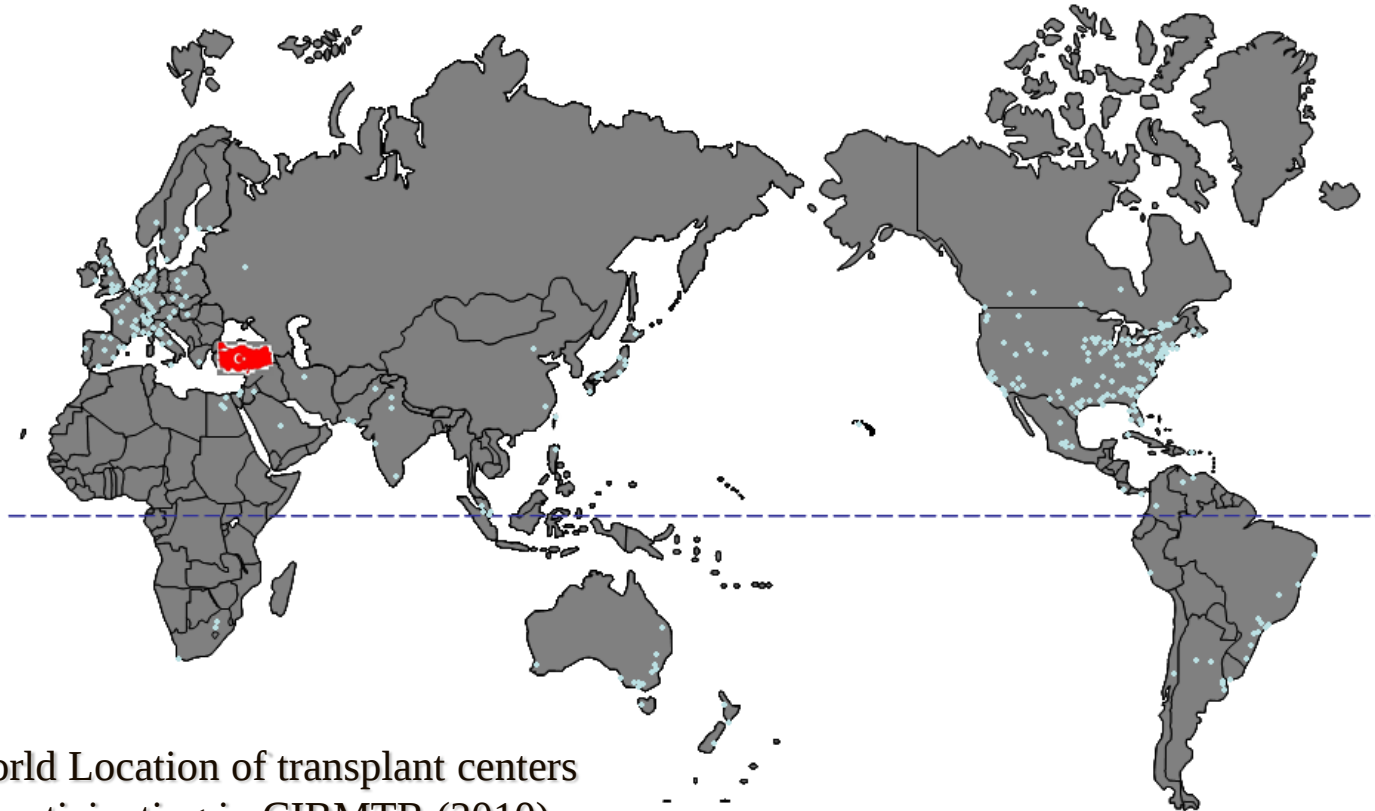


Hematopoietic Stem Cell Therapies in TURKIYE



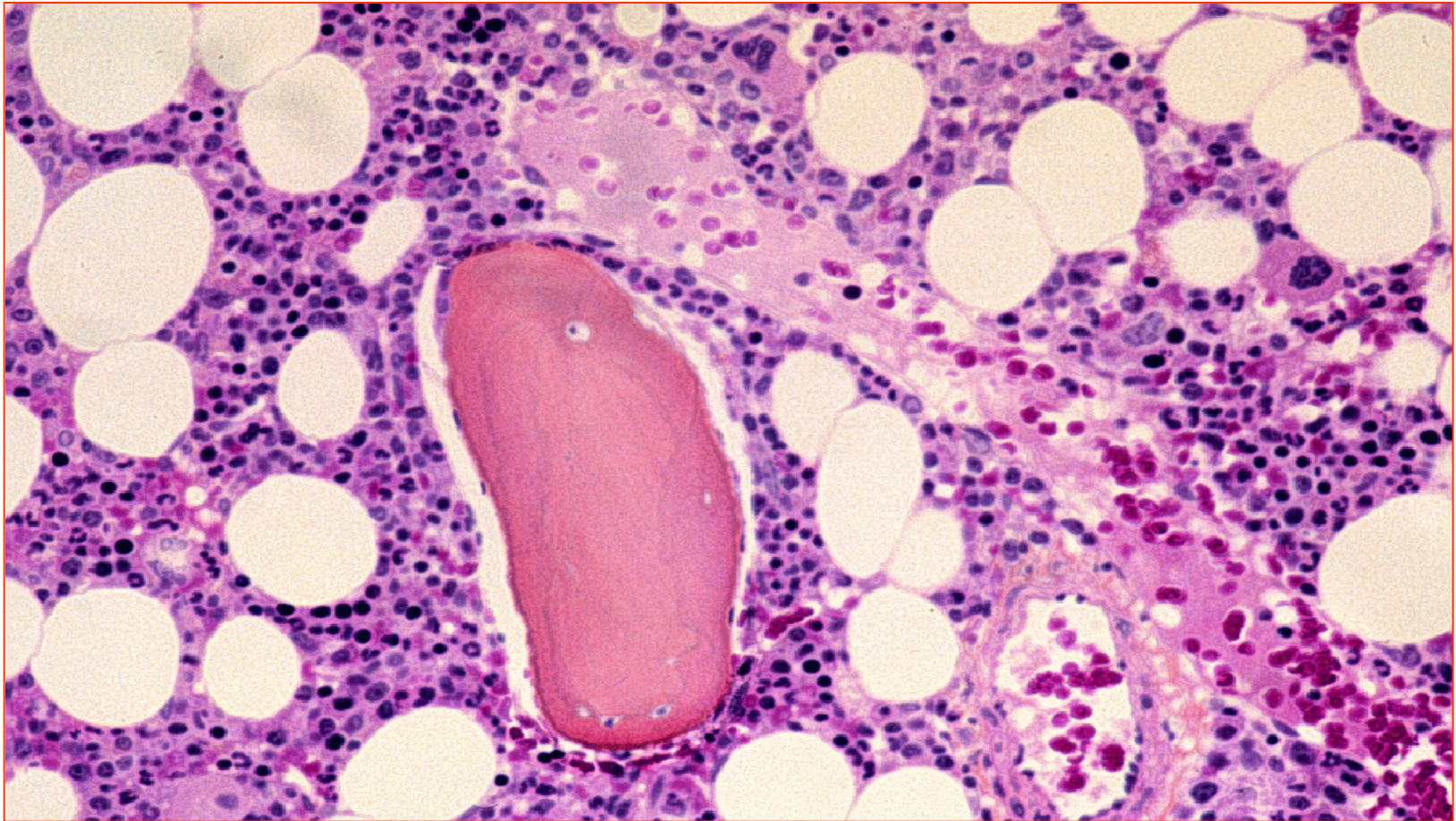
World Location of transplant centers
participating in CIBMTR (2010)

Mustafa CETIN, M.D.
Erciyes University Medical Faculty
Kayseri-TURKIYE

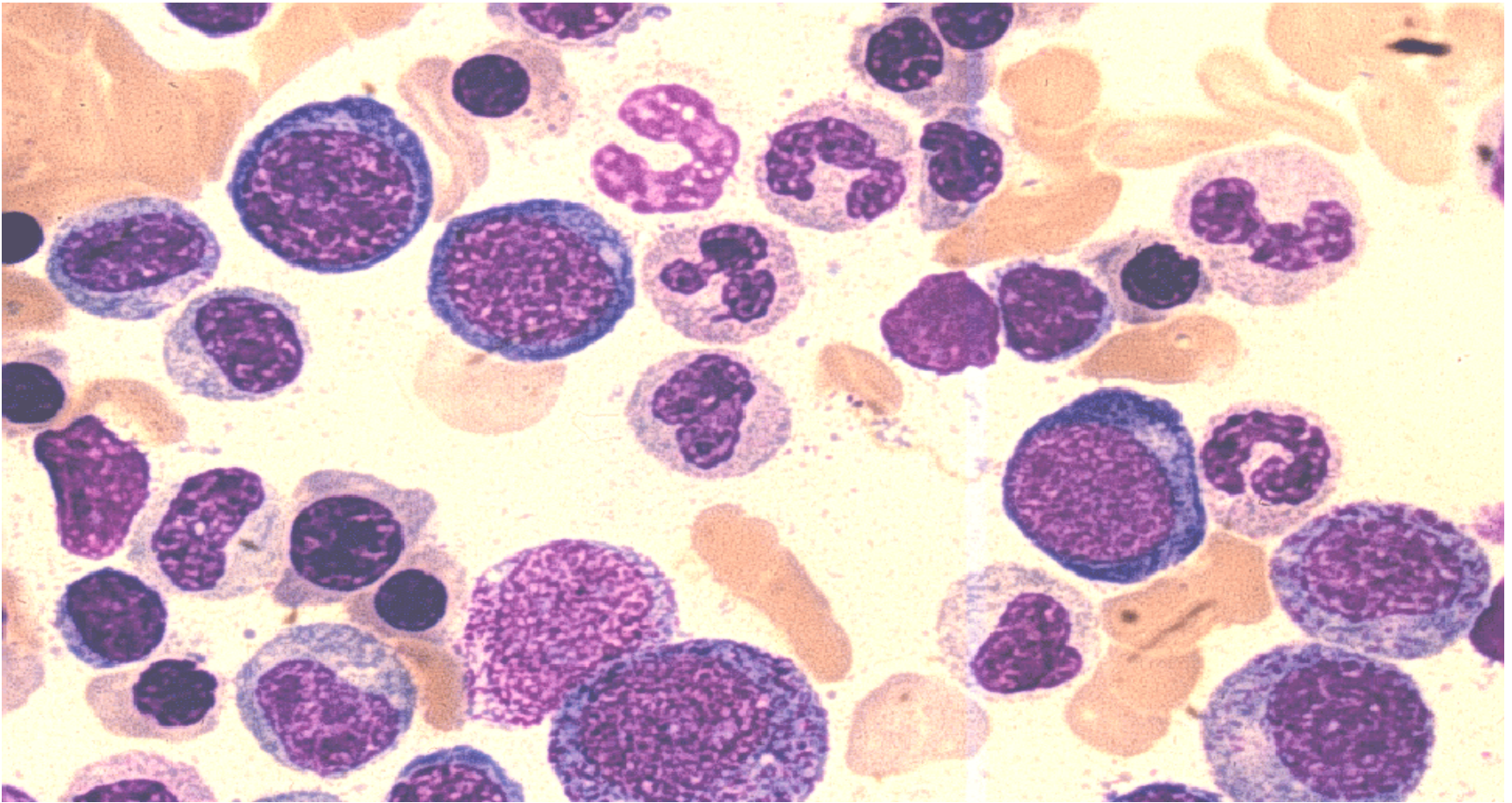
Background

- Bone Marrow Function
- Hematopoietic Stem Cell (Bone Marrow) Transplantation
- Hematopoietic Stem Cell Therapy Results
- Transplantation Activity Survey (Europa & US & World)
- Transplantation Activity Survey (TURKIYE)
- Transplantation Activity Survey (ERCIYES)

Bone Marrow: Function

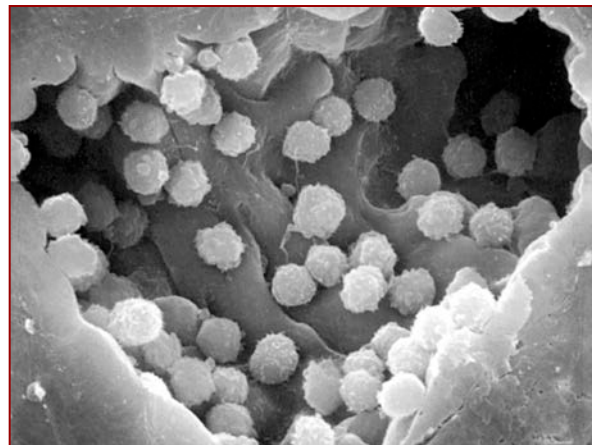
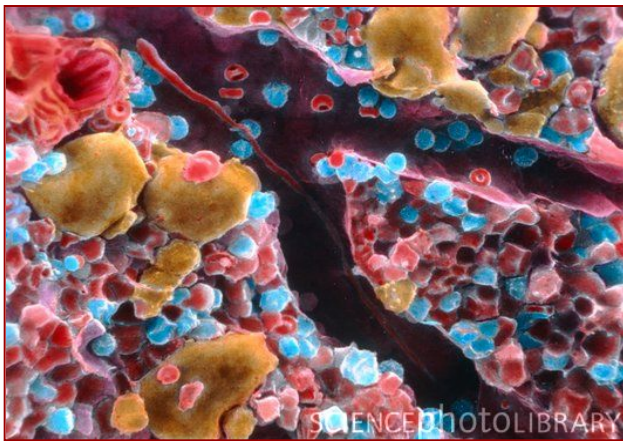


Bone Marrow: Function



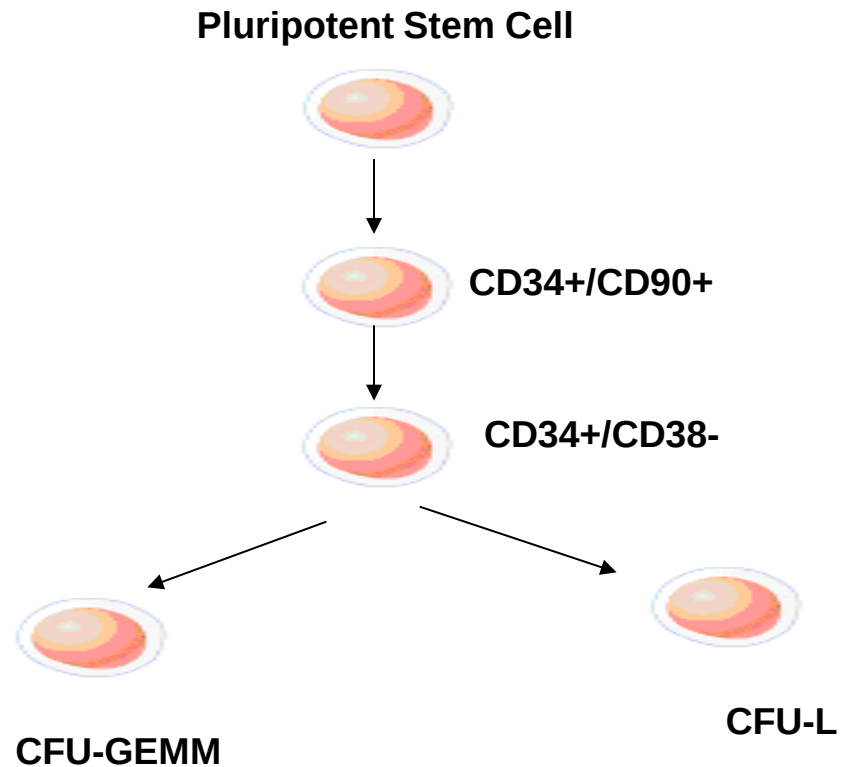
Bone Marrow: Function

- Production of blood cells,
 - 175 billion red cells/day
 - 70 billion granulocytes/day (neutrophils, eosinophils, basophils)
 - 175 billion platelets/day
 - Capable of 5-10 fold increase in production

