# „Donor suitability and donation process"

Dietger Niederwieser,
Prof. Dr. med. Dr. h.c.
Universität Leipzig

# Donor suitability and donation process



**BRIEF REPORT**

## INADVERTENT TRANSMISSION OF A DONOR'S ACUTE MYELOID LEUKEMIA IN BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOCYTIC LEUKEMIA

DIETGER W. NIEDERWIESER, M.D.,
FREDERICK R. APPELBAUM, M.D.,
GÜNTHER GASTL, M.D.,
ELISABETH GERSDORF, M.D.,
BERNHARD MEISTER, M.D.,
DIETMAR GEISSLER, M.D.,
JEANNIE A. TRATKIEWICZ, PH.D.,
JOSEF THALER, M.D., AND CHRISTOPH HUBER, M.D.

layered with 0.25 ml of medium containing various concentrations of serum samples from the patient or a control. After incubation for 12 days at 37°C, 1 ml of 2.5 percent glutaraldehyde was injected into the well to detach and fix the agar layer. Cell aggregates containing more than 50 granulocytic and monocytic cells were scored as granulomonocytic colonies.

### Analyses of Surface-Antigen Patterns

The expression of different surface antigens of bone marrow cells was measured by direct immunofluorescence and flow cytometry on a fluorescence-activated cell sorter (Becton Dickinson, Mountain View, Calif.) or by immunohistologic examination of cryostat sections of bone marrow. In the analysis of surface markers, the following monoclonal antibodies were applied: My9 (CD33, Coulter, Hialeah, Fla.), My7 (CD13, Coulter), VIM-2 (Dr. Walter Knapp, University of Vienna, Austria), BMA 0200 (CD15, Behringwerke, Marburg, Federal Republic of Germany), anti-HLA-DR (Becton

# Donor suitability and donation process

Bone Marrow Transplantation (2004) 34, 657–665

www.nature.com/bmt

**Mini review**

## Transmission of donor illness by stem cell transplantation: should screening be different in older donors?

D Niederwieser[1], C Gentilini[1], U Hegenbart[1], T Lange[1], P Moosmann[1], W Pönisch[1], H Al-Ali[1], M Raida[1], P Ljungman[2], A Tyndall[3], A Urbano-Ispizua[4], HM Lazarus[5] and A Gratwohl[6]

[1]*Department of Internal Medicine II, Division of Hematology and Oncology, University of Leipzig, Leipzig, Germany;* [2]*Department of Hematology, Huddinge University Hospital, Karolinska Institutet, Stockholm, Sweden;* [3]*Department of Rheumatology, University of Basle, Felix Platter-Spital, Basle, Switzerland;* [4]*EBMT Secretariat, Hospital Clinic, Barcelona, Spain;* [5]*Deptartment of Medicine, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH, USA; and* [6]*Deptartment of Hematology, Kantonspital, Basel, Switzerland*

# Donor suitability and donation process

**Table 1** Transmission of donor diseases to recipients

| *Transmission of* | *Donor disease* |
|---|---|
| *Infectious diseases* | |
| Viruses | HIV[12] |
| | Hepatitis B and C[12] |
| | HTLV-1[13] |
| | CMV[14–16] |
| | EBV |
| | Parvovirus B19[17] |
| | West Nile[18,19] |
| Bacteria | Contaminants[a] |
| | Brucellosis[20] |
| Parasites | Toxoplasmosis[21,22] |
| | Malaria[23–26] |
| | Leishmania[12] |
| | Babesia[12] |
| Fungi | Candida, Aspergillus |
| Prions | Creutzfeld Jakob disease[b] |

[a]Contamination rates of one in 3000 units in platelet concentrates. No information available on stem cell grafts.
[b]No known cases in HCT and blood transfusions.
[c]Not reported in HCT.

# Donor suitability and donation process

**Table 1** Transmission of donor diseases to recipients

| *Transmission of* | *Donor disease* |
|---|---|
| *Acquired disorders* | |
| Autoimmune diseases | Myasthenia gravis[28] |
| | Atopy[29] |
| | SLE specific autantibodies[30] |
| | Thyreotoxicosis[31–33] |
| | Diabetes mellitus type I[34] |
| | Sarcoidosis[35] |
| | Coeliac disease[36] |
| | Autoimmune thrombocytopenia[37] |
| Hematological malignancies | AML[38] |
| | CML[39] |
| | T-cell lymphoma[55] |
| Nonhematological malignancies[c] | Small-cell lung cancer from renal transplantation[40] |
| | Glioblastoma multiforme from liver transplantation[41] |

[a]Contamination rates of one in 3000 units in platelet concentrates. No information available on stem cell grafts.
[b]No known cases in HCT and blood transfusions.
[c]Not reported in HCT.

