“Allogeneic Hematopoietic Stem cell Transplantation for Aplastic Anemia”

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❖ INTRODUCTION:

✓Aplastic Anemia definition:

- The term refers to a clinical syndrome of bone marrow hypo-cellularity accompanied by progressive loss of hematopoietic progenitor stem cells (HPSC), resulting in peripheral pancytopenia.

- Patients may present along a spectrum, ranging from being asymptomatic with incidental findings on peripheral blood testing to having life-threatening neutropenic infections or bleeding.

- Aplastic anemia results from either **inherited** or **acquired** causes, and the pathophysiology and treatment approach vary significantly between these 2 causes.

❖ INTRODUCTION:

✓Acquired AA:

- The cause of most cases of acquired aplastic anemia is that **a dysregulated immune system destroys HPSCs** which implicates **cytotoxic T-lymphocyte–mediated destruction of CD34+ hematopoietic stem cells.**

- Etiologies implicated in the development of acquired AA include :

  - ✓ **Pregnancy**
  - ✓ **Infection**
  - ✓ **medications**
  - ✓ **exposure to certain chemicals, such as benzene.**

- Cytogenetic abnormalities in up to 10% of true SAA
- A close relation between PN and concomitant SAA in 40% of cases
- Prior to treatment.
  - Stable the patient
  - Control infection and bleeding
  - Asses the severity
  - Family HLA typing and donor search

Rovo et al,2016;Barone et al;2015

❖ INTRODUCTION:

✓Acquired AA:

- The basis **treatment** of acquired aplastic anemia is **immunosuppressive therapy**, **predominantly anti-thymocyte globulin (ATG) combined with cyclosporine A**.

- More recent work has focused on **cytokine interactions**, particularly the **suppressive role of interferon (IFN)-γ** on hematopoietic stem cells independent of T-lymphocyte–mediated destruction.

- **Eltrombopag**, a thrombopoietin receptor antagonist,has shown promise in the treatment of refractory aplastic anemia, with studies indicating that its effectiveness is independent of IFN-γ levels.

❖ INTRODUCTION:

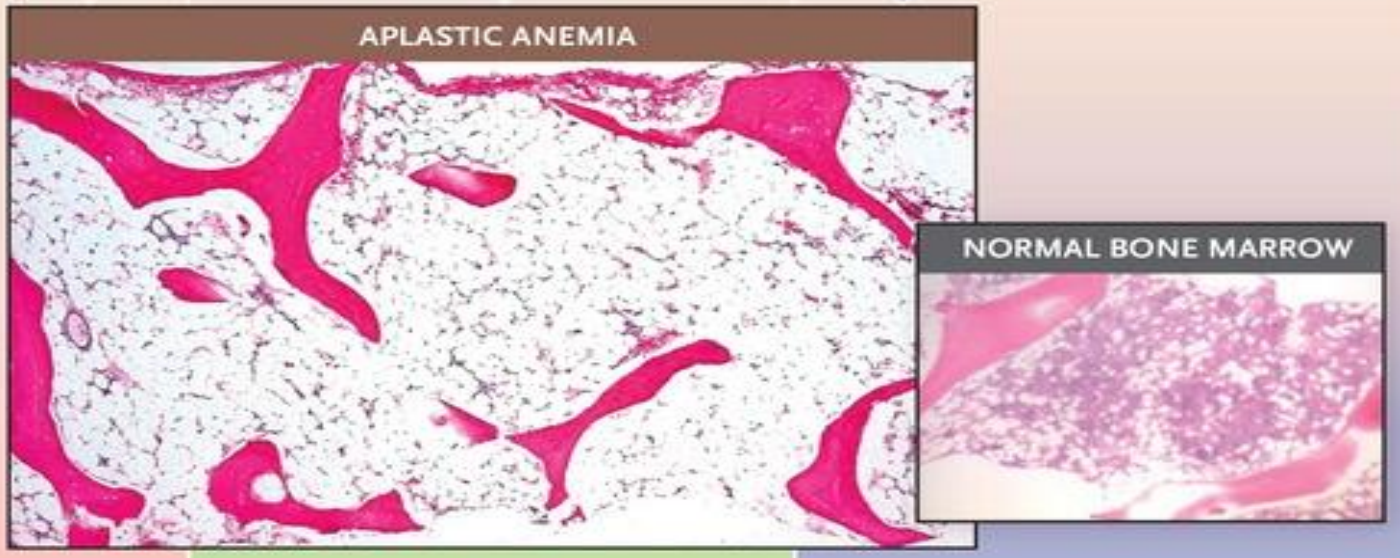
✓Inherited AA:

- The **inherited marrow failure syndromes (IMFSs)** are a group of disorders characterized by cellular maintenance and repair defects, leading to cytopenias, increased cancer risk, structural defects, and risk of end organ damage, such as liver cirrhosis and pulmonary fibrosis. The pathophysiology of inherited aplastic anemia relates to the defective HPSCs and an accelerated decline of the hematopoietic stem cell compartment.

- The most common diseases include:

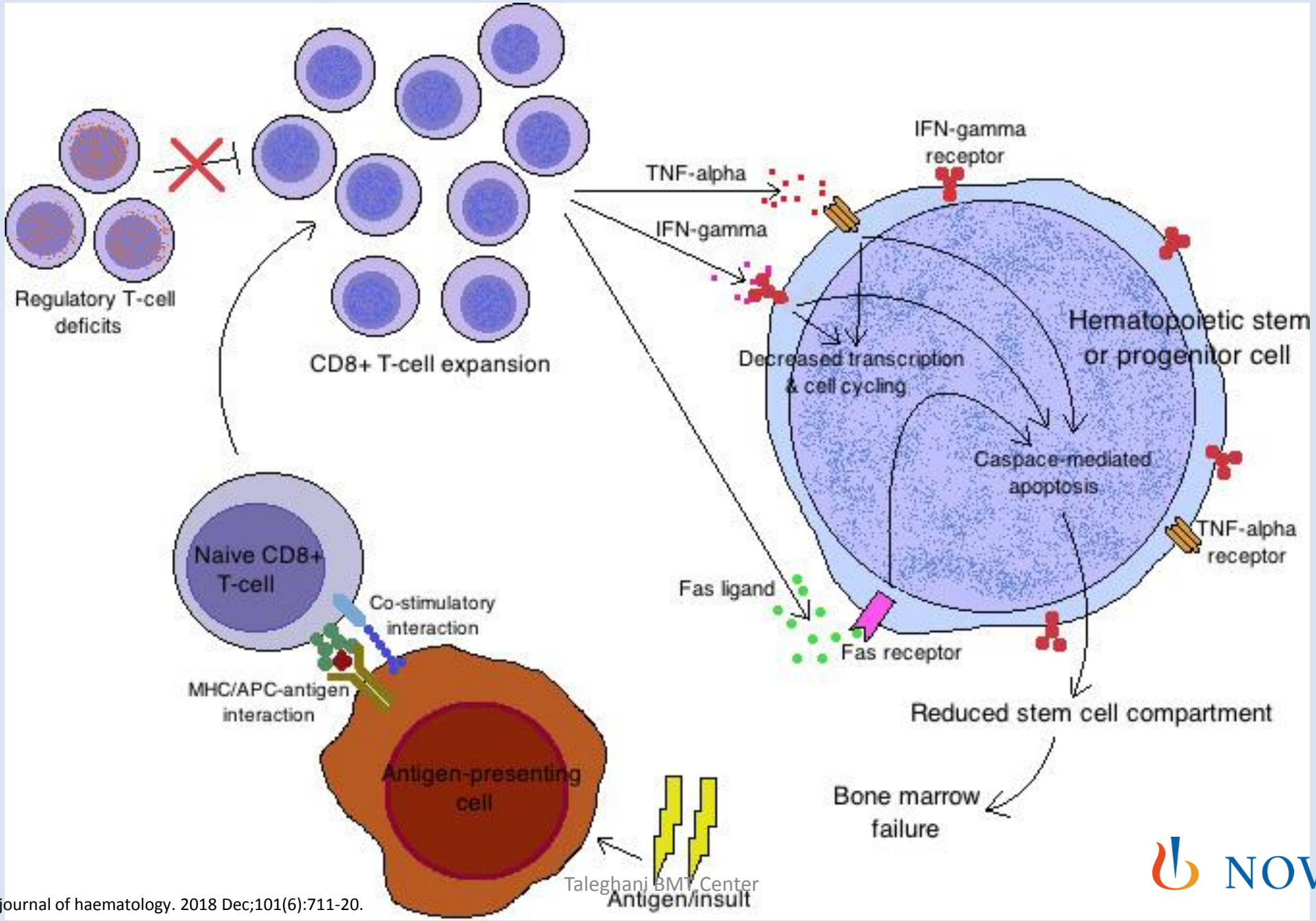
  - ✓ **Fanconi anemia**
  - ✓ **dyskeratosis congenita/telomere biology disorders**
  - ✓ **Diamond-Blackfan anemia**
  - ✓ **Shwachman-Diamond syndrome**

