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MRD status nel paziente unfit è clinicamente utile

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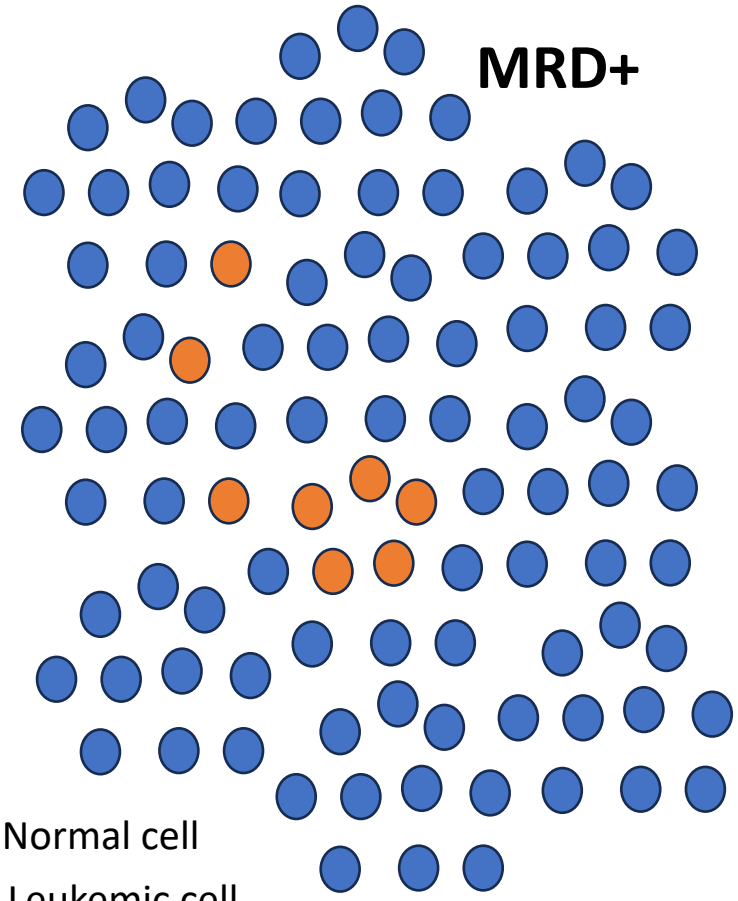
Disclosures of Name Surname

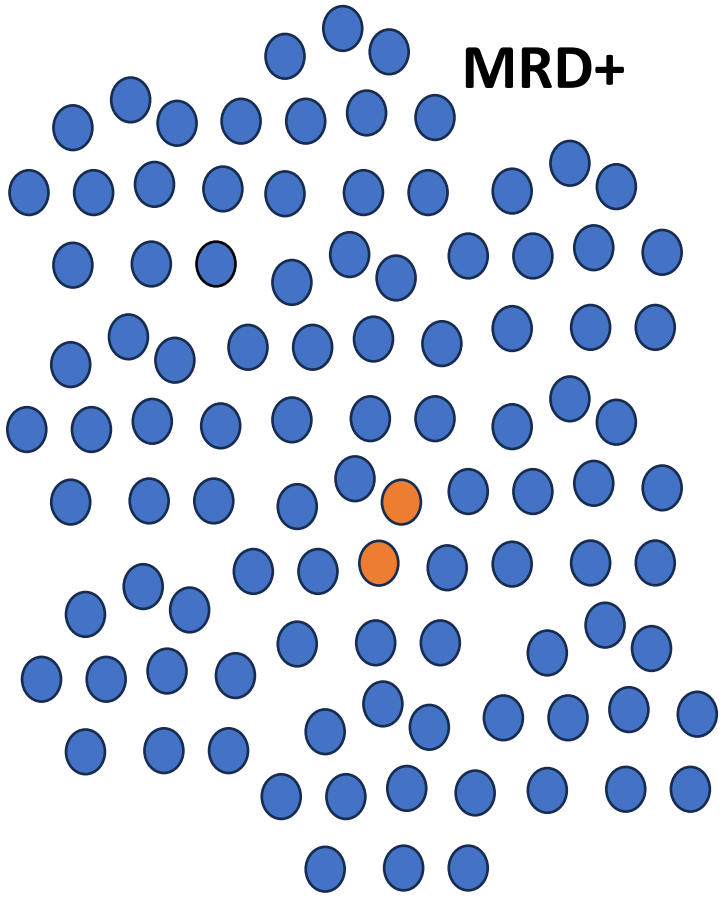
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Incyte			X				
Jazz Pharmaceuticals						X	
Abbvie							X

