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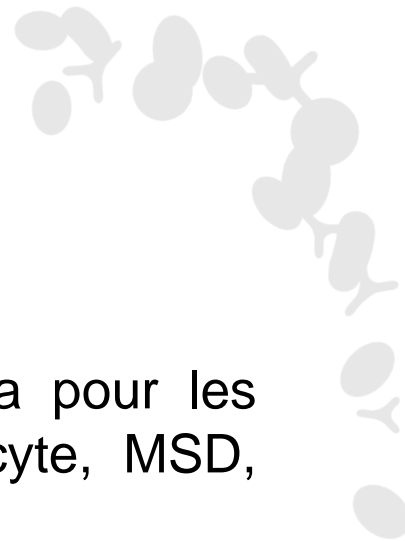
# Allogeneic BMT in older patients with aplastic anemia (40, 50...)

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**Régis Peffault de Latour, MD, PhD**

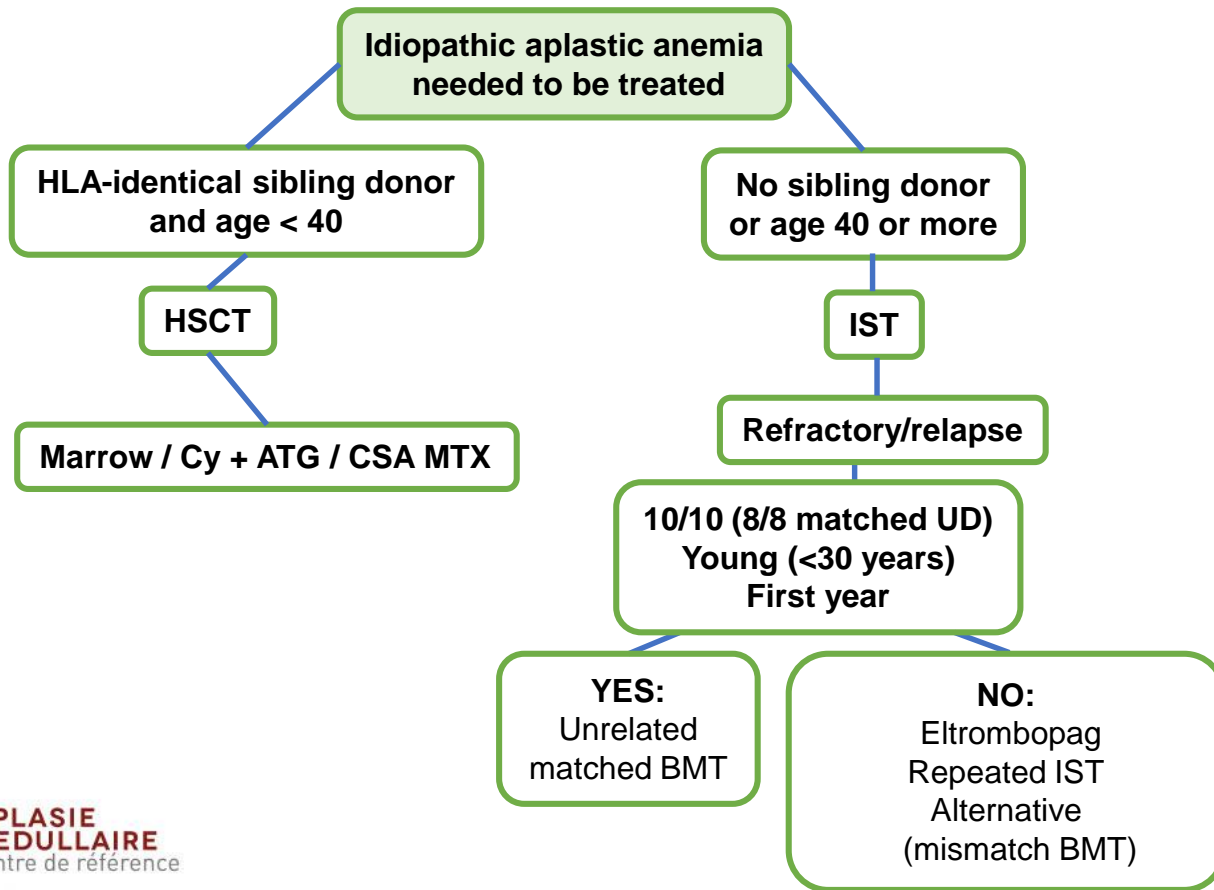
French reference center for aplastic anemia & PNH  
French network for rare immunological & hematological disorders (MaRIH)  
Severe aplastic anemia working party of EBMT (SAAWP EBMT)  
Hôpital Saint-Louis, Paris, France

# Disclosures

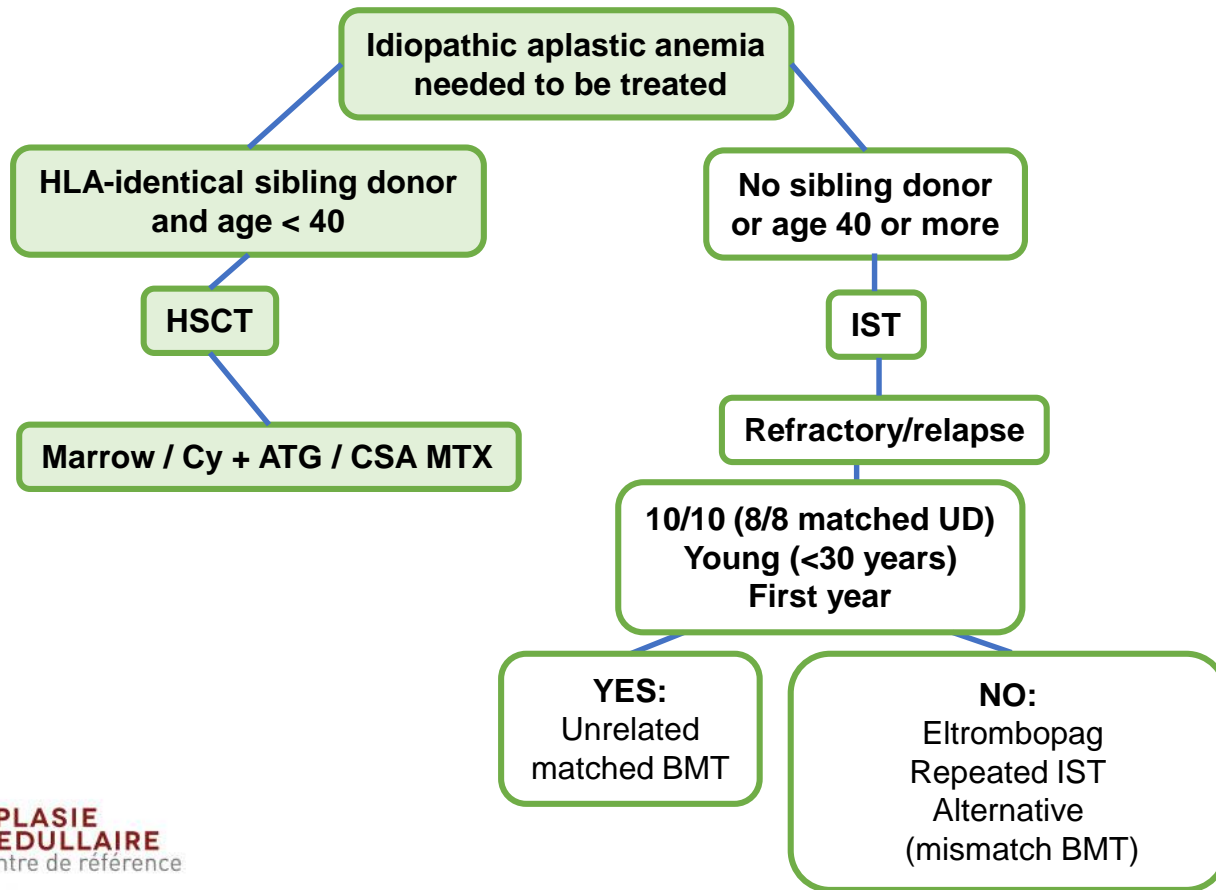


- **Expert consultant / orateur** pour des symposia pour les laboratoires Alexion, Amgen, Gilead, Jazz, Keocyte, MSD, Novartis, Pfizer, Roche, Samsung & Therakos
- **Bourse de recherche** des laboratoires Alexion, Amgen, Jazz pharmaceutical, Novartis, Pfizer