- The recognition of an **underlying genetic disorder** or **telomere biology disorder** leading to constitutional aplastic anemia is significant, as these conditions are associated not only with marrow failure, but also with endocrinopathies, organ fibrosis, hematopoietic and solid organ malignancies.

CAUSES	Cytotoxic drugs Radiation Benzene	Idiopathic Seronegative hepatitis Eosinophilic fasciitis Thymoma	Telomere disease Fanconi anemia Other germline gene mutations
PATHOPHYSIOLOGY	Chemical and physical damage	Immune destruction	Constitutional genetic defects
PATHOLOGY			
TREATMENTS	Supportive care Hematopoietic growth factors Hematopoietic stem-cell transplantation	Immunosuppressive therapy Hematopoietic stem-cell transplantation Eltrombopag	Sex hormones Hematopoietic stem-cell transplantation

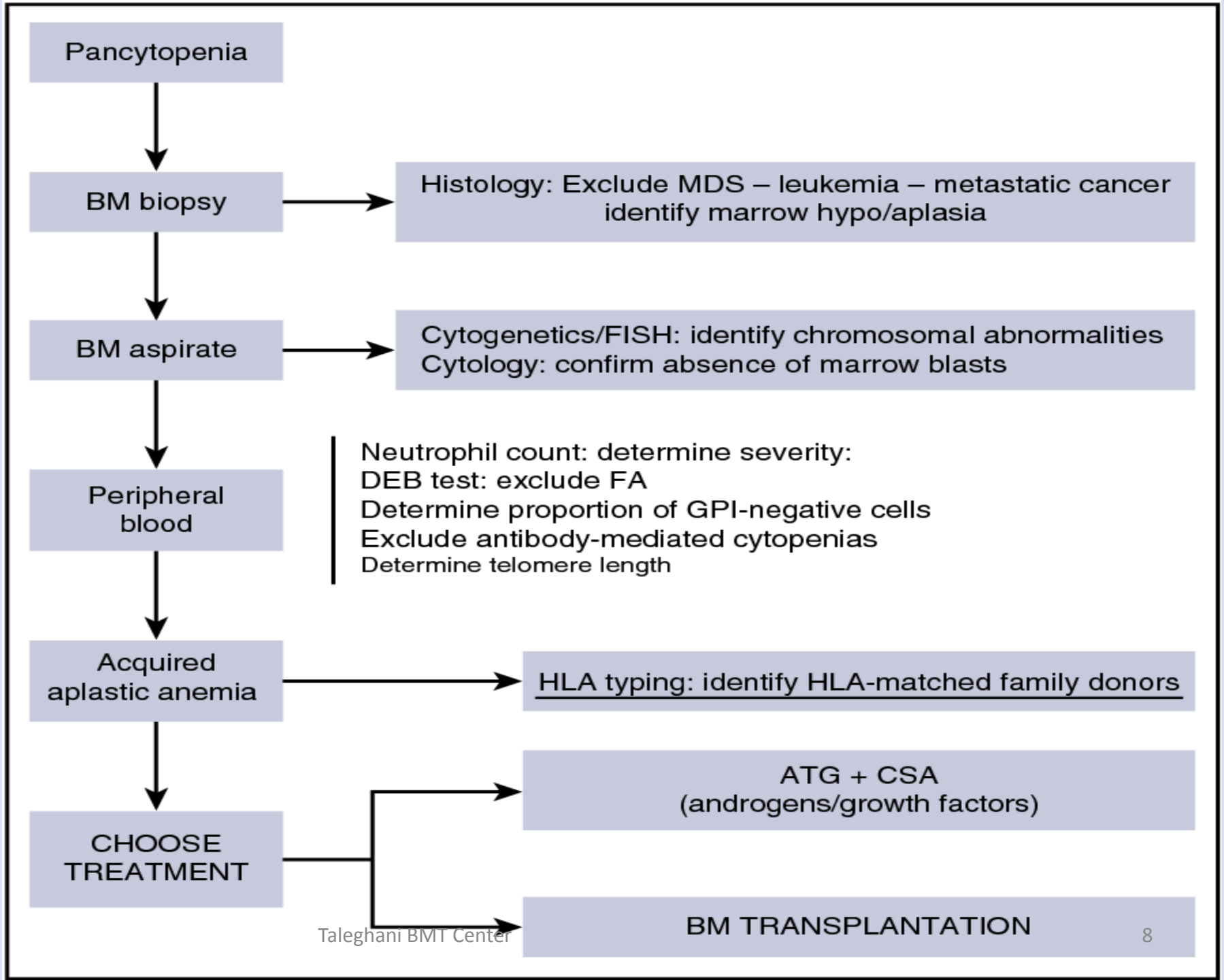
Young NS, et al. Current opinion in hematology. 2008 May;15(3):162.

Immunopathogenic mechanism of hematopoietic stem or progenitor cell apoptosis in the AA bone marrow



Shallis RM, et al. European journal of haematology. 2018 Dec;101(6):711-20.