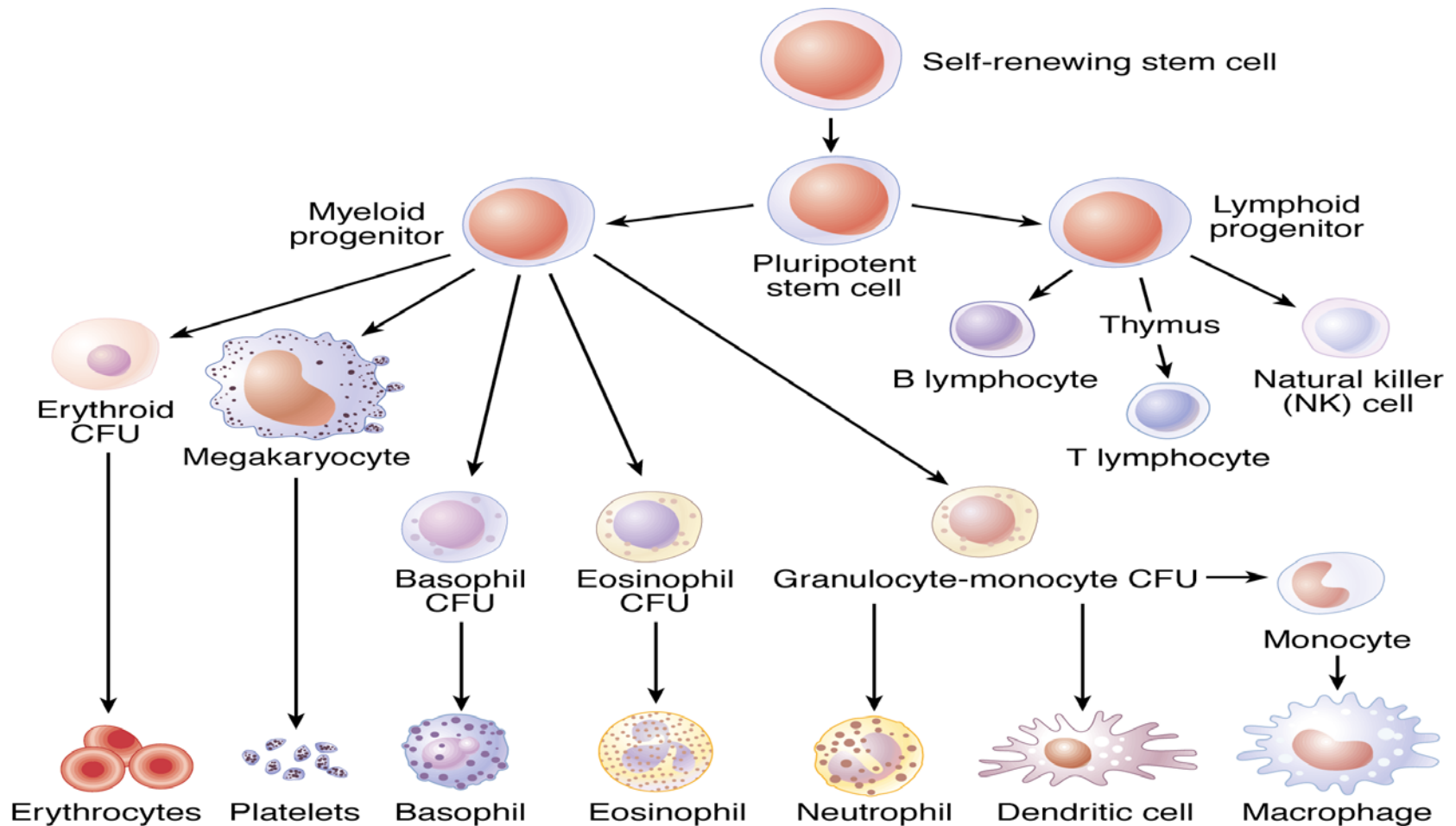


1- 0.1% human
bone marrow
cells are early
hematopoietic
cell precursors

Experimental Model of Early Hematopoiesis

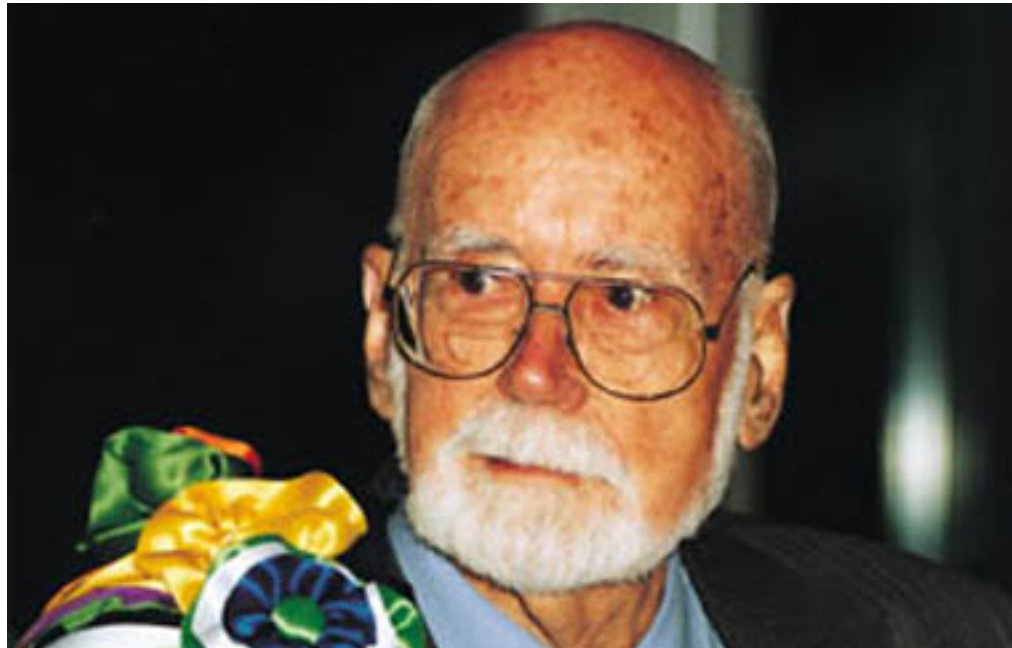


Bone Marrow hematopoiesis



The Nobel Prize, 1990

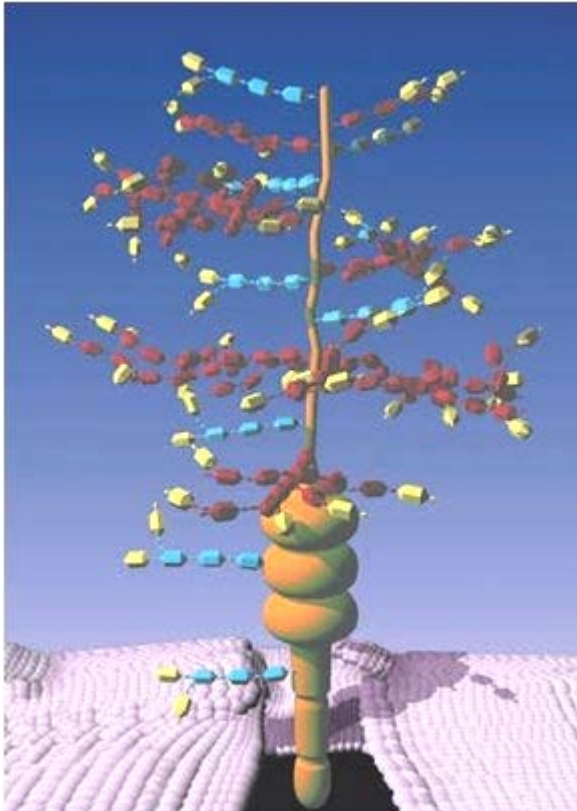
E. Donnall Thomas



first successful clinical HSCT in treatment of acute leukemias

Thomas ED, Lochte HL, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N. Engl. J. Med. 1957; 257: 491.

What is CD 34 anyway ?



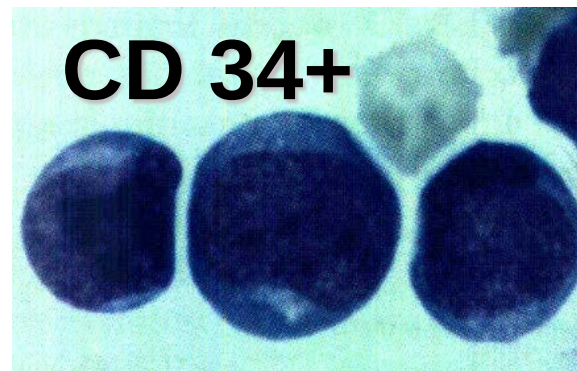
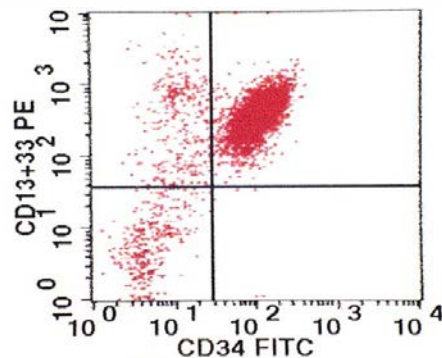
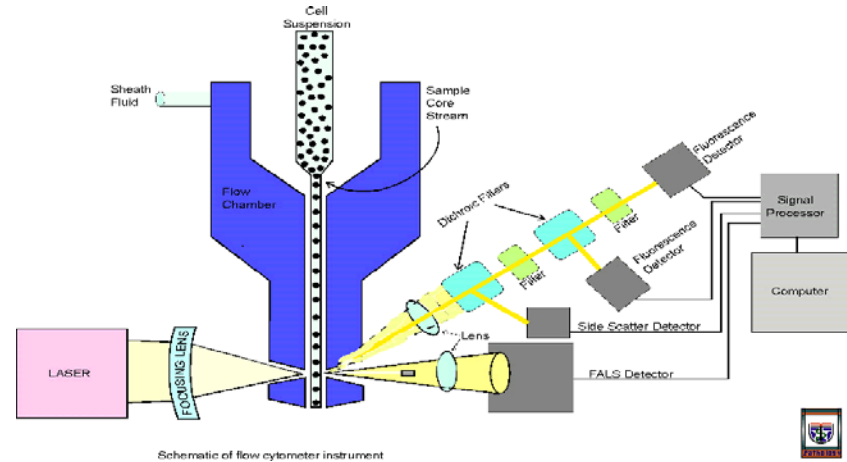
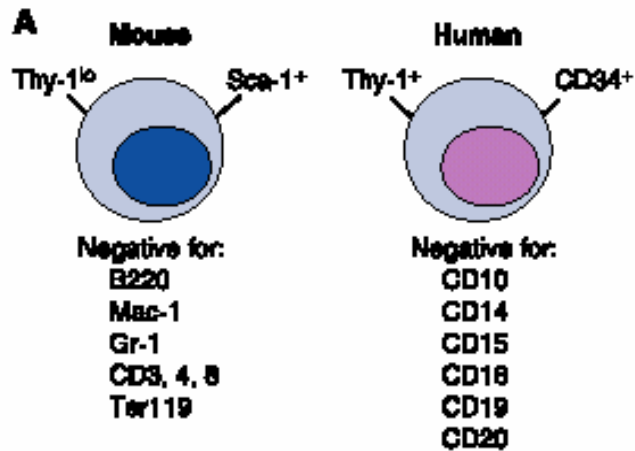
- 105-120 kDa transmembrane Glycoprotein
- Present in early hematopoietic cell precursors
- Present in 0.1% of peripheral mononuclear cells
1-4% human bone marrow cells

Probably an adhesion molecule.



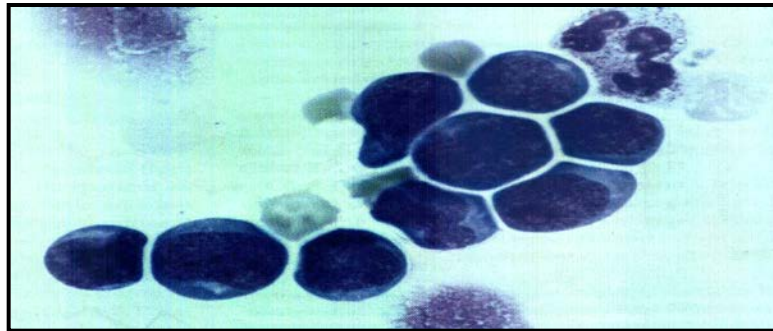
Hematopoietic stem cell (immunophenotyping)

CD34+, Thy1+, CD38-, HLA-DR-, c-kit+, Lin-, AC133+, CD33-, CD4-, CD8-, CD14-, CD19-,



Hematopoietic stem cell harvesting

**How can we get CD34+
hematopoietic stem cell ?**



- Bone marrow harvesting
- Peripheral blood harvesting

Bone marrow harvesting

- General anaesthetic
- Marrow aspirated from pelvis (+sternum)
- Marrow filtered to remove debris
- Marrow may be administered “fresh” or cryo-preserved



Peripheral blood harvesting

- **Stem cells mobilised –**
 - G-CSF in healthy donors
 - Cyclophosphamide + G-CSF in patients
- **On day 5 (donors), day 10 (patients)**
 - 3 hours session on stem cell collection machine
- **Stem cells given fresh or cryopreserved**