# Treatment (guidelines)

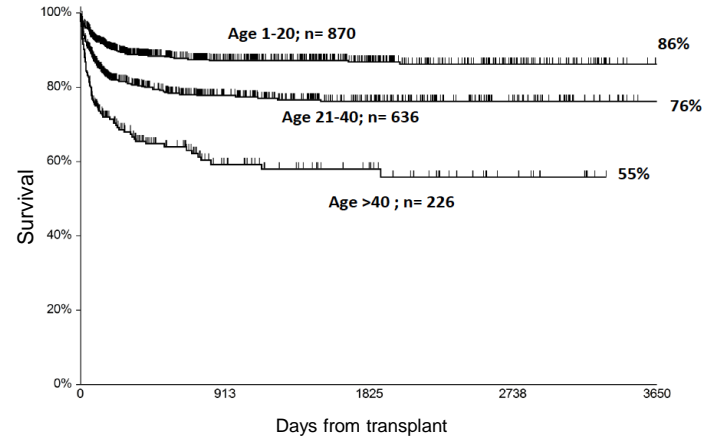
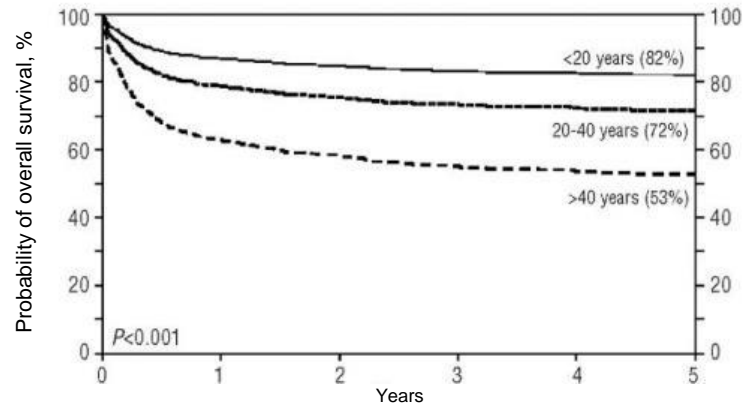
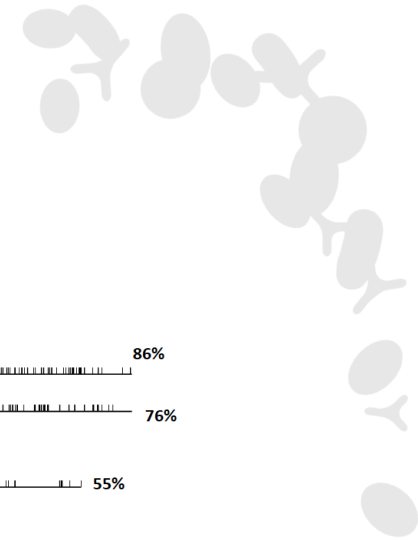