❖ Diagnosis:



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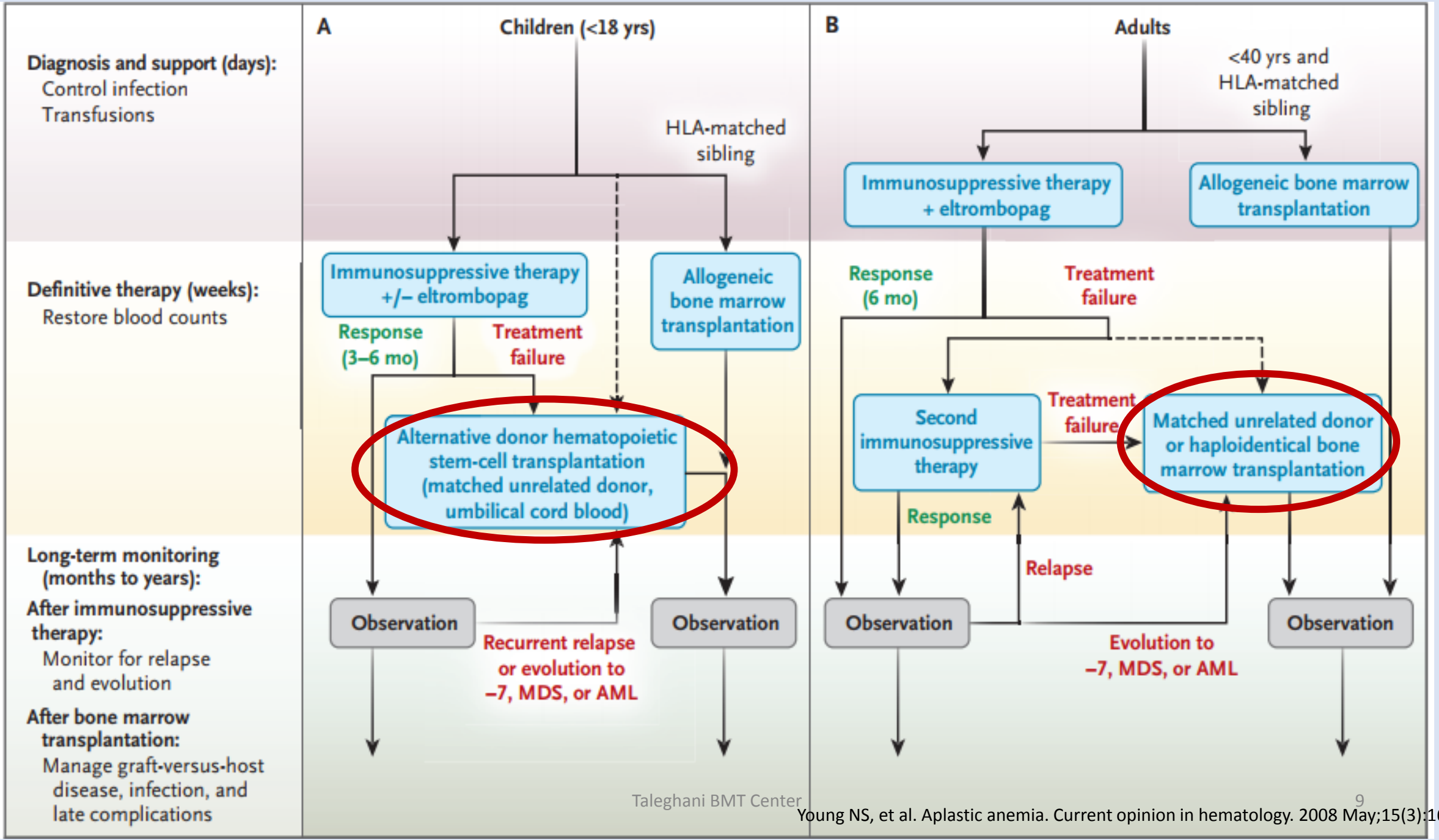

Young NS, et al. Aplastic anemia. Current opinion in hematology. 2008 May;15(3):162.

Historical points: should be lessoned

- 1970: the first successful marrow transplant from an HLA-identical sibling donor
- the hematopoietic recovery seen in some patients was derived from the host and not from the graft.
- a large percentage (36% in the Seattle experience) rejected their grafts, and some remaining patients succumbed to GVHD.
- Rejection:sensitization of patients to minornon-HLA antigen disparities with their respective donors through prior blood transfusions
- normal growth and development and Fertility
- The problems seen after IST with ATG :clonal disorders, including PNH mMDS, and AML were seen in surviving patients. Tichelli et alreported a 26% incidence of MDS/AML, and a larger European study reported a 20% incidence of cancer

Blood. 1997;90(3):1009-1013.

❖ ALLO-HSCT for AA:

✓ Replacement of failed bone marrow is curative of the AA. However, transplantation is limited by its complications graft rejection and graft-versus-host disease (GVHD) and the need for suitable donors.

✓ Bone marrow grafts :superior OS compared to peripheral blood stem cell (PBSC) grafts in both pediatric and adult AA patients, due to lower rates of GVHD.

✓ More recent efforts to improve outcomes with PBSC showed encouraging results with partial T cell depletion ; larger randomized prospective studies are needed to confirm the efficacy and safety of this approach.

✓ Increased age is correlated with greater transplantation related complications and worse survival. the decision to pursue MSD HSCT in this age group may need to be individualized by taking into account comorbidities, transplantation center experience, history of complications associated with pancytopenia, access to transplantation, and patient preference.

✓ The current standard of care for patients older than 40 years is frontline IST, while BMT is the treatment of choice for children and young adults with SAA who have a MSD.

Hematopoietic Stem-Cell Transplantation for Severe Aplastic Anemia

Study	Transplant Source and Recipient Status	No. of Patients	Age	Conditioning and Prophylaxis	Overall Survival	Acute and Chronic GVHD†	Graft Failure
			yr		%	%	%
IBMTR prospective RCT, 1994–2001[64]‡	MFD — 50% of recipients had no previous treatment	70	Median, 23	Conditioning: Cy, ATG Prophylaxis: CsA, MTX	80 at 5 yr	Acute: 11 Chronic: 32	16
King's College retrospective study, 1999–2009[65]§	MFD — most recipients had no previous treatment; MUD — most recipients had refractory disease	100	Median, 18	Conditioning: Alemtuzumab+Cy Prophylaxis: CsA for MSD, FLU+Cy for MUD, FLU+Cy+TBI for mismatched MUD	90 at 5 yr	Acute: 29 Chronic: 3	9
EGBMT registry, children, 2000–2009[61]	MFD — no previous treatment	396	Range, 0–12	Conditioning: mainly Cy, some Cy+FLU Prophylaxis: CsA±ATG±MTX	87 at 3 yr	Acute: 8 Chronic: 6	2
EGBMT registry, adolescents, 2000–2009[63]	MFD — no previous treatment	394	Median, 15	Conditioning: mainly Cy, some Cy+FLU±ATG Prophylaxis: mostly MTX+CsA, some CsA+MMF	86 at 3 yr	Acute: 12 Chronic: 8	8
EGBMT registry, 2005–2009[66]	MFD — previous recipient treatments not described	940	50% >20	—	83 at 5 yr	Acute: 13 Chronic: 6	9
EGBMT registry, 2005–2009[66]	MUD — previous recipient treatments not described	508	53% >20	—	76 at 5 yr	Acute: 26 Chronic: 11	9
French national prospective study, 2011–2015[67]	UCB — refractory SAA	26	Median, 16	Conditioning: FLU+Cy+ATG+TBI Prophylaxis: CsA	85 at 2 yr	Acute: 46 Chronic: 36	12
JSHCT registry, 2001–2012[68]	UCB — refractory adult SAA	69	Median, 49	Conditioning: mainly FLU+melphalan+low-dose TBI Prophylaxis: MTX or MMF± glucocorticoids±CIN	69 at 3 yr	Acute: 32 Chronic: 21	29
Eurocord and EBMT retrospective registry, 1988–2014[69]	Sibling UCB with or without bone marrow — mainly for refractory disease	20	Median, 5.6	Conditioning: variable but mainly Cy+FLU Prophylaxis: variable but mainly CsA+glucocorticoids	81 at 7 yr	Acute: 6 Chronic: 8	10

