## Supplemental Appendix

# Treatment free remission after ceasing venetoclax-based therapy in patients with acute myeloid leukemia

Chua et al, 2022

This appendix has been provided by the author to give readers additional information about their work

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## SUPPLEMENTAL METHODS

Data was retrospectively collected from the Alfred Hospital in Melbourne, the University of Texas MD Anderson Cancer Center and the University of Colorado. To limit the analysis to a homogenous cohort with long-term follow-up, only patients enrolled and treated on the phase 1/2 clinical trials examining venetoclax lower-intensity combinations were included in this analysis to minimize selection bias (supplemental Figure 1). Patients who received <12 months of venetoclax-combination therapy and/or proceeded to allogeneic stem cell transplantation in first remission were excluded from this study. Reasons for treatment cessation were identified from the medical records.

Key endpoints included overall survival (OS, from day 1 of therapy), relapse free survival (RFS, as per European LeukemiaNet (ELN) 2017 definition[1]) and treatment free remission (TFR).

Measurable residual disease (MRD) data was collected from each site based on assays performed as per local institutional practice. MRD results from both flow cytometric (limit of detection, LoD, 0.01%) and molecular assays were collected where available. Only ELN recommended molecular MRD markers such as *NPM1* performed via leukemia-specific reverse-transcriptase quantitative polymerase chain reaction assays (RT-qPCR, LoD $10^{-4}$-$10^{-6}$) or digital droplet PCR (LoD $10^{-4}$) were collected.[2]

Kaplan-Meier survival curves were compared using the log-rank test. Group comparisons were evaluated using the Mann-Whitney-U test for continuous data and Chi squared test or Fishers exact test for categorical variables. A two-tailed p-value of <0.05 was used to indicate statistical significance.

Ethics approval was obtained from the Human Research Ethics Committees of the Alfred Hospital, the University of Texas MD Anderson Cancer Center and the University of Colorado. The study was conducted according to the Declaration of Helsinki.

