

El trasplante de Progenitores Hematopoyéticos en el mundo

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HCUVA. Universidad de Murcia

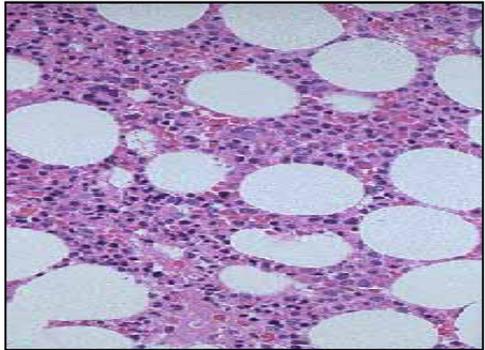
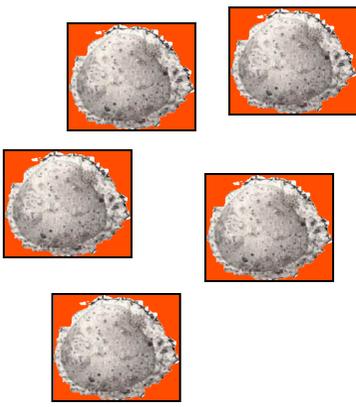
Sumario

1. Fundamentos
2. Tipos
3. Técnica. Complicaciones
4. Indicaciones
5. Resultados

Fundamentos del TPH

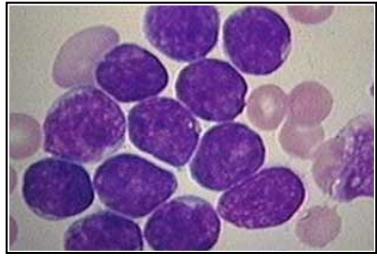
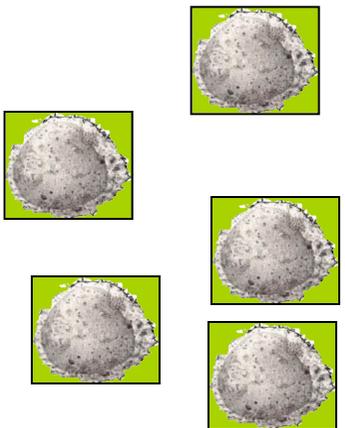
**Células
Prog. hem.**

Reconstitución
Hemopoyética



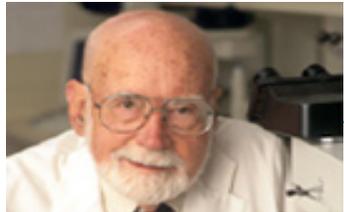
Injerto Hemopoyético

**Progenitores
inmunológicos**



Reconstitución Inmune

Trasplante de PH



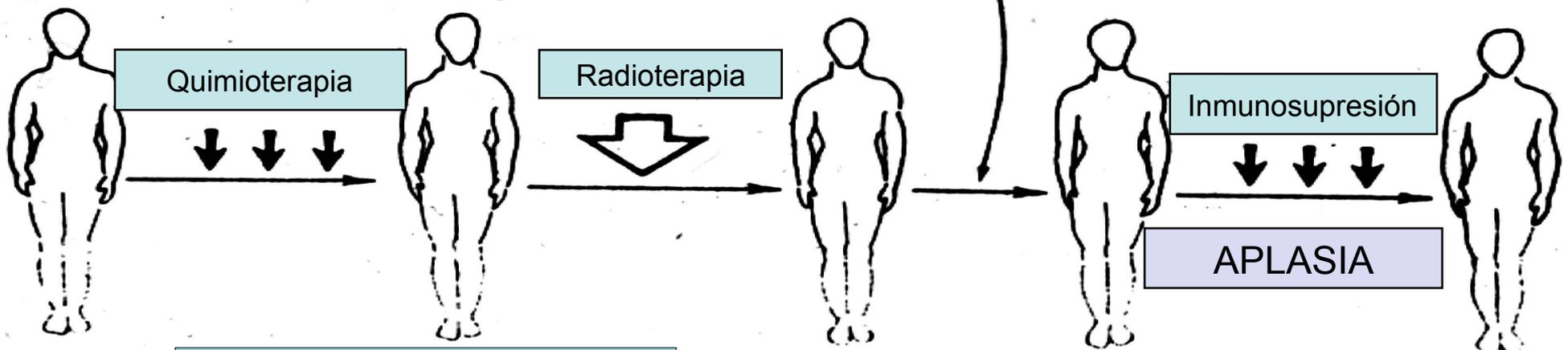
1. Obtención PH: Medula ósea, SP, CU



Donante

3. Infusión de PH

Paciente



2. Acondicionamiento

4. Injerto

Objetivos del TPH

- Restaurar la Hematopoyesis:
 - Infusión de Progenitores Hematopoyéticos (Auto – Alo)
- Eliminar células anormales (malignas /disfuncionales)
 - Terapia mieloablativa (acondicionamiento) (Auto - Alo)
- Proporcionar inmunidad normal derivada del donante
 - Anti-infecciosa. Antitumoral (Alo)

Indicaciones TPH

NEOPLASIAS

- Hematológicas: Leucemias, SMD, Linfomas, Mieloma.
- Tumores sólidos

ENFERMEDADES NO MALIGNAS

Trastornos adquiridos de la hematopoyesis y el sistema inmune:

- Aplasia medular severa.
- Enfermedades Autoinmunes

Trastornos congénitos:

- Anemias Hemolíticas (talasemias, drepanocitosis)
- Inmunodeficiencias (Wiskott-Aldrich, ISC)
- Enf. De depósito (mucopolisacaridosis, mucopolipidosis)

Tipos de TPH

Tipos de TPH según diferencias inmunológicas Donante - Receptor

1. Autólogo: el paciente es su propio donante
2. Singénico: hermano gemelo univitelino
3. Alogénico: donante HLA compatible
 1. Familiar: hermano HLA compatible
 2. Donante no emparentado

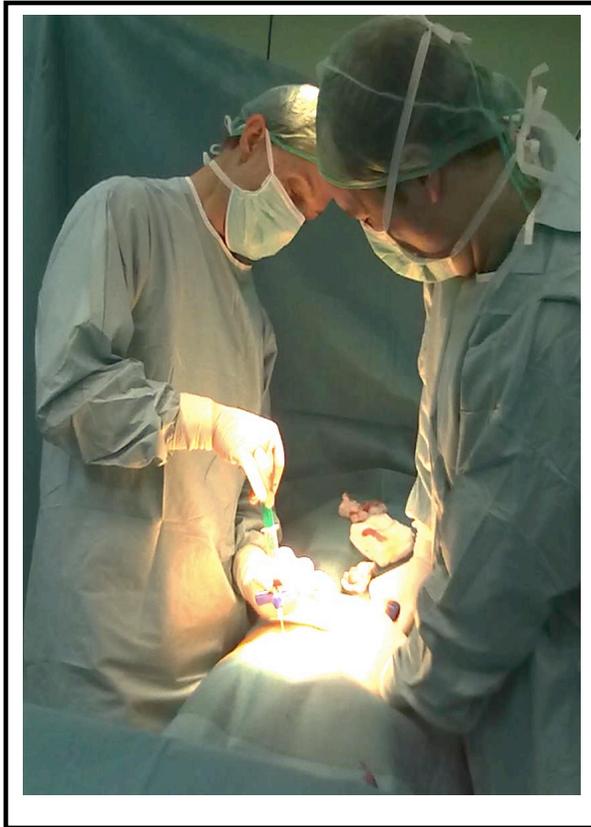
Características diferenciales del TPH

	TOXICIDAD	EICH*	RECAIDA
• ALO-TPH	++	+++	+
• AUTO-TPH	+	--	+++

* Efectos inmunes: EICH, Fallo injerto, EICL

Tipos de TPH según la fuente de PH

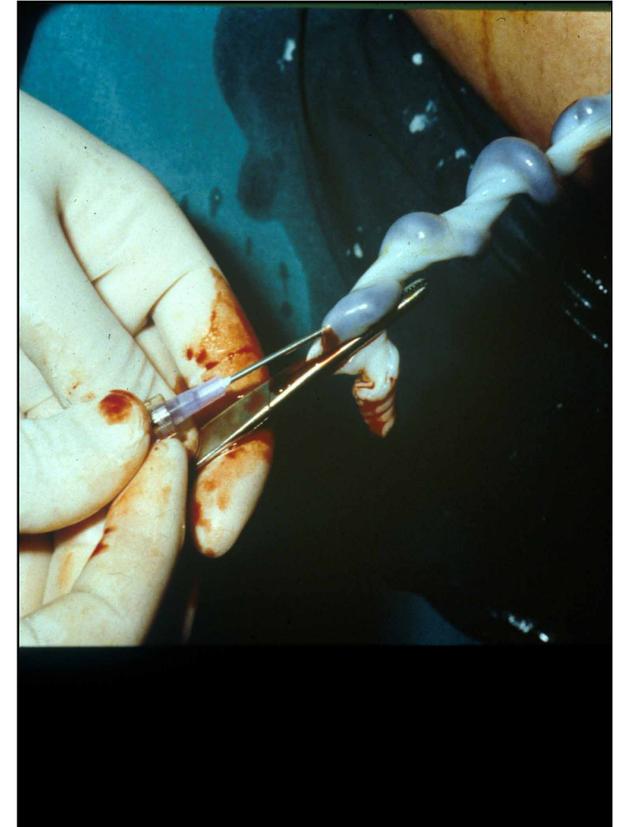
MO (20%)



SP (75%)

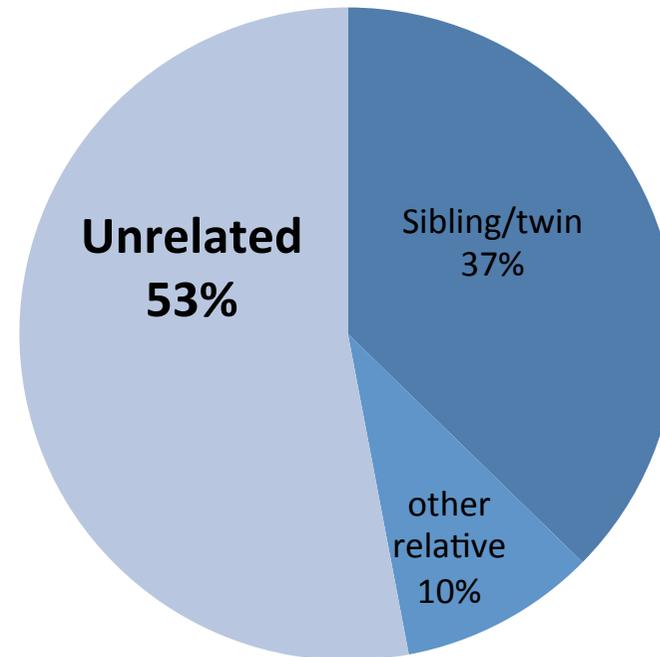
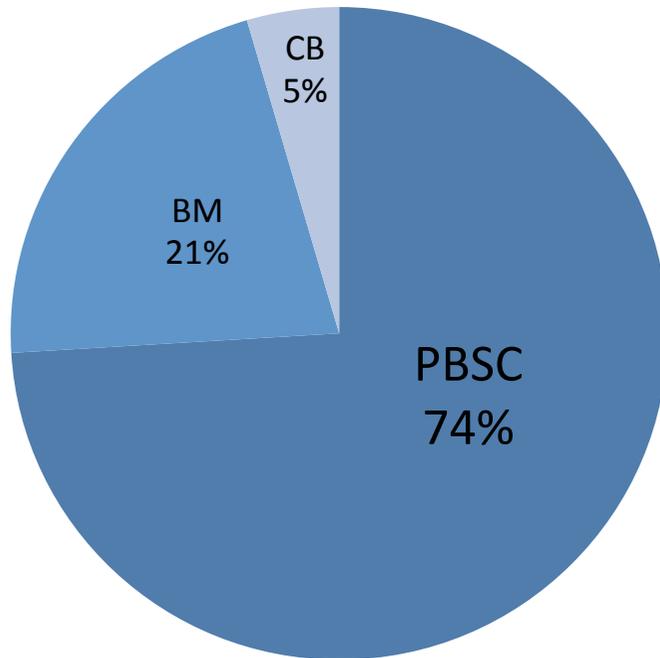


CU (5%)



HSCT Activity in Europe 2013:

Stem cell source and donor type: all transplants



Tipos de TPH según intensidad del régimen de acondicionamiento

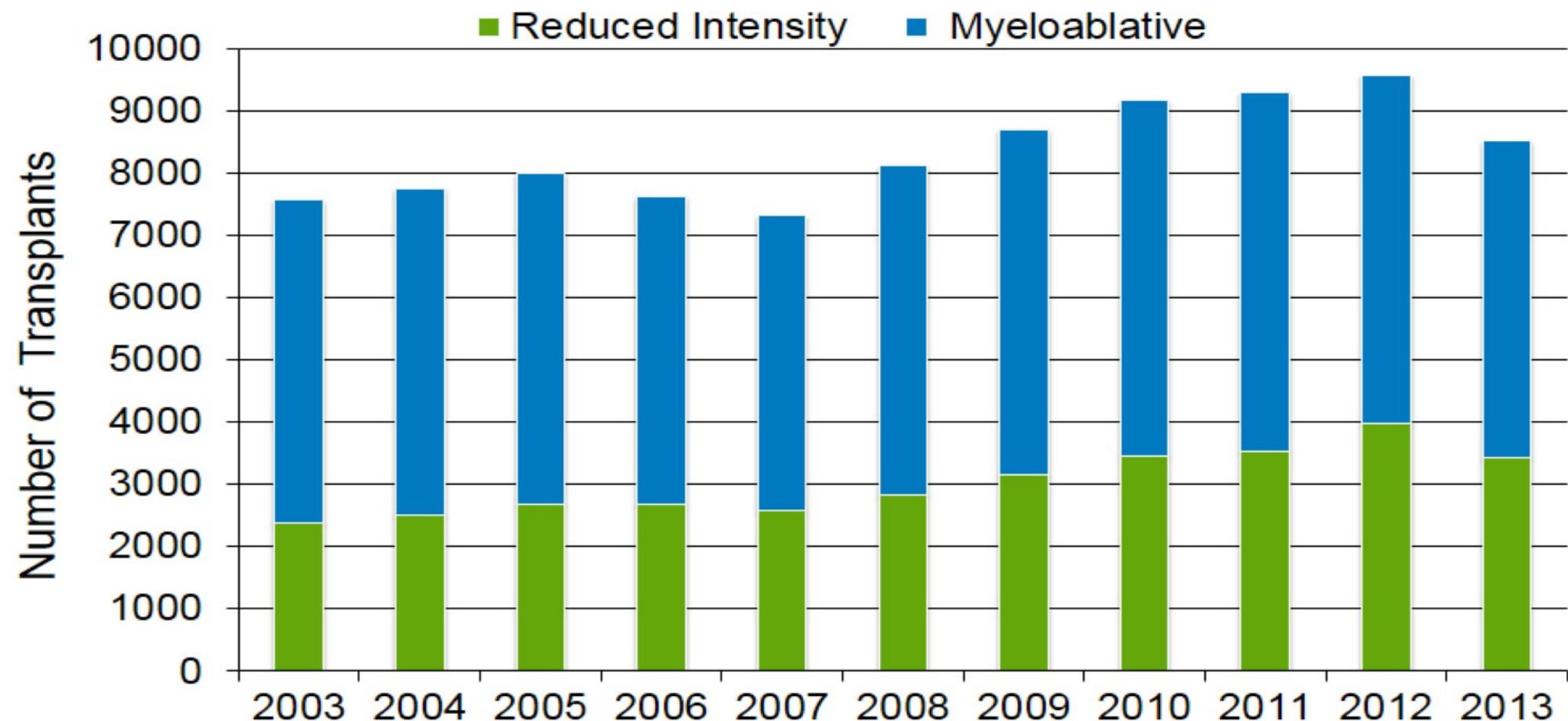
1. TPH Mieloablatoivo

- TPH convencional: Alta MRT

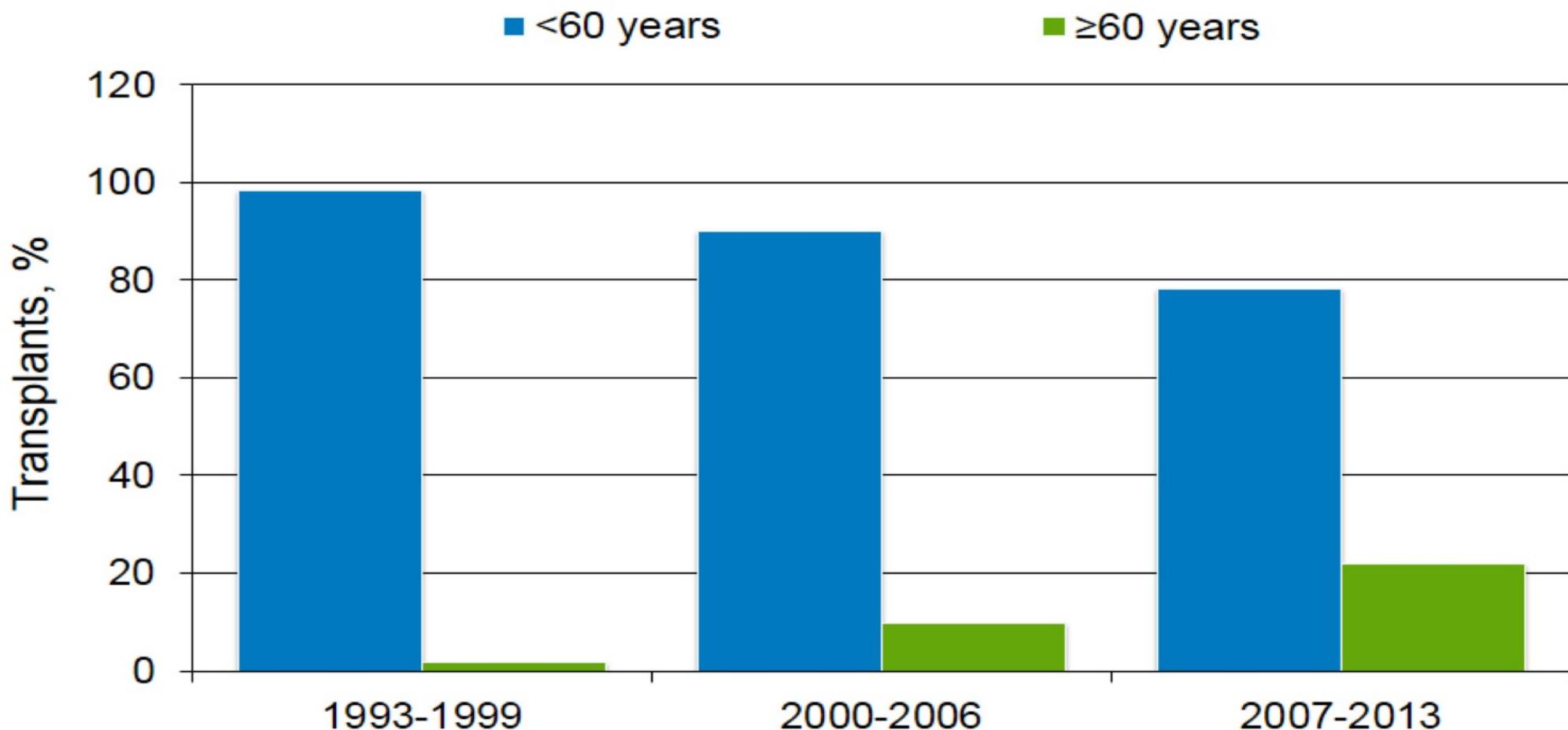
2. TPH No-Mieloablatoivo

- TPH de intensidad reducida: ↓↓MRT
- “mini-TPH”, “micro-TPH”

Allogeneic Transplants Registered with the CIBMTR



Trends in Allogeneic Transplants by Recipient Age*

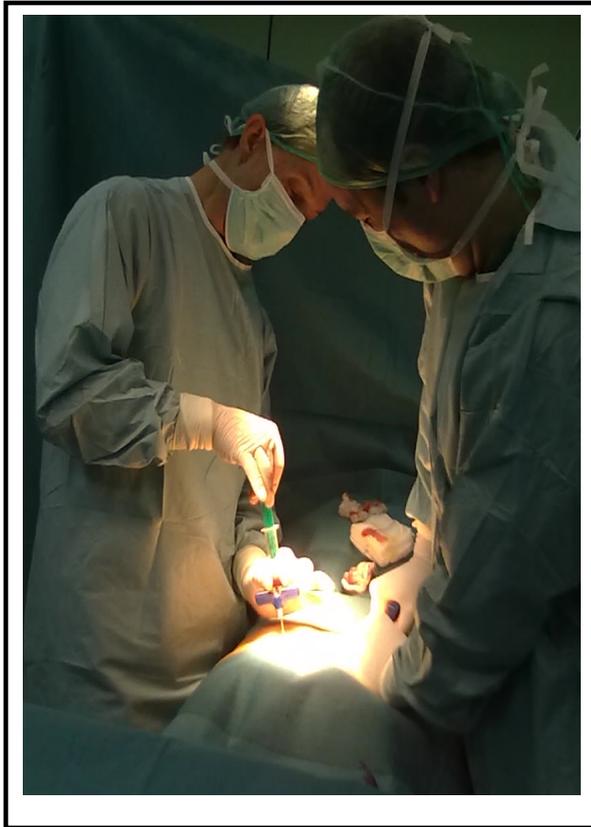


TPH. Técnica

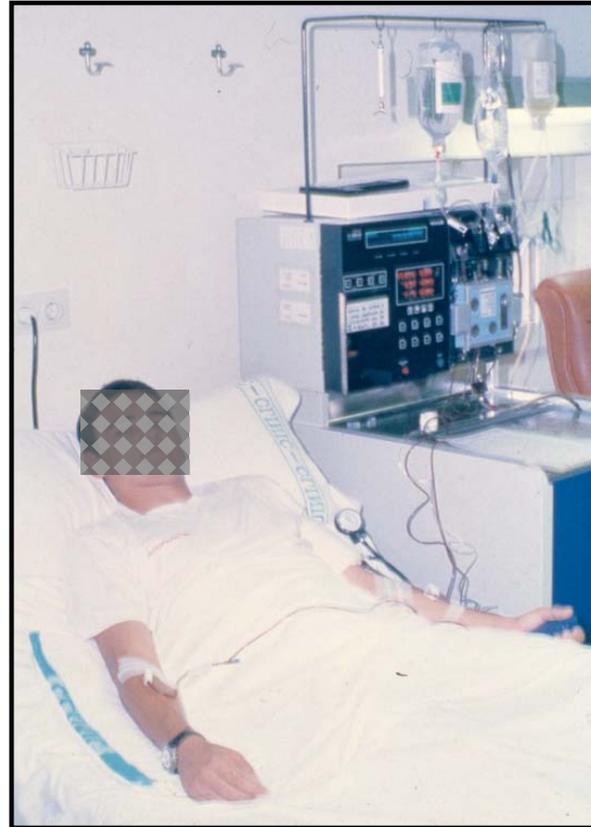
Complicaciones

Recolección de PH (“Harvest”)

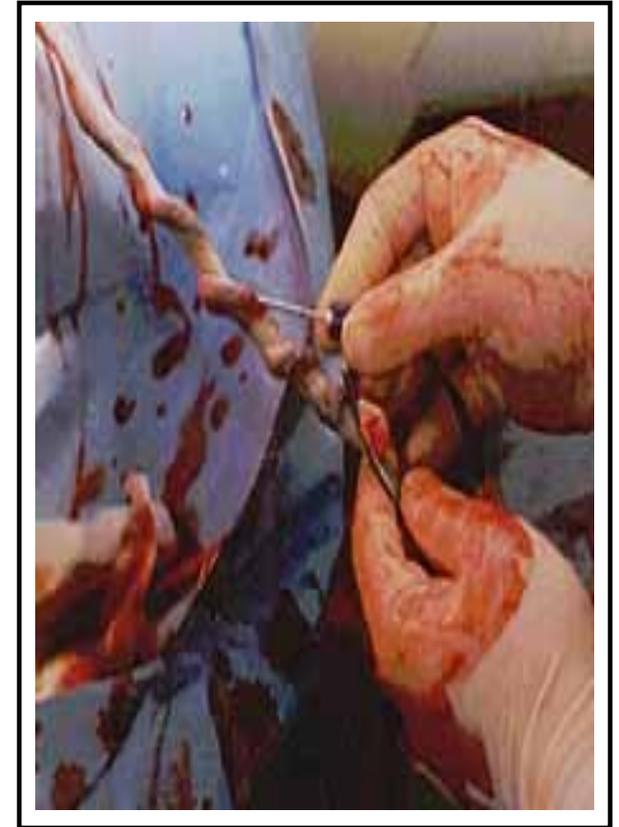
BM (20%)



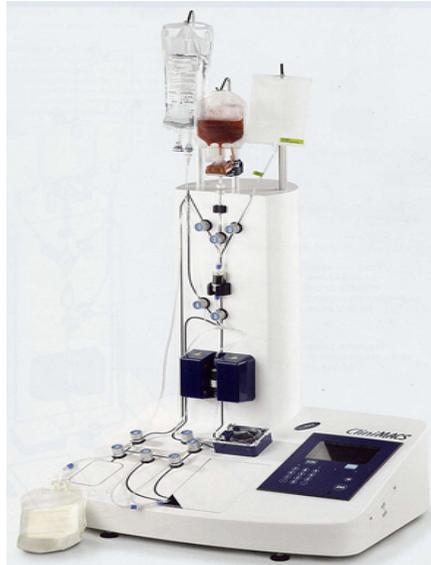
PB (75%)



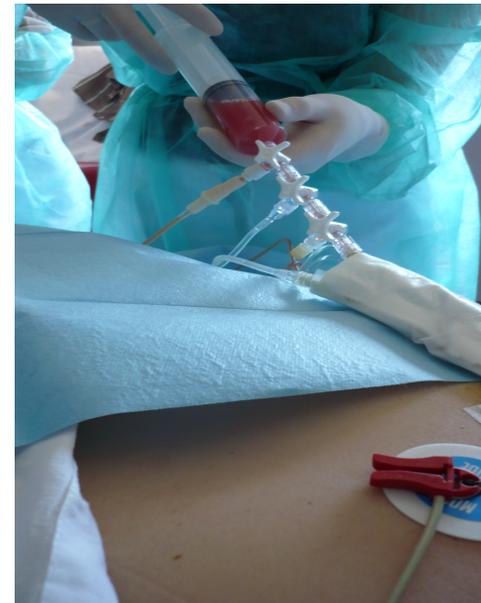
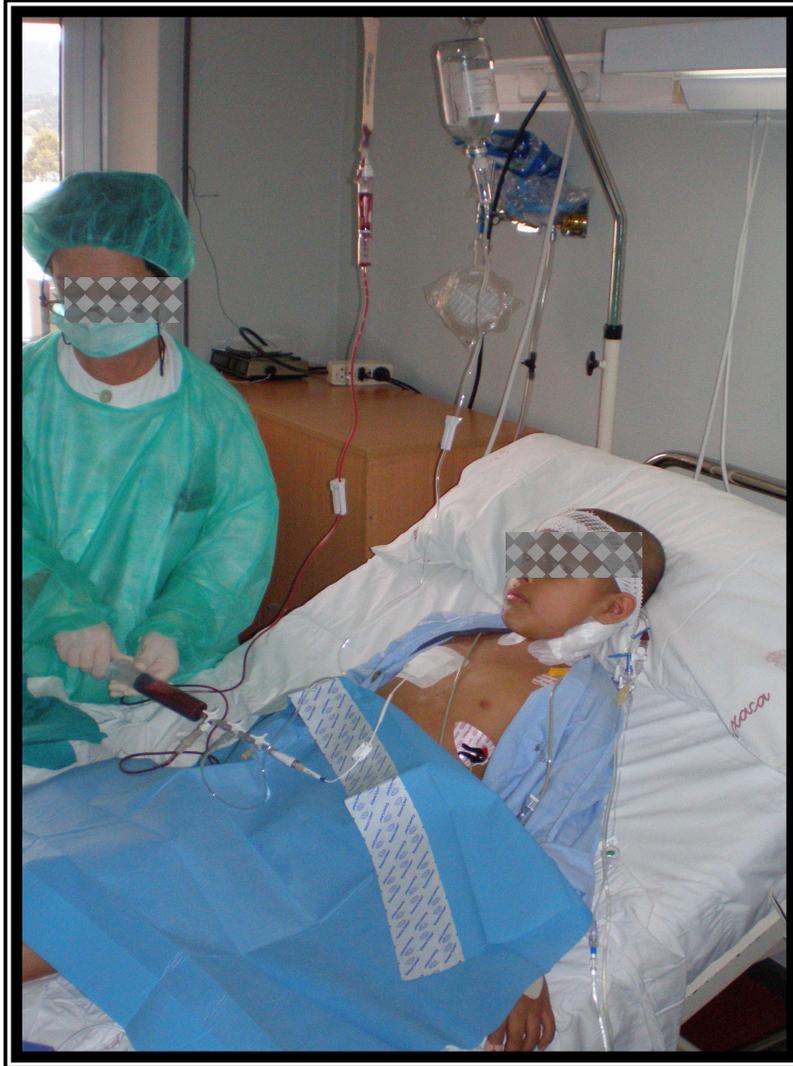
UC (5%)



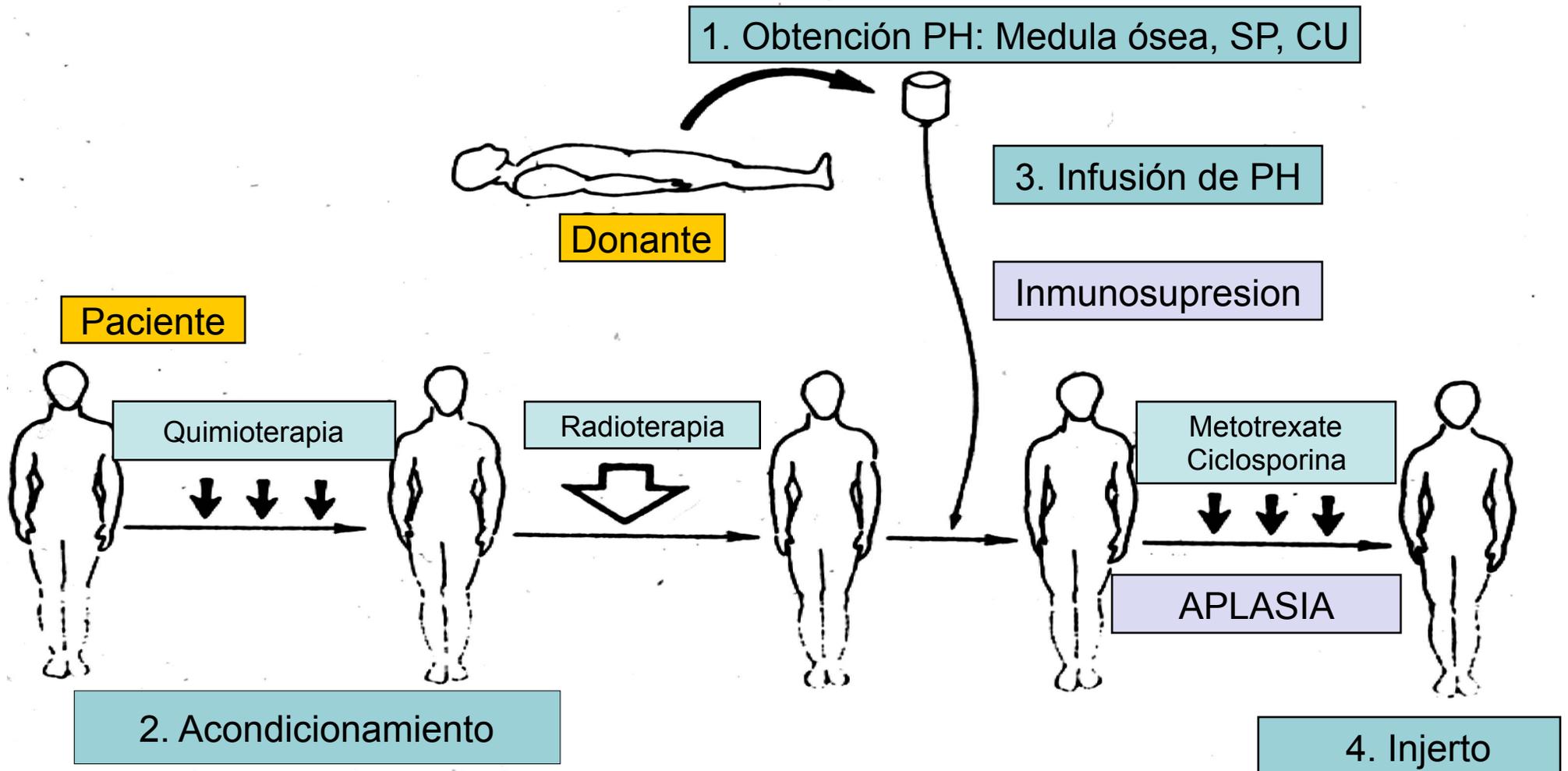
Manipulación “in vitro” y criopreservación



