Deklaration Interessenskonflikte

- Finanzielle oder Eigentümerinteressen:
  - keine
- Tätigkeiten für die pharmazeutische Industrie und andere Firmen des Gesundheitssystems:
  - Verwaltungsrat Blutspende SRK Schweiz AG
- Drittmittel / Spenden:
  - keine
- Persönliche Beziehungen:
  - keine
- Sonstige Mitgliedschaften:
  - Präsident Swiss Blood Stem Cell Transplantation
  - Stiftungsrat Stiftung zur Förderung der Knochemarktransplantation

Stammzelltransplantation

Blut-Stammzelltransplantation

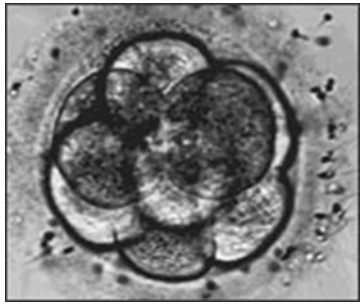
Knochenmark-Transplantation

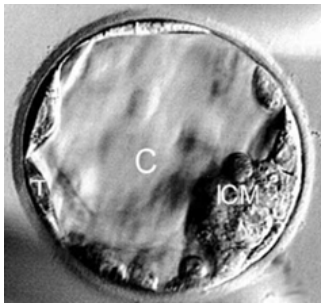
Urs Schanz

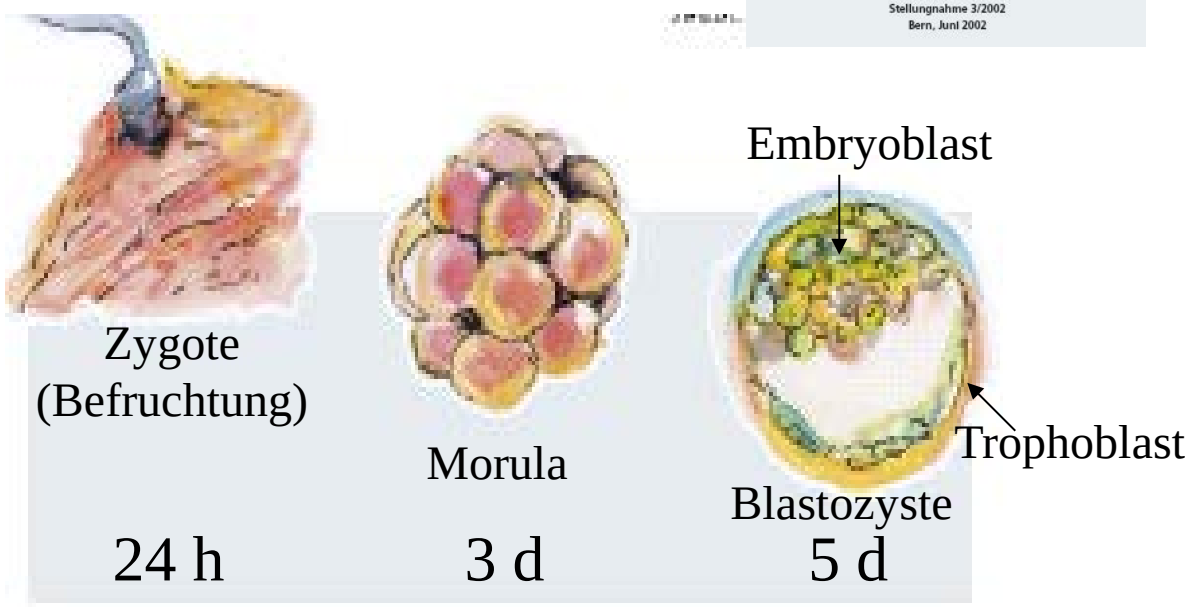
Klinik für Hämatologie

UniversitätsSpital Zürich

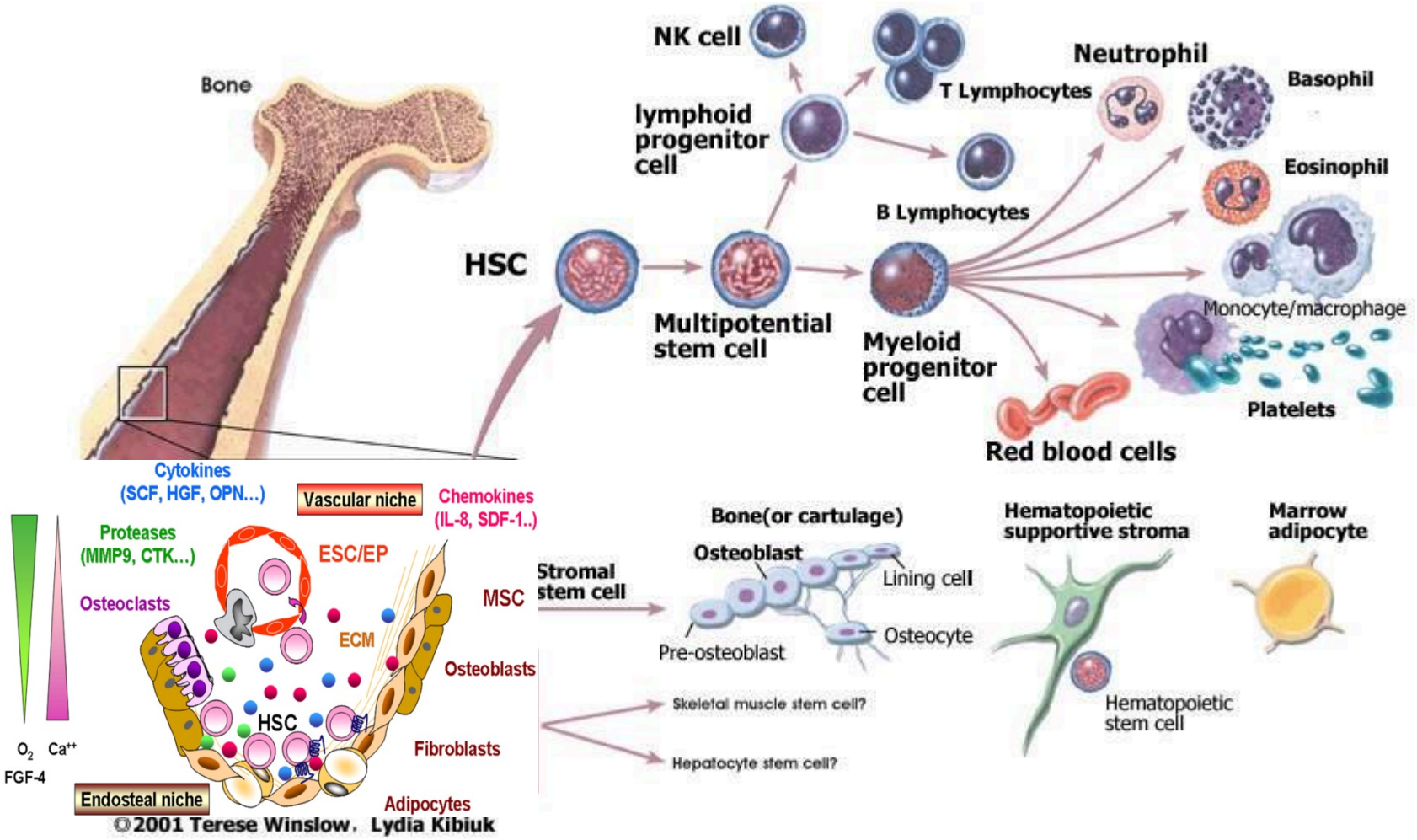
Stammzellen







Adulte Stammzellen



Definition Stammzellen (embryonal und adult)

Stammzellen sind unspezialisierte Zellen mit zwei wichtigen Eigenschaften, die sie von den übrigen Körperzellen unterscheiden

