IPIG
International PNH Interest Group

Optimizing Stem Cell Transplantation for Patients with PNH
European Experience – Update from EBMT

Camilla Frieri, MD, PhD,
AORN San Giuseppe Moscati , Avellino, Italy
Orlando, 5 December 2025

Disclosure statement

Advisory board : Sobi, Novartis, Roche

Speakers bureau: Alexion, Novartis, Sobi

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Please scan the QR code to participate in the Audience Response and Q&A

Live polling question

Do you currently perform allogeneic HSCT for PNH patients in your center?

A. Yes, regularly

B. Occasionally

C. Rarely

D. Never

Live polling question

If YES, for which PNH patients do you consider HSCT?

(more than one answer is allowed)

A. Classical hemolytic PNH, because I don't have access to CI

B. Poor Responder Classical hemolytic PNH to terminal CI, because I don't have access to proximal CI

C. PNH with thrombosis despite CI

D. PNH with SAA

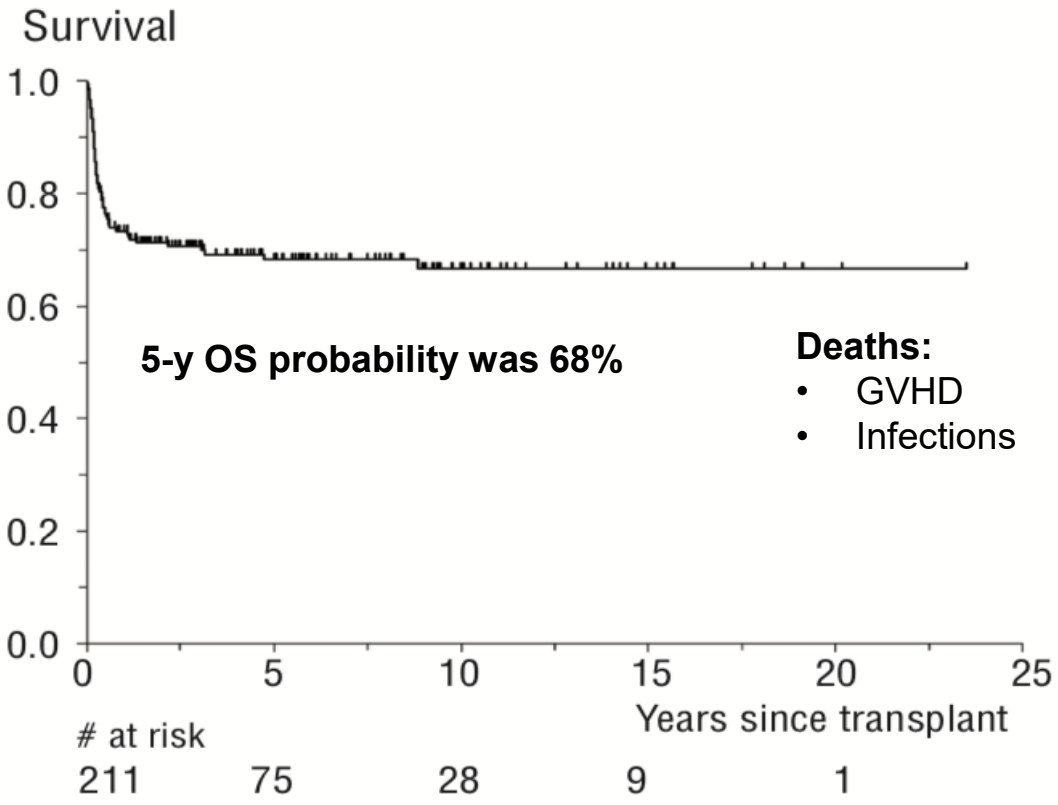
Background

Allogeneic stem cell transplantation in paroxysmal nocturnal hemoglobinuria

Régis Peffault de Latour,[1] Hubert Schrezenmeier,[2] Andrea Bacigalupo,[3] Didier Blaise,[4] Carmino A. de Souza,[5] Stephane Vigouroux,[6] Roelf Willemze,[7] Louis Terriou,[8] Andre Tichelli,[9] Mohamad Mohty,[10] Sophie de Guibert,[11] Judith C. Marsh,[12] Jakob Passweg,[13] Jean Yves Mary,[14]* and Gerard Socié[1,15]*

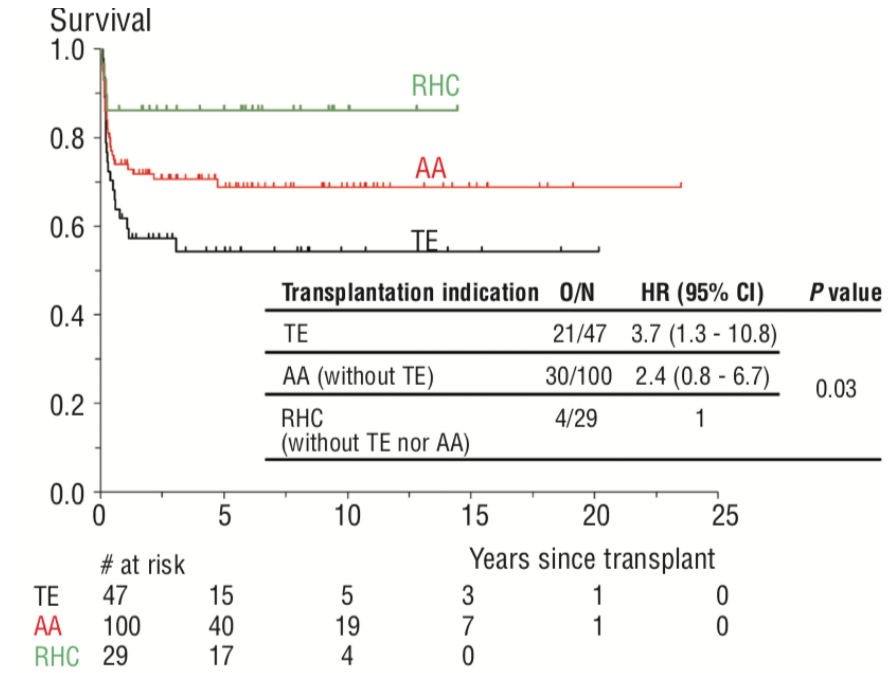
Haematologica, 2012

Largest study: 211 PNH patients transplanted between 1978 to 2007



5-y OS probability was 68%

Deaths:
- GVHD
- Infections



Transplantation indication	O/N	HR (95% CI)	*P* value
TE	21/47	3.7 (1.3 - 10.8)	0.03
AA (without TE)	30/100	2.4 (0.8 - 6.7)	
RHC (without TE nor AA)	4/29	1	

The indication for SCT was the only significant predictor of survival, with patients transplanted for TE having the worst outcome.

EBMT-SAAWP Study

Improved outcomes in Paroxysmal Nocturnal Hemoglobinuria (PNH) patients undergoing Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) in 2011-2020: a retrospective EBMT-SAAWP Study.