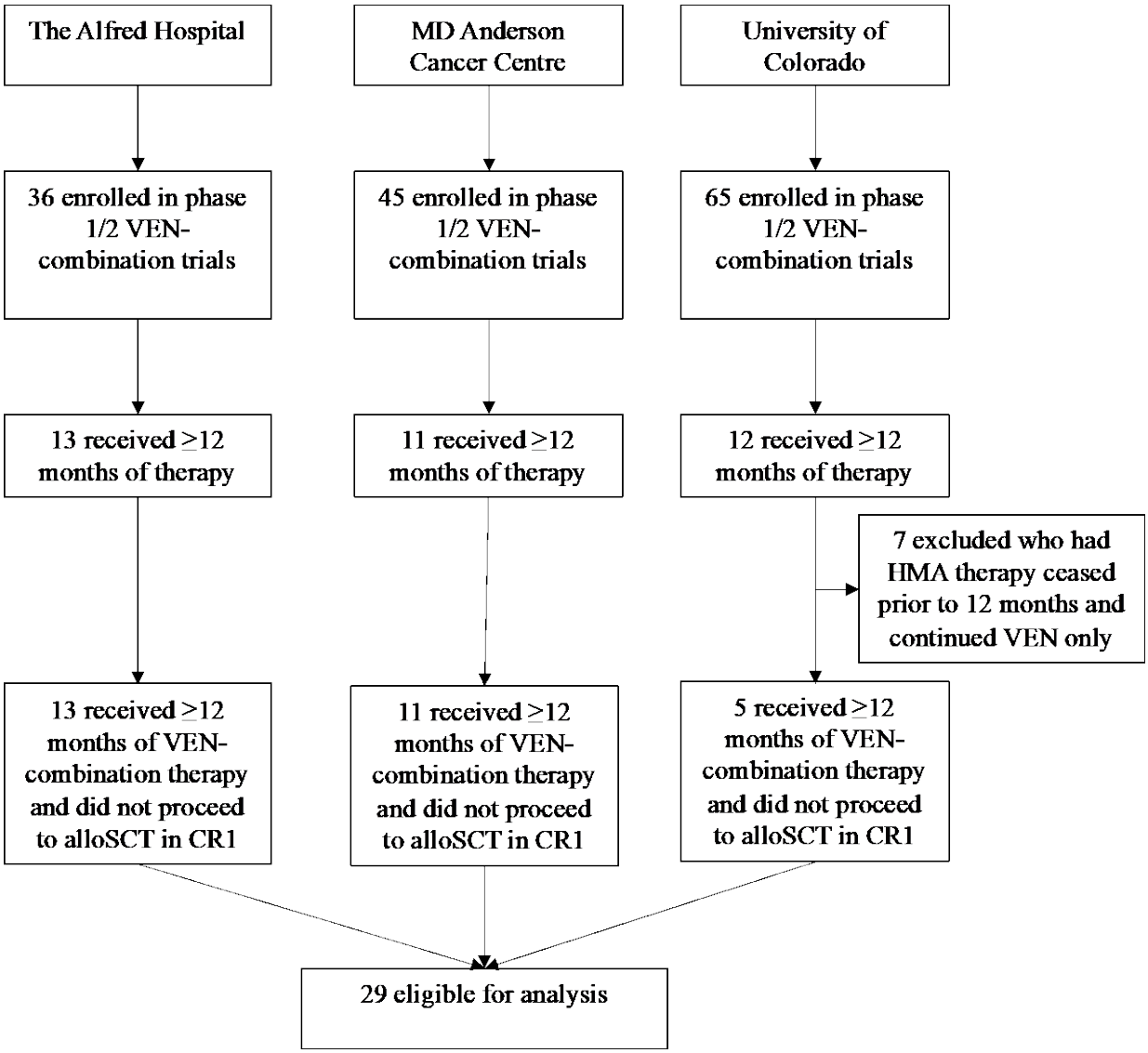
**SUPPLEMENTAL TABLE**

**Supplemental Table 1. Measurable residual disease (MRD) assessments in *NPM1* and/or *IDH2* mutant cases**

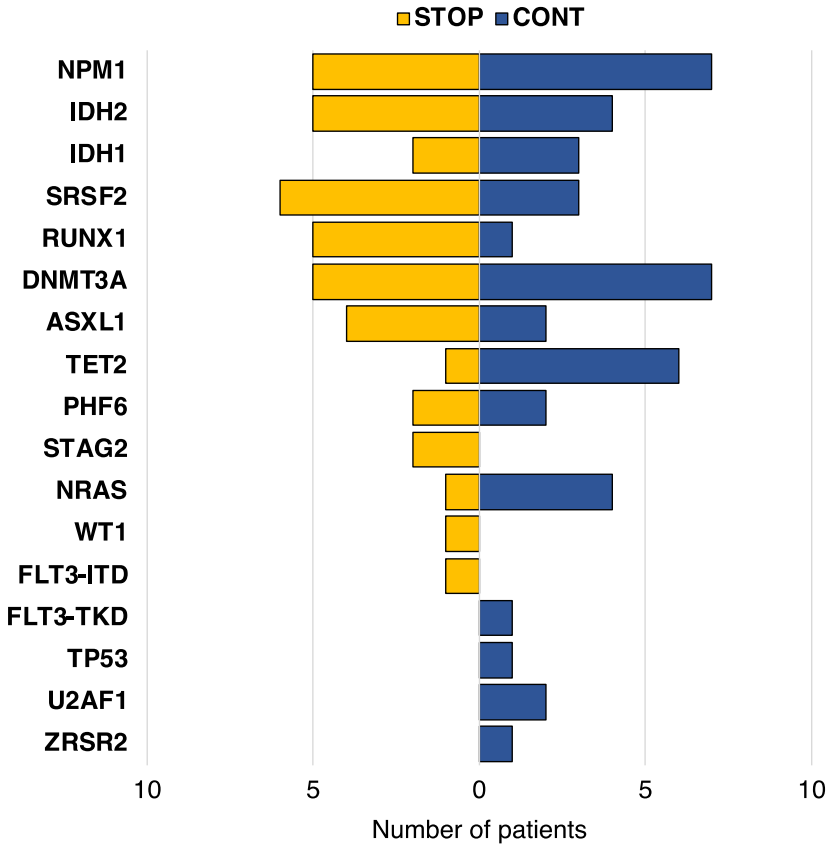
| N, (%) | Elective cessation in remission (STOP) | Continuous therapy (CONT) |
|---|---|---|
| *NPM1/IDH2* mutant cases | 8/13 (62%) | 10/16 (63%) |
| MRD analysis performed | 6/8 (75%) | 9/10 (90%) |
| MRD results<br>• Achieved MRD negative<br>• Persistent MRD positive | <br>6/6 (100%)<br>- | <br>8/9 (89%)<br>1/9 (11%) |
| Methodology<br>• Flow cytometry<br>• Molecular | <br>3/6 (50%)<br>5/6 (83%) | <br>9/9 (100%)<br>6/9 (67%) |
| Flow cytometry<br>• Achieved MRD negative<br>• Persistent MRD positive | <br>3/3 (100%)<br>- | <br>8/9 (89%)<br>1/9 (11%) |
| Molecular methods<br>• Achieved MRD negative<br>• Persistent MRD positive | <br>5/5 (100%)<br>- | <br>6/6 (100%)<br>- |

