haematologica
Journal of the Ferrata Storti Foundation

Blinatumomab for measurable residual disease relapse in acute myeloid leukemia with t(8;21) translocation: the BlinAML Trial

by Carlos Jimenez-Vicente, Jad Othman, Nicola Potter, Jelena Jovanovic, Manohursingh Runglall, Phoebe Aucken, Laura Barr, Jennifer O'Sullivan, Hugues de Lavallade, Michael Lim, Patrick Harrington, Nigel Russell and Richard Dillon

Received: April 21, 2026.
Accepted: July 14, 2026.

Citation: Carlos Jimenez-Vicente, Jad Othman, Nicola Potter, Jelena Jovanovic, Manohursingh Runglall, Phoebe Aucken, Laura Barr, Jennifer O'Sullivan, Hugues de Lavallade, Michael Lim, Patrick Harrington, Nigel Russell and Richard Dillon. Blinatumomab for measurable residual disease relapse in acute myeloid leukemia with t(8;21) translocation: the BlinAML Trial.
Haematologica. 2026 July 23. doi: 10.3324/haematol.2026.301120 [Epub ahead of print]

Blinatumomab for measurable residual disease relapse in acute myeloid leukemia with t(8;21) translocation: the BlinAML Trial

Carlos Jiménez-Vicente[1], Jad Othman[1,2,3], Nicola Potter[1], Jelena Jovanovic[1], Manohursingh Runglall[1], Phoebe Aucken[1], Laura Barr[2], Jennifer O'Sullivan[2], Hughes de Lavallade[2], Michael Lim[1,2], Patrick Harrington[2], Nigel Russell[1,2], Richard Dillon[1,2]

1. Department of Medical and Molecular Genetics, King's College, London, UK
2. Department of Clinical Haematology, Guy's Hospital, London, UK
3. Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

Corresponding author: Richard Dillon, Department of Medical and Molecular Genetics, Kings College London, Floor 7 Tower Wing, Guy's Hospital, London SE1 9RT, United Kingdom. richard.dillon@kcl.ac.uk

Contribution: R.D., and N.R. designed and were principal investigators of the trial. C.J-V and.J.O curated data. C.J-V performed statistical analysis. N.P., J.J., M.R., and P.A performed measurable residual disease analyses. J.O., L.B., J.O'S., H.d.L., M.L., P.H. and R.D. provided clinical support to the patients, C.J-V, J.O., N.R. and R.D. drafted the paper, which was revised and approved by all authors.

Data Availability Statement: Access to deidentified data and supporting information can be requested from the corresponding author by qualified researchers who engage in rigorous, scientific research. Data may be provided following review and approval of a research proposal, statistical analysis plan, and execution of a data sharing agreement.

Funding Sources: Amgen provided the study drug and contributed funding; they had no role in the study's design, oversight, data analysis, or preparation of the manuscript. CJ-V received travel grant funding from the Societat Catalana d'Hematologia I Hemoteràpia (SCHH). JO was supported by fellowship grants from the Haematology Society of Australia and New Zealand and the RCPA Foundation.

Conflict of interest disclosure: CJ-V serves as educational speaker for AbbVie and Pfizer. RD declares consultancy for Astellas, Abbvie, Kura, ThermoFisher and Syndax. There are no other conflicts of interest to report.

Key words: Acute myeloid leukaemia (AML), blinatumomab, measurable residual disease (MRD), AML with t(8;21), bispecific t-cell engager (BiTE)

Acute myeloid leukaemia (AML) with t(8;21)(q22;q22.1)/*RUNX1::RUNX1T1* accounts for 8–10% of younger adults with the disease, and has a generally favourable prognosis (1), however about one third of patients relapse. For these patients the current standard of care is salvage chemotherapy followed by allogeneic haematopoietic stem cell transplantation (allo-HSCT) if feasible (2).

The *RUNX1::RUNX1T1* fusion is a recommended target for sequential monitoring of measurable residual disease (MRD) by real time quantitative polymerase chain reaction (RT-qPCR) (3) allowing early detection of molecular failure before overt relapse, however there are no established pre-emptive treatments in this situation.

Blinatumomab, a bispecific CD19xCD3 T-cell engager (BiTE), has demonstrated potent activity in clearing MRD in B-cell acute lymphoblastic leukaemia (B-ALL) (5). Since CD19 is aberrantly expressed in over 80% of t(8;21) AML cases (4), we investigated whether it may also be effective as pre-emptive therapy for MRD relapse in this disease subtype.