Camilla Frieri, Dirk-Jan Eikema Sr., Joe Tuffnell, Brian Piepenbroek, Malek Benakli, MD, Grzegorz Helbig, MD, PhD, Thomas Cluzeau, MD, PhD, Cécile Renard, MD, Philippe Lewalle, Victoria Potter, Krzysztof Kalwak Sr., Johan Maertens, MD, PhD, Gerard Michel, MD, PhD, Andrew Bruce McDonald, MBCh, Péter Pál Reményi, MD, Ladislav Sopko, Kazimierz Halaburda, Depei Wu, MD, PhD, Zubeyde Nur Ozkurt, Xavier Poiré, MD, PhD, Morag Griffin, MBChB, MRCP, Mahmoud Aljurf, Ashrafsadat Mousavi, Jose Antonio Pérez-Simón, MD, PhD, Henrik Sengeloev, Ben Carpenter, MD, Eric Deconinck, Arancha Bermúdez, Stéphanie Nguyen-Quoc, MD, PhD, Matteo Parma, MD, Ibrahim Yakoub-Agha, MD, PhD, Shankara Paneesha, Lutz Peter Hermann Mueller, MD, Regis Peffault De Latour, Austin G. Kulasekararaj, MD, MBBS, FRCPath, MRCP and Antonio M Risitano, MD, PhD

Design and Methods

- ✓ It is a **retrospective multicentre study** conducted through the SAAWP of the EBMT;
- ✓ All consecutive **first HSCT** for PNH performed at EBMT centers;
- ✓ Data were retrieved from the EBMT registry **Promise** (looking specifically for the diagnosis of PNH), which includes detailed information about the underlying disease;
- ✓ From **2011 to 2020**, data on **259 patients** transplanted for PNH in Europe were reported to the EBMT by **125 centres**;
- ✓ An additional **questionnaire** was sent to all centres with PNH patients requiring more specific details regarding **PNH history**: pre-transplant treatment, presentation of disease and type of PNH at the diagnosis and at the time of the transplant (classical PNH or AA-PNH syndrome).
- ✓ We received answers on **142 pts (54%)**

Results

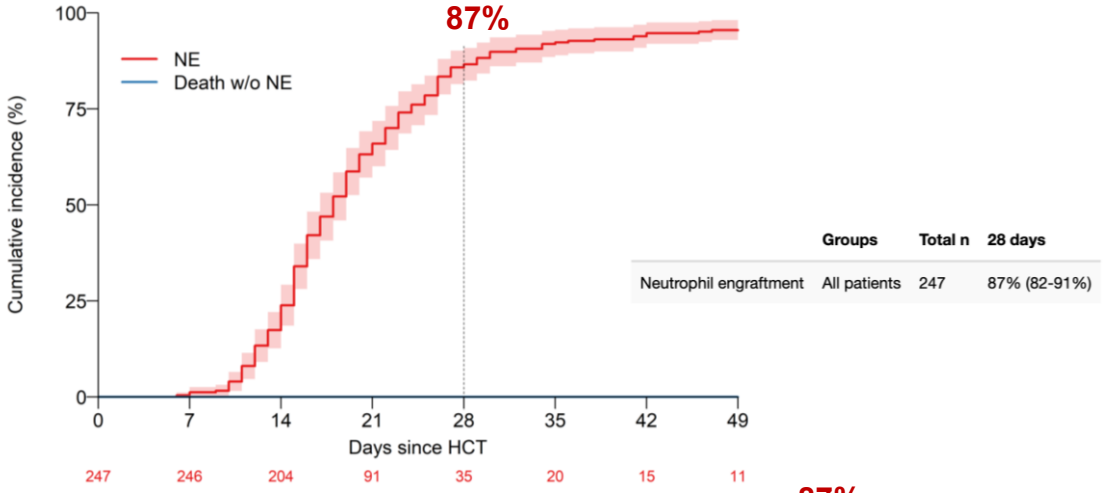
Patients' characteristics

A total of **259** patients from **125** centers, who underwent SCT for PNH between **2011 and 2020**, were included in this study.

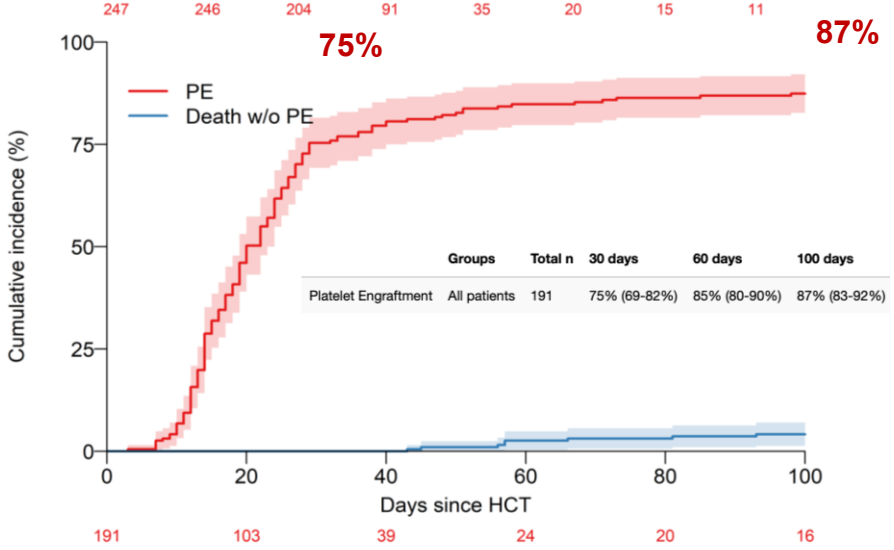
	n/N (%) or median (IQR), N	
Gender/female		130 (49,8%)
Age at transplantation, years		26.2 (18.4-36.5)
Interval diagnosis to allo1 (months)		10.6 (4.7-36.8)
PNH subcategory at diagnosis *	Classical PNH PNH/AA Missing	99 (53.2%) 87 (46.8%) 73
Clinical presentation at transplant	Classical PNH PNH/AA Missing	92 (49.5%) 94 (50.5%) 73
Donor type	MSD MUD MMUD Haplo	123 (47.5%) 96 (37.1%) 33 (12.7%) 7 (2.7%)
Source of stem cells	BM PB CB	129 (49.8%) 126 (48.6%) 4 (1.5%)
Conditioning regimen	RIC MAC	197 (78.2%) 55 (21.8%)
GVHD prophylaxis	CNI ATG ALEMTUZUMAB PTCy	37 (14.6%) 175 (69.2%) 29 (11.5%) 12 (4.7%)
ECU	YES NO	42 (28.6%) 105 (71.4%)

