

## Molecular MRD status and outcome after transplantation in NPM1-mutated AML

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DOI:

[10.1182/blood.2019002959](https://doi.org/10.1182/blood.2019002959)

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*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Dillon, R, Hills, RK, Freeman, SD, Potter, N, Jovanovic, J, Ivey, A, Kanda, AS, Runglall, M, Foot, N, Valganon, M, Khwaja, A, Cavenagh, J, Smith, ML, Ommen, HB, Overgaard, U, Dennis, M, Knapper, S, Kaur, H, Taussig, DC, Mehta, P, Raj, K, Novitzky-Basso, I, Nikolousis, E, Danby, RD, Krishnamurthy, P, Hill, K, Finnegan, D, Alimam, S, Hurst, E, Johnson, P, Khan, AB, Salim, R, Craddock, CF, Ruth Lilian Spearing, D, Gilkes, AF, Gale, RE, Alan Kenneth Burnett, Russell, NH & Grimwade, D 2020, 'Molecular MRD status and outcome after transplantation in NPM1-mutated AML', *Blood*, vol. 135, no. 9, pp. 680-688.  
<https://doi.org/10.1182/blood.2019002959>

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## Supplementary Appendix

### Molecular MRD status and outcome after transplantation in *NPM1* mutated AML: results from the UK NCRI AML17 study

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We gratefully acknowledge the support of all haematologists, nurses and laboratory scientists who contributed to the molecular monitoring arm of the National Cancer Research Institute AML17 trial.

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## Supplementary methods

### Calculation of the NCRI risk score

The NCRI risk score was derived from outcome data from the UK Medical Research Council (MRC) AML10 and AML12 trials and was validated using data from the MRC / National Cancer Research Institute (NCRI) AML15 trial<sup>1</sup>. The score takes into account age, sex, presenting white blood cell count, cytogenetics, secondary disease status and response to induction cycle 1.

In the study reported in this manuscript, patients with a score of greater than 2.667 were considered high risk and recommended for allogeneic transplant in first complete remission.

The score is calculated as follows:

$0.01325 * \text{age (in years)} + 0.16994 * \text{sex (1=male, 0=female)} + 0.22131 * \text{diagnosis (1=de novo, 2=secondary)} + 0.65082 * \text{cytogenetics (1=favourable, 2=intermediate, 3=adverse)} + 0.19529 * \text{status post C1 (1=complete remission, 2=partial remission, 3=refractory disease)} + 0.00169 * \text{WBC (x10}^9\text{/L)}$ .