Shallis RM, et al. European journal of haematology. 2018 Dec;101(6):711-20

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❖ Matched Sibling Donor Transplantation:

- ✓ MSD HSCT is the treatment of choice for patients diagnosed with **SAA <40 years old.**
- ✓ This standard of care has been adopted internationally and is recommended by different national treatment algorithms .
- ✓ IST leads to worse overall outcomes compared to MSD HSCT, given higher risk of clonal evolution and relapse.
- ✓ Older age is a risk factor for worse outcome with MSD HSCT for SAA, and even among children in one report, survival appears better for patients aged 0–11 years versus 12–18 years; with three year overall survival (OS) of 91% and 86% respectively, and event-free survival (EFS) of 87% and 83% respectively.
- ✓ The historically high rate of graft rejection in SAA is now less problematic, probably because of patients moving faster to this treatment and thus avoiding heavy transfusion burdens, less immunogenic blood products, and more efficacious conditioning regimens.

❖ MSD HSCT conditioning regimen:

- **The original "Seattle protocol" for SAA included :**

- **cyclophosphamide** 200 mg/kg and **ATG** → This approach yielded consistently good results with survival up to 95% in younger patients.

- To reduce the dose of cyclophosphamide and its associated side effects, **fludarabine** was incorporated by some groups.

- Using **fludarabine** 120 mg/m2, **cyclophosphamide** 1200 mg/m2 and **ATG**, patients over age 30 had an OS of 80% versus 60% (p=0.04) for those conditioned with conventional cyclophosphamide dosing, with no primary engraftment failures and acceptable rates of acute and extensive chronic GVHD (10% and 13% respectively).

- To reduce cGVHD grafts were limited to #2.5 3 108nucleated cells per kilogram

- With these excellent results using chemotherapy based regimens, especially in children, there is no current role for the use of TBI in MSD HSCT for pediatric SAA.

- AHSCT for AA in Seattle in children: %100 OS.

❖ Serotherapy in preparative regimens improves outcomes:

- ✓ Very early data reported improved survival with the **addition of ATG to cyclophosphamide** in the preparative regimen.

- ✓ A retrospective study from the European Society for Blood and Marrow Transplantation (EBMT) with 1886 MSD HSCT between 1999 and 2009 showed that the omission of ATG resulted in significantly lower survival.

- ✓ **Alemtuzumab** was tested in a retrospective study with 50 pediatric and adult patients showing a low incidence of chronic GVHD (4%), hinting at a significant role of alemtuzumab in GVHD prevention.

- ✓ A second retrospective study compared outcomes in 155 patients receiving ATG or alemtuzumab during conditioning with no difference between groups in engraftment, time to count recovery, full chimerism achievement and acute GVHD, but less chronic GVHD with alemtuzumab (11 vs 26%, p=0.031)

Bacigalupo et al,2012

Peffault et al.2016

❖ Matched Unrelated Donor Transplantation:

- In the last 20 years, results of MUD HSCT have dramatically improved with better HLA matching, suppor care and reduced intensity regimens.
- The EBMT : fludarabine based conditioning in this setting without TBI
- American and Japanese groups: de-escalated the TBI dose to 200–300 cGy, and still achieved survival in the range of 60–65%.
- More recent results report even better outcomes.

- In 2015, Dufour and colleagues described:

- 2 years OS for MUD recipients of 96%.
- front-line MUD recipients had better EFS compared to IST recipients (92% vs 40%, p=0.0001).
- 29 patients undergoing MUD HSCT received a fludarabine, alemtuzumab, and cyclophosphamide conditioning regimen.
- GVHD was low with 10% acute grade II–IV GVHD and 19% chronic GVHD.
- One patient experienced graft failure after 1-antigen mismatched transplant
- And there was one case of transplant related mortality reported. Cumulative incidence of rejection at 2 years was 4%.

Dufour et al.2014,2015

Samarasinghe and Webb ,2012

MUD BMT in AA

Table 1. **Select recent reports of HLA-matched sibling and unrelated donor hematopoietic cell transplantation for severe aplastic anemia**

Reference (year)	Year of transplant	Patients, n	Age range (median), y	Conditioning program	Hematopoietic source (n)	Prevention of GVHD	Graft rejection/ failure, %	GVHD, %		Survival, %	Follow-up, range (median), y
								Acute	Chronic		
HLA-identical sibling donor transplantation											
30 (2012)	1971-1984 1981-1988 1989-2010	96 19 31	1.8-19 (12.8)	CY CY CY+ATG	BM	MTX CSP+MTX CSP+MTX	22 32 7	21 11 39	21 21 10	66 95 100	11-37.2 (31.1) 15.2-27.1 (23) 0.3-21.6 (6.1)
49 (2012)	1999-2009	1886	1-68 (18)	CY+ATG (41%) and various	BM (1163)	CSP+MTX (41%) or other	9	11	11	Age ≤20 y: 90 Age >20 y: 74	(2.1)
			1-69 (24)		PBSCs (723)		10	17	22	Age ≤20 y: 76 Age >20 y: 64	(2.0)
52 (2009)	1998-2007	30	31-66 (46)	FLU+CY+ATG	BM (20) PBSCs (10)	CSP+MTX or other	3	10	13	77	1.1-6.8 (4.1)
82 (2016)	1999-2014	BMT: 1732 IST: 802	0-20 21-40 >40	BMT various IST various	Compare BMT vs IST	Various for BMT	N/A	N/A	N/A	Age 0-20 y: 86 (BMT); 84 (IST) Age 21-40 y: 76 (BMT); 66 (IST) Age >40 y: 56 (BMT); 58 (IST)	0.2-10
50 (2015)	2006-2009	940	Age >20 y: 50%	Various	BM (566) PBSCs (374)	Various	9	13	14	Low risk: 93 Int. risk: 76 High risk: 67	0.1-9.1 (3.1)
31 (2016)	2006-2015	21	3-52 (15)	CY+ATG	BM <2.5 × 10⁸ TNC/kg	CSP+MTX	0	47	16 (24)	100	1-8 (4.0)
Unrelated donor transplantation											
57 (2012)	2000-2010	44	3-19 (8)	FLU+CY+Alem various doses	BM (26) PBSCs (18)	CSP or CSP+MMF or MTX	0	38	12	95	1-6.3 (2.9)
50 (2015)	2006-2009	508	Age >20 y: 53%	Various	BM (264) PBSCs (244)	Various	9	25	26	Low risk: 83 Int. risk: 77 High risk: 64	0.1-9.1 (3.1)
58 (2016)	2006-2014	29 Upfront MUD HCT (no prior IST)	1.7-19.1 (8.4)	FLU+CY+Alem (+2-3-Gy TBI for 1 Ag-MM)	BM (21) PBSCs (8)	CSP or CSP/MMF	4	10	19	96 OS 92 2-y EFS	0.2-8.5 (1.7)
56 (2015)	2006-2013	79	0.5-66 (24)	ATG +2-Gy TBI+ CY-100 (n = 41) vs CY-60 (n = 38)	BM	CSP/MTX	CY-100: 15 CY-60: 12	27 24	32 23	81 at 1 y 97 at 1 y	1.0-4.2 (2.0) 0.3-2.2 (1.4)
53 (2014)	1999-2009	55 URD	1-67 (18)	FLU+CY+Alem	BM (36) PBSCs (19)	Tacrolimus/MMF	9	38	13	88 97 BM 70 PBSCs	0.5-10

Alem, alemtuzumab; BM, bone marrow; CY-60, 60 mg/kg CY; CY-100, 100 mg/kg CY; EFS, event-free survival; HCT, hematopoietic cell transplantation; Int., intermediate; MMF, mycophenolate mofetil; MUD, matched unrelated donor; N/A, not available; OS, overall survival; TBI, total body irradiation; TNC, total nucleated cell; URD, unrelated donor; 1 Ag-MM, 1 HLA-antigen mismatch.