# Donor suitability and donation process

**Table 2** Recommendations for donor work-up

| *Test* | *WMDA*[6] | *NMDP 18th Edition Standards/ September 2002* | *JACIE 2 edition/June 2003* | *Proposal* |
|---|---|---|---|---|
| Medical history | Yes | Infectious (including risk for infections), pregnancy, blood donation history | Vaccination, travel and blood transfusion history, questions to identify persons at high risk for transmittable infections | Familiar, travel, vaccination, smoking, blood transfusion and donation, infectious, pregnancy, allergy, autoimmune, vaccination and tumor history |
| Physical examination | Yes | Yes | Yes | Particular attention to cardiovascular, bleeding and malignant diseases |
| ECG | Yes | Yes | Not specified | Yes |
| Chest X-ray | Yes | Yes | Not specified | Yes |
| Blood counts | Full blood count and differential with blood film | Complete blood count | Not specified | Complete blood count, manual differential on blood film |
| Blood group | Yes with antibody screen | ABO group and Rh type | ABO group and Rh type and appropriate red cell compatibility with the recipient | ABO group and Rh type and appropriate red cell compatibility with the recipient |
| Coagulation screen | Yes | No | No | **PT**, **PTT**, fibrinogen |
| HLA-typing | Yes | Yes | Yes | HLA typing HLA-A, -B, -C, DRB1, HLA-DQ |
| Biochemial profile | Urea, electrolytes, creatinine, liver function tests, blood sugar | Urinalysis, electrolytes, blood urea nitrogen or creatinine, bilirubin, serum protein plus albumin or serum protein electrophoresis, hemoglobin S for **PBSC** donors only | Not specified in detail | Urea, electrolytes, creatinine, liver function tests (bili, **ASAT**, **ALAT**, **AP**, γ-**GT**), LDH, blood sugar, protein electrophoresis, urine analysis |
| Infectious disease markers (within 30 days prior to collection) | Syphilis, hepatitis B surface antigen, HIV antigen and antibodies, hepatitis B core antigen, hepatitis C, **HTLV**-1, herpes simplex virus, CMV, *Varicella zoster* virus, and EBV | HIV type 1 and 2, HBV, HCV, HTLV type 1 and 2, *Treponema pallidum* (syphilis), CMV | HIV type 1 and 2, HBV, HCV, HTLV type I and II, *Treponema pallidum* and CMV | HIV type 1 and 2, HBV (HBs Ag, HBsAb, HBcAb) HCV (HCVAb), HTLV type I and II, *Treponema pallidum*, CMV (IgG, IgM), **T**oxoplasmosis (IgG, IgM) and EBV |
| **P**regnancy test (when indicated) | Yes | Yes | Yes | Gynecological visit including pregnancy test and physical breast examination |
| Malignant diseases in donors >55 years of age (related **HCT**) | | | | **PSA** in males, physical, occult blood in the stool. Bone marrow aspiration if medical history or tests are abnormal. **CT** chest scan in case of a long smoking history |
| Congenital disorders | | | | **T**esting for congenital disorders of planned recipient within family donors; testing for congenital disorders of the family |

# Donor suitability and donation process



**Table 3** Donor selection in case of donors with abnormal findings: (a) family donors, (b) unrelated donors and (c) unrelated cord blood

