In the name of GOD

HEMATOPOIETIC STEM CELL TRANSPlANTATION (HSCT) IN Aplastic Anemia(AA) OF CHILDREN

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Bone Marrow Failure in children

Mofid Children Hospital (during 7.1394-12.1401)

Full name	Disease	Sex	Ageat HSCT(Y)	Type& timeoF HSCT- ALLO HSCT	Source / HSCT	Donor Type	Result
1-Mahila Jahan bakhsh	AA	F	10	X (1395)	CB	sibling	**Live, Full chimerism**
2- A M , Mir Hosseni	AA	M	13	X(1396)	PB	MSD	Live , full chimersm
-3 -HaniehMohammadi	FA	F	4	X(1397)	BM	MRD	Live, full chimerism
4- MehdeiZomorodi	AA	M	12	X(1397)	BM	MSD	Live, full chimerism
5-Fatemeh Maagholi x 2HSCT , the same donor	FA	F	6	X(1397)	BM /second time PB	MSD	Live, full chimerissm
6-Panisa Mameli	AA	F	5.5	X(1397)	**CB**	**Cord blood unrelated**	**Live-Primary rejection**
-7-Sajad Dadash poor	FA	M	7	X(1397)	PB	MRD	Live mixedchimersm
8-Mehdi Jafari	DC	M	9	X(1398)	PB	**MURD 9/10 HLA**	Primary Graft rejectionDeath:3 moaft , bleeding
9- ZohaBarahooei	CHA	F	1.2	X(1398)	PB	MSD	Live , full chimersm
10-Mahan karimi	AA	M	3	X(1398)	BM	MSD	Live mixed chimerism
11- M. HZareei	AA	M	3.7	X(1398)	PB	MURD- Germany	Live, full chimerism
12- Donya Ebrahimi	FA	F	6	X(1399)	PB	MRD (Grand Ma)	Live mixed chimerism
13-Ahoora Sarikhani	FA	M	10	X(1400)	PB	MURD- Germany	Live full chimerism
14-A. T Ilka	FA	M	8	X(1400)	PB	MRD (Grand Father)	Death(sepsis)
15-Fatemeh Gholi	DC	F	11	X(1400)	PB	MURD 12/12	Live , full chimerism
16-Mehrazad Mirzaloo	FA	M	9	X(1400)	PB	MRD, Father	Live, full chimerism
17-Shaver Saeedi	AA	M	14	X(1400)	PB	MSD	Live, full chimerism
18-Ermia Hashemi	AA	M	7	X(1400)	PB	**MSD, 9/10 HLA**	**, live-Primary rejection**
19 AMIR, A Zeini	FA	M	11	X(1400)	PB	MURD- Germany	Live, full chimerism
20-Sajedeh Dehghan	FA	F	11	X(1400)	PB	MRD, FATHER	Live, full chimerism

Bone marrow failure syndrome , Mofid children hospital(7/ 1394 , 12/1401)

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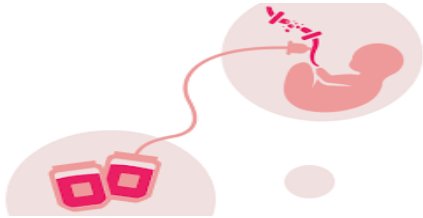
Bone marrow failure syndrome , Mofid children hospital(7/ 1394 , 12/1401)