1. Selbsterneuerung über lange Zeit

2. Differenzierung in spezialisierte Gewebe und Zellen mit spezifischer Funktion

Unterschied: Embryonale und adulte Stammzellen

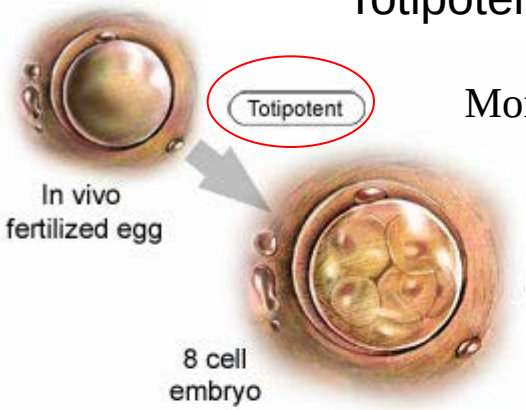
Diffenzierungspotenzial

totipotente Stammzellen

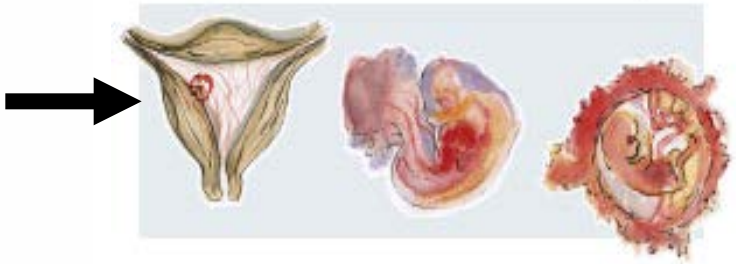
pluripotente Stammzellen

multipotente Stammzellen

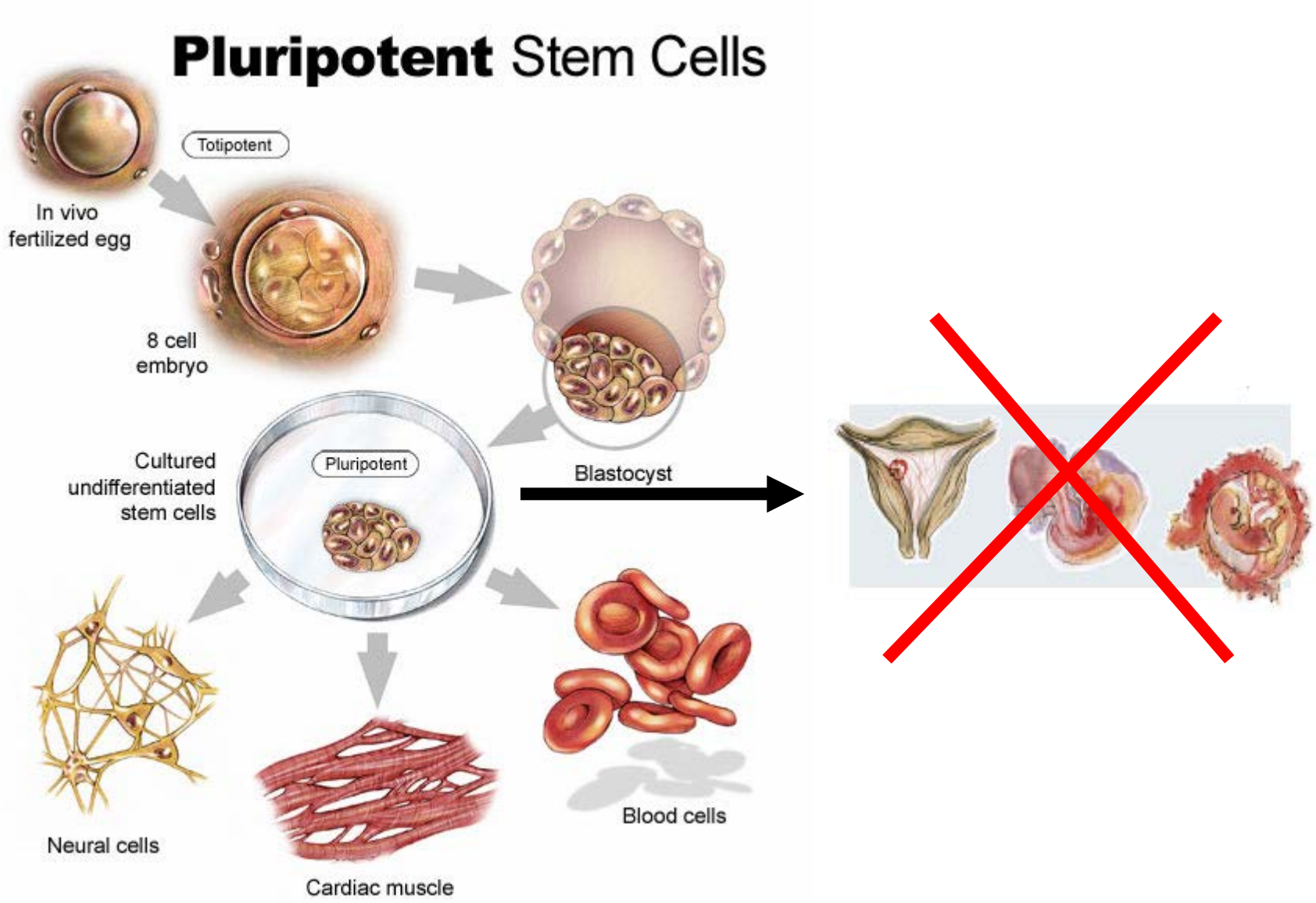
Totipotente Stammzellen



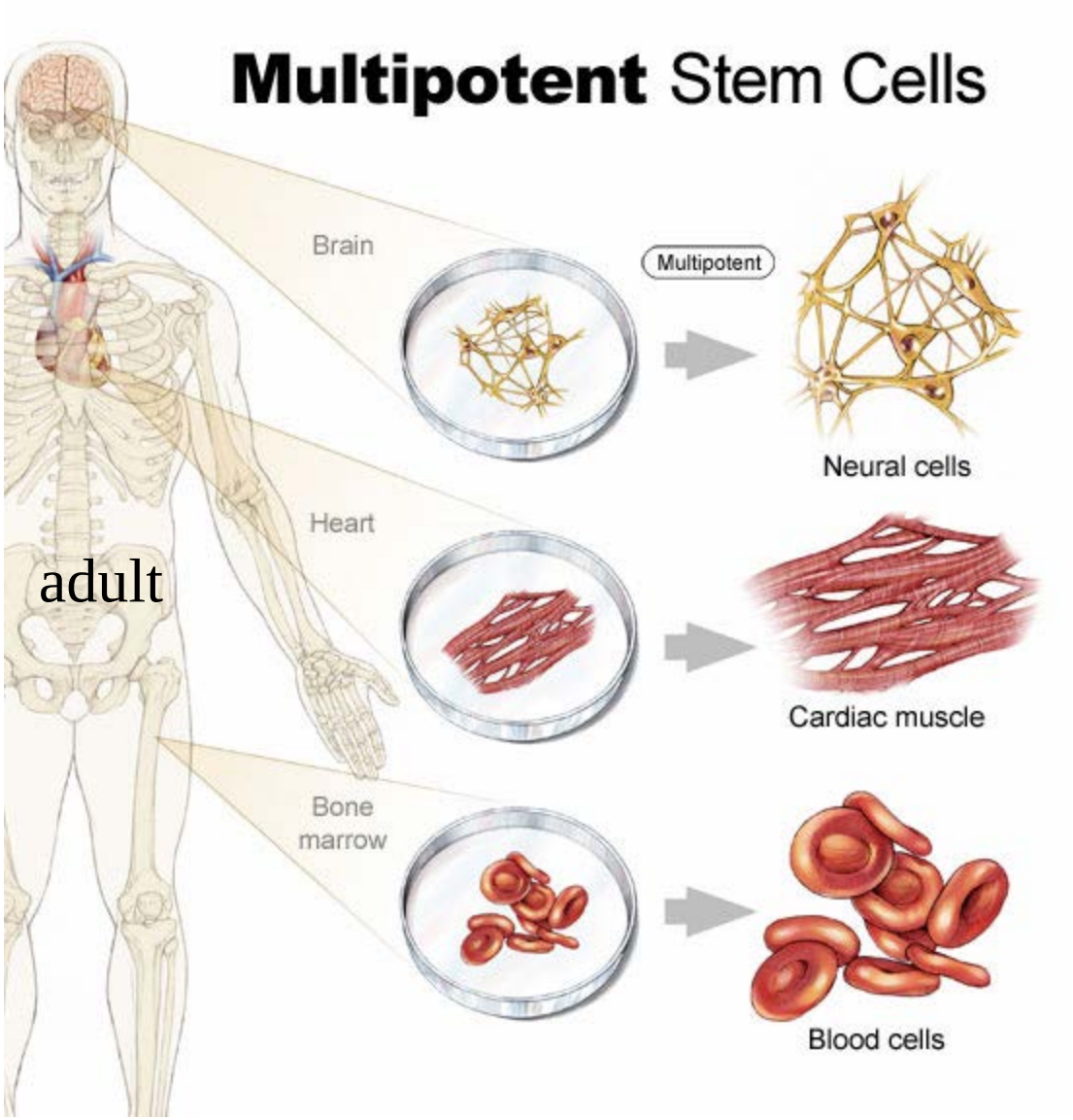
Morula



Gesamt Organismus



Verschiedene Organe und Gewebe



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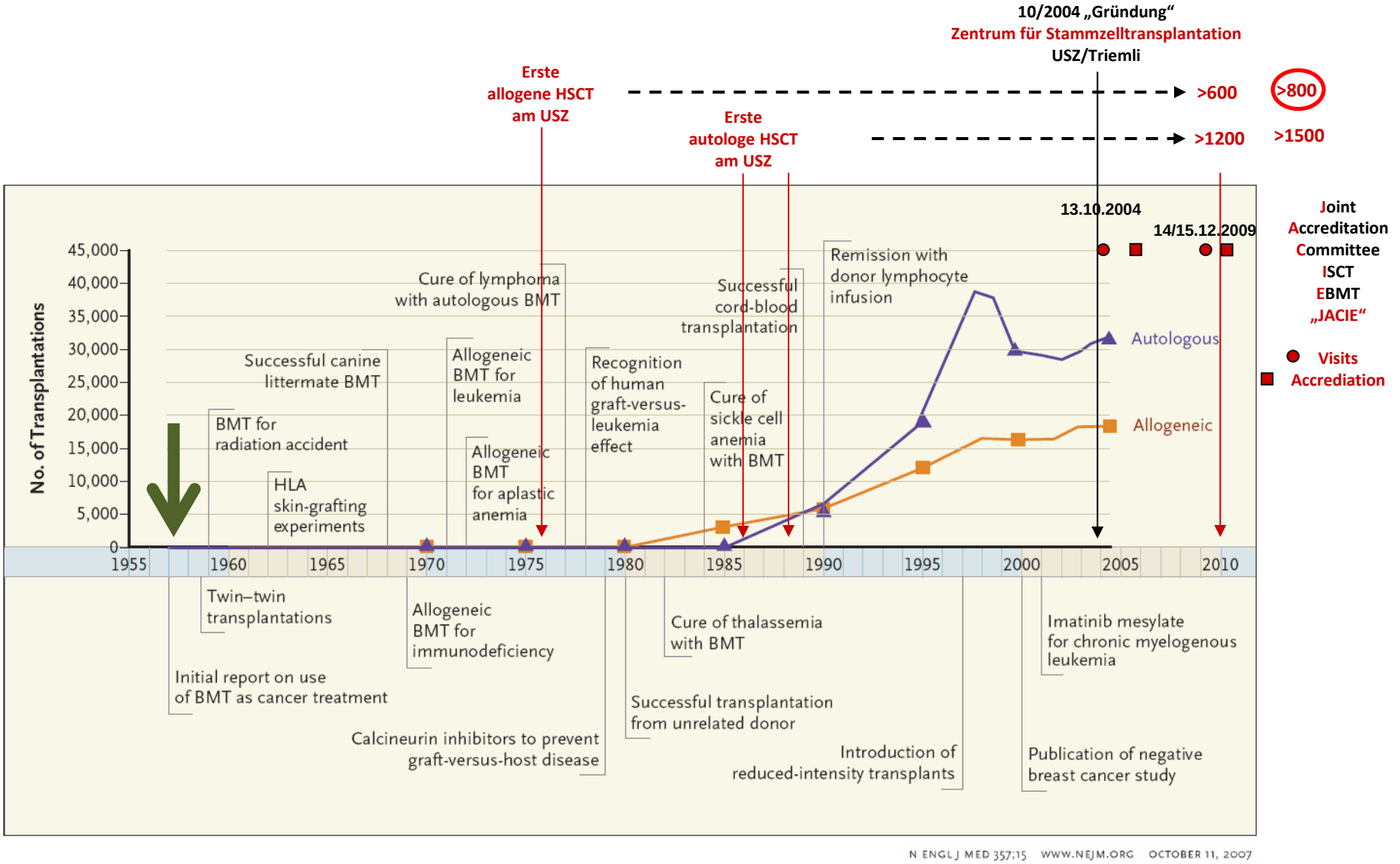
Ein Organ oder Gewebe

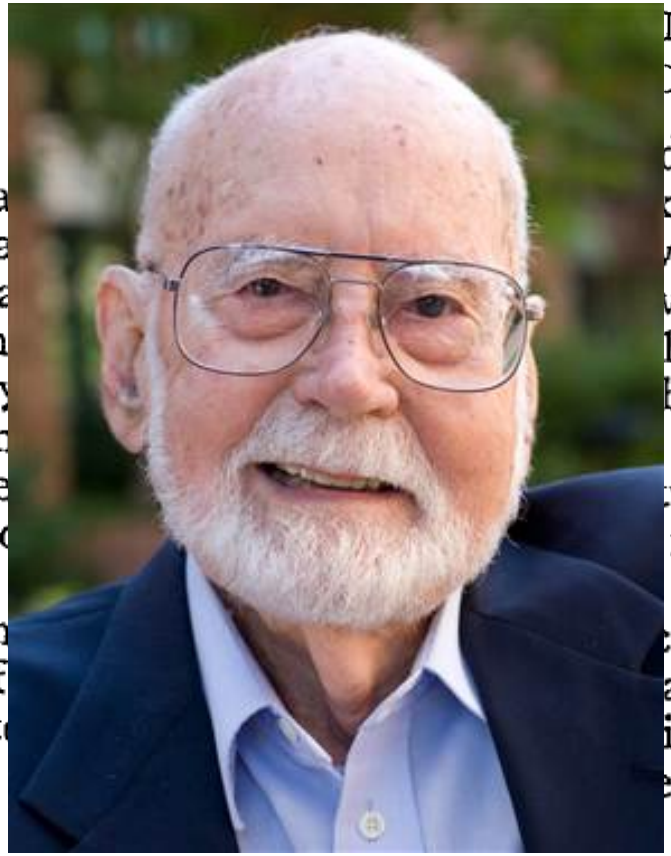
Geschichte der Zürcher Stammzelltransplantation



N ENGL J MED 357;15 WWW.NEJM.ORG OCTOBER 11, 2007

INTRAVENOUS INFUSION OF BONE MARROW IN PATIENTS RECEIVING RADIATION AND CHEMOTHERAPY*

E. DONNALL THOMAS, D.,‡ WAN CHING LU, PH.D.,§ D.¶



CASE
leukemia d chronic myelogenous
leran) a k-rays, busulfan (My-
in the la vent downhill rapidly
infection ver, anemia, bleeding,
pital day 1st, 22d and 23d hos-
kv, 5 m body irradiation (250
was give on the 23d day he
died. Pe y-four hours later he
marrow no evidence of bone-

The m came from the 4 long
bones of arrow was removed 1
hour aft il given to the patient
9 hours ed marrow cells were
given.

NEJM 1957

A COMPENDIUM OF REPORTED HUMAN BONE MARROW TRANSPLANTS[1]

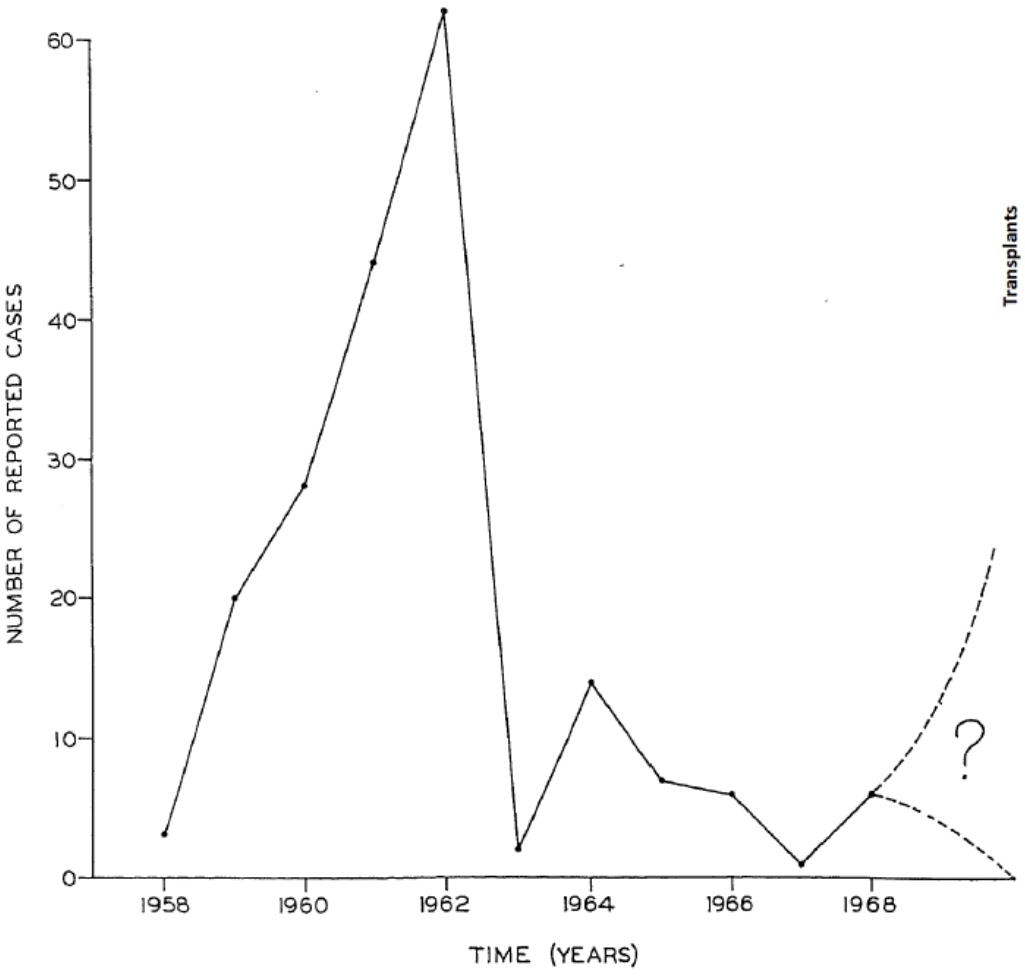
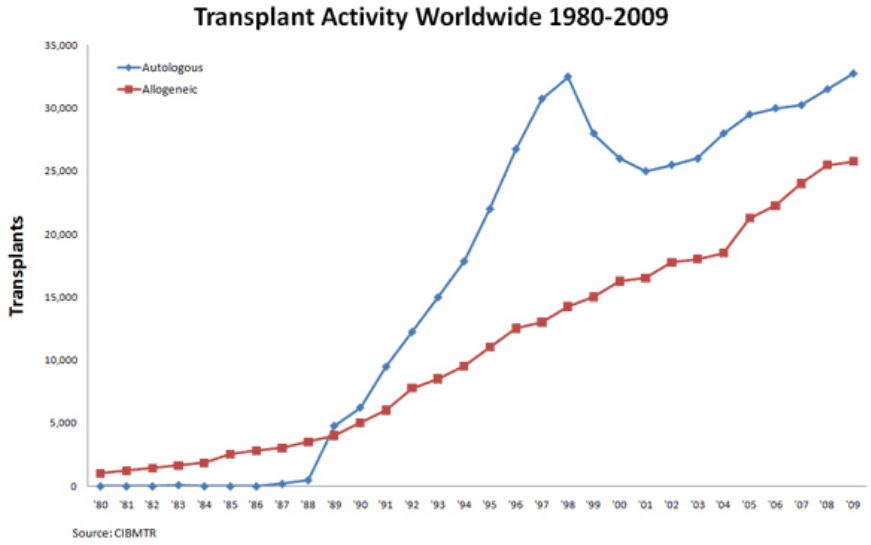
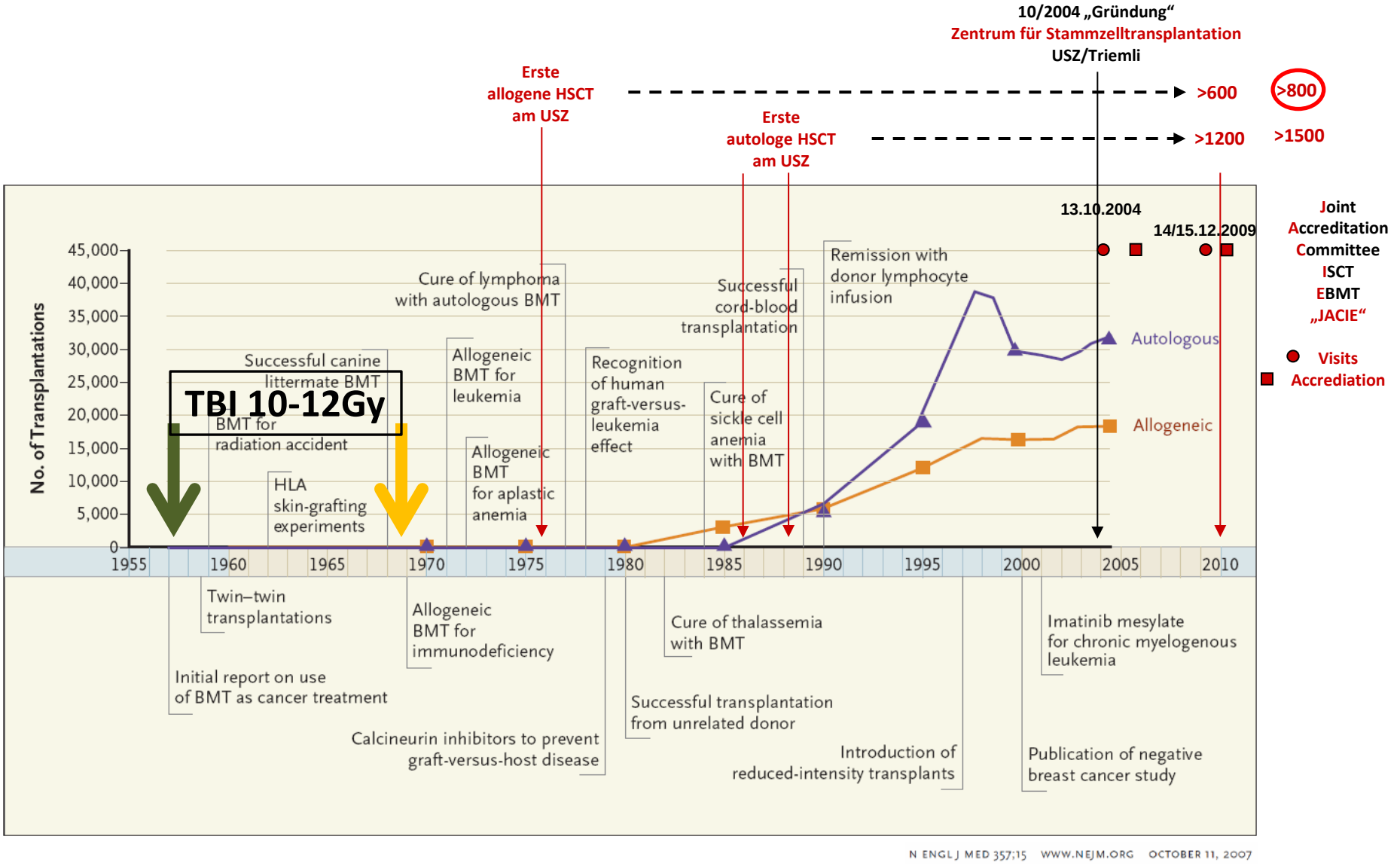


FIGURE 1. Reported human bone marrow transplants from 1958 to 1968.



