



*Hospital Pediátrico*  
**Luis Calvo Mackenna**  
Hospital Autogestionado de Alta Complejidad - Fundado en 1942

# Starting a transplant program: A perspective from the front line.

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PINDA - Luis Calvo Mackenna  
Santiago –Chile  
October 3rd, 2013

# **HSCT CHILEAN PROGRAM 1999- 2012**

- **Introduction**
- **HSCT Program**
- **Overall Ongoing Results**
- **Future Plans**

# CHILE



GOBIERNO DE CHILE  
MINISTERIO DE SALUD

## DEMOGRAPHICS

### Total Population

16.928.873 inhabitants

	< 15 yr %
Total	22.8



**Public Health System**

**75,0 %**

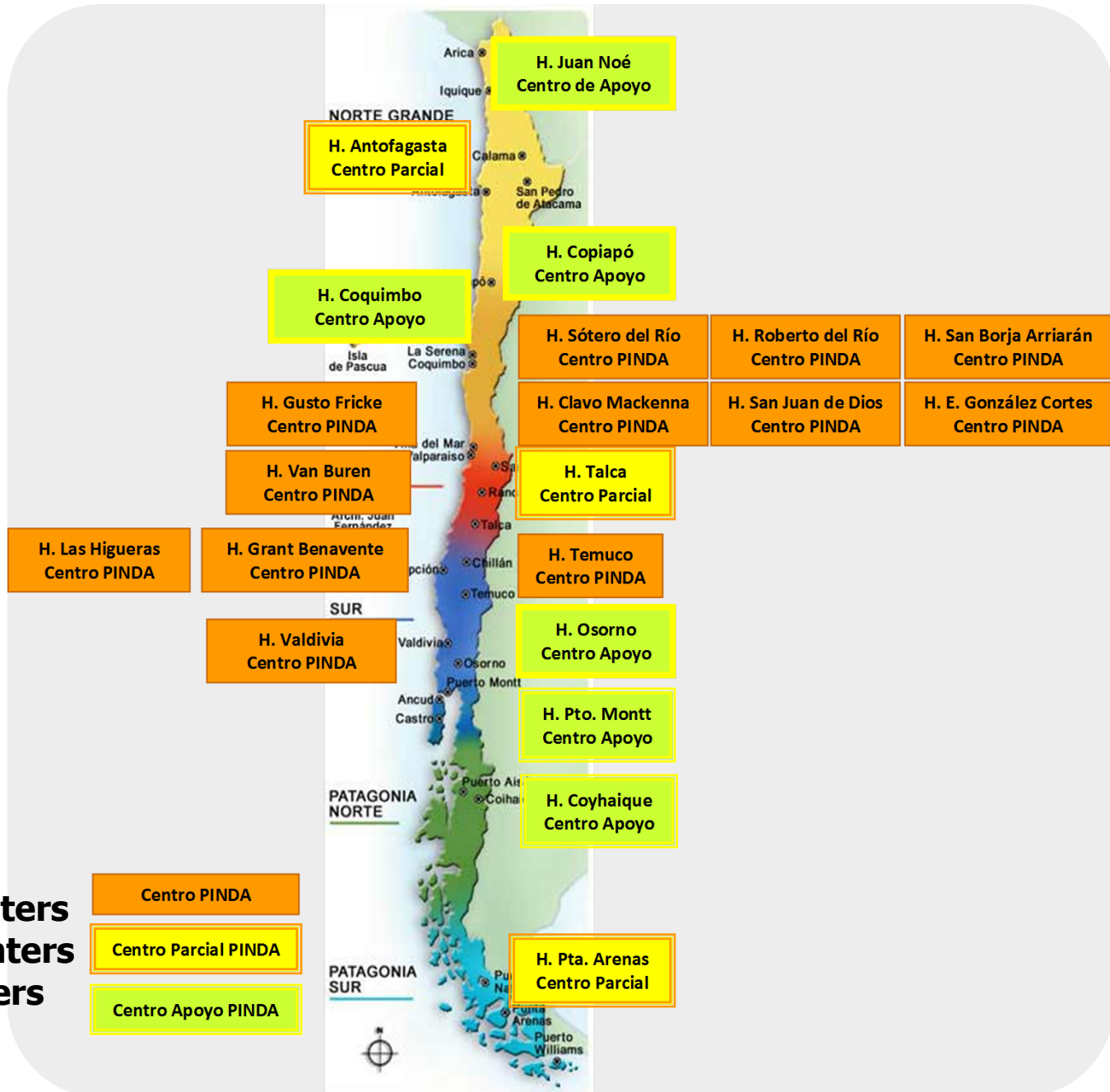
# Highlights of Chilean Public Health

In 1986

Cancer  
2<sup>nd</sup>  
cause of  
death in  
Chile

The **NATIONAL CANCER COMMITTEE** was established with members from the scientific societies, universities, private and public system: **PINDA**

# PINDA NETWORK



**12 PINDA centers**  
**7 Satellite centers**  
**4 partial centers**

- Centro PINDA
- Centro Parcial PINDA
- Centro Apoyo PINDA

**MINSAL**  
**Non communicable disease department**



**Cancer Unit**

**Chair**

**Directive Committee**

**General Committees**

**Trial Committees**

**Center Chairs**

**BMT**  
**Nurse**  
**Infectology**  
**Pathology**  
**Radiotherapy**  
**Pharmaceutical**  
**Paliative Care**

**30 Trials**

**Network**  
**13 PINDA Centers**  
**7 Satellite Centers**

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# SCT program PINDA-HLCM

