SEVERE APLASTIC ANEMIA TRANSPLANTATION

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SEVERE APLASTIC ANEMIA CASE PRESENTATIONS:

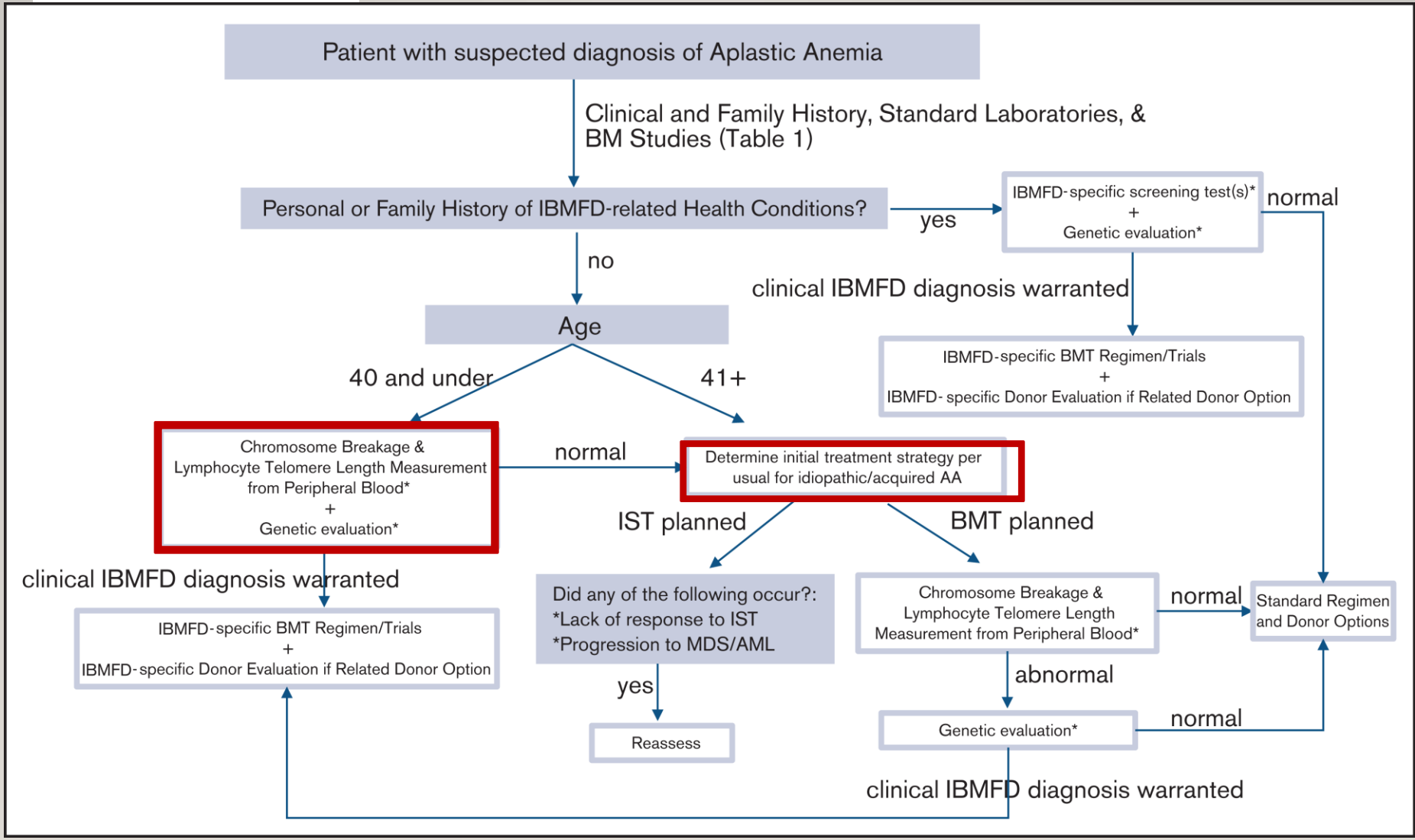
AGE/SEX	GRAFT SOURCE RECIPIENT STATUS	CONDITIONING GVHD PROPHYLAXIS	ENGRAFTEMENT /GVHD	OUTCOME
36/Male	MRD/Female 32 yr Limited blood products transfusions Transplantation in 4 months	CPM 120mg/kg,FLU 120 mg/kg,ATG 7.5 mg/kg CSA ,MTX Cell dose :3.5 X 10. 6/Kg T cell depletion: NO	Day. + 12 NO GVHD	14 months Chimeris m99%
33/Female	MUD/Female 32 yr No blood products transfusions Transplantation in 2 months	CPM 90mg/kg,FLU 120 mg/kg,ATG 7.5 mg/kg CSA ,MTX Cell dose 10 x 10 6/kg T cell depletion: YES	Day. + 14 NO GVHD	30months Chimeris m99%

SEVERE APLASTIC ANEMIA CASE PRESENTATIONS:

AGE/SEX	GRAFT SOURCE RECIPIENT STATUS	CONDITIONING GVHD PROPHYLAXIS	ENGRAFTEMENT /GVHD	OUTCOME
10/Female	MRCB Limited blood products transfusions hATG+CSA	CPM 90mg/kg,FLU 120 mg/kg,ATG 7.5 mg/kg CSA ,MTX TNC dose :3.19X 10. 7/Kg post thaw:2.93 x10 7/kg T cell depletion: NO	Day. + 21 NO GVHD	6years Chimeris m95%
20/male	HLA DR ,PermissiveDP MMUD /male Heavily transfused. Transplantation after 2 yrars IST hATG & r ATG Fungal infection +	CPM 90mg/kg,FLU 120 mg/kg,ATG 7.5 mg/kg CSA ,MTX,PTCP 50 mg/kg x2,cellcept Cell dose 9x 10 6/kg CD 3,169 T cell depletion: NO	Day + 15 NO GVHD	+60 Chimeris m99% BUT rejection on +180

blood advances

Blood Adv (2021) 5 (12): 2660–2671.



CLASSIFICATION OF TRANSPLANT INDICATIONS

The eighth report from EBMT April 2022, [Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, Bone Marrow Transplantation **(Springer Nature**) (2022) 57:1217–1239.]