Results

Engraftment

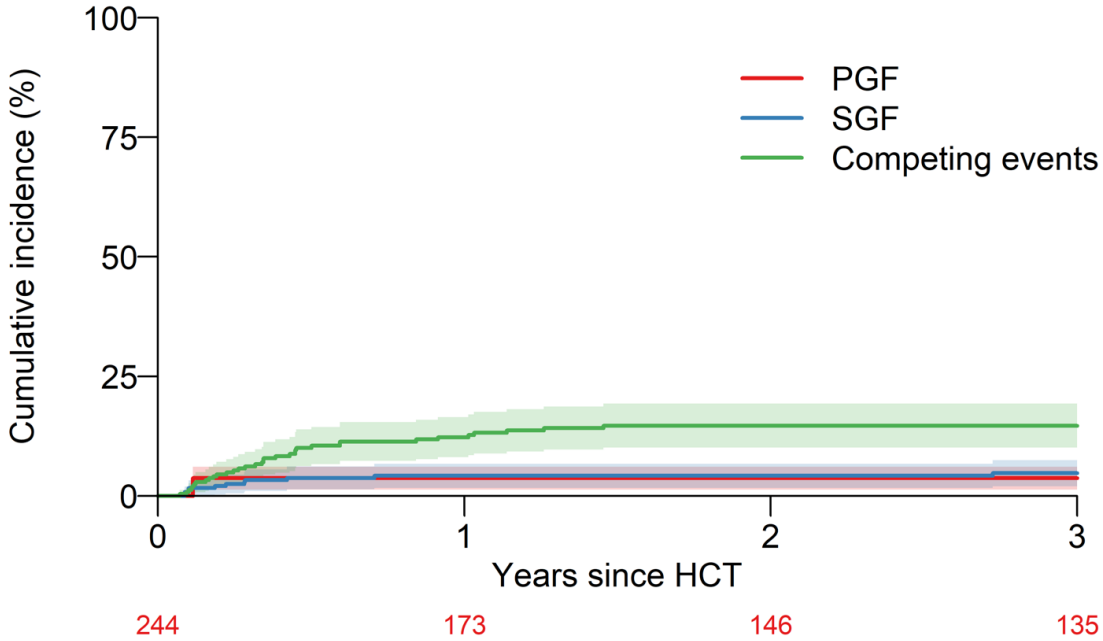


Groups	Total n	28 days
Neutrophil engraftment All patients	247	87% (82-91%)



Groups	Total n	30 days	60 days	100 days
Platelet Engraftment All patients	191	75% (69-82%)	85% (80-90%)	87% (83-92%)

Graft failure



PGF

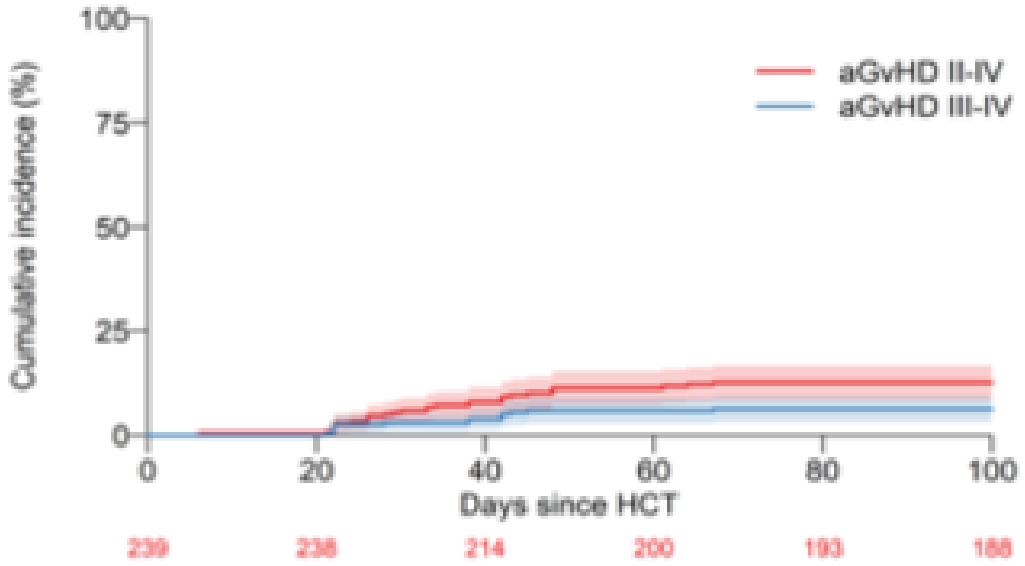
Groups	Total n	42 days
All patients	244	4% (1-6%)

Graft failure

Outcome	N	1y	3y
SGF	244	4% (2-7%)	5% (2-7%)
Competing events	244	12% (8-16%)	15% (10-19%)

Results

aGVHD

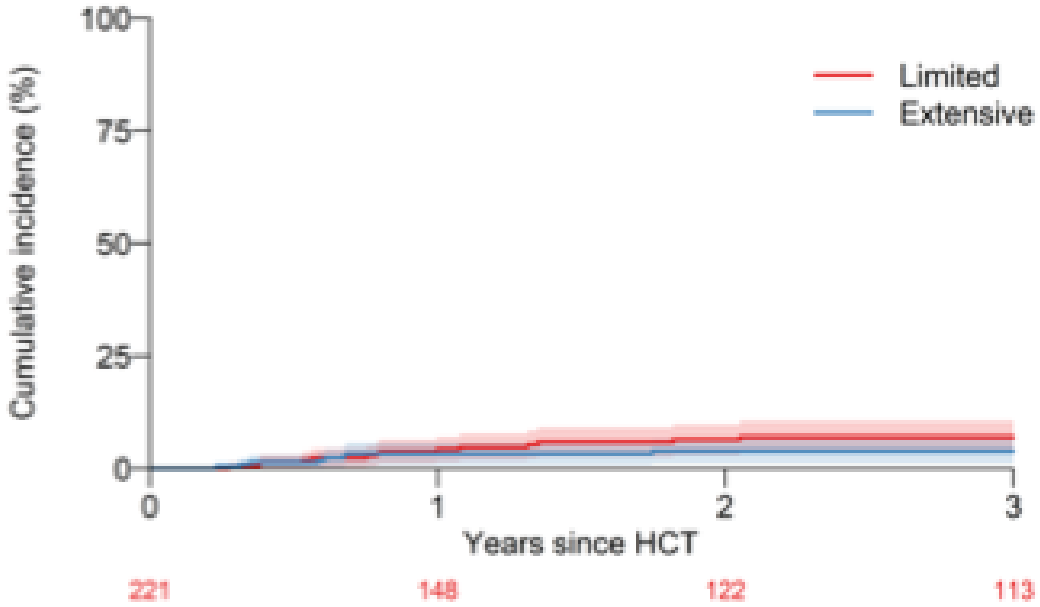


Group	N	aGvHD II-IV (95% CI) 100 days	Fail w/o aGvHD (95% CI) 100 days
All patients	239	13% (8-17%)	8% (5-11%)

aGvHD

Group	N	aGvHD III-IV (95% CI) 100 days	Fail w/o aGvHD (95% CI) 100 days
All patients	239	6% (3-9%)	8% (5-11%)

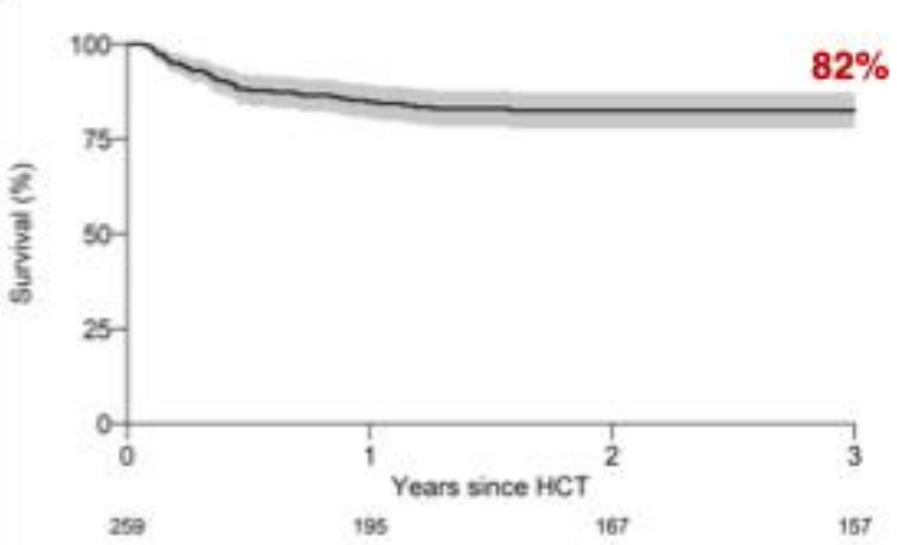
cGVHD



Group	N	Limited (95% CI) 1y	Limited (95% CI) 3y	Extensive (95% CI) 1y	Extensive (95% CI) 3y
All patients	221	4% (2-7%)	7% (3-10%)	3% (1-6%)	4% (1-6%)