Measurable residual disease (MRD)

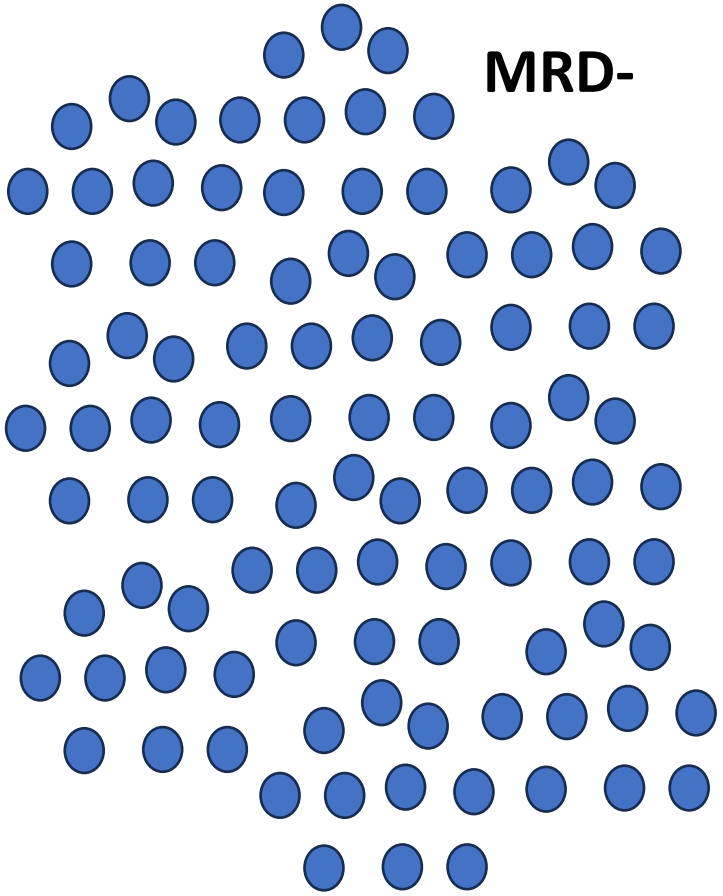
Paz.1
Complete remission



Paz.2
Complete remission



Paz.3
Complete remission



Normal cell

Leukemic cell

“Universal” information provided by MRD

- How deep the response
- How fast the response

} Biology of the disease

Recommended MRD techniques in AML (as of today)

- Flow cytometry
  - Good sensitivity (~1 cell/10000)
  - Very good specificity, but…

- Quantitative PCR (NPM1mut; RUNX1::RUNX1T1; CBFB::MYH11)
  - Very good sensitivity (ca. 1 cell/100000)
  - Excellent specificity

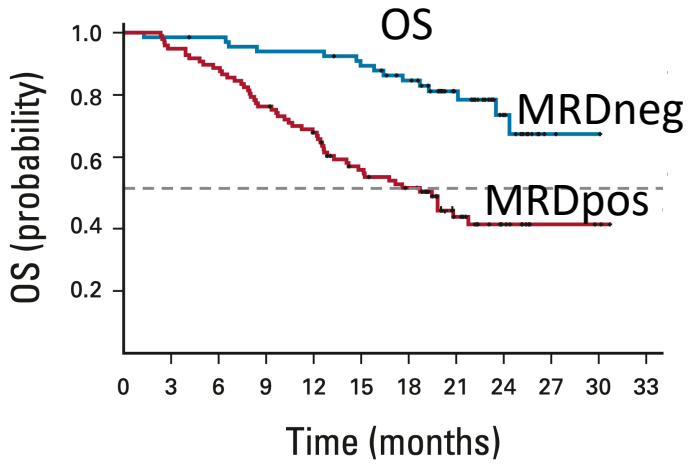
2021 Update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party

