]

Integration of myelodysplasia-related gene mutations into the new 2022 ELN risk classification has meant that a significant proportion of patients with intermediate cytogenetic risk have switched to the adverse group.[1] Our result showed that the 2022 ELN classification poorly discriminated intermediate and adverse risk groups in patients selected based on cytogenetics only.[13]

The DEXAML-02 trial had some limitations such as the limited number of participants and the single arm trial design. We also acknowledge that lomustine in the induction chemotherapy backbone is not widely used. A randomised trial is required to confirm whether dexamethasone may improve outcome in this patient population. Nevertheless, this study updates the results of intensive chemotherapy in older patients with a high CR rate, an early death rate <5% and a median survival not reached.

References

1. Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377.
2. Castaigne S, Pautas C, Terré C, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012;379(9825):1508-1516.
3. Lancet JE, Uy GL, Newell LF, et al. CPX-351 versus 7+3 cytarabine and daunorubicin chemotherapy in older adults with newly diagnosed high-risk or secondary acute myeloid leukaemia: 5-year results of a randomised, open-label, multicentre, phase 3 trial. Lancet Haematol. 2021;8(7):e481-e491.
4. Pigneux A, Béné MC, Salmi LR, et al. Improved Survival by Adding Lomustine to Conventional Chemotherapy for Elderly Patients With AML Without Unfavorable Cytogenetics: Results of the LAM-SA 2007 FILO Trial. J Clin Oncol. 2018;36(32):3203-3210.
5. Bertoli S, Picard M, Bérard E, et al. Dexamethasone in hyperleukocytic acute myeloid leukemia. Haematologica. 2018;103(6):988-998.
6. Cerrano M, Chevret S, Raffoux E, et al. Benefits of dexamethasone on early outcomes in patients with acute myeloid leukemia with hyperleukocytosis: a propensity score matched analysis. Ann Hematol. 2023;102(4):761-768.
7. Récher C. Clinical Implications of Inflammation in Acute Myeloid Leukemia. Front Oncol. 2021;11:623952.
8. Peterlin P, Garnier A, Le Bourgeois A, et al. Tocilizumab in combination with a standard induction chemotherapy in acute myeloid leukaemia patients (TOCILAM study): a single-centre, single-arm, phase 1 trial. EClinicalMedicine. 2023;64:102254.
9. Inaba H, Pui CH. Glucocorticoid use in acute lymphoblastic leukaemia. Lancet Oncol. 2010;11(11):1096-1106.
10. Löwenberg B, Ossenkoppele GJ, van Putten W, et al. High-dose daunorubicin in older patients with acute myeloid leukemia. N Engl J Med. 2009;361(13):1235-1248.
11. Niederwieser D, Lang T, Krahl R, et al. Different treatment strategies versus a common standard arm (CSA) in patients with newly diagnosed AML over the age of 60 years: a randomized German inter-group study. Ann Hematol. 2023;102(3):547-561.
12. Corrigan DJ, Luchsinger LL, Justino de Almeida M, Williams LJ, Strikoudis A, Snoeck HW. PRDM16 isoforms differentially regulate normal and leukemic hematopoiesis and inflammatory gene signature. J Clin Invest. 2018;128(8):3250-3264.
13. Rausch C, Rothenberg-Thurley M, Dufour A, et al. Validation and refinement of the 2022 European LeukemiaNet genetic risk stratification of acute myeloid leukemia. Leukemia. 2023;37(6):1234-1244.

Table 1: Characteristics of the AML patients included in DEXAML-02

	DEXAML-02
	114
Age (years)	
Median	70
IQR	66;73
Min;Max	61;80
<70	54 (47%)
>=70	60 (53%)
Sex, n (%)	
Male	72 (63%)
Female	42 (37%)
ECOG performance status, n (%)	
0	46 (40%)
1	59 (52%)
2	9 (8%)
HCT-Comorbidity index	
Median	0
IQR	0; 1
Min;Max	0; 4
AML status, n (%)	
de novo	108 (95%)
therapy related	6 (5%)
WBC (x 10^9/L)	
Median	4·99
IQR	2;11
Min;Max	0·6; 137
Bone marrow blasts (%)	
Median	55%
IQR	35;83
Min;Max	6; 98
Cytogenetic risk, n (%)	
favorable	5 (4%)
intermediate	108 (96%)
2022 ELN risk classification, n (%)	
favorable	33 (31%)
intermediate	31 (29%)
adverse	44 (40%)
Mutations, n (%)	
NPM1	43 (38%)
FLT3-ITD	23 (20%)
FLT3-TKD	10 (9%)
CEBPA bZIP	5 (4%)
RUNX1	23 (21%)
ASXL1	23 (21%)
BCOR	6 (5%)
EZH2	5 (5%)
SF3B1	3 (3%)
SRSF2	27 (24%)
STAG2	18 (16%)
U2AF1	7 (6%)
ZRSR2	3 (3%)
TP53	2 (2%)

IQR=Inter-quartile Range. Min, Max=minimum, maximum.