**SUPPLEMENTAL FIGURES**

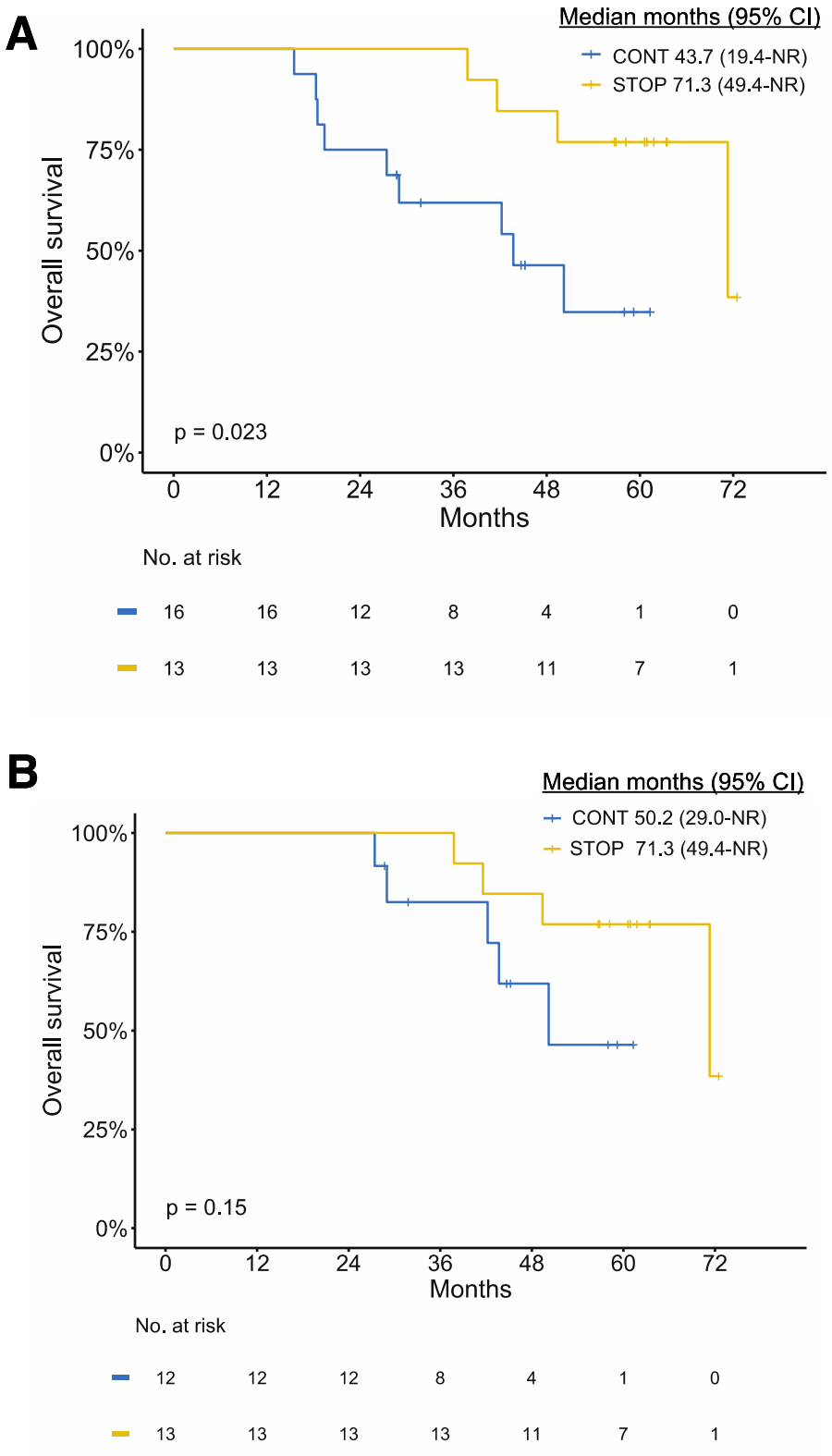
**Supplemental Figure 1. Consort diagram of patient selection from the Alfred Hospital, MD Anderson Cancer Centre and University of Colorado**