Infusión PH / TPH

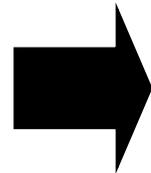
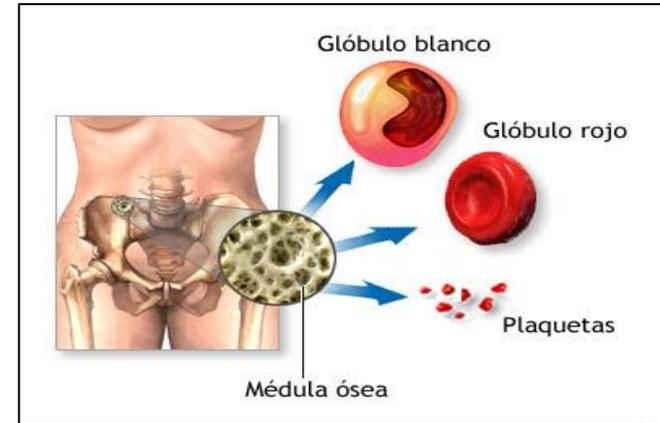
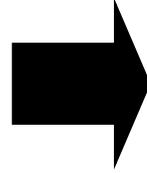


Trasplante Alogénico de PH



TPH. Complicaciones

- Aplasia medular
- Mucositis
- Toxicidad Hepática
- Toxicidad Pulmonar
- Immunologicas

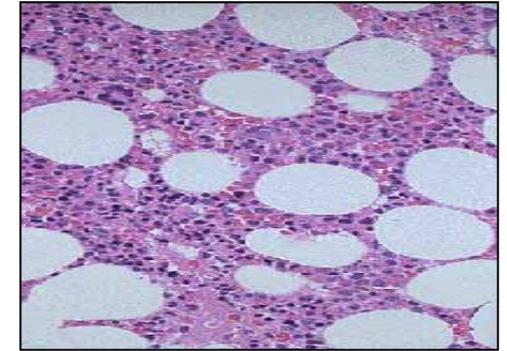
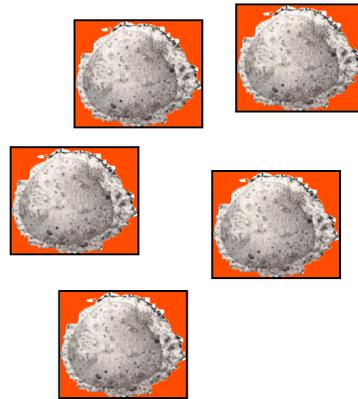


EICH

Patogenia EICH

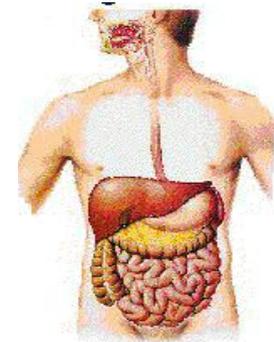
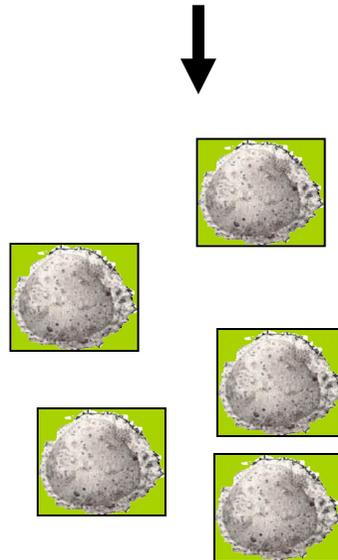
**Células
Prog. Hem.**

Reconstitución
Hemopoyética



Injerto Hemopoyético

**Linfocitos del
Donante**
(células T, NK, CPA)

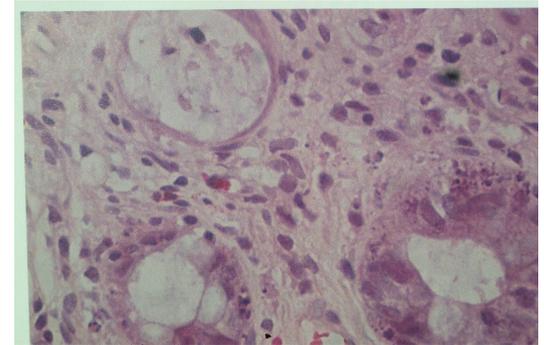
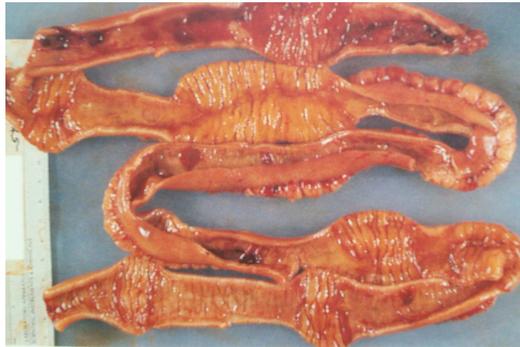


Enfermedad Injerto contra huesped.
Ataque a los tejidos del huésped
mediado por linfocitos T aloreactivos

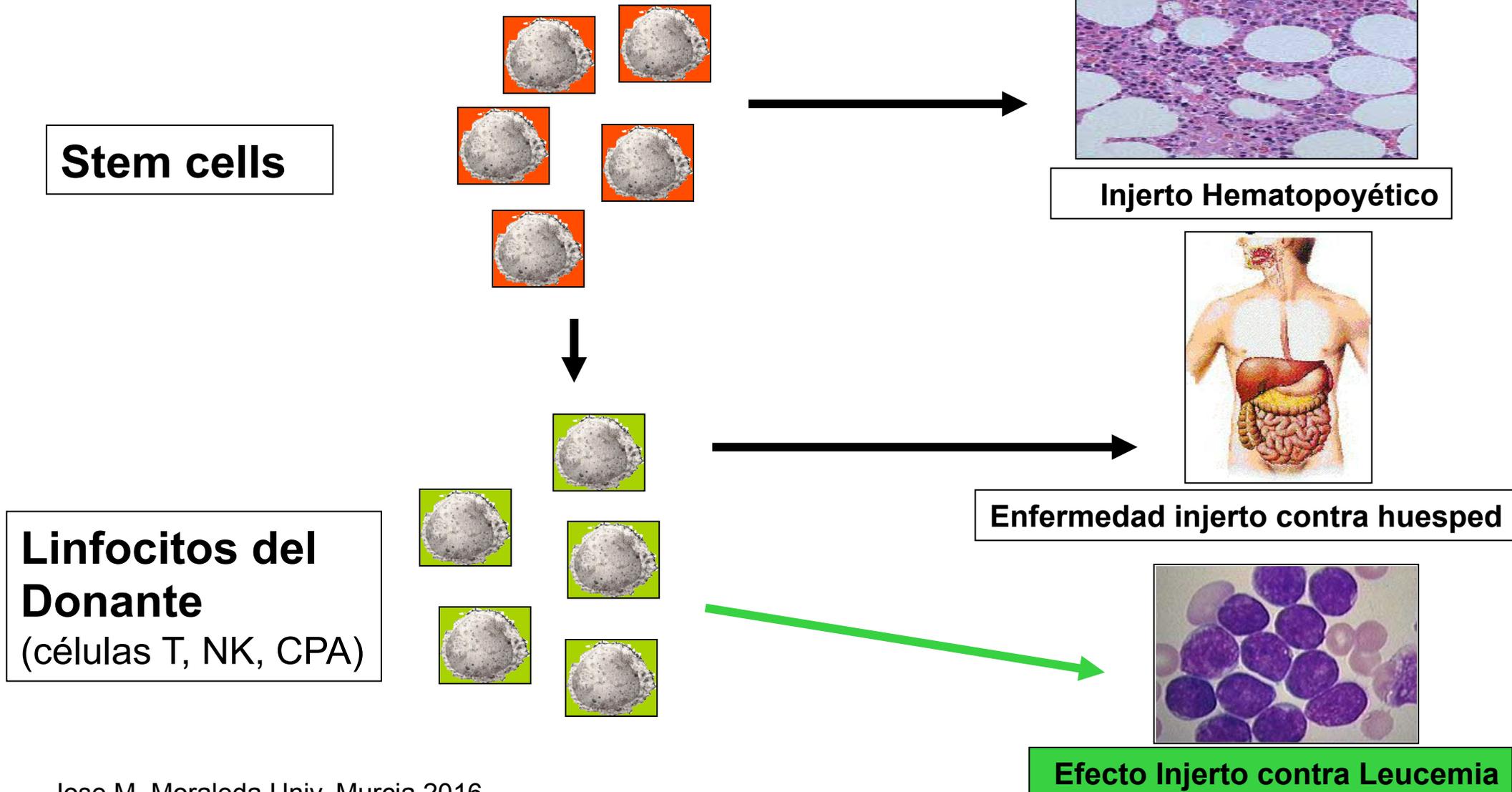
EICH aguda. Organos diana

Manifestaciones Clínicas

- Piel:
 - Exantema
 - Palmas- plantas
- Digestivo:
 - Diarrea
- Hígado:
 - Ictericia



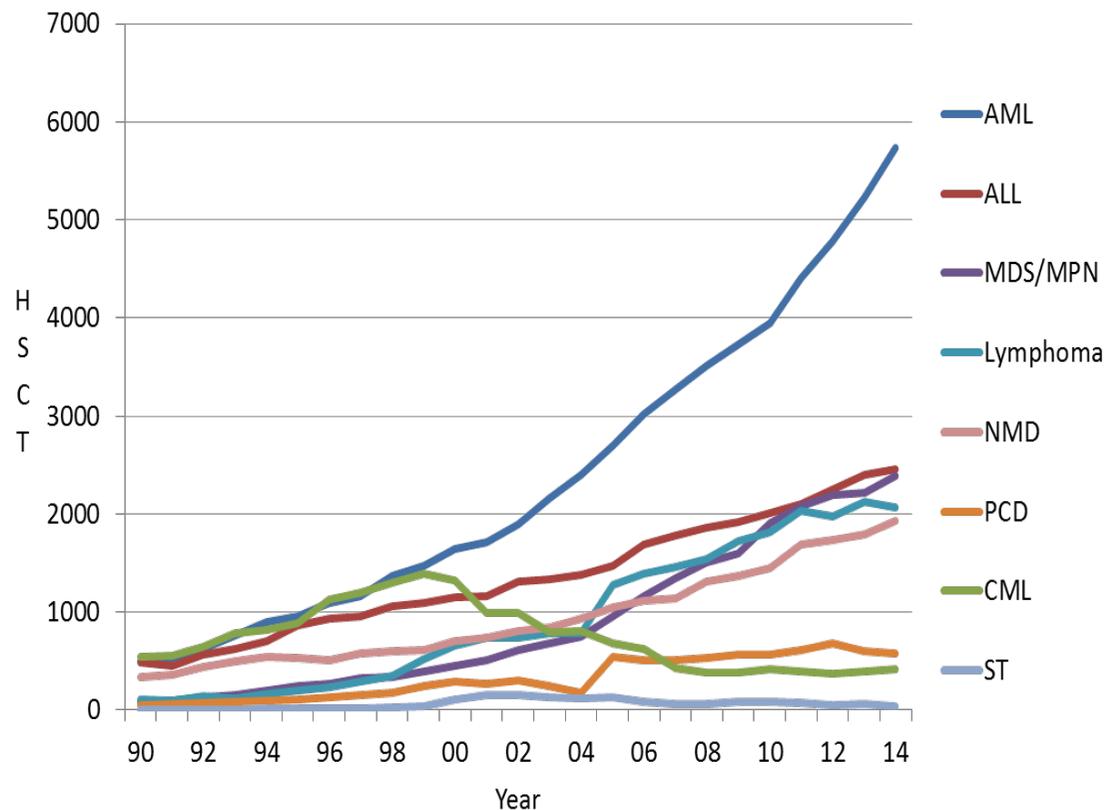
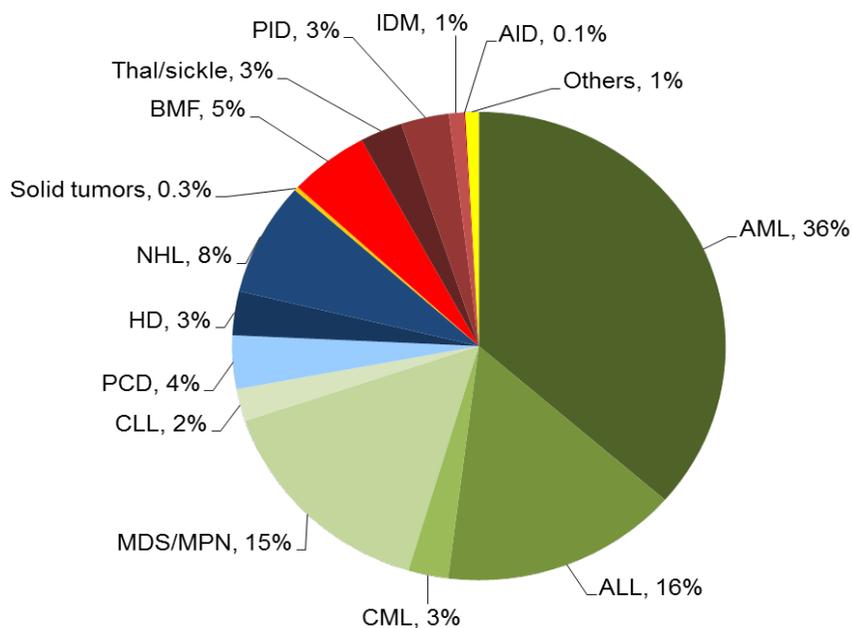
Efecto injerto contra leucemia (*inmunidad antitumoral*)



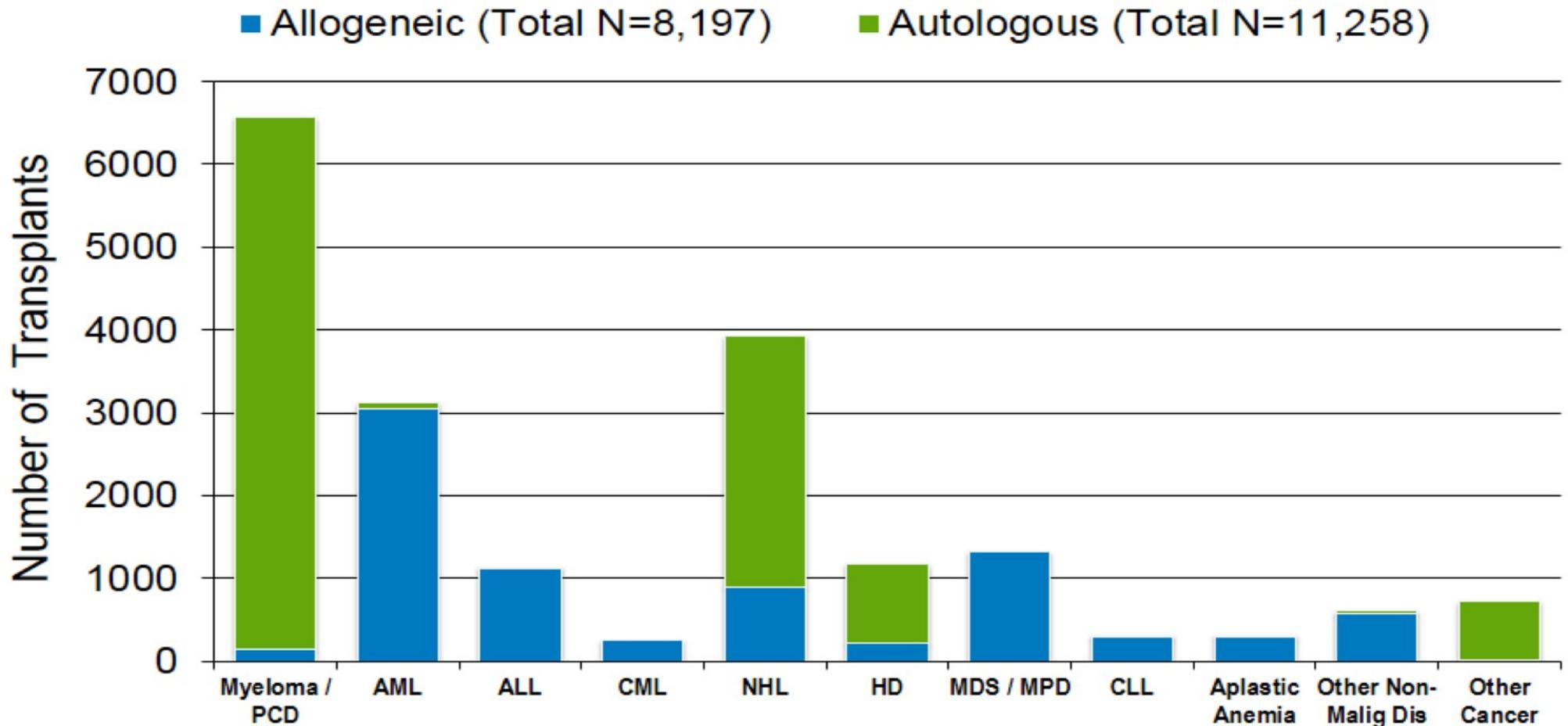
Indicaciones del TPH

Indicaciones. TPH Alogénico en Europa 2014

1st HSCT



Indications for Hematopoietic Stem Cell Transplants in the US, 2013



Indicaciones TPH en España.