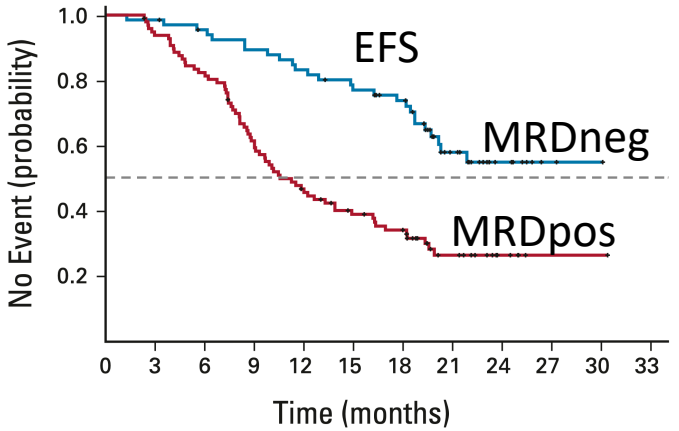
Michael Heuser,[1] Sylvie D. Freeman,[2] Gert J. Ossenkoppele,[3] Francesco Buccisano,[4] Christopher S. Hourigan,[5] Lok Lam Ngai,[3] Jesse M. Tettero,[3] Costa Bachas,[3] Constance Baer,[6] Marie-Christine Béné,[7] Veit Bücklein,[8] Anna Czyz,[9] Barbara Denys,[10] Richard Dillon,[11] Michaela Feuring-Buske,[12] Monica L. Guzman,[13] Torsten Haferlach,[6] Lina Han,[14] Julia K. Herzig,[12] Jeffrey L. Jorgensen,[15] Wolfgang Kern,[6] Marina Y. Konopleva,[14] Francis Lacombe,[16] Marta Libura,[17] Agata Majchrzak,[18] Luca Maurillo,[4] Yishai Ofran,[19] Jan Philippe,[10] Adriana Plesa,[20] Claude Preudhomme,[21] Farhad Ravandi,[14] Christophe Roumier,[21] Marion Subklewe,[8] Felicitas Thol,[1] Arjan A. van de Loosdrecht,[3] Bert A. van der Reijden,[22] Adriano Venditti,[4] Agnieszka Wierzbowska,[23] Peter J. M. Valk,[24] Brent L. Wood,[25] Roland B. Walter,[26] Christian Thiede,[27,28] Konstanze Döhner,[12] Gail J. Roboz,[13] and Jacqueline Cloos[3]

Patients treated with lower-intensity treatment?

Prognostic impact of flow MRD in patients treated with venetoclax

- VIALE-A
- 164 patients treated AZA+VEN in CR/CRi
- Flow cytometry bone marrow
- MRD neg if < 0.1% at any time
- 67 achieved MRD neg