Disease	Disease status	MSD allo	MUD allo	MMAD allo	Auto	CAR-T
SAA (for adult)	Newly diagnosed	S/II	CO/II	GNR/III	NA	
	Relapsed/ Refractory	S/II	S/II	CO/II	NA	
SAA (for children and adolescents)		S/II	S/II	CO/II	NA	

S: Standard of care (generally indicated in suitable patients), **CO:** clinical option (can be carried after careful assessment of risks and benefits), **GNR:** generally, not recommended, **NA:** not applicable.
Grade I: Evidence from at least one well-executed randomized trial.
Grade II Evidence from at least one well-designed clinical trial without randomization.
Grade II: Evidence from opinions of respected authorities based on clinical experience.

EBMT GUIDLINE

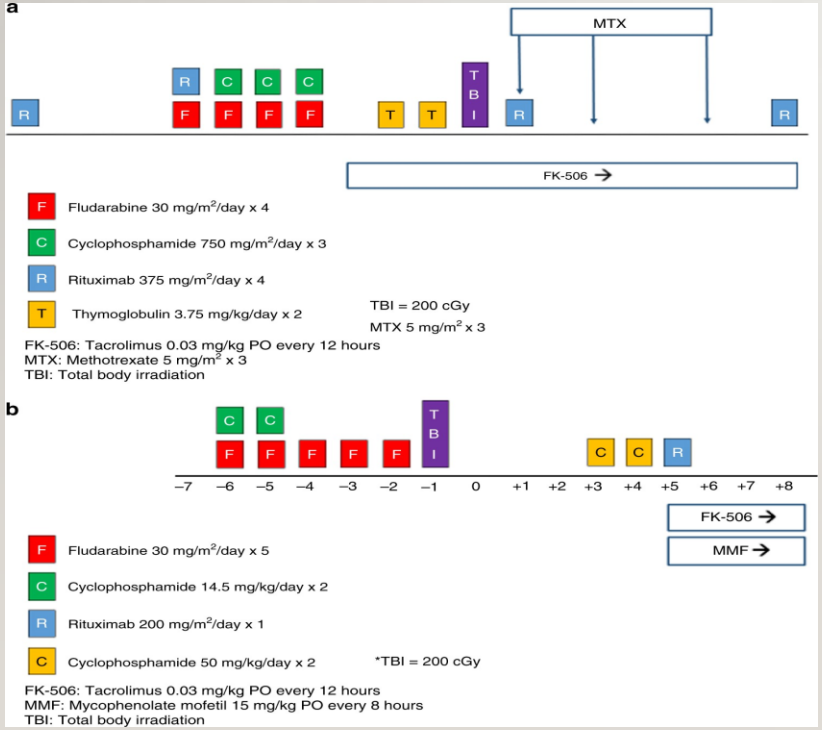
	Volume collected	Med CD34 content	Med CD3 content	Target cell dose
Bone marrow	10–20 mL/kg	2–3 × 10^6/kg[a]	25 × 10^6/kg	>2 × 10^8 TNC/kg
Peripheral blood	150–400 mL	8 × 10^6/kg	250 × 10^6/kg	5–10 × 10^6 CD34+/kg
Umbilical cord blood	80–160 mL	0.2 × 10^6/kg	2.5 × 10^6/kg	>3 × 10^7 TNC/kg

[a]Per kg recipient body weight

STANDARD CONDITIONING FOR MATCHED SIBLING TRANSPLANTS

- Under the age of 40 Cyclophosphamide 200mg/kg (CY 200) and ATG, as originally described.
- For older patients, current guidelines support the use of FLU-CY-ATG-low dose irradiation (FCA) or FLU-Cy alemtuzumab (CAMPATH) .
- Rituximab 200mg on day +5 should be added in patients receiving alternative donor grafts.

NOVEL RITUXIMAB-BASED NON-MYELOABLATIVE CONDITIONING REGIMEN FOR HEMATOPOIETIC CELL TRANSPLANTATION IN SEVERE APLASTIC ANEMIA



- improved efficacy
- decreased toxicity
- decreased risk of infectious complications

https://doi.org/10.1016/j.bbmt.2017.12.766

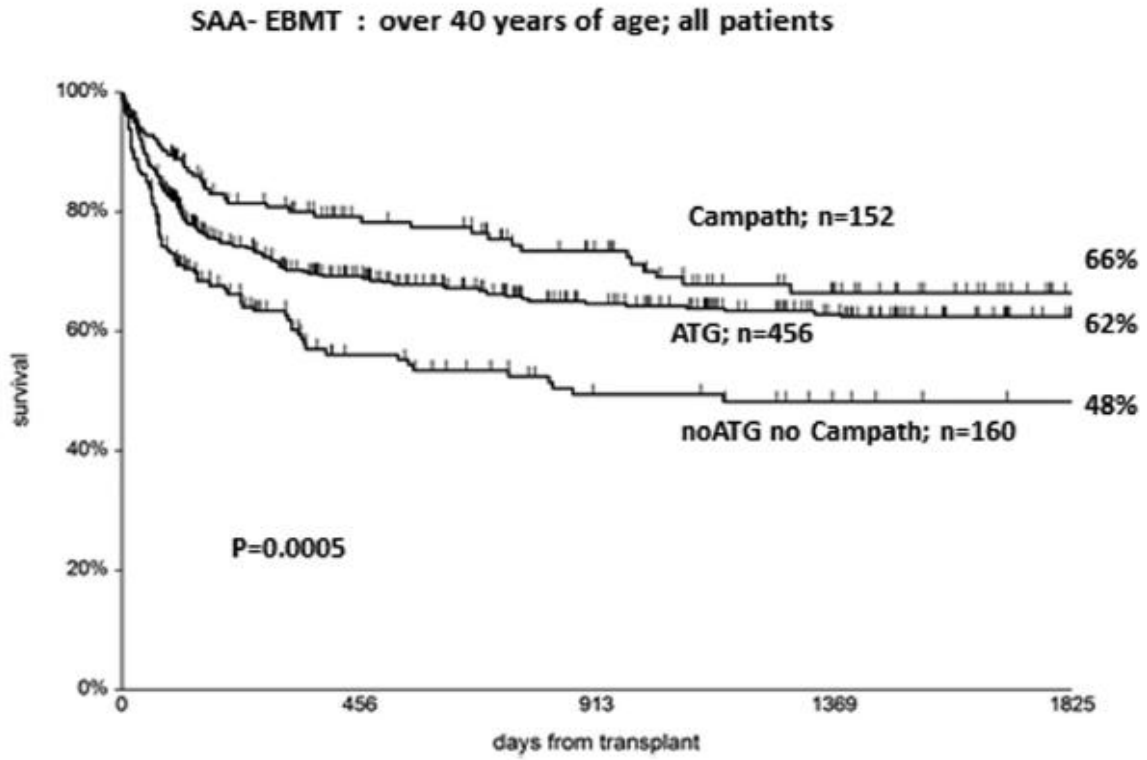


Figure 1. Actuarial survival of patients undergoing a SCT from HLA identical siblings or unrelated donors: shown is the effect of GvHD prophylaxis with Campath (alemtuzumab), ATG, or no Campath/ATG. The difference is highly significant.