Enfermedades malignas

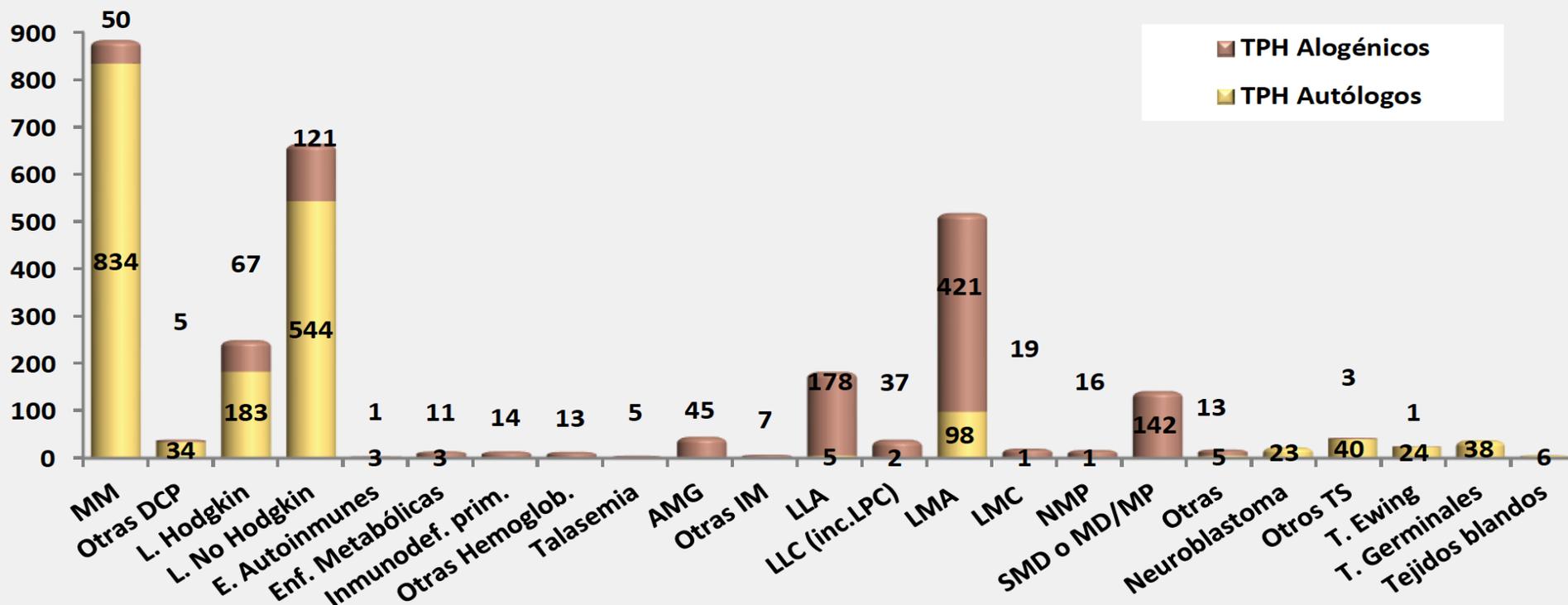


Fig. 29 Indicaciones de TPH Autólogos y Alogénicos. España 2014

TPH. Resultados

El TPH es una terapia consolidada

One million haemopoietic stem-cell transplants: a retrospective observational study.

Gratwohl A, Pasquini MC, Aljurf M, et al.

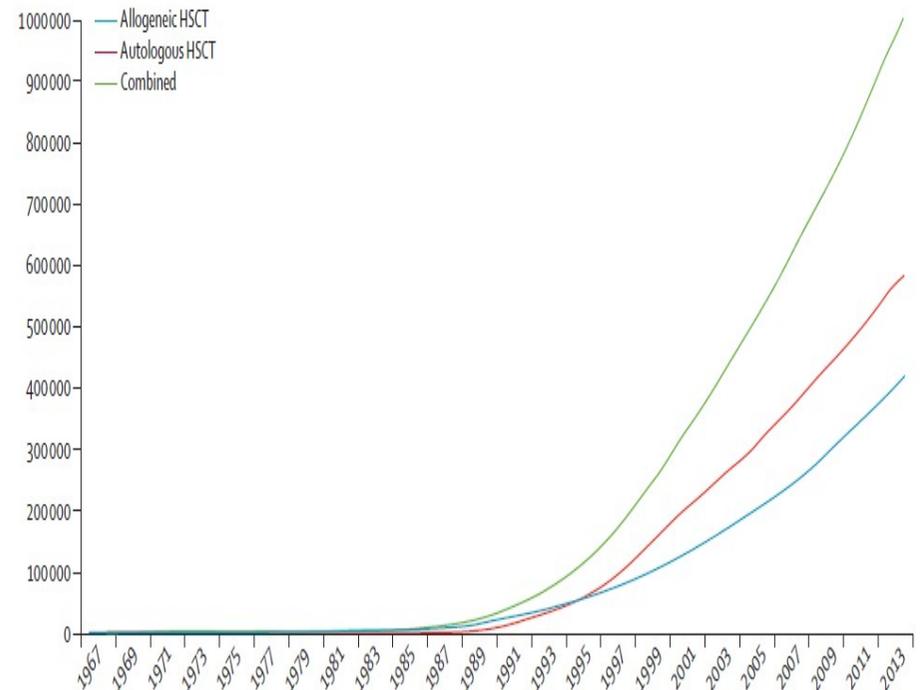
Lancet Haematol. 2015 Mar;2(3):e91-e100.

METHODS:

Between Jan 1, 2006, and Dec 31, 2014, the Worldwide Network for Blood and Marrow Transplantation collected data for the evolution of haemopoietic stem-cell transplantation (HSCT) activity and volunteer donors in the 194 WHO member states.

FINDINGS:

953 651 HSCTs (553 350 [58%] autologous and 400 301 [42%] allogeneic) were reported by 1516 transplant centres from 75 countries. No transplants were done in countries with fewer than 300 000 inhabitants, a surface area less than 700 km², and a gross national income per person of US\$1260 or lower. Use of HSCT increased from the first transplant in 1957 to almost 10 000 by 1985. We recorded a cumulative total of about 100 000 transplants by 1995, and an estimated 1 million by December, 2012. Unrelated donor registries contributed 22·3 million typed volunteer donors and 645 646 cord blood products by 2012. Numbers of allogeneic HSCTs increased in the past 35 years with no signs of saturation ($R(2)=0\cdot989$). **Transplant rates were higher in countries with more resources, more transplant teams, and an unrelated donor infrastructure.**



EBMT Activity Survey in 2014: Patient and transplant numbers

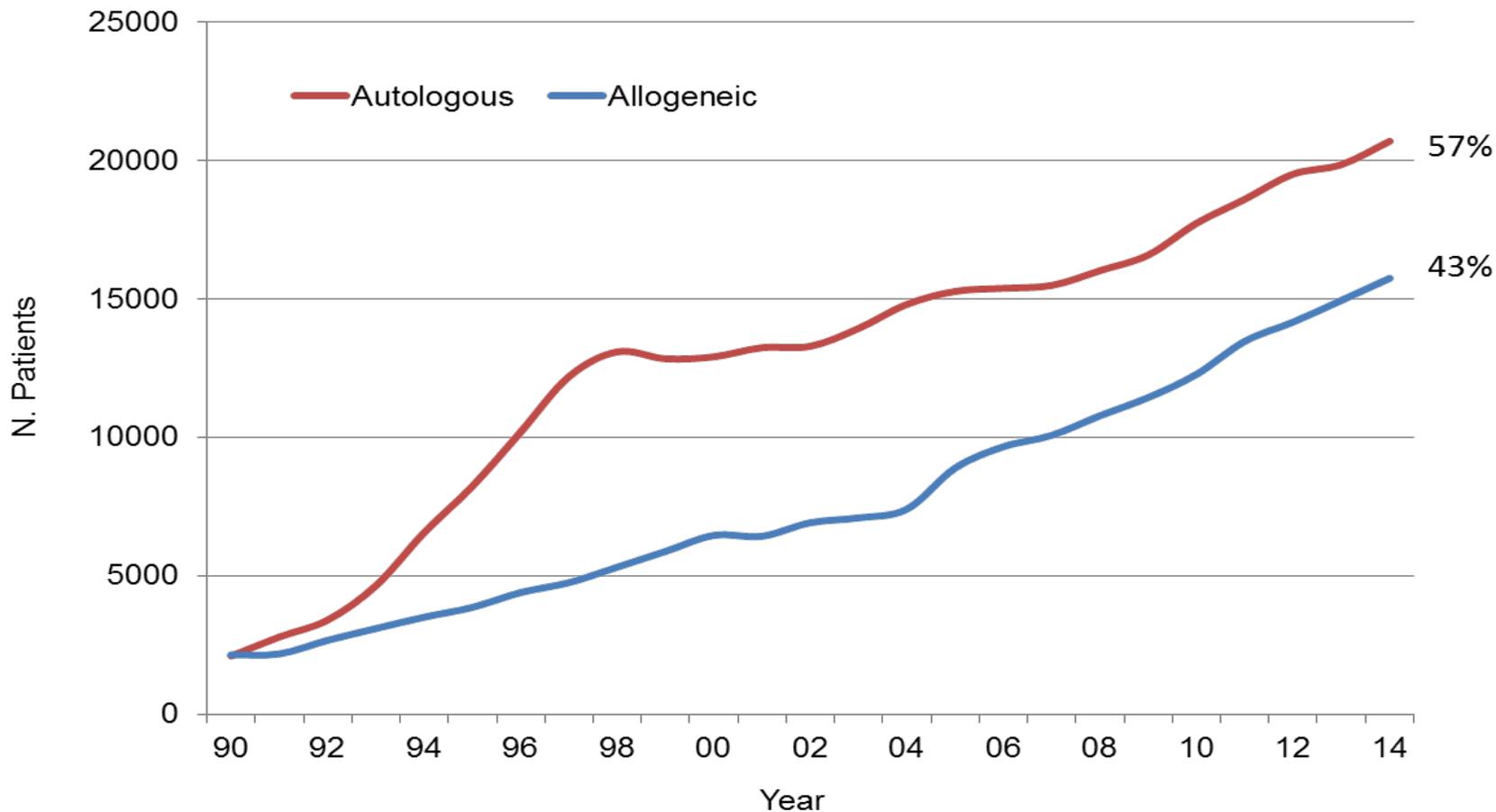
Indication	Allogeneic HSCT	Autologous HSCT	Total
1st allo/1 st auto HSCT	15765	20704	36469
Retransplants	1106	1594	2700
Additional transplants	76	1585	1661
TOTAL	16947	23883	40830

Teams: 656 (of 680)

Countries reporting data: 48

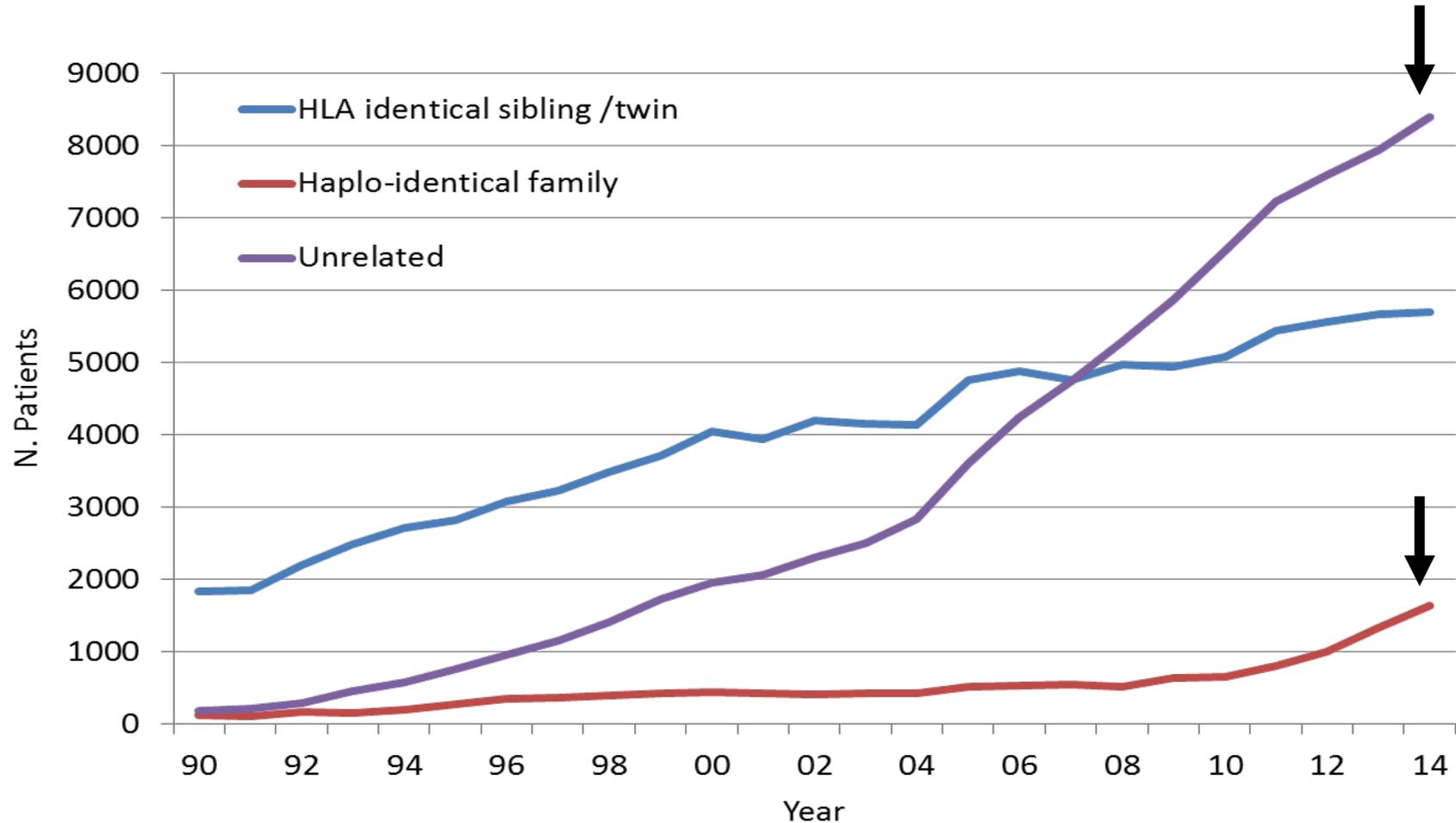
HSCT Activity in Europe 1990-2014:

Transplant type 1st HSCT



HSCT Activity in Europe 1990-2014:

Donor origin: 1st HSCT



España. Tipos TPH 1994-2014

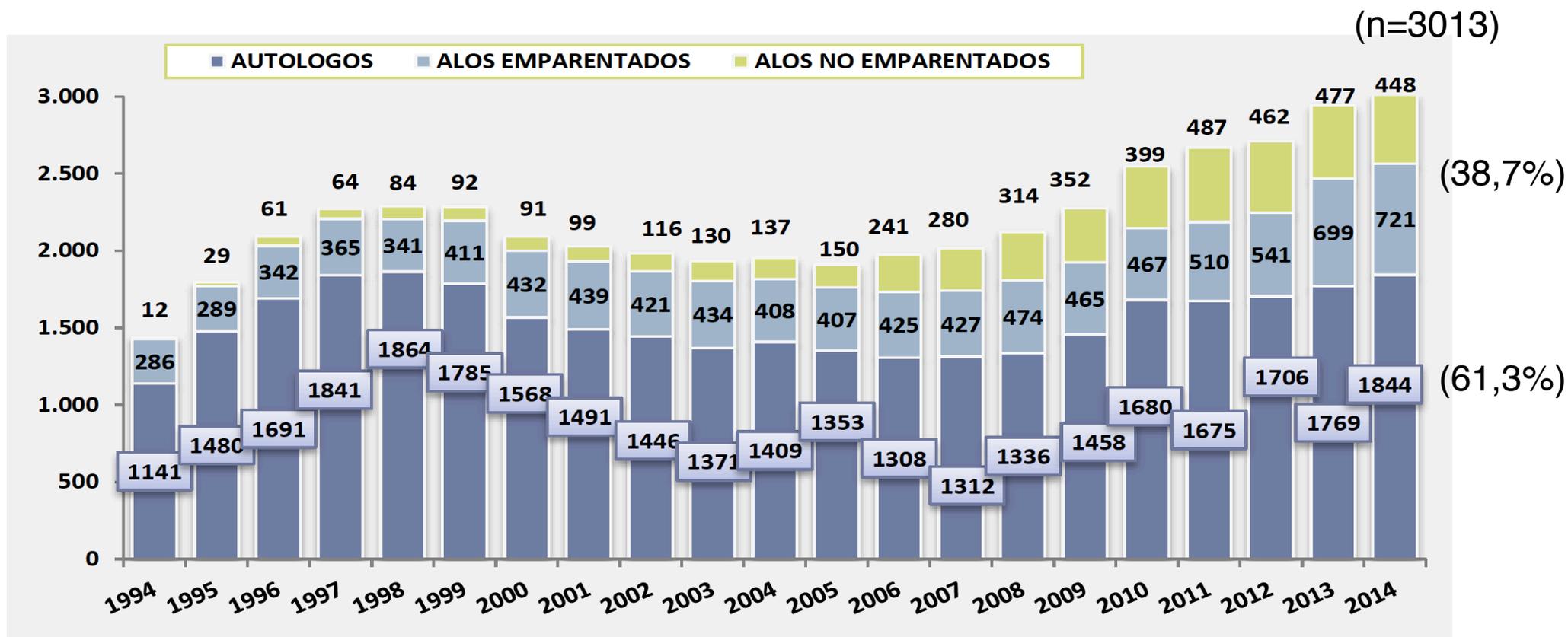
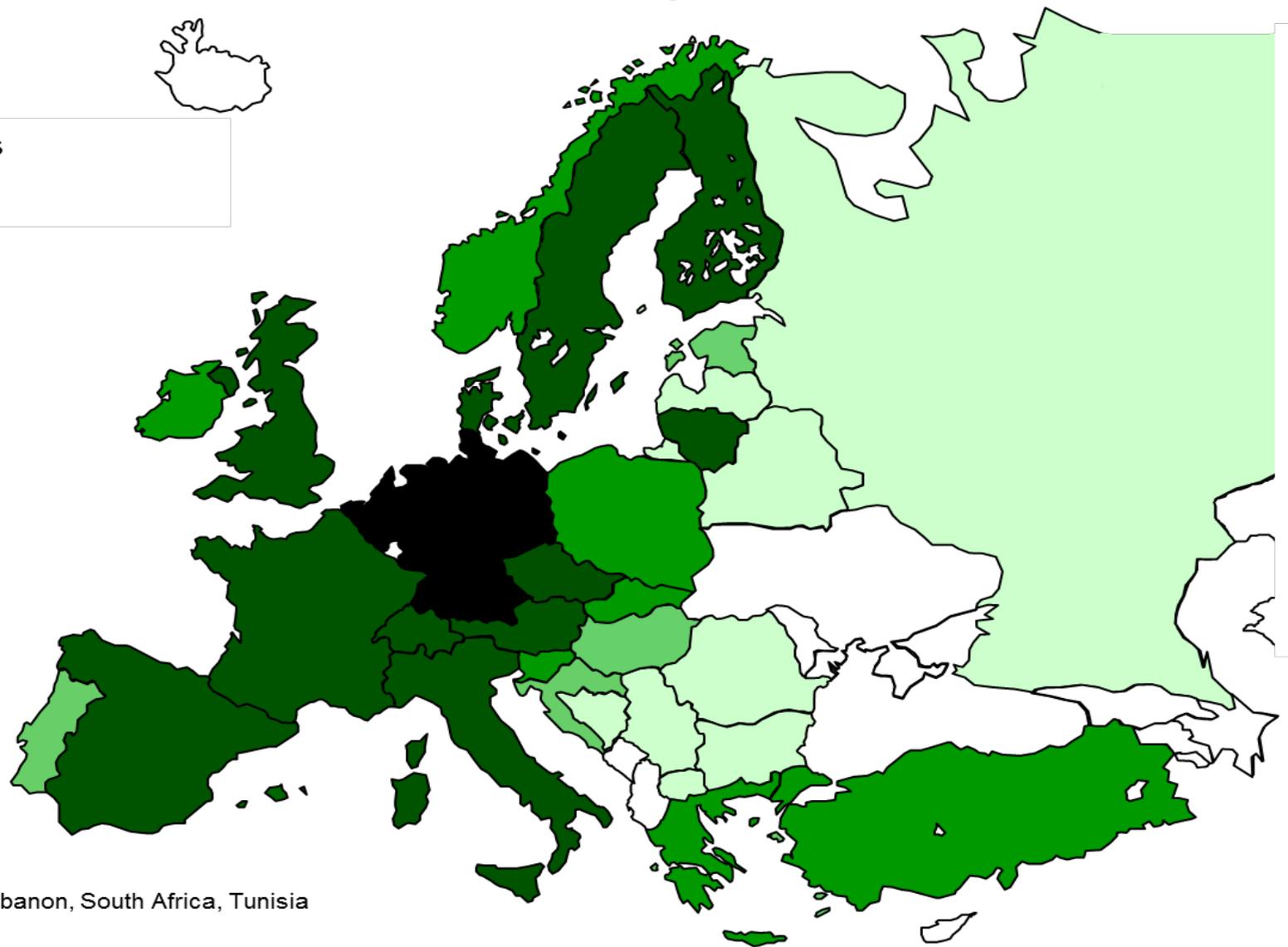
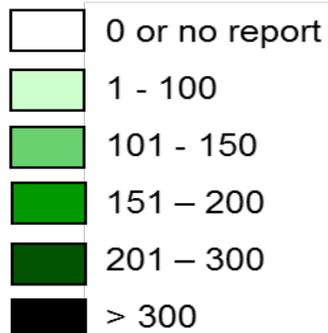


Fig.4. Trasplantes de progenitores hematopoyéticos Tipos. España. 1994-2014

HSCT - rates in Europe 2014

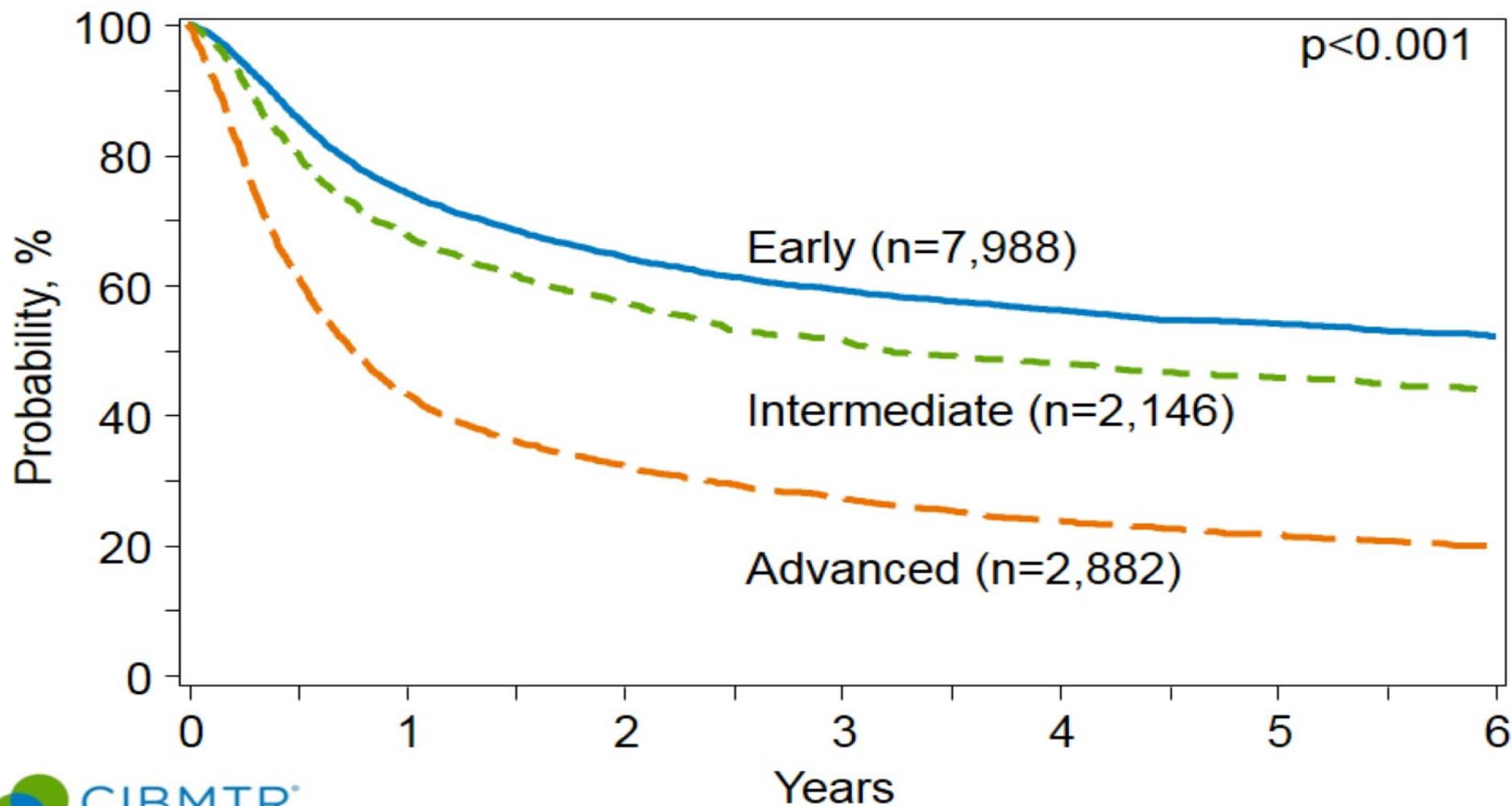
N. allogeneic transplants
per 10 million population



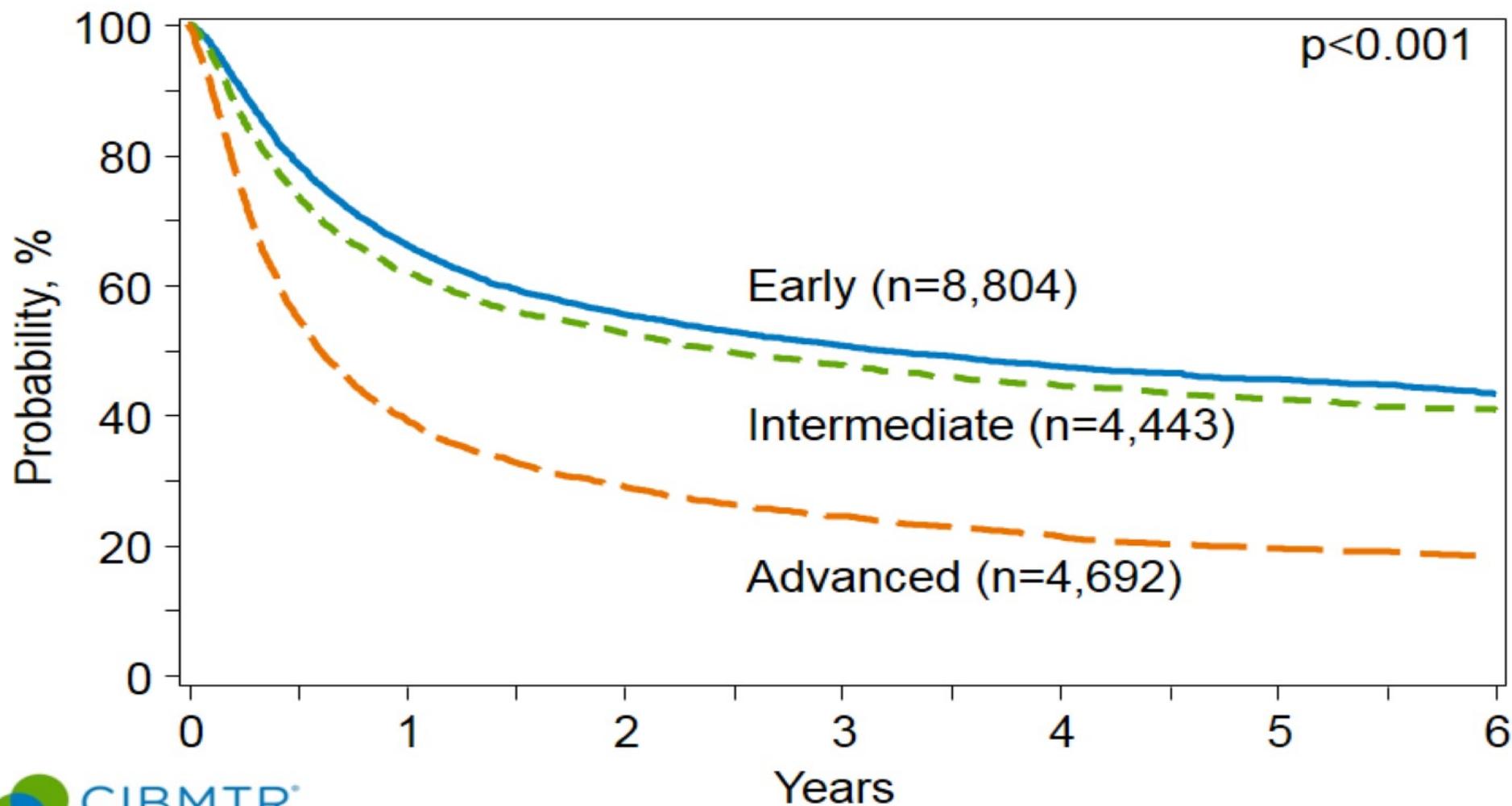
TPH Resultados

Enfermedades

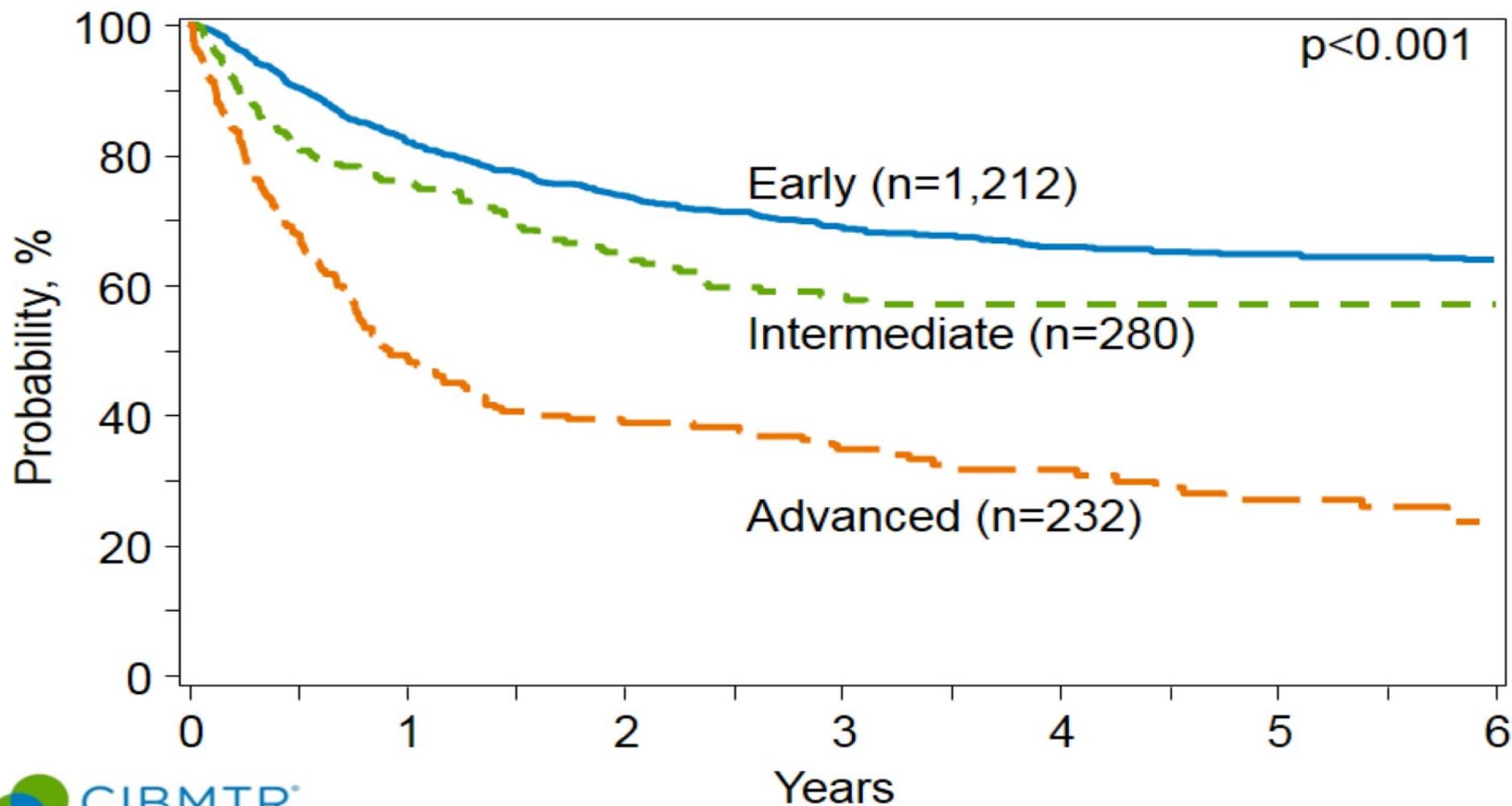
Survival after HLA Match Sibling Donor Transplants for AML, 2003-2013