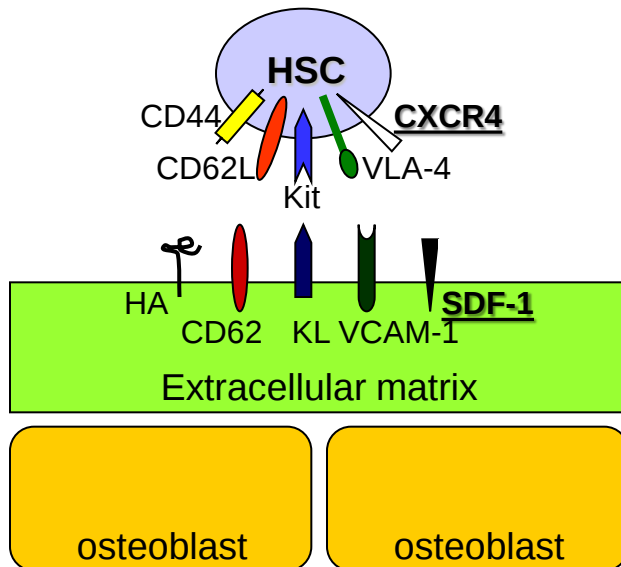


G-CSF mobilization

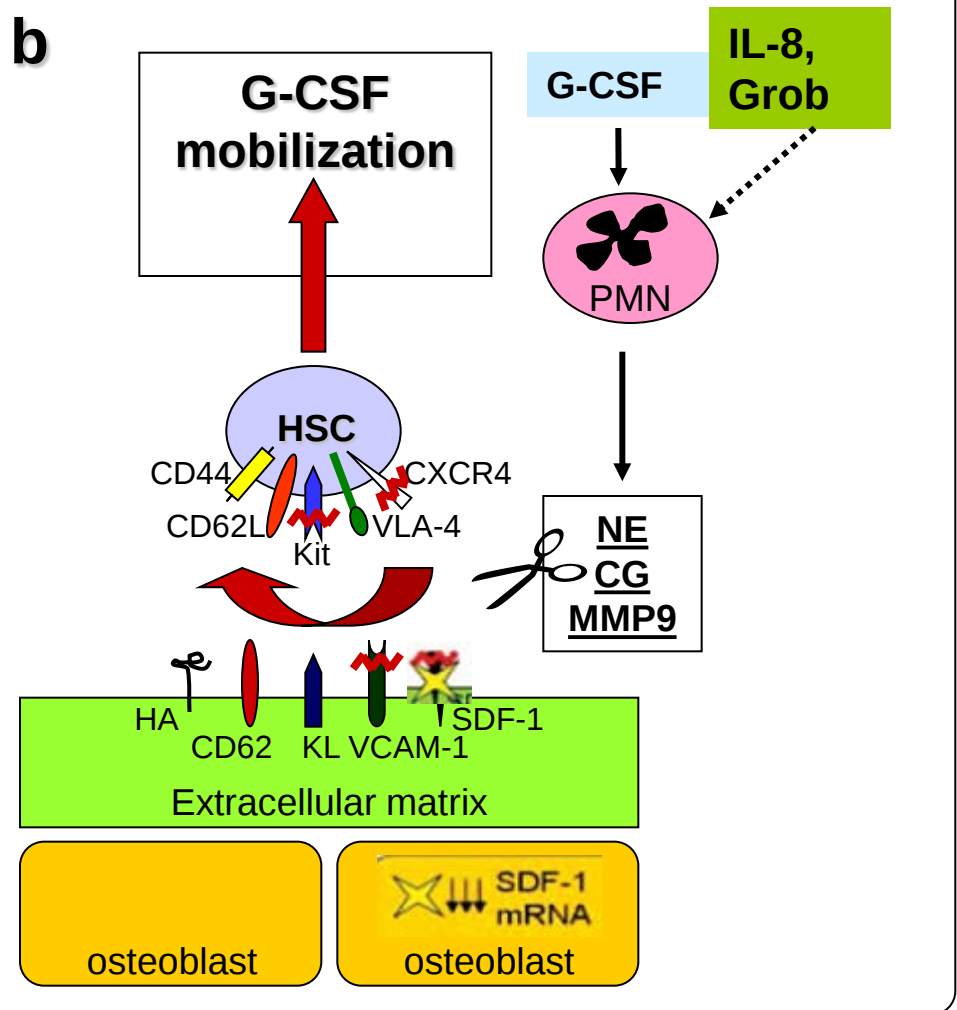
The role of proteases (NE, CG, and MMP9)

a

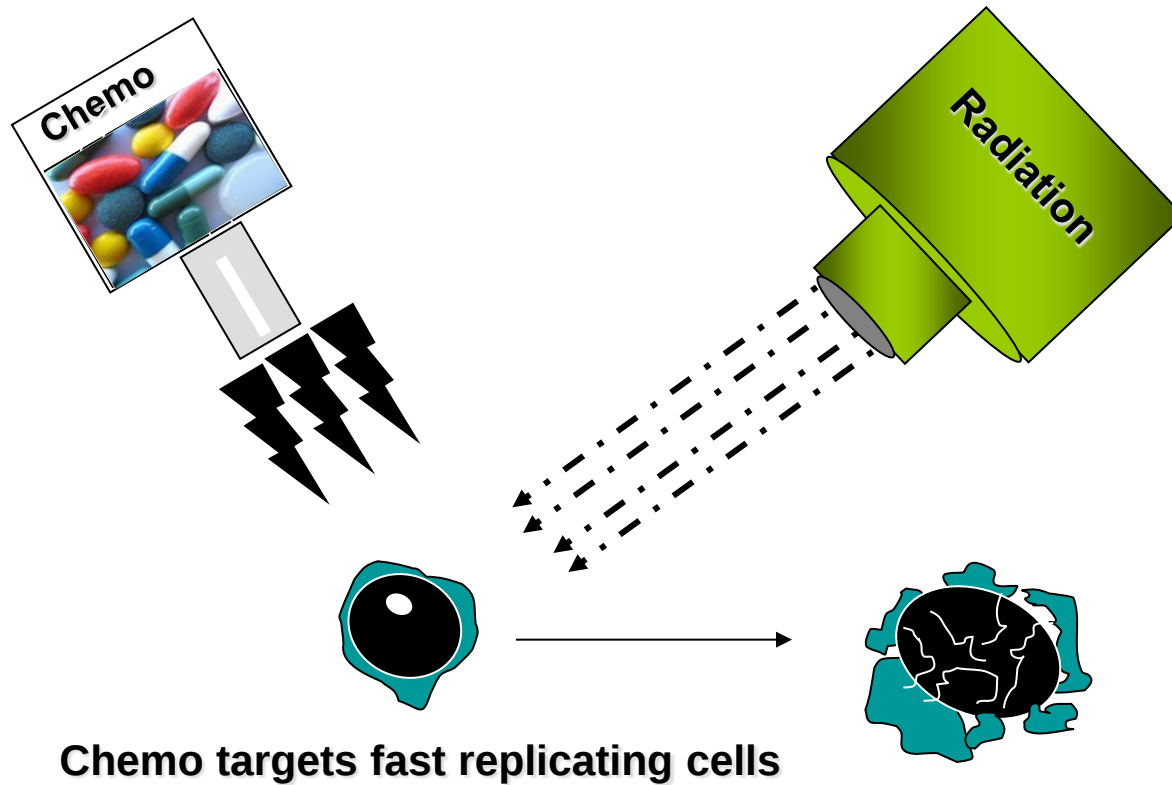
adhesive interactions
between HSC and BM:
cell adhesions molecules



b

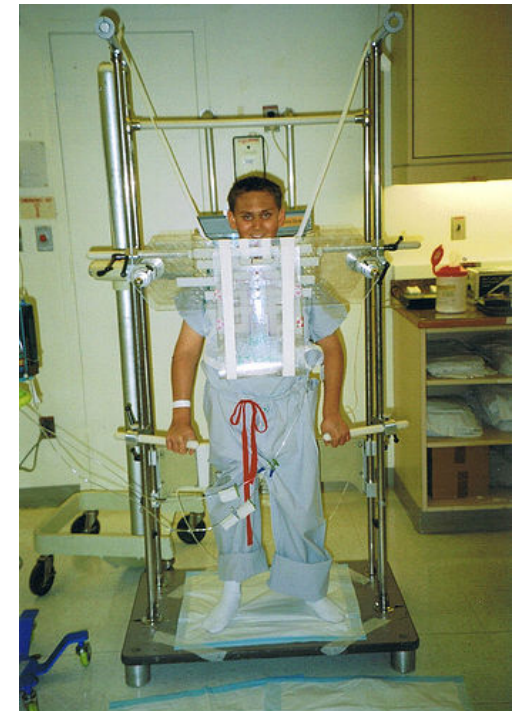
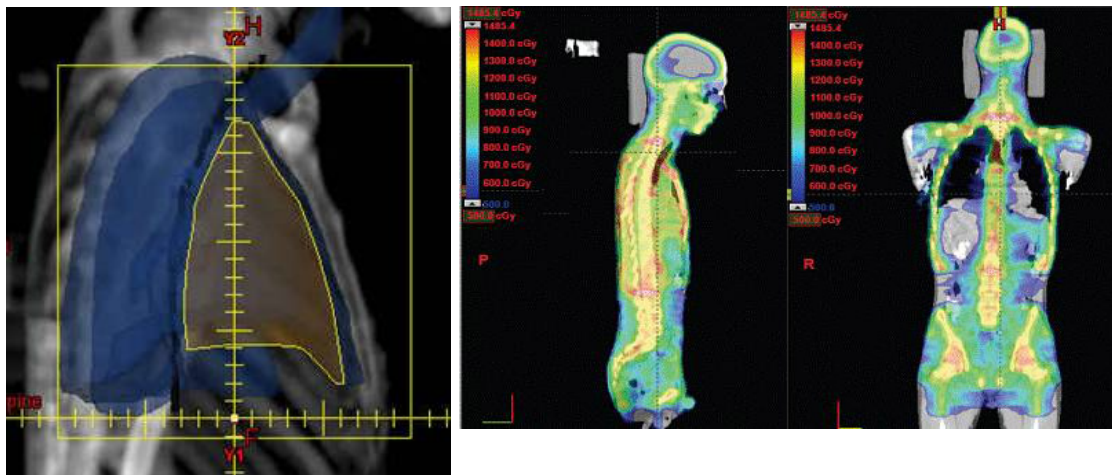


Stem Cell Transplant: Effects of Treatment



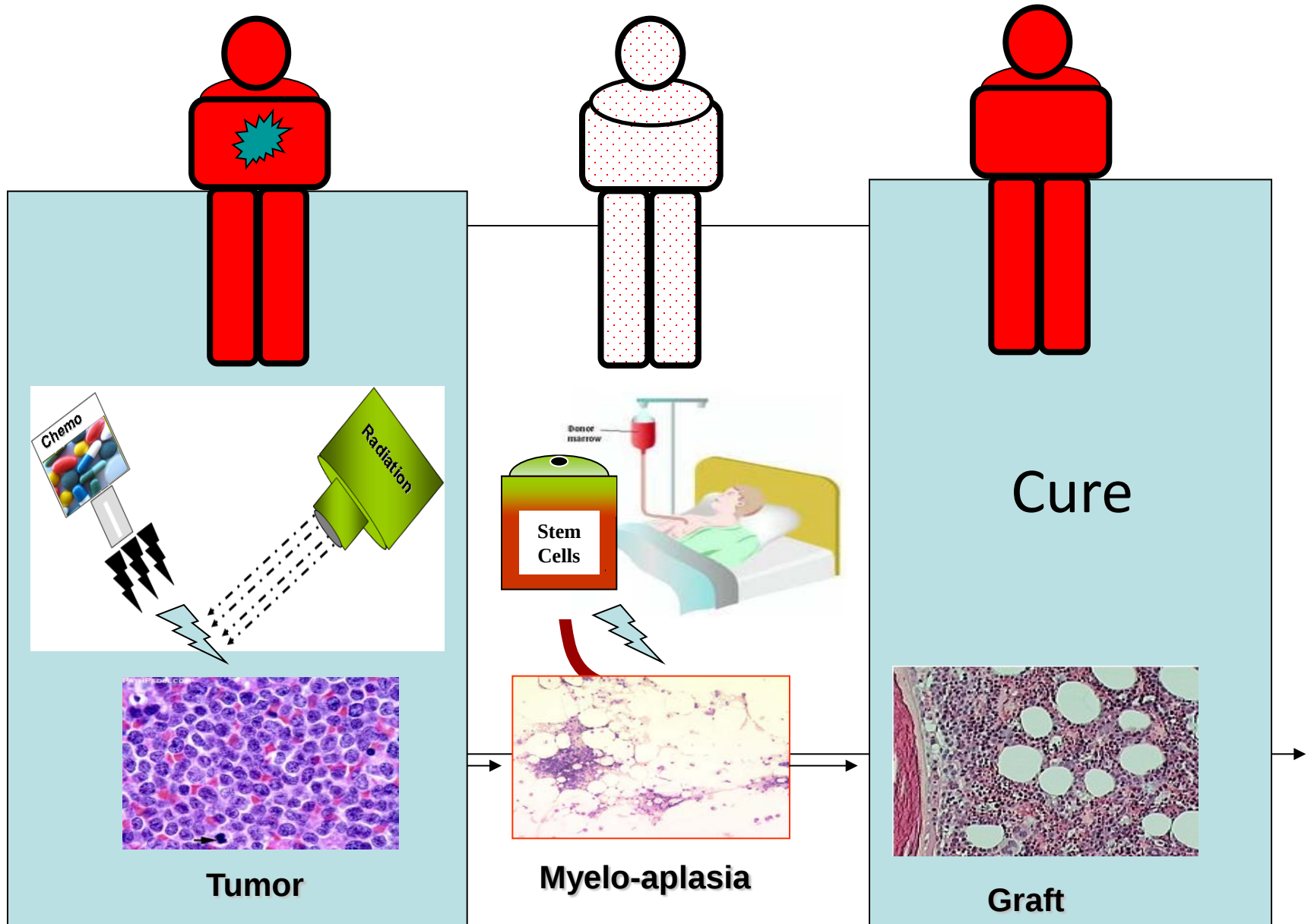
Myelo-ablation

- Total body irradiation 10-12 Gy (fractionated) + cyclophosphamide
- Cyclophosphamide + busulfan