OVERALL SURVIVAL: HLA-MATCHED SIBLING TRANSPLANT

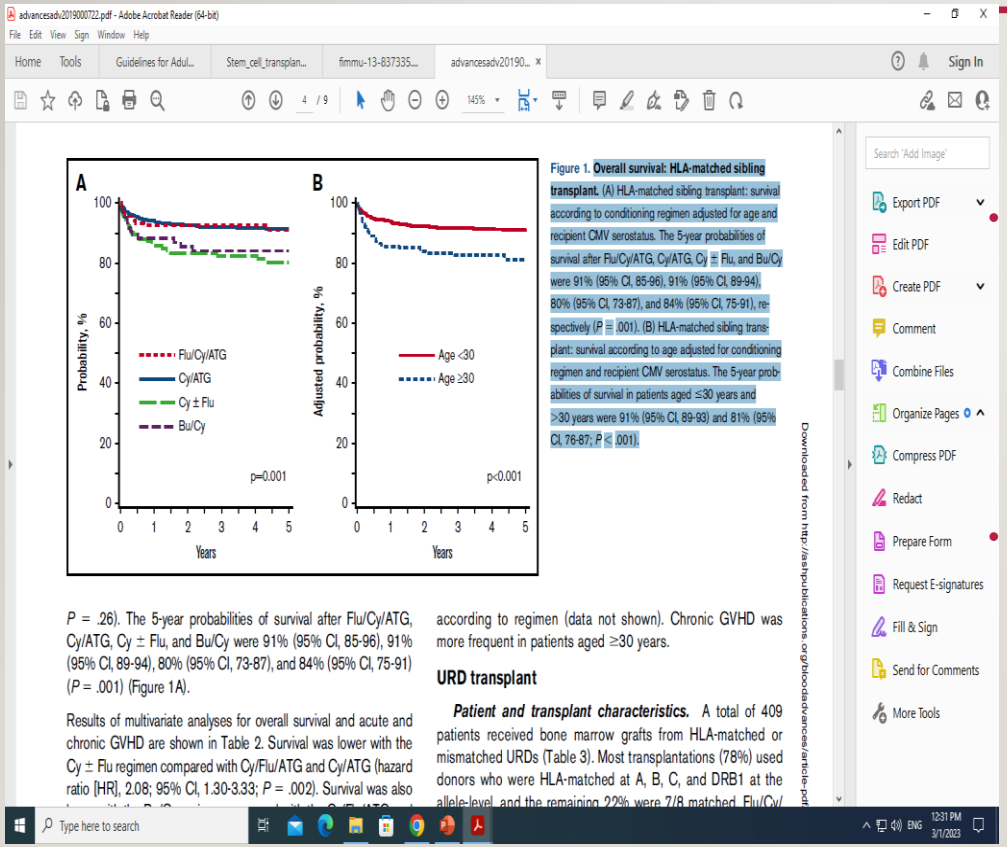


Figure 1. Overall survival: HLA-matched sibling transplant. (A) HLA-matched sibling transplant: survival according to conditioning regimen adjusted for age and recipient CMV serostatus. The 5-year probabilities of survival after Flu/Cy/ATG, Cy/ATG, Cy ± Flu, and Bu/Cy were 91% (95% CI, 85-96), 91% (95% CI, 89-94), 80% (95% CI, 73-87), and 84% (95% CI, 75-91), respectively (P = .001). (B) HLA-matched sibling transplant: survival according to age adjusted for conditioning regimen and recipient CMV serostatus. The 5-year probabilities of survival in patients aged ≤30 years and >30 years were 91% (95% CI, 89-93) and 81% (95% CI, 76-87; P < .001).

P = .26). The 5-year probabilities of survival after Flu/Cy/ATG, Cy/ATG, Cy ± Flu, and Bu/Cy were 91% (95% CI, 85-96), 91% (95% CI, 89-94), 80% (95% CI, 73-87), and 84% (95% CI, 75-91) (P = .001) (Figure 1A).

Results of multivariate analyses for overall survival and acute and chronic GVHD are shown in Table 2. Survival was lower with the Cy ± Flu regimen compared with Cy/Flu/ATG and Cy/ATG (hazard ratio [HR], 2.08; 95% CI, 1.30-3.33; P = .002). Survival was also

according to regimen (data not shown). Chronic GVHD was more frequent in patients aged ≥30 years.

URD transplant

Patient and transplant characteristics. A total of 409 patients received bone marrow grafts from HLA-matched or mismatched URDs (Table 3). Most transplantations (78%) used donors who were HLA-matched at A, B, C, and DRB1 at the allele-level, and the remaining 22% were 7/8 matched. Flu/Cy/

(A) HLA-matched sibling transplant: survival according to conditioning regimen adjusted for age and recipient CMV serostatus. The 5-year probabilities of survival after Flu/Cy/ATG, Cy/ATG, Cy 6 Flu, and Bu/Cy were 91% (95% CI, 85-96), 91% (95% CI, 89-94), 80% (95% CI, 73-87), and 84% (95% CI, 75-91), respectively (P 5 .001).

(B) HLA-matched sibling transplant: survival according to age adjusted for conditioning regimen and recipient CMV serostatus. The 5-year probabilities of survival in patients aged #30 years and .30 years were 91% (95% CI, 89-93) and 81% (95% CI, 76-87; P , .001).

UNRELATED DONOR TRANSPLANT

- Flu/Cy/ ATG/TBI 200 cGy
- Cy/ATG/TBI 200 cGy

were the predominant regimens

Low-dose total body irradiation is often added to Cy and ATG for URD transplantation.