The single-center, single-arm phase II BlinAML trial (ISRCTN52962455) enrolled patients between September 2022 and October 2024. The study used a Simon's two-stage design, with a target of 7 patients in the first, and 10 in the second stage. The criteria for progression to stage II were that at least 4 of 7 patients achieved complete molecular remission at any time during trial treatment, and that treatment was discontinued due to toxicity in less than 3 patients. After withdrawal of drug supply by the manufacturer the study was terminated after 5 patients had been recruited. Patients had to be diagnosed with AML with t(8;21), have aberrant CD19 expression at diagnosis, and have molecular relapse or persistence defined according to the European LeukaemiaNet criteria (2) after receiving at least one previous line of treatment which included at least two courses of an anthracycline based regimen. Each cycle comprised 4 weeks of blinatumomab (28mcg/day) in a continuous intravenous infusion followed by an infusion free interval of 2 weeks. Patients were admitted during the first three days of cycle 1, and the first two days of subsequent cycles. MRD testing for *RUNX1::RUNX1T1* transcripts was performed as previously described following the Europe Against Cancer

(EAC) guidelines(6,7). The study was approved by the Wales Research Ethics Committee 2 (reference 21/WA/0243).

The primary endpoint was molecular complete remission (CR_{MRD-}) after one cycle of treatment defined as RT-qPCR test negativity. Secondary endpoints included: molecular response rate during treatment, defined as 1 log_{10} reduction of MRD, overall survival (OS), leukaemia-free survival (LFS), duration of molecular response, and adverse events. Patients could undergo allo-HSCT any time after cycle 1 if medically eligible with a suitable donor and could receive donor lymphocyte infusions (DLI) at any time after first day of cycle 1 (C1D1) if they had previously been allografted.

Categorical variables are presented as counts and percentages and continuous variables as medians with range. OS and LFS were estimated using the Kaplan-Meier method. Time-to-event endpoints were analysed from C1D1 onwards, and failure to achieve a molecular response, or subsequent molecular relapse, were considered leukaemia-free survival (LFS) events.

Baseline and response characteristics are summarized in Table 1. Five patients were included, their median age was 42 years (range 24–67) and all were male. All entered the study because of molecular relapse having achieved CR_{MRD-} with previous lines of therapy. Four patients had isolated t(8;21)(q22;q22.1) and one had a deletion of chromosome 9 in addition. Median number of previous treatments was 2 (range 2-4). Three patients had previously received allo-HSCT of whom two were treated with DLI before starting treatment (one patient received two infusions 12 and 5 weeks before starting blinatumomab and the other a single infusion five weeks before) without achieving molecular response. Median baseline *RUNX1::RUNX1T1* transcript level was 142 copies / 10^5 *ABL* (range 37-5624). All patients presented with a CD19 expression higher than 25% at diagnosis. This information was not possible to reassess before treatment due to the low disease burden at inclusion.

CR_{MRD-} was achieved in 2 patients after cycle 1, and a further one patient after cycle 2. One patient achieved a molecular response short of CR_{MRD-} with a 1.6 log_{10} reduction in MRD after two cycles, maintaining low level positive MRD status for more than 12

months of follow-up. The final patient was refractory to treatment, with a 0.75 log_{10} increase of MRD (Figure 1). Median duration of response was 16 months (range 6-31). Median number of cycles administered was 2 (range 2-4). There was not a correlation between transcript levels and response to treatment in this trial (Supplementary Figure 1) Reasons for treatment discontinuation before the completion of cycle 4 included lack of response in one case and physician decision in two cases.

At the cutoff date of 1st November 2025, with a median follow-up of 21 months (range 9-34), all patients are still alive. Two-year median LFS rate was 60% (95% confidence interval (CI): 29.3-100) (Supplementary Figure 2). Of the two patients that experienced an LFS event, one had no response to blinatumomab but achieved durable CR_{MRD-} after a second transplant and one experienced central nervous system relapse with concurrent MRD relapse six months after treatment discontinuation. Of the three patients that did not experience an LFS event, one received allo-HSCT after blinatumomab and two received pegylated interferon at an initial dose of 90mcg every two weeks as maintenance therapy.

Four patients experienced at least one adverse event during the first 2 cycles of blinatumomab. Three patients had a grade 3 non-haematological adverse event, including ALT increase in one case, upper gastrointestinal bleeding in another and two patients experienced viral infections without concomitant neutropenia or lymphopenia. Haematological adverse events included grade 3 neutropenia in two cases and grade 3 anaemia in one patient (Supplementary Table 1).