| *Abnormal finding on donors* | *Absolute contraindications* | *Relative contraindications* | *Specific consideration* |
|---|---|---|---|
| *(a) Family donors*[a] | | | |
| Infectious | HIV, HTLV-1, | Lues, HBV, HCV, malaria after 3 years; parvovirus B19 | EBV, CMV, toxoplamosis |
| Congenital | Thalassemia major; combined immune deficiency. Congenital disease with severely reduced life expectancy | Thalassemia minor; M Gaucher | Targeted cord blood should be tested for congenital disease of planned recipient |
| Malignancies | Every malignancies except *in situ* cancer | Skin cancer removed *in toto* | |
| Pregnancy | | Marrow donation and G-CSF-stimulated apheresis, unstimulated apheresis | |
| *(b) Unrelated donors*[a] | | | |
| Infectious | As for blood donation | Parvovirus B19, if known after collection: Gram-positive graft infection | EBV, CMV, toxoplamosis |
| Congenital | As for blood donation | | |
| Malignancies | Every malignancies except *in situ* cancer | Skin cancer removed *in toto* | |
| Pregnancy | Any donation | | |
| *(c) Unrelated cord blood*[a] | | | |
| Infectious | As for blood donation Gram-positive, Gram-negative contamination | | EBV, CMV, toxoplamosis |
| Congenital | As for blood donation; exclude, if congenital diseases known in family | | |
| Malignancies | Any, in child | | |

[a]No enough information is available for West Nile virus. Contamination of stem cell graft with epidermal bacteria might be a relative contraindication.

# Donor suitability and donation process

Bone Marrow Transplantation (2010), 1–7

www.nature.com/bmt

ORIGINAL ARTICLE

## The impact of the age of HLA-identical siblings on mobilization and collection of PBSCs for allogeneic hematopoietic cell transplantation

HK Al-Ali[1], M Bourgeois[1], R Krahl[1], E Edel[2], S Leiblein[1], W Poenisch[1], N Basara[1], T Lange[1] and D Niederwieser[1]

[1]*Department of Hematology/Oncology, University of Leipzig, Leipzig, Germany and* [2]*Institute of Transfusion Medicine, University of Leipzig, Leipzig, Germany*

# Donor suitability and donation process

**Table 1** Characteristics of patients and their HLA-identical donors ($n$ 167)

| | |
|---|---|
| *Patients* | |
| Median age (years) | 48 (18 74) |
| Gender | No. (%) |
| Male | 95 (57) |
| Female | 72 (43) |
| *Diagnosis* | |
| Acute leukemia | 67 (40) |
| Chronic leukemia | 37 (22) |
| MM | 24 (14) |
| MDS | 13 (8) |
| Others | 26 (16) |
| *Conditioning regimens* | |
| RIC | 88 (52.7) |
| Conventional | 79 (47.3) |
| *Donors* | |
| Median age (years) | 47 (18 74) |
| < 50 years | 100 (59.9) |
| ⩾50 59 years | 33 (19.8) |
| ⩾60 years | 34 (20.3) |
| *Gender* | |
| Male | 85 (51) |
| Female | 82 (49) |
| Patient/donor gender | |
| Male/male | 51 (30.5) |
| Male/female | 44 (26.3) |
| Female/female | 38 (22.8) |
| Female/male | 34 (20.4) |
| *History of hypertension in the donor* | |
| No | 75 (45) |
| Yes | 92 (55) |
| *History of drug intake in the donor* | |
| No | 111 (66.5) |
| Yes | 56 (33.5) |

Abbreviations: MDS myelodysplastic syndrome; MM multiple myeloma; RIC reduced intensity conditioning.