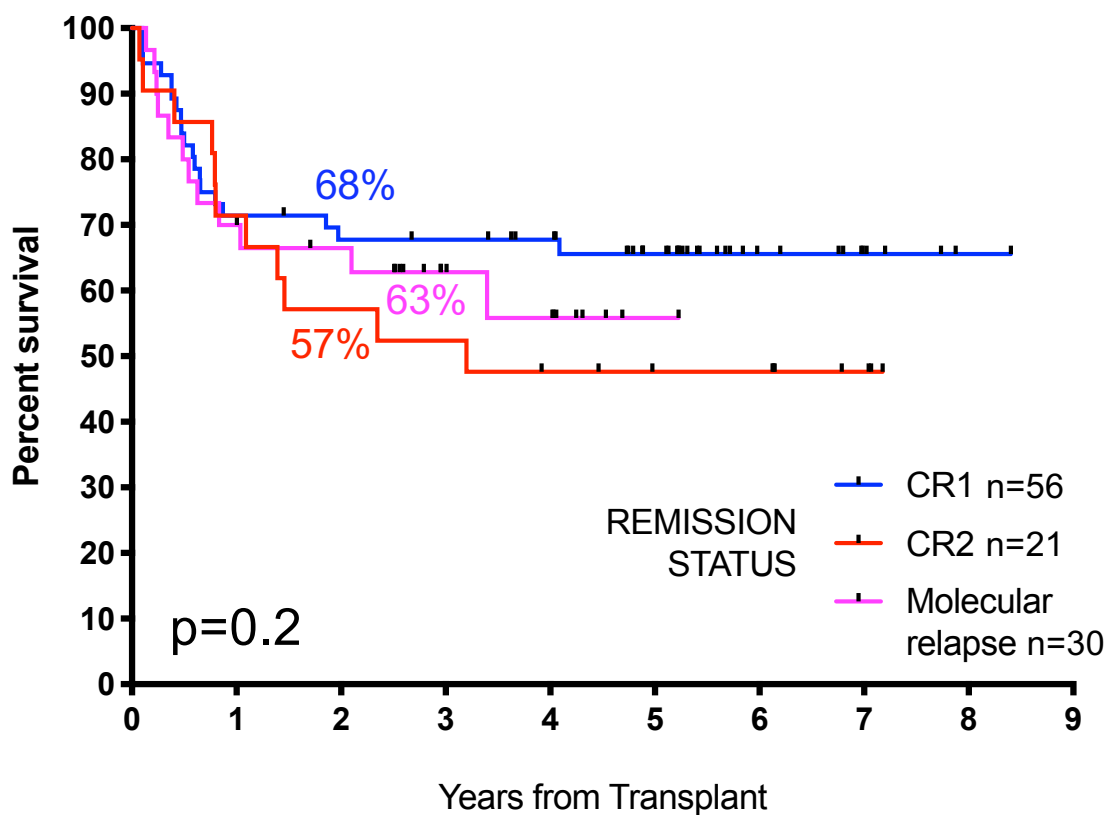
### References

1. Burnett A.K., R. K. Hills, K. Wheatley, A. H. Goldstone, A. G. Prentice, and D. Milligan. A sensitive risk score for directing treatment in younger patients with AML. *Blood* 108 (11):10a, 2006

## Supplementary Figures

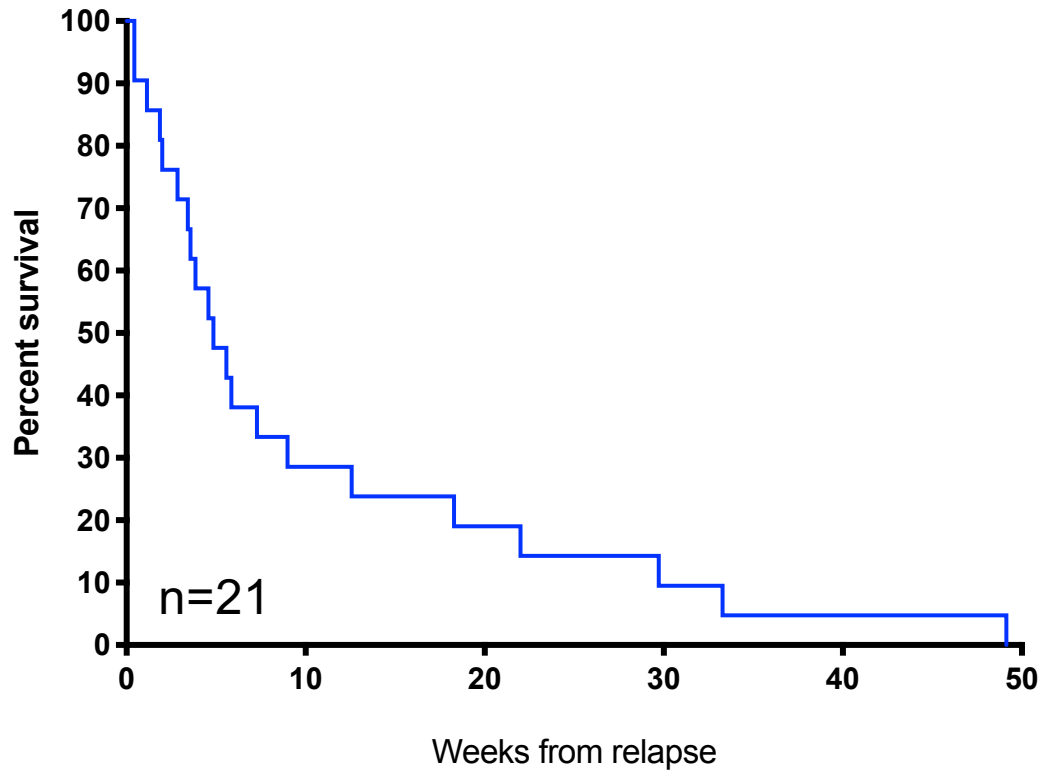
Supplementary figure 1.

**Overall survival from the date of transplant according to remission status at the time of transplant.** CR1 = 1<sup>st</sup> morphological complete remission without molecular relapse. CR2 = second morphological complete remission following a documented morphological relapse. Molecular relapse = 1<sup>st</sup> morphological complete remission with confirmed molecular relapse according to the definition of the European Leukaemia Network (ELN)<sup>43</sup>. Estimates for 2-year overall survival are shown. Overall  $p=0.2$  for trend;  $p=0.25$  for CR1 vs other;  $p=0.63$  for molecular vs haematological relapse;  $p=0.22$  for CR1 vs CR2.



Supplementary figure 2.