## How to do it?



- Develop goals and objectives for the HSCT program
- To define and have the necessary infrastructure for starting...



# Goals: short-term (December 1998)

- To establish a protocol for the study of donor and recipient prior HSCT (IBMTR) ✓
- To establish a protocol: for infectious prophylaxis, VOD prevention and transfusional norms ... ✓
- To define conditioning protocols to be used based on specific diseases ✓
- To create the PINDA transplant committee (June 1998) ✓
- To define transplant indications according to PINDA's protocols and EBMT Guidelines ✓
- Selection of patients for transplantation in the committee ✓

# Goals: mid-term (December 1999)

- Accreditation process ✓
- To start an autologous and identical sibling transplant program ✓
- To obtain financial support through the Ministry of Health for autologous and identical sibling transplants ✓

**Allogeneic transplant US\$ 54,000**

**Autologous transplant US\$ 28,000**

# Goals: Long-term

- UCB transplant ✓
- Haploidentical HSCT program ✓
- Unrelated stem cells transplant program
- To create a umbilical cord blood bank
- To establish a national donor registry

# HSCT RESULTS

## PINDA-HLCM

- National Program ✓
- BMT Program in the public health system ✓
- Started: October 1999 ✓
- Accredited (NMDP) ✓
- PINDA selection committee ✓
- Routine indications ✓

# PINDA Chile

500 new cases every year in Chile

Second cause of death!

60 patients!