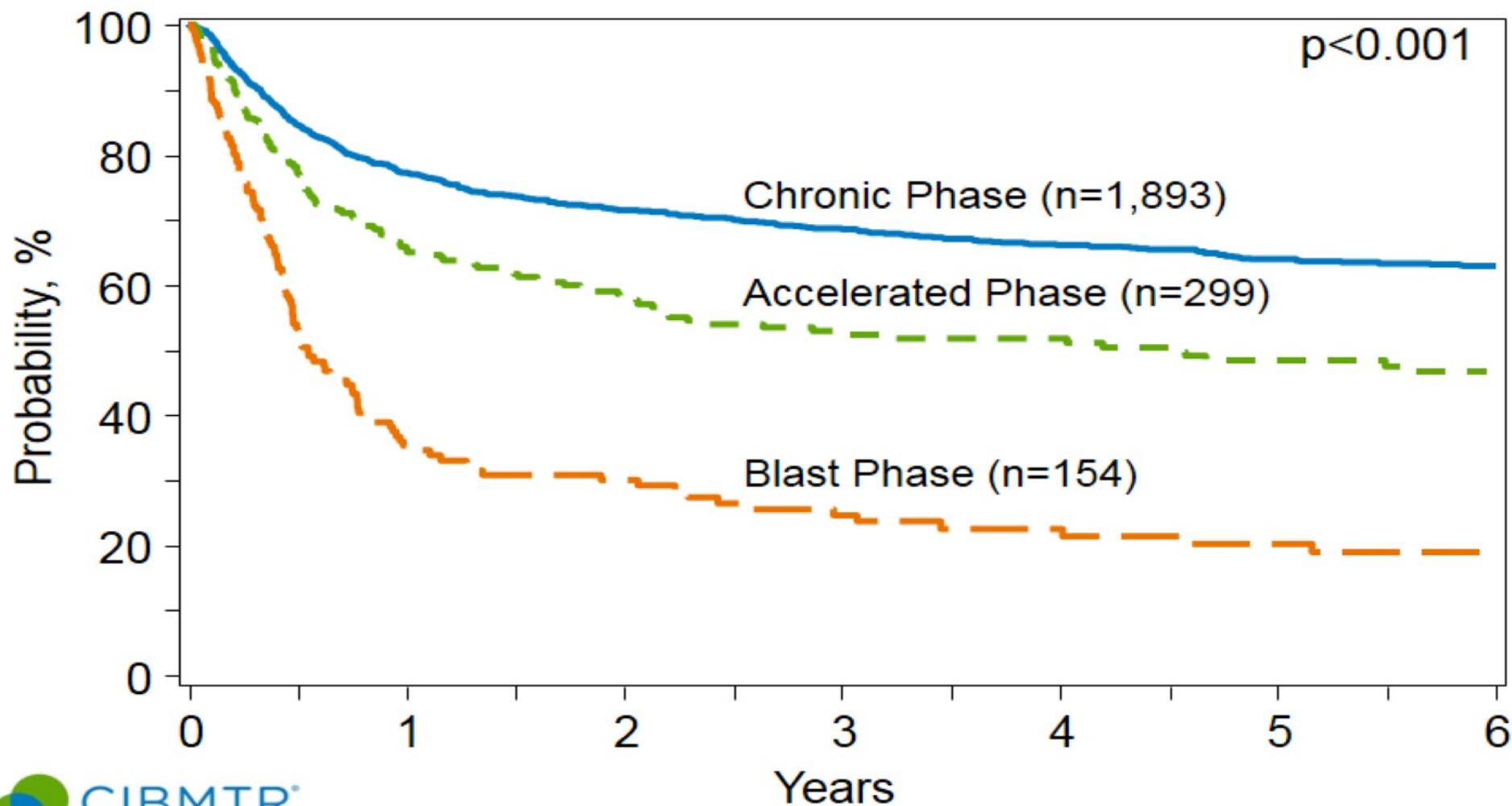
Survival after Unrelated Donor Transplants for AML, 2003-2013



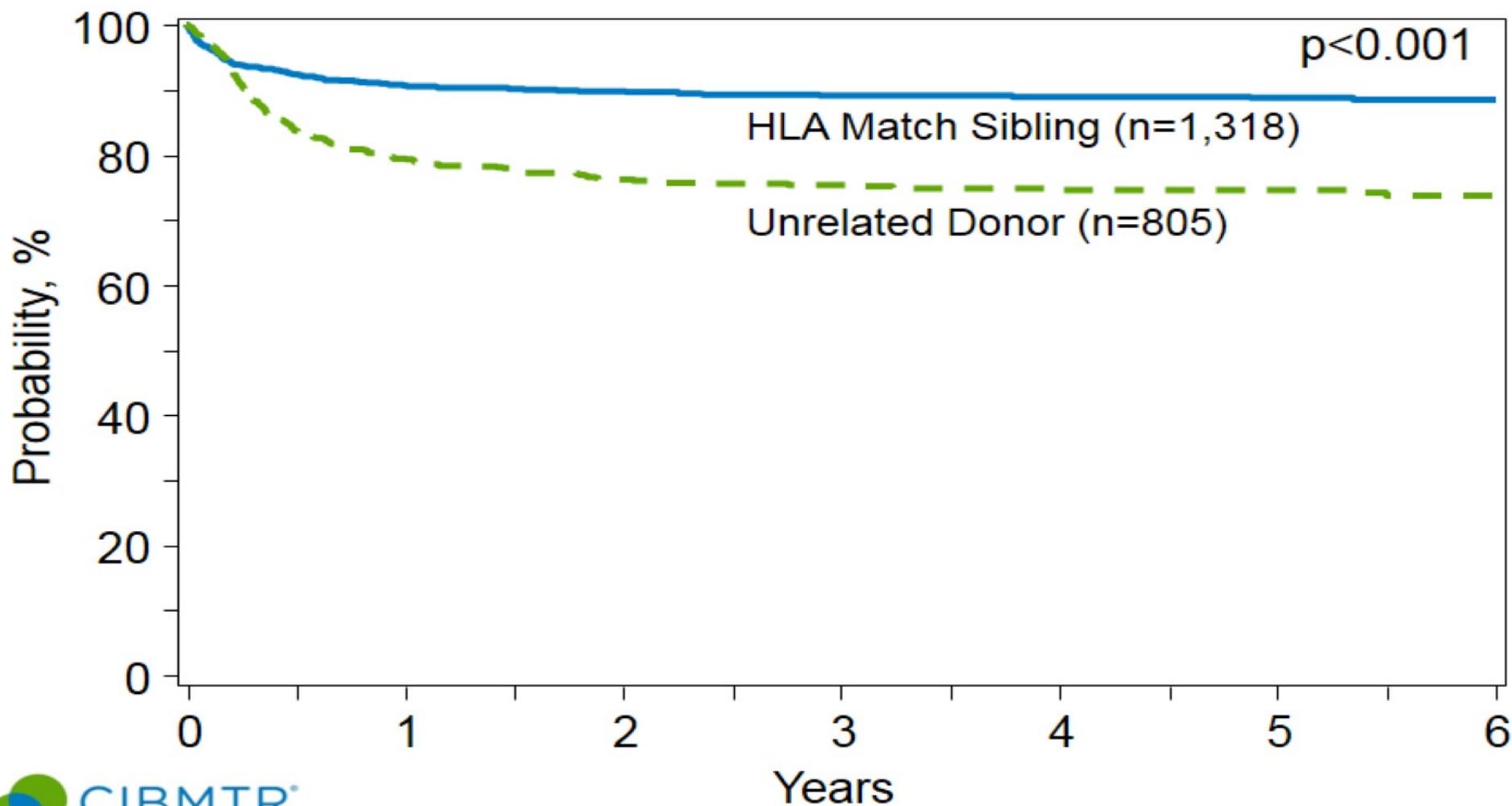
Survival after HLA Match Sibling Donor Transplants for AML, Age <20 Years, 2003-2013



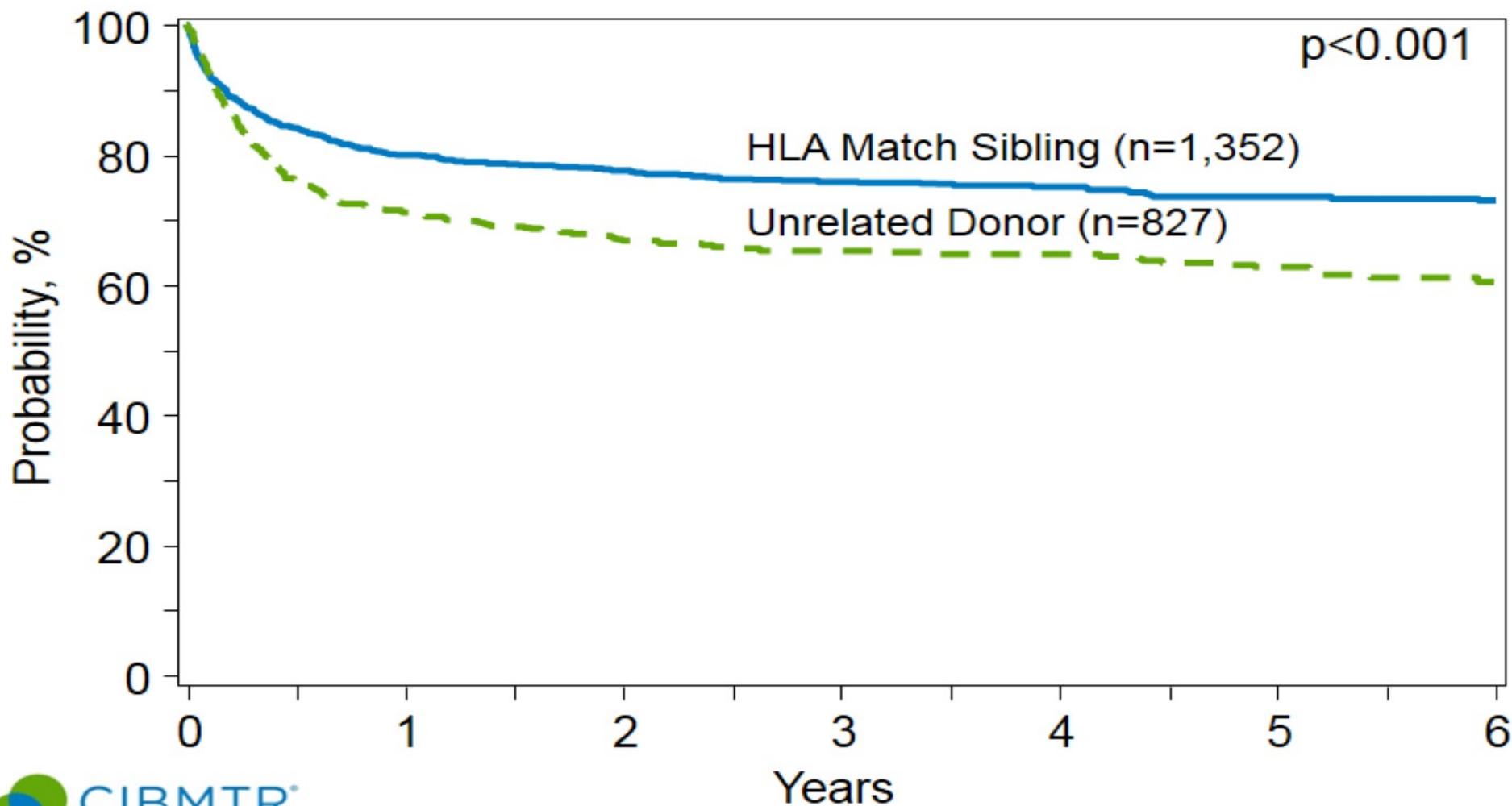
Survival after HLA Match Sibling Transplants for CML, 2003-2013



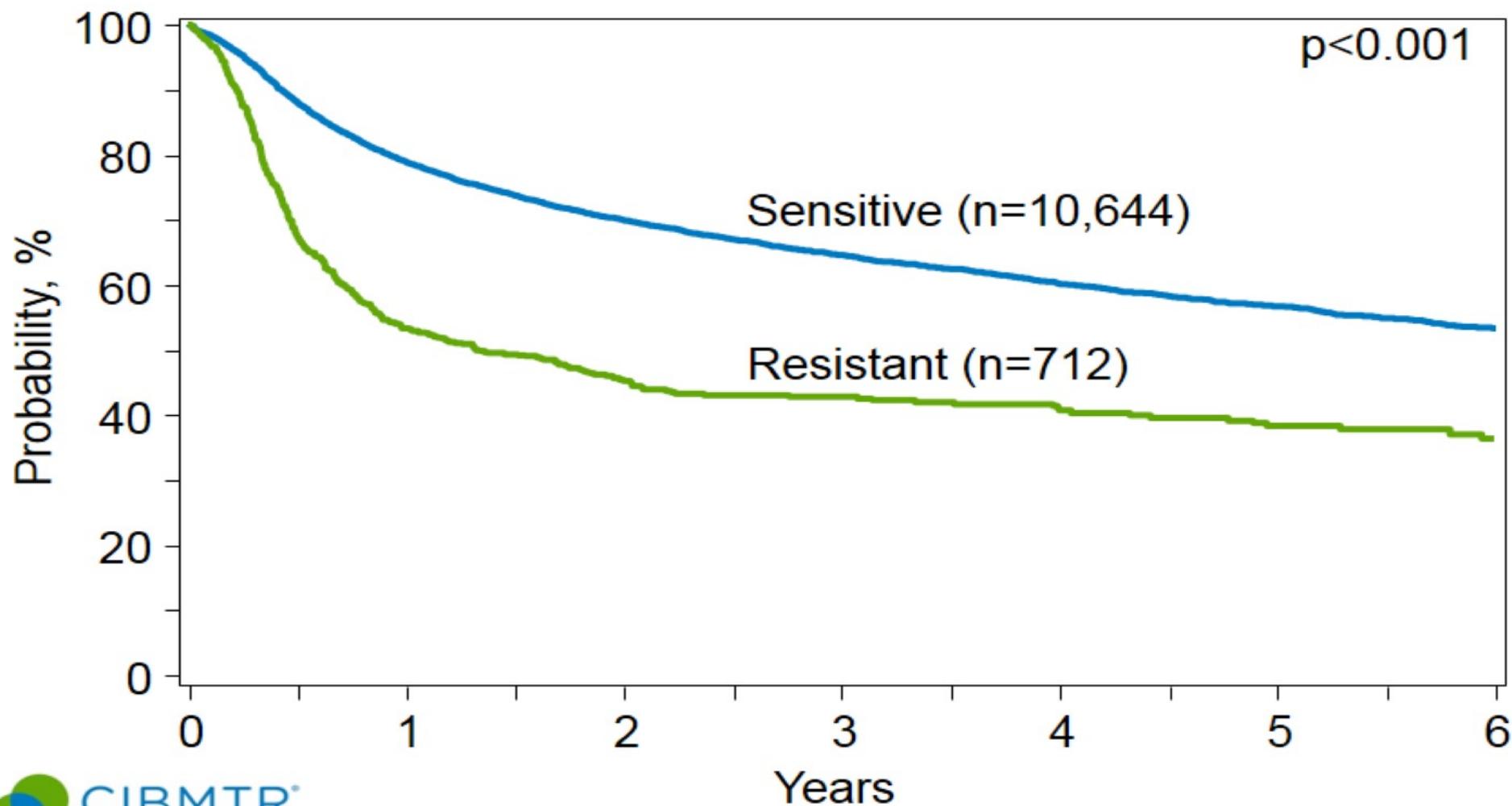
Survival after Allogeneic Transplants for Severe Aplastic Anemia, <20 Years, 2003-2013