# Treatment (guidelines)

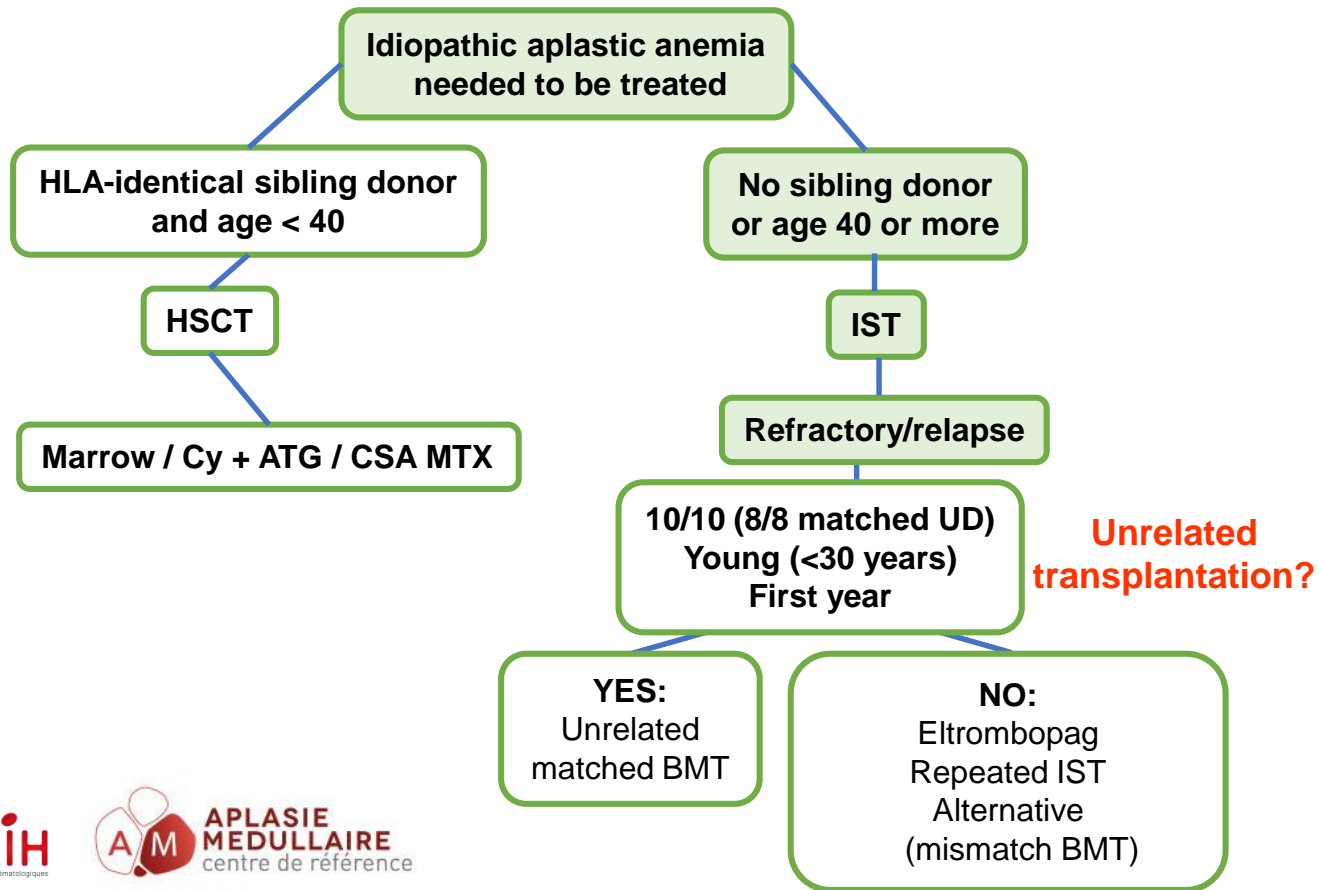


# Sibling transplantation

## Limitation - Age

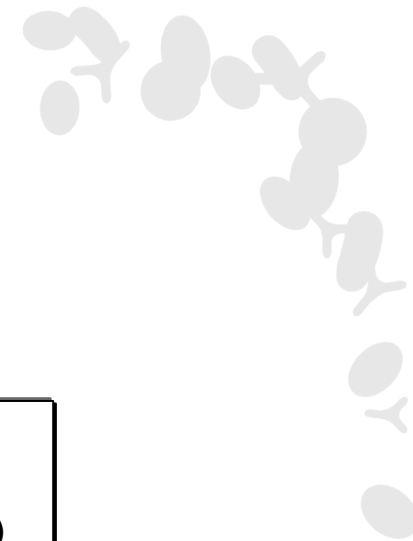


# Treatment (guidelines)



# Unrelated transplantation

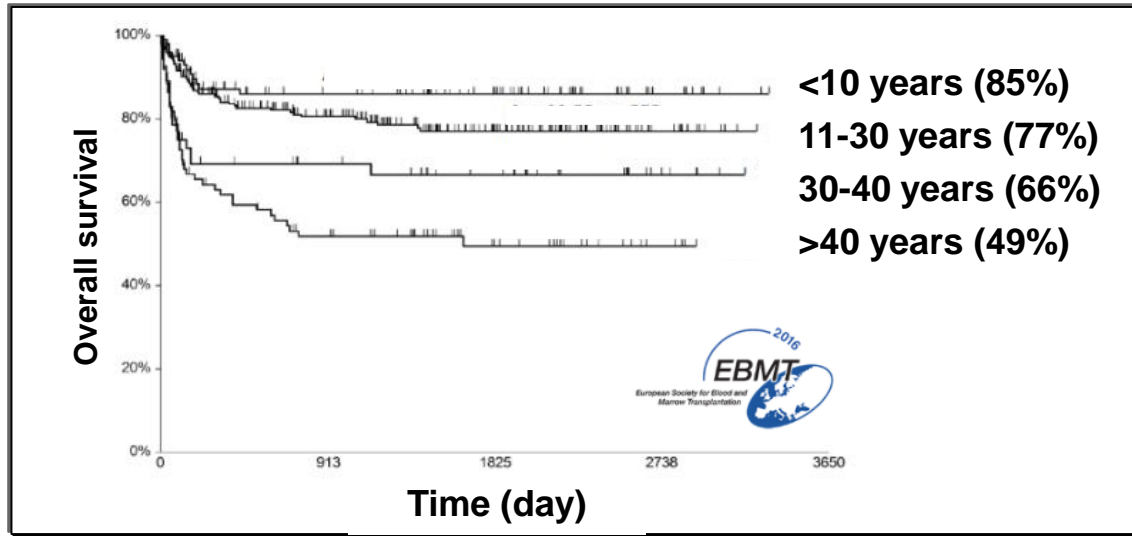
## Guidelines & role of age



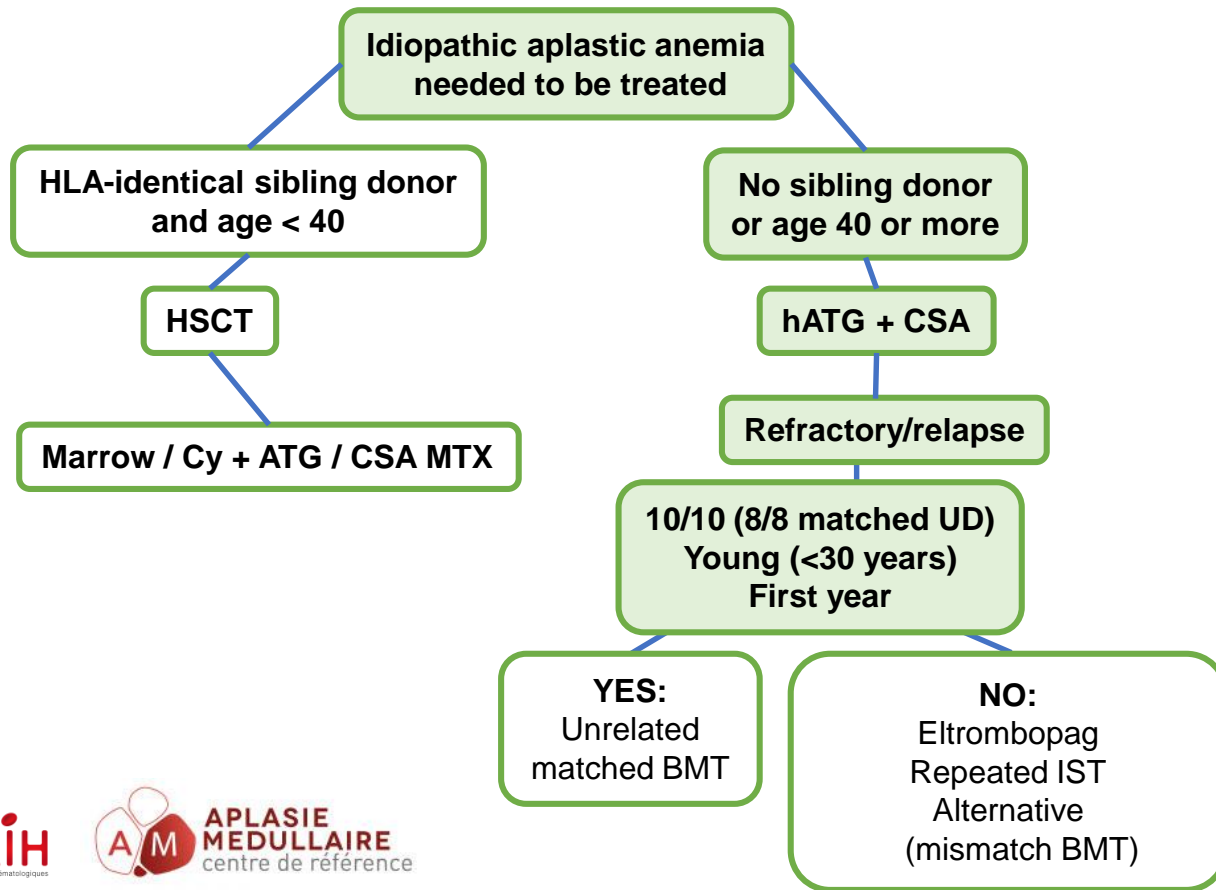
Marrow as source of stem cells

In the first year after diagnosis for refractory patients

Flu Cy ATG Low dose TBI (EBMT / BMT CTN / Japan)

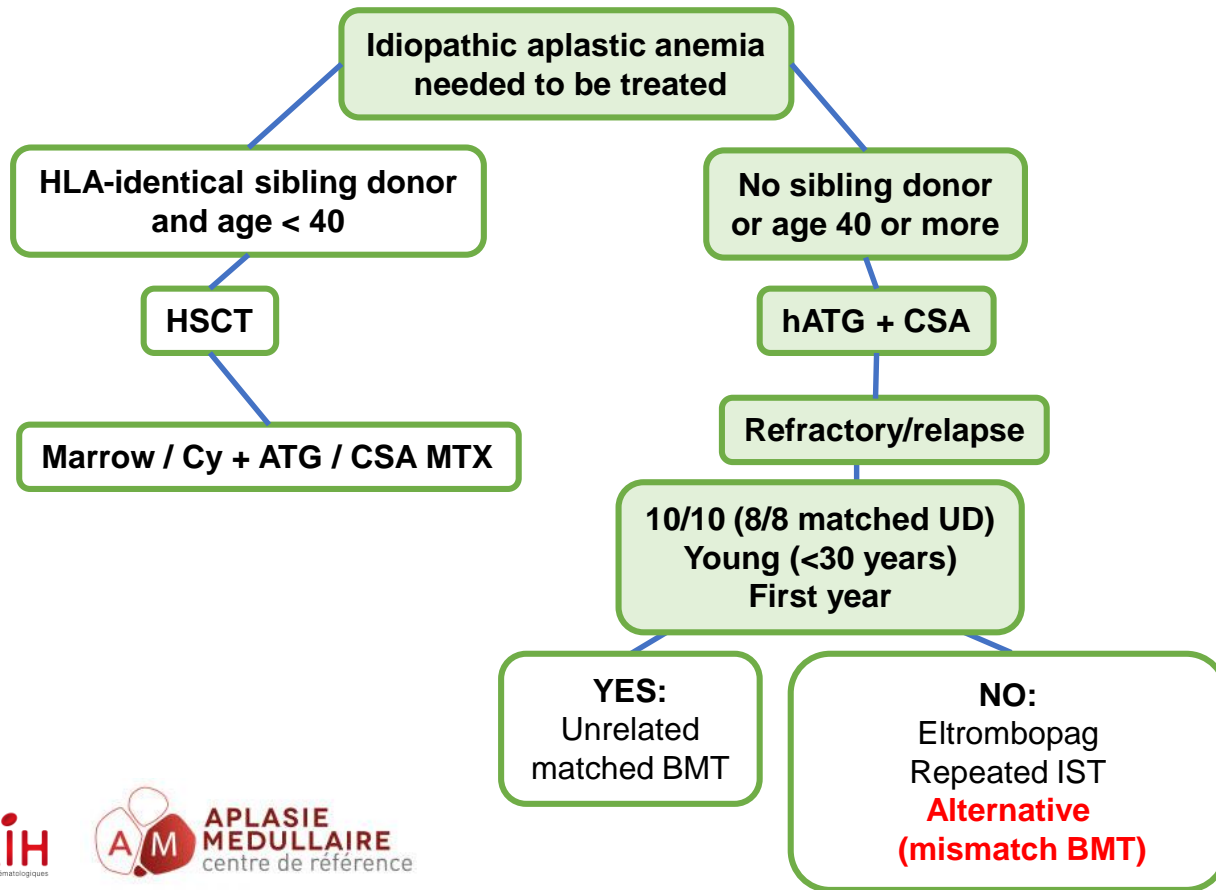


# Treatment (guidelines)





# Treatment (guidelines)



TO THE EDITOR:

