What should we consider about the donor when performing HCT in NMD?

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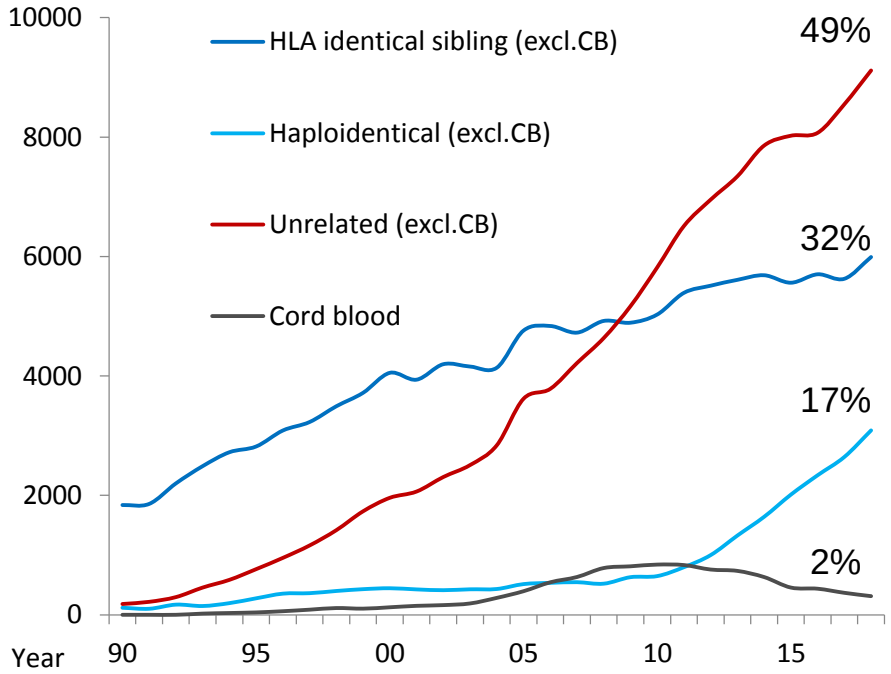
Donor Type in non-malignant diseases (NMD)

- Approx. 46% of patients <18 yrs are affected with non- malignant diseases.[1]
- Nonmalignant diseases do not benefit of any alloreactivity -> the closest HLA matching (possibly “10 out of 10” HLA alleles) is recommended.[2]
- Some patients are considered eligible for HSCT only in case an HLA-identical sibling is available.
- Some inherited disorders (e.g. SCD) have higher incidences in non- Caucasian ethnicities, which are less represented within stem cell donor registries.
- As a consequence well-matched donors often are lacking.

1 Passweg et al. 2014; 2 EBMT handbock 2019

Haploidentical related donors

- Improved outcome in haploidentical HSCT broadened its indications:
  - pre-transplant ATG[1]
  - Post-transplant cyclophosphamide (PT-CY[2])
  - alpha-beta T-cell depletion (TCD[3])
- -> increasing use of haploidentical related donor transplantation[4]
- Several retrospective comparison studies have reported similar outcome for haploidentical and MUD transplants[5].



1 Huang et al. 2006, 2 Luznik et al. 2008, 3 Bertaina et al. 2014 , 4 Passweg et al. 2020, 5 Fuchs et al. 2017

Haploidentical donors in NMD

- Similar outcome between TCR αβ-depleted and matched sibling and matched unrelated donors HSCT in children with acute leukemia[1] and in NMD[2], was recently confirmed by a multicenter phase I/II study[3].
- One of the parents mostly serves as a donor in haploidentical donors for pediatric recipients. The choice between the mother and the father is still debated.
- Better survival after T cell depleted HSCT was shown in patients transplanted from the **mother** than from the father (51% vs 11%; $P < 0.001$)
  - reduced incidence of relapse and TRM
  - protective effect on the risk of failure (HR 0.42; $P = 0.003$) -> transplacental leukocyte trafficking during pregnancy, inducing long-term, stable, reciprocal microchimerism in mother and child[4].

