Cytoreduction Should Not (Uniformly) Precede Transplant for MDS

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Disclosures

- None

Definition

- Cytoreduction: some type of therapy prior to transplant conditioning
  - Chemotherapy (7+3, Vyxeos)
  - Hypomethylating agents with or without venetoclax
- In this talk, term is irrespective of blast count

Cytoreduction does not improve outcomes

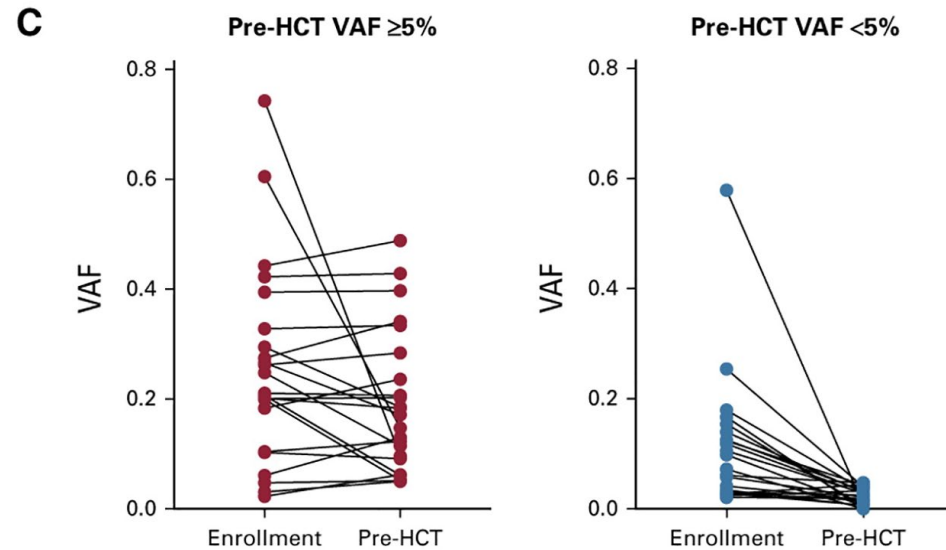| Relapse-Free Survival		P-value	Study
Cytoreduction	No cytoreduction		
37%	42%	0.78	Damaj et al, BBMT 2014
38-41%	38%	0.9	Schroeder et al, BBMT 2019
41%	51%	0.3	Field et al, BMT 2010
NA	NA	0.5	Allesandrino et al, JCO 2013

Caveats:

1. All retrospective studies
2. Differences between patients who did/did not receive cytoreduction
   - Many studies include both secondary AML and MDS
3. Patients who achieved CR may have better outcomes – mostly AML

MDS is a heterogeneous disease and is largely lumped together in these studies!
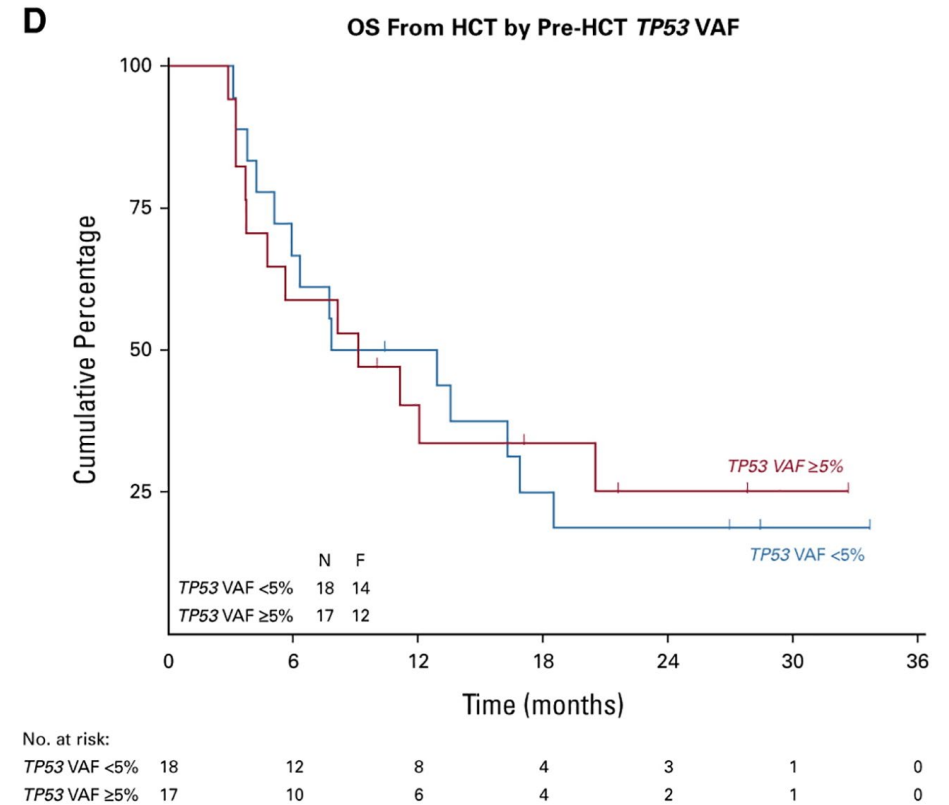
"Effective" cytoreduction may not improve outcomes either