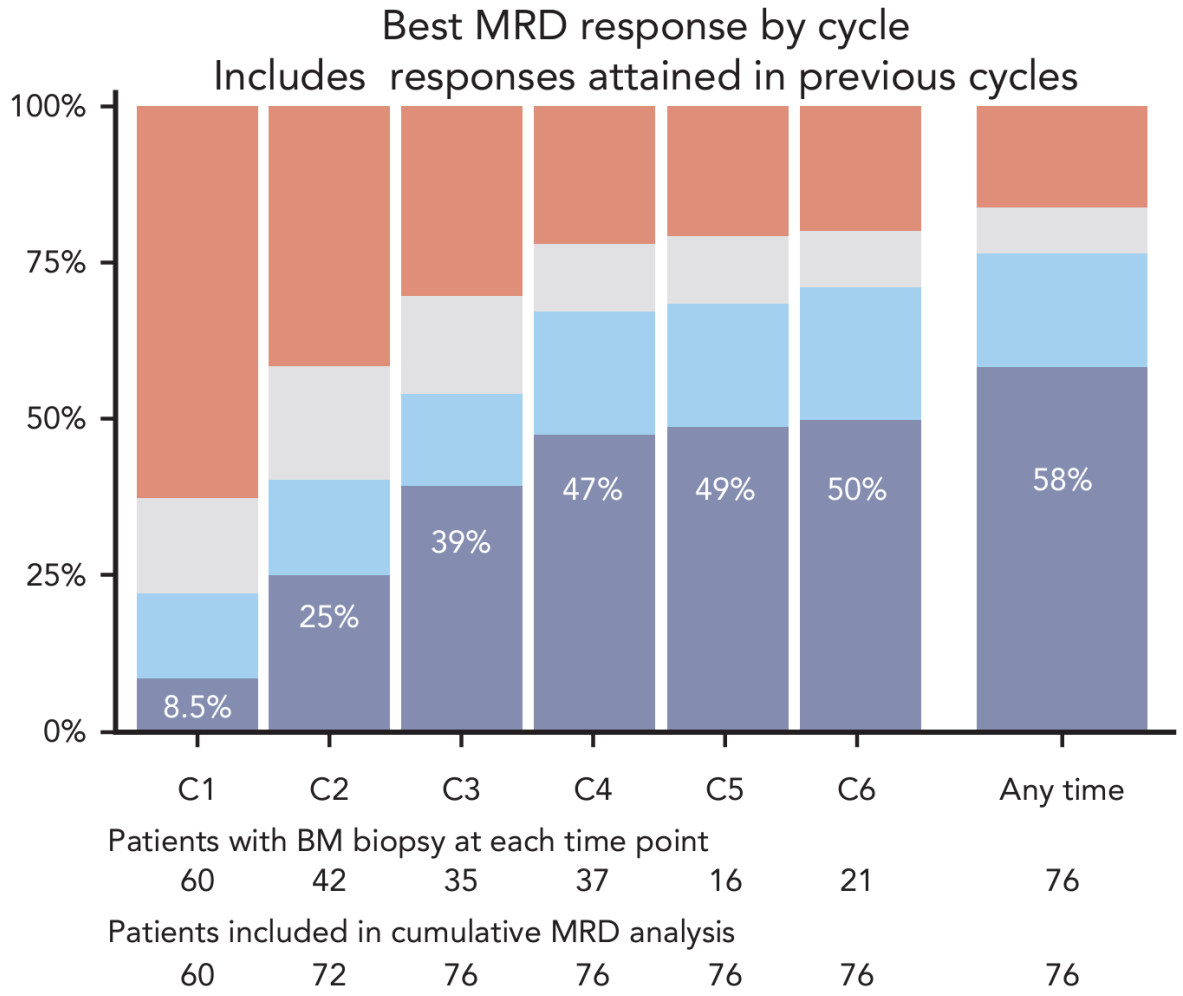




Pratz, et al. JCO 2021

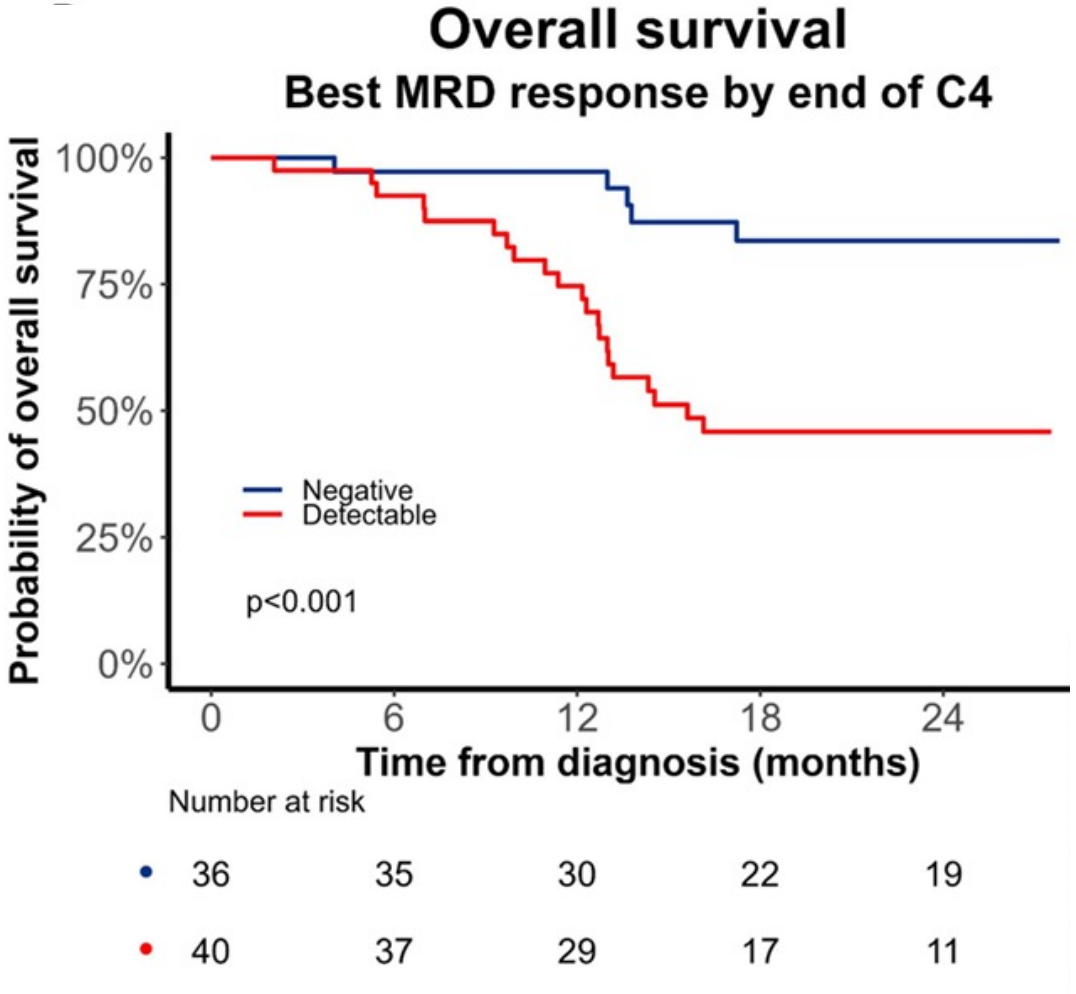
Prognostic impact of NPM1mut MRD in patients treated with venetoclax