## Transplant outcome for patients with acquired aplastic anemia over the age of 40: has the outcome improved?

Sabrina Giammarco,<sup>1</sup> Régis Peffault de Latour,<sup>2</sup> Simona Sica,<sup>1</sup> Carlo Dufour,<sup>3</sup> Gerard Socie,<sup>2</sup> Jakob Passweg,<sup>4</sup> Nicolaus Kroger,<sup>5</sup> Eefke Petersen,<sup>6</sup> Maria Teresa Van Lint,<sup>7</sup> Rosi Oneto,<sup>1</sup> Alessio Signori,<sup>8</sup> and Andrea Bacigalupo,<sup>1</sup> for the European Group for Blood and Marrow Transplantation Severe Aplastic Anemia Working Party

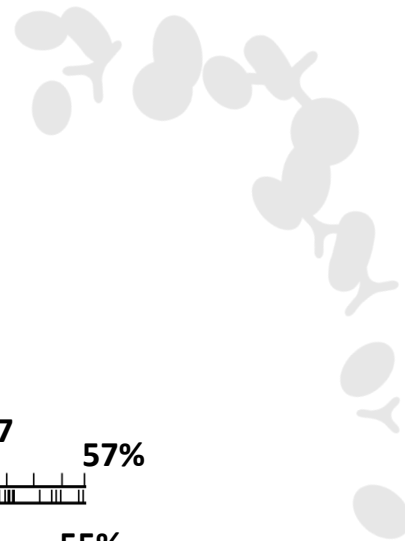
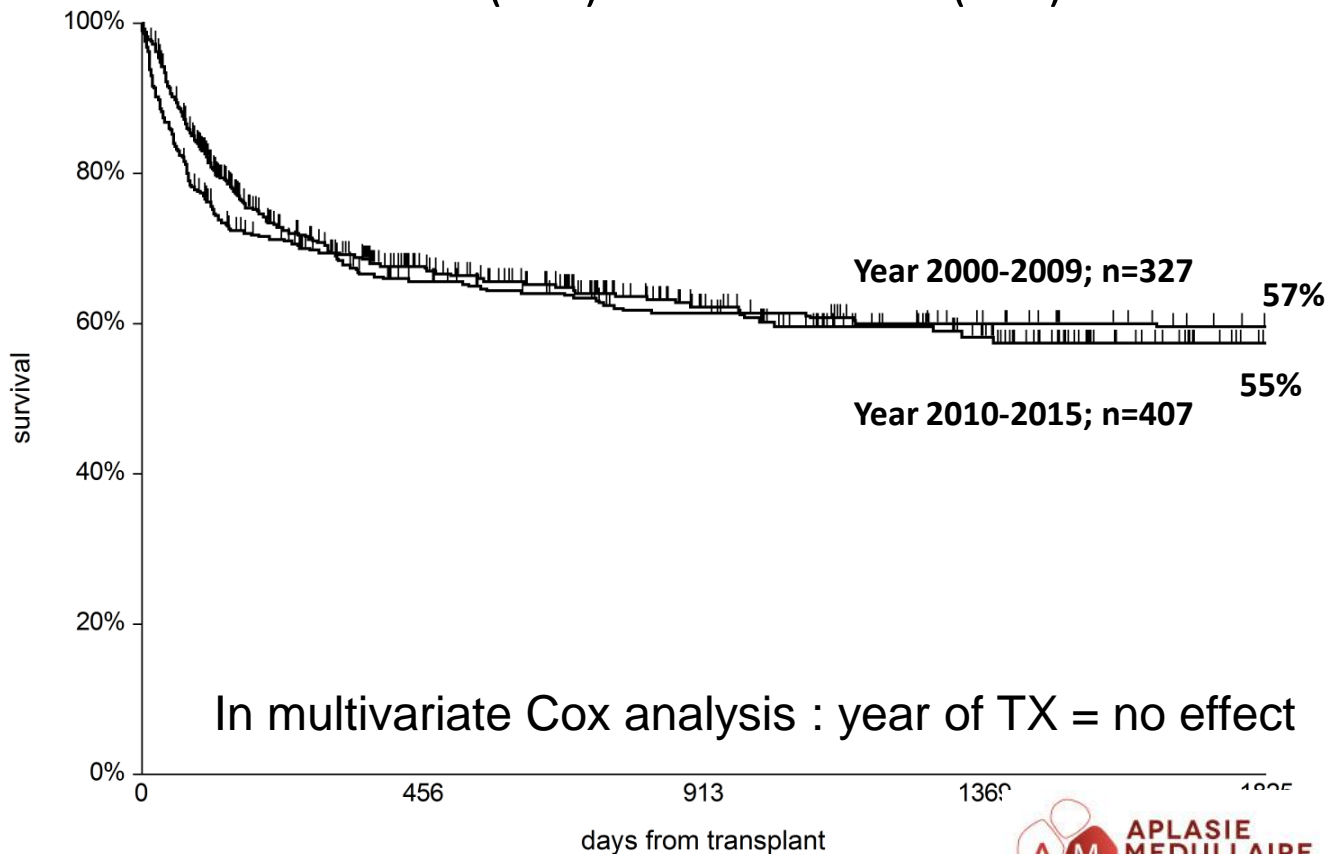
Blood 2018; 17:1989

Year of transplant	2001-2009	2010-2015	
<b>N patients</b>	<b>329</b>	<b>439</b>	
Median age (rang)	50 (40-69)	52 (40-77)	0.001
>60 years	12%	21%	0.001
Alternative donor	29%	52%	0.001
Interval Dx-BMT days	246 (10-10340)	313 (11-13512)	-

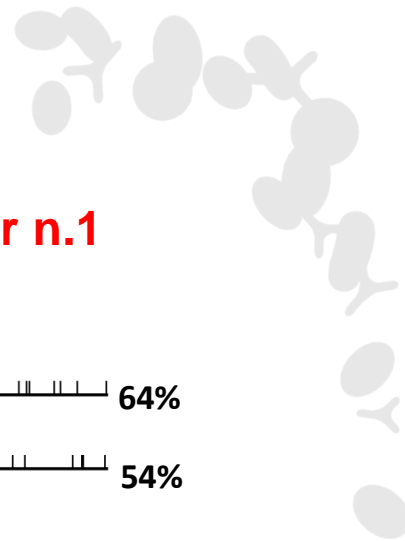
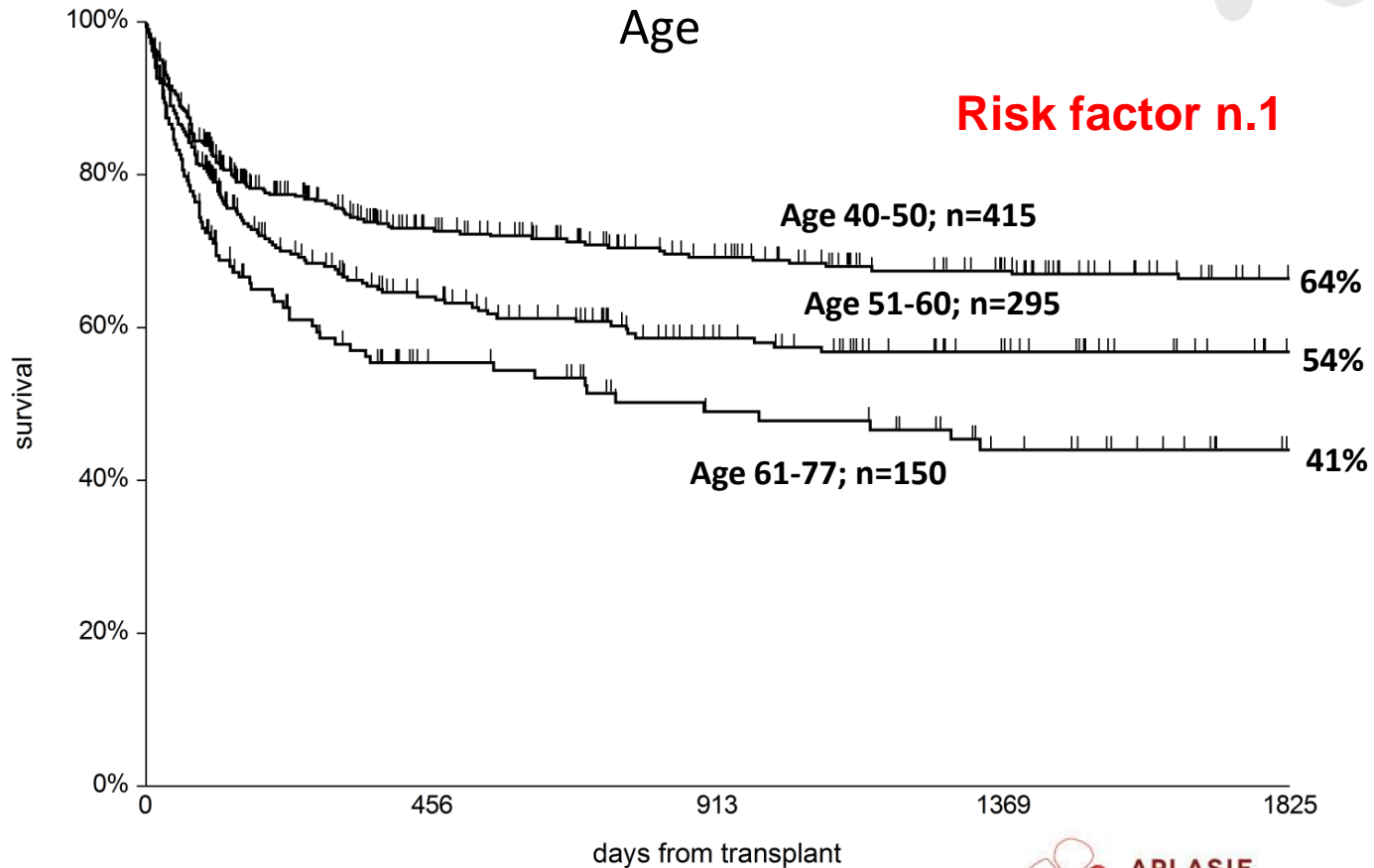