To our knowledge, we report the first prospective study a CD19 targeted therapy for AML with t(8;21) and MRD relapse. Previously small case series have shown efficacy of blinatumomab in patients with overt haematological relapse in AML with t(8;21) (8,9). In this series, we provide evidence of the safety and efficacy of blinatumomab as pre-emptive therapy to prevent overt relapse.

When compared with MRD-positive acute lymphoblastic leukaemia, where 78% of patients achieve a molecular response after a single treatment cycle (5), our cohort

displayed slower response kinetics. Two of the four patients who achieved a molecular response required two cycles of blinatumomab to reach that milestone.

In t(8;21) AML, overt relapse is sensitive to chemotherapy-based salvage regimens and allo-HSCT consolidation, with durable second remissions reported in over 60% of patients (10). Pre-emptive therapies may improve outcomes in patients presenting with MRD failure (11), however, the management of this clinical situation remains challenging. Variability in MRD kinetics may impact on the ability to identify patients with MRD relapse before they progress to overt haematological relapse(10,12), and pre-emptive treatment options are not well defined. When feasible, salvage chemotherapy followed by allo-HSCT consolidation is the standard of care, despite high toxicity and requirement for prolonged hospital admission. There is very little data to support the use of targeted therapies which have been shown to be effective in other molecular subtypes of AML such as venetoclax-based regimens in patients with *NPM1* mutation (13), or gilteritinib (14) in patients with *FLT3* mutation.

In this cohort, blinatumomab showed promising efficacy and a good safety profile. The low disease burden at treatment initiation may explain the limited toxicity. None of the patients discontinued treatment because of adverse events, and no blinatumomab-related neurologic or cytokine-release syndromes were reported. This supports its role as a therapeutic alternative for patients unfit for aggressive treatments, offering the additional advantage of outpatient administration and potential improvement in quality of life.

The favourable tolerability also enabled post-blinatumomab consolidation strategies such as Peg-INF (15) or DLI to be delivered, and their use may have influenced the sustained responses observed.

The main limitations of this study are the small sample size and the use of interventions such as DLI and Peg-INF before or after Blinatumomab therapy. Nonetheless, our results provide strong initial evidence of safety and efficacy, which warrant confirmation in larger, multicentre prospective studies.

REFERENCES

1. Grimwade D, Ivey A, Huntly BJP. Molecular landscape of acute myeloid leukemia in younger adults and its clinical relevance. Blood. 2016;127(1):29-41.

2. 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.

3. Heuser M, Freeman SD, Ossenkoppele GJ, et al. 2021 update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party. Blood. 2021;138(26):2753-2767.

4. Kita K, Nakase K, Miwa H, et al. Phenotypical characteristics of acute myelocytic leukemia associated with the t(8;21)(q22;q22) chromosomal abnormality: frequent expression of immature B-cell antigen CD19 together with stem cell antigen CD34. Blood. 1992;80(2):470-477.

5. Gökbuget N, Dombret H, Bonifacio M, et al. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia. Blood. 2018;131(14):1522-1531.

6. Gabert J, Beillard E, van der Velden VHJ, et al. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia – a Europe Against Cancer program. Leukemia. 2003;17(12):2318-2357.

7. Potter N, Jovanovic J, Ivey A, et al. Molecular monitoring versus standard clinical care in younger adults with acute myeloid leukaemia: results from the UK NCRI AML17 and AML19 randomised, controlled, phase 3 trials. Lancet Haematol. 2025;12(5):e346-e356.

8. Plesa A, Labussière-Wallet H, Hayette S, Salles G, Thomas X, Sujobert P. Efficiency of blinatumomab in a t(8;21) acute myeloid leukemia expressing CD19. Haematologica. 2019;104(10):e487-e488.

9. Yin J, Cui QY, Dai HP, et al. CD19 CAR-T in relapsed t(8;21) AML: a single-center prospective phase II clinical trial. J Hematol Oncol. 2025;18(1):53.

10. Yin JAL, O'Brien MA, Hills RK, Daly SB, Wheatley K, Burnett AK. Minimal residual disease monitoring by quantitative RT-PCR in core binding factor AML allows risk stratification and predicts relapse: results of the United Kingdom MRC AML-15 trial. Blood. 2012;120(14):2826-2835.