Aplastic Anemia-Case presentation CORD BLOOD HSCT

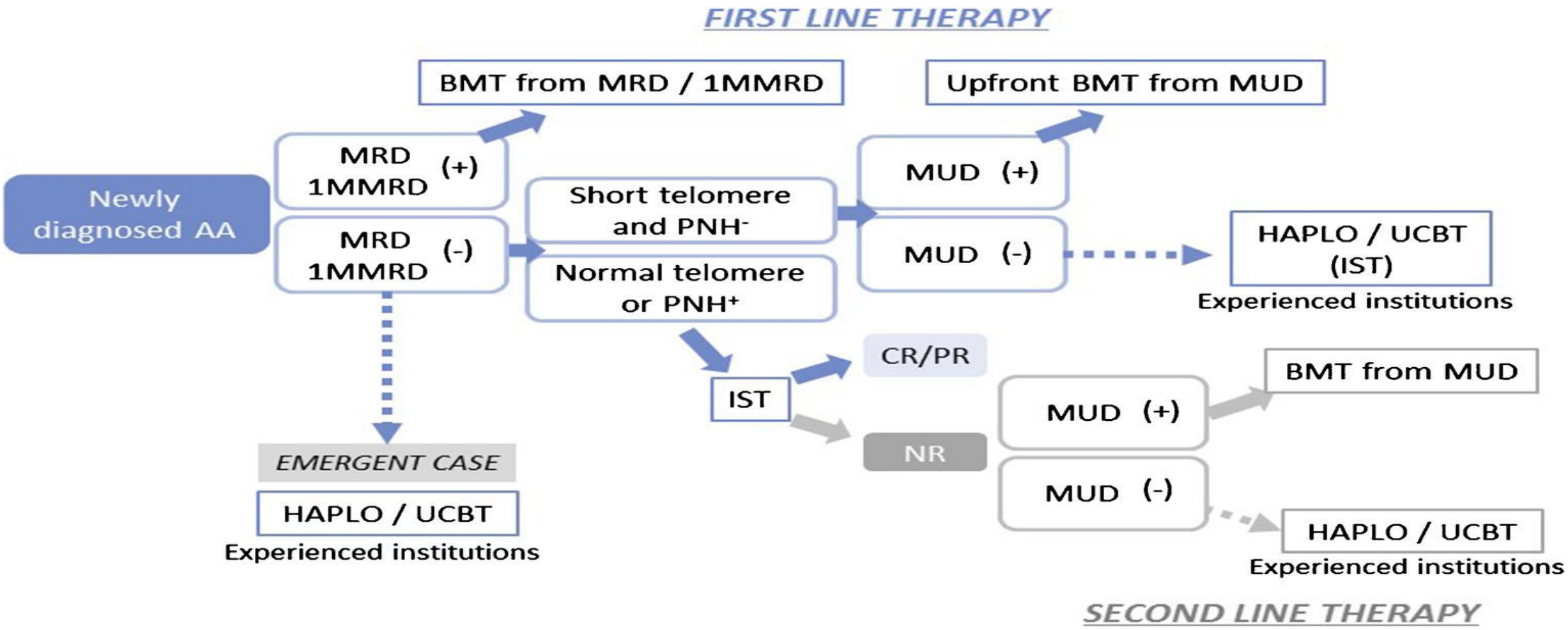


- **A 10 Y old age female, first child ,parents : first cousin Patient : 25kg .**
- **Data birth :22/10/1385**
- First presentation (6/95) Ecchymoses, pancytopenia, BMA & BMB , Sever hypocellular BM, Flowcytometry : NL Cytogenetic : 46xx , DEB test ; neg , otherwise : NL
  Diagnosis: Aplastic Anemia
- **1 course of horse ATG and Cyclospurine,** Blood & plate transfusion < 10 times, She received Oxymetolon , 25 mg/day
- **Admission for ALLO-HSCT : 21/5/96**
- EF: Nl GFR : 95 CMV IgG : pos HBsAg : neg HBsAb : neg BG : AB pos
- WBC: 1100 Hb: 7.5 Plate; 35000
- **Condition : FLU + Cyclophosfamide + ATG**
- **GVHD prophylaxis : Cyclospurine + Methyl prednisone**