# Outcome of acquired SAA $\geq 40$ years

2000-2009 (327) and 2010-2015 (407)



# Outcome of acquired SAA $\geq 40$ years



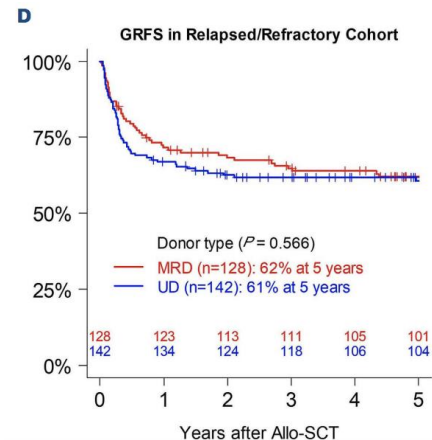
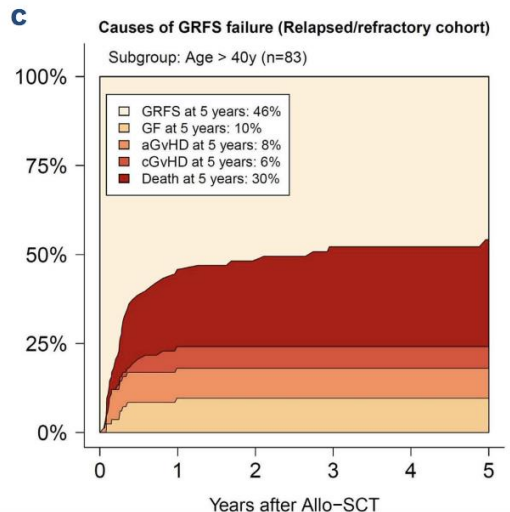
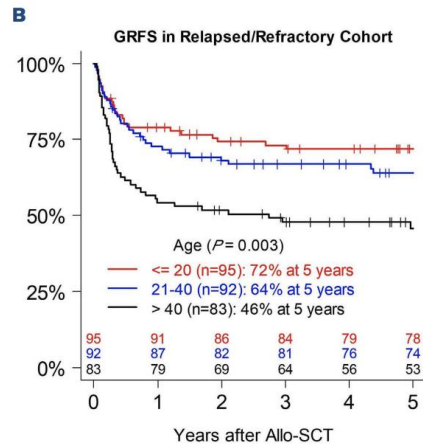
# Graft versus host disease and relapse/rejection-free survival

ARTICLE - Aplastic Anemia

## Graft-versus-host disease and relapse/rejection-free survival after allogeneic transplantation for idiopathic severe aplastic anemia: a comprehensive analysis from the SAAWP of the EBMT

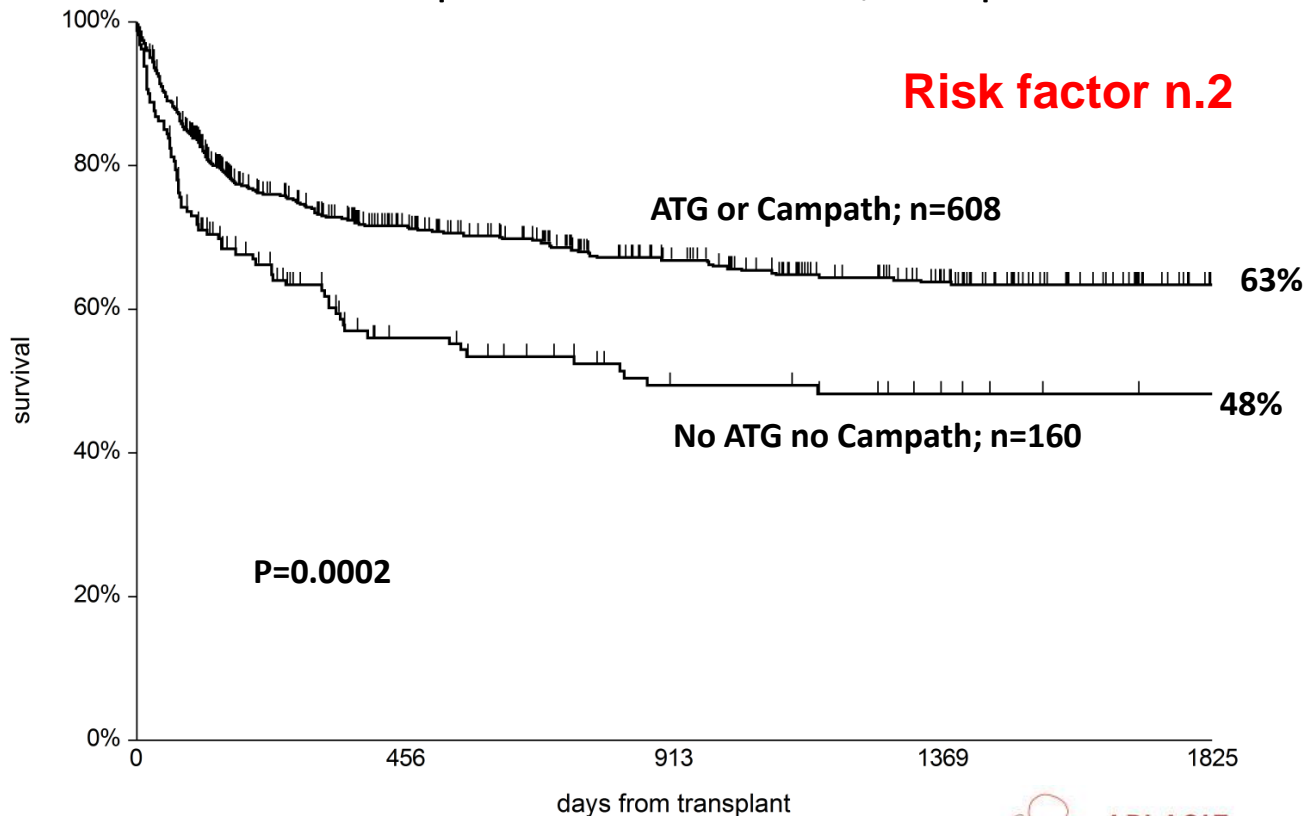
Raynier Devillier,<sup>1</sup> Dirk-Jan Eikema,<sup>2</sup> Carlo Dufour,<sup>3</sup> Mahmoud Aljurf,<sup>4</sup> Depei Wu,<sup>5</sup> Alexei Maschan,<sup>6</sup> Alexander Kulagin,<sup>7</sup> Constantijn J. M. Halkes,<sup>8</sup> Matthew Collin,<sup>9</sup> John Snowden,<sup>10</sup> Cécile Renard,<sup>11</sup> Arnold Ganser,<sup>12</sup> Karl-Walter Sykora,<sup>12</sup> Brenda E. Gibson,<sup>13</sup> Johan Maertens,<sup>14</sup> Maija Itälä-Remes,<sup>15</sup> Paola Corti,<sup>16</sup> Jan Cornelissen,<sup>17</sup> Martin Bornhäuser,<sup>18</sup> Mercedes Colorado Araujo,<sup>19</sup> Hakan Ozdogu,<sup>20</sup> Antonio Risitano,<sup>21</sup> Gerard Socie<sup>22</sup> and Régis Peffault de Latour<sup>22</sup>