11. Orvain C, Bertoli S, Peterlin P, et al. Molecular relapse after first-line intensive therapy in patients with CBF or NPM1-mutated acute myeloid leukemia – a FILO study. Leukemia. 2024;38(9):1949-1957.

12. Puckrin R, Atenafu EG, Claudio JO, et al. Measurable residual disease monitoring provides insufficient lead-time to prevent morphologic relapse in the majority of patients with core-binding factor acute myeloid leukemia. Haematologica. 2021;106(1):56-63.

13. Tiong IS, Hiwase DK, Abro E, et al. Targeting molecular measurable residual disease and low-blast relapse in AML with venetoclax and low-dose cytarabine: a prospective phase II study (VALDAC). J Clin Oncol. 2024;42(18):2161-2173.

14. Othman J, Potter N, Mokretar K, et al. FLT3 inhibitors as MRD-guided salvage treatment for molecular failure in FLT3 mutated AML. Leukemia. 2023;37(10):2066-2072.

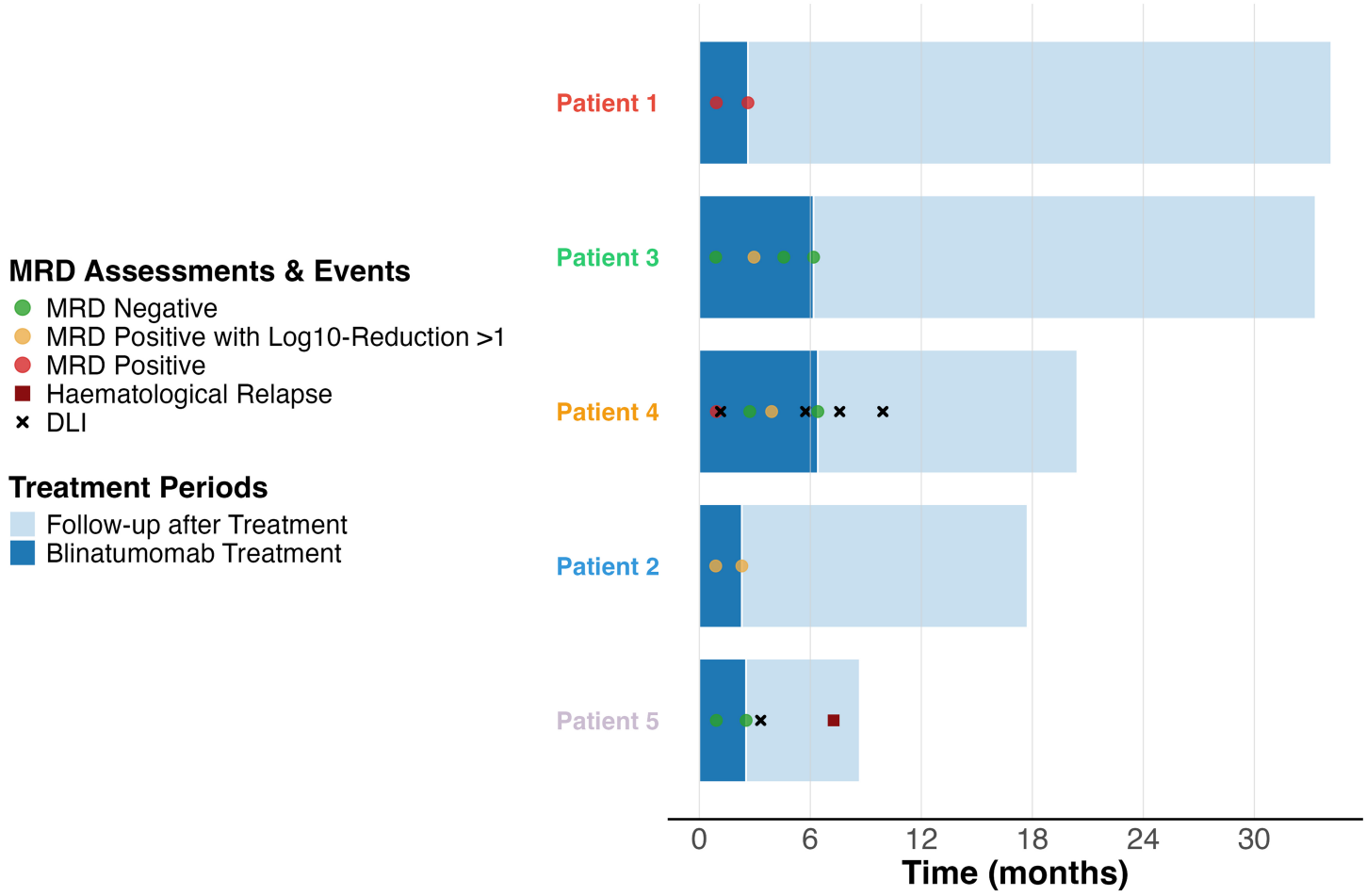
15. Fan S, Pan TZ, Dou LP, et al. Preemptive interferon-α therapy could prevent relapse of acute myeloid leukemia following allogeneic hematopoietic stem cell transplantation: a real-world analysis. Front Immunol. 2023;14:1091014.