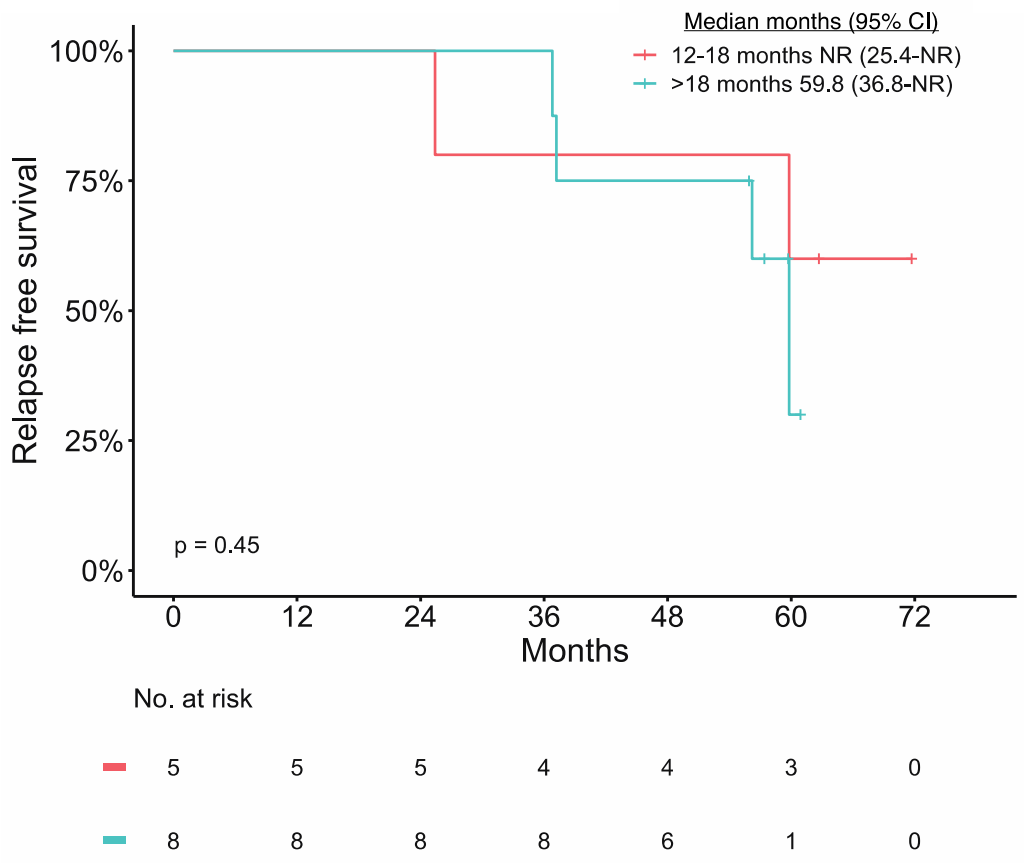
**Supplemental Figure 2. Comparison of molecular mutation profile at diagnosis in the STOP and CONT cohorts**