Sept 2023



# Outcome of acquired SAA $\geq 40$ years

## ATG or Campath versus no ATG /Campath



# Campath

## UK experience

REGULAR ARTICLE

 blood advances

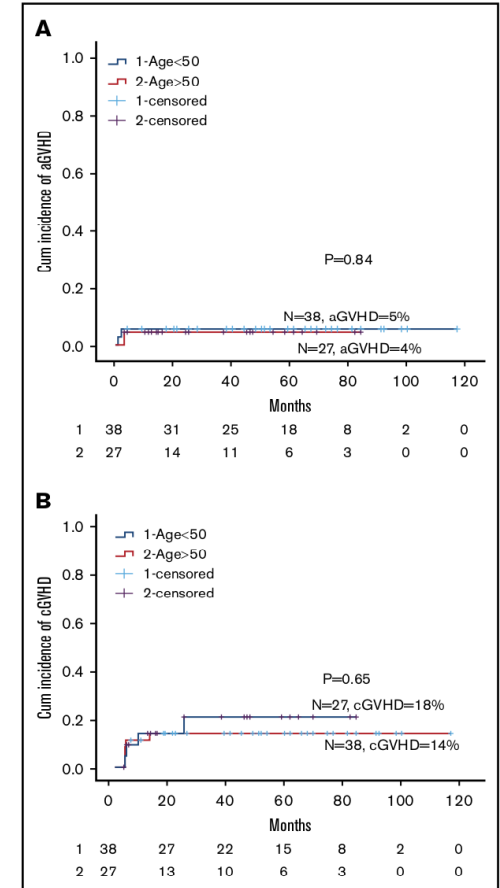
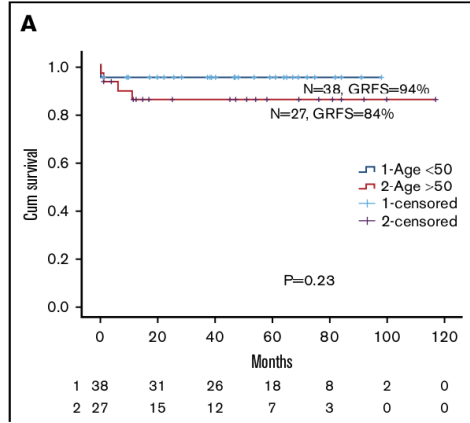
### Similar outcomes of alemtuzumab-based hematopoietic cell transplantation for SAA patients older or younger than 50 years

Vipul Sharad Sheth,<sup>1</sup> Victoria Potter,<sup>1</sup> Shreyans A. Gandhi,<sup>1,2</sup> Austin Gladston Kulasekararaj,<sup>1</sup> Hugues de Lavallade,<sup>1,2</sup> Petra Muus,<sup>1</sup> Antonio Pagliuca,<sup>1,2</sup> Carmel F. M. Rice,<sup>1</sup> Varun Mehra,<sup>1</sup> Francesco Grimaldi,<sup>2,3</sup> Shafqat Inam,<sup>1</sup> Linda D. Barber,<sup>2</sup> Ghulam J. Mufti,<sup>1,2</sup> and Judith C. Marsh<sup>1,2</sup>

<sup>1</sup>Department of Haematological Medicine, King's College Hospital, London, United Kingdom; <sup>2</sup>Department of Haematological Medicine, King's College London, London, United Kingdom; and <sup>3</sup>Department of Hematology, Federico III University of Naples, Naples, Italy

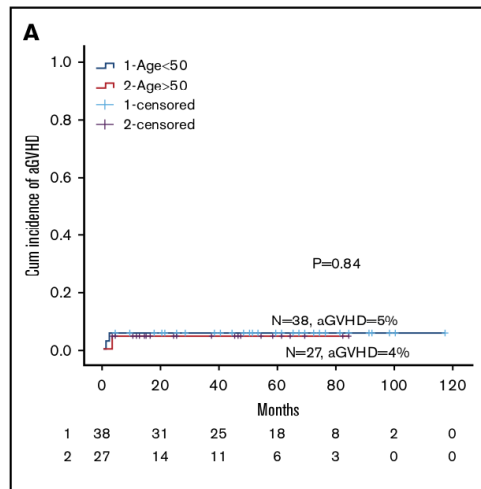
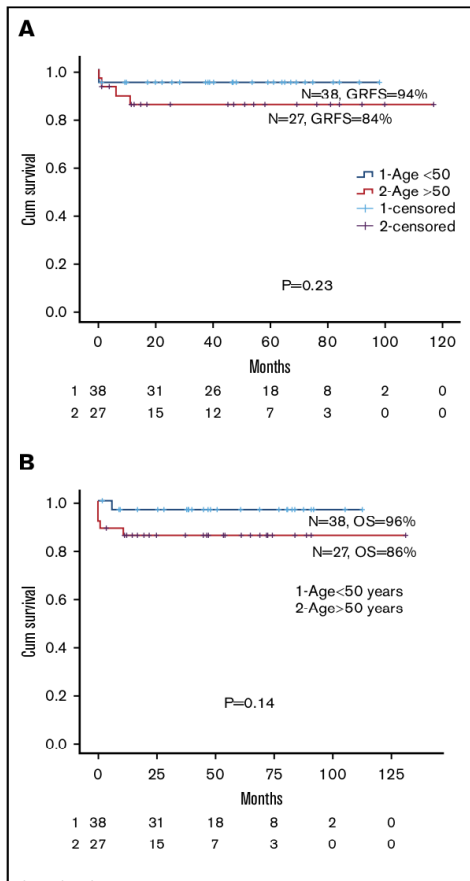
- 65 consecutive patients (38 patients < 50 years / 27 aged 50 or more)
- Older cohort: 21 MUD (3 MMUD) and 6 siblings
- FCC conditioning regimen: 30 mg/m<sup>2</sup> (4 days), CY 300 mg/m<sup>2</sup> (4 days) and alemtuzumab (0.2 mg/kg each day, days -7 to -3).

# Campath (UK experience)





# Campath (UK experience)

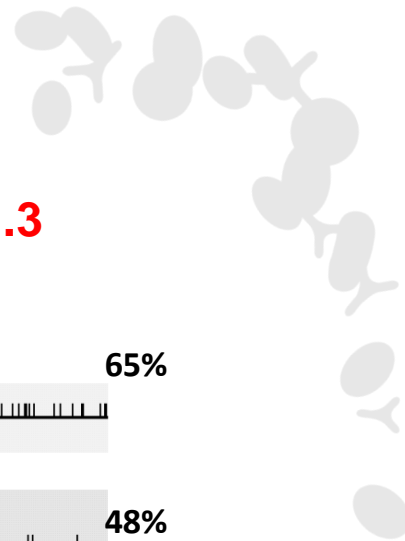
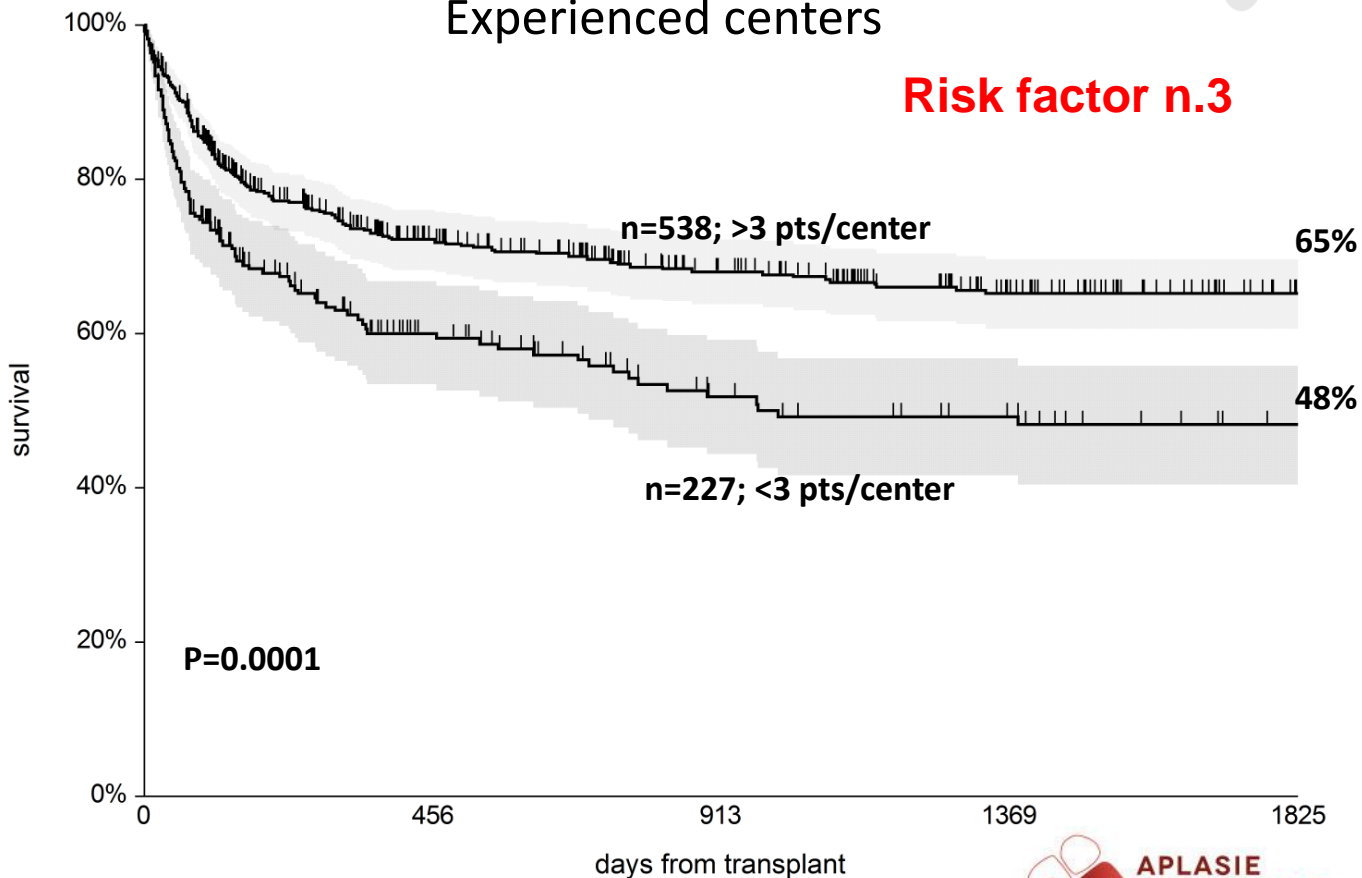