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❖ MUD HSCT conditioning regimen:

- ✓ The EBMT SAA working party recommends: **fludarabine** 120 mg/m2, **cyclophosphamide** 120 mg/kg and **ATG** (or **alemtuzumab** based on some positive experiences with this substitution)

- ✓ **TBI 200 cGy** can be added for patients **above 14 years** of age in case of mismatched grafts and may be considered for younger children if previously sensitized (transfusion refractory), to reduce the risk of graft rejection.

- ✓ A BMT CTN study explored **cyclophosphamide dose reduction** in the context of **fludarabine** (120 mg/m2), **ATG** (9 mg/kg) and 200 **cGy TBI**.

- ✓ Both 100 and 50 mg/kg cyclophosphamide doses led to good outcomes, but superior early survival was noted in the 50 mg/kg cohort (97.4% at 1-year) with 11.7% graft failure, 23.7% grades II-IV acute GVHD and 22.5% chronic GVHD, suggesting this approach is also reasonable.

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 matchingmay also be considered, but there are insufficient data to proposesuch donors for first-line treatment. Clinical

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Haplotransplant in SAA

- The use of PT-CY has simplifiedthe clinical use of HLA-haploidentical grafts encouraging early results
- Johns Hopkins group challenge: HLA-haploidentical grafts should be used as second-line therapy
- Cord blood transplantation is probably inferior to HLAhaploidentical
- marrow grafts because of the low cell dose infused,
- the high risk for graft rejection, and delayed engraftment/immune
- recovery.65,66

❖Mismatched Donor, and Haploidentical Transplantation:

✓Haploidentical HSCT:

- Transplants from **mismatched family donor** had been reported in the past by different groups for refractory patients, generally with suboptimal outcomes.

- Recently both **T-cell depleted** and **T-cell replete** haploidentical strategies have been reported for multiply relapsed SAA patients lacking a matched donor.

- Im and colleagues describe 21 patients who underwent fludarabine, cyclophosphamide, 400 cGy TBI and ATG conditioning followed by either CD3/19 or CD3alfa beta/CD19 depleted grafts. OS was reported as 94% at 3 years, without cases of chronic GVHD.

- T-replete haploidentical approaches have been taken by Wang (17 children, full intensity conditioning and 4 agent GVHD prophylaxis: OS 71% at 1 year, 20% chronic GVHD).

✓ **Mismatched HSCT in SAA** is improving, but with published outcomes lagging behind MUD and MSD survival, until studies demonstrate improvements, this approach should be restricted to refractory or multiply relapsed patients.

❖Mismatched Donor, and Haploidentical Transplantation:

Studies of UD HSCT in SAA

Study	N	Design	Conditioning	Graft failure	Median age, y	Acute GVHD grade II-IV	Chronic GVHD	Survival
Kim et al[67]	40	Prospective	Cy/TBI	5%	27	30%	38%	75% at 3 y
Maury et al[47]	89	Retrospective	Various	14%	17	50%	28%	42% at 5 y
Viollier et al[51]	349	Retrospective	Various	11%	18	28%	22%	57% at 5 y
Kosaka et al[68]	31	Prospective	Cy/ATG/TBI Flu/Cy/ATG/TBI	16%	8	13%	13%	93% at 3 y
Perez-Albuerne et al[32]	195	Retrospective	Various	15%	10	43%	35%	51% at 5 y
Bacigalupo et al[29]	100	Retrospective	Flu/Cy/ATG Flu/Cy/ATG-TBI	17%	20	18%	27% (no TBI) 50% (TBI group)	75% at 5 y
Kang et al[69]	28	Prospective	Flu/Cy/ATG	0%	13	46%	35%	68% at 3 y
Yagasaki et al[30]	31	Retrospective	Various	3%	9	37%	27%	94% at 5 y
Lee et al[70]	50	Prospective	Cy/TBI	0%	28	46%	50%	88% at 5 y
Marsh et al[18]	29	Retrospective	Flu/Cy/Alem	15%	35*	14%*	4%*	83% at 2 y

Outcomes shown are for the entire cohort reported in each study. Studies that include 4 or more conditioning regimens are reported as “various.” Only studies with greater than 20 patients reported in the past 5 years are depicted.

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Scheinberg P. Hematology 2010, the American Society of Hematology Education Program Book. 2012 Dec 8;2012(1):292-300.

Haploidentical Hematopoietic Stem-Cell Transplantation for Severe Aplastic Anemia