TRANSPLANTATION

Geschichte der Stammzelltransplantation



N ENGL J MED 357;15 WWW.NEJM.ORG OCTOBER 11, 2007

IMMUNOLOGICAL RECONSTITUTION OF SEX-LINKED LYMPHOPENIC IMMUNOLOGICAL DEFICIENCY

RICHARD A. GATTI
M.D. St. Louis
RESEARCH FELLOW

HILAIRE J. MEUWISSEN
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RESEARCH FELLOW

HUGH D. ALLEN
M.D. Cincinnati
PEDIATRIC RESIDENT

RICHARD HONG
M.D. Illinois
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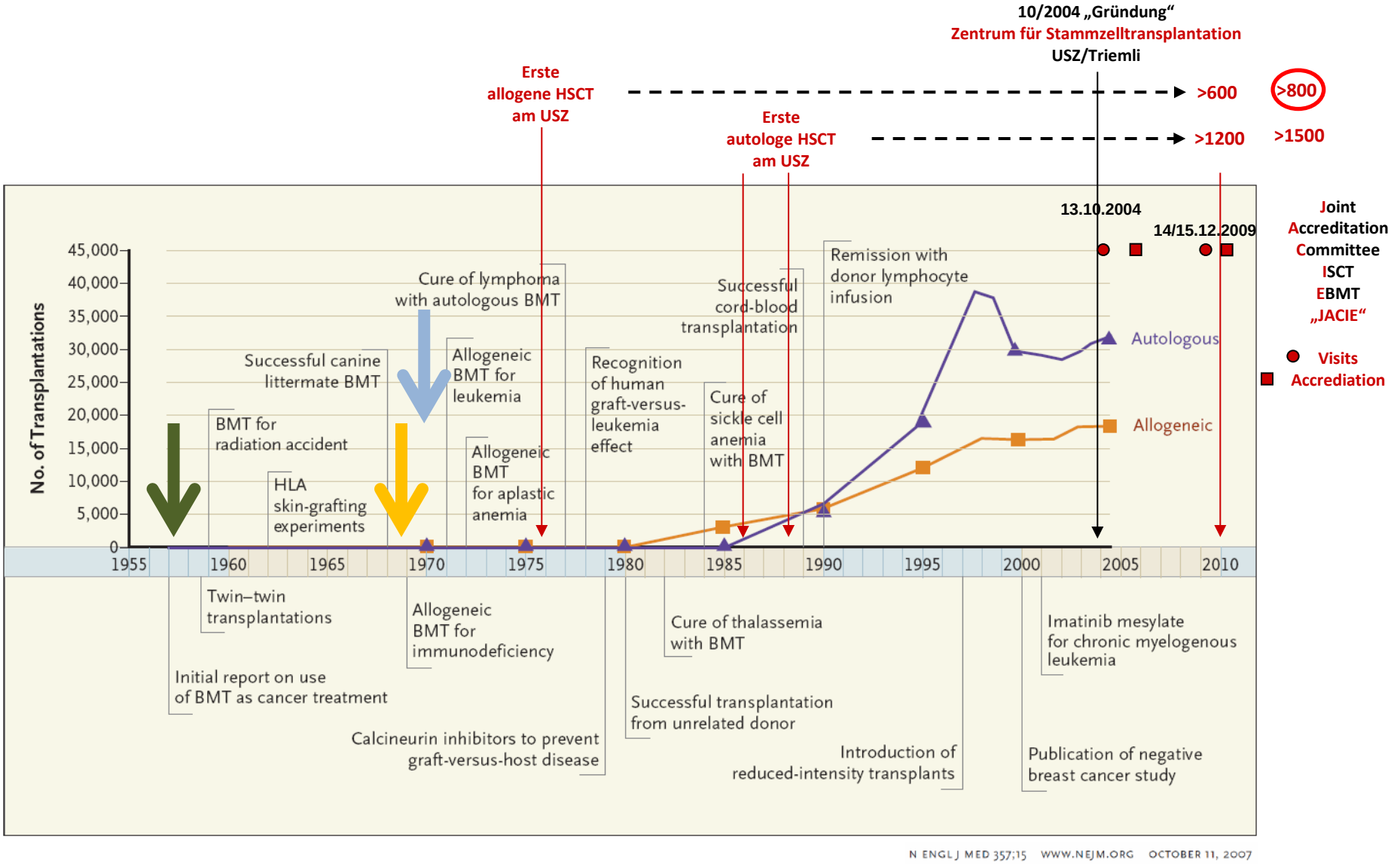
ROBERT A. GOOD
M.D., Ph.D. Minneapolis
AMERICAN LEGION MEMORIAL HEART RESEARCH PROFESSOR OF PEDIATRICS AND MICROBIOLOGY

Summary Treatment of a 5-month-old male with sex-linked lymphopenic immunological deficiency utilising immunologically competent cells from peripheral blood buffy coat and bone-marrow of a sibling donor resulted in reconstitution of both cellular and humoral immunity. Fatal graft-versus-host disease was compatible with the patient's cells with respect to the HL-A locus, as determined by both mixed lymphocyte cultures and lymphocytotoxic assay. A mild graft-versus-host reaction appeared at 8 days post-implantation but resolved spontaneously. Biopsies of rectal mucosa and skin indicate a continuing round-cell infiltration of host tissue 2 months post-implantation; the patient, however, remains clinically well.

Geschichte der Stammzelltransplantation



N ENGL J MED 357;15 WWW.NEJM.ORG OCTOBER 11, 2007

Allogeneic Marrow Engraftment Following Whole Body Irradiation in a Patient with Leukemia

C. DEAN BUCKNER, ROBERT B. EPSTEIN, ROBERT H. RUDOLPH, REGINALD A. CLIFT, RAINER STORB and E. DONNALL THOMAS

Irradiation

Total body irradiation was administered on March 10, 1969 using opposing ^{60}Co sources. The patient lay on an aluminum stretcher transversely between the two sources which were 400 cm. apart. At the midpoint of the irradiation field, the dose rate in air was 5.8 R./minute and the total dose 1620 R. The tissue/air ratio was calculated to be 0.62 on the basis of an 1100-cm.^{2} field and a 16-cm. tissue depth. A factor of 0.95 was used to convert from R. to rads. Thus, the calculated midline tissue dose was 954 rads. The exposure rate in air was determined by a Victoreen R. meter model 570 with its associated model 553 high-energy 25-R. chamber bearing a recent certification by the Bureau of Standards and checked for constancy against a Victoreen model 540B radium standard just prior to use. The readings were corrected for deviations of atmospheric conditions from those at calibration and for shutter time. Lithium fluoride radioluminescence dosimeters were taped to the patient's skin at various locations. The dosimeters contained dosimetry grade lithium fluoride powder having grain size between 80 and 200 mesh contained in polyethylene having sufficient wall thickness to produce electron equilibrium and sufficient capacity to contain four aliquots of the powder for readout. The largest standard deviation on these readings was three per cent. The results were as follows: forehead 1156 rads, umbilicus 1380 rads, left midiliac crest 1410 rads, right midiliac crest 1515 rads, inner aspect of left thigh 1114 rads, left foot 885 rads.

Two hours before irradiation, the patient was given 100 mg. of pentobarbital and 100 mg. of chlorpromazine. The irradiation lasted approximately five hours and was interrupted for brief intervals on six occasions because of nausea and vomiting. These symptoms ceased at the end of the irradiation. Following completion of the irradiation, the patient was transferred to a regular hospital room and placed on reverse isolation (personnel wore mask, gown and gloves). No attempt was made to sterilize the gastrointestinal tract, and he received the regular hospital diet.

Blood 35(6):741-750 (1970)

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TABLE 1. RESULTS OF CYTOTOXICITY TYPING TESTS

			Leukocyte Groups											
	Sex	*Red Cell Type*	*HLA 1*	*HLA 2*	*HLA 3*	*B 4*	*HLA 5*	*HLA 7*	*HLA 8*	*B 9*	*B 11*	*B 6*	*B 10*	*B 12*
Recipient	M	A	−	+	−	−	−	−	−	+	−	−	+	−
Donor	F	A	−	+	−	−	−	−	−	+	−	−	−	−
Father	M	A	−	+	−	−	−	−	−	+	−	−	+	−
Mother	F	A	−	+	−	+	−	−	−	+	−	−	+	−
Sibling	M	A	−	+	−	−	−	−	−	+	−	−	+	−
Sibling	F	O	−	+	−	−	−	−	−	+	−	−	+	−

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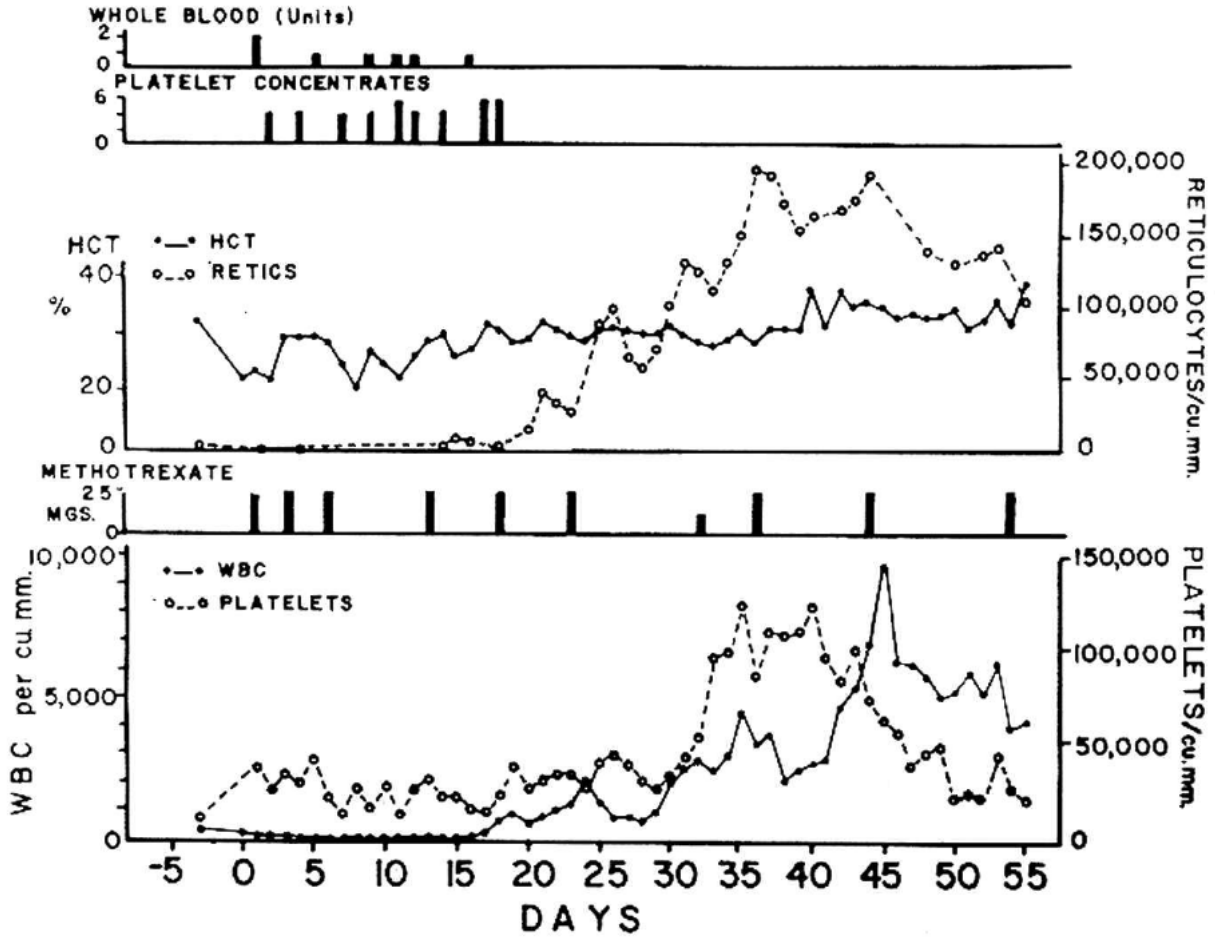

FIG. 1. Hematological events in patient given 950 rads whole-body irradiation and allogeneic bone marrow.

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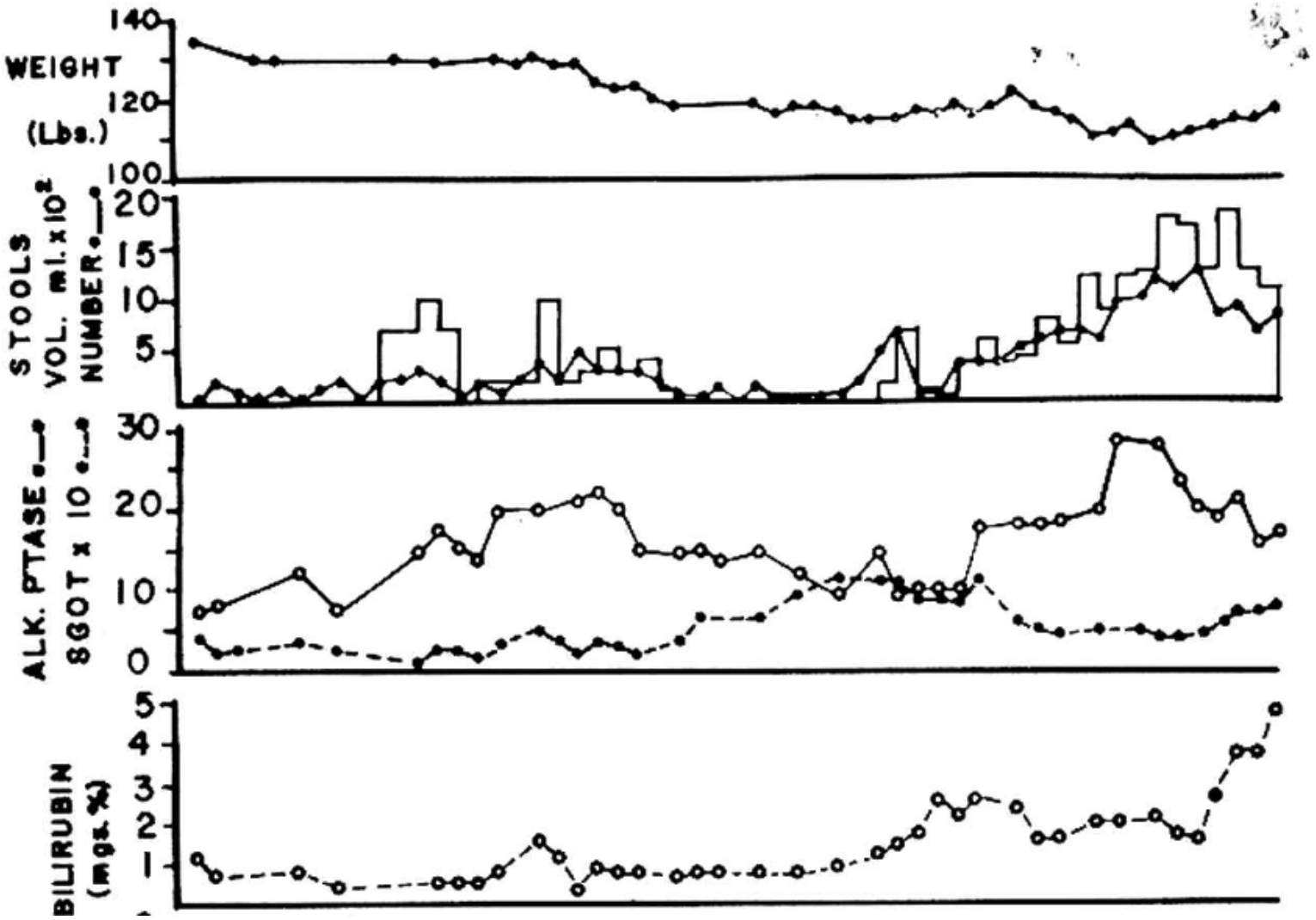

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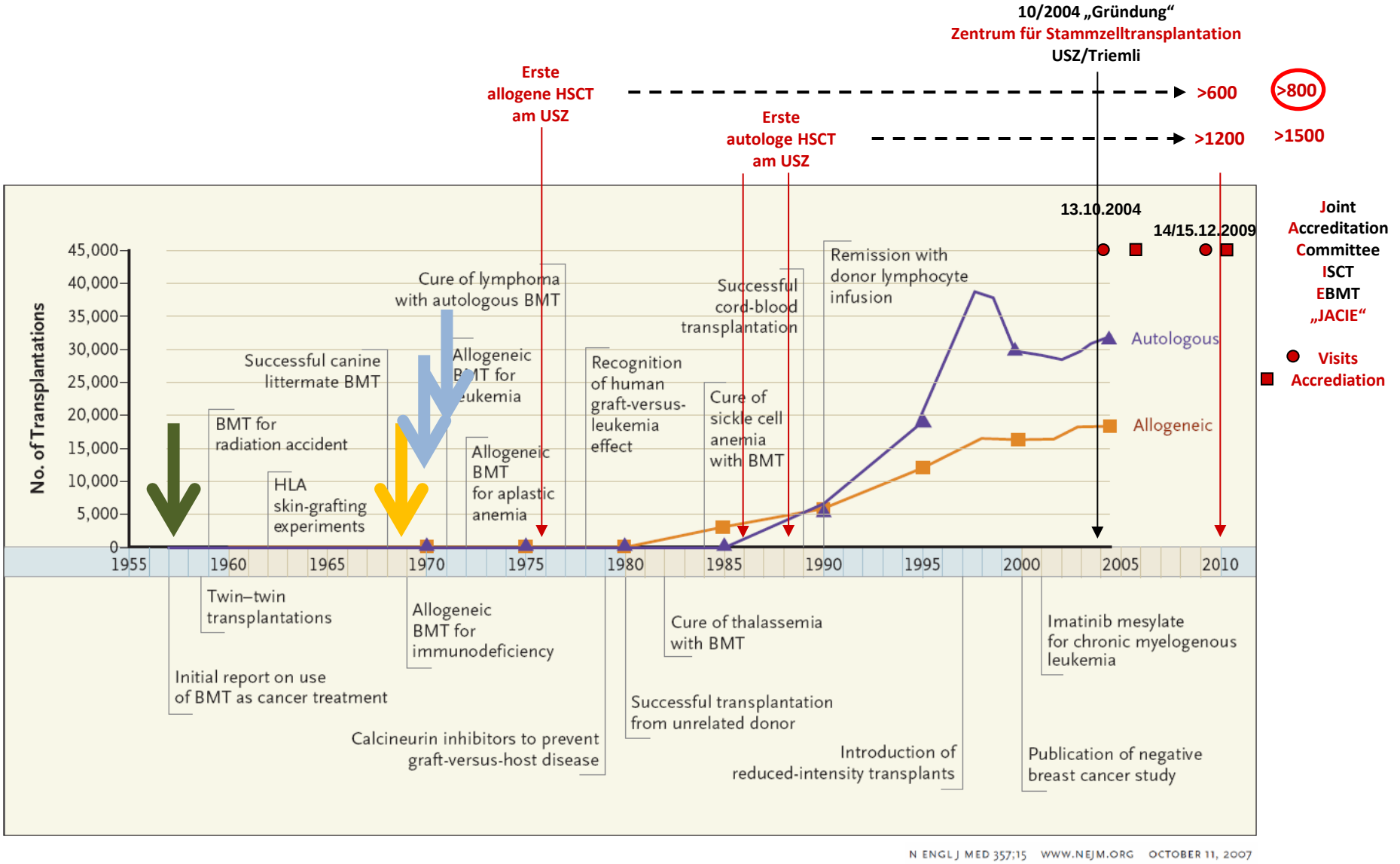
Geschichte der Stammzelltransplantation



N ENGL J MED 357;15 WWW.NEJM.ORG OCTOBER 11, 2007

BLOOD *The Journal of Hematology*

SEPTEMBER, 1971 VOL. XXXVIII, NO. 3

Allogeneic Marrow Grafting for Hematologic Malignancy Using HL-A Matched Donor-Recipient Sibling Pairs

By E. D. Thomas, C. D. Buckner, R. H. Rudolph, A. Fefer, R. Storb, P. E. Neiman, J. I. Bryant, R. L. Chard, R. A. Clift, R. B. Epstein, P. J. Fialkow, D. D. Funk, E. R. Giblett, K. G. Lerner, F. A. Reynolds, and S. Slichter

Seven patients with hematologic malignancy refractory to conventional therapy were treated with 1000 rads midpoint tissue dose of whole-body irradiation followed by infusion of marrow from an HL-A matched sibling. Three patients with advanced leukemia showed histologic evidence suggestive of engraftment but the graft did not function and they died after 18, 26, and 30 days. Four patients, three with acute lymphoblastic leukemia and one with Hodgkin's disease, treated while in good clinical condition, showed evidence of a functioning marrow graft within 3 wk. Engraftment was proved by cytogenetic analysis in three cases with donors of the opposite sex. One patient died with graft-vs.-host disease (GVH) after 37 days. The other three had mild to moderate GVH. Two patients showed recurrent leukemia and died after 85 and 102 days. In one of these patients, a girl, the recurrent leukemia was in male donor cells. One patient, a boy, is alive and well after 200 days with only female donor cells in the marrow. He shows no evidence of GVH and, as yet, no leukemia.