- <50: fungal disease (2); MOF (1)
- 50 or more: fungal disease (3); MOF and CMV (1)

# Outcome of acquired SAA $\geq 40$ years

Experienced centers

**Risk factor n.3**



# Outcome of acquired SAA $\geq 40$ years

2000-2009 (327) and 2010-2015 (407)

## Cox analysis

		<i>HR</i>	<i>P</i>
Center	>3 pts	0.59	0.0001
Age	50-59	1.3	0.05
	>60	2.0	0.0001
ATG/C	yes	0.3	0.0001
Year	$\geq 2010$	0.9	0.5
DxTx	>180	1.17	0.2
Donor	UD	1.24	0.1



## Outcome of acquired SAA $\geq 40$ years

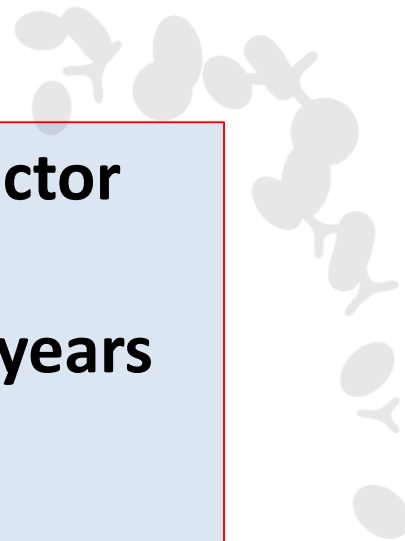
**# Age  $> 40$  (50) remains a significant risk factor for BMT**

**# results have not improved over the past years**

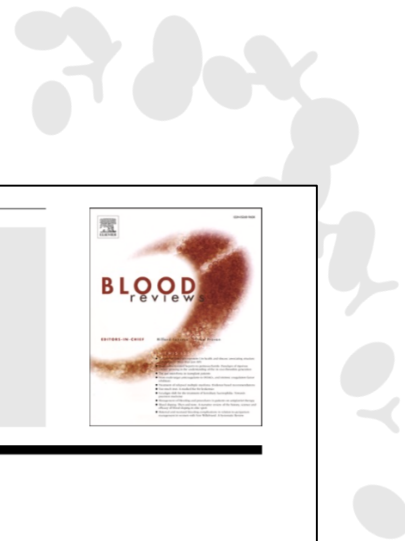
**# additional risk factors are**

- . No ATG/CAMP**
- . Unexperienced centers**

**# different transplant platform needed**



# Different transplant platform needed



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## Blood Reviews

journal homepage: [www.elsevier.com/locate/issn/0268960X](http://www.elsevier.com/locate/issn/0268960X)



### Review

## Combining PTCy and ATG for GvHD prophylaxis in non-malignant diseases

Amy E. DeZern<sup>a,\*</sup>, Robert A. Brodsky<sup>b</sup>

<sup>a</sup> Division of Hematologic Malignancies, The Johns Hopkins University School of Medicine, 1650 Orleans Street, CRBI Room 3M87, Baltimore, MD 21287-0013, United States of America

<sup>b</sup> Division of Hematology, The Johns Hopkins University School of Medicine, 720 Rutland Avenue | Ross 1025, Baltimore, MD 21205, United States of America

# Different transplant platform needed



**Table 1**  
Lessons learned in aplastic anemia.

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PTCy expands the donor pool	<ul style="list-style-type: none"><li>• Allows use of HLA-haploidentical bone marrow donors</li><li>• Engraftment, risk of GVHD and survival appears comparable to outcomes using matched sibling or matched unrelated donors</li></ul>
400 cGy is superior to 200cGy in treatment-naïve patients	<ul style="list-style-type: none"><li>• Full donor chimerism is 100% with the use of 400 cGy TBI in the Flu/CY/TBI backbone</li><li>• 200 cGy TBI may sufficient if patient previously received high dose immunosuppressive therapy</li></ul>
Oral IST post-transplant is only needed to 6 months, not 12 months with intensive ATG and PTCy regimens for GVHD	<ul style="list-style-type: none"><li>• Represents a shortened period of immune compromise than immunosuppressive therapy as front-line treatment in acquired AA.</li></ul>
Quality of the bone marrow graft is imperative	<ul style="list-style-type: none"><li>• Donor bone marrow should be harvested with a target yield of <math>4 \times 10^8</math> nucleated marrow cells per kilogram of recipient ideal body weight (IBW)<sup>31</sup></li><li>• Recommended minimum yield of <math>2.5 \times 10^8</math> nucleated marrow cells per kilogram of recipient IBW allows engraftment and best outcomes</li></ul>

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# Different transplant platform needed



## Bone marrow transplantation for acquired aplastic anemia: What's new

Andrea Bacigalupo<sup>a,b,\*</sup>, Giulia Benintende<sup>b</sup>

<sup>a</sup> Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy

<sup>b</sup> Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Roma, Italy

Furthermore, PTCy can be of use even in SIB BMT. Small case series from the Baltimore group, including old patients at high risk of graft failure and GvHD due to massive transfusions and alloimmunization, demonstrated its feasibility [41]. Research also investigated the possibility to use PTCy as the sole GvHD prophylaxis compared to CsA and MTX in patients receiving PBSC, owing lower rates of grade II-IV acute GvHD (22.2% vs 37.1%,  $p = 0.56$ ) and chronic GvHD (22.7% vs 63.6%,  $p = 0.013$ ) but higher rate of viral infections (60% vs 23.3%,  $p = 0.008$ ) [42]. The combination of PTCy with standard immunosuppression (CsA + MTX) has proven superiority to CsA + MTX alone in patients receiving PBSC – who are known to have higher rates of graft failure and GvHD – with lower grade II-IV acute GvHD (22-6% vs 52.2%,  $p = 0.0015$ ) but similar chronic GvHD (16.7% vs 26%,  $p = 0.306$ ) [43].

Further studies are needed to explore the use of PTCy for SIB BMT with bone marrow stem cells source and to validate its role in MUD BMT.

- The combination of Flu and CY has changed the paradigm of conditioning regimen.
- PTCy may be the turning point of GvHD prophylaxis, but new trials are needed to validate its use with donors other than HLA mismatched related HAPLO donors.