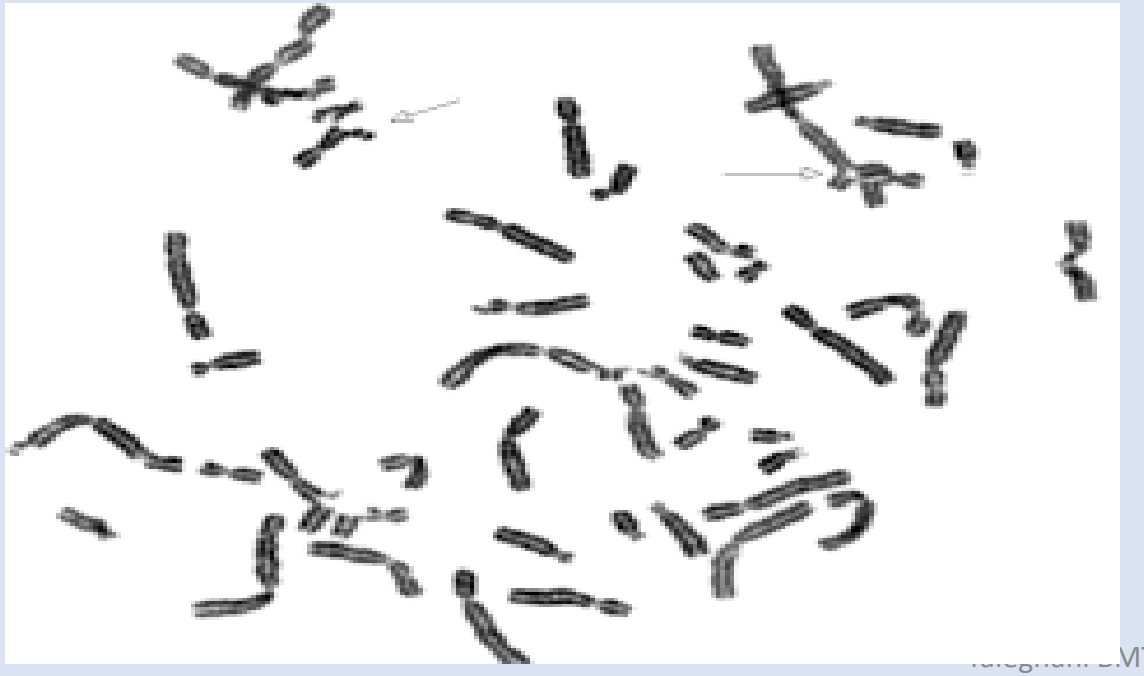
Study	No. of Patients	Median Age	Conditioning and Prophylaxis	Overall Survival	Acute and Chronic GVHD†	Graft Failure
		yr		%	%	*no. of cases*
Prospective study in Korea, 2009–2010[85]	4	18	Conditioning: Cy, FLU, ATG Prophylaxis: CsA, MMF; graft depleted of CD3 or CD3–CD19 cells	100 at 19 mo	0	0
King's College study[86]	6	30	Conditioning: Cy, FLU, low-dose TBI Prophylaxis: Cy (after transplantation), tacrolimus, MMF; GCSF-mobilized peripheral blood	67% at 1 yr	Acute: 17 (skin) Chronic: 0	2 primary
Retrospective study in Brazil, 2010–2014[87]	16	17	Conditioning: Cy, FLU, low-dose TBI Prophylaxis: Cy (after transplantation), CNI, MMF	67% at 1 yr	Acute: 13 Chronic: limited, 20; severe, 7	1 primary, 1 secondary
Multicenter prospective study in China, 2012–2015[88]	101	19	Conditioning: BU, Cy, ATG Prophylaxis: CsA, MMF, MTX	89 at 3 yr	Acute: 34 Chronic: 20 (extensive, 9)	2 secondary
Prospective pediatric study in Beijing, 2007–2015[89]	52	9	Conditioning: BU, Cy, ATG Prophylaxis: CsA, MMF, MTX	85 at 3 yr	Acute: 14 (grade III–IV) Chronic: 13	3 secondary
Multicenter retrospective study in China, 2012–2015[90]	89		Conditioning: BU, Cy, ATG Prophylaxis: CsA, MMF, MTX	86 at 3 yr	Acute: 30 Chronic: 3	1 primary
Johns Hopkins study, 2011–2016[59]	13	30	Conditioning: Cy, FLU, low-dose TBI, ATG Prophylaxis: Cy (after transplantation), MMF, tacrolimus	100 at 21 mo	0	0
Retrospective study in Langfang, China, 2012–2016[91]	41	13	Conditioning: Cy, FLU, BU, ATG, and GCSF-mobilized bone marrow and peripheral blood Prophylaxis: CIN, MMF, MTX	80 at 3 yr	Acute: 44 Chronic: 12	0

Allo transplant in PNH

- The treatment should target the specific clinical presentation
- Eculizumab is the treatment of choice in patients presenting with hemolysis or thromboembolic
- In concomitant heemolysis or thromboemboly ad BMF ECULIZUMAB should be added to IST
- Allotransplant indications is similar to SAA
- Novel anti C5and C3 and even factor B is available

Risitano and Marotta ,2018

Fanconi anemia and other hereditary bone marrow failure syndromes



Indications of HSCT

- bone marrow failure
- Development of an abnormal clone/MDS
- Leukemia

- the genomic. instability of FA cells and the resulting hypersensitivity to alkylating agents was a major obstacle
- FA patients should receive considerably reduced doses of alkylating agents and radiation for conditioning

- Individual decision making for each patient based on age and risk factors
- Specific consideration for conditioning regimen
  - FLU 150 mg/m2 /CPM up to 50mg/m2 and /or TBI100-300 cGy in the unrelated cases+/_ ATG

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Prognostic factors

- Conditioning regimen:
  - incorporation of fludarabine inthe conditioning regimen has had a very positive impacton outcome. The CY dose has subsequently varied fromone study to another; doses as low as 20 mg/kg and up to80 mg/kg have been used with favorable outcomes
- Age
- Donor type
- Clonal disease
- Stem cell source

- Post transplant secondary malignancy

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FA

- There are no data in the literature to suggest that carriers of FAshould be avoided as donors

- FA with pretransplantation cytogeneticabnormalities, myelodysplastic syndrome, or acuteleukemia are a special challenge.long-term survival is achievable, younger patients and recipients of (HLA)-matched related donor transplantations

J Clin Oncol 2013;31:1669–76.

Unrelated or alternative HSCT in FA

- a study from theUniversity of Minnesota130 FA patients after alternative donor HCT Patientsreceived CY, single TBI, and ATG with or without fludarabine,and then T cell-depleted bone marrow or unmanipulated umbilical cord blood transplantation.
-
- The best results were obtained in patients without a history of opportunistic infection or transfusions and who received conditioning with TBI 300 cGy, CY, fludarabine, and ATG ,survival of 94% at 5 years

- Severe toxicity was highest inpatients >10 years of age or those with a history of opportunistic infections or transfusions prior to HCT.

- haploidentical HCT with post-transplant CY??

Blood 2015;125:3798–804.

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Allotransplant in dyscratosis congenita

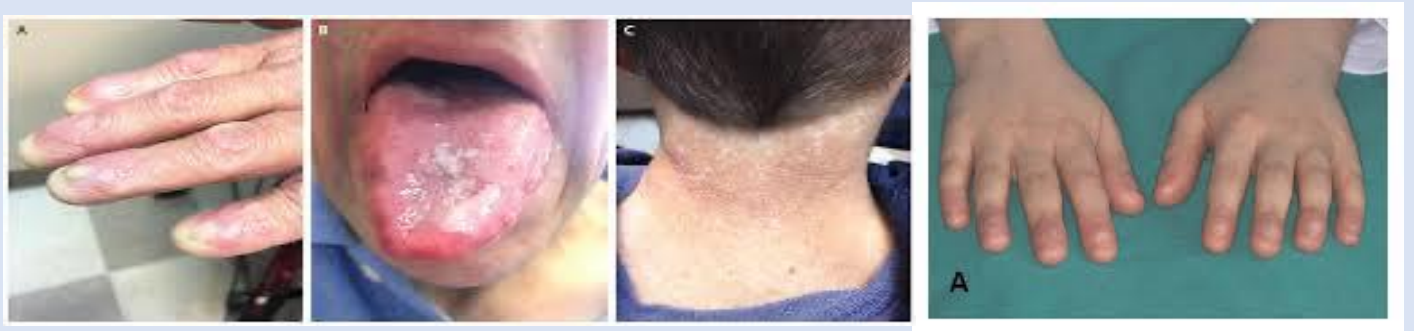
- bone marrow failure due to abnormal telomere maintenance, predisposition to malignancy and fatal pulmonary complications

- The only curative treatment but it is not indicated preemptive , it is recommended in progressive BMF
- reported outcomesare markedly inferior to those seen in FA patients

- Cohort of 34 DC patientsafter HCT, over 3 decades, was reported by CIBMTR showed a 10-year probability of survival of 30% with 14patients alive at last follow-up.

- a systematic review by Barbaro and Vedi 109 DC patients who underwent HCT; the take-home message was that the outcome was poor, with 5- and 10-year survival estimates of only 57% and 23%, respectively

Biol Blood Marrow Transplant 2013;19:1238–43.