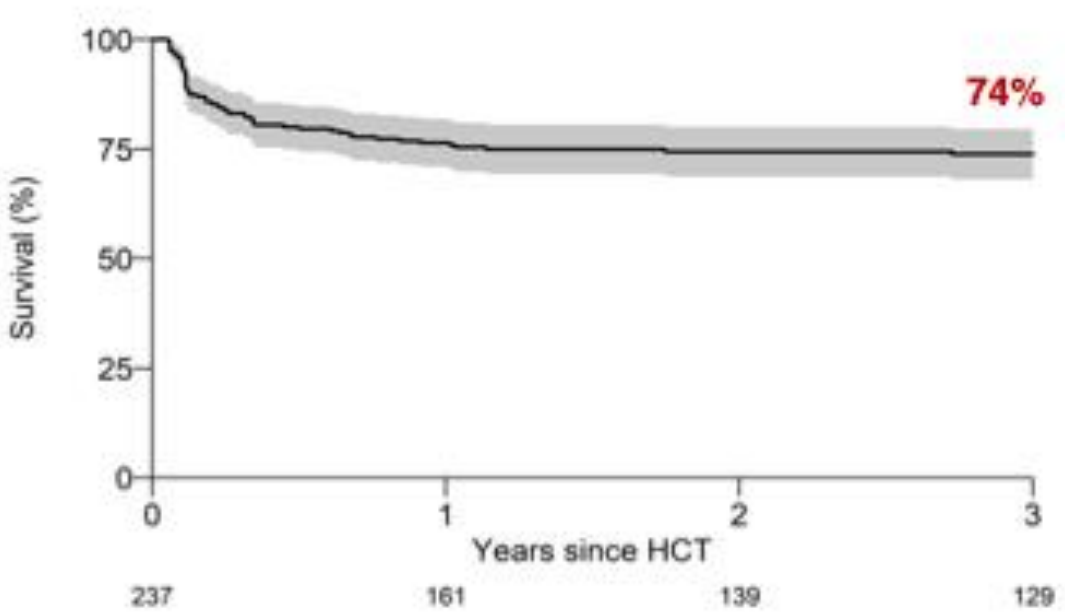
Results

Overall Survival



Group		Total	
		Missing	N (%)
Total			46 (100%)
Main cause of death	HCT-related	1 (2.2%)	35 (77.8%)
	Other; specify:		5 (11.1%)
	Relapse or progression/persistent disease		3 (6.7%)
	Secondary malignancy		2 (4.4%)

GRFS



GRFS

			GRFS (95% CI)	
Group		N	1y	3y
GRFS	All patients	237	76% (71-82%)	74% (68-80%)

From theory to practice…we need to discuss case by case!

#1 Clinical case

Female, 37 y
No comorbidities
WBC 3800 Ne 1600
Hb 6,2 gr/dl
Plt 100,000
LDH 1200 (vn 243U/L)
Bilirubin 4,1 mg/dl
PNH clone: 98%
BM: normal
Normal karyotype
Donor: no siblings

Classical PNH

Severe anemia + active homolysis

Our goal: to control hemolysis and prevent complications

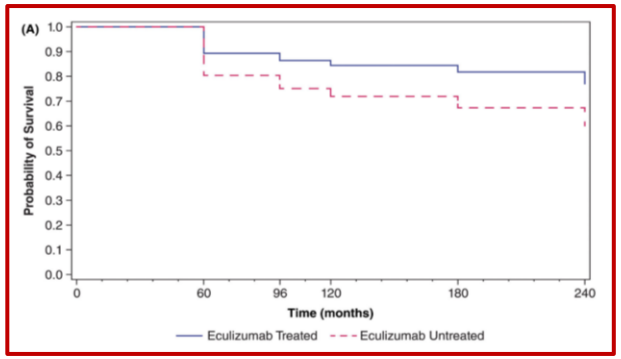
Complement inhibitors available ? YES
Which one (as "first line")?

In Italy : anti- C5 and anti-C3
(think about efficacy/safety)

Long-term safety and efficacy of anti-C5

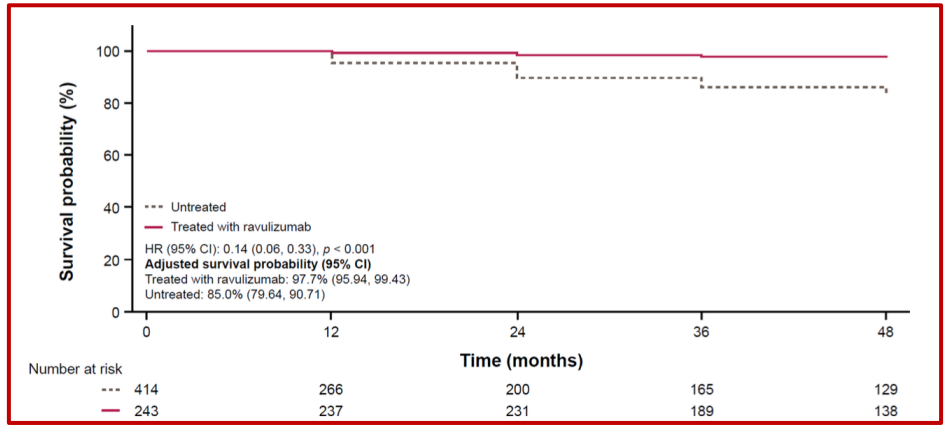
2023
Terriou et al, EJH

- ✓ **From 2007 to 2022 (International PNH Registry)**
- ✓ **4,118 patients, 1613 eculizumab-treated/2505 untreated individuals**
- ✓ **Thromboembolic Events**: Approximately 60% reduction
- ✓ **Better OS.**



2025
Kulasekararaj et al, Annals of Hematology

C5i-naïve: N = 246
Ravulizumab-experienced: N = 195 treated for up to 6 years.
Incidence TE and MAVE and survival are reported, including a comparison of survival with untreated patients from the International PNH Registry.