Table 4.—Summary of Histocompatibility Typing of Patients and Their Marrow Donors

	Blood Type	Number of Family Members Studied To Determine HL-A Genotype: Parents	Siblings	Children	HL-A Genotype*	Mixed Leukocyte Culture†: Control	Sibling Mixture	Unrelated Mixture
Patient 1	O	2	5	—	2, x/9, 12	639	263	24,906
Donor	O				2, x/9, 12	1,027	883	24,004
Patient 2	A	2	4	—	x, 5/2, 12	2,857	1,867	13,738
Donor A	A				x, 5/2, 12	299	707	51,532
Donor B	A				x, 5/2, 12	457	974	32,894
Patient 3	O	0	9	3	3, —/10, —		Not tested	
Donor ‡	O				3, 7/10, 12	601	3,935	31,017
						384	1,267	7,034
Patient 4	O	2	8	—	2, 5/2, 12	1,423	1,311	7,400
Donor	O				2, 5/2, 12	387	314	15,493
Patient 5	A	2	6	—	9, 12/2, Te55	117	136	2,736
Donor	A				9, 12/2, Te55	350	177	36,541
Patient 6	O	2	3	—	1, Te64/2, 8	737	933	23,218
Donor	O				1, Te64/2, 8	3,572	2,727	47,323
Patient 7	O	2	3	—	1, 8/2, 12	387	318	2,925
Donor	O				1, 8/2, 12	280	310	2,836

* Numerals indicate HL-A designations or Terasaki designations. x = any unknown antigenic group.

† Means of duplicate cultures expressed as counts per minute of tritiated thymidine per culture.

‡ Two tests performed on different days.

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2015

Die allogene Blut-Stammzelltransplantation

Ziel der allogenen Transplantation ist es, bei mittels konventioneller Chemotherapie nur schwer oder nicht heilbaren hämato-onkologischen Erkrankungen, durch eine hochdosierte Chemo- und oder Radiotherapie möglichst viele (maligne) Zellen zu zerstören oder zumindest zu reduzieren.

Die transplantierten Stammzellen dienen als Ersatz des (irreversibel) geschädigten Knochenmarkes

Residuelle Tumorzellen können immunologisch durch den sog. graft versus tumour Effekt des Transplants eliminiert werden.

→ **Heilung**

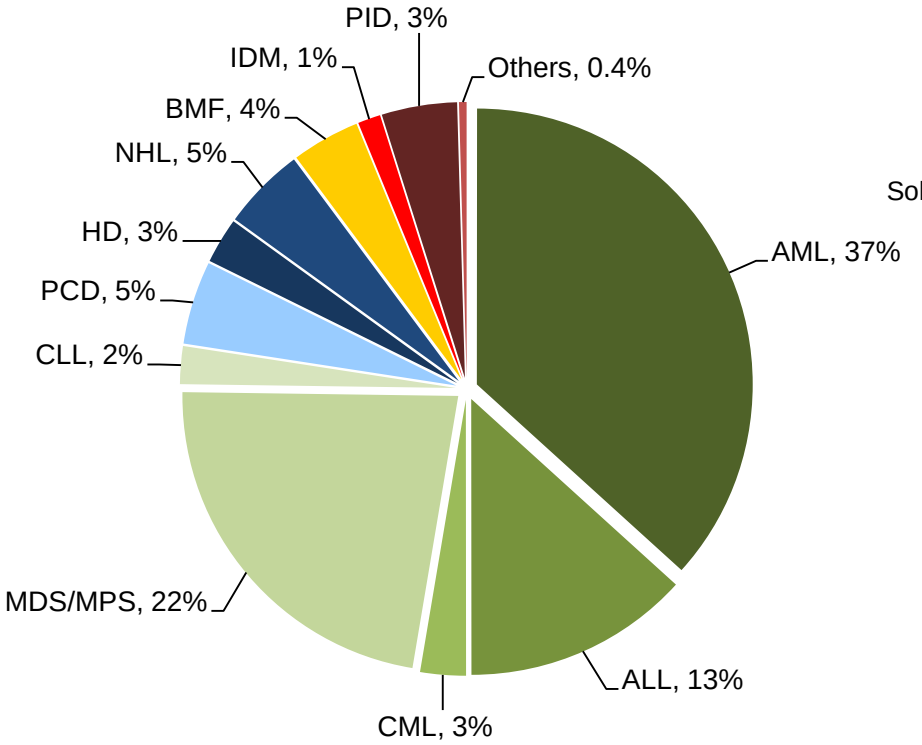
Autologe, syngene und allogene Blut-Stammzelltransplantation

Autolog: Verwendung von eigenen Stammzellen des Patienten

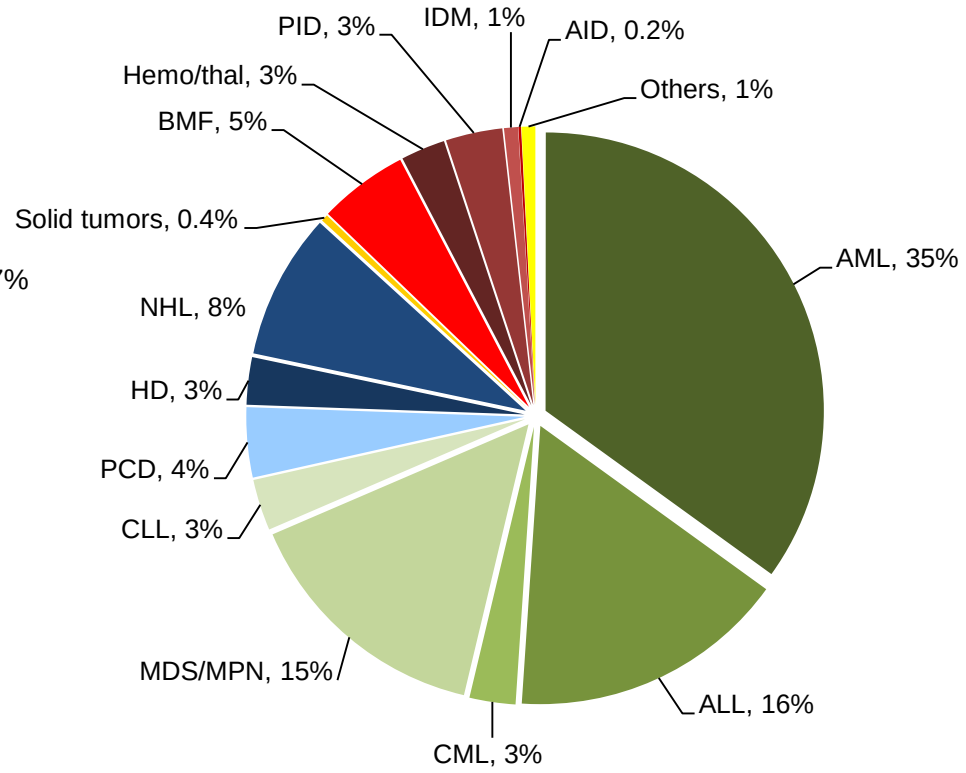
Syngen: Verwendung von Stammzellen eines eineiigen Zwillings

Allogen: Verwendung von Stammzellen eines ‚kompatiblen' Spenders

Indications: Switzerland - Europe



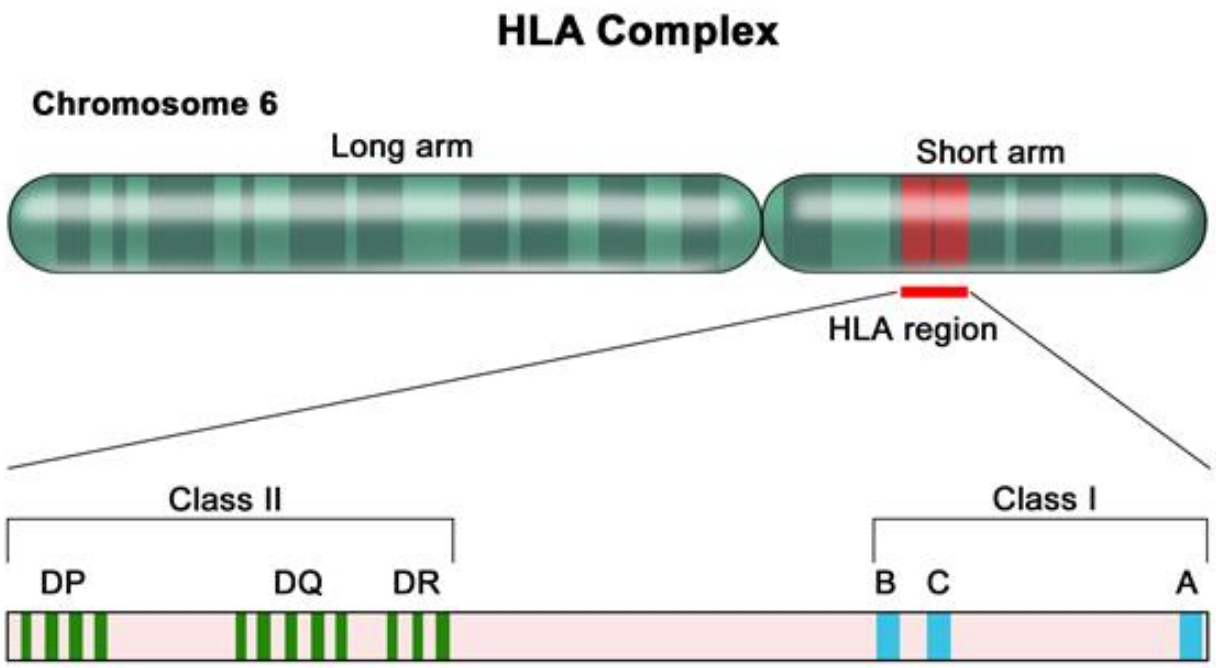
Switzerland 2014



Europe 2013

Data source MedAB database: 2014 final data

Die allogene **Spenderin** / der allogene **Spender**



Theoretisch mehr mögliche HLA-Kombinationen als Menschen auf der Welt leben

Number of Confidential Alleles										5
HLA Class I										
Gene	A	B								
Alleles	3,285	4,077								
Proteins	2,313	3,011								
Nulls	153	128								
Gene	H	J							X	Y
Alleles	12	9							0	3
Proteins	0	0							0	0
Nulls	0	0							0	0
Gene	DRA	DRB							DOB	
Alleles	7	1,932							13	
Proteins	2	1,412							5	
Nulls	0	47							0	
Gene	DRB1	DRB2								
Alleles	1,825	1								
Proteins	1,335	0								
Nulls	41	0	1	3	2	0	0	0	0	
Other non-HLA Genes										

	HLA-A	HLA-B	HLA-C
Anzahl unterschiedlicher Proteine	1 119	1 601	750
mögliche Kombinationen zweier Proteine eines HLA-Typs	1 251 042	2 561 600	562 500
theoretische Kombinationen aller HLA-Klasse-I-Proteine	$1{,}8 \times 10^{18}$		

	HLA-DR α	HLA-DR β	HLA-DQ α	HLA-DQ β	HLA-DP α	HLA-DP β
Anzahl unterschiedlicher Proteine	2	738	26	103	16	127
mögliche Kombinationen zweier α- und zweier β-Ketten eines HLA-Typs	1 087 812		6 828 900		3 840 480	
theoretische Kombinationen aller HLA-Klasse-II-Proteine	$2{,}8 \times 10^{19}$					

Gesamtzahl aller möglichen HLA-Proteinkombinationen (Klasse I × Klasse II)	5×10^{37}

Aufgrund unterschiedlicher Häufigkeiten der einzelnen Allele besteht jedoch eine 70-80%ige Chance einen Spender zu finden

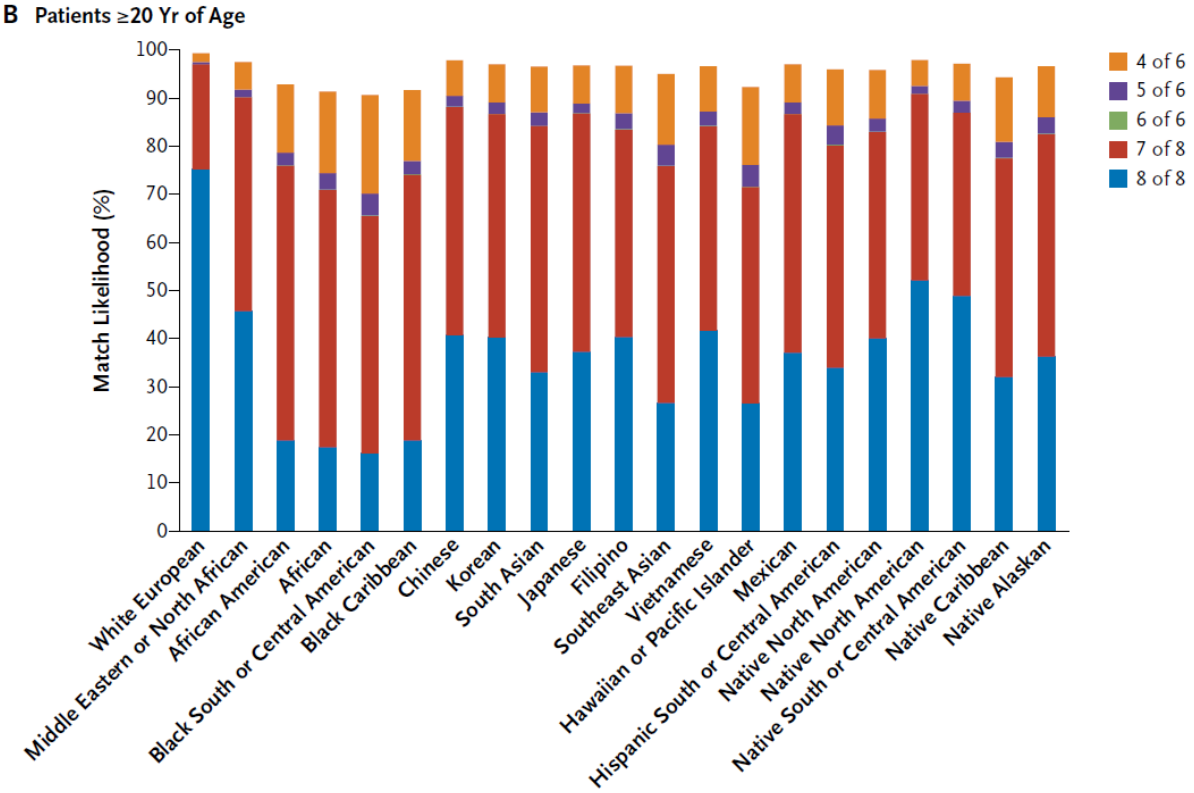
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

HLA Match Likelihoods for Hematopoietic Stem-Cell Grafts in the U.S. Registry

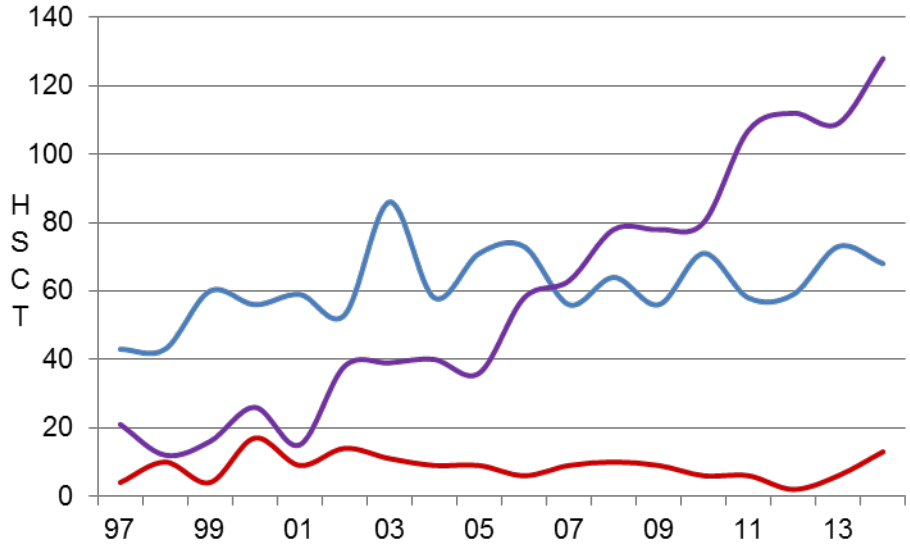
Loren Gragert, B.S., B.A., Mary Eapen, M.B., B.S., Eric Williams, Ph.D., John Freeman, B.S., Stephen Spellman, M.B.S., Robert Baitty, M.P.P., Robert Hartzman, M.D., J. Douglas Rizzo, M.D., Mary Horowitz, M.D., Dennis Confer, M.D., and Martin Maiers, B.A.