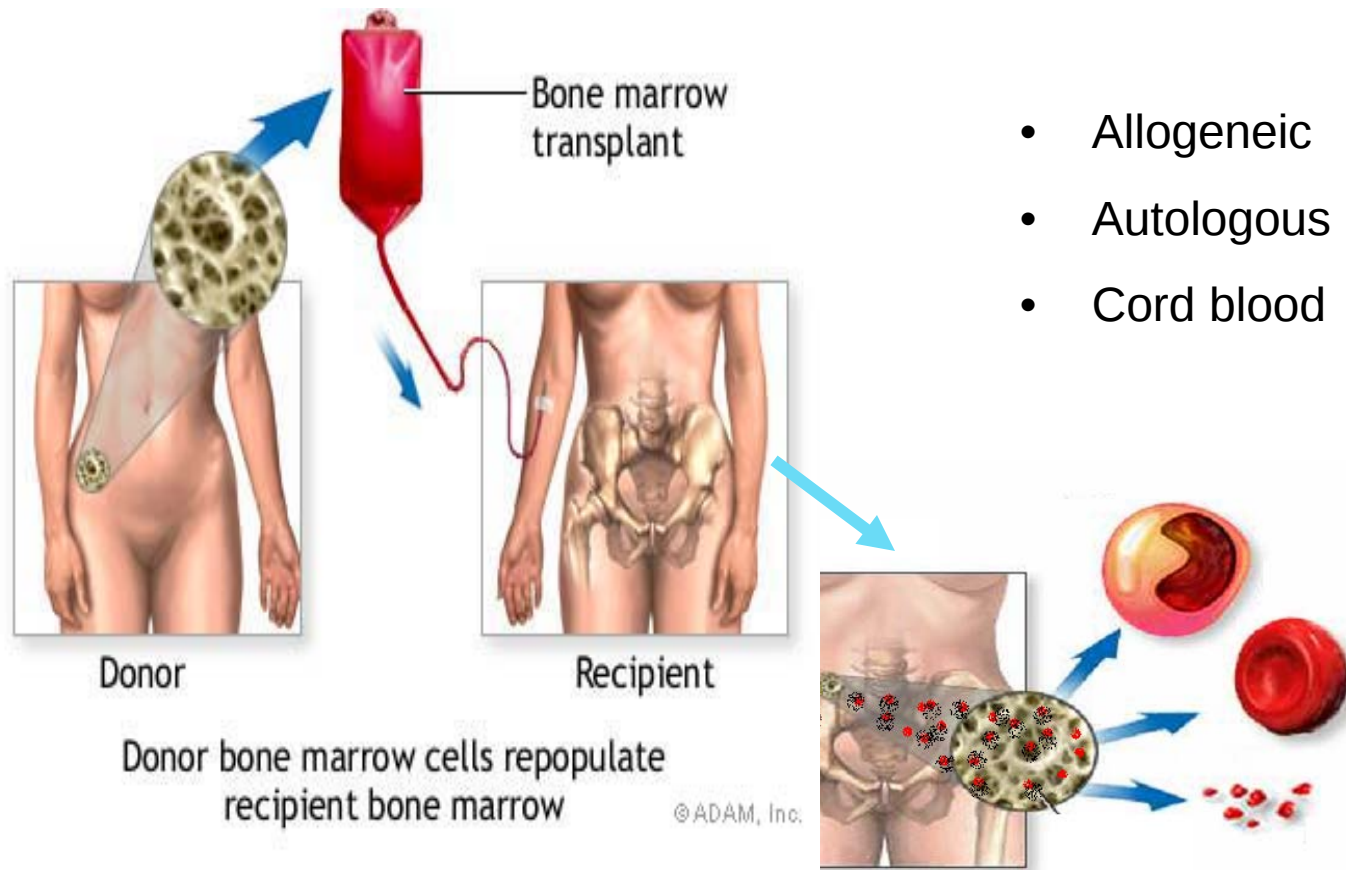


Nb 4.5 Gy fatal in 50% exposed individuals

Rational of BMT



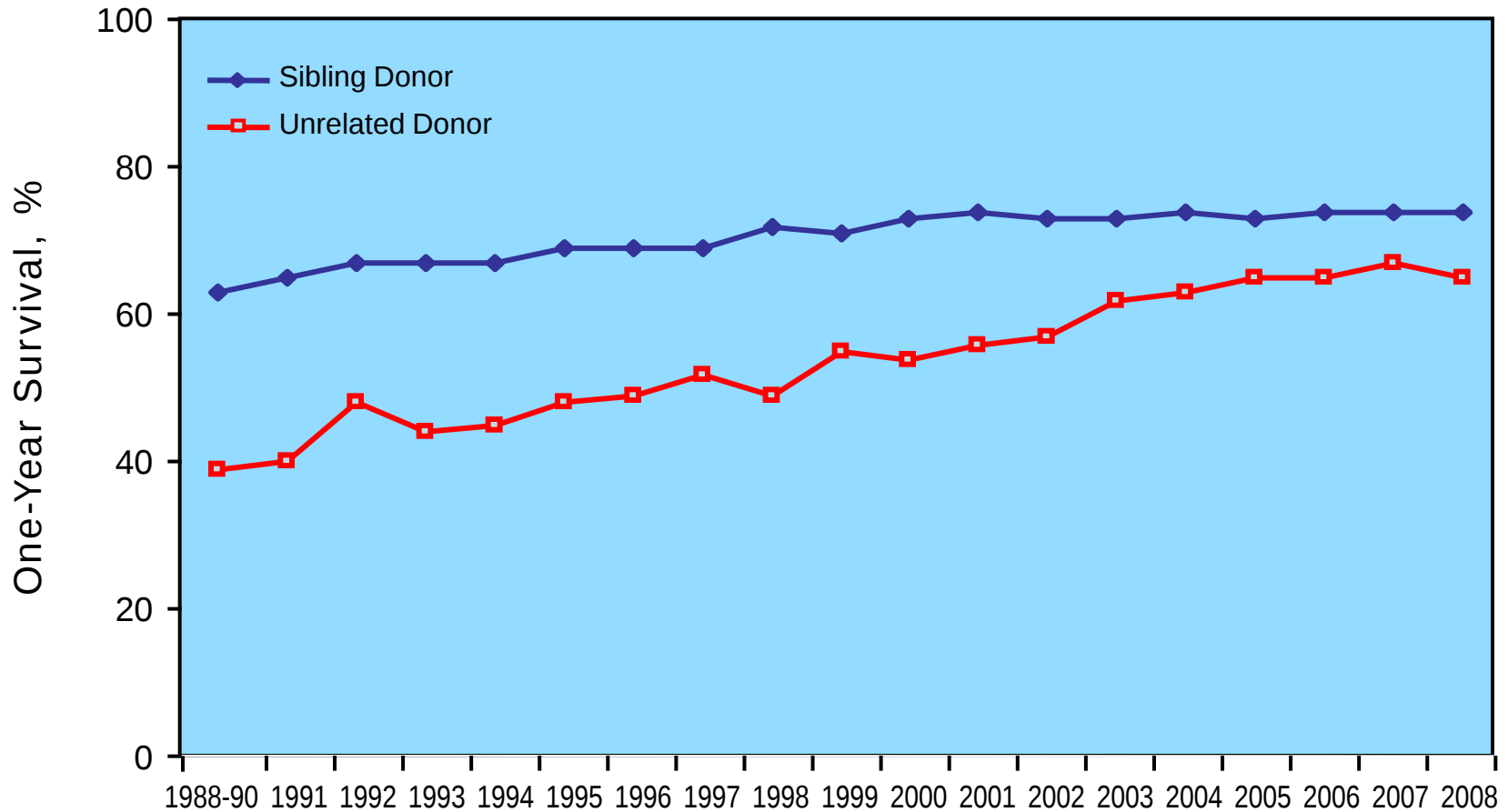
Types of stem cell for transplantation



BMT/ PBSC Transplants: Indications

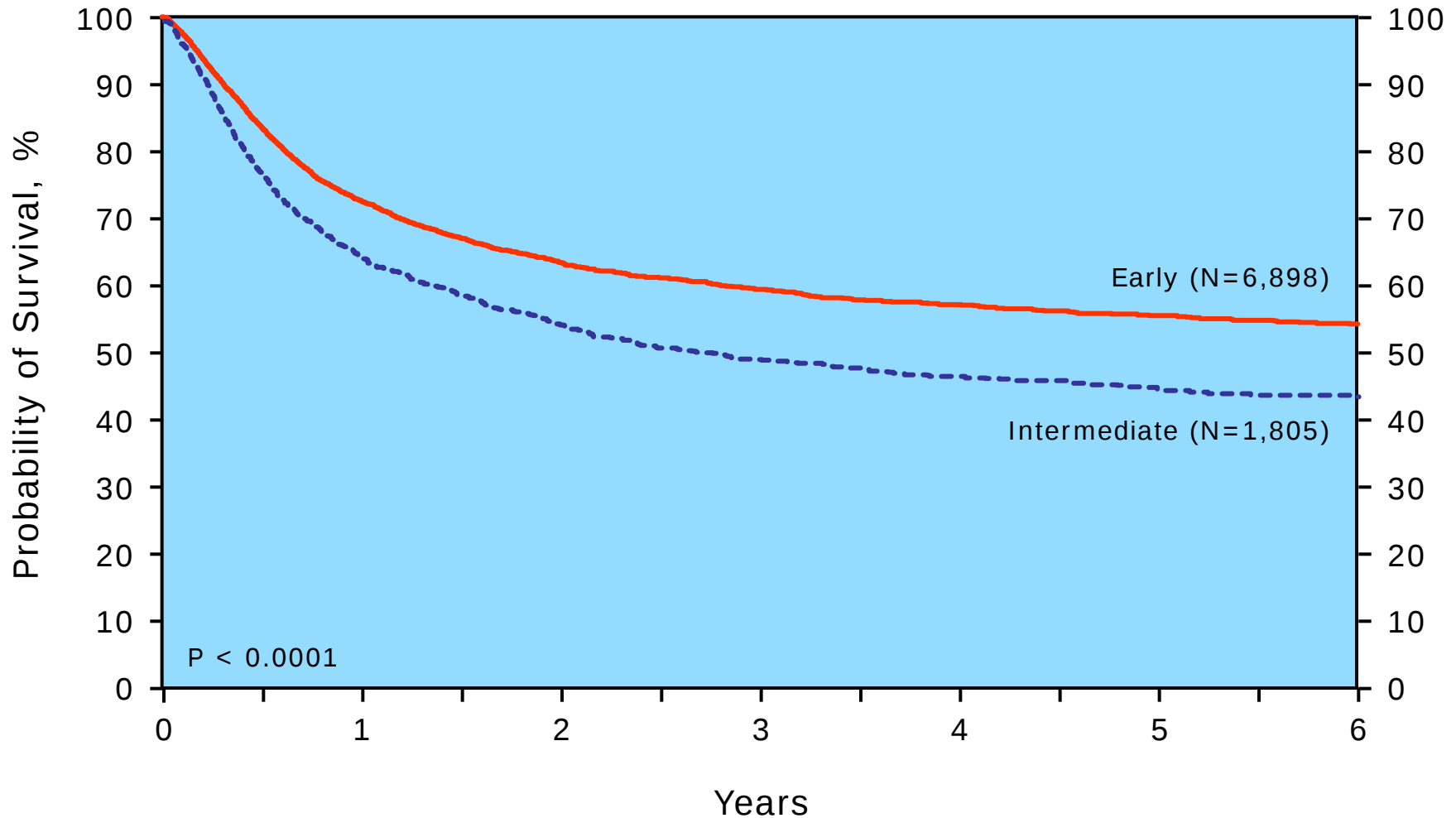
- Leukemias (acute and chronic)
- Lymphomas (Hodgkin's and non-Hodgkin's)
- Multiple myeloma
- Myelodysplastic and myeloproliferative disease
 - (myelofibrosis, polycythemia vera, essential thrombocytosis)
- Aplastic anemia
- Metastatic breast cancer *
- Some metabolic diseases
- childhood cancers (neuroblastoma, sarcomas, high grade gliomas, Wilm's tumor)
- Congenital immunodeficiencies (CGD, SCID, Wiskott-Aldrich)
- Rheumatologic/autoimmune diseases (RA, jRA, Lupus, AIHA)
- Hemoglobinopathies
- Metabolic diseases (osteopetrosis, Hurler's, adrenaleukodystrophy)

Trends of transplant survival RATE & succes , age <50 years, by year of transplant and graft source, 1988-2008