Survival after Allogeneic Transplants for Severe Aplastic Anemia, ≥ 20 Years, 2003-2013

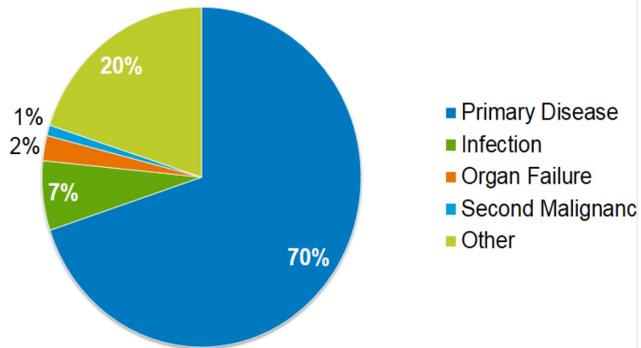


Survival after Autologous Transplants for Diffuse Large B-cell Lymphoma (DLBCL), 2003-2013

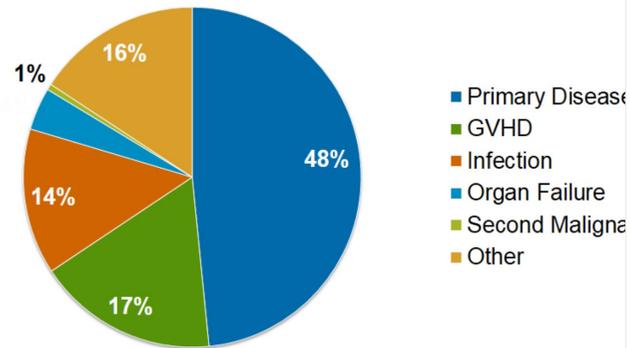


Causas de muerte tras el TPH CIBMTR 2012-13

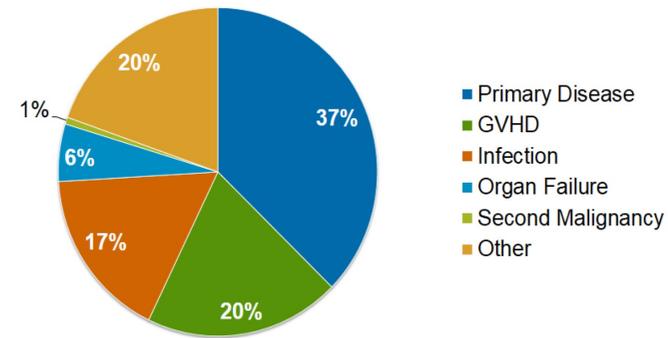
Causes of Death after Autologous Transplants done in 2012-2013



Causes of Death after HLA Match Sibling Transplants done in 2012-2013



Causes of Death after Unrelated Donor Transplants done in 2012-2013



Factores que influyen en resultados TPH.

Indice de riesgo EBMT

Table 2. European Group for Blood and Marrow Transplantation Risk Score Definition

Risk Factor	Score Point
Age of the patient, y	
<20	0
20-40	1
>40	2
Disease stage*	
Early	0
Intermediate	1
Late	2
Time interval from diagnosis to transplant, mo†	
<12	0
>12	1
Donor type	
HLA-identical sibling donor	0
Unrelated donor	1
Donor-recipient sex combination	
All other	0
Donor female, male recipient	1

HLA indicates human leukocyte antigen.

* See text for the definitions according to main disease category; does not apply for patients with severe aplastic anemia (score 0).

† Does not apply for patients transplanted in first complete remission

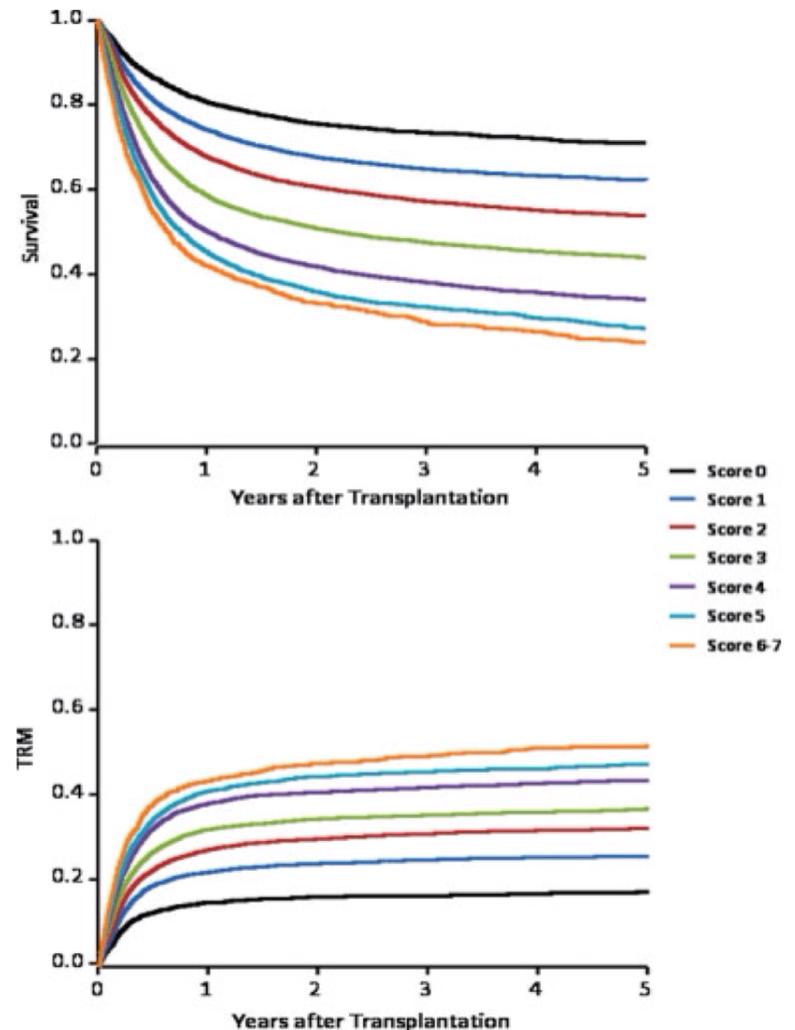


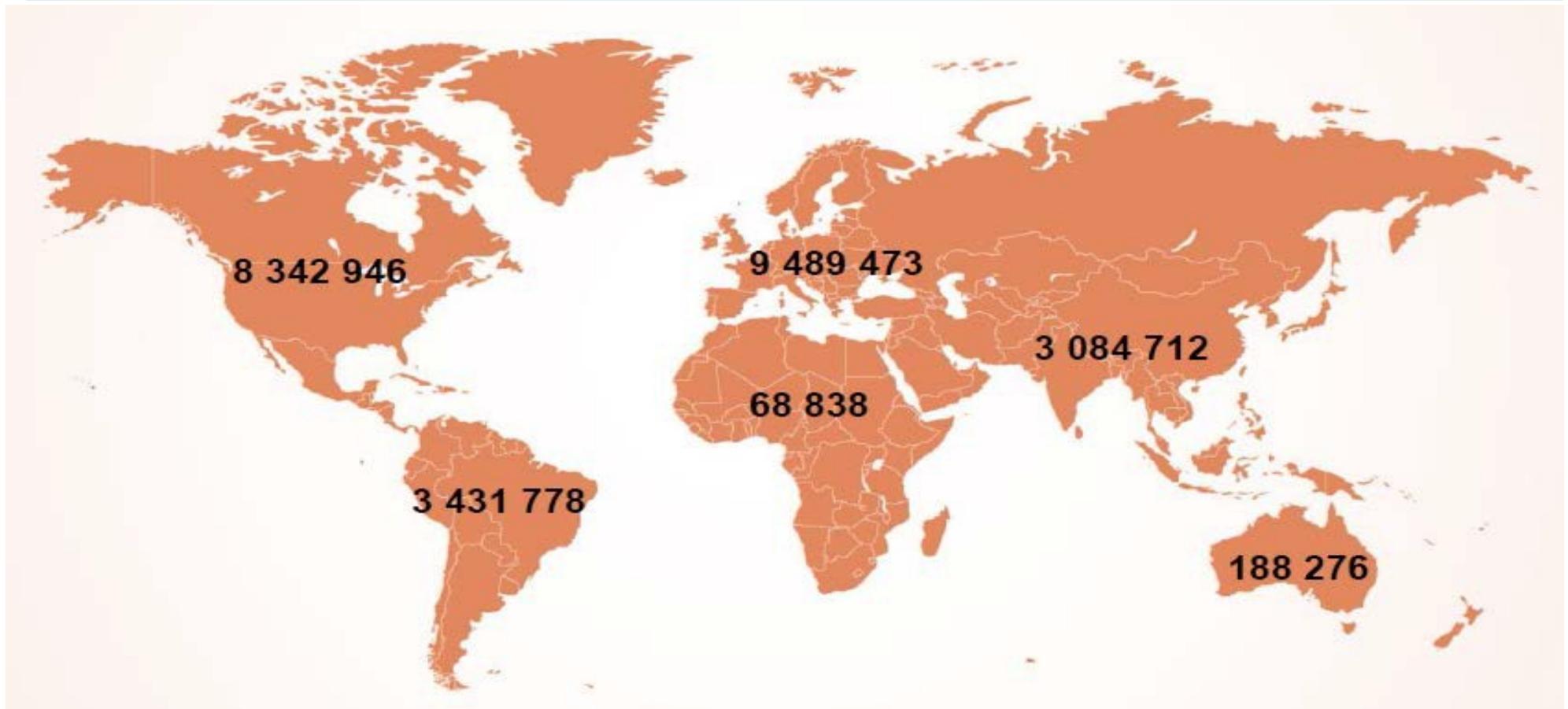
FIGURE 1. Survival (*Top*) and transplant-related mortality (TRM) (*Bottom*) of 56,605 patients with an allogeneic hematopoietic stem cell transplantation (HSCT) for an acquired hematological disorder is shown by risk score. Graphs reflect probability of survival (*Top*) and transplant-related mortality (*Bottom*) over the first 5 years after HSCT.

¿Como mejorar los resultados?

Objetivos de futuro en el TPH

- ↑ Disponibilidad de donantes: Disponer de un donante y fuente de PH adecuados en el tiempo preciso
- Modular y mejorar la reconstitución inmune. Terapia celular:
 - ↓ EICH: Immunomodulacion
 - ↓ Infecciones: acelerar reconstitución inmune
 - ↓ Recaída: inmunoterapia celular

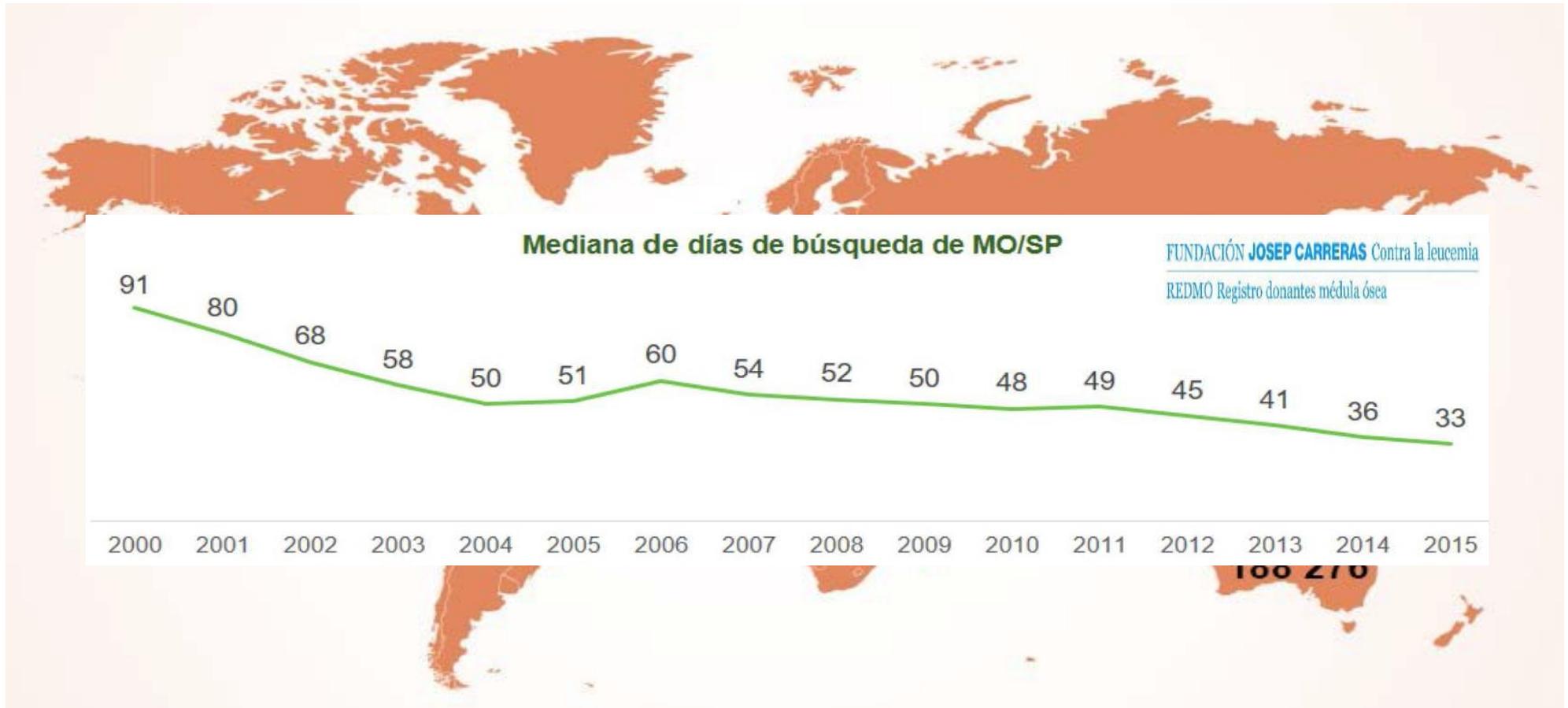
Donantes no emparentados en registros



Total (Enero 2016) 27,673,102 (26,992,207 donantes y 680.895 unidades CU)

España: 207.572 donantes de PHSP y 61.000 cordones de alta calidad (2º país mundo) gracias a los planes nacionales de SCU y MO promocionados por la ONT