CME Article

Treatment outcomes of complement protein C5 inhibition in 509 UK patients with paroxysmal nocturnal hemoglobinuria

..between May 2002 and July 2022

Richard J. Kelly,[1] Matthew Holt,[1] Jennifer Vidler,[2] Louise M. Arnold,[1] Joanna Large,[2] Briony Forrest,[1] Catherine Barnfield,[1] Alexandra Pike,[1] Morag Griffin,[1] Talha Munir,[1] Petra Muus,[1] Sateesh K. Nagumantry,[3] Abraham Varghese,[1] John R. Davies,[4] Roochi Trikha,[2] Austin G. Kulasekararaj,[2] Lindsay Mitchell,[5] and Shreyans Gandhi[2]

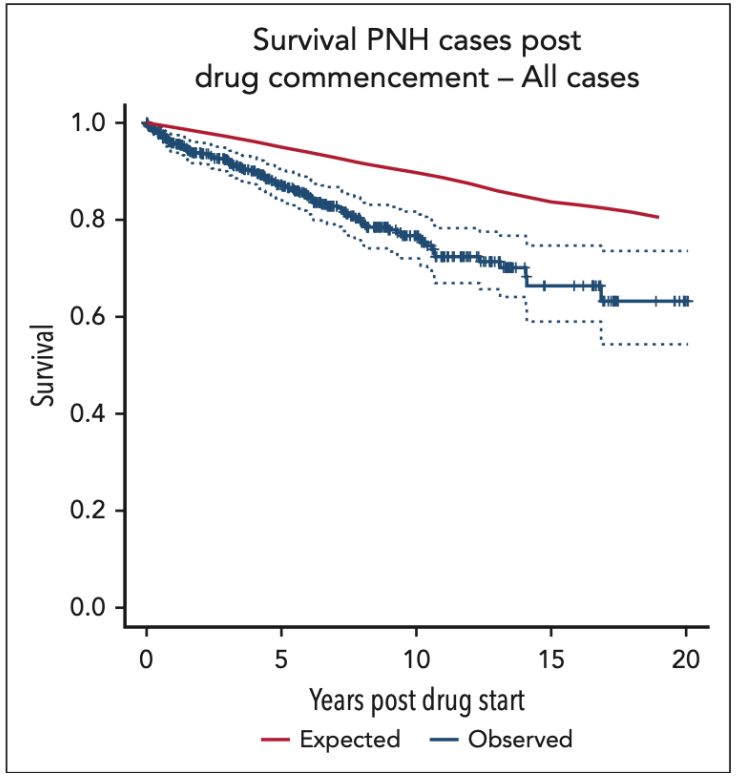


Figure 1. OS of all 509 patients compared with that of age- and sex-matched controls.

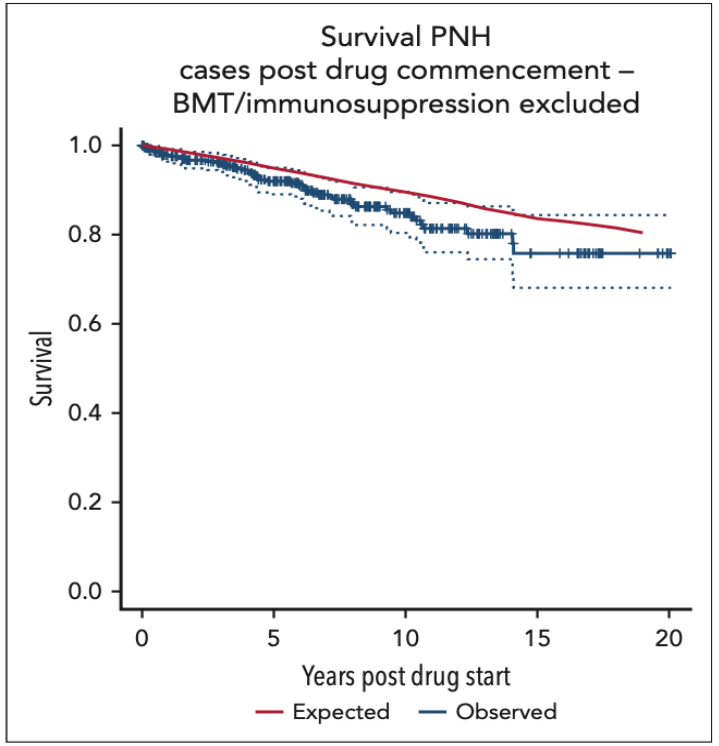


Figure 2. OS of patients with PNH, excluding those with clonal evolution or treatment for AA.

Complications

There have been 11 cases of Neisseria meningitidis septicemia in 10 individuals over 3130 treatment years of C5i, with 1 fatality. This equates to a meningococcal infection rate of 0.35 events per 100 patient-years.

Thrombosis occurred in 23 patients, consistent with a thrombotic rate of 0.73 events per 100 patient-years.

Clonal evolution to AML occurred in 7 cases and to MDS in 10 cases.

#1st take home message

Complement inhibitors remain the standard of care for hemolytic PNH patients

#2 Clinical case

Man, 45 y
Bud-Chiari syndrome
WBC 2500 Ne 1000
Hb 7 gr/dl
Plt 60,000
LDH 950 (vn 243)
Bilirubin 3,2 mg/dl
PNH clone: 85%
BM: moderate hypocellularity
Normal karyotype
Donor: HLA sib

PNH associated with a specific bone marrow disorder

Severe anemia + active homolysis + thrombosis + MAA

TRANSPLANT OR NOT TO TRANSPLANT ?

Live polling question

Would you transplant this patient?

A. Yes, directly

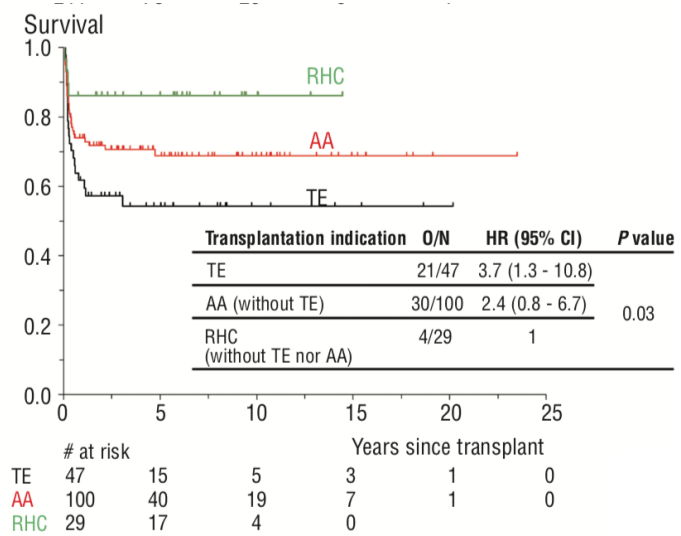
B. Yes, but try CI first (if available) / “bridge to transplant”