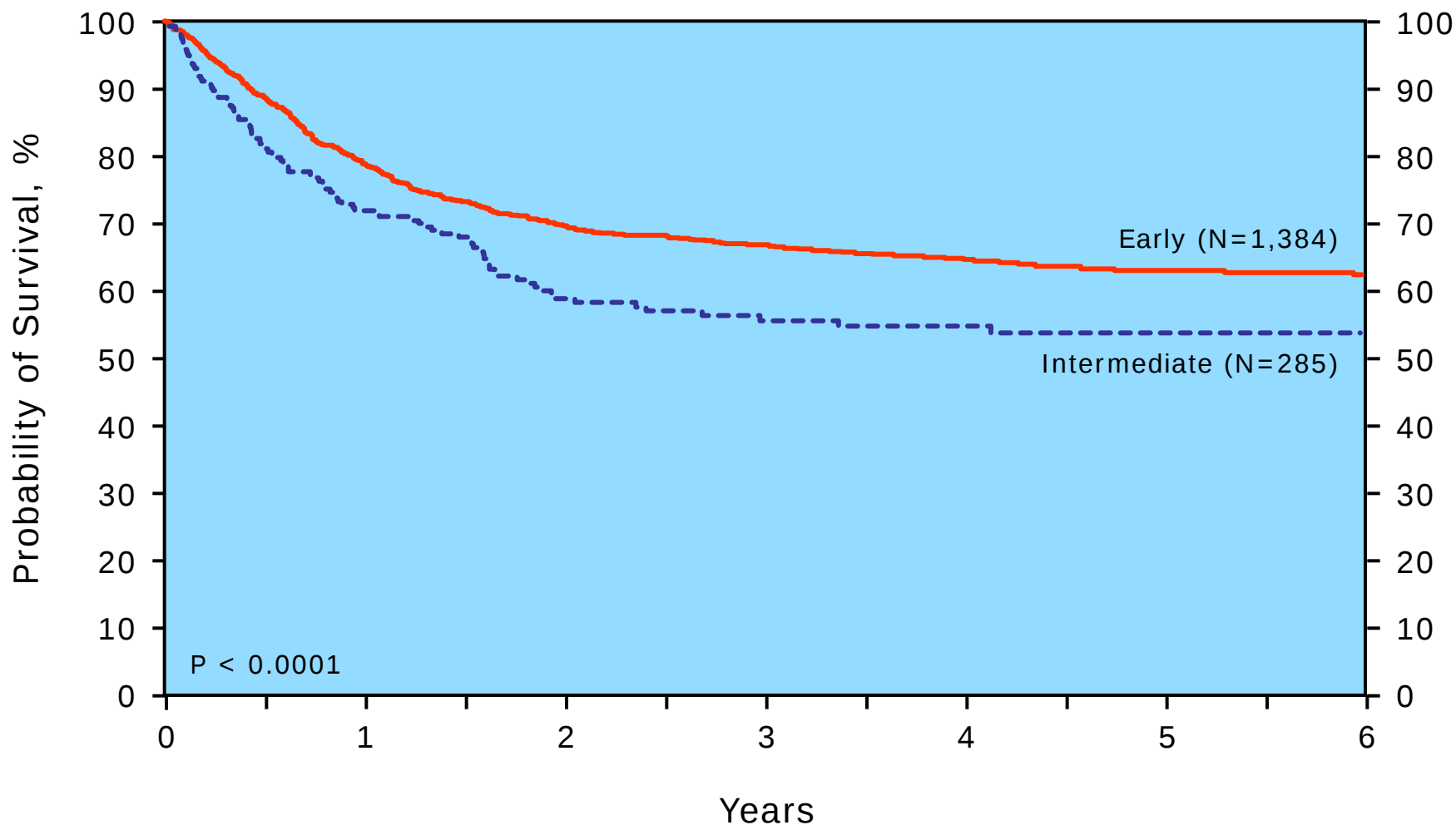


Probability of survival for AML

HLA-matched sibling donor transplant, by disease status, 1998-2008

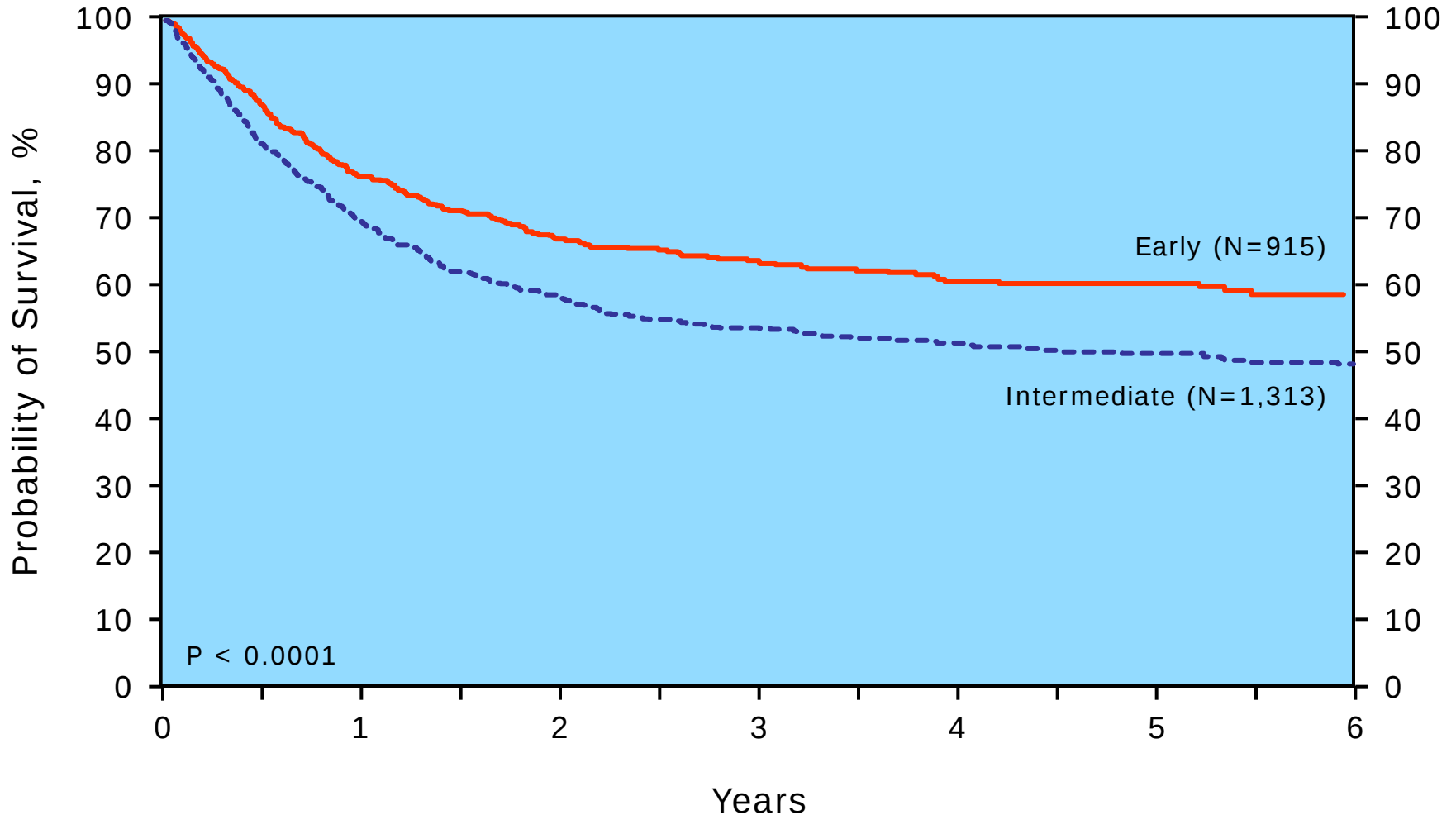


Probability of survival for AML , HLA-matched sibling donor transplant, age <20 years, by disease status, 1998-2008



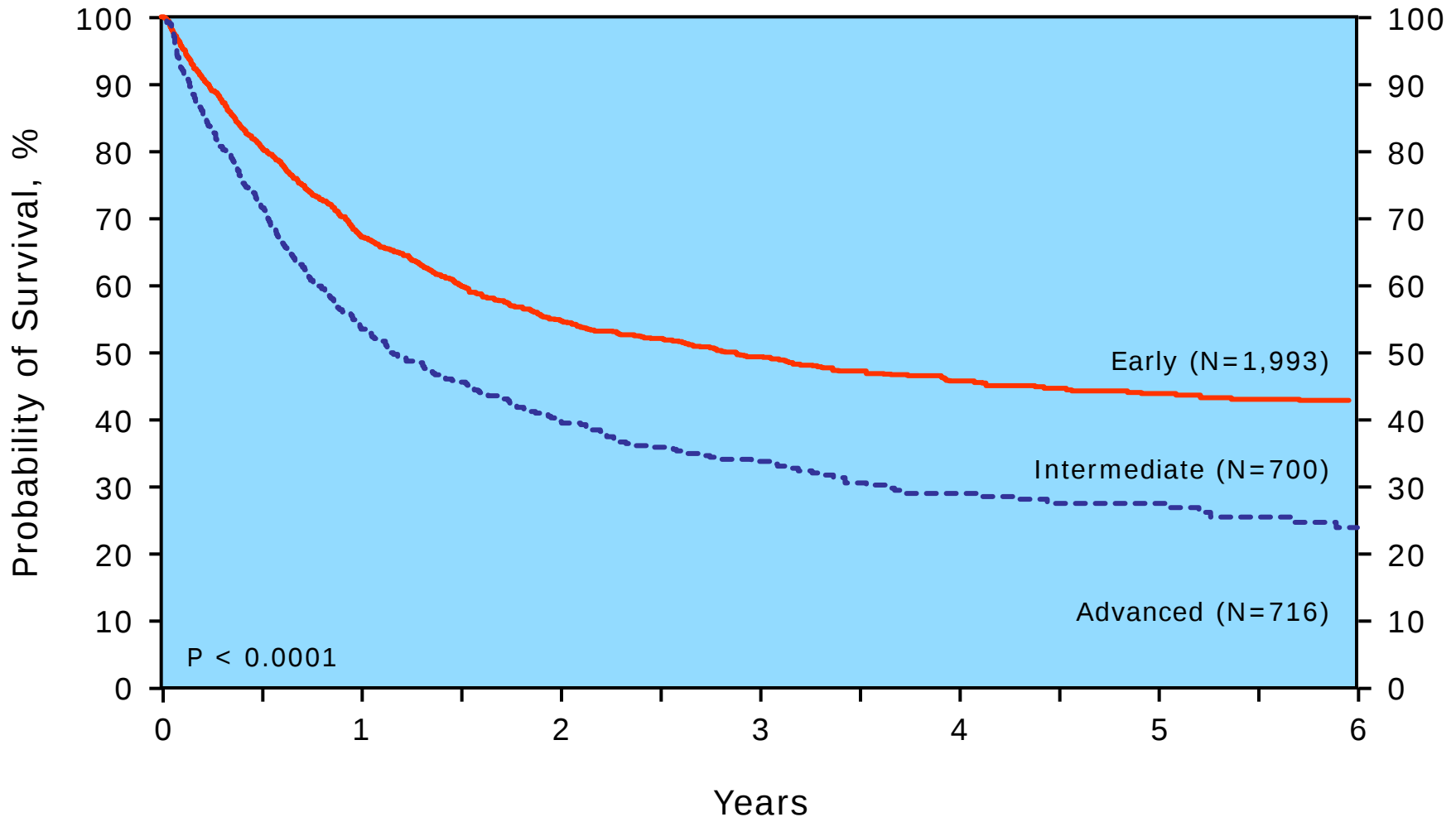
Probability of survival for ALL

HLA-matched sibling donor transplant, age <20 years, by disease status, 1998-2008



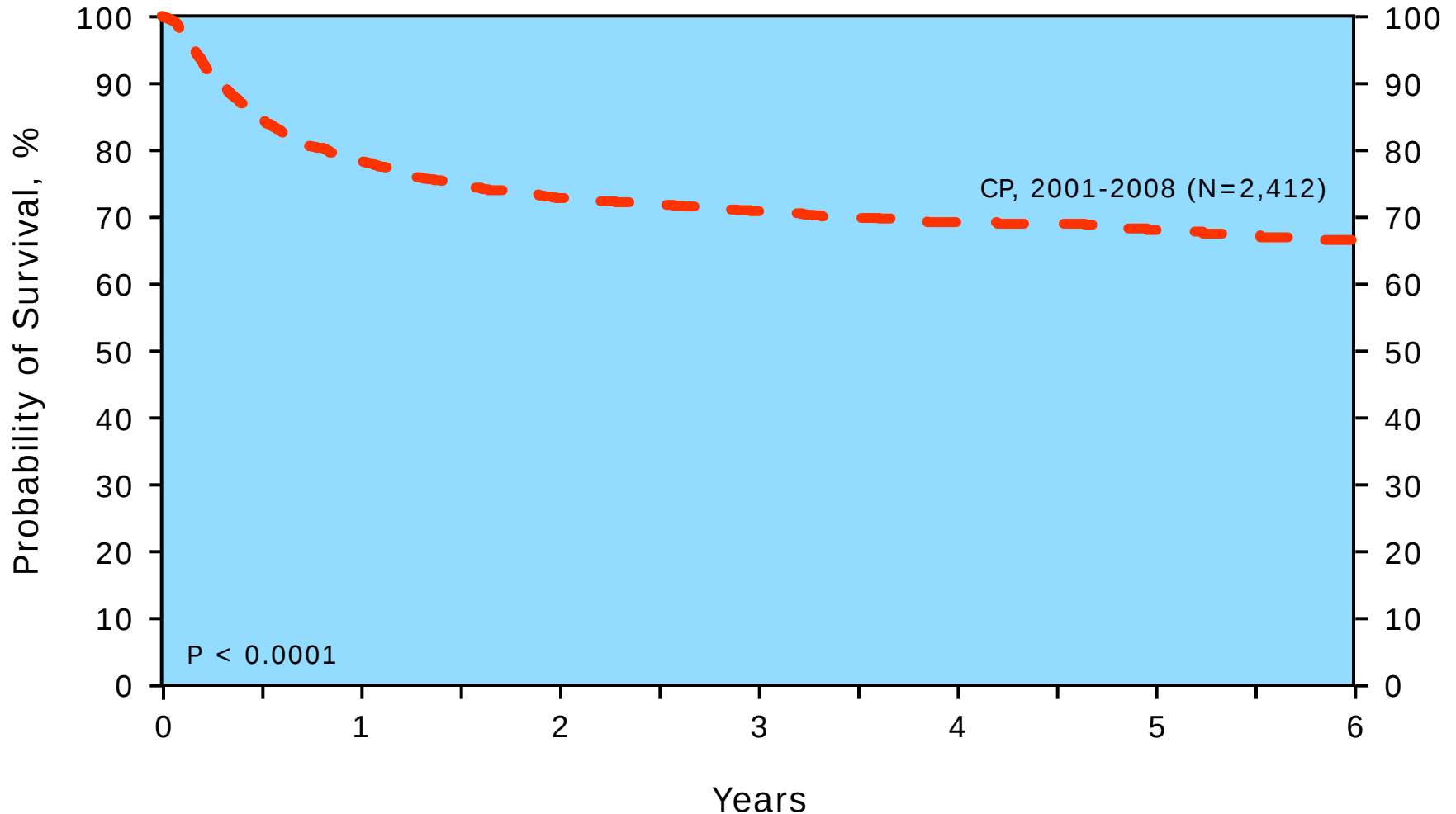
Probability of survival for ALL

HLA-match sibling donor transplant, age ≥ 20 years, by disease status, 98-2008



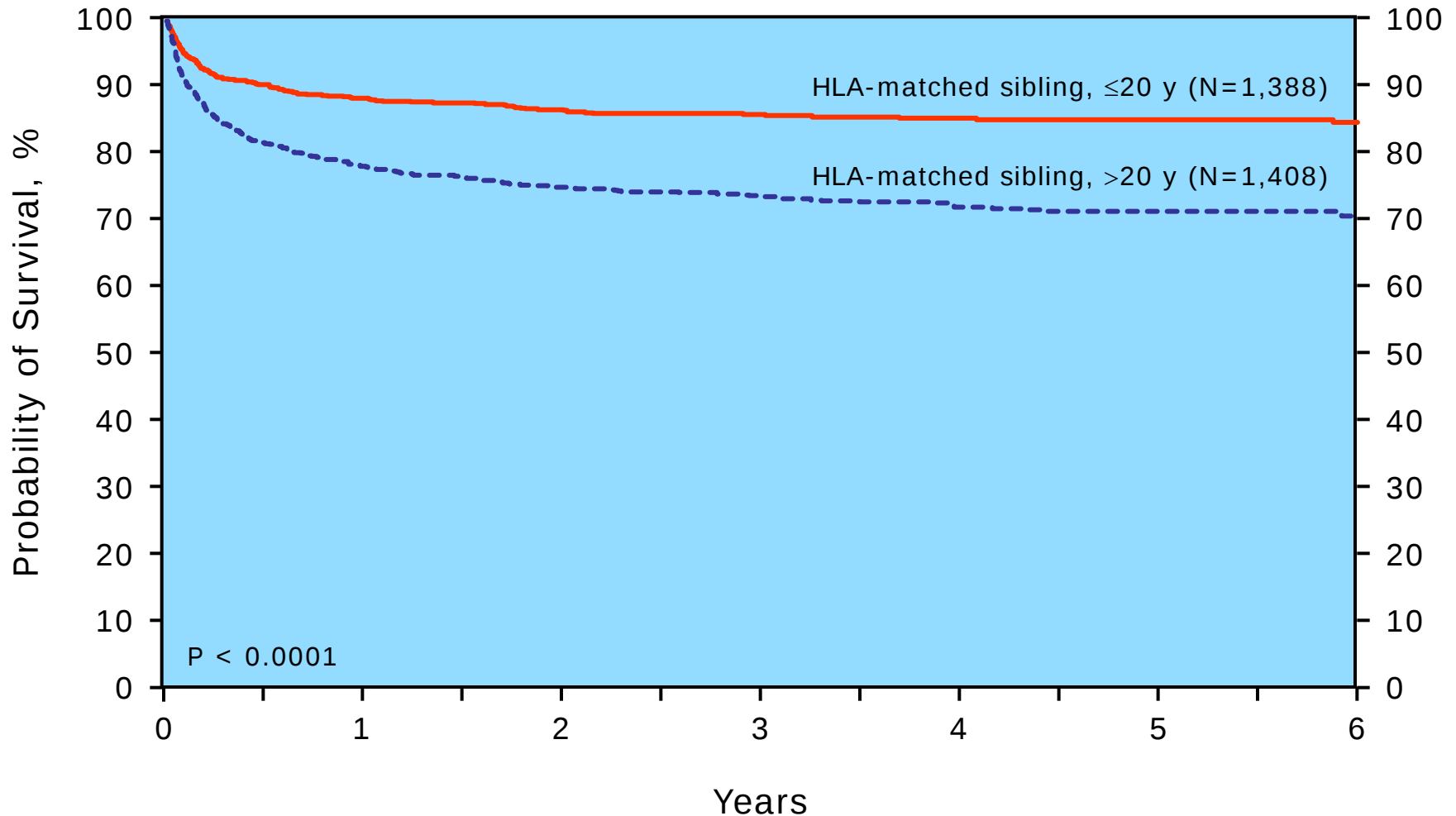
Probability of survival for CML

HLA-match sibling donor transplant, by disease status and transplant year, 98-2008