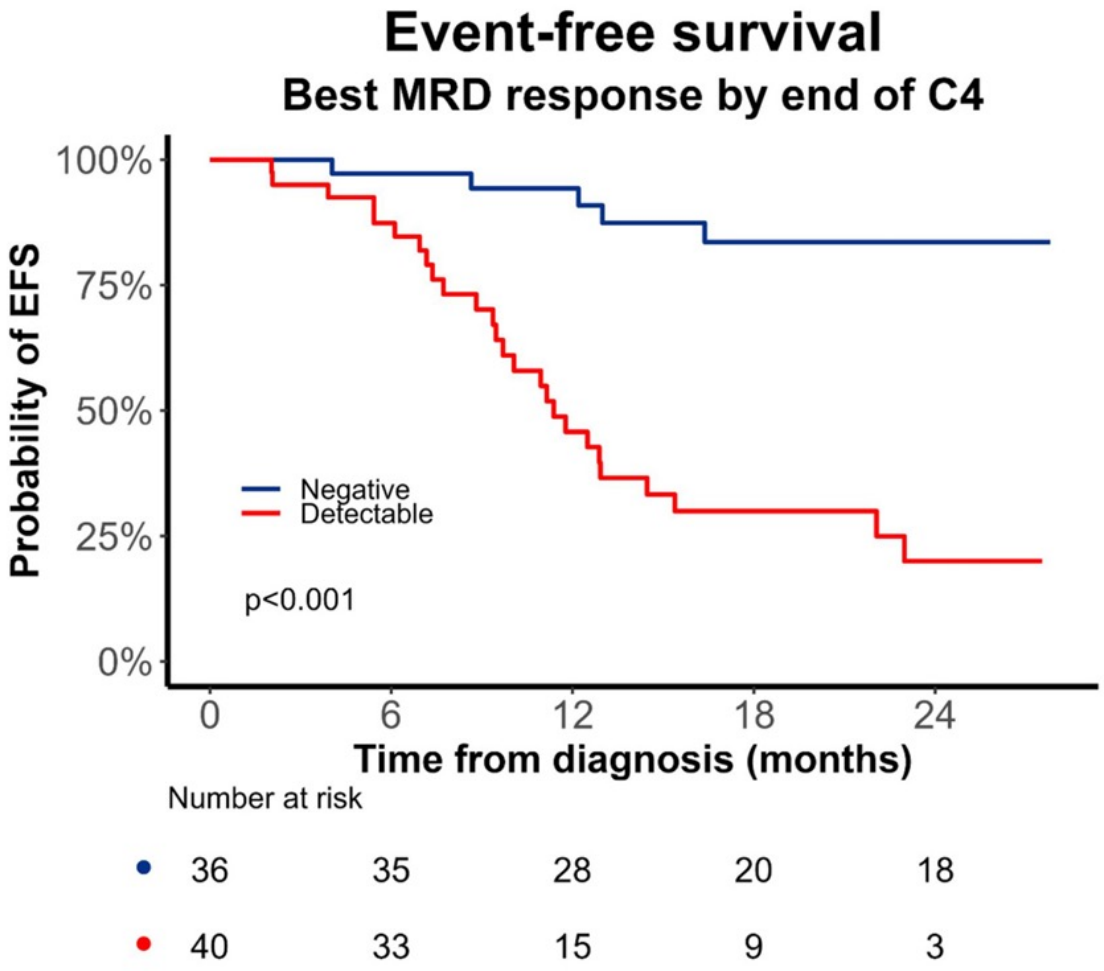
- Retrospective data
- 76 NPM1mut patients who achieved CR/CRi
- LDAC/HMA + VEN
- Median age 72 (34-86)
- 24% FLT3-ITD
- qPCR bone marrow