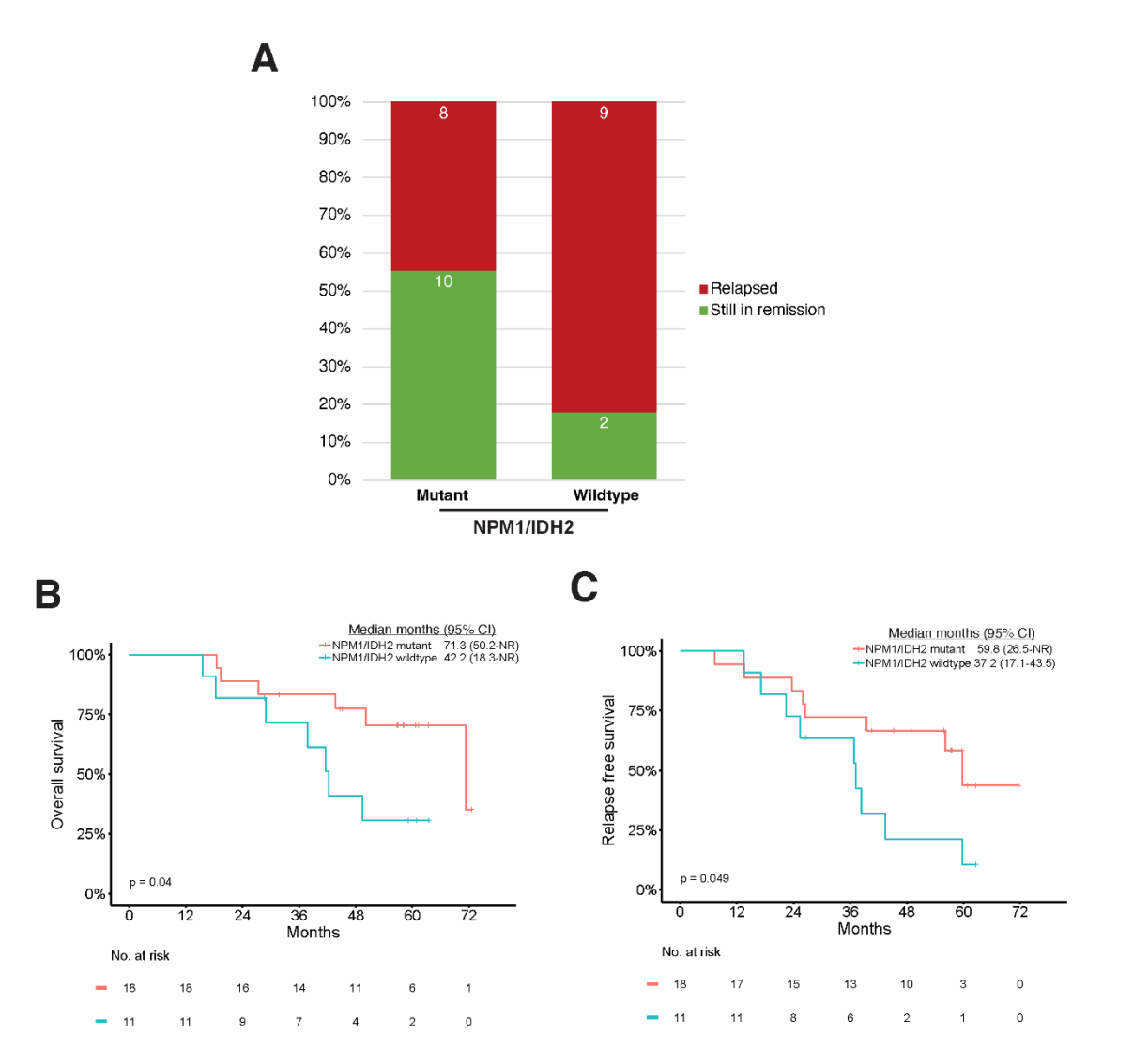
**Supplemental Figure 3. Overall survival in the STOP vs CONT cohorts.** (A) Overall survival from day 1 of therapy for all patients. (B) Overall survival landmarked from the median duration of therapy received in the STOP cohort (19.3 months)