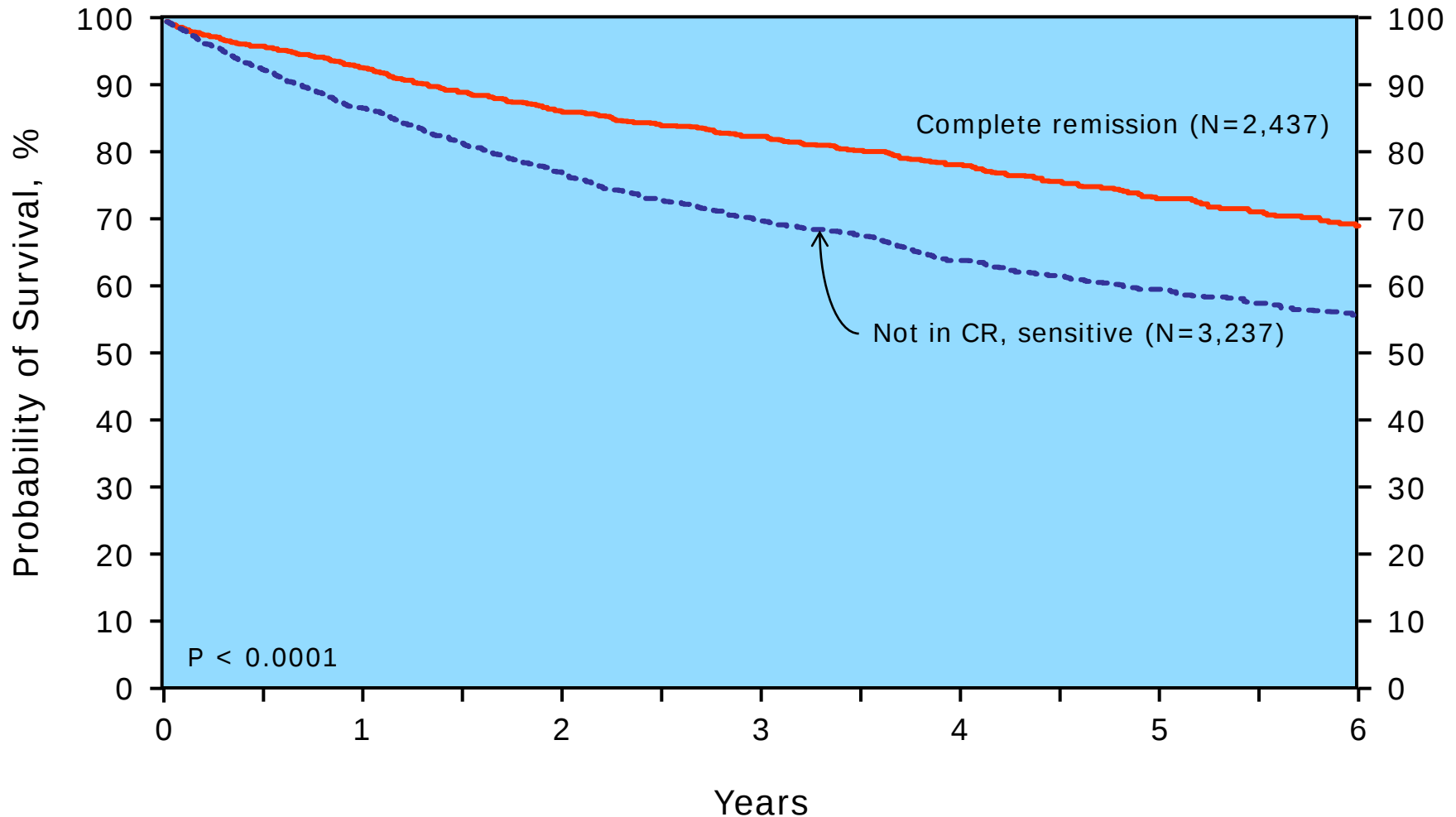
Probability of survival for severe aplastic anemia

allogeneic transplant for, by donor type and age, 1998-2008

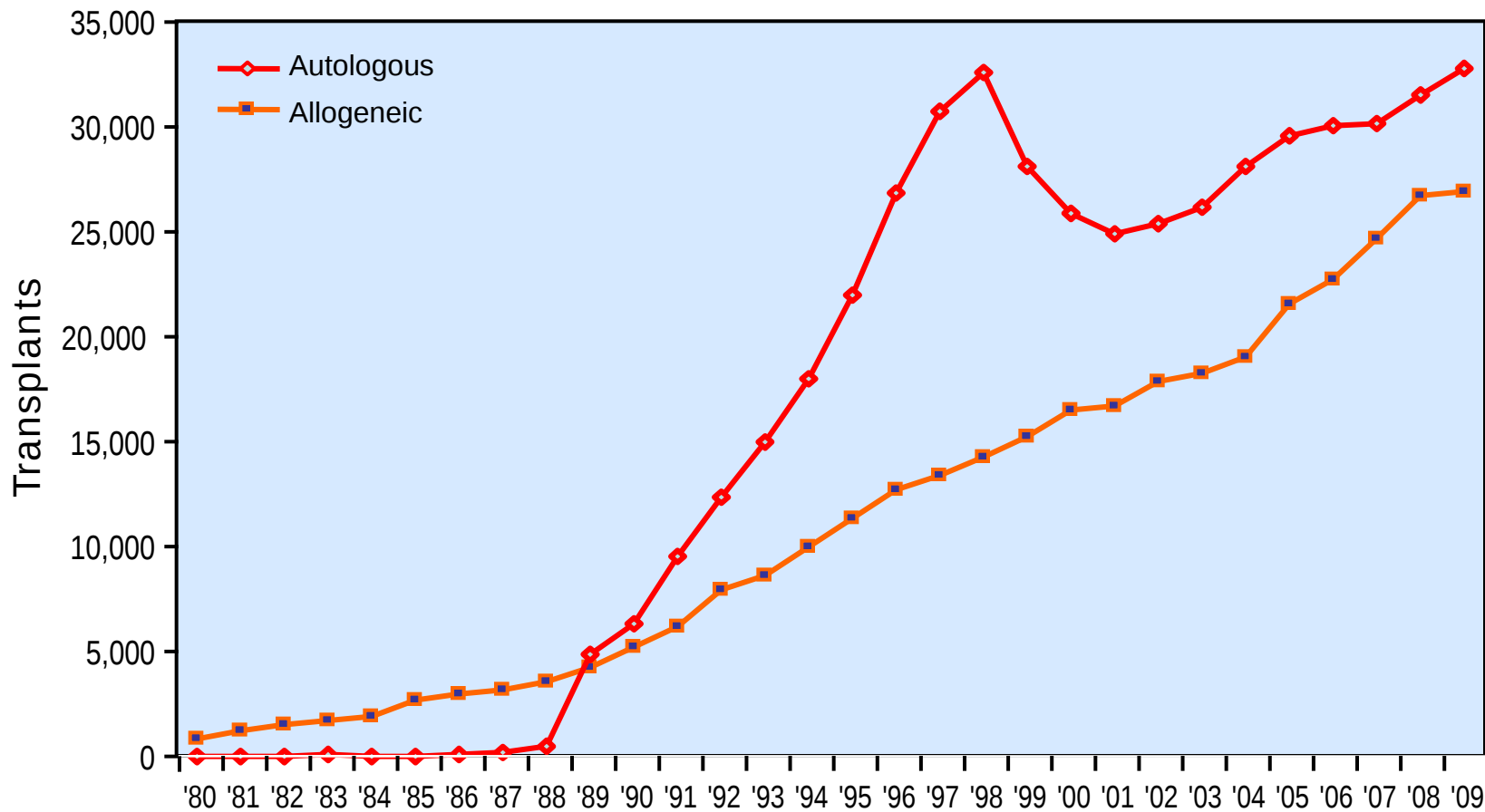


Probability of survival for Hodgkin disease

autologous transplant , by disease status, 1998-2008

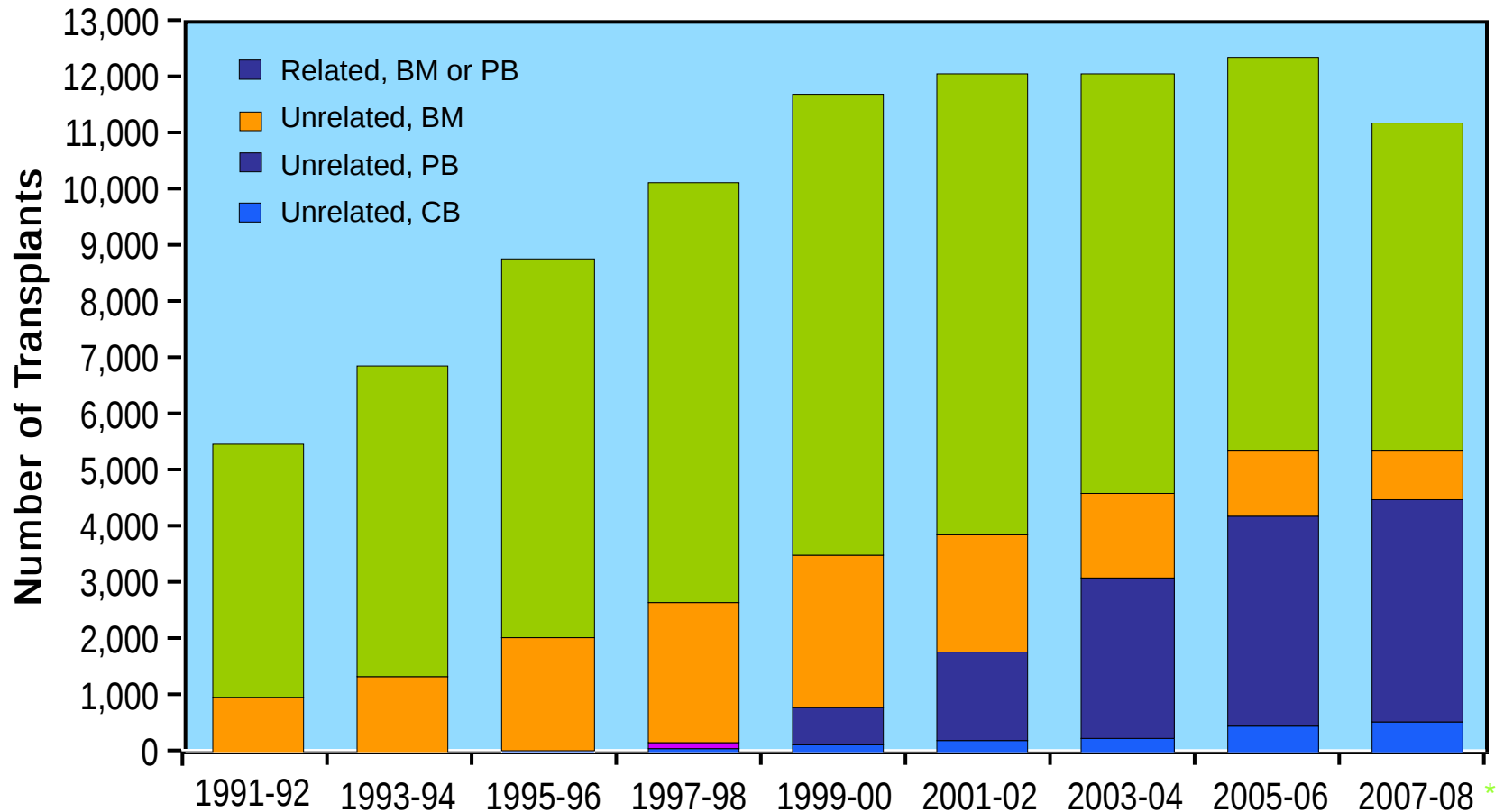


Transplant Activity Worldwide 1980-2009



Allogeneic transplant donor type

in patients >20 years, by and graft source, registered with CIBMTR, 1991-2008



* Data incomplete

European Transplant Activity 2010

HSCT - rates in Europe 2010

Total transplants (all)