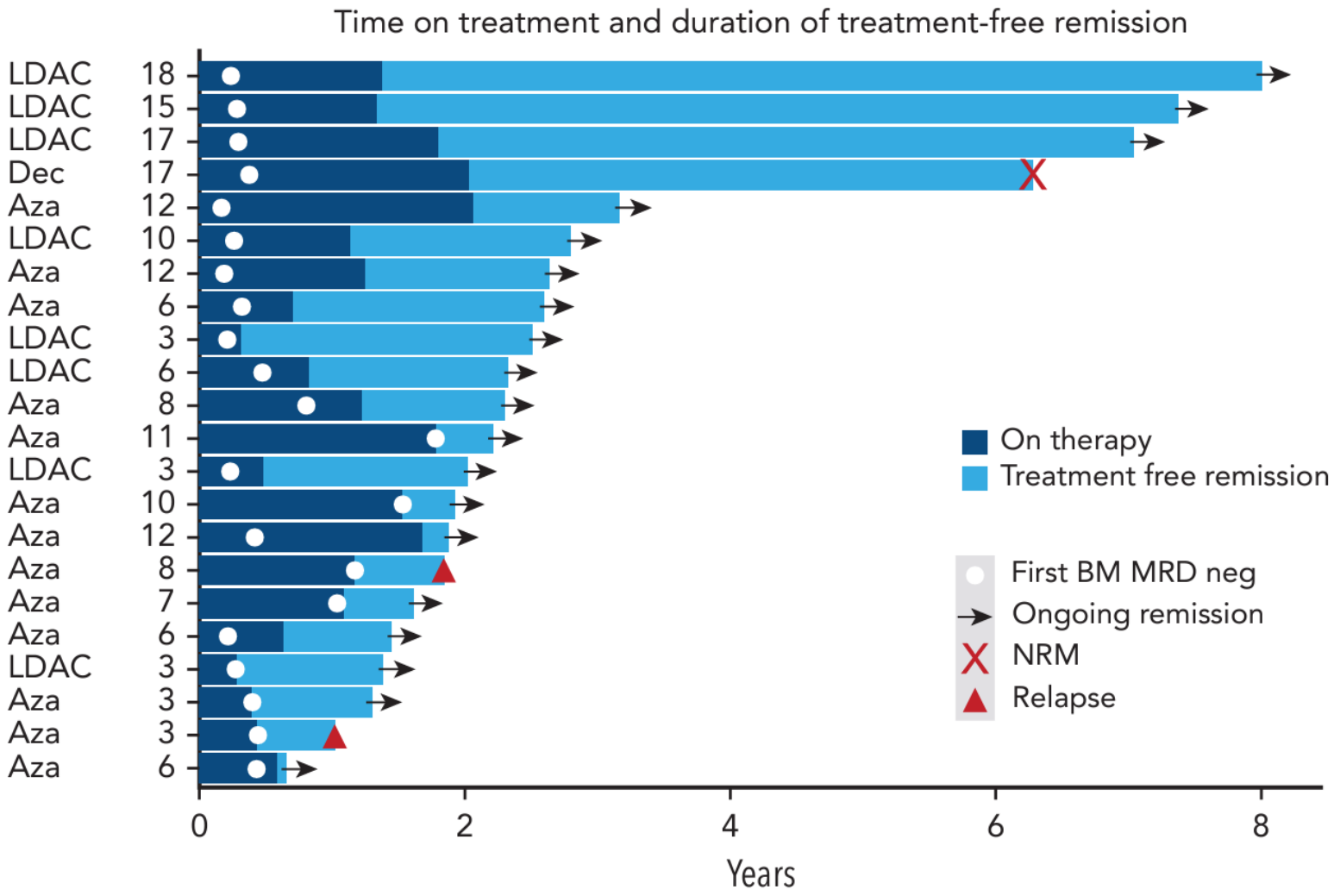
Othman et al. Blood 2023

Prognostic impact of NPM1mut MRD in patients treated with venetoclax Othman et al. Blood 2023