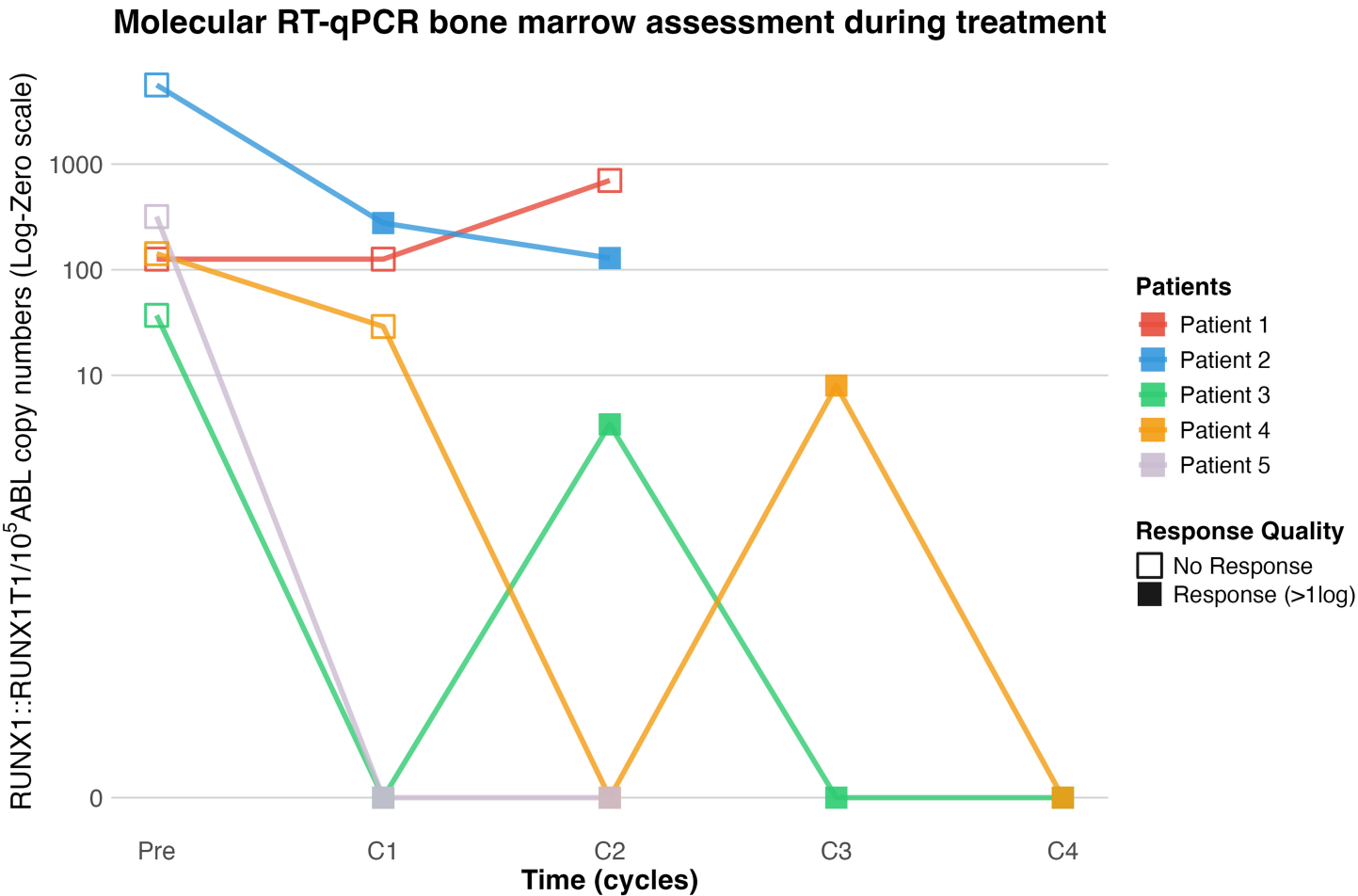
Patient	Age /Sex	Cytogenetics	ELN 2022 Risk	NGS	MRD status	Previous treatments	Initial BM *RUNX1::RUNX1T1/10^5 ABL* copies	Best response	Cycle to best response	Best log reduction	Treatment cycles	Treatment after Blinatumomab	Relapse after Blinatumomab
1	24/M	t(8;21)(q22;q22.1)	Favorable	NA	Relapse	DAx2+HDACx2 + FLAG-Ida + Quizartinib + IDAC+GO + MRD allo-HSCT + DLI x1	126	NR	NR	-0.75	2	Peg-INF allo.HSCT	Refractory
2	42/M	t(8;21)(q22;q22.1) + del(9)	Favorable	NA	Relapse	DA+GO + HDAC	5624	MR	1	1.6	2	allo HSCT	No
3	67/M	t(8;21)(q22;q22.1)	Favorable	NA	Relapse	DA-GO + HDAC + IDAC	37	MCR	2	Max	4	Peg-INF	No
4	35/M	t(8;21)(q22;q22.1)	Favorable	*KIT*	Relapse	DA-GO + HDAC + FLAG-Ida + MSD allo-HSCT	142	MCR	2	Max	4	Peg-INF DLI x4	No
5	43/M	t(8;21)(q22;q22.1)	Favorable	*ASXL1* *KIT* *NRAS*	Relapse	DA-GO + HDAC + FLAG-IDA + MRD allo-HSCT +DLI x2	319	MCR	1	Max	2	Peg-INF DLI x1	CNS haematological relapse