per 10 million

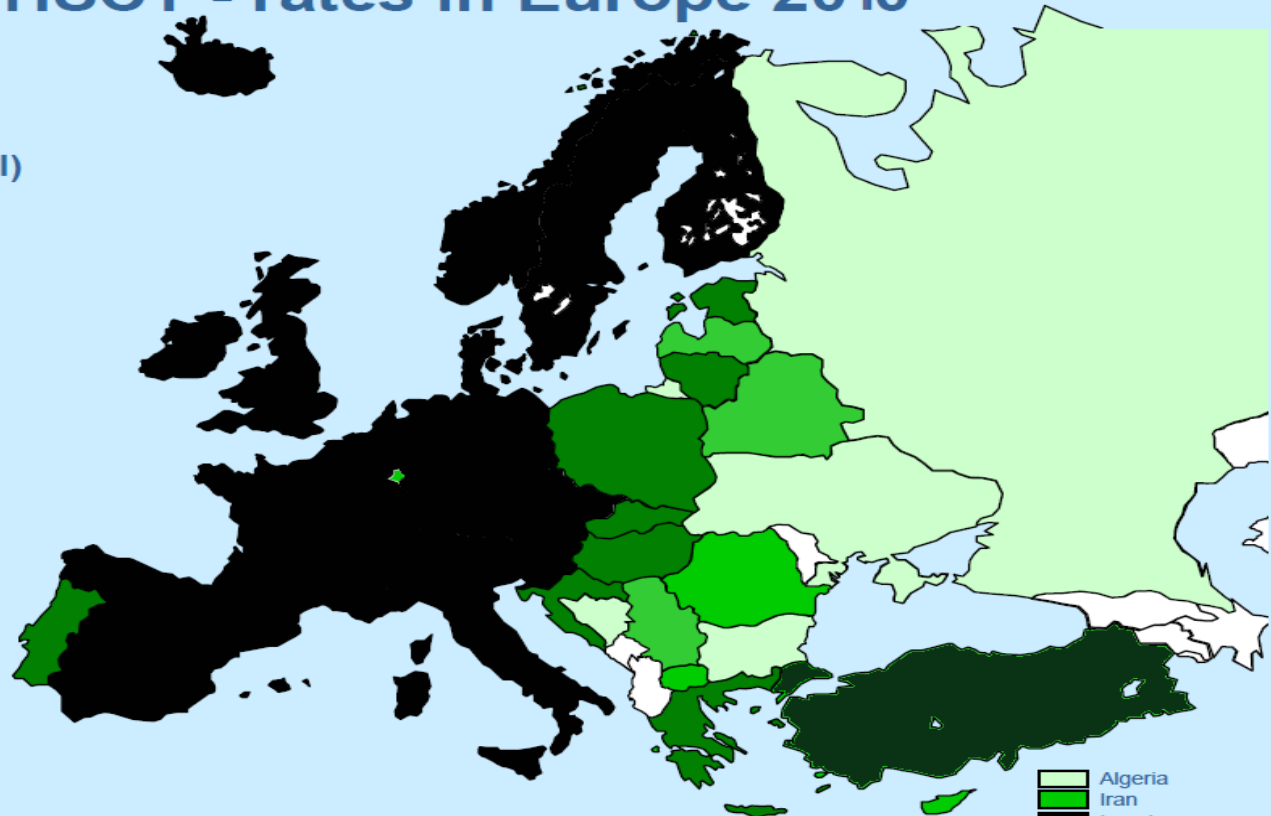
0 or no report

1 - 50

51 - 200

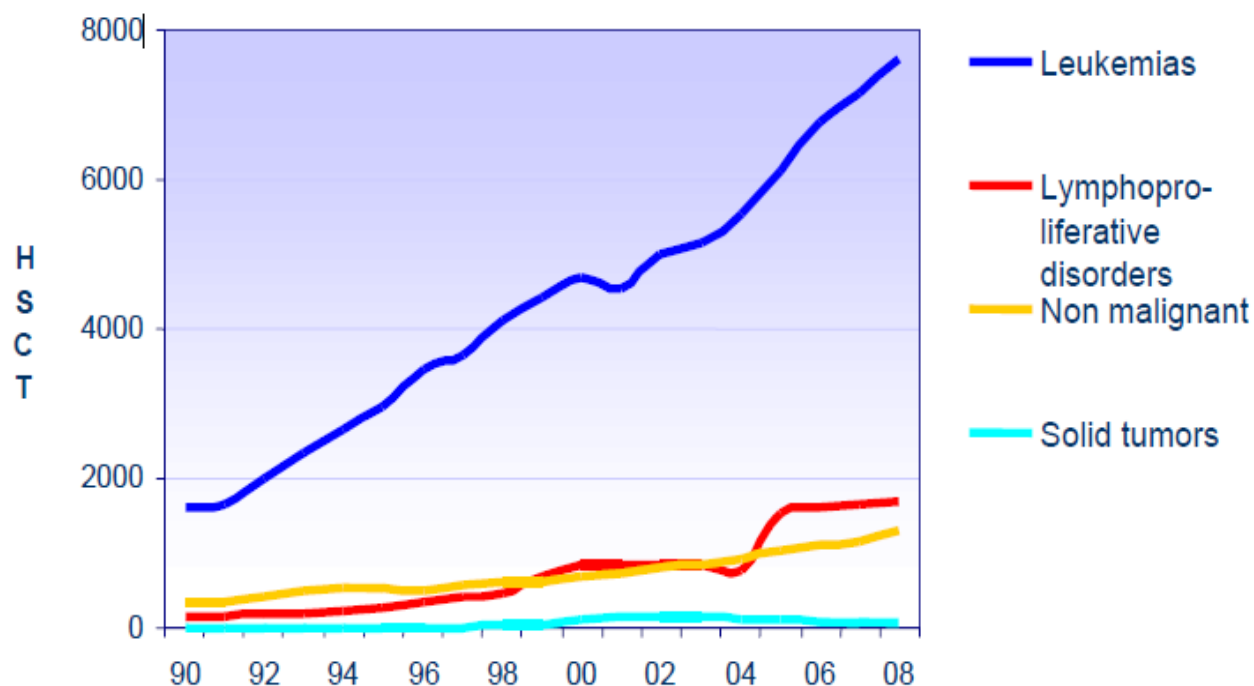
201 - 400

> 400



Algeria
Iran
Israel
Lebanon
Saudi Arabia
South Africa
Tunisia
Jordan

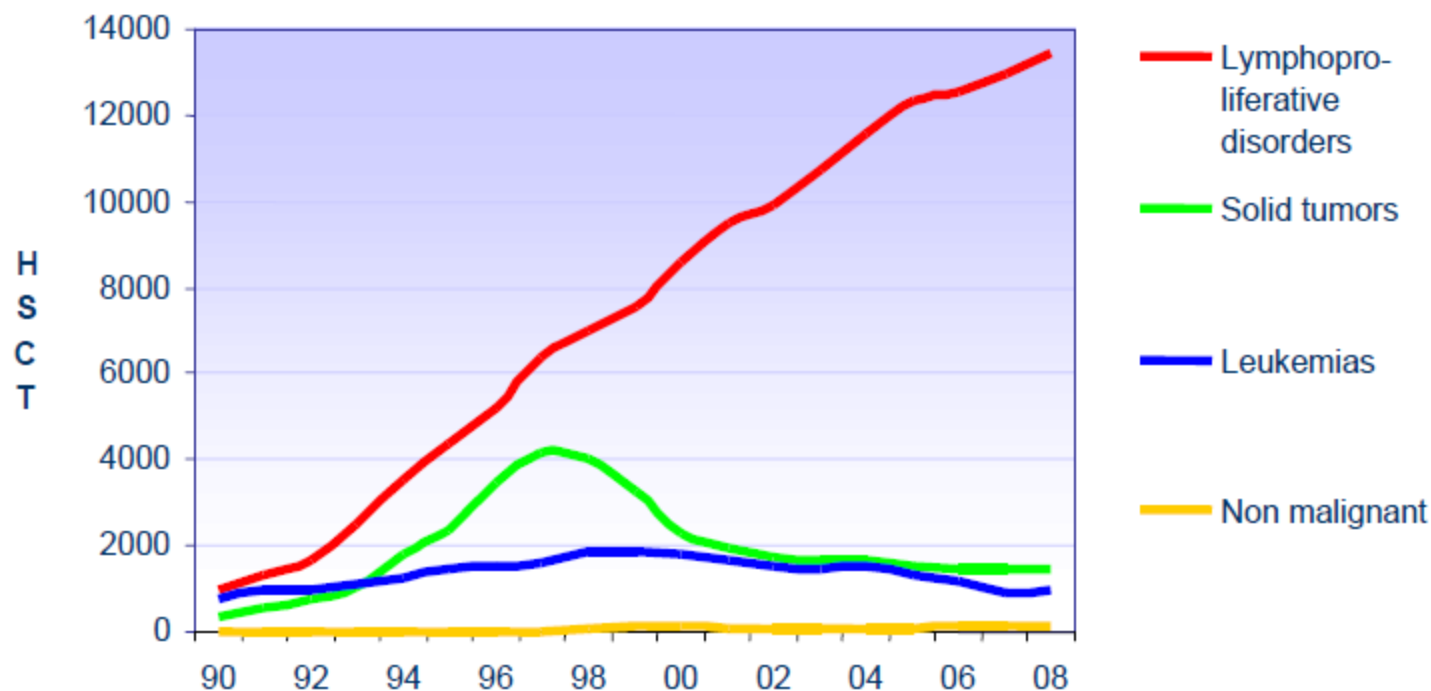
EBMT Activity Survey on HSCT 1990-2008: allogeneic



2008: final data

The European Group for Blood and Marrow Transplantation

EBMT Activity Survey on HSCT 1990-2008: autologous



2008: final data

The European Group for Blood and Marrow Transplantation

EBMT Activity survey on HSCT in 2008: main indications

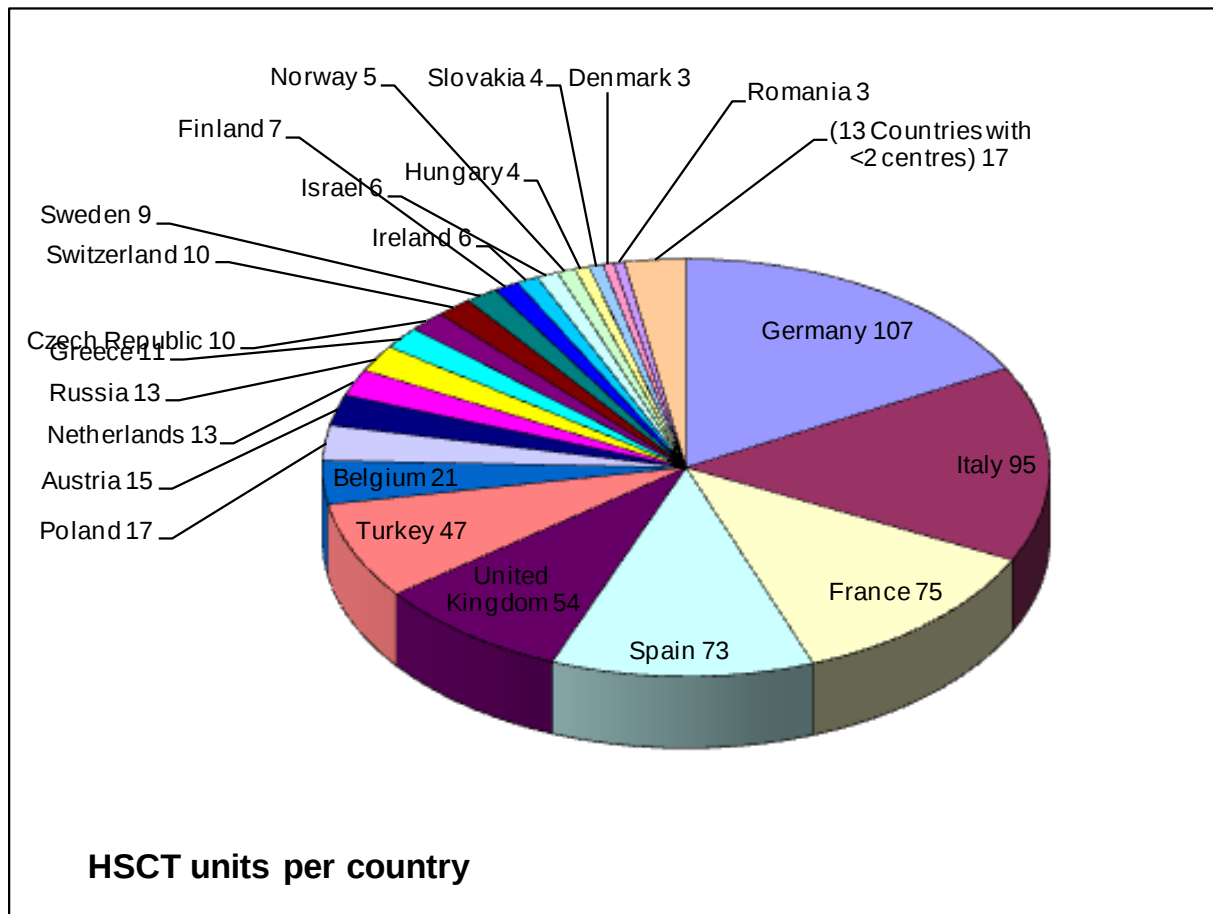
Indication	Allogeneic 1st Tx.	Autologous 1 st Tx.	Total
Leukaemias*	7632	978	8610
Lymphoproliferative disorders	1699	13428	15127
Bone marrow failures	615	2	617
Solid tumours	62	1424	1486
Non-malignant disorders	699	172	869
Others	75	26	101
Total	10782	16028	26810

* includes CLL

2008: final data

The European Group for Blood and Marrow Transplantation

Activity survey centers 2010

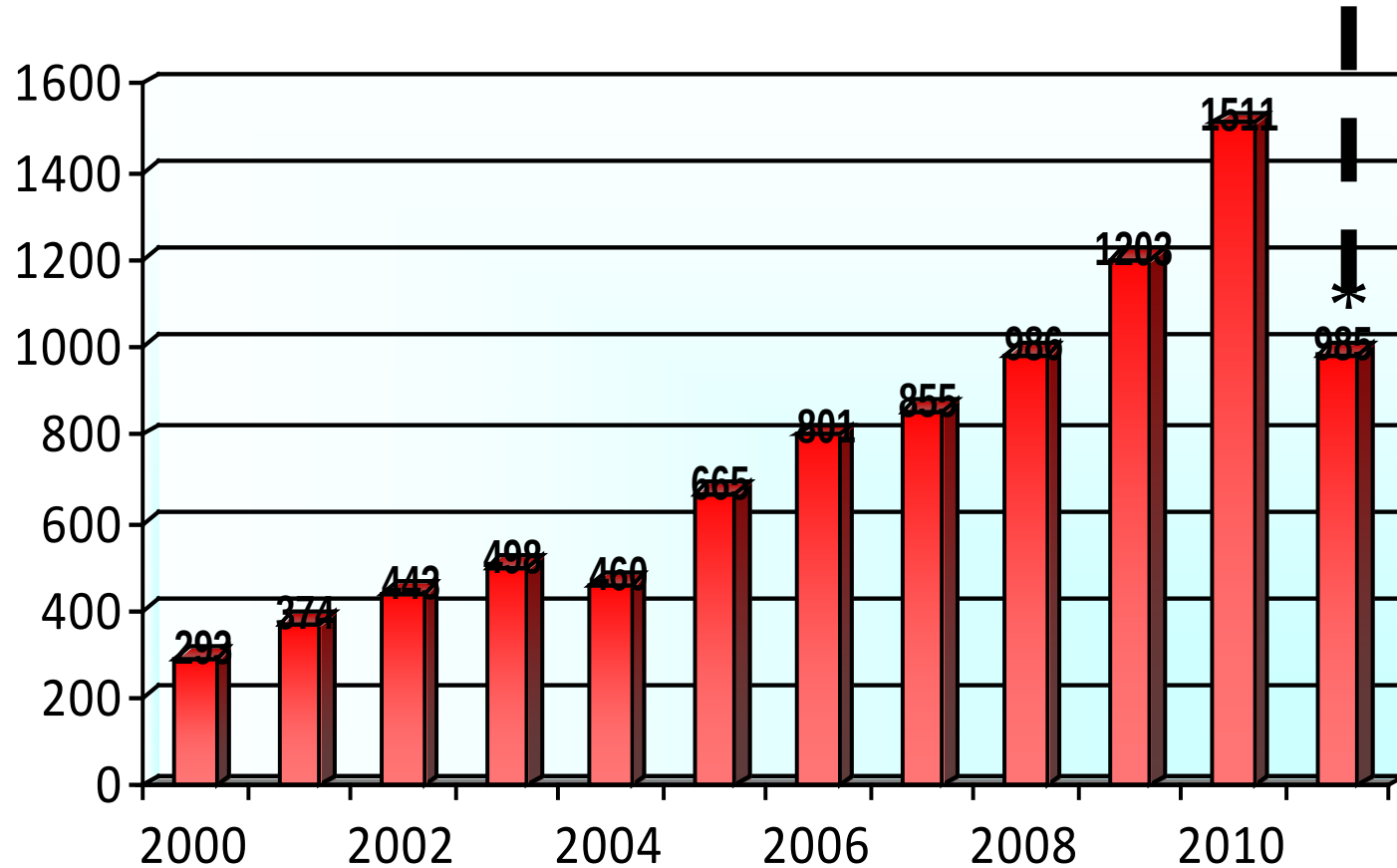


COUNTRY	Activity Survey
Germany	107
Italy	95
France	75
Spain	73
United Kingdom	54
Turkey	47
Belgium	21
Poland	17
Austria	15
Netherlands	13
Russia	13
Greece	11
Czech Republic	10
Switzerland	10
Sweden	9
Finland	7
Ireland	6
Israel	6
Norway	5
Hungary	4
Slovakia	4
Denmark	3
Romania	3
(13 Countries with <2 centres)	17
	625