Al-Ali et al, BMT 2010

# Donor suitability and donation process

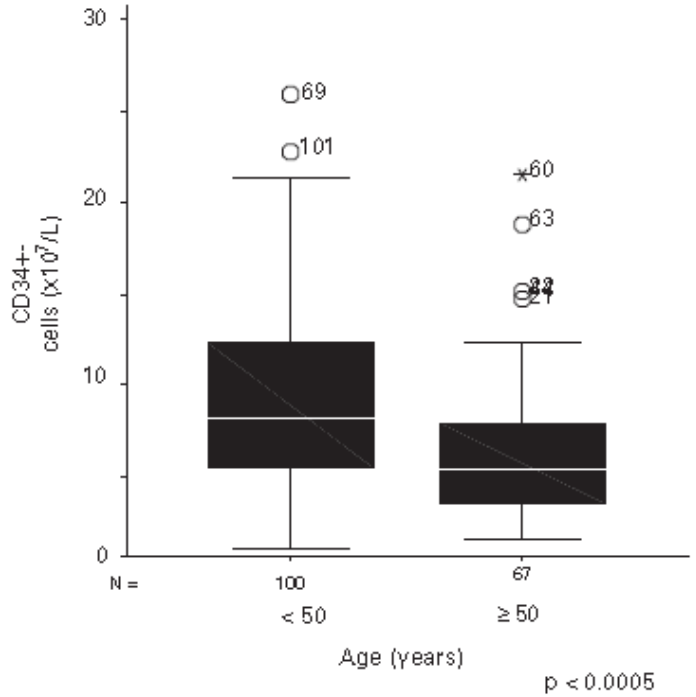


**Figure 1** Age of the donor and peripheral blood CD34 + cell count before apheresis.

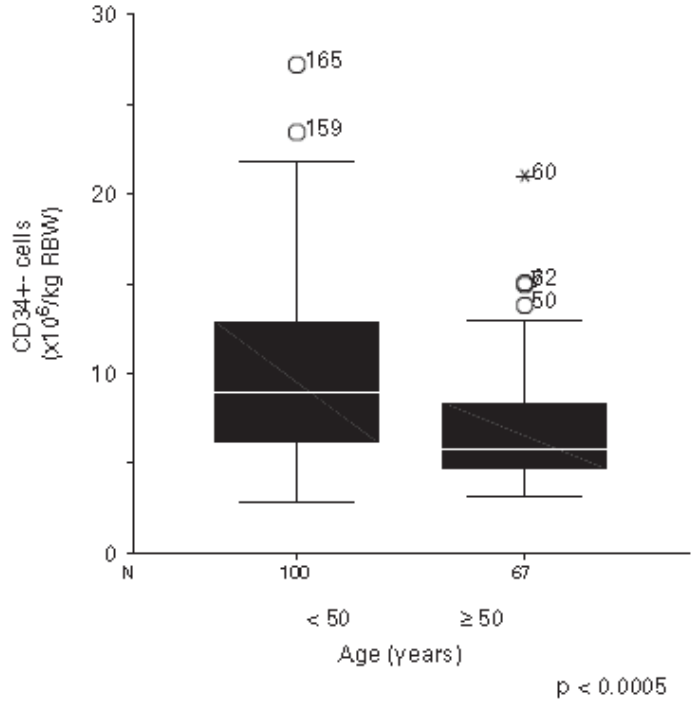


**Figure 2** Age of the donors and CD34 + cell counts in the transplants.

Al-Ali et al, BMT 2010

# Donor suitability and donation process

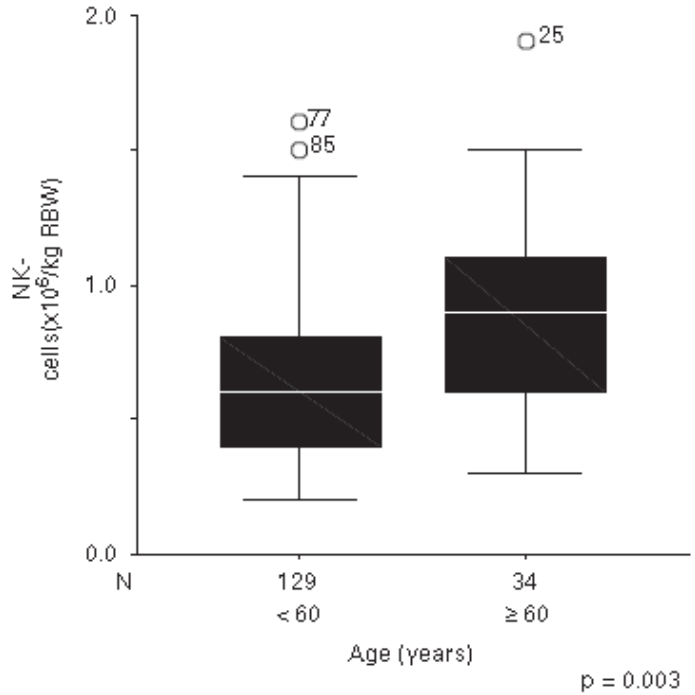


**Figure 3** Age of the donor and NK-cell counts in the transplant.

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# Donor suitability and donation process