OVERALL SURVIVAL: URD TRANSPLANT

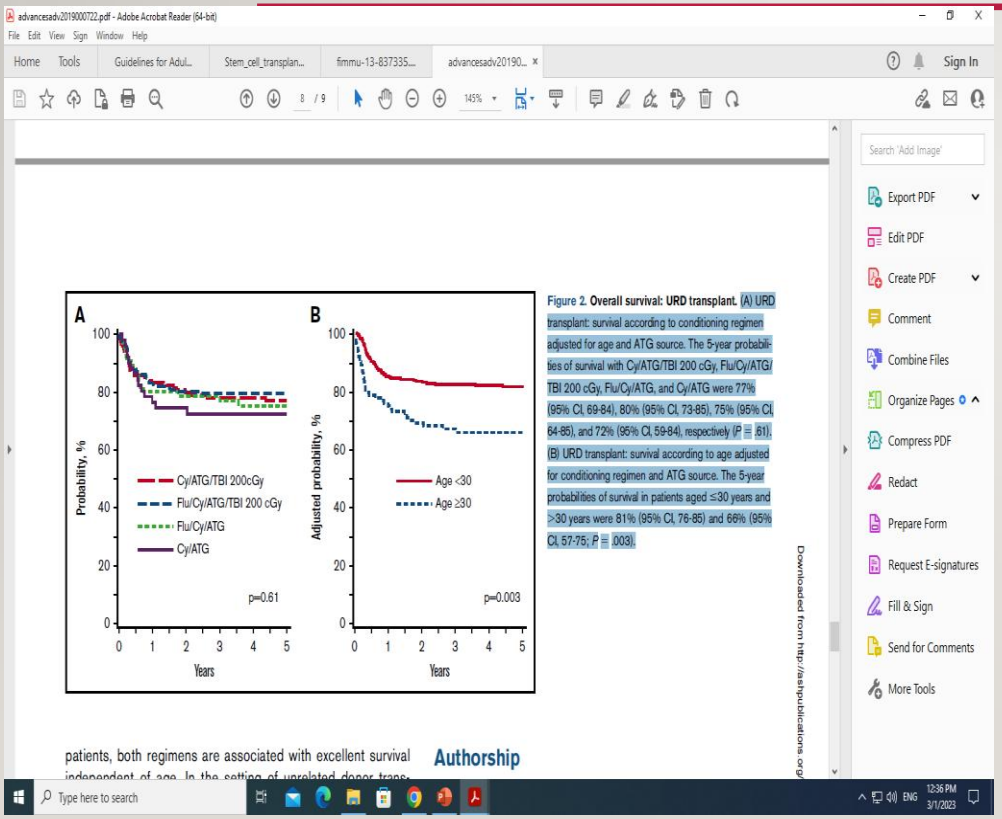


Figure 2. Overall survival: URD transplant. (A) URD transplant: survival according to conditioning regimen adjusted for age and ATG source. The 5-year probabilities of survival with Cy/ATG/TBI 200 cGy, Flu/Cy/ATG/TBI 200 cGy, Flu/Cy/ATG, and Cy/ATG were 77% (95% CI, 69-84), 80% (95% CI, 73-85), 75% (95% CI, 64-85), and 72% (95% CI, 59-84), respectively ($P = .61$). (B) URD transplant: survival according to age adjusted for conditioning regimen and ATG source. The 5-year probabilities of survival in patients aged ≤30 years and >30 years were 81% (95% CI, 76-85) and 66% (95% CI, 57-75; $P = .003$).

patients, both regimens are associated with excellent survival

Authorship

- (A) URD transplant: survival according to conditioning regimen adjusted for age and ATG source. The 5-year probabilities of survival with Cy/ATG/TBI 200 cGy, Flu/Cy/ATG/ TBI 200 cGy, Flu/Cy/ATG, and Cy/ATG were 77% (95% CI, 69-84), 80% (95% CI, 73-85), 75% (95% CI, 64-85), and 72% (95% CI, 59-84), respectively (P 5 .61).
- (B) URD transplant: survival according to age adjusted for conditioning regimen and ATG source. The 5-year probabilities of survival in patients aged #30 years and .30 years were 81% (95% CI, 76-85) and 66% (95%CI, 57-75; P 5 .003).

ALEMTUZUMAB CONDITIONING REGIMENS

- Alemtuzumab (CAMPATH) monoclonal Ab against CD52
- CD52, a GPI-linked membrane protein expressed on almost all WBC but not on CD34 HSC
- Potent lympholytic agent
- Detected in the plasma for several weeks after administration resulting in depletion of recipient auto reactive lymphocytes
  - Prevents GVHD by depletion of donor allo-reactive T-cells

Gandhi S,et al. Int J Hematol. 2013 May;97(5):573-80

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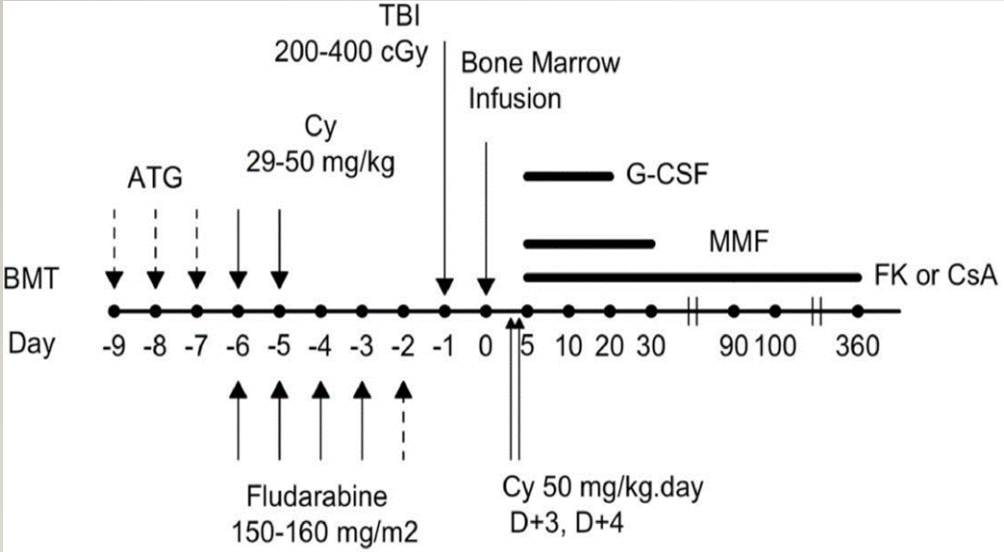
The Official Journal of ASTCT
ASTCT American Society for Transplantation and Cellular Therapy