N Engl J Med 2014;371:339-48

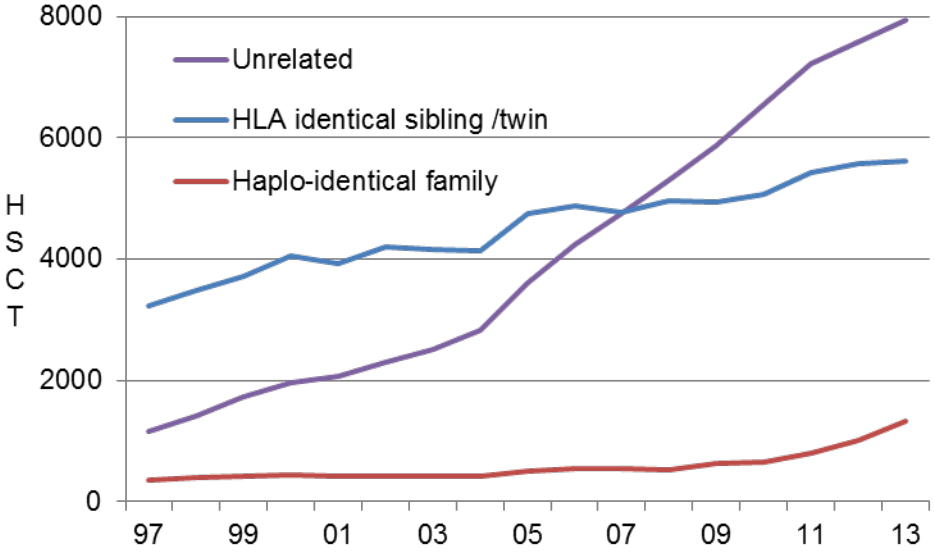


Donor selection: 1st allo HSCT

- Unrelated HSCT exceeded sibling donor HSCT in 2007 in both Europe and CH
- Haplo-identical HSCT started to rise in Europe in 2005
- Switzerland appears to follow later in 2013



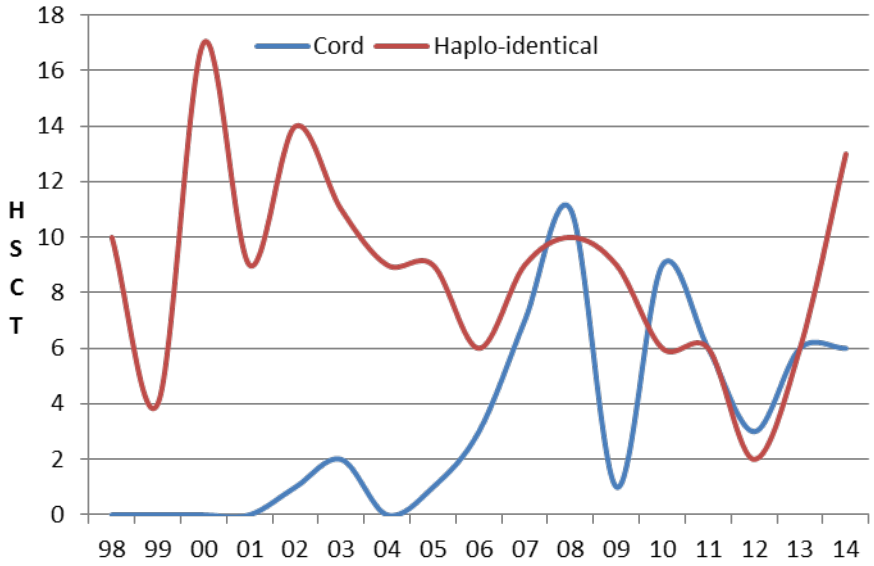
Switzerland 97-2014



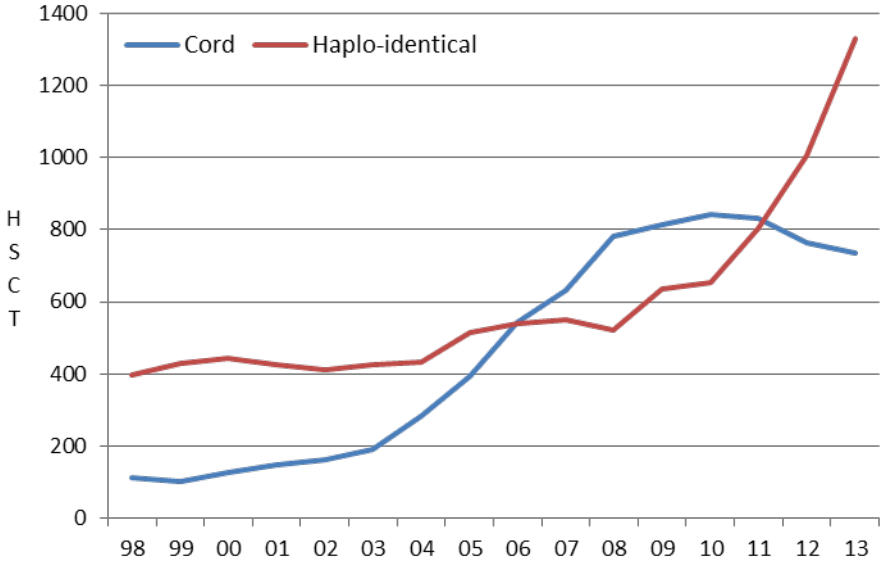
Europe 97-2013

Data source MedAB database: 2014 final data

Unrelated **cord vs haplo-identical**: 1st allo HSCT



Switzerland 98-2014



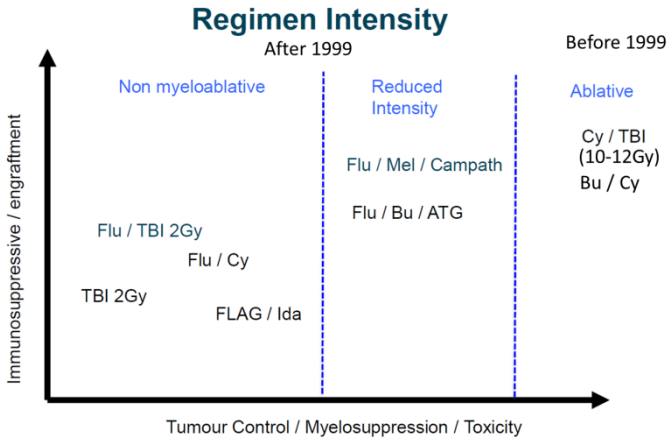
Europe 98-2013

Data source MedAB database: 2014 final data

Ablauf der allogenen Stammzelltransplantation

Konditionierung

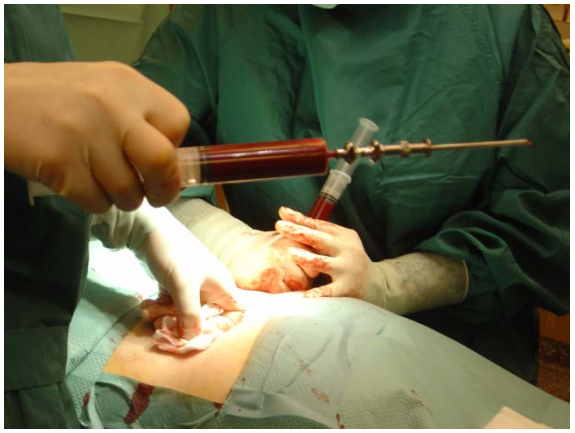
Chemotherapie+/-
Radiotherapie
6 – 10 d

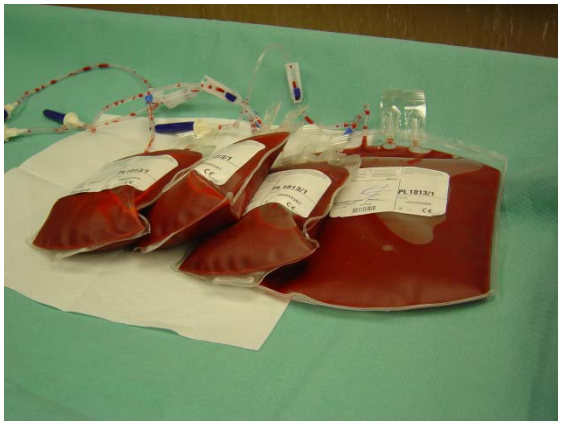


Gewinnung der Stammzellen

Aus dem Knochenmark:

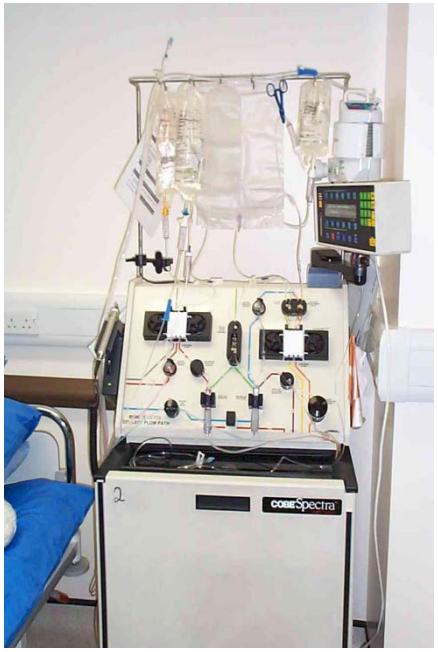
In Narkose wird aus dem Beckenknochen in Narkose durch multiple Punktionen das Blut-Knochenmarkzell-Gemisch (ca. 800 bis 1500ml) gewonnen





Aus dem peripheren Blut:

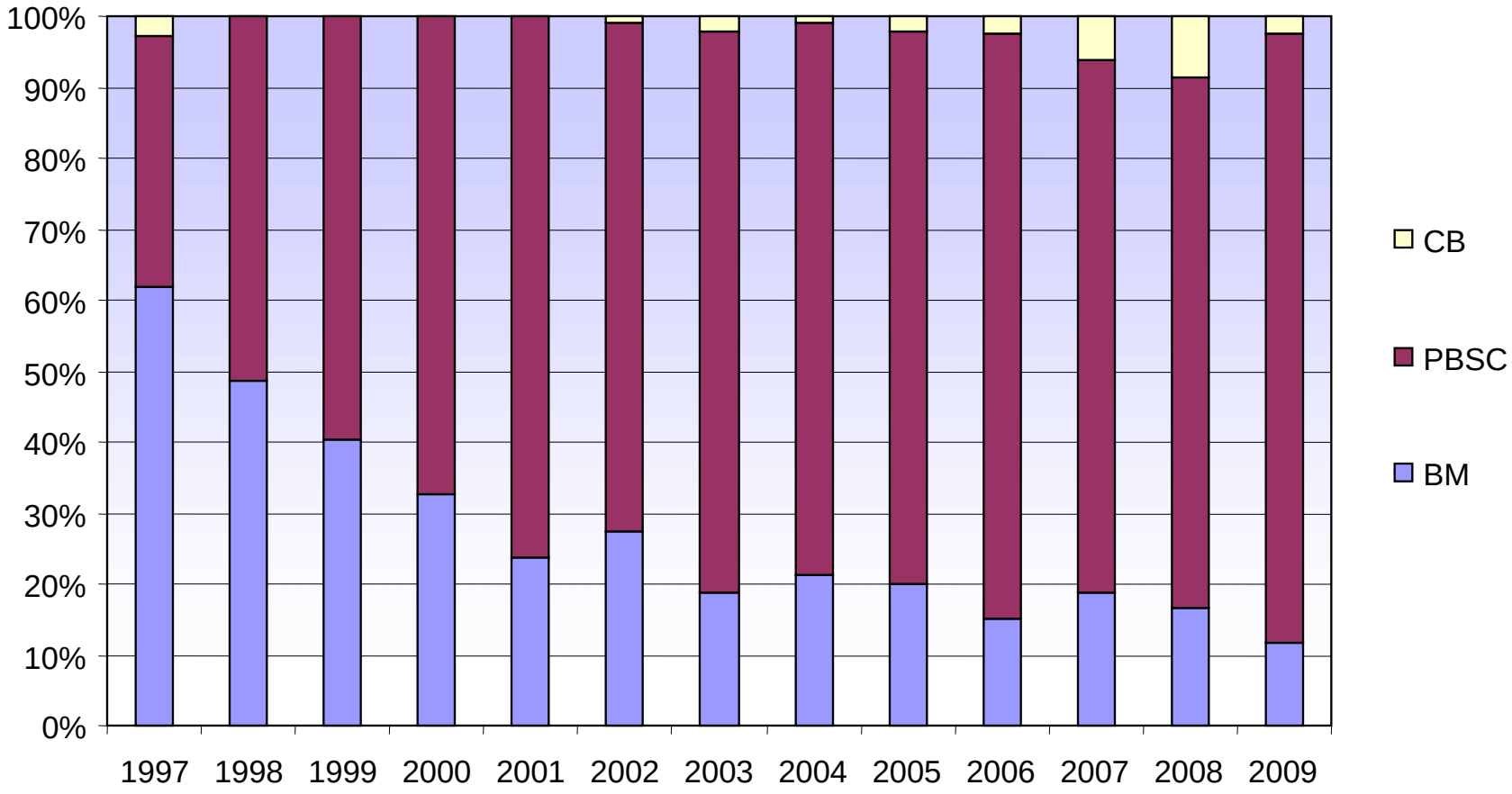
Ohne Narkose werden nach vorgängiger sog. Mobilisation (G-CSF) mittels eines Zellseparators Stammzellen aus dem peripheren Blut gewonnen



Aus dem Nabelschnurblut:

Bei der Geburt wird Nabelschnurblut (40 bis 180ml), welches sehr reich an Stammzellen ist, gewonnen und zum späteren Gebrauch für eine Transplantation eingefroren und bei -196°C gelagert