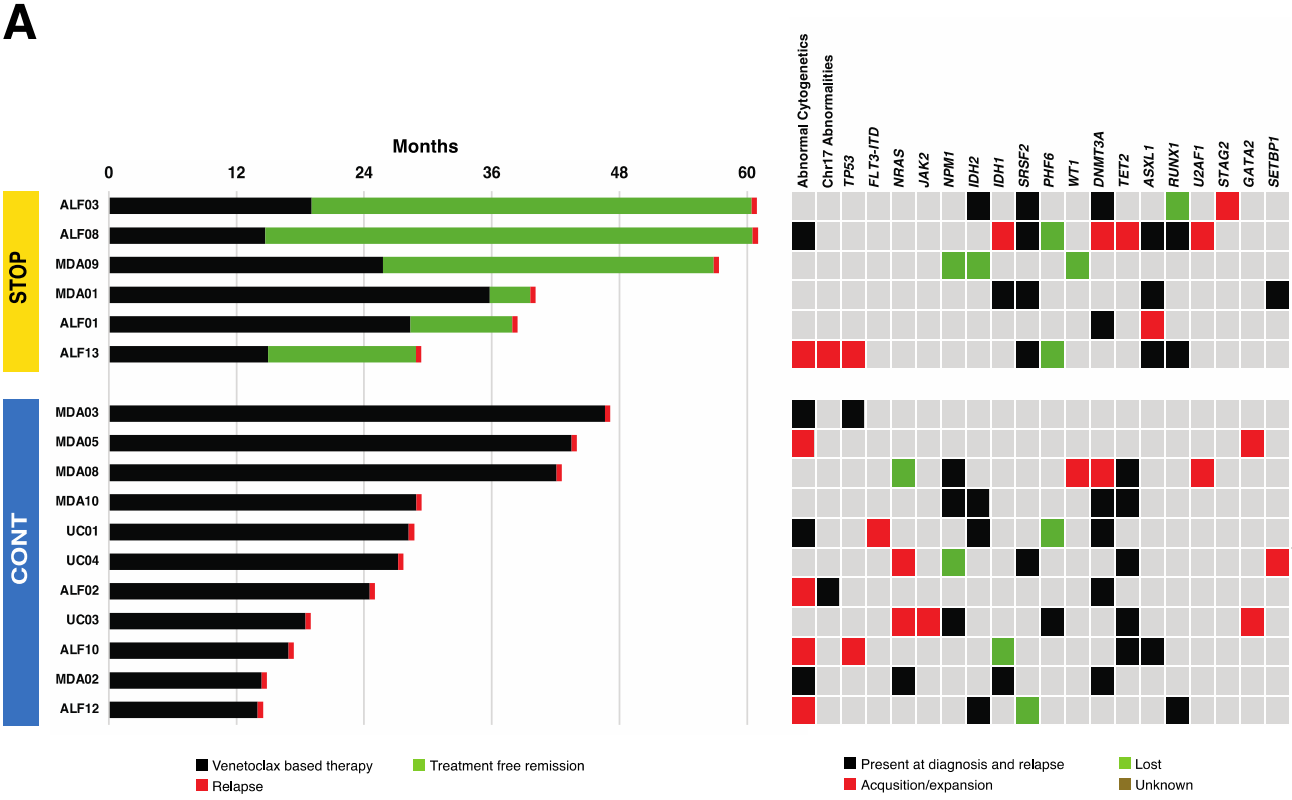
**Supplemental Figure 4. Comparison of relapse free survival within the STOP cohort according to whether prior duration of therapy was for 12-18 vs >18 months.**