**BMT COMMITTEE PINDA**

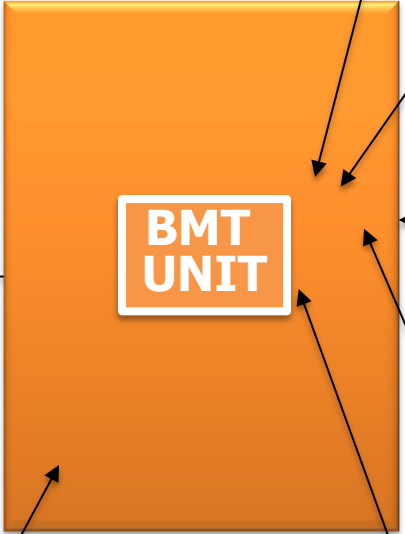


**Ministry of Health  
FONASA  
AMICAM**

**IOP  
St. Jude Children's  
Research Hospital**

**Internal Support**

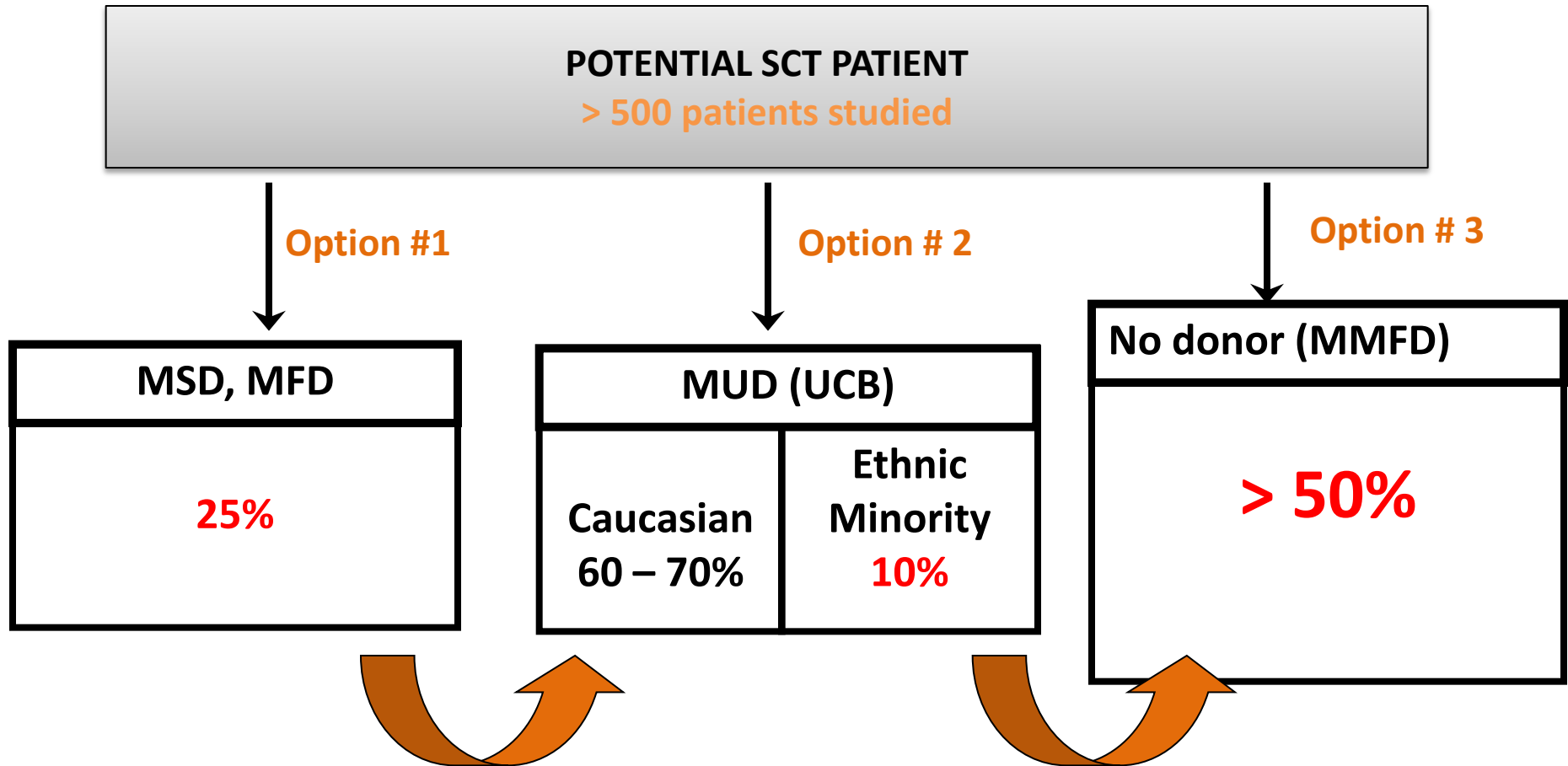
**External Support**



**Hosp. Valle Hebron  
Barcelona, Spain  
Curitiba, Brasil  
Londres, UK**

**Universidad  
de  
Chile**

# SCT Donors



# **HSCT CHILEAN PROGRAM 1999- 2012**

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- **263 transplants**
- **Age: 3 months – 24 years**
- **Average: 8,8 years**