Table 2: Response to induction and outcomes

	DEXAML-02
	N=114
Response to induction chemotherapy, n (%)	
CR or CRi	95 (83%)
Refractory disease	14 (12%)
Day-30 death	4 (4%)
Day-60 death	9 (8%)
Outcomes	
Median event-free survival, months (IQR)	19·7 (6-NR)
2-year event-free survival (%)	46% (95% CI 36-54)
Median relapse-free survival, months (IQR)	26·7 (9-NR)
2-year relapse-free survival (%)	52% (95% CI 42-62)
Median overall survival, months (IQR)	NR (12-NR)
2-year overall survival (%)	63% (95% CI 54-71)
Outcomes per 2022 ELN risk	
Favorable	**N=33**
CR or CRi, n (%)	31 (94%)
Median event-free survival, months (IQR)	NR (9-NR)
2-year event free survival (%)	61% (95% CI 42-75)
Median relapse-free survival, months (IQR)	NR (14-NR)
2-year relapse-free survival (%)	61% (95% CI 42-76)
Median overall survival, months (IQR)	NR (24-NR)
2-year overall survival (%)	76% (95% CI 57-87)
Intermediate	**N=31**
CR or CRi, n (%)	28 (90%)
Median event-free survival, months (IQR)	20·4 (7-NR)
2-year event free survival (%)	45% (95% CI 27-61)
Median relapse-free survival, months (IQR)	20·1 (7-NR)
2-year relapse-free survival (%)	50% (95% CI 30-66)
Median overall survival, months (IQR)	NR (11-NR)
2-year overall survival (%)	58% (95% CI 39-73)
Adverse	**N=44**
CR or CRi, n (%)	32 (73%)
Median event-free survival, months (IQR)	12·4 (2-NR)
2-year event free survival (%)	36% (95% CI 23-50)
Median relapse-free survival, months (IQR)	22·3 (9-NR)
2-year relapse-free survival (%)	47% (95% CI 29-63)
Median overall survival, months (IQR)	27·5 (9-NR)