# Different transplant platform needed



## Bone marrow transplantation for acquired aplastic anemia: What's new

Andrea Bacigalupo<sup>a,b,\*</sup>, Giulia Benintende<sup>b</sup>

<sup>a</sup> Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy

<sup>b</sup> Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Roma, Italy

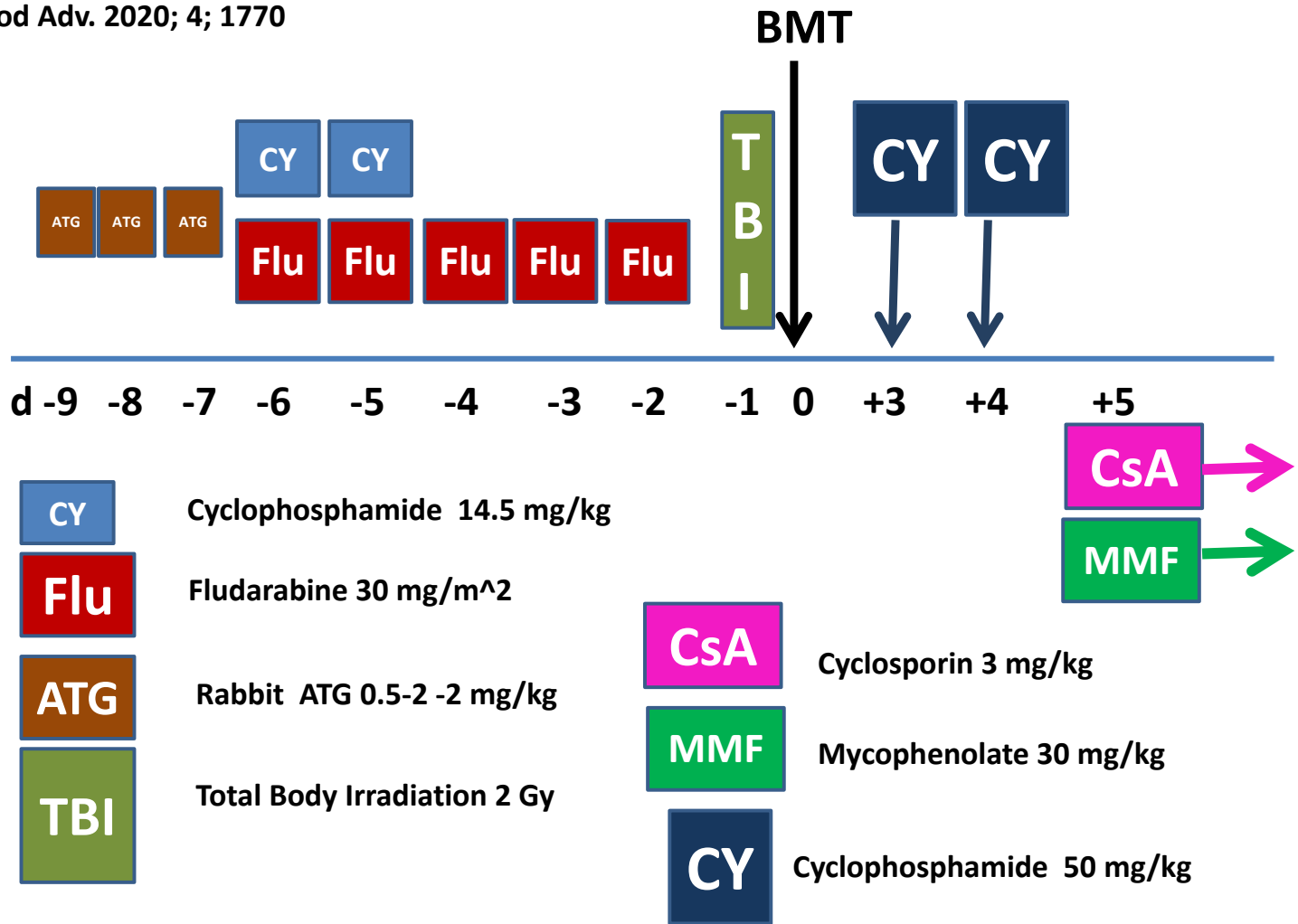
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- The combination of Flu and CY has changed the paradigm of conditioning regimen.
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# HSCT for older AA patients – FCA-TBI 2gray / PTCy CsA+MMF

Roma, Perugia, Cuneo, Alessandria, Milano, Bolzano, Verona, Udine, Palermo, Torino

MUD =16

UD 7/8 = 6

HAPLO = 2

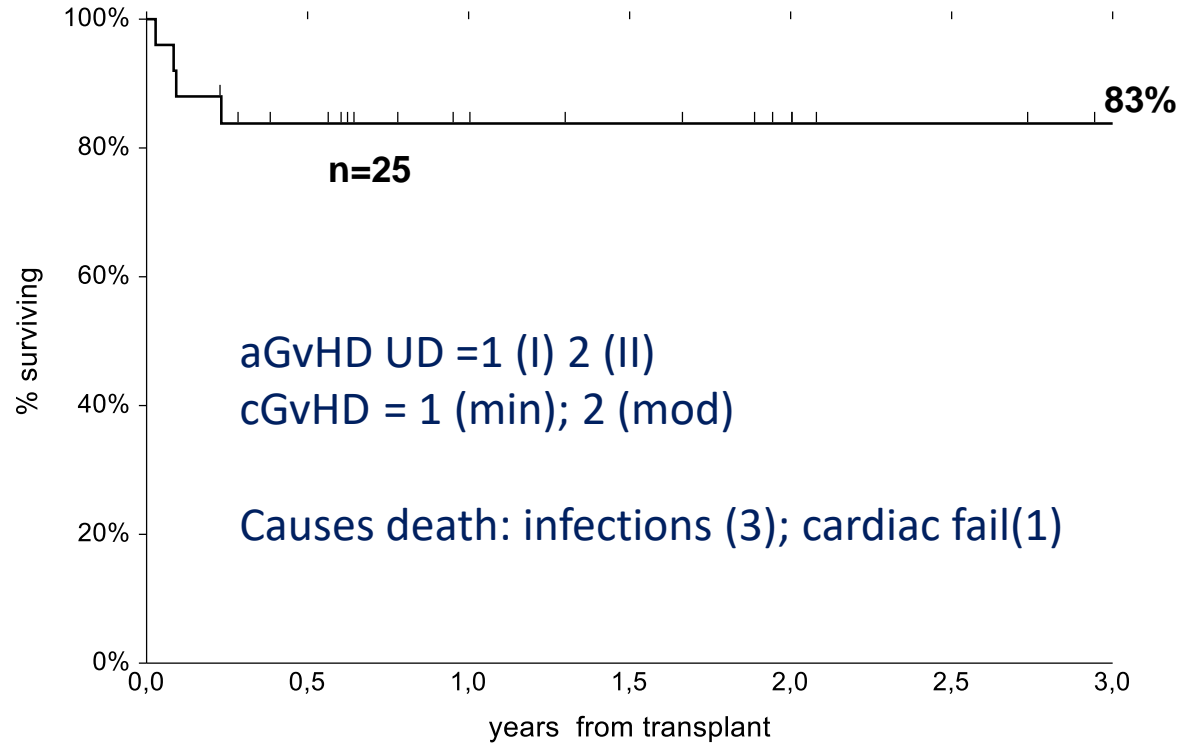
SIB =1

Age = 42 (26-70)

Int DxTx 536 (90-3000)

Engr PMN 500 = day 19

Engr Plt 20 = day 22



## Conclusion – APARR 😊

**Allogeneic hematopoietic stem cell transplantation in Patients Aged 40 to 60 years old with acquired aplastic anemia Refractory or in Relapse after immunosuppression**

- **Main endpoint:** to demonstrate a benefit in term of the 2-year GRFS (Graft Versus Host Disease {GvHD} and Relapse/rejection-Free Survival) from 50% (historical rates in patients with refractory/relapse AA undergoing HSCT) up to 70% using marrow as source of stem cells and a PTCy strategy.
- **Design:** A phase II multicenter, national, prospective cohort study in patients aged from 40 to 60 years with refractory/relapse AA after IST eligible to HSCT.
- **Regimen:** FCA-TBI / Bone marrow / PTCy+CSA+MMF
- **Number of participants:** 52 patients in 28 centres
- **Duration of the study:** Inclusion period: 36 months / Participation period (treatment + follow-up): 24 months. Total duration: 60 months

# Thank you!

## The French Reference Center for aplastic anemia and PNH in Paris



Saint-Louis Hospital



Robert Debré Hospital



Institute of Hematology, IUH St-Louis

**F Sicre, T Leblanc, M Fahd, JH Dalle, A Baruchel, G Socié,  
N Vasquez, W. Cuccuini, J Soulier (Fanconi team),  
C Kannengiesser, E Lainey, L Da Costa (Telomeres team)**