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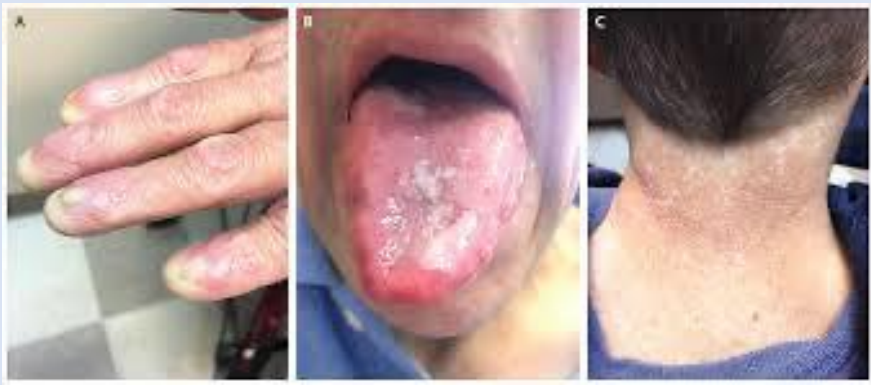
D yscrattosis congenita



- Avoid related carrier donors
- MRD>MUD>Alternative donor
- RIC >myeloabelative conditioning regimen
- 5 and 10 years OS is 57% and 23%
- Age>20 ,alternative donor,transplant before. 2000 are worse
- mortality due to pulmonary complicationsis a major cause of late death in of DC patients after HCT, even with RIC

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Severe congenital neutropenia and Shwashman syndrome

- Considerable mortality in HSCT

- HSCT indicates only in MDS/AL OR absent response to GCSF
- In SCN myeloabelative regimen is better while in SDS RIC regimen is preferred due to possible organ failure
- 82% overal survival in cohort of 136 p atients,better result in age under 10 and MSD transplants

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Diamond Blackfan anemia

- Indications:
  - Non responders to steroids
  - Steroid dependency at the dose>0.3 mg/kg/day
  - Transfusion dependent(individual decision making)
  - Alloimmunization
  - Progressive pancytopenia
  - MDS/AML
- Better outcome
  - Age<10 years

Congenital Amegacaryocytic Thrombocytopenia

- The only curative treatment
- Indications:
  - Transfusion dependency
  - Pancytopenia
  - Clonal evolution
- SPECIFIC CONCIDERATION IN CONDITIONING REGIMEN
- Successful reports of mismatch donors

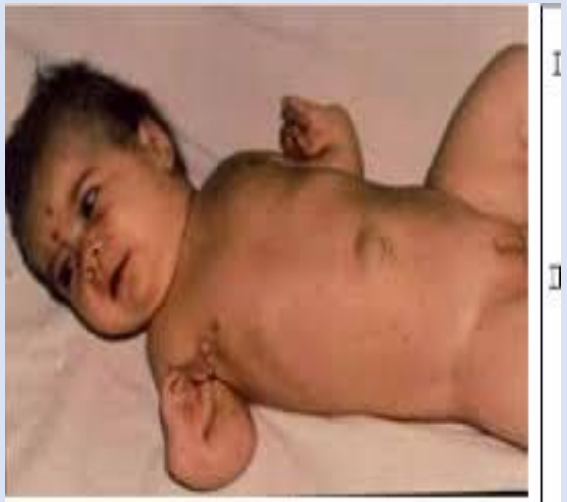
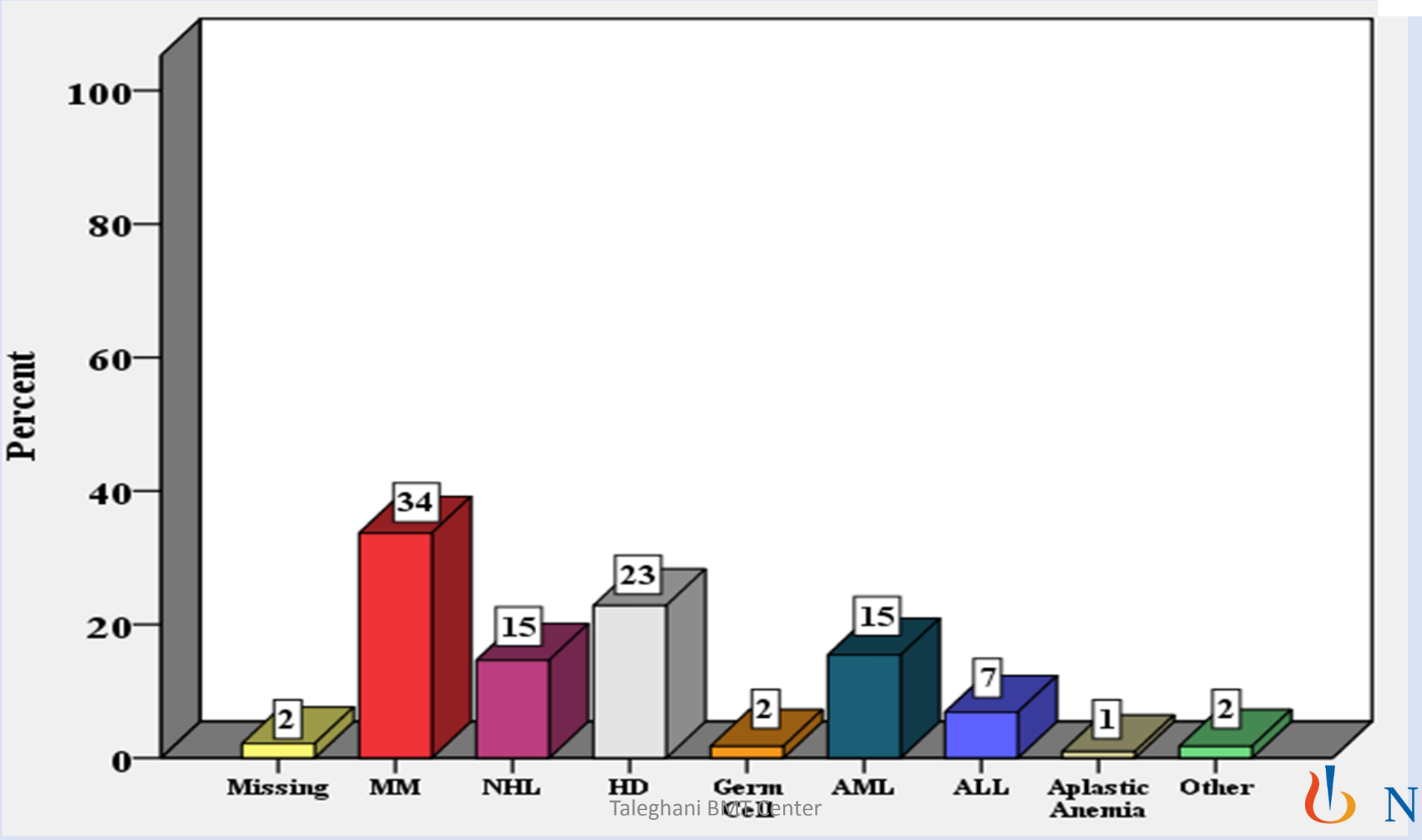