**Table 2** Impact of donors' age on mobilization and harvest of HPC ($n$ 167)

| *Parameter* | *< 60 years vs ≥60 years* | | *< 50 years vs ≥ 50 years* | |
|---|---|---|---|---|
| | *Uni* (**P**-*value*) | *Multi* (**P**-*value*) | *Uni* (**P**-*value*) | *Multi* (**P**-*value*) |
| No. of apheresis sessions, median 1 (range 1 3) | 0.07 | NS | NS | |
| Filgrastim dose required for mobilization | NS | | NS | |
| **P**eripheral CD34+ cells before apheresis, median 6.3 (range 1 25.2) × $10^9$/L | 0.001 | NS | <0.0005 | 0.01 |
| *Hb, median (range) g per 100mL* | | | | |
| Before mobilization, 14.3 (11 17.6) | NS | | NS | |
| Before apheresis14, (9.5 16.8) | NS | | NS | |
| After apheresis, 13 (8.1 15.8) | NS | | NS | |
| *WBC, median (range)* × $10^9$/L | | | | |
| Before mobilization, 6.7 (2.8 14.5) | NS | | NS | |
| Before apheresis, 50.4 (22.5 94.5) | NS | | 0.04 | 0.08 |
| After apheresis, 40.9 (10.3 82.8) | NS | | 0.009 | NS |
| *Plts, median (range)* × $10^9$/L | | | | |
| Before mobilization, 246 (127 467) | NS | | NS | |
| Before apheresis, 225 (85 459) | NS | | 0.09 | NS |
| After apheresis, 94 (22 275 | NS | | 0.02 | NS |
| CTC toxicity ≥grade II | NS | | NS | |
| *Graft, median (range)* | | | | |
| Vol, 295 (83 1499) ml | NS | | NS | |
| CD34+ cells, 7.2 (2.8 33) × $10^6$/kg | 0.003 | 0.006 | <0.0005 | NS |
| CD3+ cells, 3.8 (0.8 21.8) × $10^8$/kg | NS | | NS | |
| NK cells, 0.7 (0.2 1.9) × $10^6$/kg | 0.003 | 0.001 | 0.01 | 0.07 |
| *Non-hematological CTC toxicity ≥ grade II* | NS | | NS | |
| **AP** | 0.005 | 0.07 | 0.04 | NS |
| **PPT** | NS | | NS | |
| **P**otassium | NS | | NS | |

Abbreviations: **AP** alkaline phosphatase; CTC the National Cancer Institute Common Toxicity Criteria; Multi multivariate analyses; NK cells natural killer cells; **PTT** partial thromboplastin time; Uni univariate analyses.

Al-Ali et al, BMT 2010

# Donor suitability and donation process

Table 3 Acute and chronic GVHD

| *Parameter* | | *Acute GVHD, N (%)* | | *Chronic GVHD, N (%)* |
|---|---|---|---|---|
| Incidence | | 90/167 (53.9) | | 62/139 (44.6) |
| *Severity* | | | | |
| | Grade I | 41/90 (45.6) | Limited | 28/62 (45.2) |
| | Grade II | 15/90 (16.7) | Extensive | 34/62 (54.8) |
| | Grade III | 27/90 (30) | | |
| | Grade IV | 7/90 (7.7) | | |
| *Organ involved*[a] | | | | |
| Skin | | 81/90 (90) | | 35/62 (56.5) |
| | Stage ⩽2 | 58/81 (71.6) | | |
| | Stage ⩾3 | 23/81 (28.4) | | |
| Liver | | 18/90 (20) | | 23/62 (37) |
| Gut | | 36/90 (40) | | 10/62 (16.1) |
| Others | | | | 22/62 (35.5) |
| *Age of patients (years)* | | | | |
| <50 | | 58/91 (63.7) | | 37/79 (46.8) |
| | Skin | | | |
| | Stage ⩽2 | 38/91 (41.8) | | |
| | Stage ⩾3 | 13/91 (14.3) | | |
| 50–59 | | 15/37 (40.5) | | 9/31 (29) |
| | Skin | | | |
| | Stage ⩽2 | 9/37 (24.3) | | |
| | Stage ⩾3 | 6/37 (16.2) | | |
| ⩾60 | | 17/39 (43.6) | | 16/31 (51.6) |
| | Skin | | | |
| | Stage ⩽2 | 11/39 (28.2) | | |
| | Stage ⩾3 | 4/39 (10.3) | | |
| <50 vs ⩾50 | | $P=0.007$ | | $P=0.1$ |
| Female donor to male patient ($n=34$) vs the rest (133) | | $P=0.9$ | | $P=0.2$ |
| Age of donors (years) <50 vs ⩾50 | | $P=0.5$ | | $P=0.6$ |
| NK cell count in the harvest | | $P=0.95$ | | $P=0.8$ |

Abbreviation: NK cells natural killer cells.
[a]Patients had one or more organ involvement.