C. No, I start CI (if available)

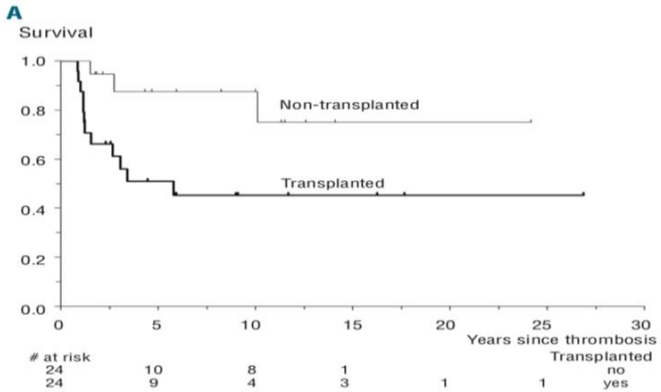
D. No, I combine CI with IST

Results

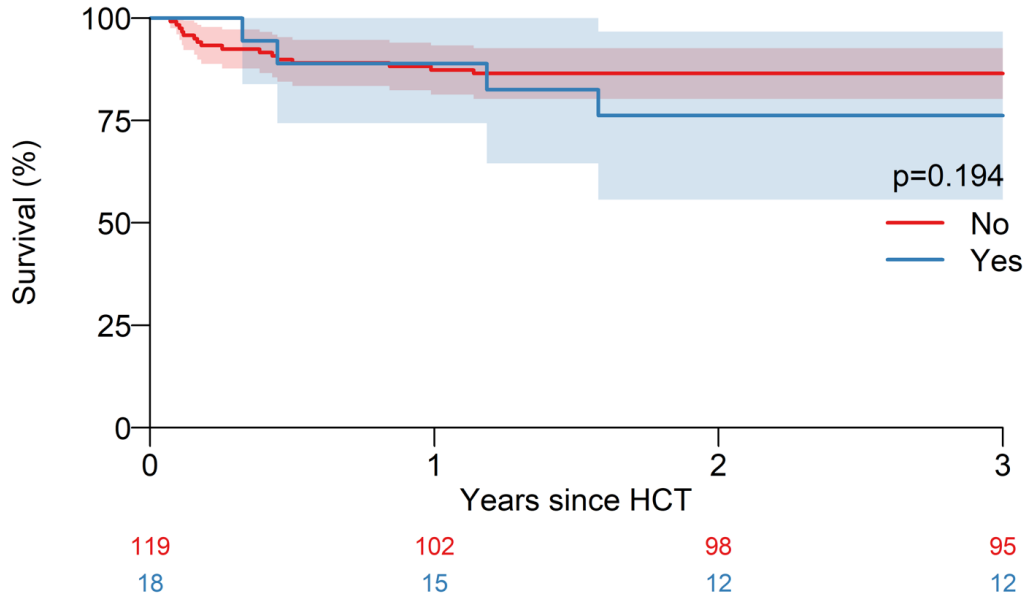
Thrombosis



Transplantation indication	O/N	HR (95% CI)	*P* value
TE	21/47	3.7 (1.3 - 10.8)	0.03
AA (without TE)	30/100	2.4 (0.8 - 6.7)	
RHC (without TE nor AA)	4/29	1	



	O/N	HR (95% CI)	*P* value
Non-transplanted	3/24	1	0.007
Transplanted	12/24	10.0 (1.3 - 78.7)	



Group	N	OS (95% CI) 1y	3y	p
No	119	87% (81-93%)	86% (80-93%)	0.19
Yes	18	89% (74-100%)	76% (56-97%)	