BRIEF ARTICLES | VOLUME 26, ISSUE 9, E222-E226, SEPTEMBER 2020

A Case Series of Post-Transplantation Cyclophosphamide in Unrelated Donor Hematopoietic Cell Transplantation for Aplastic Anemia

Leonardo Javier Arcuri • Samir Kanaan Nabhan • Gisele Loth • ... Samantha Nichele • Renato de Castro Araujo • Carmem Bonfim • Show all authors

Open Archive • Published: June 03, 2020 • DOI: https://doi.org/10.1016/j.bbmt.2020.05.023 • Check for updates



Post-transplantation cyclophosphamide is feasible for patients with severe aplastic anemia undergoing unrelated donor hematopoietic stem cell transplantation

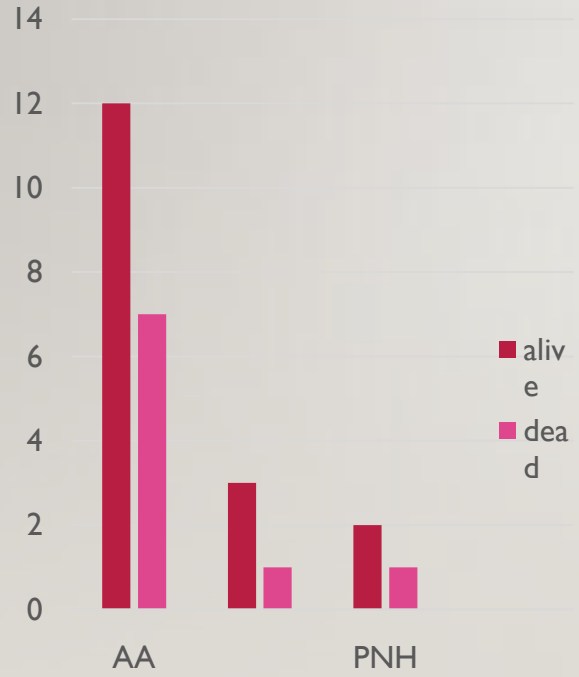
The toxicity of PTCy was low in patients with SAA undergoing URD HSCT.

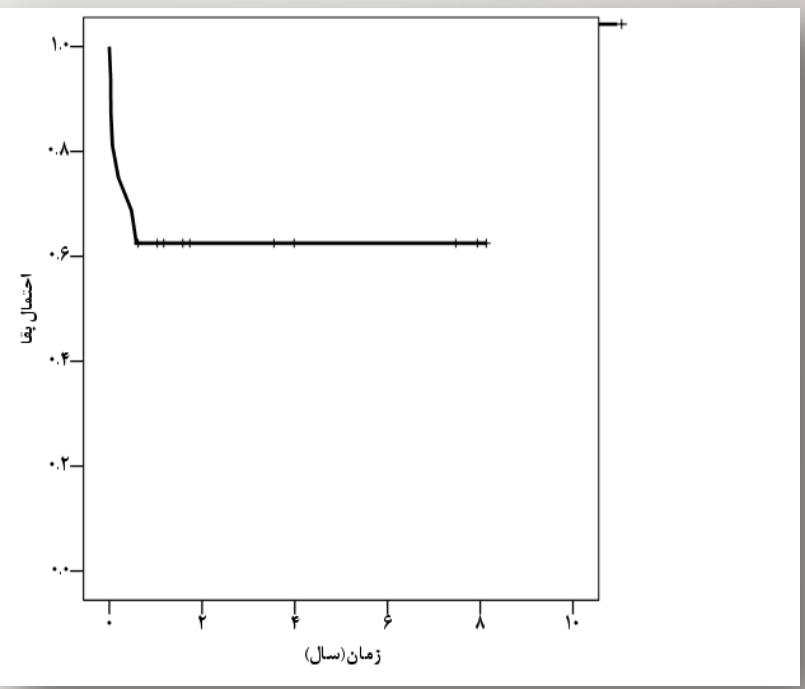
The engraftment rate of URD HSCT for SAA is promising.

High total nucleated cell number was associated with faster engraftment.

SURVIVAL STATUS OF OUR PATIENTS AFTER ALLO-HSCT

بقای ۶ ماهه و ۱ ساله





متغیر های معنی دار در سورویوال بیماران اپلاستیک آنمی

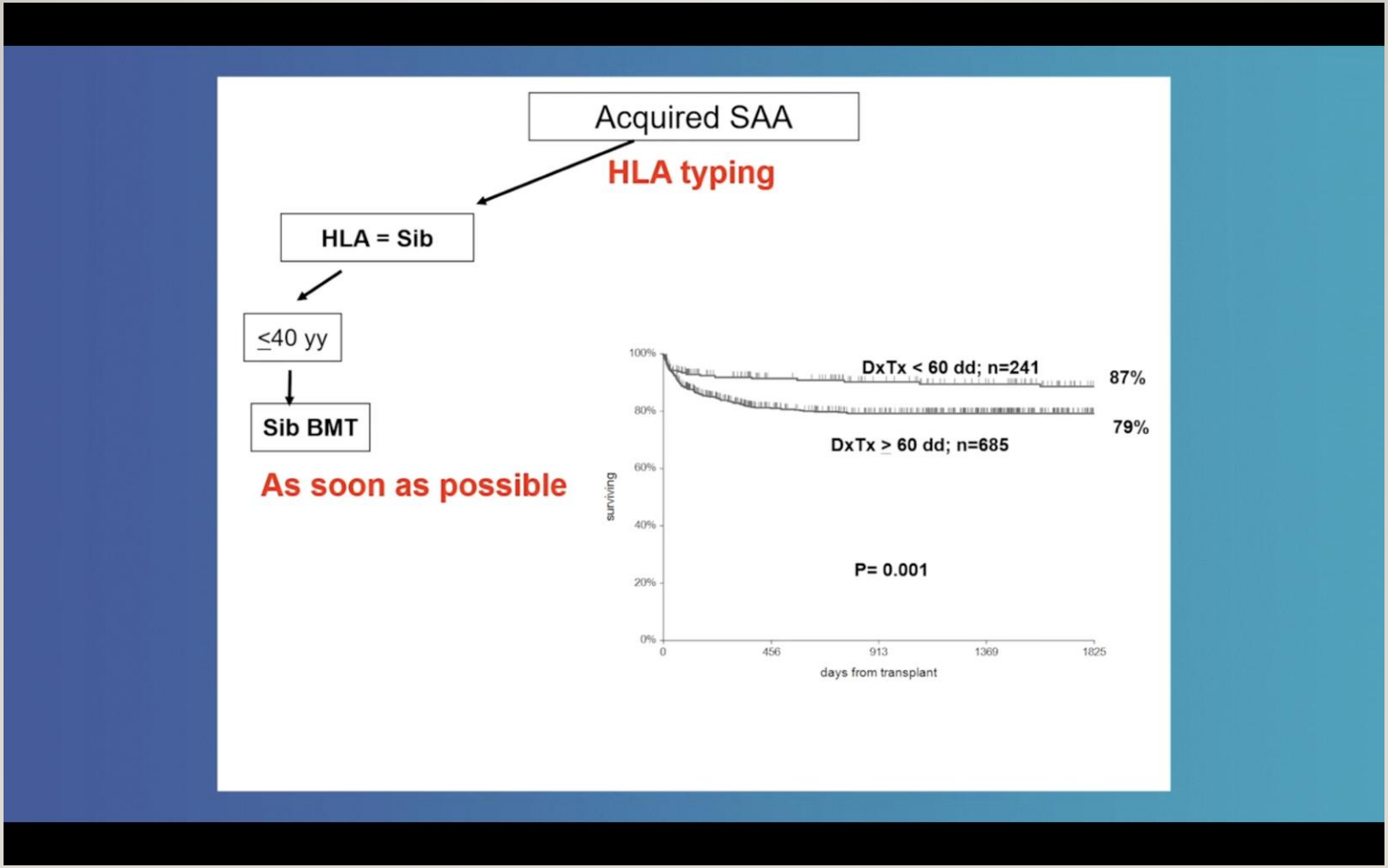
متغیر	مقدار	معنی دار
بروز سندرمSIIRS	2	S
فاصله زمانی تشخیص تا پیوند(سال)	1,82	S
زمان اینگرفتمنت wbc(روز)	14	s
عفونت سیستمیک قبل پیوند	+	s