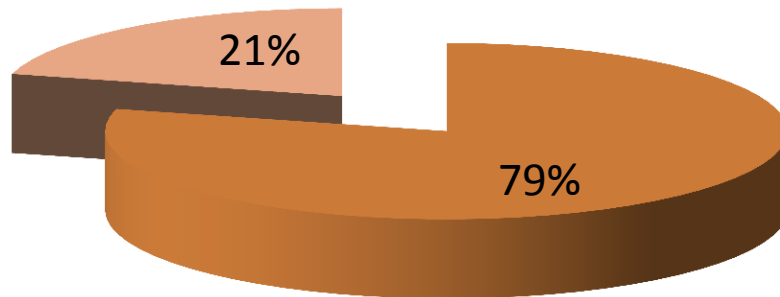


# SCT-PINDA/HLCM Experience

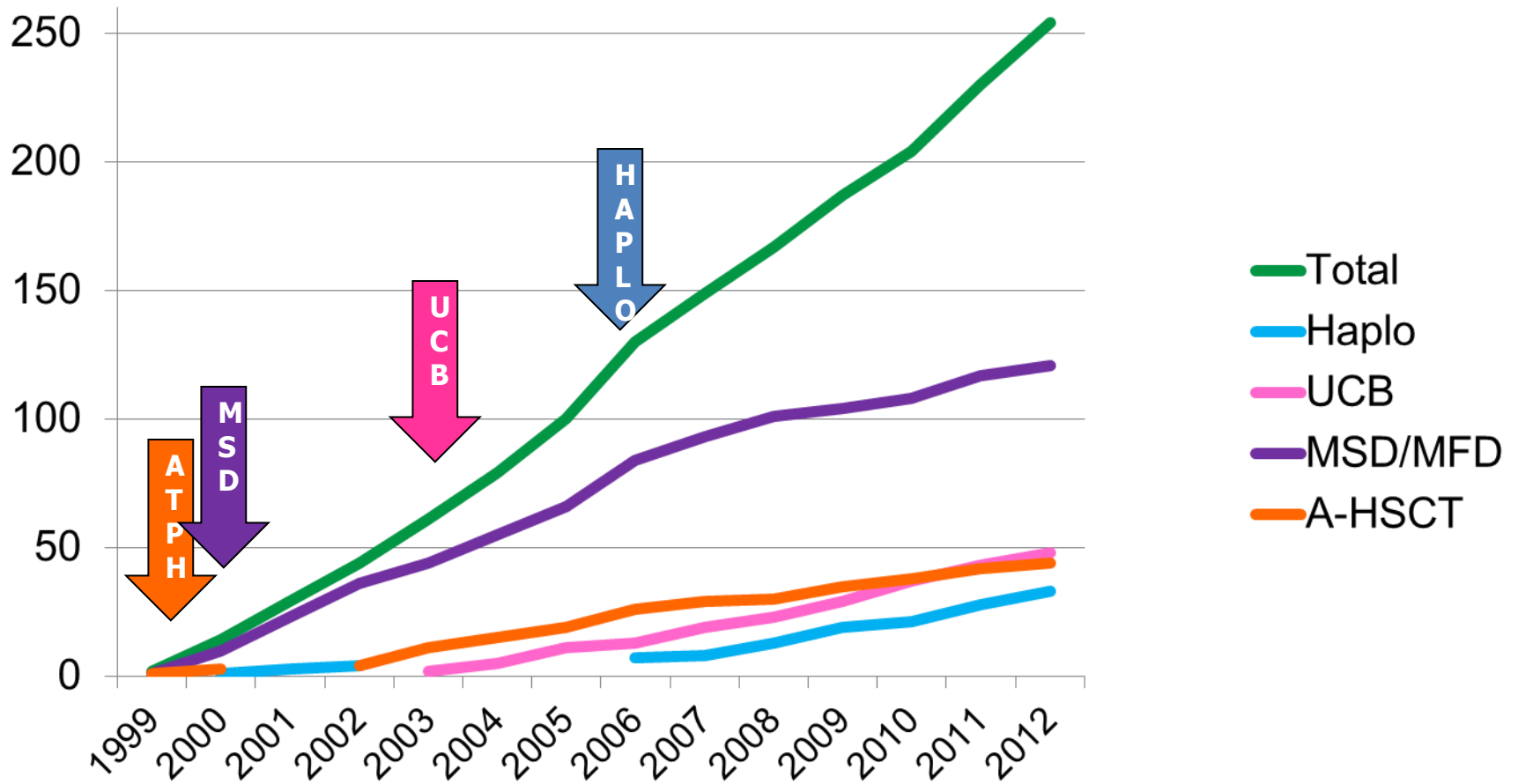
Age 3 mo – 25 y (median 8,8 y)