Aplastic Anemia-Case presentation
CORD BLOOD HSCT

- HLA typing ; (Final report) Cord blood of sibling(sister) , Cord 6/6 match(A, B , DR), BG: B+
- Cord Blood :1 unit Volume: 19cc Viablity : 92%
- TWBC: 79.8x107 T WBC/Kg: 3.19x107 Corrected WBC: 73.41x107 Corrected WBC/kg: ; 2.93x107
- **Pre Thaw : 3.19x107 Cellularity Post thaw : WBC/Kg; 2.93x107**
- **Engraftment ; day + 21 Chimerism: 85% First Discharge : Day+ 29**
- Complication: On Day + 41 after HSCT : CMV reactivation , and sinus fungal infection
- Treatment et : Gancyclovir , Amphotericin B liposomal ; response to treatment
- **Now; 16 y old age young lady , Clinically good**
- **Chimerism 5 y after HSCT 95%**

Updated treatment algorithm for children with acquired aplastic anemia. Nao Yoshida1 Current Oncology Reports (2018) 20: 67



Options for Second-Line Treatment in AA. CORD Blood

❑**Unrelated Cord Blood Transplantation in AA of children**

- **CB :in the lack of MRD or MUD or for emergency cases.**
- **For patients with SAA, CBT from an unrelated donor should be considered only in the setting of clinical trials,when a suitable BM donor is not available and after the failure of IST.**
- Cord blood : is probably inferior to HLA haploidentical marrow grafts because of the **low cell dose infused, Graft rejection, and delayed engraftment/immune recovery**.

- **2008: Japanese study** :both **pediatric & adult** patients who underwent **UCBT (n = 31)** reported a **2- year OS rate of 41% and engraftment of 55%**

Options for Second-Line Treatment in AA. CORD Blood

- Retrospective analysis by Eurocord on 71 p /SAA ,9 with (PNH) :single UCBT (n=57, 80%) or double UCBT (n=14, 20%) the 3-year OS was 37% and 43% after double UCBT
- In multivariate analysis, the only factor influencing engraftment and survival was pre-freezing total nucleated cell (TNC) dose (>3.9×107/kg, P=0.05).
- **5-year OS rate was 94% among 17 patients who UCBT after 2006**
- **ATG using in CB HSCT???**

Results of a prospective phase II study (NCT01343953, APCORD Trial: CB.
Stem Cell Investig 2019;6:39. France

Blood 2018;132:750-4.

- 26 patients ,unrelated cord blood (CB)HSCT
- Conditioning regimen : (Flu) 30 mg/m2 from day −6 to day −3, Cy 30 mg/kg from day −6 to day −3, anti-thymocyte globulin (ATG) 2.5 mg/kg from day −3 to day −2, 2-Gray total body irradiation (TBI) on day −2.
- Anti-CD20 at the dose of 150 mg/m2 was given at day +5 for prophylaxis (EBV) . **(GVHD) :cyclosporine A (CsA) alone.**
- Median age at CBT ; **16 years [9.3–23.4 years].**
- **All patients received at least 1 course of IST pre HSCT (2 courses, n=5–11)**
- with a median time between diagnosis and HSCT of 12 months
- Median follow-up was 38.8 months
- **2-year survival rate of 84.6% (95% CI, 71–100%).**
- Engraftment occurred in 23 patients (88%);1-year treatment-related mortality was 11.5%
- **CBT with units containing ≥4 × 10^7 frozen NCs per kilogram**

Stem Cell Investig 2019;6:39

- Eurocord ; 117 children & Young adult acquired and inherited BMF : related CbHSCT
- 82 patients received a single CB unit and 35 received a mixed graft (CB and BM cells from the same donor).
- **The median age HSCT ; 6.7 years.**
- 7-year OS for the whole population was **87.9%** , **89% for inherited and 81% for acquired** (P=0.66).
- **CBT from an HLA-identical sibling donor could be a good option for patients with BMF since it is associated with excellent survival outcomes and low risk of GVHD and graft failure**
- **In this setting collecting CB unit at the birth of a new sibling, especially in case of inherited BMF, should be strongly recommended.**

Stem Cell Investig 2019;6:39

- **IN BMF disorders :**
- Eurocord studies provide evidence that in these particularly high-risk patients
- **Related CBT can be associated with excellent results**
- while UCBT outcomes may be improved by an increasing of TNC dose and better HLA matching.