متغیر های معنی دار در سورویوال بیماران اپلاستیک آنمی

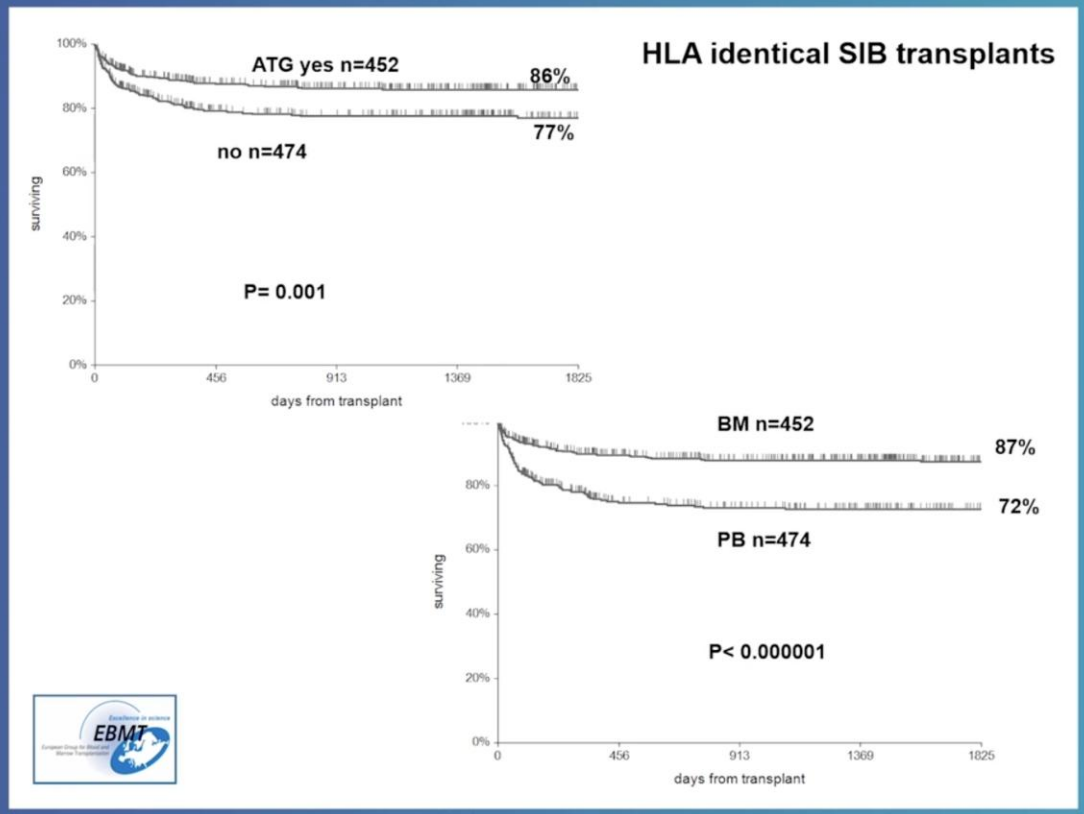
متغیر	مقدار	معنی دار
سنS	۳۱	NS
دوز سیکلوفسفامایِد		NS
خونریزی	+	
ترومبوز	+	