■ T. Oncological

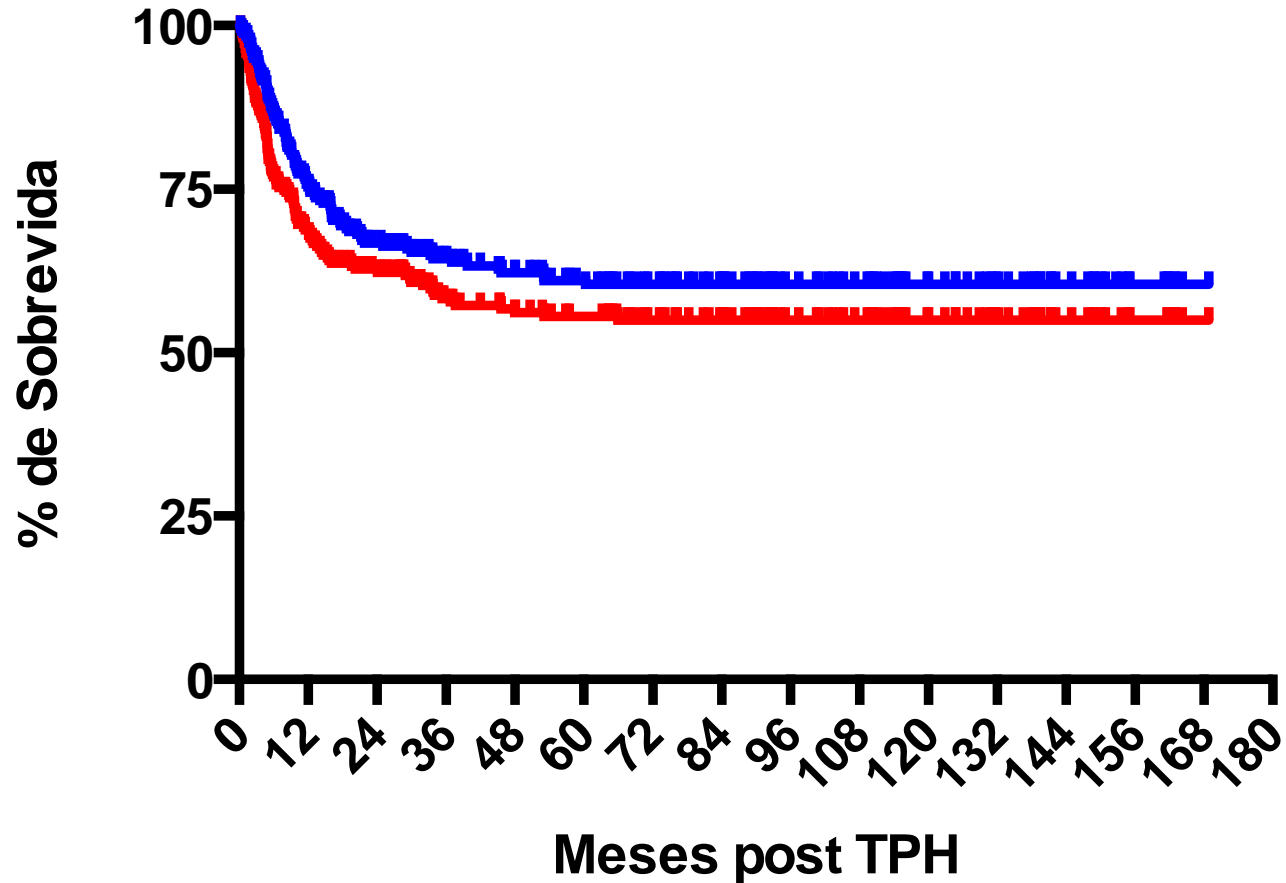
■ Non Oncological



# HSCT Activity 1999 - 2013