Table 1. Baseline characteristics, response and follow-up of all patients included in the BlinAML trial.

ELN: European LeukaemiaNet, DA: Daunorrubicin and cytarabine, HDAC: High-dose cytarabine, FLAG-IDA: Fludarabine, cytarabine, granulocyte colony-stimulating factor (G-CSF) and idarubicine, Ara-C: cytarabine, GO: gemtuzumab-ozogamicin, IDAC: intermediate-dose cytarabine, MSD: matched sibling donor, allo-HCST: allogeneic haematopoietic stem cell transplantation, BM: Bone marrow, NR: No response, MR: Molecular response, MCR: Molecular complete response, Peg-INF: Peginterferon alfa-2a, DLI: Donor lymphocyte infusion, CNS: Central Nervous System

Figure 1. Clinical course, treatment duration, and molecular response to blinatumomab. Upper panel: Swimmer-plot showing duration of blinatumomab treatment (dark blue) and follow-up (light blue) with MRD assessments and clinical events annotated. MRD results are displayed as dots: Negative (green), Positive with >1 log_{10} reduction (orange), Positive (red). Haematological relapse (red square) and DLI administration (Diamond). Lower panel: *RUNX1::RUNX1T1/10^{5}ABL1* copies in bone marrow by RT-qPCR (log_{10} scale) during treatment. Molecular responses (≥1 log_{10} reduction) are highlighted.


MRD Assessments & Events
MRD Negative
MRD Positive with Log10-Reduction >1
MRD Positive
Haematological Relapse
DLI
Treatment Periods
Follow-up after Treatment
Blinatumomab Treatment
Patient 1
Patient 3
Patient 4
Patient 2
Patient 5
0
6
12
18
24
30
Time (months)


Molecular RT-qPCR bone marrow assessment during treatment
RUNX1::RUNX1T1/10^5ABL copy numbers (Log-Zero scale)
1000
100
10
0
Pre
C1
C2
C3
C4
Time (cycles)
Patients
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
Response Quality
No Response
Response (>1log)