Proportion of **stem cell source**: 1997 – 2009
Allogeneic HSCT



Ablauf der allogenen Stammzelltransplantation

Konditionierung

Chemotherapie+/-
Radiotherapie
6 – 10 d

Transplantation

Transfusion von
Stammzellen
1 – 3 Std

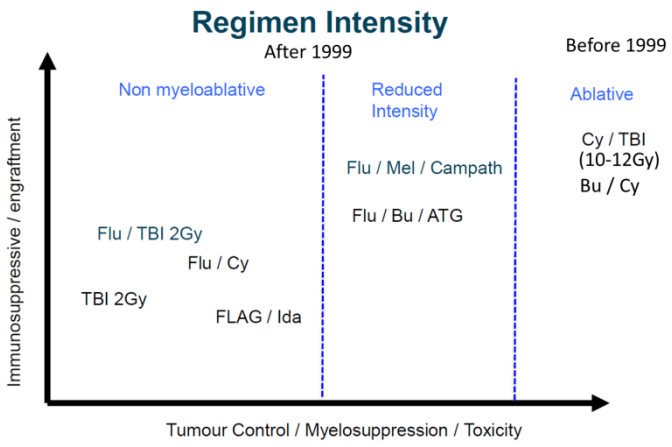
Postranspl. Phase

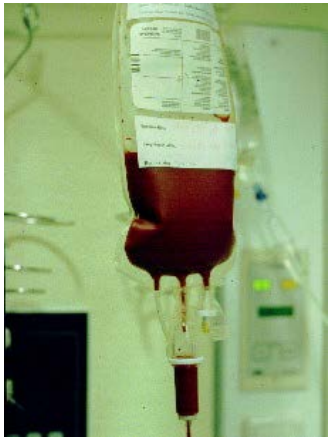
Hämatologische
Rekonstitution
14 – 21 d

Immunsuppression
3 – 6 (-12) Mte

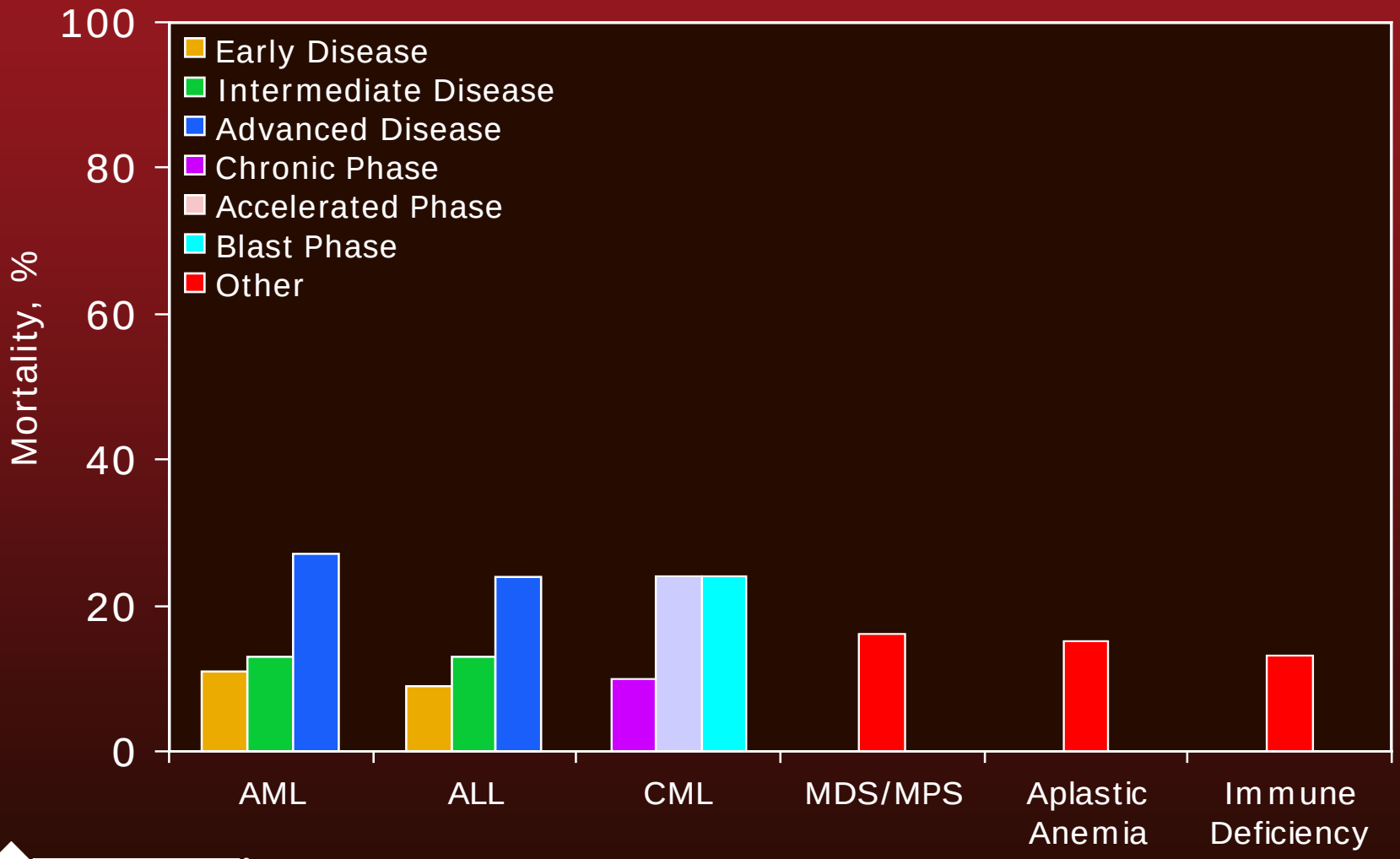
Immunologogische
Rekonstitution
6 – 12 Mte

Komplikationen
(häufig innerhalb von 100d)





100-day Mortality after Unrelated Donor Transplants, 2008-2009



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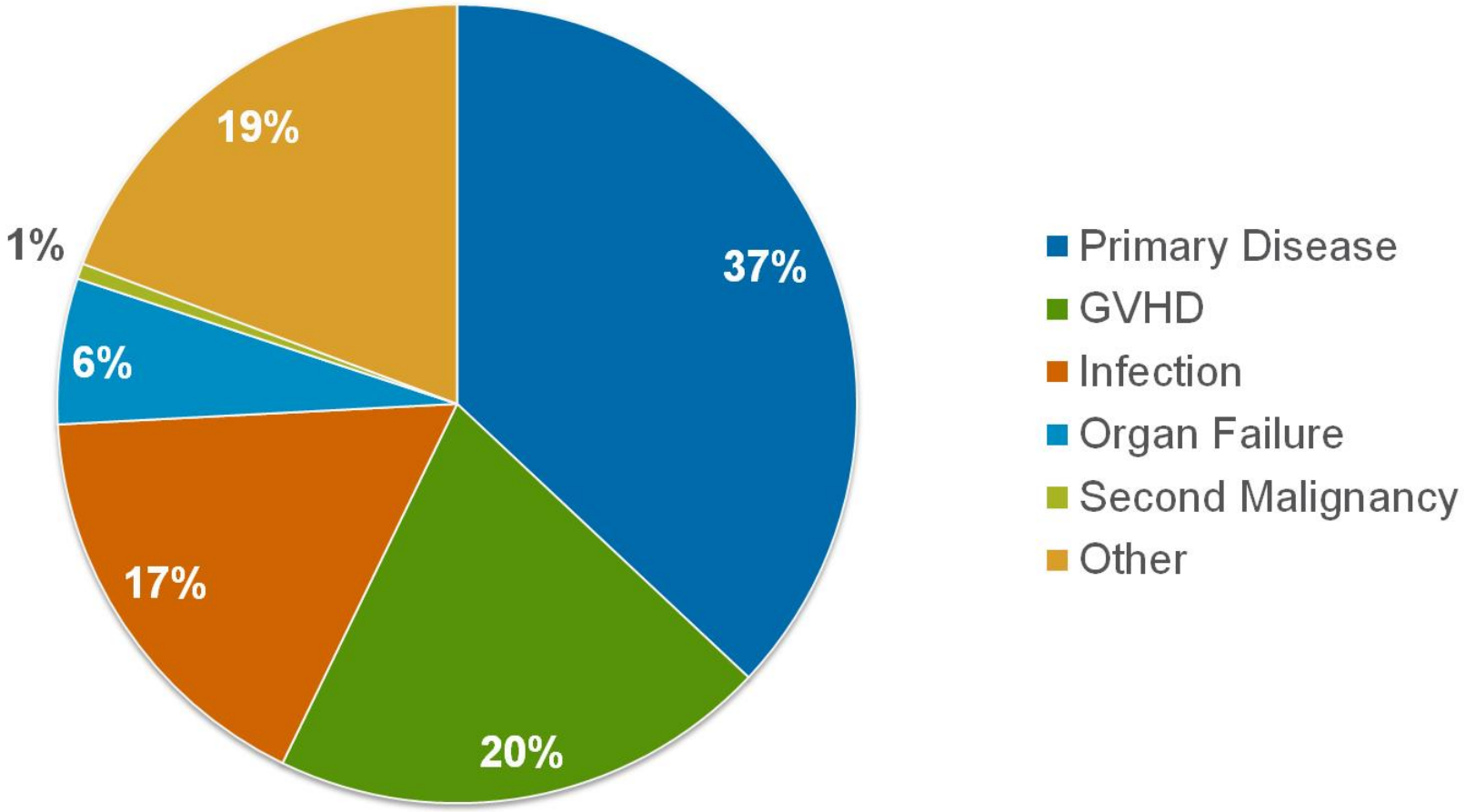
Causes of Death after Unrelated Donor Transplants done in 2011-2012



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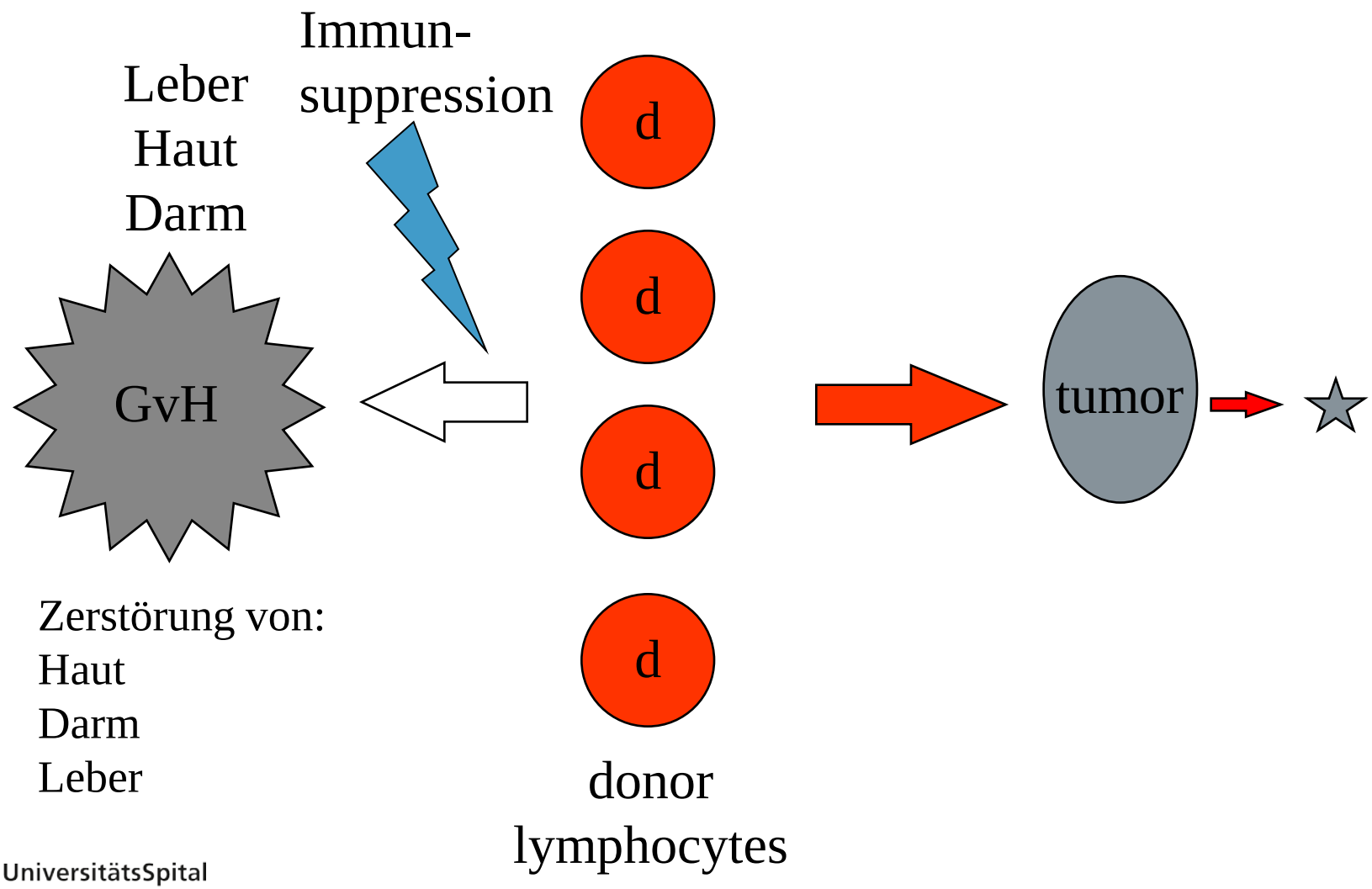
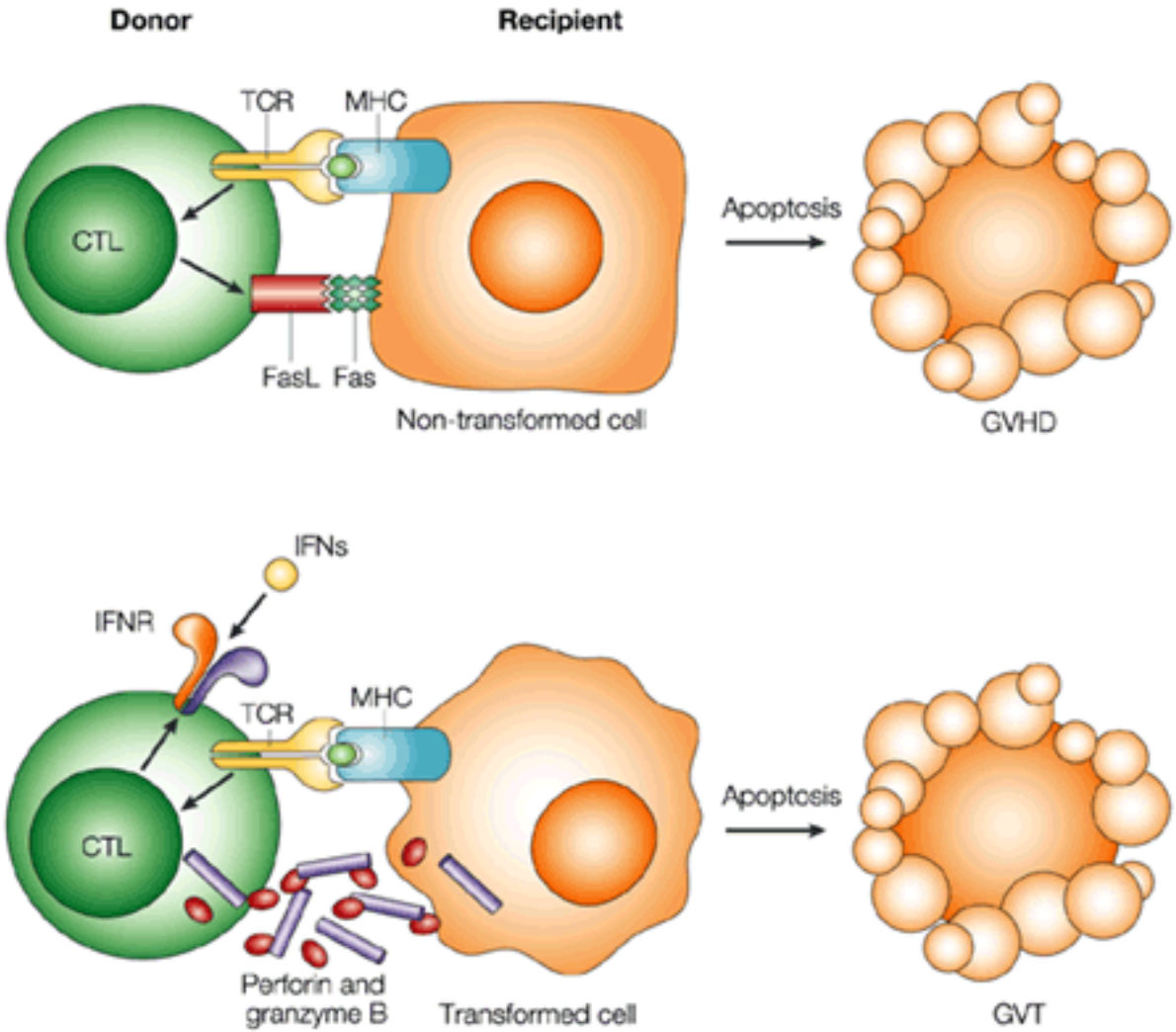
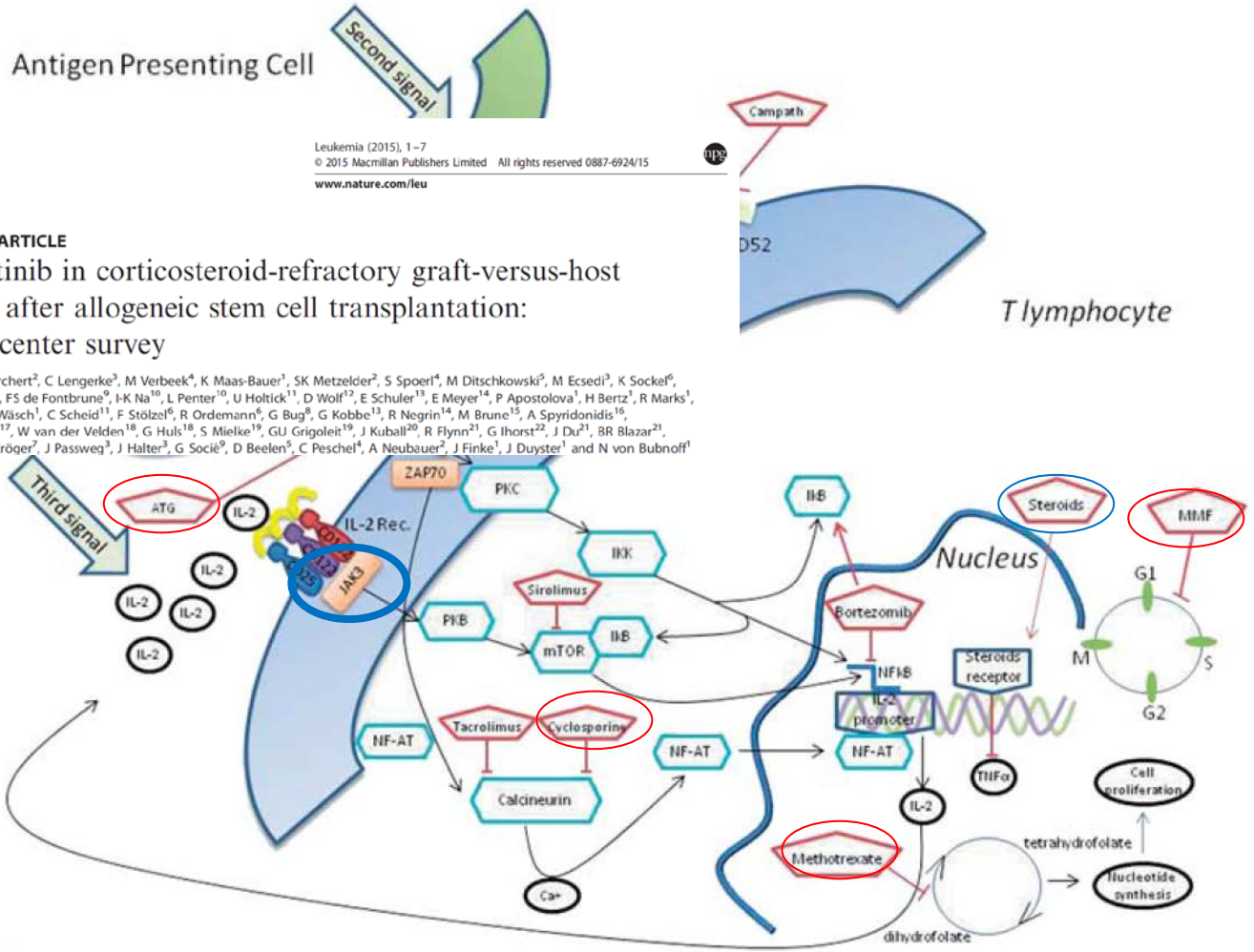
Graft versus host Erkrankung / Graft versus tumour Effekt