1 Locatelli et al. 2017; 2 Bertaina et al. 2014; 3 Lang et al. 2017; 4 Stern et al. 2008

Logistical comparison of related haplo vs MUD

	MUD	Haplo
Donor availability	20-80%[1]	>95%
Time to graft acquisition	Slower	Faster
Time between collection and infusion	Longer	Shorter
Ease of repeat donation	Harder	Easier

1 EBMT handbook 2019

Stem cell source and other donor-recipient- related factors

- Avoid PBSC due to the increased risk of cGvHD
- Donor age, gender, female parity, weight, ABO blood group, and viral serological status should be considered, whenever more than one donor is available[1].
- Survey within the PDWP of the EBMT, the features were listed in the following order of importance[2]:

1. HLA compatibility (10/10 better than 9/10)
2. CMV serological status of D+ in case of R+
3. BM as stem cell source
4. Donor age (preferable a younger donor)
5. Donor gender (male donor preferred esp. for a male recipient)
6. ABO major incompatibility
7. Donor center location
8. ABO minor incompatibility

1 Wang et al. 2018; 2 unpublished data

Special considerations for haplo donors

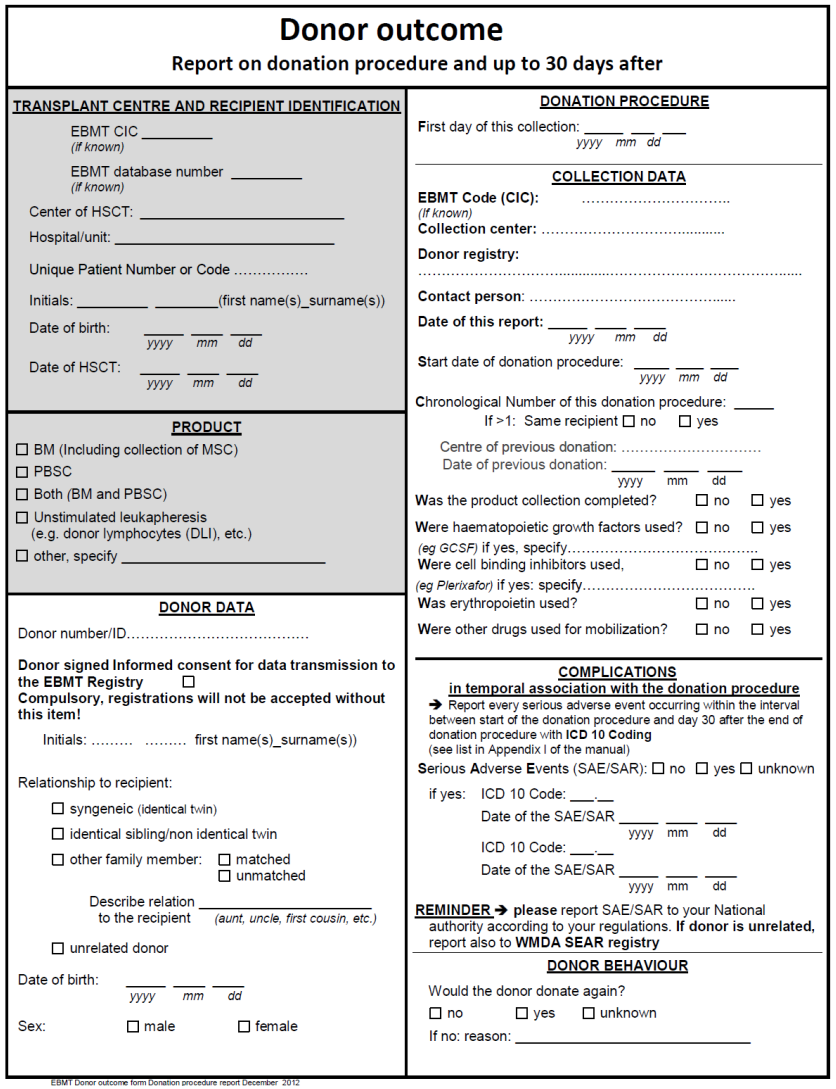
- Financial burden influences donor selection process (haplo > MUD)
- HLA-matched sibling (minor->minor) donation is accepted but how to proceed in the haplo setting?
  - Donor age is more and more coming into the focus is it ethical to use a minor haplo if an adult haplo (e.g. parents) are available?
- What degree of increase in medical risk raises red flags in minors?
  - Until now no clear evidence in minors with respect to comorbid conditions and risk of donation
  - How about multiple risks? (e.g. morbidly obese teenager with diabetes)

Outcome registries for HPC donors

- Information on short- and long-term donor outcome to ensure donor safety.
- Data on frequent early events associated with donation do exist (mostly for MUD) but are lacking especially for minor donors.
- Information on type and risk of severe adverse reactions (SAR) is limited and only few data exist on long-term donor outcome.
- Recommendations for a minimum data set for prospective related donor follow-up were developed under the auspices of WBMT in 2013.