n=263 ATPH/MSD/MFaD/SCU/Haplo



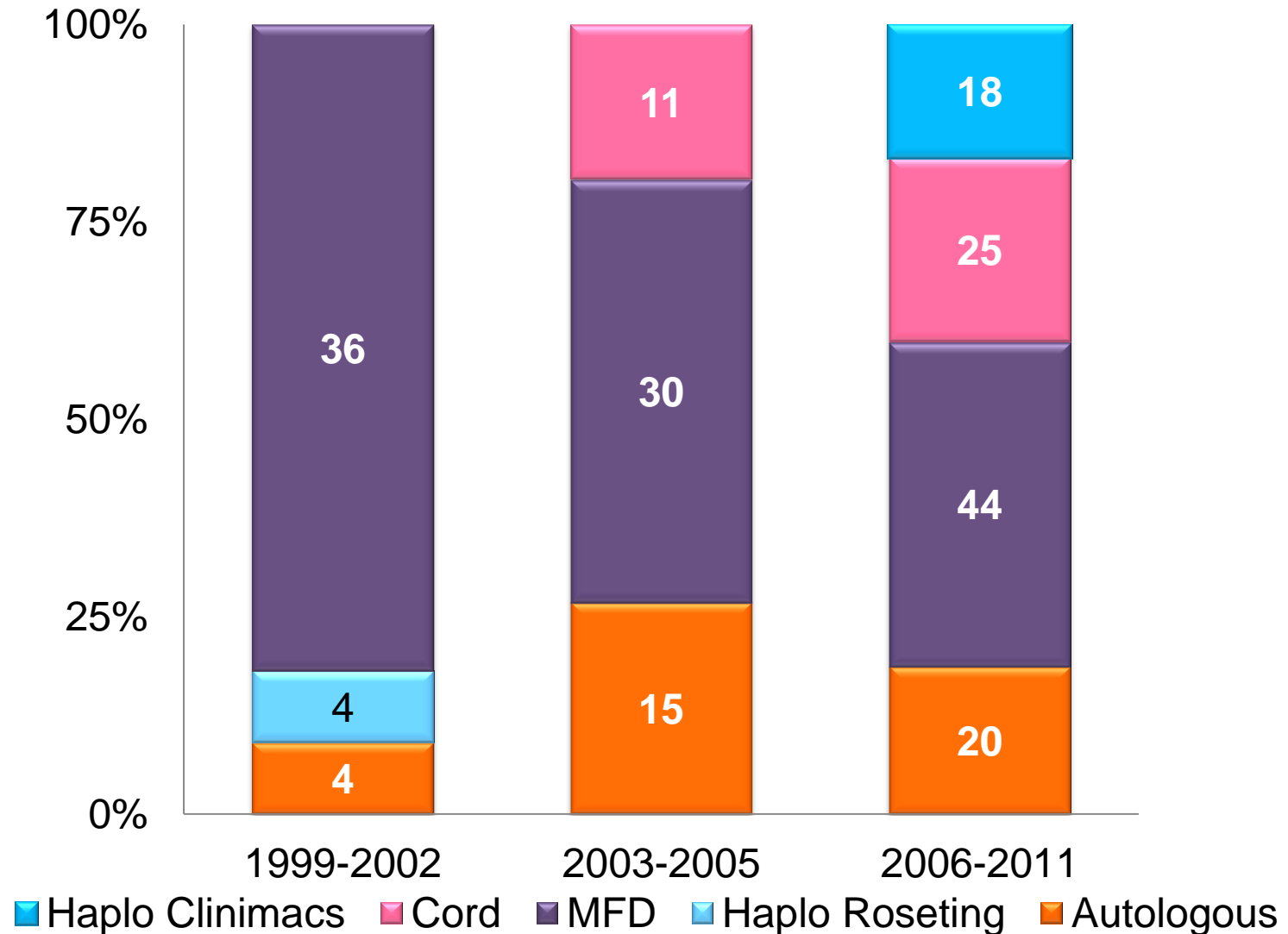
 **Total Survival**

75% a 1 año  
64% a 3 años  