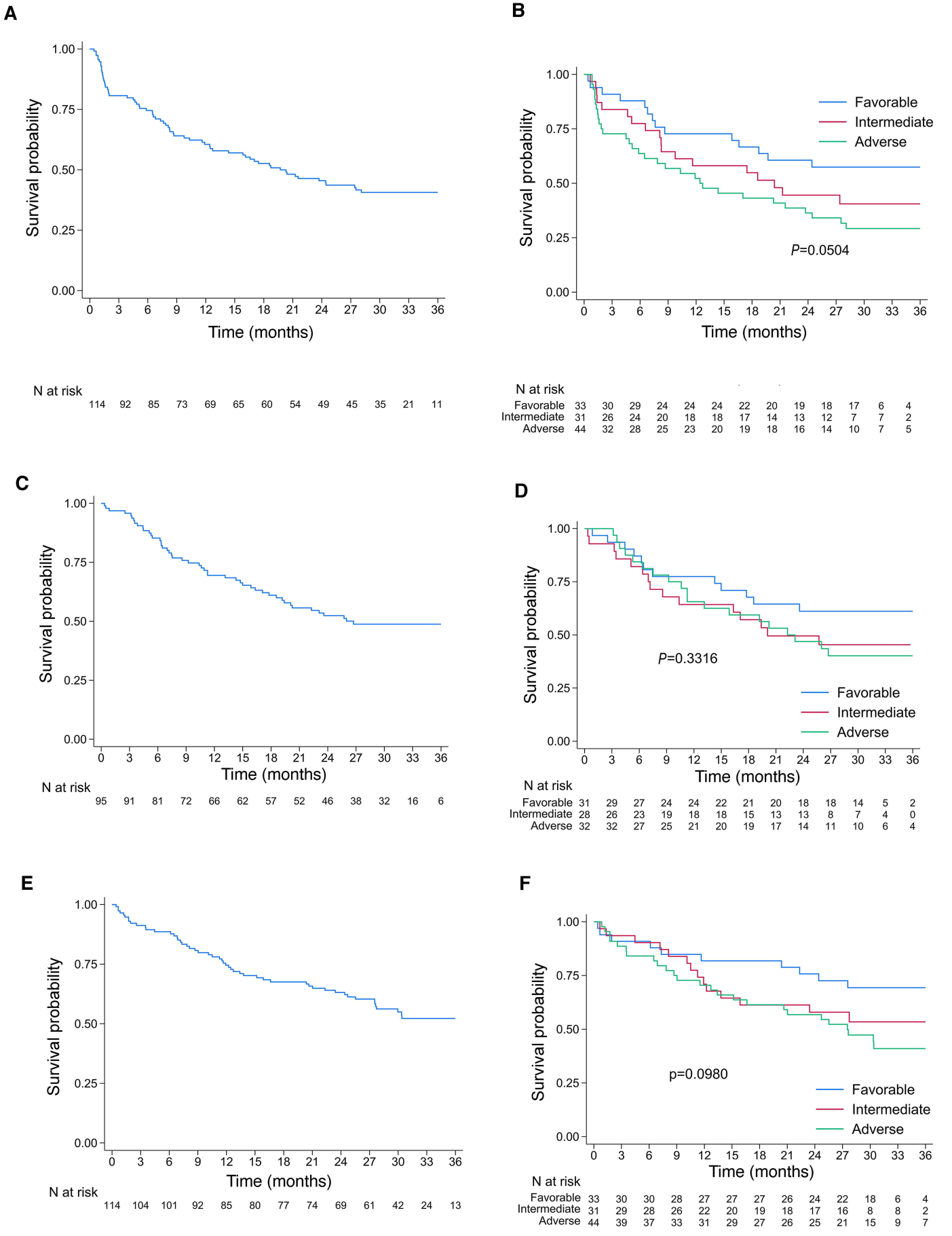
2-year overall survival (%)	57% (95% CI 41-70)

CR=complete remission. CRi=complete remission with incomplete hematological recovery. NR=not reached. IQR=inter-quartile range. CI=confidence interval.

Figure legends

Figure 1: Event-free survival, relapse-free survival and overall survival.

A. Event-free survival in the whole population. B. Event-free survival according to the 2022 ELN classification. C. Relapse-free survival in the whole population. D. Relapse-free survival according to the 2022 ELN classification. E. Overall survival in the whole population. F. Overall survival according to the 2022 ELN classification.


A
Survival probability
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33 36
Time (months)
N at risk
114 92 85 73 69 65 60 54 49 45 35 21 11
B
Survival probability
Favorable
Intermediate
Adverse
P=0.0504
Time (months)
N at risk
Favorable 33 30 29 24 24 24 22 20 19 18 17 6 4
Intermediate 31 26 24 20 18 18 17 14 13 12 7 7 2
Adverse 44 32 28 25 23 20 19 18 16 14 10 7 5
C
Survival probability
Time (months)
N at risk
95 91 81 72 66 62 57 52 46 38 32 16 6
D
Survival probability
P=0.3316
Favorable
Intermediate
Adverse
Time (months)
N at risk
Favorable 31 29 27 24 24 22 21 20 18 18 14 5 2
Intermediate 28 26 23 19 18 18 15 13 13 8 7 4 0
Adverse 32 32 27 25 21 20 19 17 14 11 10 6 4
E
Survival probability
Time (months)
N at risk
114 104 101 92 85 80 77 74 69 61 42 24 13
F
Survival probability
p=0.0980
Favorable
Intermediate
Adverse
Time (months)
N at risk
Favorable 33 30 30 28 27 27 27 26 24 22 18 6 4
Intermediate 31 29 28 26 22 20 19 18 17 16 8 8 2
Adverse 44 39 37 33 31 29 27 26 25 21 15 9 7