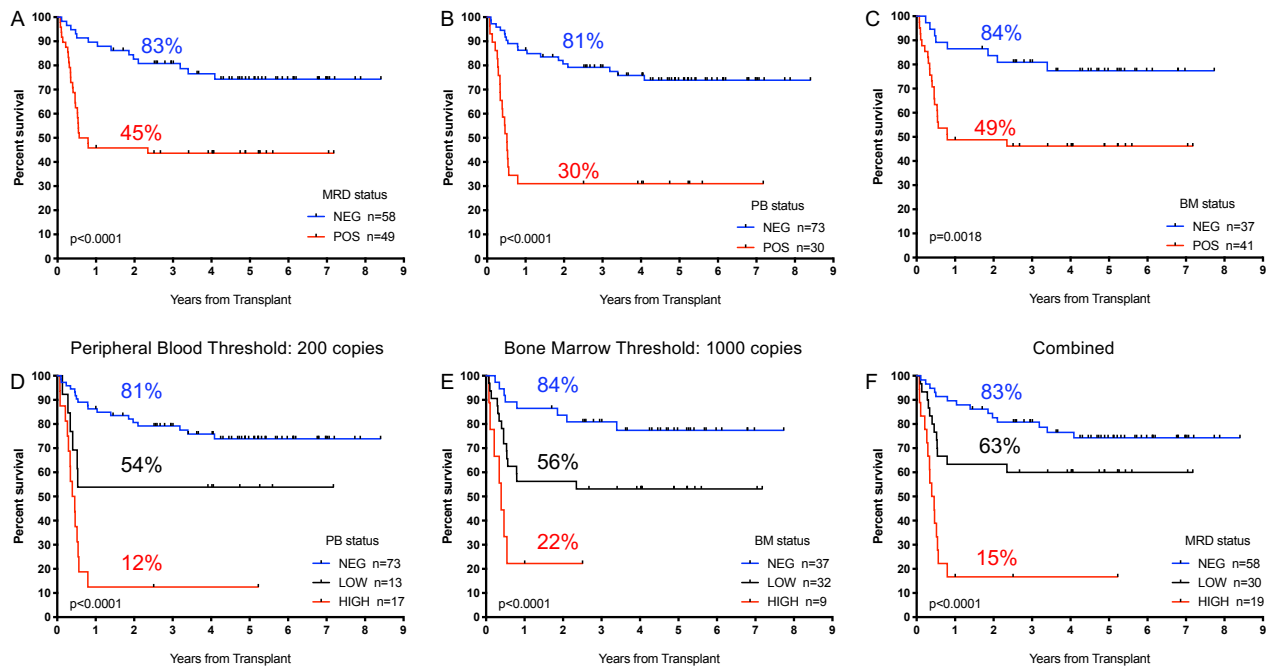
**Overall survival from the time of post-transplant relapse.** The median survival time was 34 days (range 3-344 days).





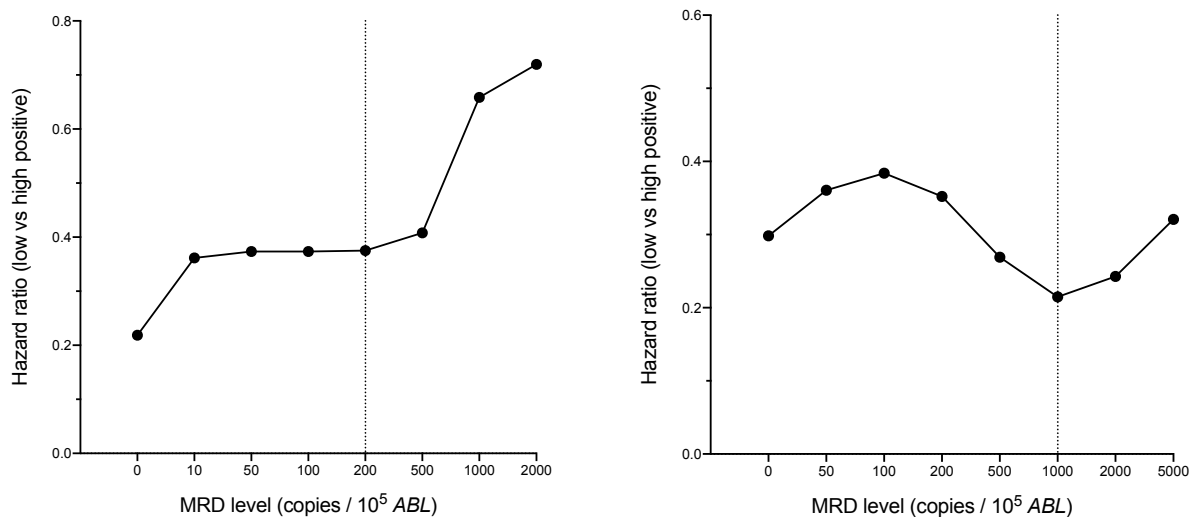
Supplementary figure 3.