FIGURE 1. Note petechial bleeding, brusing in the forehead

NOVARTIS

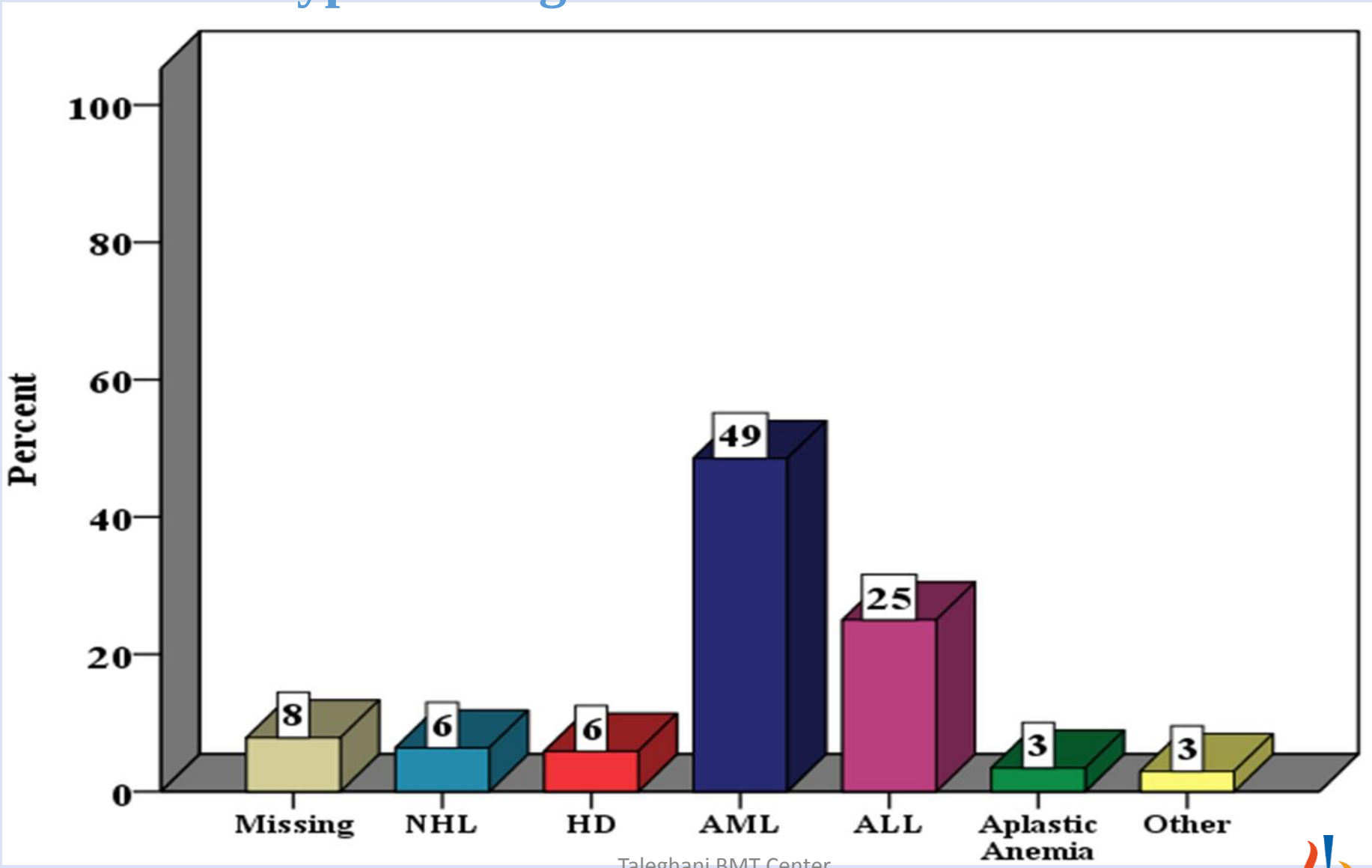
❖ ALLO-HSCT for AA patients in our center:

Type of Diagnosis Status in all Transplantations



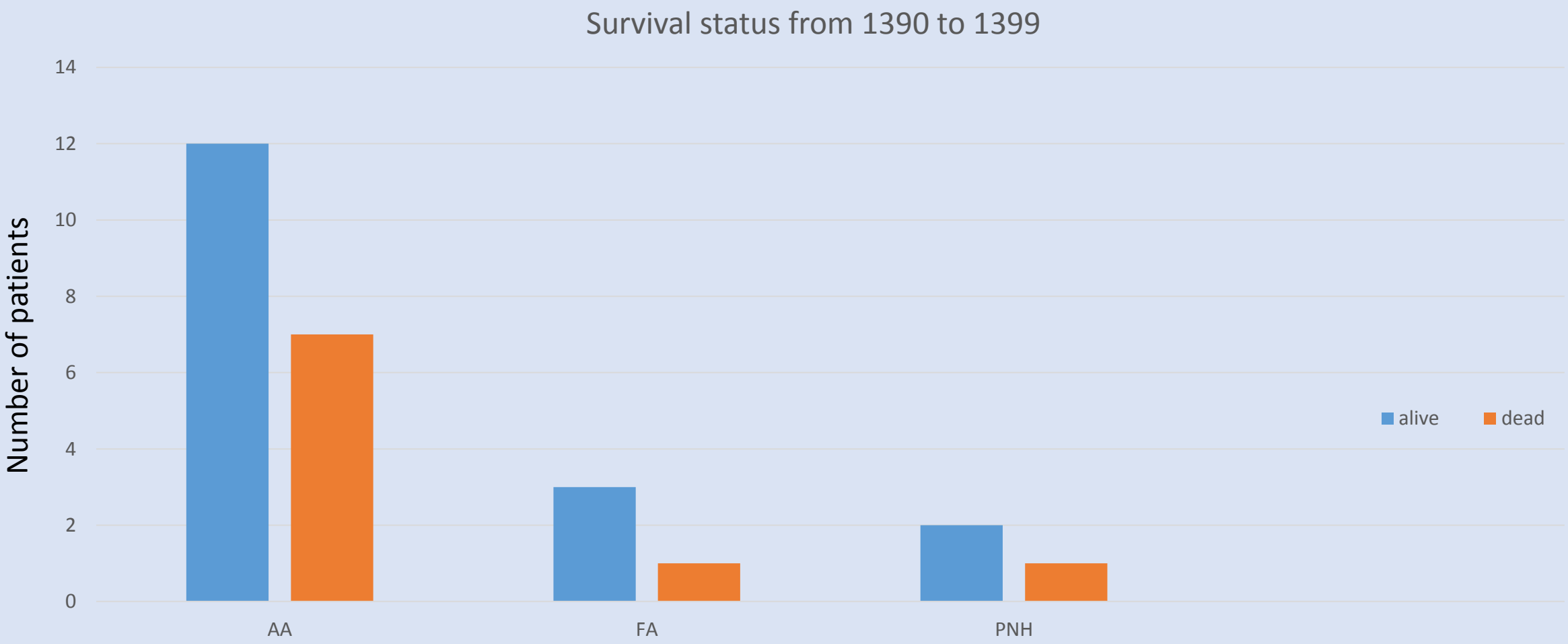
❖ ALLO-HSCT for AA patients in our center:

Type of Diagnosis Status in Allo-SCT



- Other Diagnosis : ALD, MDS and thalassemia.

Survival status of our patients after Allo-HSCT:




“thank you for
your ATTENTION
:)”