Peffault de Latour R et al, Haematologica 2012

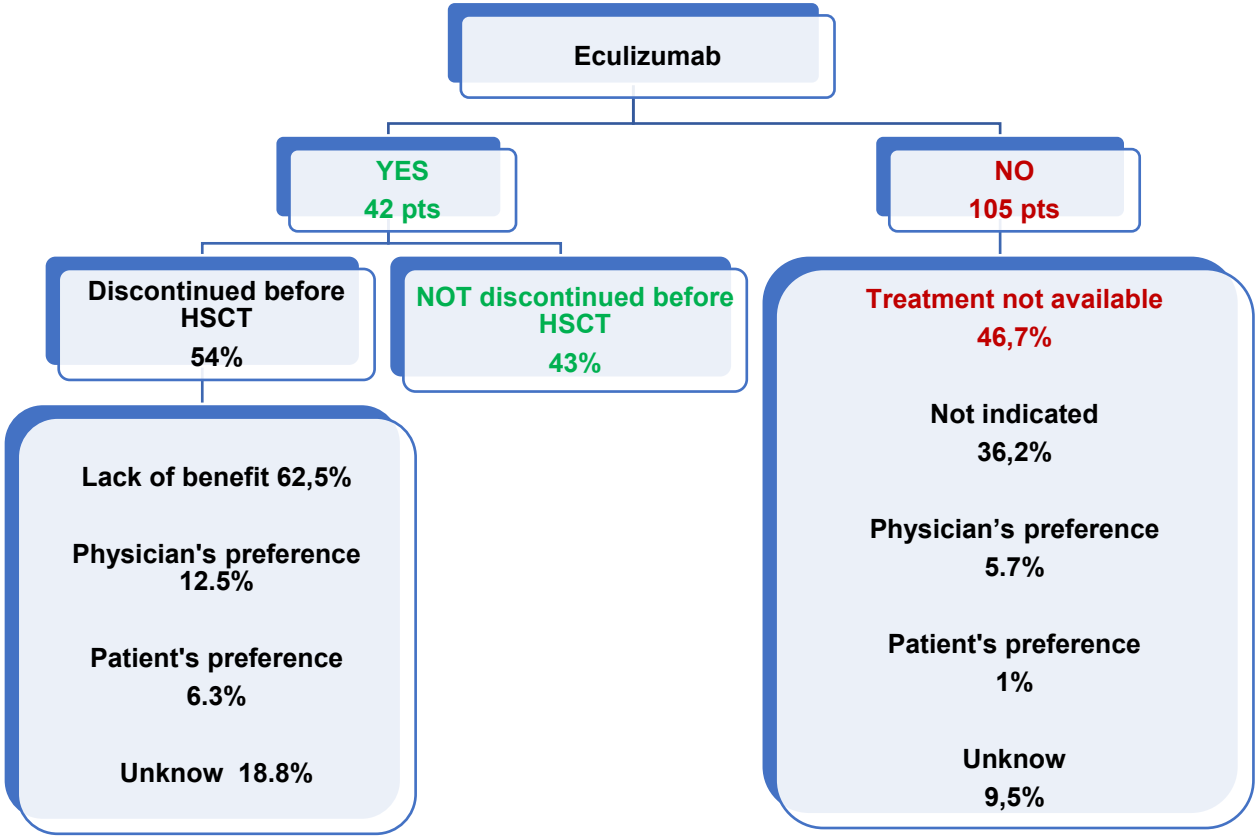
Frieri et al, ASH abstract 2024

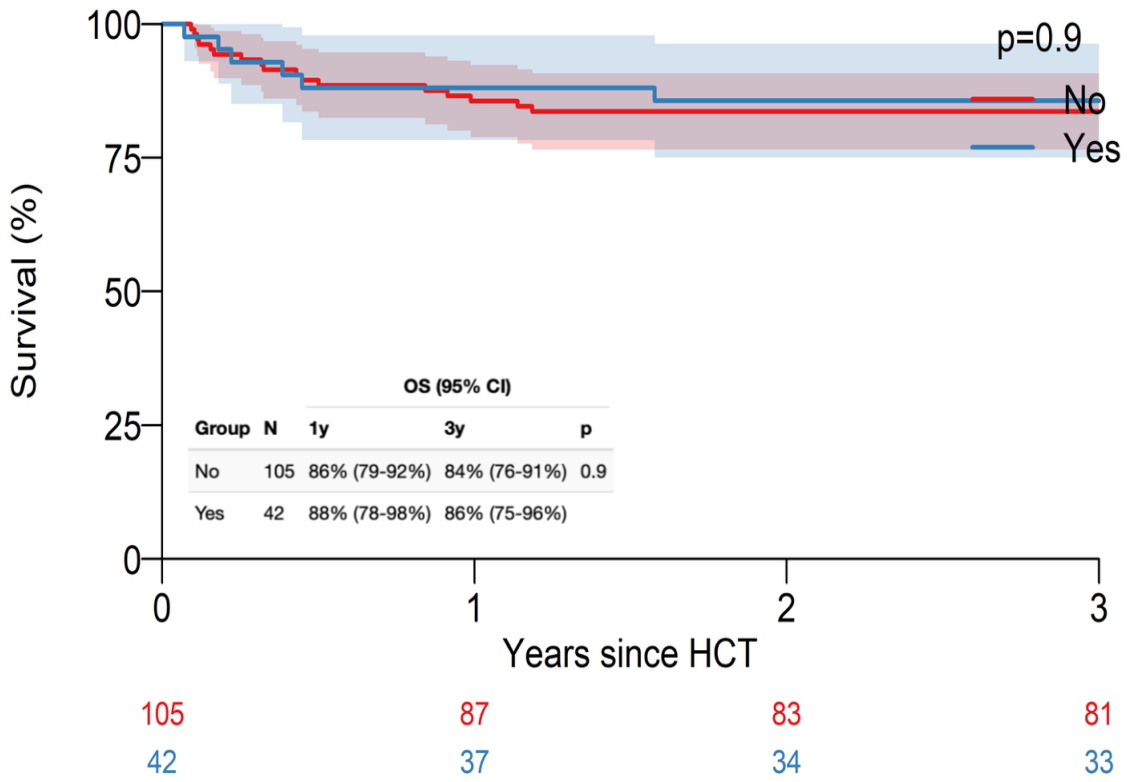
What we know from the literature

	N° of pt	Ecu management	Deaths/GVHD
DeZern et al., BBMT, 2018	8	Ecu stopped before conditioning regimen	No GVHD, infections, deaths
Cooper et al., BBMT 2018	7	5 Ecu stopped before conditioning regimen 2 Ecu continued after transplant	No infections, deaths. aGVHD/cGVHD 5/4
Vallet N, et al. Haematologica 2018	21	19 Ecu stopped before conditioning regimen 2 Ecu continued after transplant	Deaths: 6 (infections, GVHD)
M. Mei et al. BBMT, 2019	8	8 Ecu continued after transplant	Deaths: 3 (infections, clonal evolution)

EBMT-SAAWP Study

Frieri et al, ASH abstract 2024
Pt 147





#2nd take home message

→ **no significant difference in OS between thrombotic and non-thrombotic PNH**
(with the limit of retrospective data!)

→ **Practical approach to CI around HSCT:**

Before HSCT → continue CI?

During conditioning → last dose approx. day −7 to −1?

After engraftment → stop CI; monitor LDH/pnh clone ?

#3 Clinical case

Man, 39 y
No comorbidities
WBC 1800 Ne 500
Hb 7,2 gr/dl
Ret 10.000
Plt 30,000
LDH 350 (vn 243)
Bilirubin 2,8 mg/dl
PNH clone: 25%
BM: hypocellularity
Normal karyotype
Donor: HLA sib

Subclinical PNH

↓

SAA

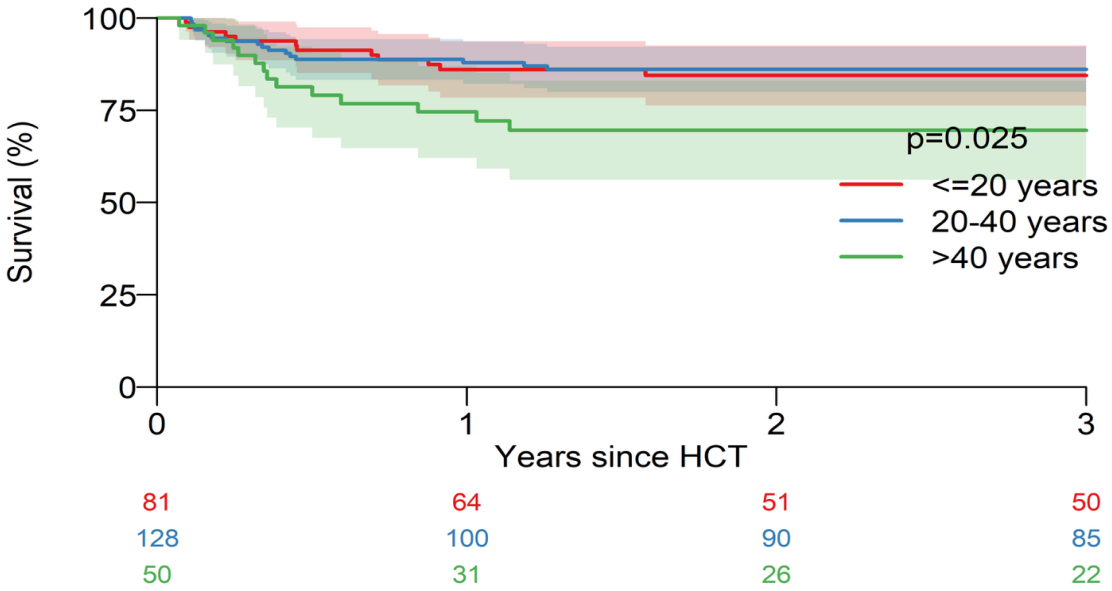
Our goal: resolve pancytopenia

HSCT VS IST

Results

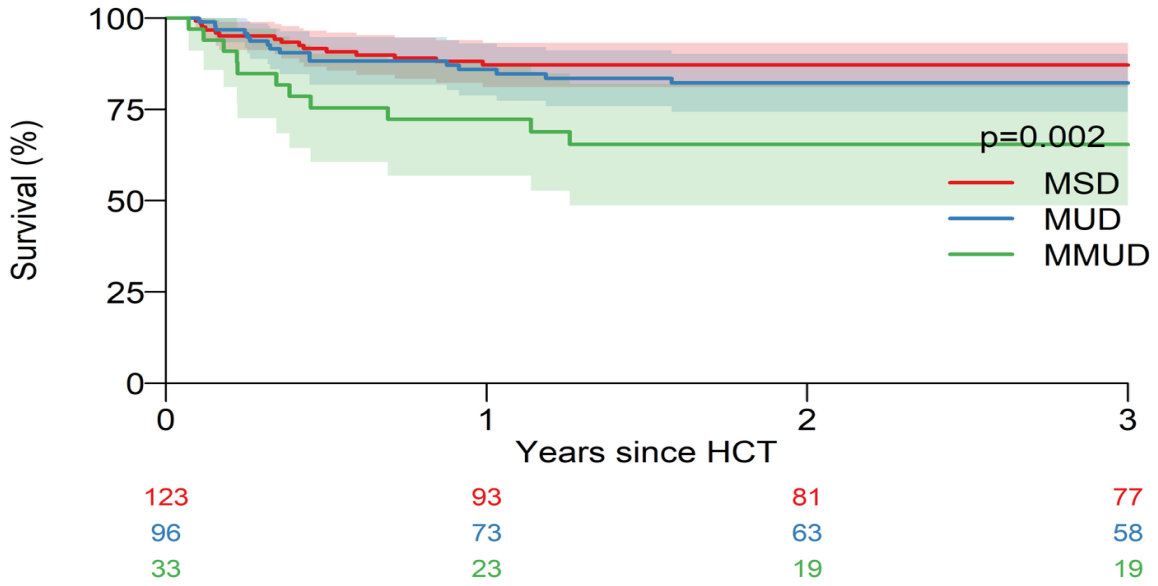
Frieri et al, ASH abstract 2024

Age



		OS (95% CI)		
Group	**N**	**1y**	**3y**	**p**
<=20 years	81	86% (78-94%)	84% (76-93%)	0.025
20-40 years	128	88% (82-94%)	86% (80-92%)	
>40 years	50	75% (62-87%)	70% (56-83%)	