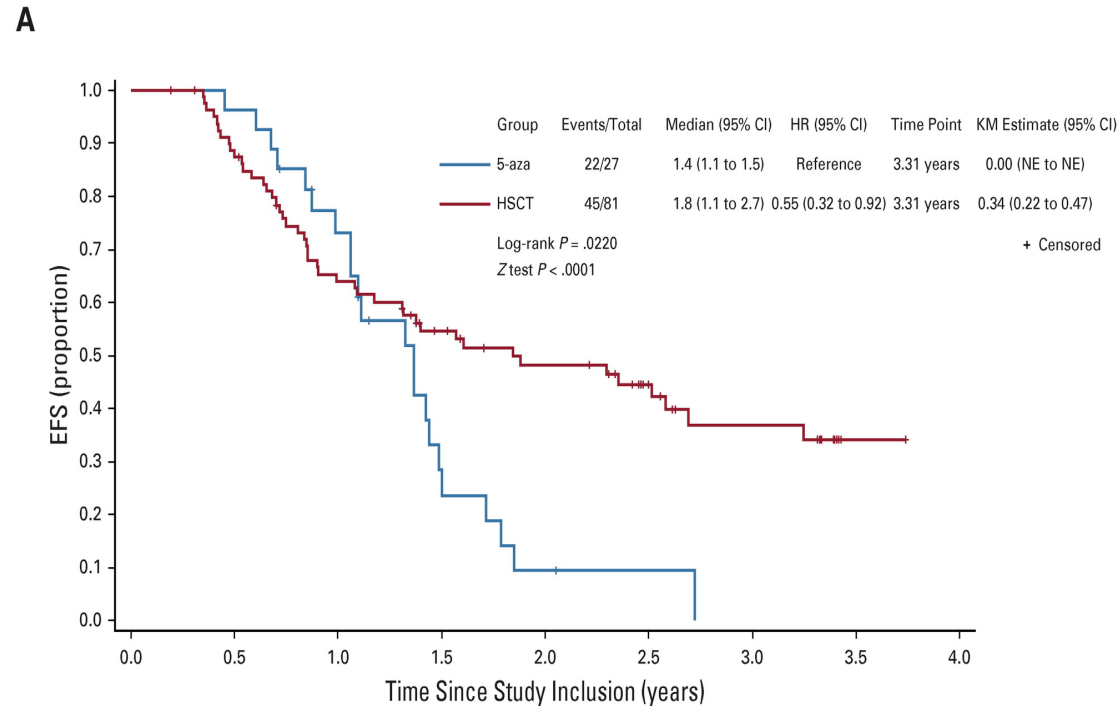*Molecular analysis of CTN 1102*

Molecular clearance of *TP53* is hard to achieve

Verslius et al, JCO 2023; 41(28):4497-4510.

Pre-transplant *TP53* mutation abundance does not correlate with post-transplant survival

Risks of delaying transplant

A

Group	Events/Total	Median (95% CI)	HR (95% CI)	Time Point	KM Estimate (95% CI)
5-aza	22/27	1.4 (1.1 to 1.5)	Reference	3.31 years	0.00 (NE to NE)
HSCT	45/81	1.8 (1.1 to 2.7)	0.55 (0.32 to 0.92)	3.31 years	0.34 (0.22 to 0.47)

Log-rank *P* = .0220

Z test *P* < .0001

+ Censored

No. at risk:

5-aza	27	26	18	6	2	1	0	
HSCT	81	69	49	36	29	19	13	1	0

Prospective RCT of continuous 5-AZA vs 5-AZA → transplant

High rate of dropout even before allocation to study arm

- 7% died due to infections
- 16% progressed to AML

Study not powered to assess primary endpoint

Kröger et al, JCO 2021; 39(30):3318-3327

My own practice: trajectory matters

- <u>I do not cytoreduce:</u>
  - MDS with < 5% blasts
  - Borderline transplant candidates (only "one shot" at curative therapy)

- <u>I nearly always cytoreduce:</u>
  - MDS with rapidly increasing blasts
    - Or other evidence of incipient transformation
  - MDS with 10-20% blasts

- <u>I *sometimes* cytoreduce:</u>
  - MDS with 5-10% blasts – depends on trajectory and scenario
  - 2-3 cycles max if possible

Thanks