Supplementary Information

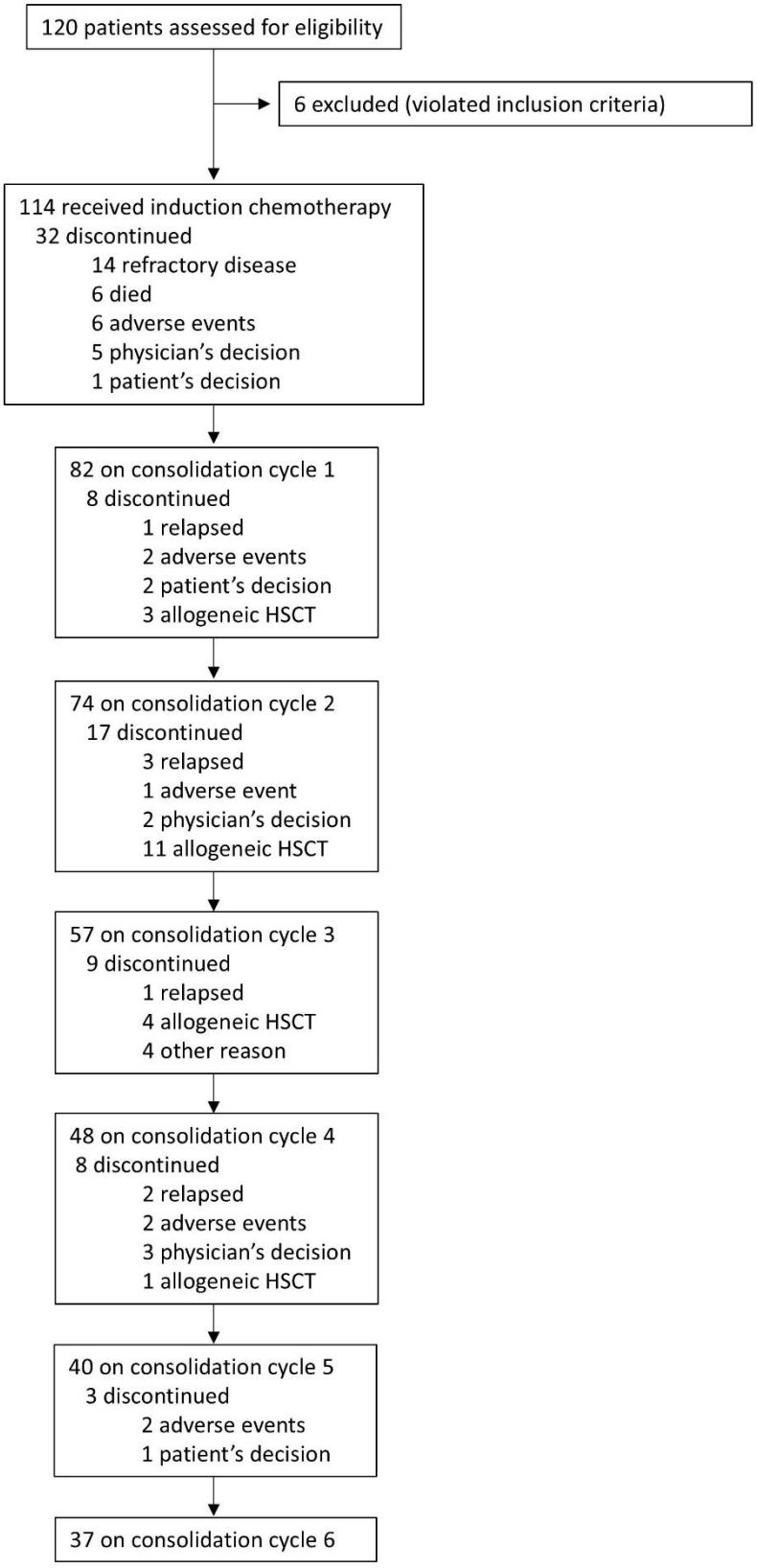
Dexamethasone added to induction and post-remission therapy in older patients with newly diagnosed acute myeloid leukemia: a multicenter, phase II trial (DEXAML-02). *Sarah Bertoli et al.*

Supplementary table 1: Hematologic toxicity and adverse events during induction chemotherapy*