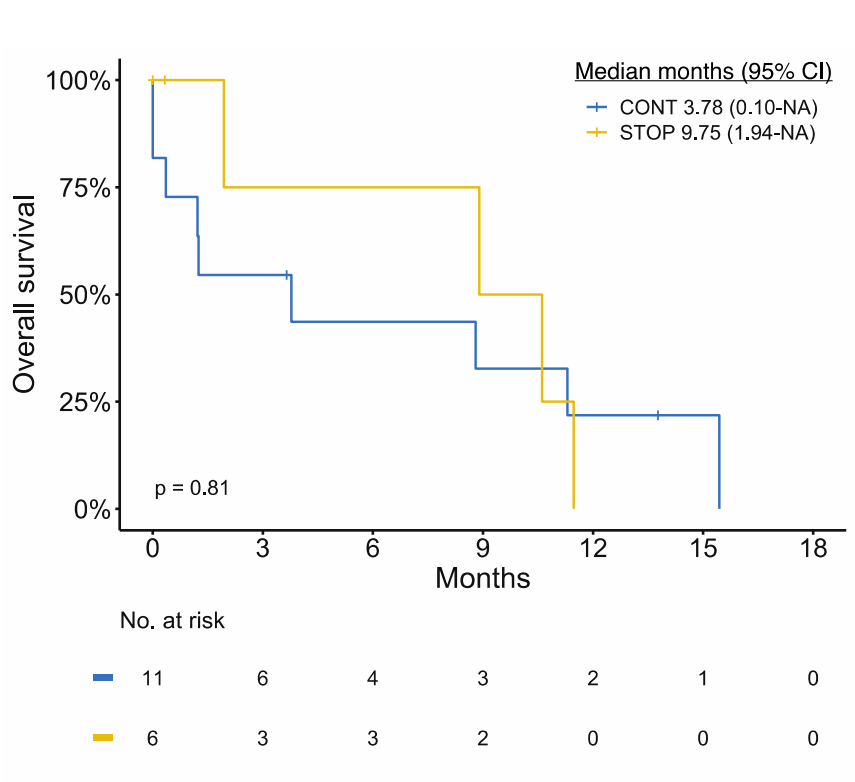


**Supplemental Figure 5. Outcomes of patients with *NPM1* and/or *IDH2* mutations vs other genotypes.** (A) Relapse rates. (B) Overall survival. (C) Relapse free survival, from day 1 of therapy.



**Supplemental Figure 6. Outcomes of patients with relapsed disease in STOP vs CONT cohorts.** (A) Cytogenetic and molecular evolution. (B) Overall survival from time of relapse.



**SUPPLEMENTAL REFERENCES**


1. Döhner H, Estey E, Grimwade D, et al: Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood 129:424-447, 2017
2. 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 138:2753-2767, 2021