Donor Type



		OS (95% CI)		
Group	**N**	**1y**	**3y**	**p**
MSD	123	87% (81-93%)	87% (81-93%)	0.002
MUD	96	86% (79-93%)	82% (74-90%)	
MMUD	33	72% (57-88%)	65% (49-82%)	

Only 7 haplo
All received PT-Cy
3 pt GF (2PGF-1SGF)
3 pt GVHD gr II-IV
1 pt dead for relapse

#3rd take home message

We treat clinical manifestations of the disease not “PNH clone”

#4th take home message

In **our study** except **age** and **donor type**, we could not identify any patient- or transplant-related factors associated with a better outcome

Conclusion #1

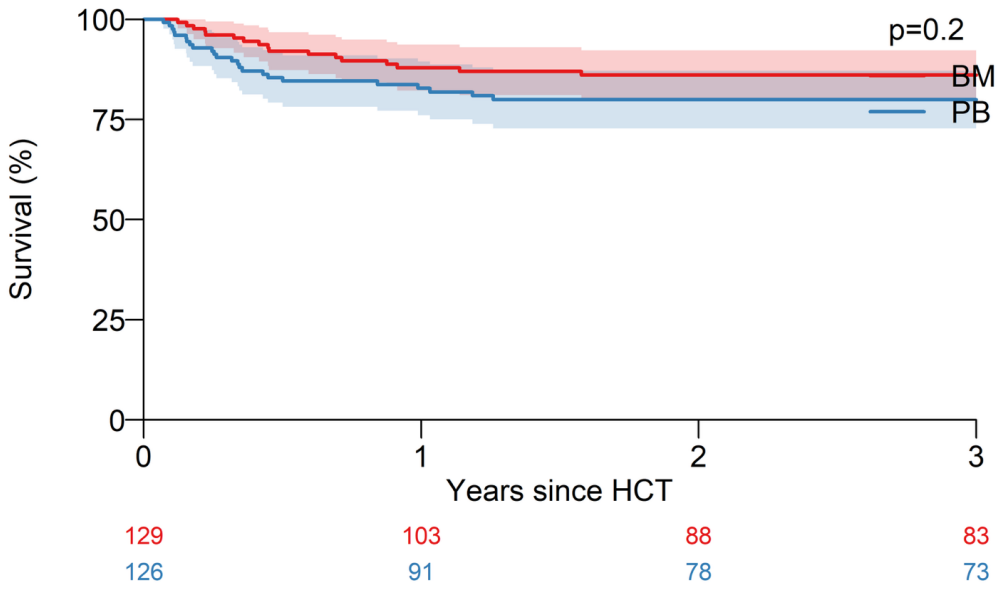
WHO to transplant?

- ✓ **PNH/AAS**
- ✓ **Clonal evolution in MDS/AML**
- ✓ Transfusion-dependent classical PNH on anti-C5 (DD between BMF and C3-mediated EVH) → ***identify candidates for proximal CI***
- ✓ Recurrent thrombotic events ***(→ better outcome in recent data, discuss case by case)***

Conclusion #2

HOW?

- ✓ Type of donor? (→ *worse outcome with MMUD, no sufficient data for haplo in our cohort*)
- ✓ Source of stem cell ?



Frieri et al, ASH abstract 2024

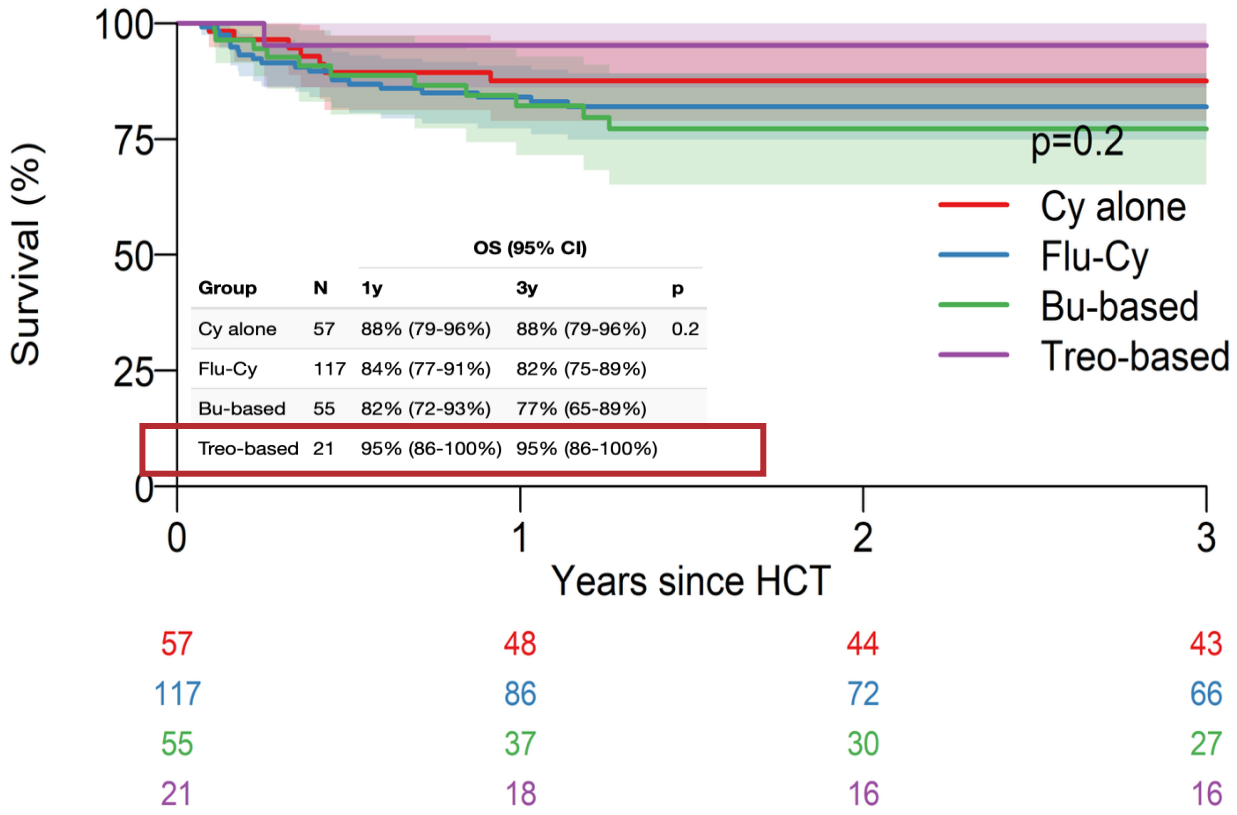
Conclusion #3

HOW?

✓ Conditioning regimen: RIC or MAC?

Markiewicz M, et al, BBMT 2020
78 pt
MAC 5 pt
RIC 73 pt
(51 pts received treosulfan-based)
NS in OS

Frieri et al, ASH abstract 2024
NS in OS bt RIC and MAC



Treosulfan as a valid alternative ?

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Dr Chiara Masucci

Thanks!

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THANK YOU!