Halter et al. 2013

Outcome registries for HPC donors



Donor outcome

Report on donation procedure and up to 30 days after

TRANSPLANT CENTRE AND RECIPIENT IDENTIFICATION

EBMT CIC _____ *(if known)*

EBMT database number _____ *(if known)*

Center of HSCT: _____

Hospital/unit: _____

Unique Patient Number or Code .....

Initials: _____ _____(first name(s)_surname(s))

Date of birth: ____ ___ ___ *yyyy mm dd*

Date of HSCT: ____ ___ ___ *yyyy mm dd*

PRODUCT

☐ BM (Including collection of MSC)
☐ PBSC
☐ Both (BM and PBSC)
☐ Unstimulated leukapheresis (e.g. donor lymphocytes (DLI), etc.)
☐ other, specify _____

DONOR DATA

Donor number/ID.....

Donor signed Informed consent for data transmission to the EBMT Registry ☐
Compulsory, registrations will not be accepted without this item!

Initials: .... first name(s)_surname(s))

Relationship to recipient:

☐ syngeneic (identical twin)
☐ identical sibling/non identical twin
☐ other family member: ☐ matched ☐ unmatched

Describe relation to the recipient _____ *(aunt, uncle, first cousin, etc.)*

☐ unrelated donor

Date of birth: ____ ___ ___ *yyyy mm dd*

Sex: ☐ male ☐ female

DONATION PROCEDURE

First day of this collection: ____ ___ ___ *yyyy mm dd*

COLLECTION DATA

EBMT Code (CIC): ..... *(If known)*
Collection center: .....
Donor registry:
.....
Contact person: .....
Date of this report: ____ ___ ___ *yyyy mm dd*
Start date of donation procedure: ____ ___ ___ *yyyy mm dd*
Chronological Number of this donation procedure: ____
If >1: Same recipient ☐ no ☐ yes
Centre of previous donation: .....
Date of previous donation: ____ ___ ___ yyyy mm dd
Was the product collection completed? ☐ no ☐ yes
Were haematopoietic growth factors used? ☐ no ☐ yes
(eg GCSF) if yes, specify.....
Were cell binding inhibitors used, ☐ no ☐ yes
(eg Plerixafor) if yes: specify.....
Was erythropoietin used? ☐ no ☐ yes
Were other drugs used for mobilization? ☐ no ☐ yes

COMPLICATIONS
in temporal association with the donation procedure
➔ Report every serious adverse event occurring within the interval between start of the donation procedure and day 30 after the end of donation procedure with **ICD 10 Coding**
(see list in Appendix I of the manual)
Serious **A**dverse **E**vents (SAE/SAR): ☐ no ☐ yes ☐ unknown
if yes: ICD 10 Code: ___.__
Date of the SAE/SAR ____ ___ ___ yyyy mm dd
ICD 10 Code: ___.__
Date of the SAE/SAR ____ ___ ___ yyyy mm dd

REMINDER ➔ **please** report SAE/SAR to your National authority according to your regulations. **If donor is unrelated,** report also to **WMDA SEAR registry**

DONOR BEHAVIOUR

Would the donor donate again?
☐ no ☐ yes ☐ unknown
If no: reason: _____

EBMT Donor outcome form Donation procedure report December 2012

EBMT

European Society for Blood and Marrow Transplantation
in collaboration with
Swiss Transfusion SRC

DONOR OUTCOME DATA MANUAL

A Guide to the completion of the EBMT Donor Outcome Data Forms

Halter et al. 2013

Conclusion

- Donor safety has been recognized by the community as an important issue.
- International standards (FACT-JACIE) already provide also examples and guidance how to handle allogeneic related donors.
- So far, related donors have been reported to be older (possibly more health problems, higher vascular risk, more cardiac events, more malignancies), however with increased haploidentical HCT more younger donors may be observed.
- Despite stem cell mobilization and donation is a safe procedure and serious or fatal events are rare, they may only be detected by large amounts of data.
- To ensure donor safety in the short- and long-term, outcome registries (e.g. as the EBMT registry funded in 2013) are urgently required.

Thank you for your attention!