Graft versus host Erkrankung / Graft versus tumour Effekt



Nature Reviews | Immunology



Leukemia (2015), 1–7
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www.nature.com/leu

ORIGINAL ARTICLE

Ruxolitinib in corticosteroid-refractory graft-versus-host disease after allogeneic stem cell transplantation: a multicenter survey

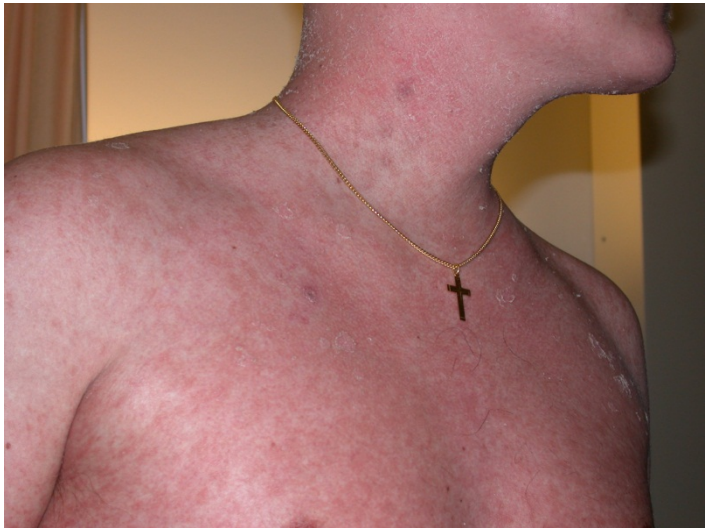
R Zeiser[1], A Burchert[2], C Lengerke[3], M Verbeek[4], K Maas-Bauer[1], SK Metzelder[2], S Spoerl[4], M Ditschkowski[5], M Ecsedi[3], K Sockel[6], F Ayuk[7], S Ajib[8], FS de Fontbrune[9], I-K Na[10], L Penter[10], U Holtick[11], D Wolf[12], E Schuler[13], E Meyer[14], P Apostolova[1], H Bertz[1], R Marks[1], M Lübbert[1], R Wäsch[1], C Scheid[11], F Stölzel[6], R Ordemann[6], G Bug[8], G Kobbe[13], R Negrin[14], M Brune[15], A Spyridonidis[16], A Schmitt-Gräff[17], W van der Velden[18], G Huls[18], S Mielke[19], GJ Grigoleit[19], J Kuball[20], R Flynn[21], G Ihorst[22], J Du[21], BR Blazar[21], R Arnold[10], N Kröger[7], J Passweg[3], J Halter[3], G Socié[9], D Beelen[5], C Peschel[4], A Neubauer[2], J Finke[1], J Duyster[1] and N von Bubnoff[1]

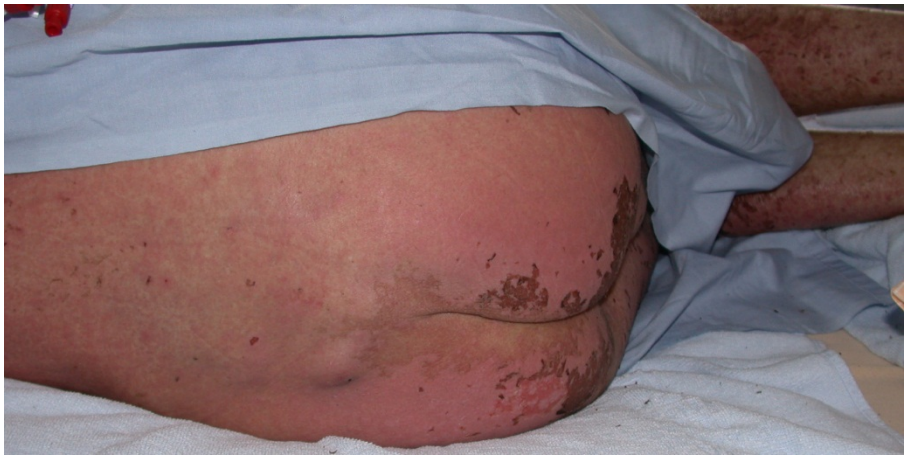
Leukemia & Lymphoma, August 2013; 54(8): 1591–1601

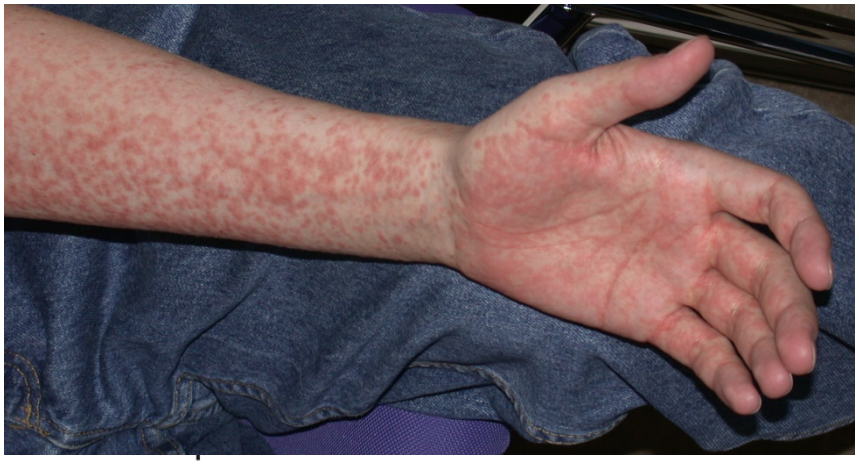
Graft versus host Erkrankung

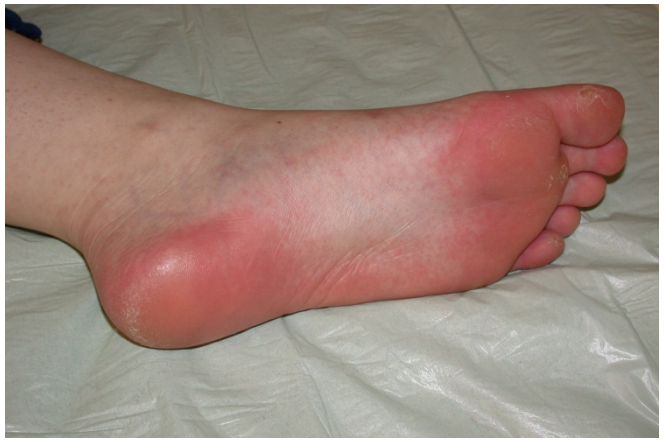
Haut	$\Rightarrow$ Rötung bis Blasenbildung
Leber	$\Rightarrow$ Ikterus
Darm	$\Rightarrow$ Diarrhoe (bis 15 Liter)

GvHD









VOLUME 32 · NUMBER 4 · FEBRUARY 1 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Allogeneic Transplantation Versus Chemotherapy as Postremission Therapy for Acute Myeloid Leukemia: A Prospective Matched Pairs Analysis

Matthias Stelljes, Utz Krug, Dietrich W. Beelen, Jan Braess, Maria C. Sauerland, Achim Heinecke, Sandra Ligges, Tim Sauer, Petra Tschanter, Gabriela B. Thoennissen, Björna Berning, Hans J. Kolb, Albrecht Reichle, Ernst Holler, Rainer Schwerdtfeger, Renate Arnold, Christoph Scheid, Carsten Müller-Tidow, Bernhard J. Woermann, Wolfgang Hiddemann, Wolfgang E. Berdel, and Thomas Büchner

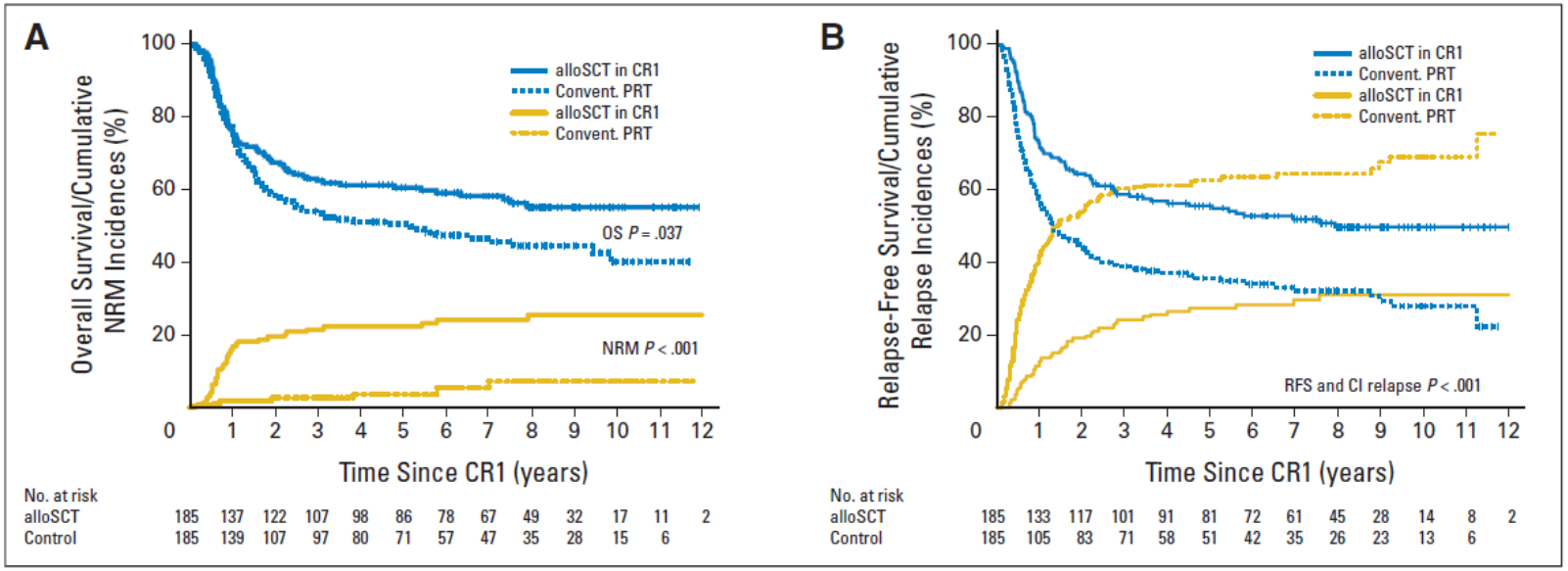
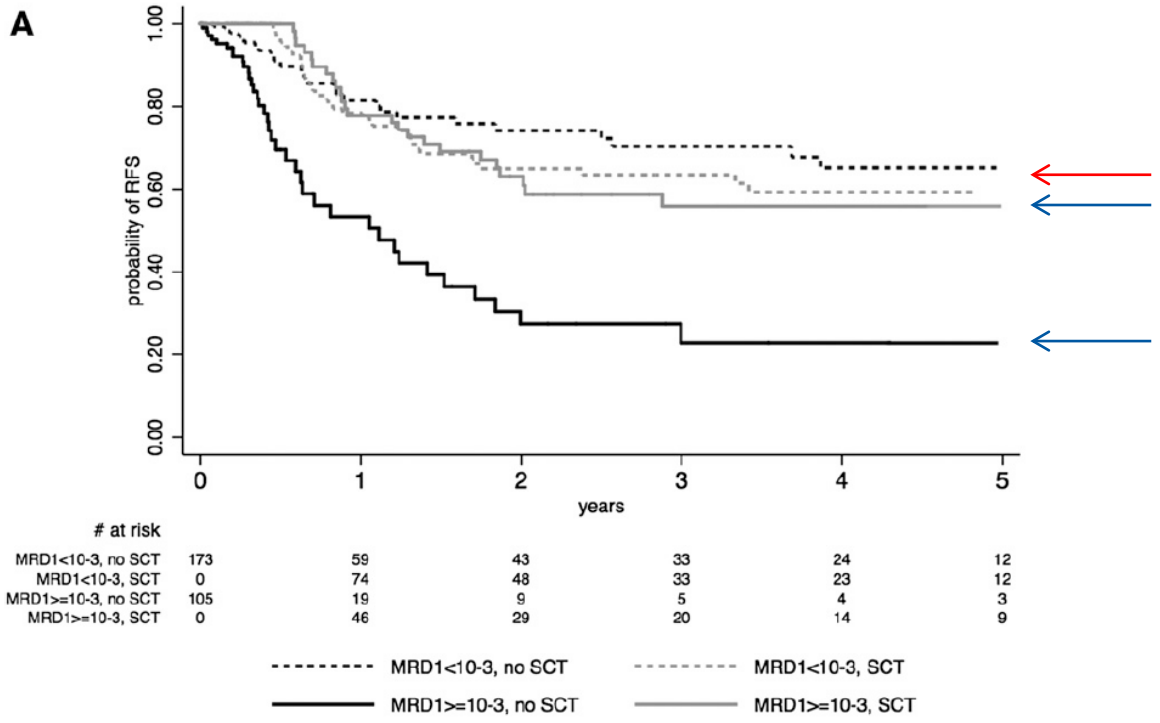


Fig 2. Kaplan-Meier survival estimates and cumulative incidences of nonrelapse mortality (NRM) and relapse according to postremission therapy. Data are shown for (A) overall survival (OS) and cumulative incidences of NRM and (B) relapse-free survival (RFS) and cumulative incidences (CI) of relapse. Gold lines depict cumulative incidences, blue lines survival curves. Tick marks represent (A) patients whose data were censored at the last time they were known to be alive or (B) whose data were censored at the last time they were known to be alive and in complete remission. NRM events for the postremission therapy (PRT) group were deaths in CR1 (first complete remission). alloSCT, allogeneic stem-cell transplantation; convent. PRT, conventional PRT.

Role of allogeneic stem cell transplantation in adult patients with Ph-negative acute lymphoblastic leukemia

Nathalie Dhédin,[1] Anne Huynh,[2] Sébastien Maury,[3] Reza Tabrizi,[4] Kheira Beldjord,[1] Vahid Asnafi,[5] Xavier Thomas,[6] Patrice Chevallier,[7] Stéphanie Nguyen,[8] Valérie Coiteux,[9] Jean-Henri Bourhis,[10] Yosr Hichri,[11] Martine Escoffre-Barbe,[12] Oumedaly Reman,[13] Carlos Graux,[14] Yves Chalandon,[15] Didier Blaise,[16] Urs Schanz,[17] Véronique Lhéritier,[18] Jean-Yves Cahn,[19] Hervé Dombret,[1] and Norbert Ifrah,[20] on behalf of the GRAALL group