**Relapse-free survival from date of transplant according to pre-transplant molecular MRD status.** Panels A-C show the difference in relapse-free survival between patients with positive and negative MRD (A) overall (B) in the peripheral blood, (C) in the bone marrow. Panels D-F show the difference in relapse-free survival between patients with negative, low and high levels of MRD (D) in the peripheral blood using a cut-off at 200 copies per  $10^5$  ABL (E) in the bone marrow with level of >1000 copies and (E) with either, defining “high level” MRD. Percentages indicate estimated 2-year relapse-free survival. p-values are indicated in the plots.

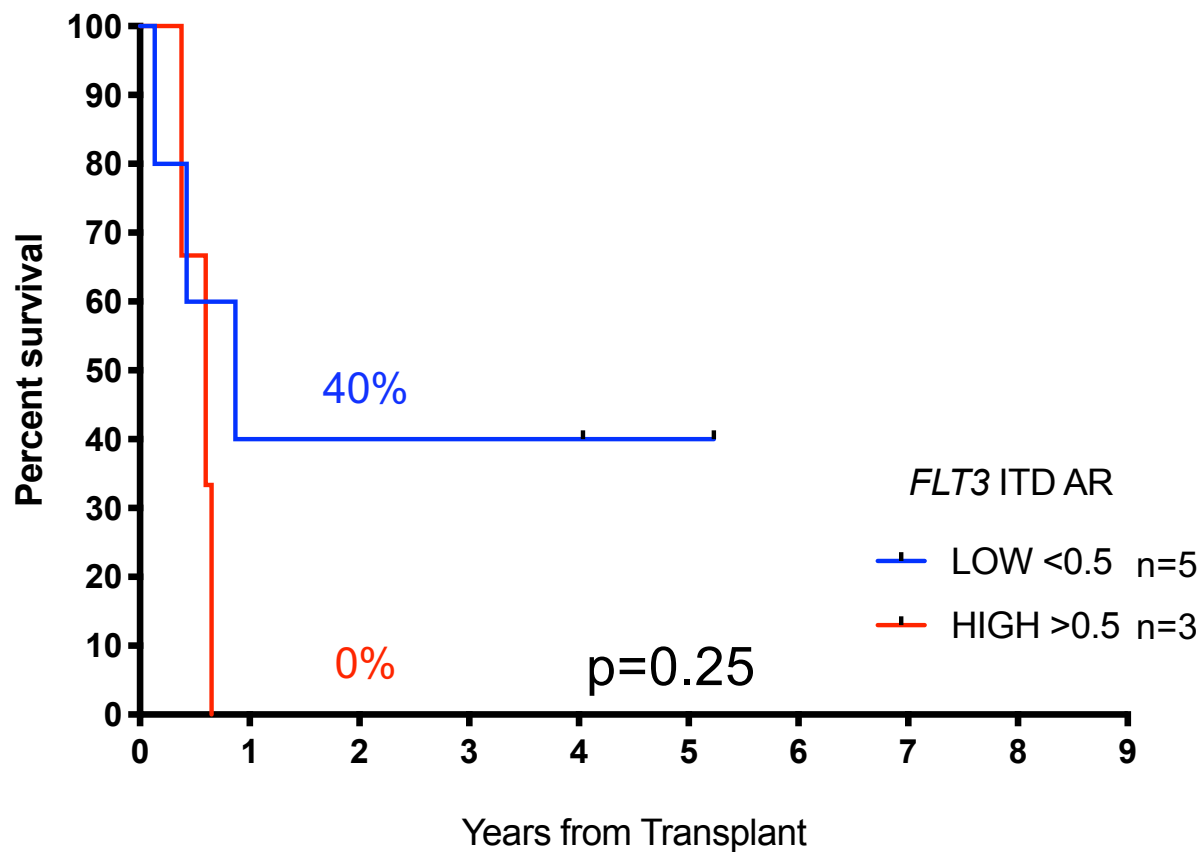


Supplementary figure 4.

**Identification of thresholds defining low and high levels of MRD.** The hazard ratio for overall survival for low vs. high positive MRD is plotted against the threshold level for peripheral blood (left panel) and bone marrow (right panel) samples. Thresholds chosen are indicated by a dotted line.



Supplementary figure 5. Overall survival from date of transplant for patients with low level MRD positivity and *FLT3* ITD mutation according to the *FLT3* allelic ratio (AR).



Supplementary figure 6. **Relapse-free survival according to risk group.** Risk group is defined in the main text. Percentages indicate estimated 2-year relapse-free survival.