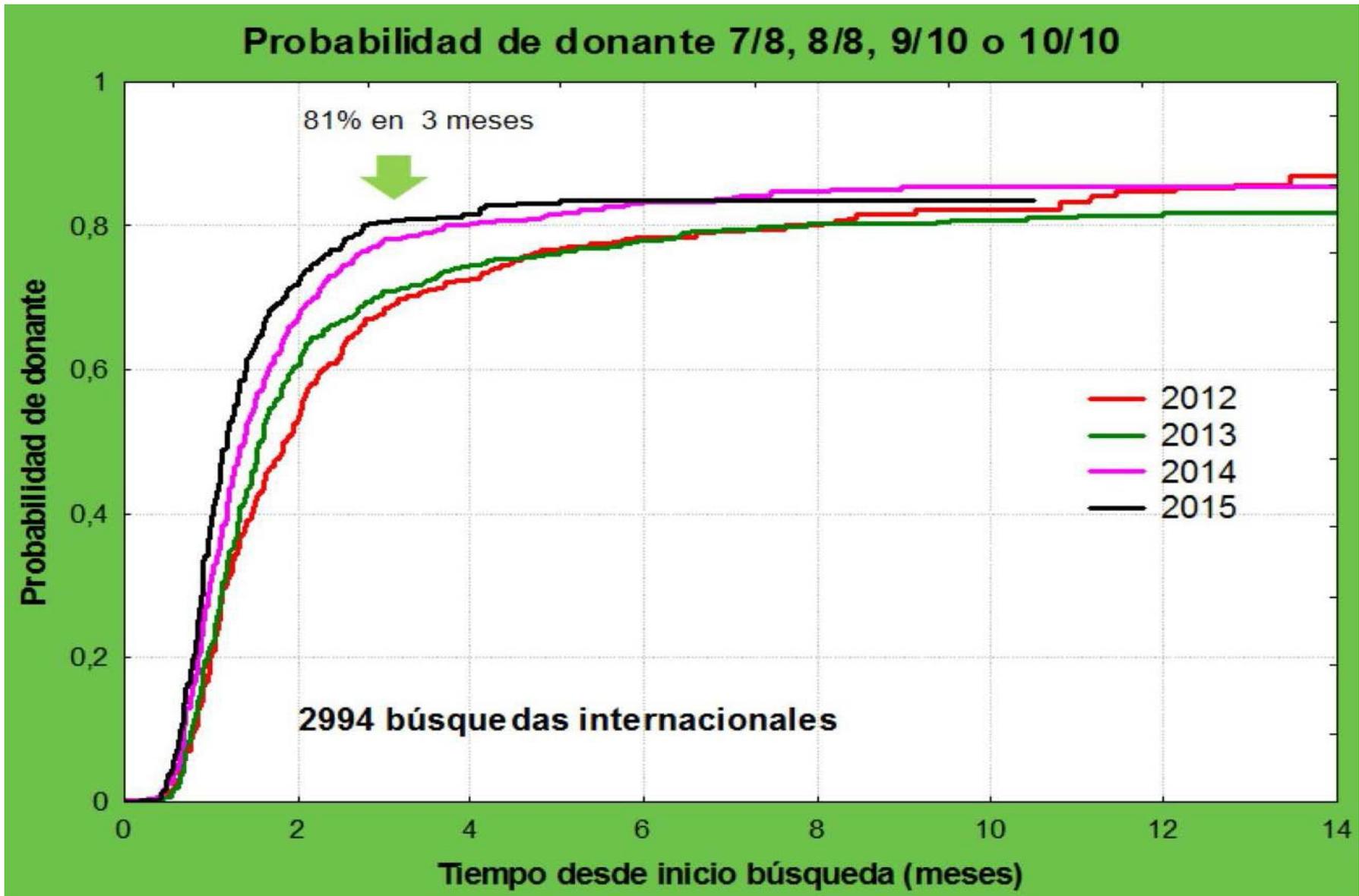
Donantes no emparentados en registros



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Memoria anual REDMO 2015



España. Tipos TPH 1994-2014

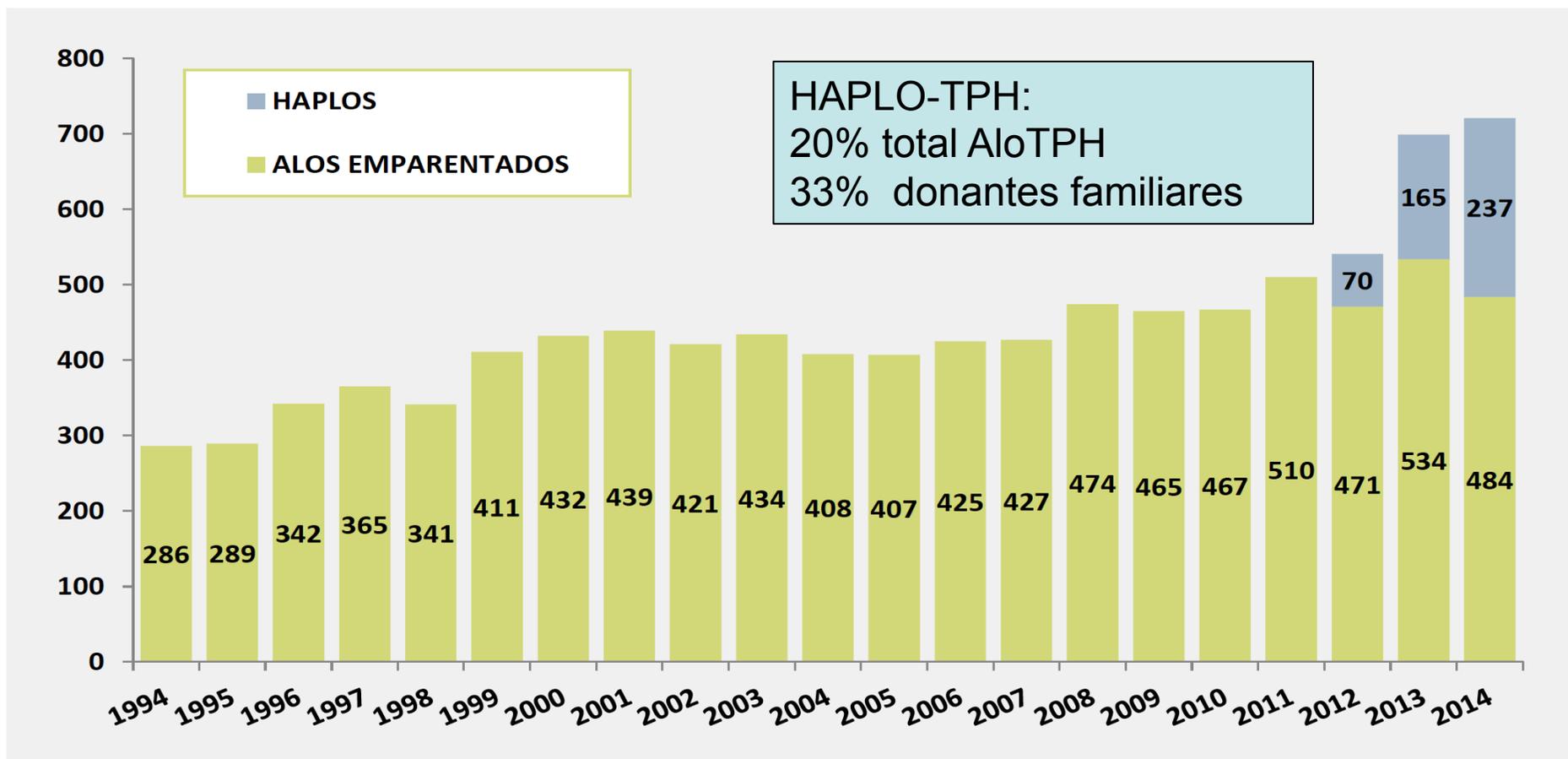
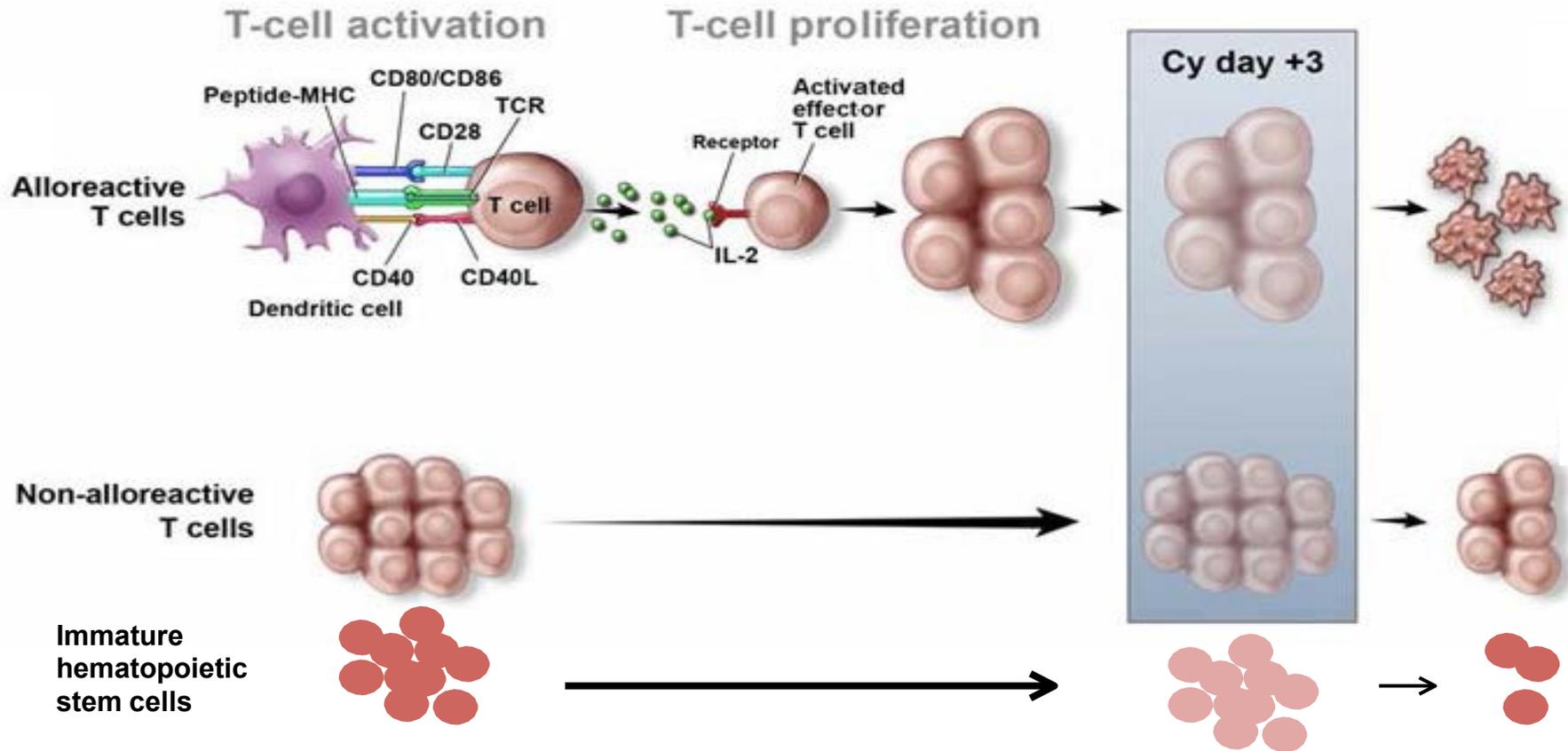


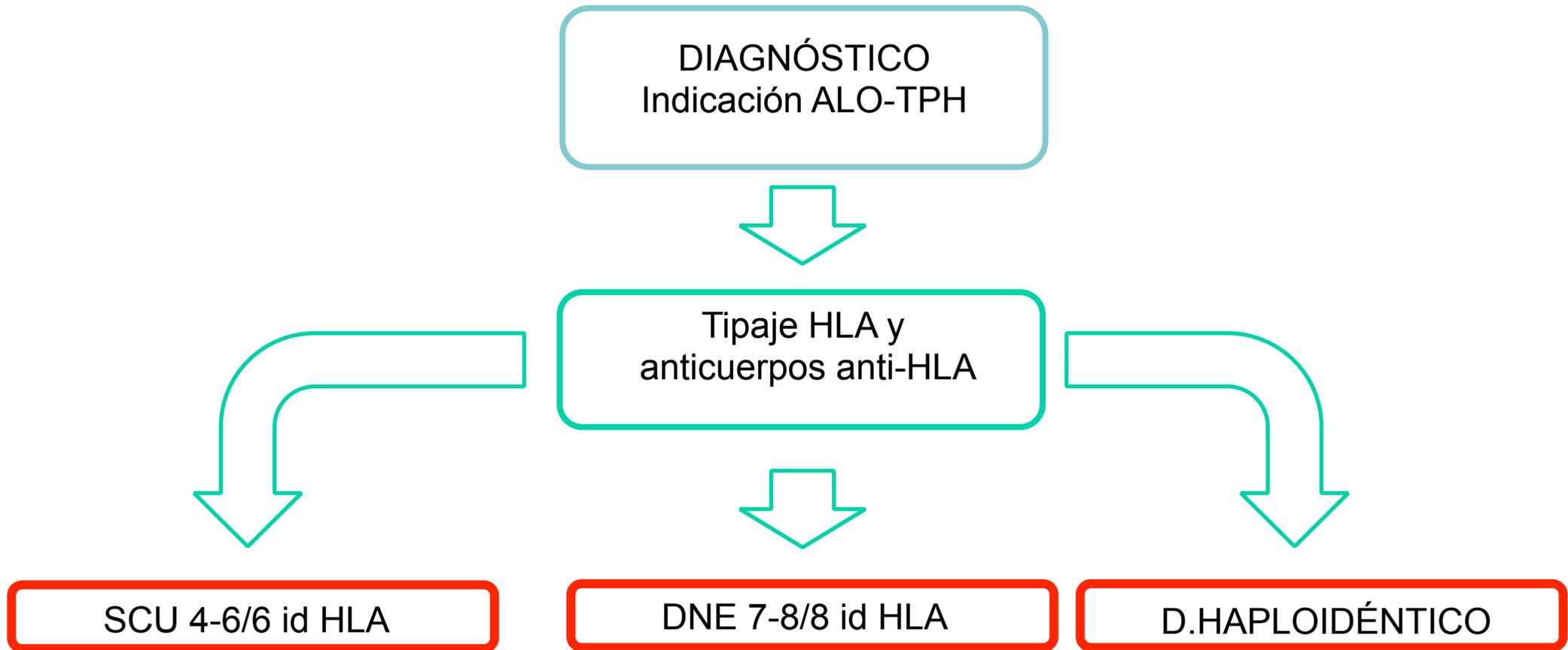
Fig. 18. TPH emparentados- haploidénticos 1994-2014

TPH haploidéntico con Ciclofosfamida pos trasplante

Day 0



Leo Luznik, MD

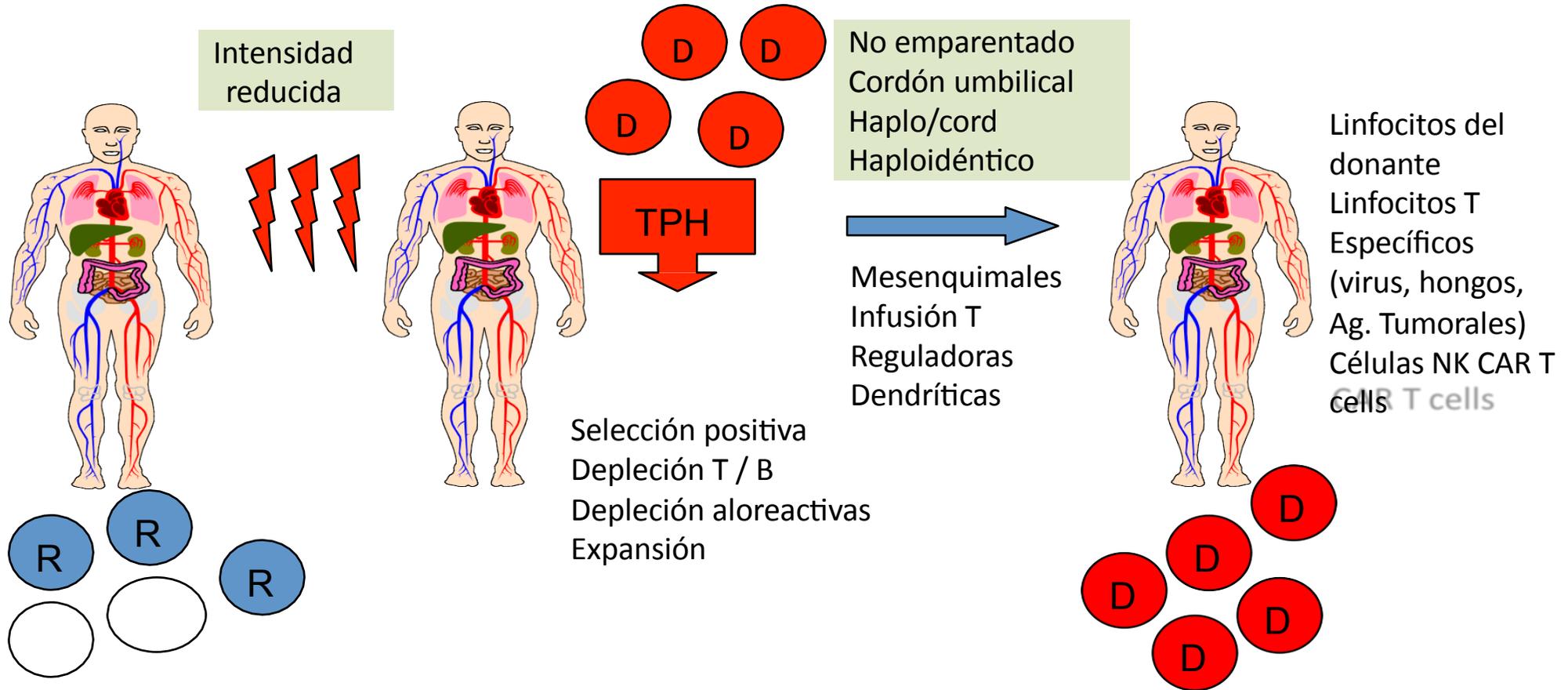


El TPH del futuro

Terapia en dosis alta
(acondicionamiento)

Autólogo (PH sangre periférica)
Hermano HLA-idéntico (PHSP, MO)

Intensidad
reducida



Conclusiones

1. El TPH es un tratamiento curativo para enfermedades malignas y no malignas.
2. Los nuevos tipos de TPH permiten trasplantar a pacientes frágiles y con más edad.
3. Plantearse cada caso individualmente, sopesando siempre riesgo/beneficio. Cada paciente y enfermedad requiere un tipo de TPH
4. El TPH alogénico tiene más poder antileucémico, pero más toxicidad que el autólogo, y antes de indicarlo hay que tener un donante.
5. La búsqueda de un donante debe iniciarse precozmente tras el diagnóstico.
6. Cualquier paciente que precisa alo-TPH, tiene posibilidades de tener donante