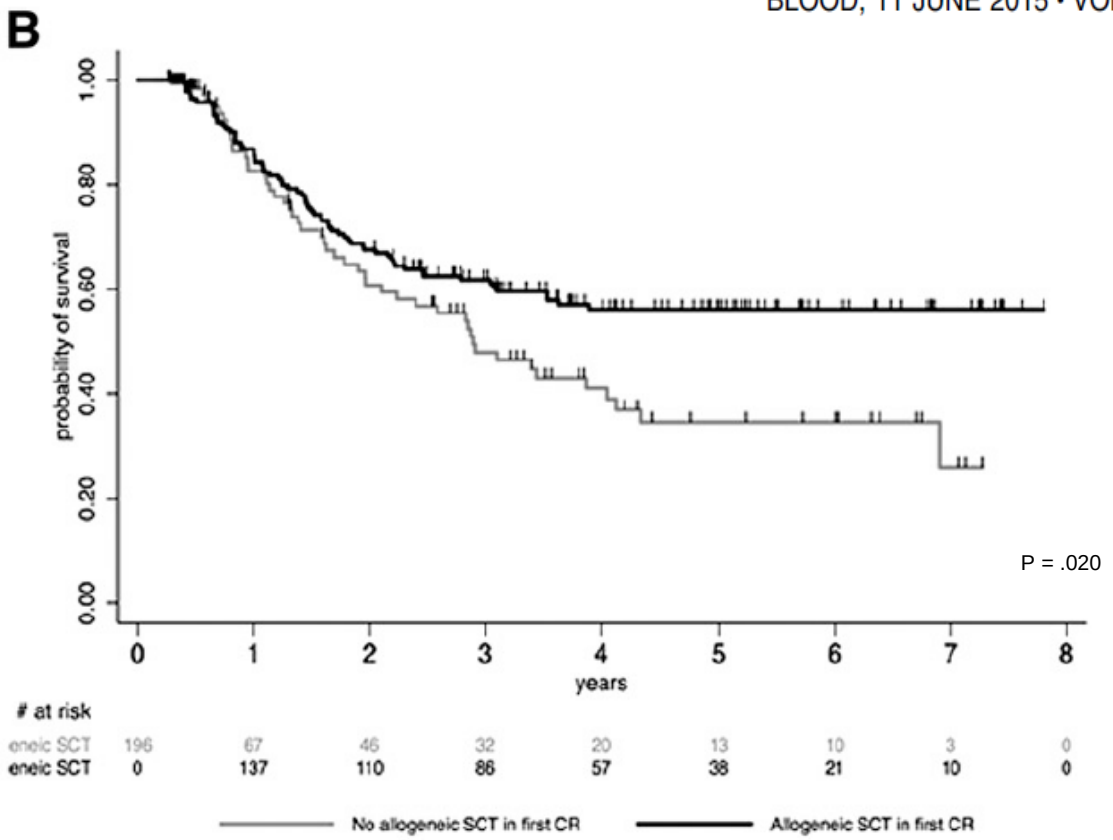


BLOOD, 16 APRIL 2015 • VOLUME 125, NUMBER 16

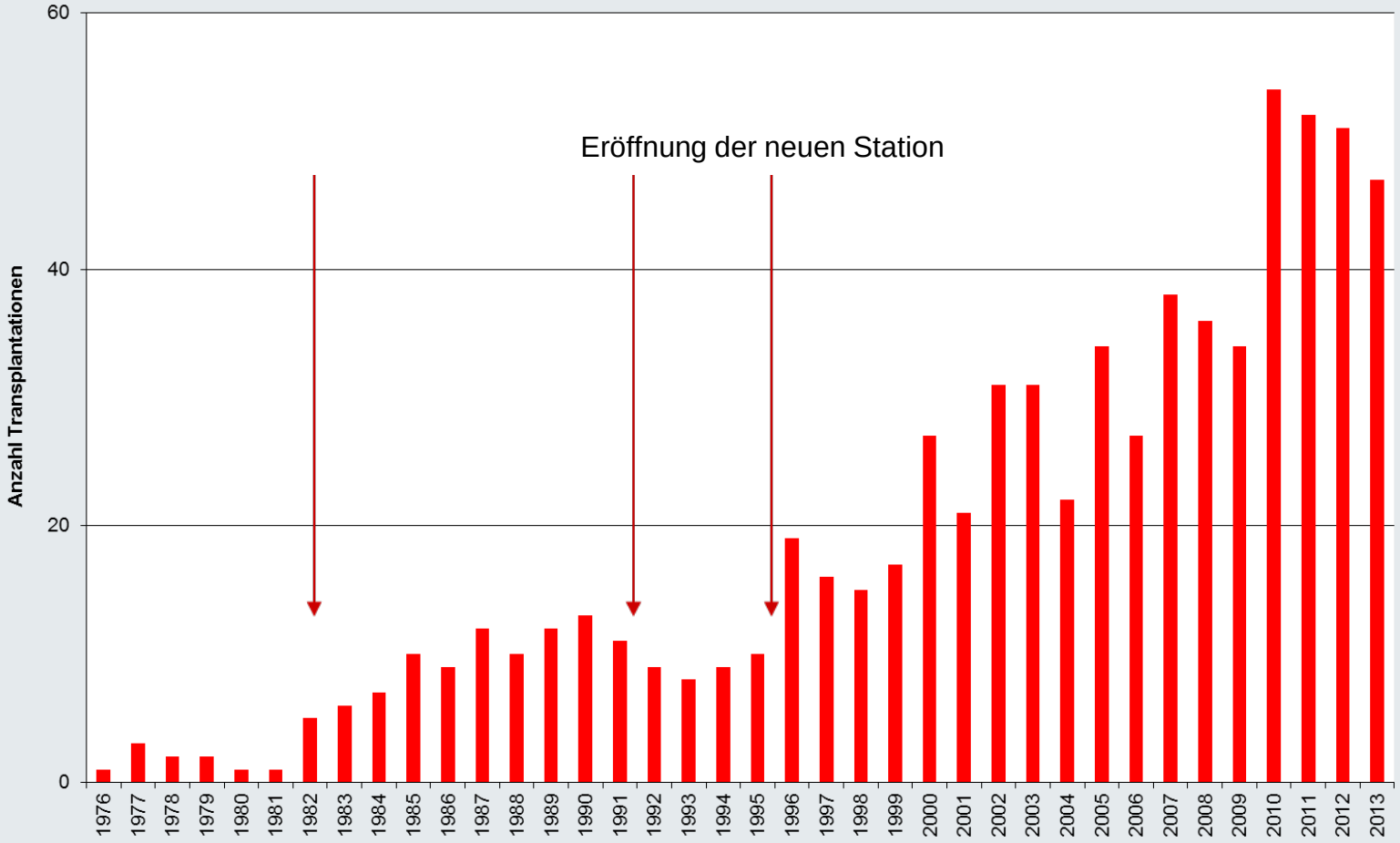
Randomized study of reduced-intensity chemotherapy combined with imatinib in adults with Ph-positive acute lymphoblastic leukemia

Yves Chalandon,[1,2] Xavier Thomas,[3] Sandrine Hayette,[3] Jean-Michel Cayuela,[4] Claire Abbal,[5] Françoise Huguet,[6] Emmanuel Raffoux,[4] Thibaut Leguay,[7] Philippe Rousselot,[8] Stéphane Lepretre,[9] Martine Escoffre-Barbe,[10] Sébastien Maury,[11] Céline Berthon,[12] Emmanuelle Tavernier,[13] Jean-François Lambert,[2,5] Marina Lafage-Pochitaloff,[14] Véronique Lhéritier,[15] Sylvie Chevret,[16] Norbert Ifrah,[17] and Hervé Dombret,[4] for the Group for Research on Adult Acute Lymphoblastic Leukemia (GRAALL)

BLOOD, 11 JUNE 2015 • VOLUME 125, NUMBER 24



Transplantationszahlen Zürich



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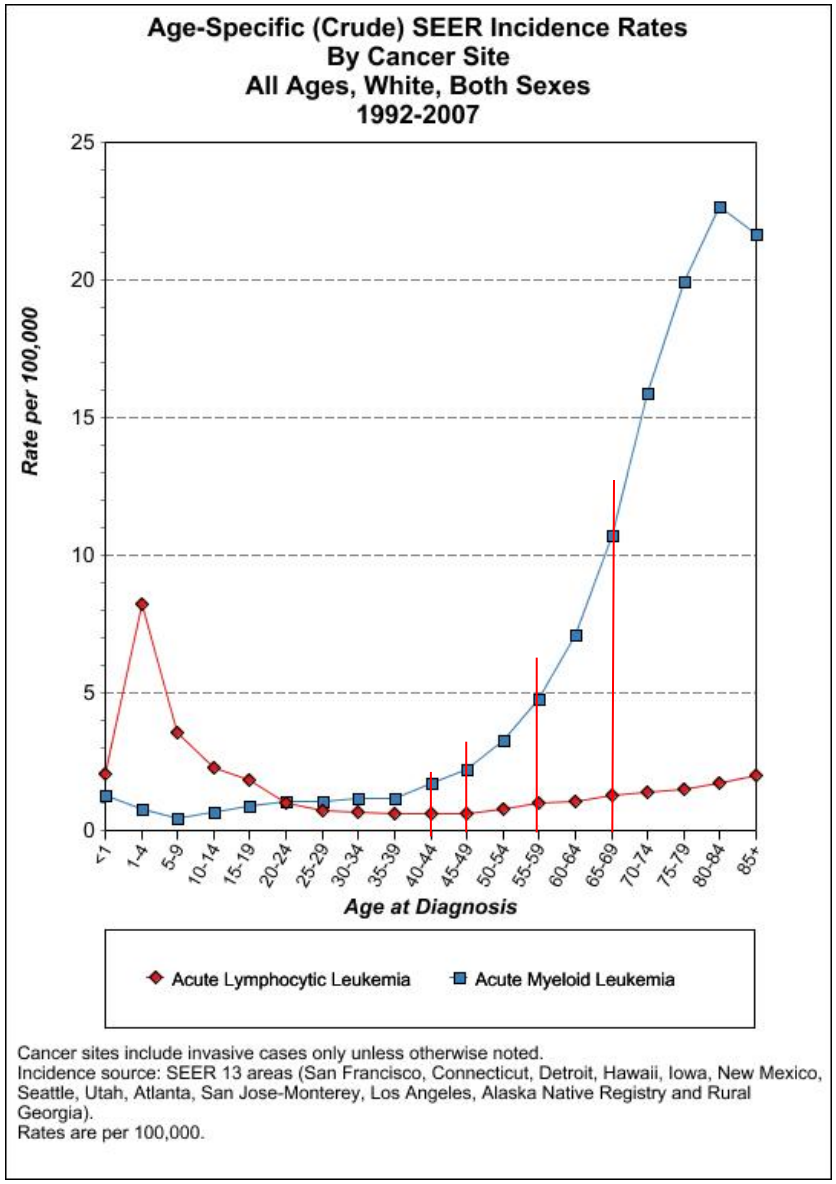
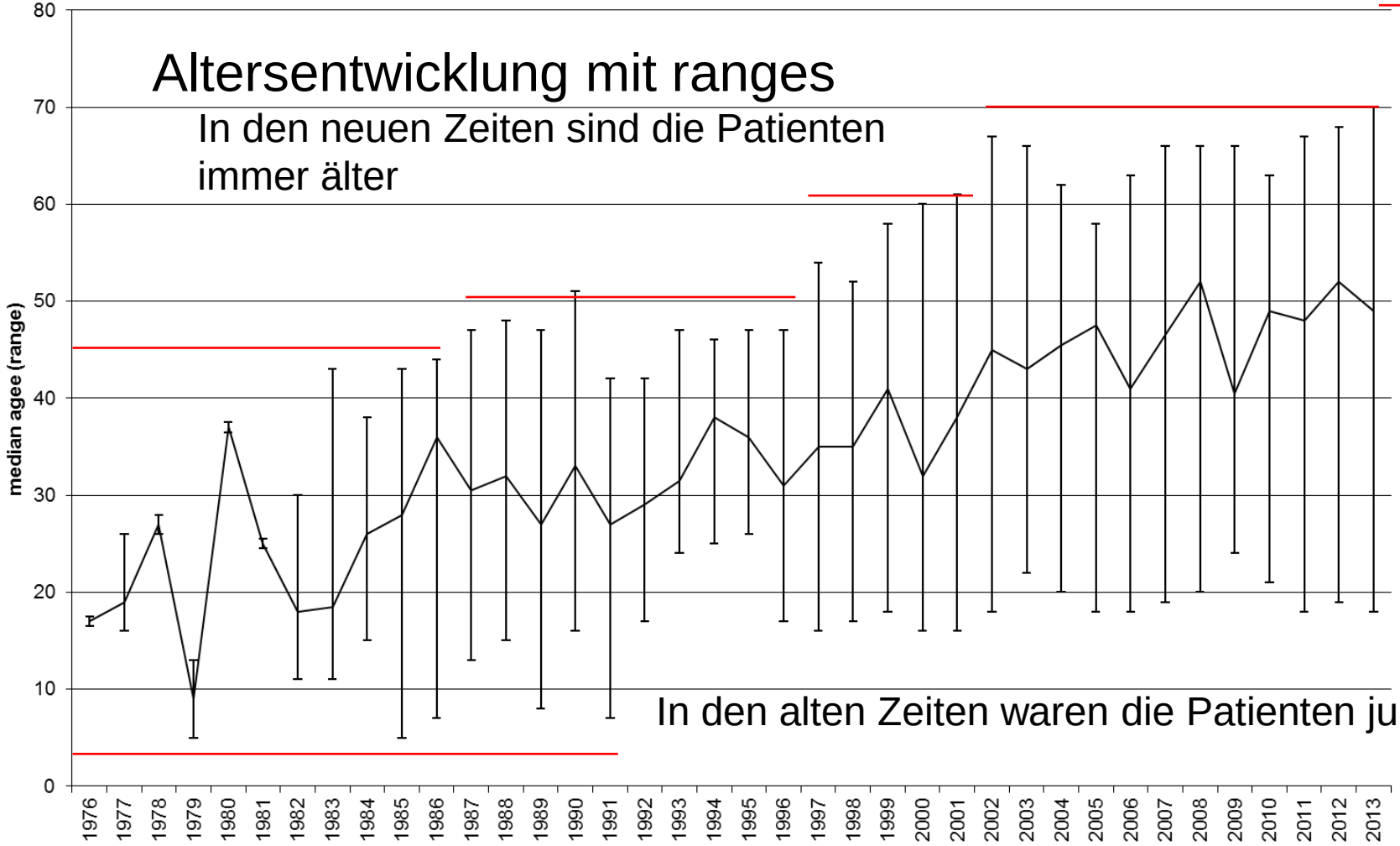
Age distribution of acute leukemias



Altersentwicklung mit ranges

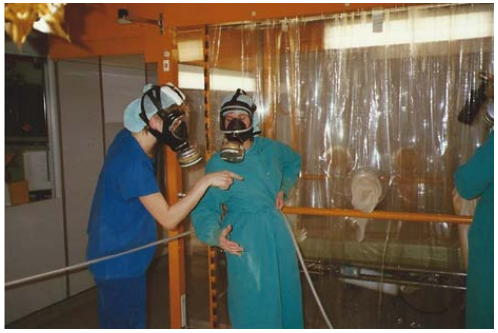
In den neuen Zeiten sind die Patienten immer älter

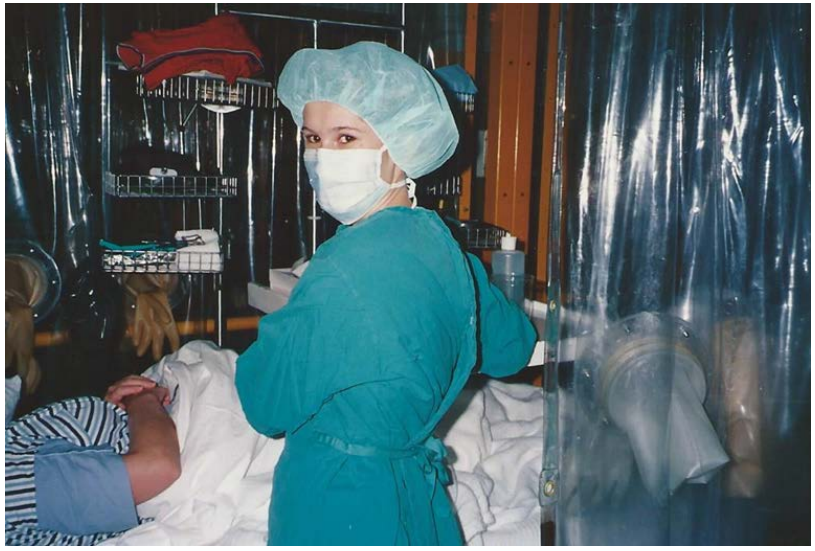


?

In den alten Zeiten waren die Patienten jung

Die alte Sterilpflegestation





1976: 2 Bettenstation
1995: Eröffnung neue Sterilpflegestation (8 Betten)
2010: Namensänderung Stammzell-Transplantationsstation

2013: Planung neue 16 Betten Station, aber es kann nicht gebaut werden: Denkmalpflege

09/2014: es darf doch gebaut werden

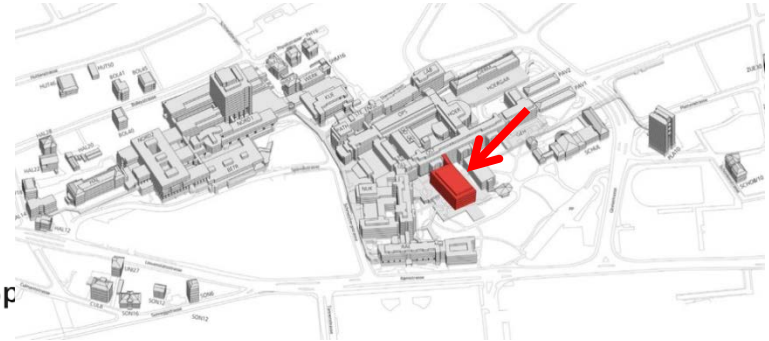
Tages-Anzeiger

Front **Zürich** Schweiz International Wirtschaft Börse Sport Kultur Leben Wissen Auto Blogs Panorama Mehr

Stadt Zürich Region Bellevue Bildstrecken Marktplatz

Grünes Licht für Provisorium des Zürcher Unispitals

Das Universitätsspital darf im Spitalpark ein Provisorium erstellen. Dies hat das Baurekursgericht entschieden. Der Beschluss der kantonalen Baudirektion sei «denkmalpflegerisch vertretbar».



Eröffnung 2019?

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TRANSFUSION CRS SUISSE
TRASFUSIONE CRS SVIZZERA

SWISS BLOOD STEM CELLS
BLUTSTAMMZELLEN
CELLULES SOUCHES DU SANG
CELLULE STAMINALI DEL SANGUE

GEMEINSAM GEGEN LEUKÄMIE

Startseite | Medien | Stammzell-Transplantationsstation

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Wydäckerring 57, 8047 Zürich

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