TAKE HOME MESSAGES OF THIS PANEL

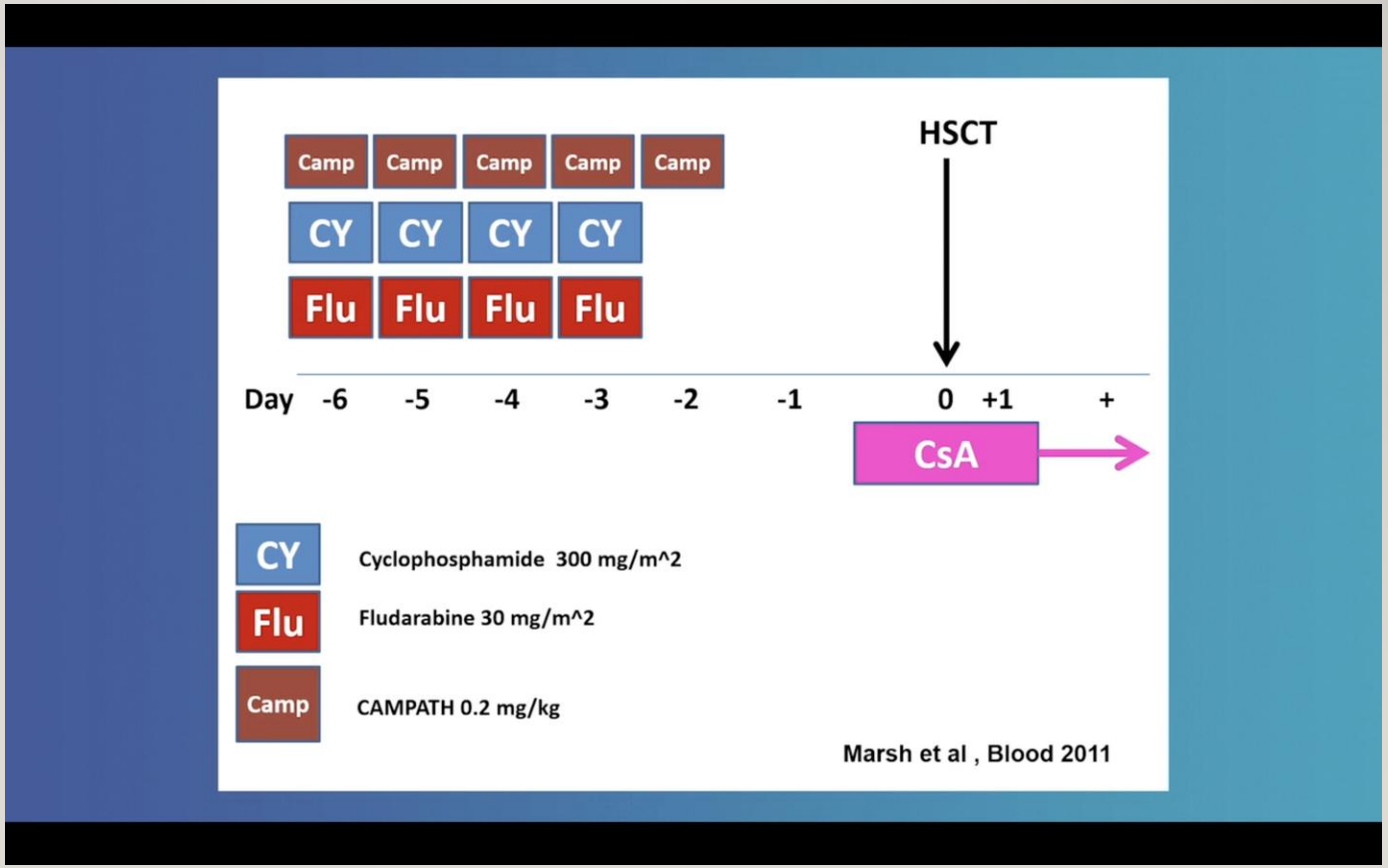
AS SOON AS POSSIBLE



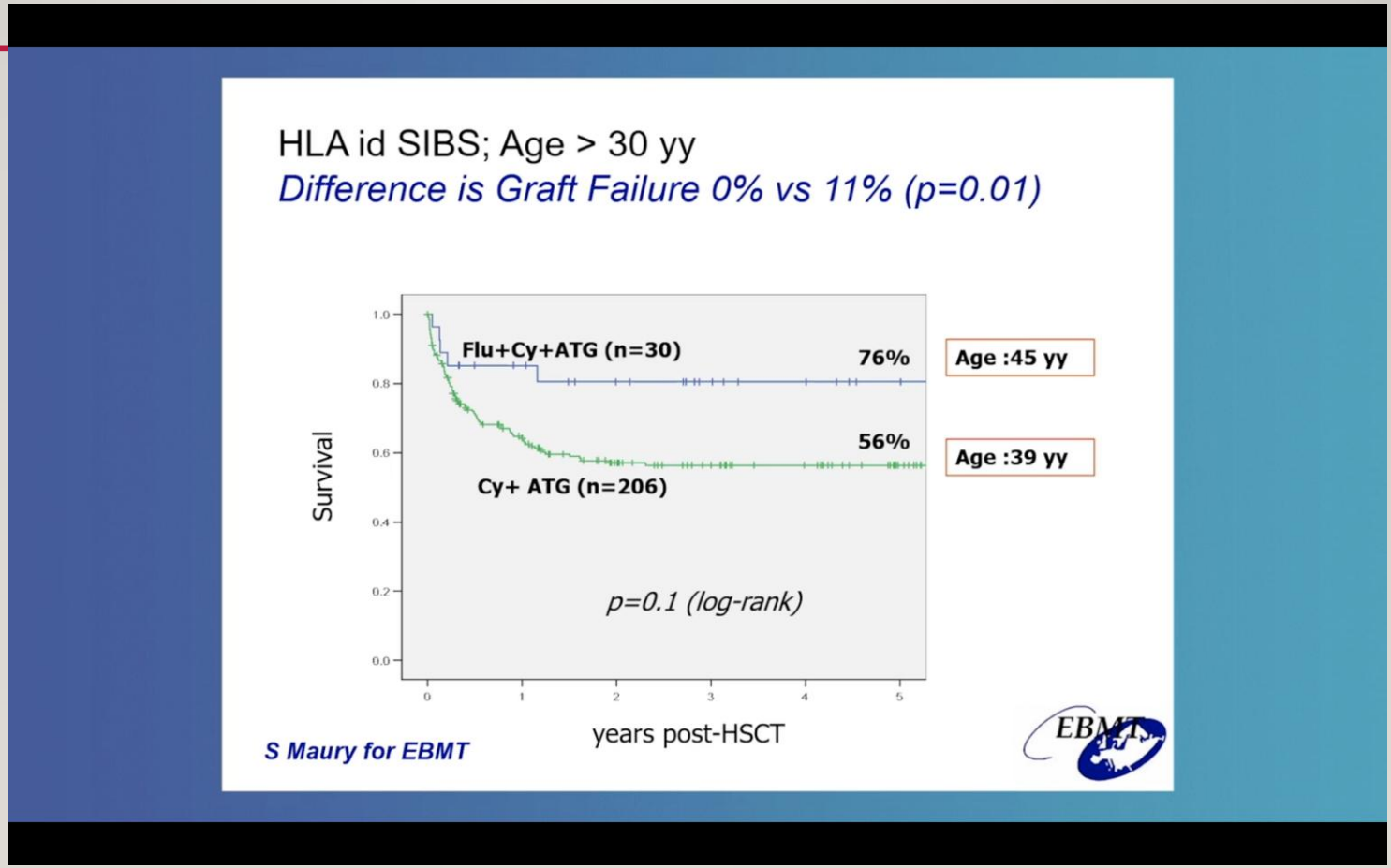
BONE MARROW SOURCE OF GRAFT & SEROTHERAPY IS RECOMMENDED