	DEXAML-02
	N=114
Number of days with platelets < 10 x 10^9/L	
Median	10·5
IQR	1·50; 19·00
Number of days between day 1 of induction and day when ANC ≥ 0·5 x 10^9/L	
Median	26
IQR	24; 30
Number of RBC transfusions during induction	
Median	9
IQR	6; 13
Number of platelets transfusions during induction	
Median	9·5
IQR	7; 15
Number of days with fever ≥ 38 degrees C	
Median	6
IQR	3; 11
Number of days with antibiotics	
Median	23
IQR	18; 29
Infections, n (%)	
Documented infection	65 (57%)
Grade 3-4	57 (50%)
Septic shock	3 (3%)
Grade 3-4 cutaneous, n (%)	6 (5%)
Grade 3-4 mucositis, n (%)	20 (18%)
Grade 3-4 haemorrhage, n (%)	5 (4%)
Grade 3-4 nausea or diarrhea or vomiting, n (%)	10 (9%)
Grade 3-4 pain, n (%)	4 (4%)
Grade 3-4 constipation , n (%)	2 (2%)
Grade 3-4 pulmonary events, n (%)	8 (7%)
Grade 3-4 arrhythmia, n (%)	2 (2%)
Grade 3-4 other cardiac toxicity, n (%)	7 (6%)
Grade 3-4 central nervous system, n (%)	3 (3%)
Grade 3-4 peripheral nervous system, n (%)	1 (1%)
Grade 3-4 alkaline phosphatases increased, n (%)	4 (4%)
Grade 3-4 ASAT increased, n (%)	4 (4%)
Grade 3-4 ALAT increased, n (%)	5 (4%)
Grade 3-4 bilirubin increased, n (%)	7 (6%)
Grade 3-4 creatinine increased, n (%)	1 (1%)
Grade 3-4 hyperglycemia, n (%)	12 (11%)
Grade 3-4 lipase increased, n (%)	1 (1%)
Grade 3-4 amylase increased, n (%)	1 (1%)

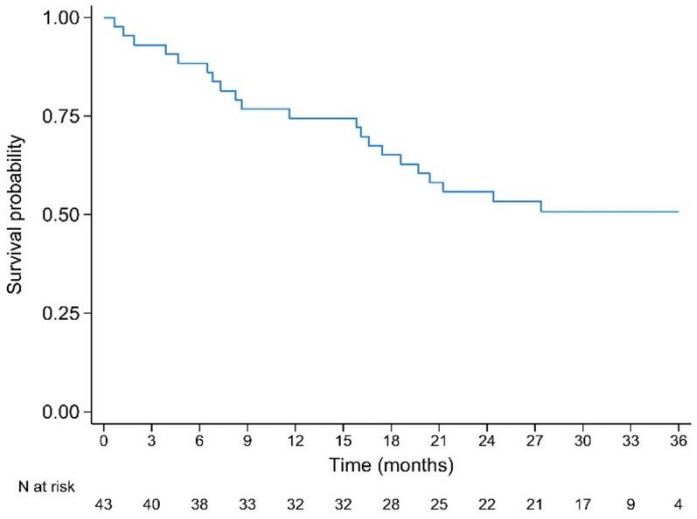
N=number. ANC=absolute neutrophil count. IQR=inter-quartile range. RBC=red blood cell. C=Celsius. NA=not applicable.
*Investigators were requested to monitor for and report adverse events as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0). Safety reports were monitored by the sponsor.

Supplementary figure 1: Consort diagram

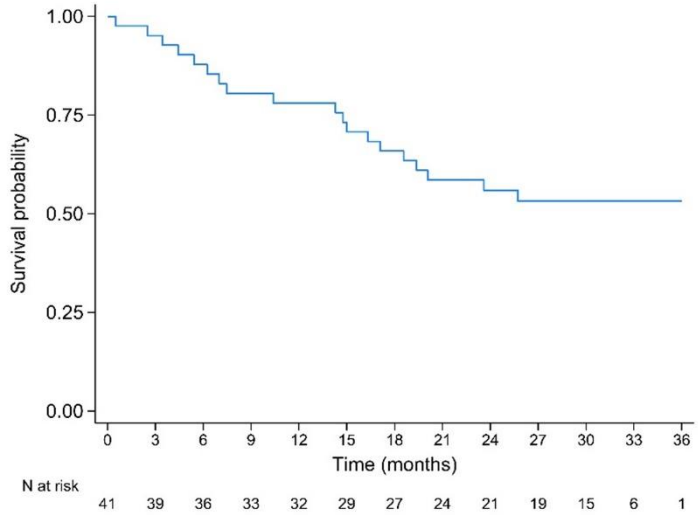


Supplementary figure 2: Event-free survival, relapse-free survival and overall survival in patients with *NPM1* mutations. A. Event-free survival. B. Relapse-free survival. C. Overall survival.

A



B



C