CB HSCT in Bone Marrow Failure

- Intra-bone infusion of CB cells may be beneficial in some contexts ,even if this technique is far to be recommended.
- Expansion of HSCs
- Co-culture of CB cells with mesenchymal stem cells (MSCs) is a strategy whose basic principle is to simulate the physiological microenvironment of the BM & **co-transplantation of those two constituents**
- **Recommendation :**
- Idiopathic context **1 or 2 CB units may be used with no more than 2 of 6 HLA mismatches**
- Inherited BMF, **particularly in the setting of FA**, the current recommendation is to **choose a donor with no more than one HLA mismatch** because of the **risk of unacceptable toxicity**
- To avoid the risk of graft failure due to an allogeneic immunization, donor-specific antibodies should be screened before transplantation
- cytomegalovirus (CMV) status is important

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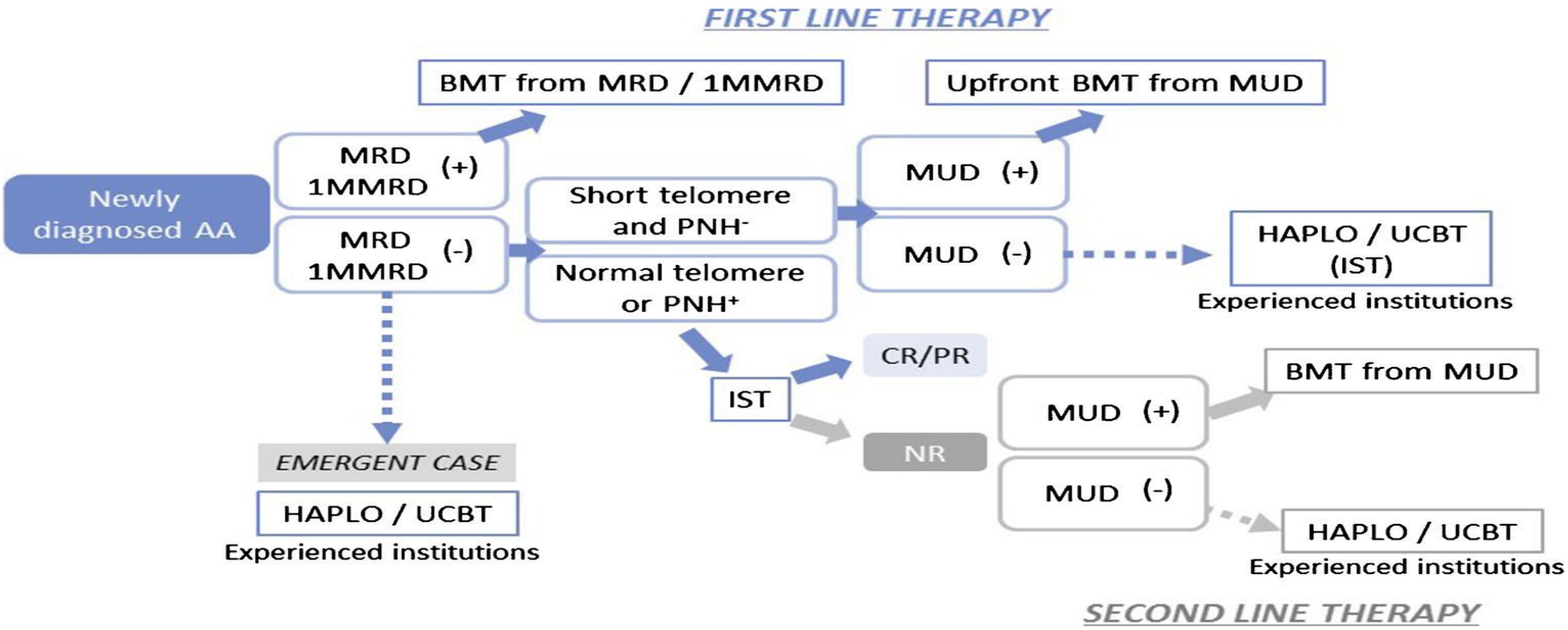

Thank YOU