Hematopoietic Stem Cell Transplantation

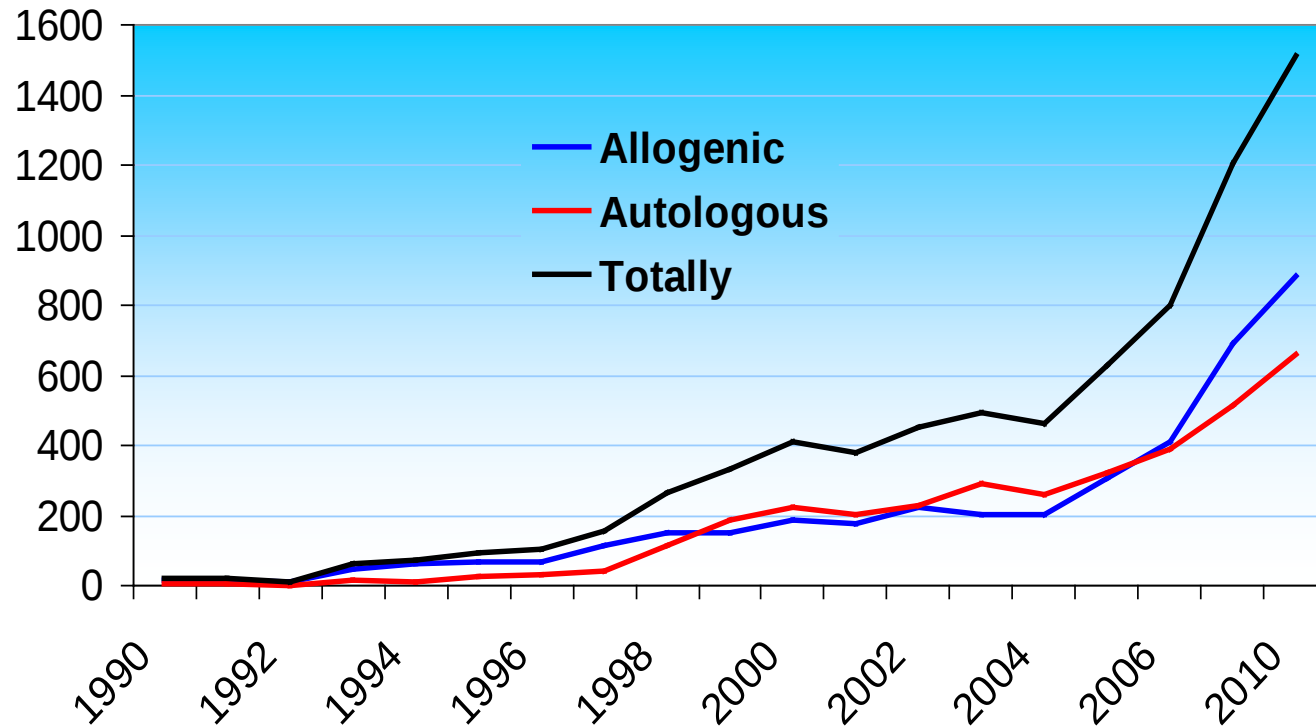
Activity survey of Turkish Center T

2000



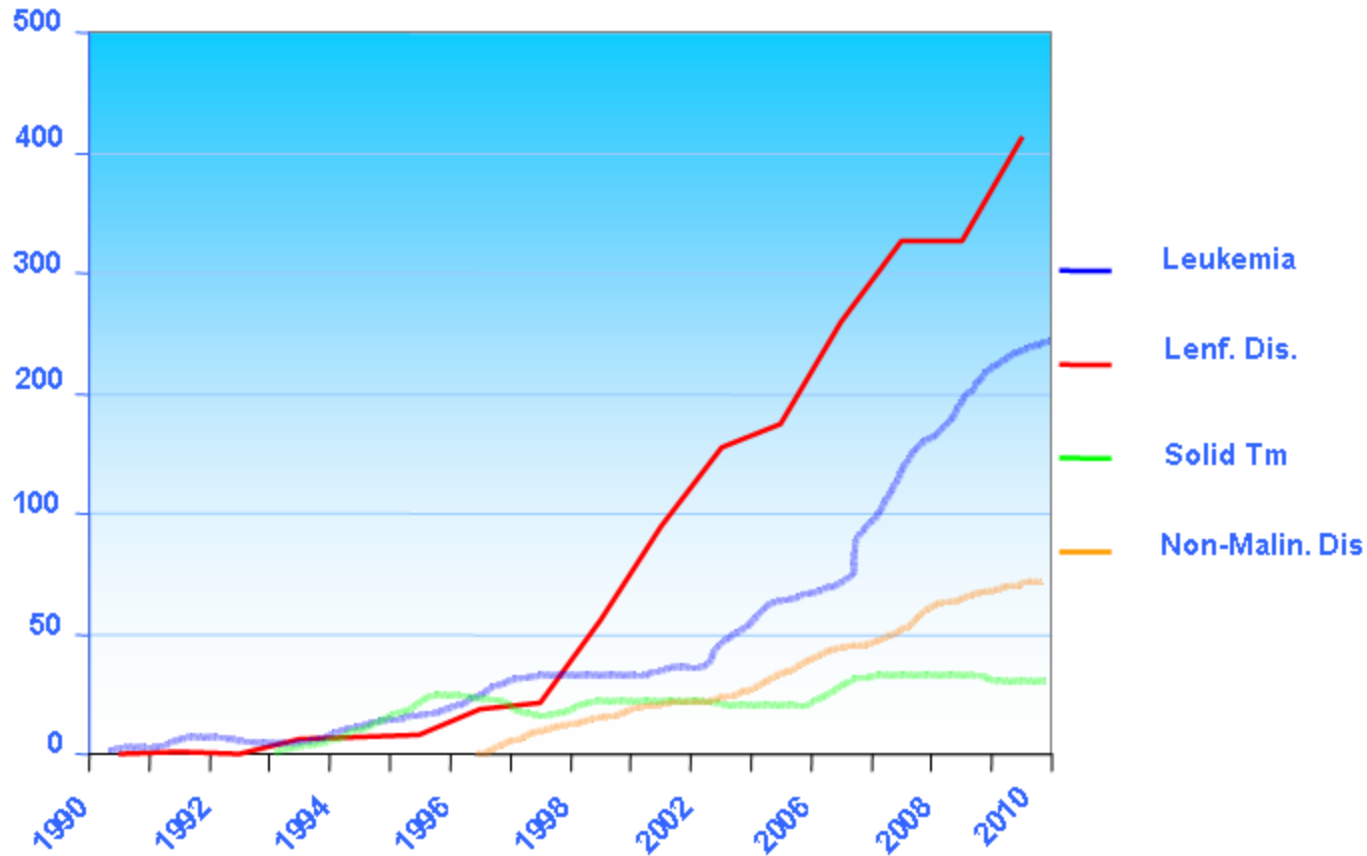
* Sixt month (incomplet data)

TTR (Turkish Transplant Registry) Hematopoietic Stem Cell Activity Survey



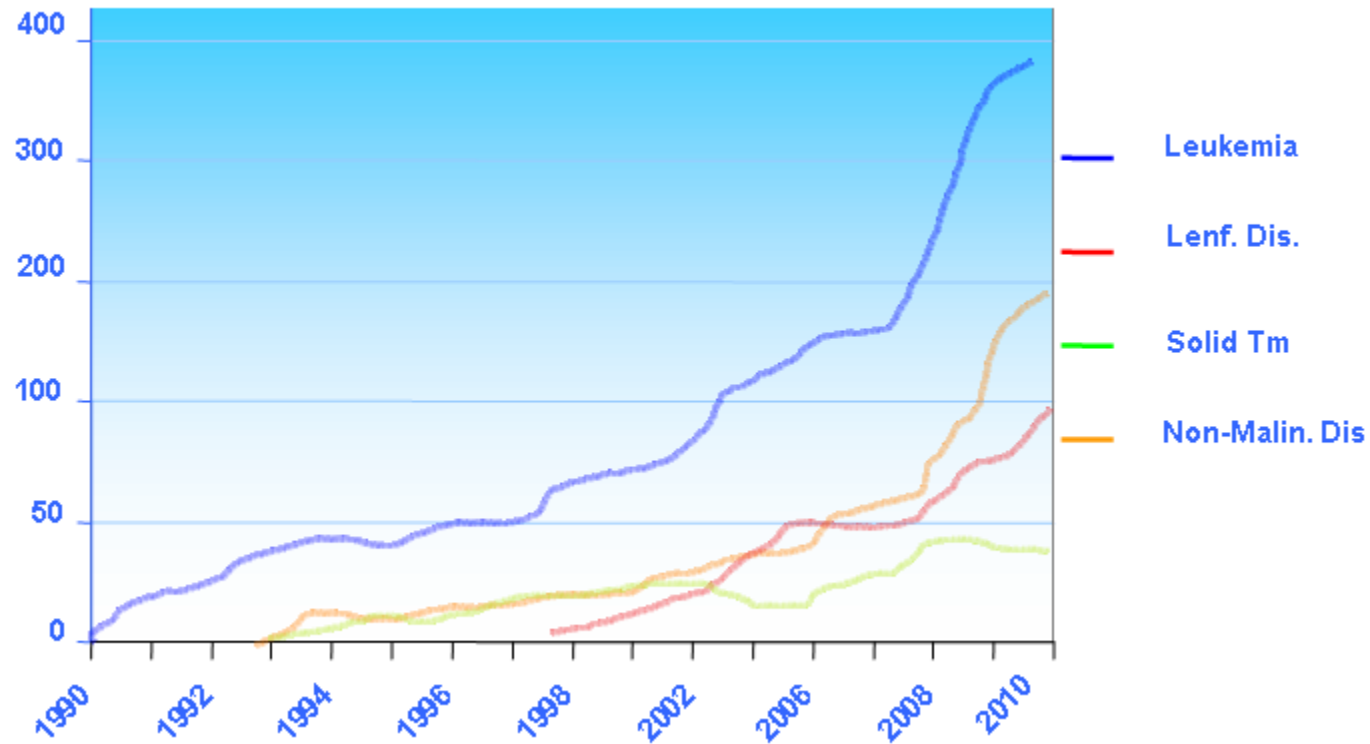
TTR (Turkish Transplant Registry)

Autologous Hematopoietic Stem Cell Activity Survey



TTR (Turkish Transplant Registry)

Allogeneic Hematopoietic Stem Cell Activity Survey

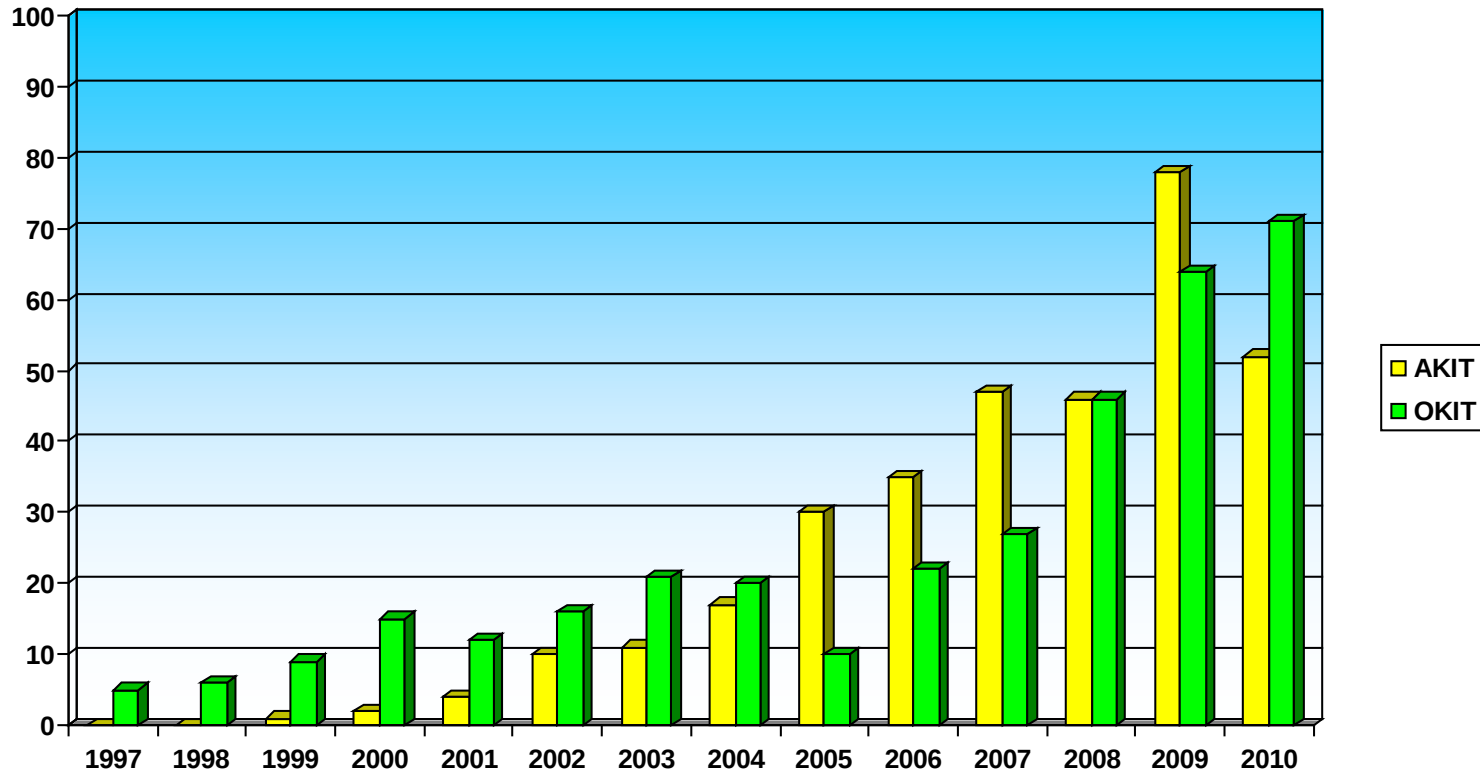




Erciyes University

Cappadocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

Hematopoietic Stem Cell Transplantation Activity Survey

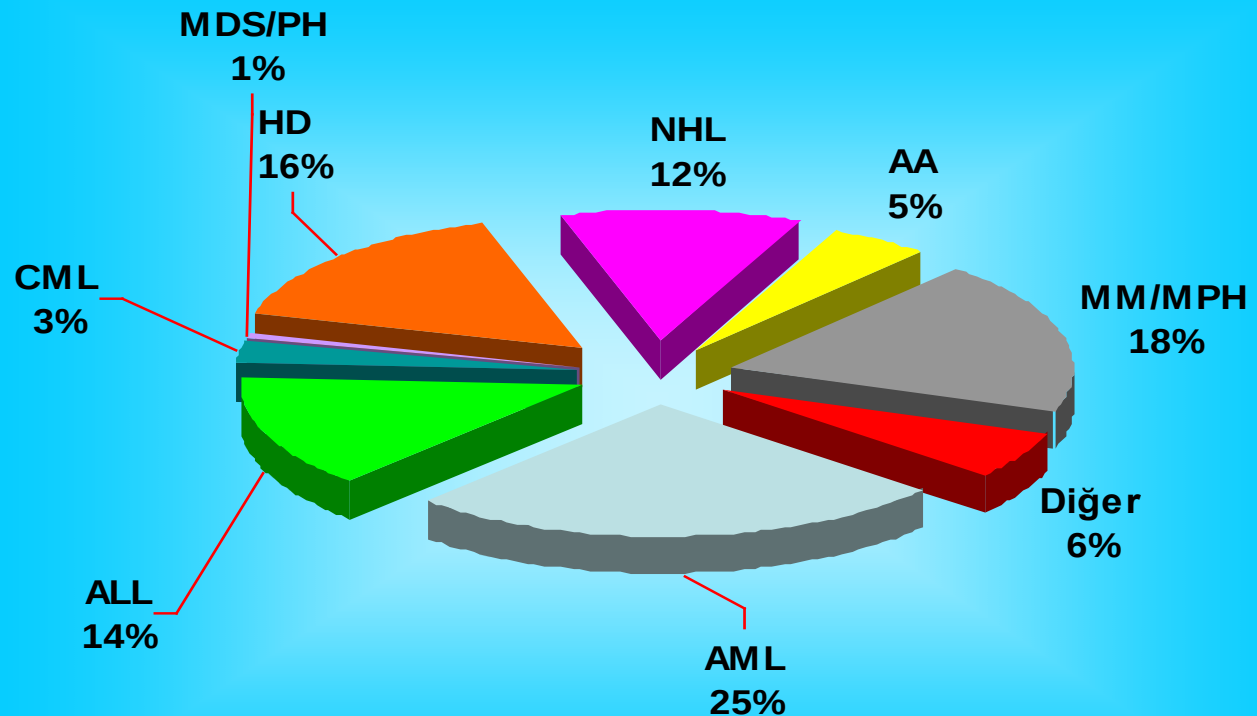




Erciyes University

Cappodocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

Hematopoietic Stem Cell Transplantation Activity Survey



Erciyes University

Cappodoccia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

Hematopoietic Stem cell Transplantation Activity Survey



Erciyes University

Cappodoccia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)



**Thank you for
your attention**

Teşekkürler