In NPM1mut patients with stable MRDneg, TFR is possible



Othman, et al. Blood 2023

MRD in (my) clinical practice in patients treated with venetoclax

- Integration with genetics for accurate survival estimates
- More accurate patient information
- Helps decision-making if poor tolerance/toxicities

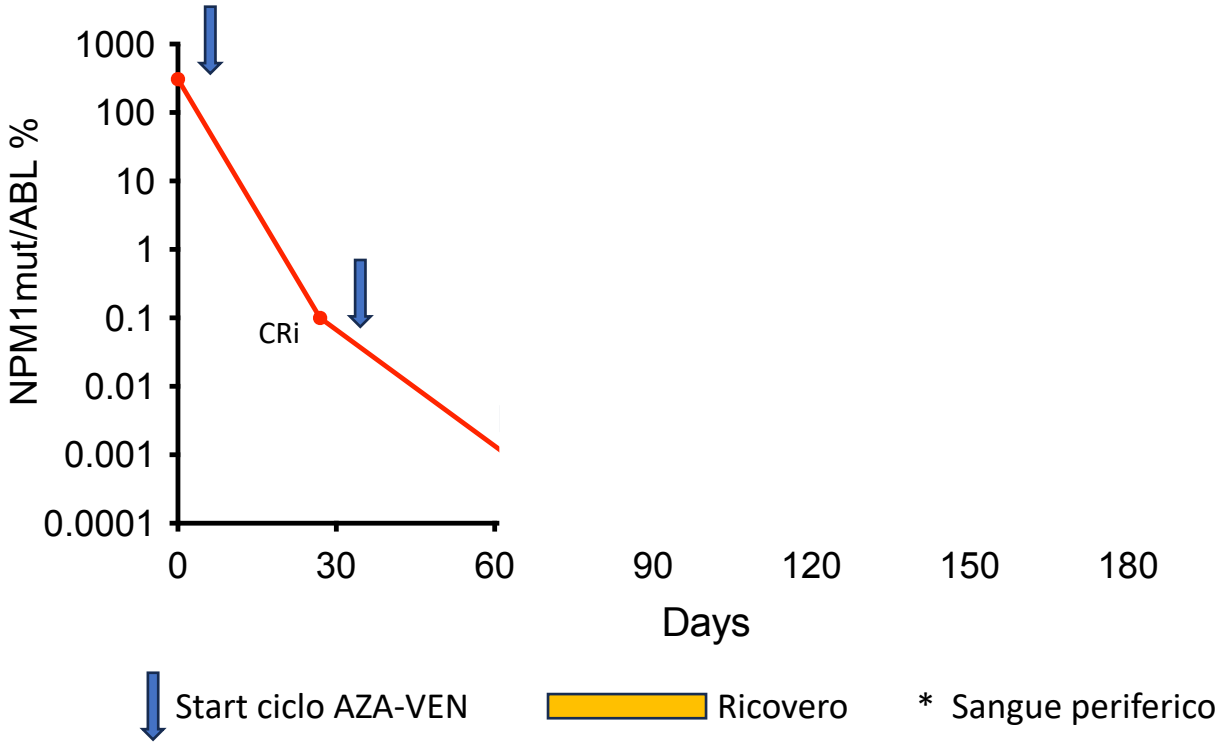
Integration with genetics: ELN 2024 for lower intensity treatments

Rischio	Anomalie genetiche	Sopravvivenza mediana
Favorevole	NPM1 mutato (FLT3-ITDneg; NRASwt; KRASwt; TP53wt) IDH2 mutato (FLT3-ITDneg; NRASwt; KRASwt; TP53wt) IDH1 mutato* (TP53wt) DDX41 mutato Anomalie genetiche MDS-relate (FLT3-ITDneg; NRASwt; KRASwt; TP53wt)	39 mesi 37 mesi 29 mesi 24 mesi 23 mesi
Intermedio	Anomalie genetiche MDS-relate (FLT3-ITDpos e/o NRASmut e/o KRASmut, TP53wt) Altre anomalie citogenetiche e/o molecolari** (FLT3-ITDpos e/o NRASmut e/o KRASmut, TP53wt)	13 mesi 12 mesi
Sfavorevole	TP53 mutato	5-8 mesi