LESS C GVHD WITH ALEMTUZOMAB



BETTER OUTCOME WITH REDUSED DOSE OF CPM ESPECIALLY IN >30 YEARS



MUD ALLOTRANSPLANT IS BECOMING UPFRONT FOR YOUNG PATIENT WITH SAA

- strong considerationshould be given to first-line marrow transplantation for patients whoare younger than 30 years old with aplastic anemia if a 10/10 HLAmatchedunrelated donor is rapidly identified

- Your time is:4-6 weeks
- Unrelated donors with 9/10 high-resolution HLA matching may also be considered, but there are insufficient data to propose such donors for first-line treatment. Clinical

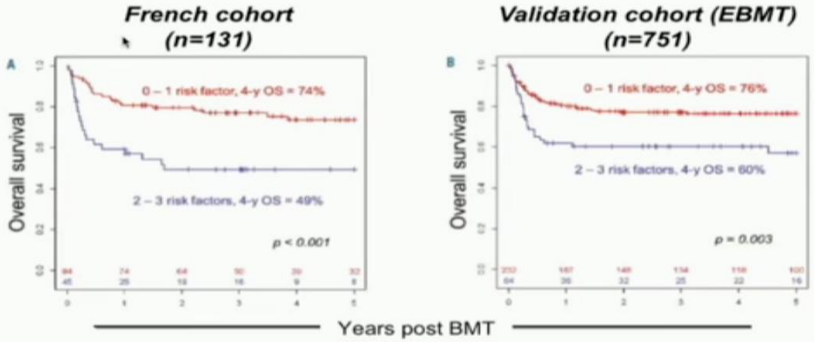
MUD ALLOTRANSPLANT IS BECOMING UPFRONT FOR YOUNG PATIENT WITH SAA

MUD for refractory patients: no change

Decision making process

3 Risk factors

- Age (30)
- MUD versus mismatch UD
- BMT in the first year post AA versus after



Bacigalupo, Blood 2016; Devillier R, *et al.* Haematologica. 2016;101:884-90.

CONSIDER RITUXIMAB IN UD TRANSPLANT CONDITIONING

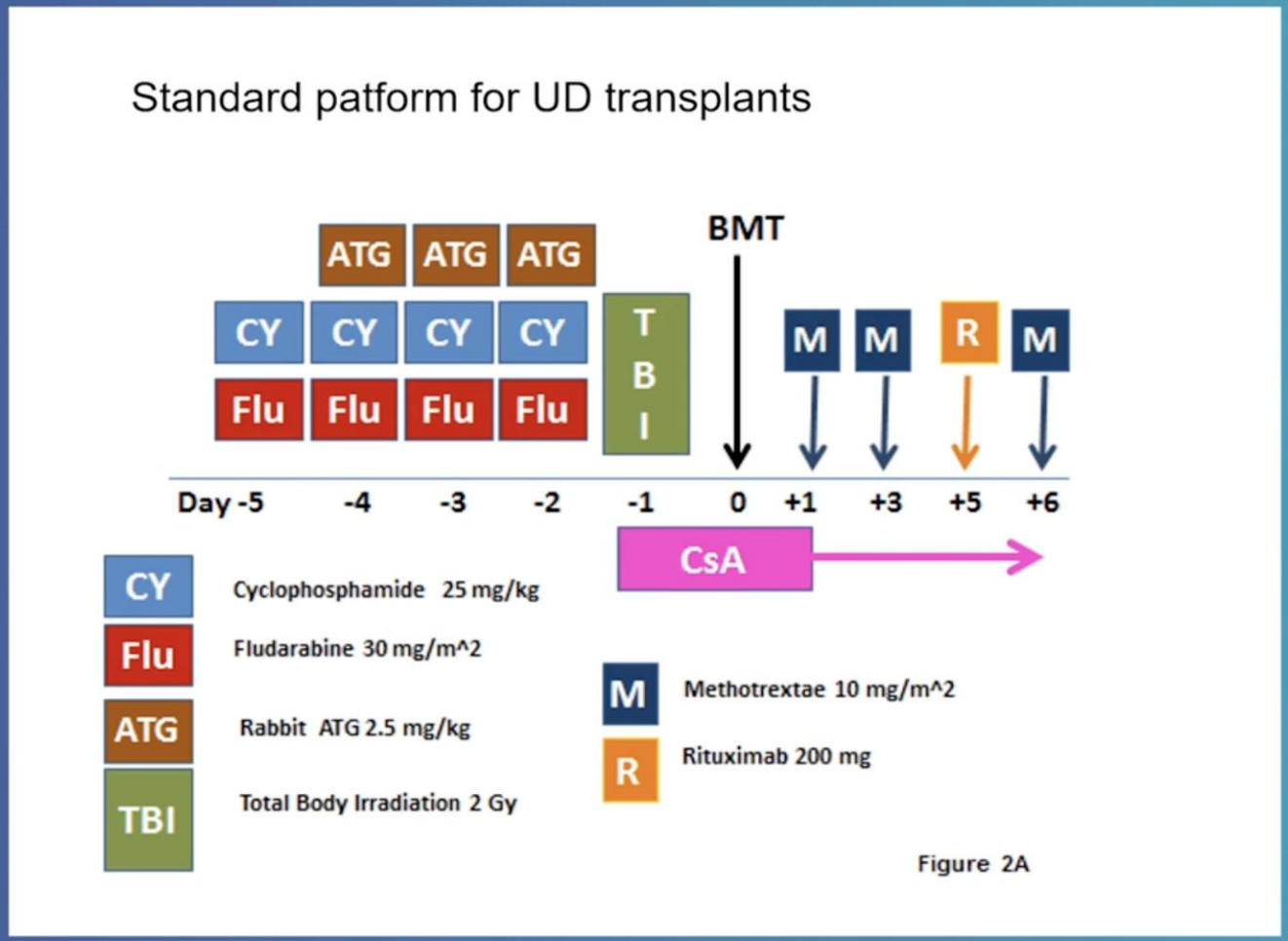


Figure 2A

SAA TRANSPLANTATION IN ERA OF ELTHROMBOPAG

- No difference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