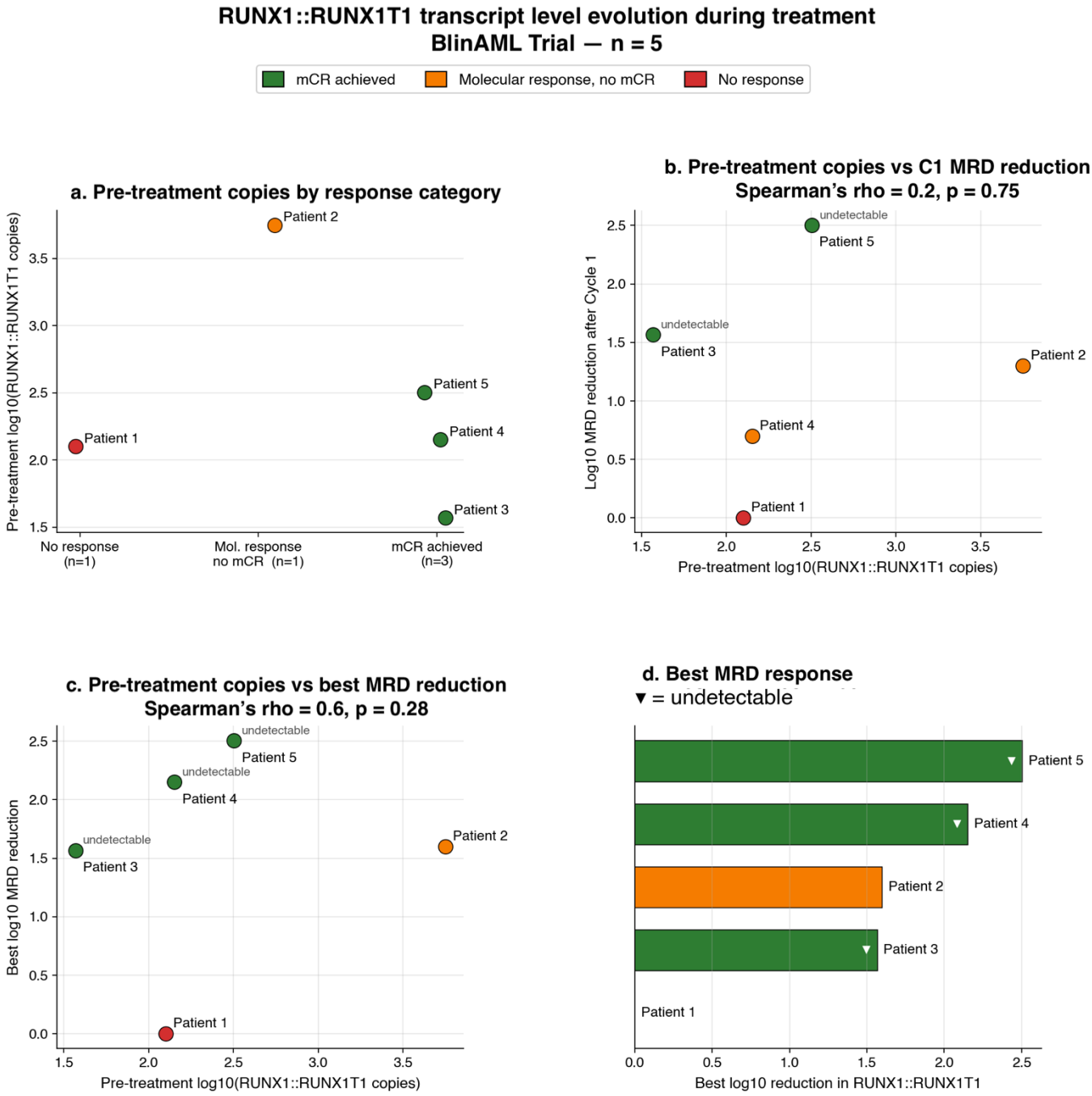
Supplementary Appendix

Blinatumomab for minimal disease burden in acute myeloid leukaemia with t(8;21) translocation: the BlinAML trial.

Carlos Jiménez-Vicente[1], Jad Othman[1,2,3], Nicola Potter[1], Jelena Jovanovic[1], Manohursingh Runglall[1], Phoebe Aucken[1], Laura Barr[2], Jennifer O'Sullivan[2], Hughes de Lavallade[2], Michael Lim[1,2], Patrick Harrington[2], Nigel Russell[1,2], Richard Dillon [1,2]