Döhner, et al. Blood 2024

Scenario 1

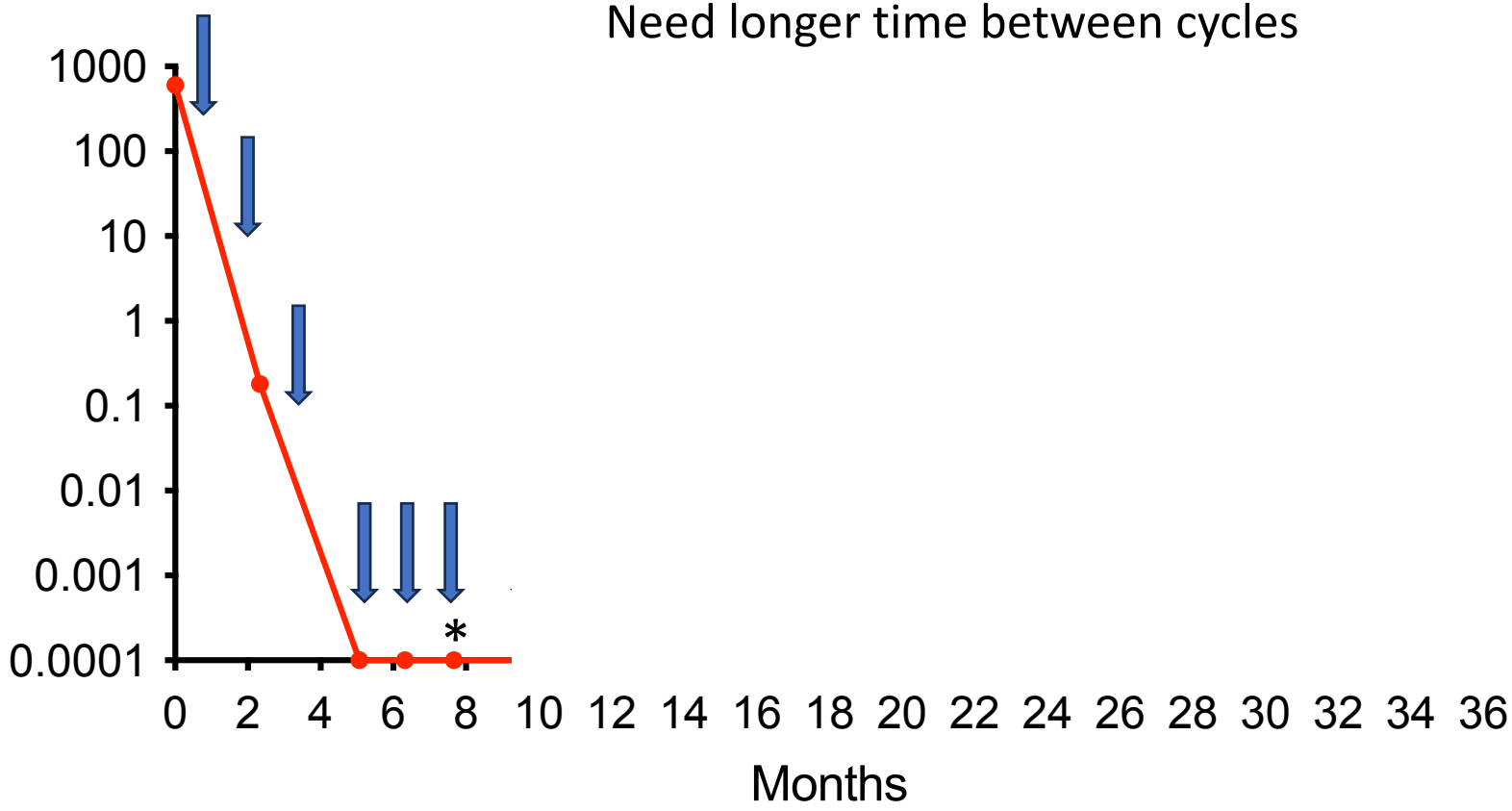
75 years
NPM1mut, FLT3-D835
46,XY



Scenario 2

74 years,
NPM1mut, FLT3 wt
46,XX

Poor QoL
Need longer time between cycles



* Peripheral blood

Start cycle AZA-VEN

Conclusions e take-home messages

- More data needed
- If CR/CRi is target, MRD provides more accurate info on the quality of response
- MRD negativity should not be pursued at all costs
- Prognostic impact: integration with genetics
- Helps in decision-making if toxicity/poor tolerance
- Imperative studying TFR in NPM1mut MRDneg patients