61% a 5 años

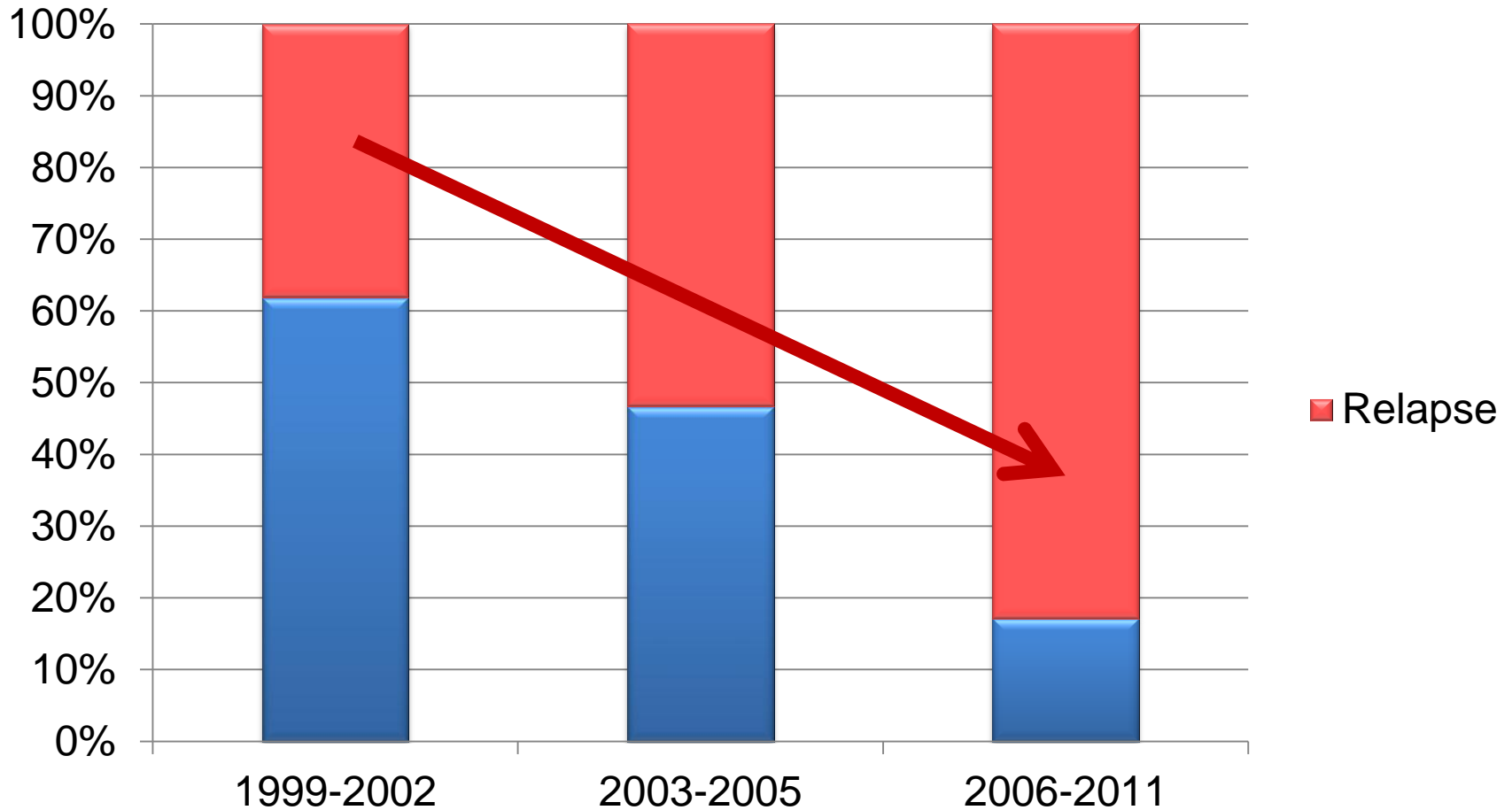
 **Event Free Survival**

69% a 1 año  
58% a 3 años  