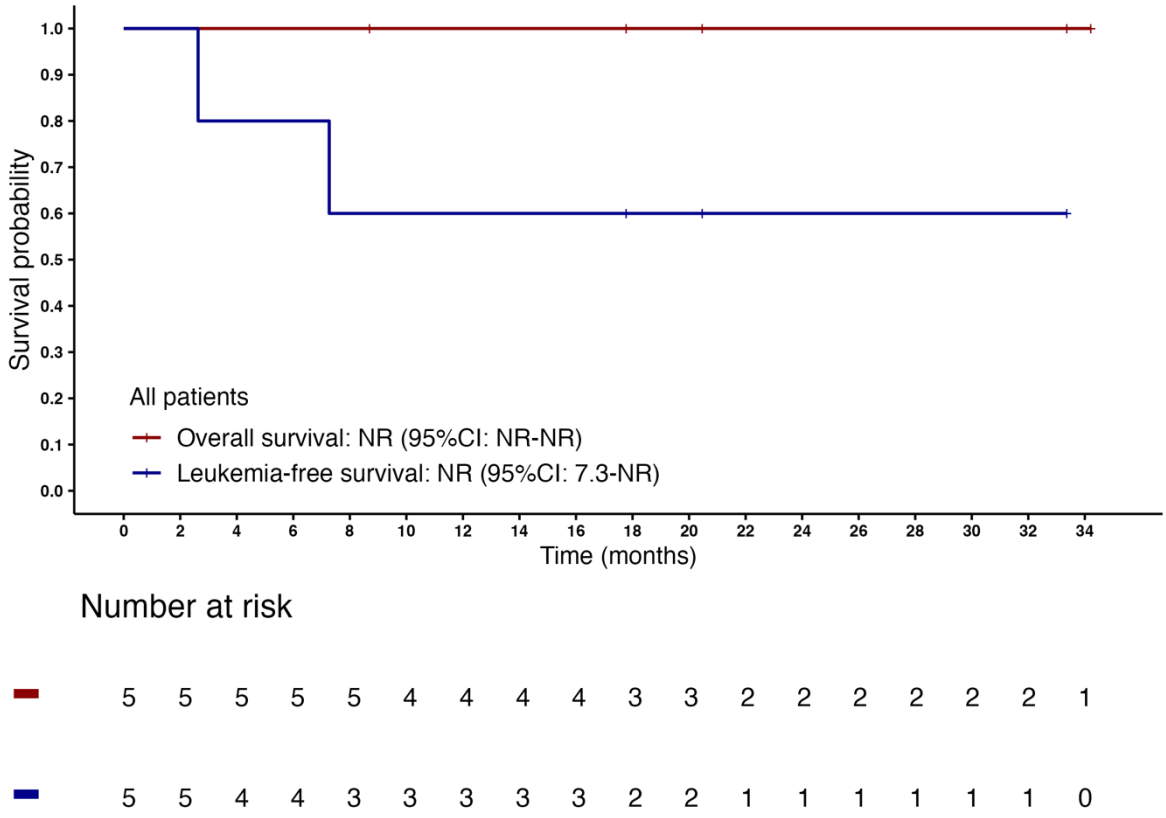
1. Department of Medical and Molecular Genetics, King's College, London, UK
2. Department of Clinical Haematology, Guy's Hospital, London, UK
3. Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

Corresponding author: Richard Dillon, Department of Medical and Molecular Genetics, Kings College London, Floor 7 Tower Wing, Guy's Hospital, London SE1 9RT, United Kingdom. richard.dillon@kcl.ac.uk



Supplementary Figure 1

Evolution of *RUNX1::RUNX1T1* fusion transcript levels during treatment in the trial. Patients are colour-coded by best molecular response throughout: green, mCR achieved (Patients 3, 4 and 5); orange, molecular response without mCR (Patient 2); red, no response (Patient 1).



Number at risk

5	5	5	5	5	4	4	4	4	3	3	2	2	2	2	2	2	1
5	5	4	4	3	3	3	3	3	2	2	1	1	1	1	1	1	0

Supplementary Figure 2.

Overall survival (red) and leukaemia-free survival (blue) in patients with AML t(8;21) and MRD failure treated with blinatumomab.

	N (%)
Any adverse event	3 (60)
Non-haematological adverse events ≥ grade 3	
ALT increase	1 (20)
Upper gastrointestinal bleeding	1 (20)
Viral infection	1 (20)
Non-haematological adverse events < grade 3	
Viral infection	2 (40)
Vascular access complication	1 (20)
Febrile neutropenia	1 (20)
ALT increase	1 (20)
Diarrhoea	1 (20)
Headache	1 (20)
Haematological adverse events ≥ grade 3	
Neutropenia	2 (40)
Anaemia	1 (20)

Supplementary Table 1.

Adverse events of all patients during treatment with blinatumomab. Adverse events were graded using the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0