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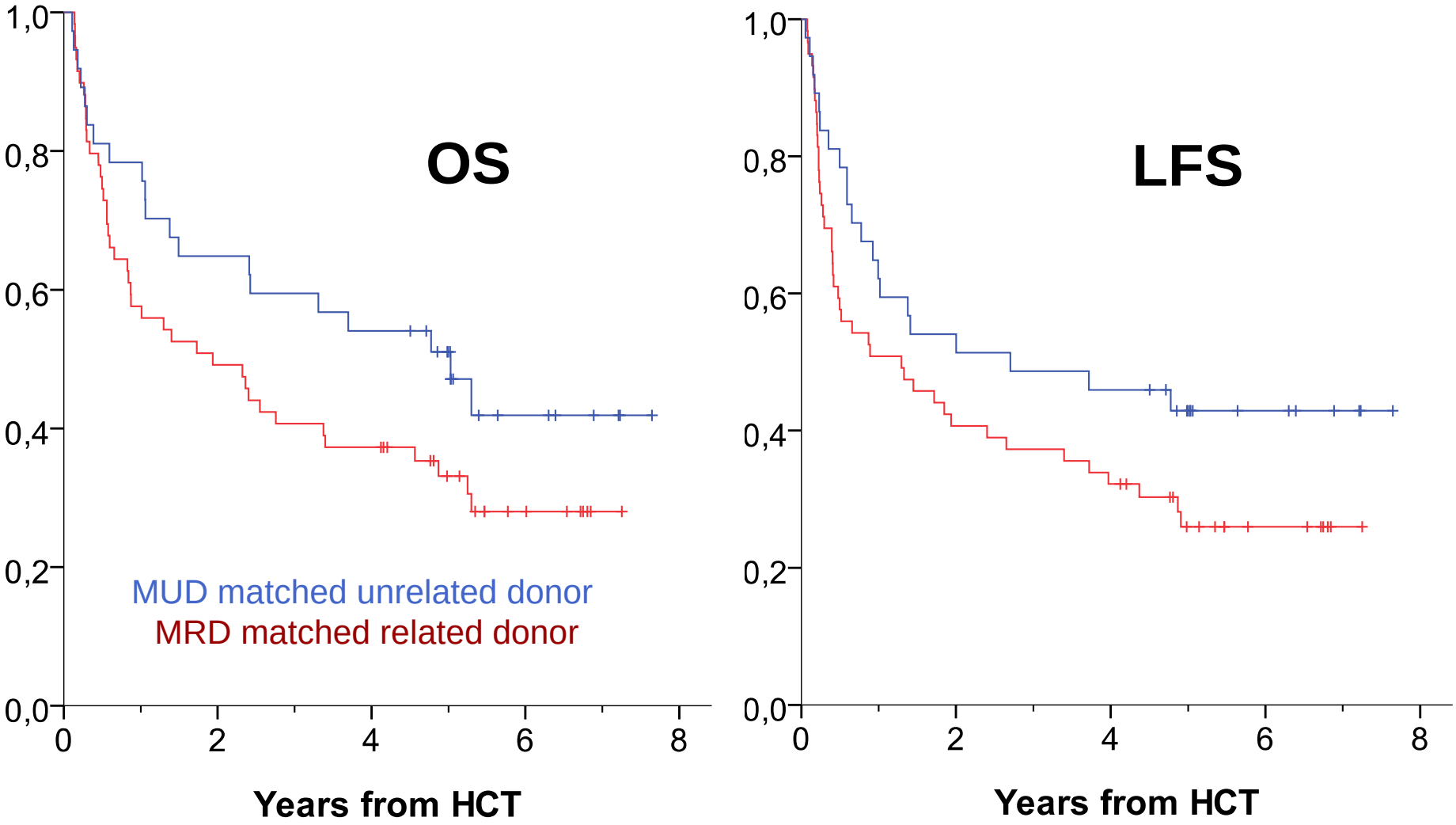
# HOVON – OSHO study

## Outcome of HCT after TBI based regimens (n=96) in AML



# EBMT study in AML > 60 yrs