56% a 5 años

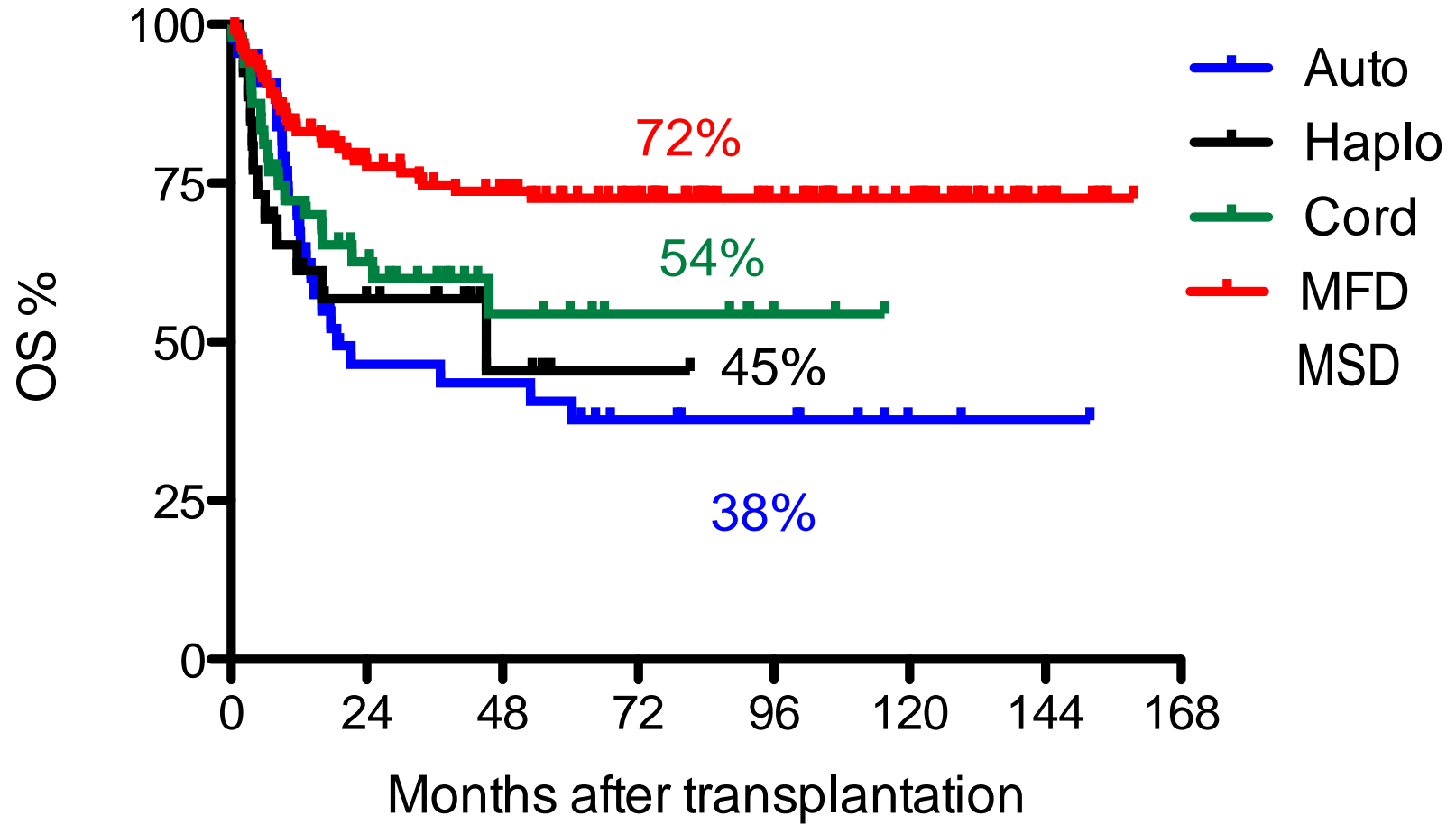
# Type of procedure by time period



# Cause of death

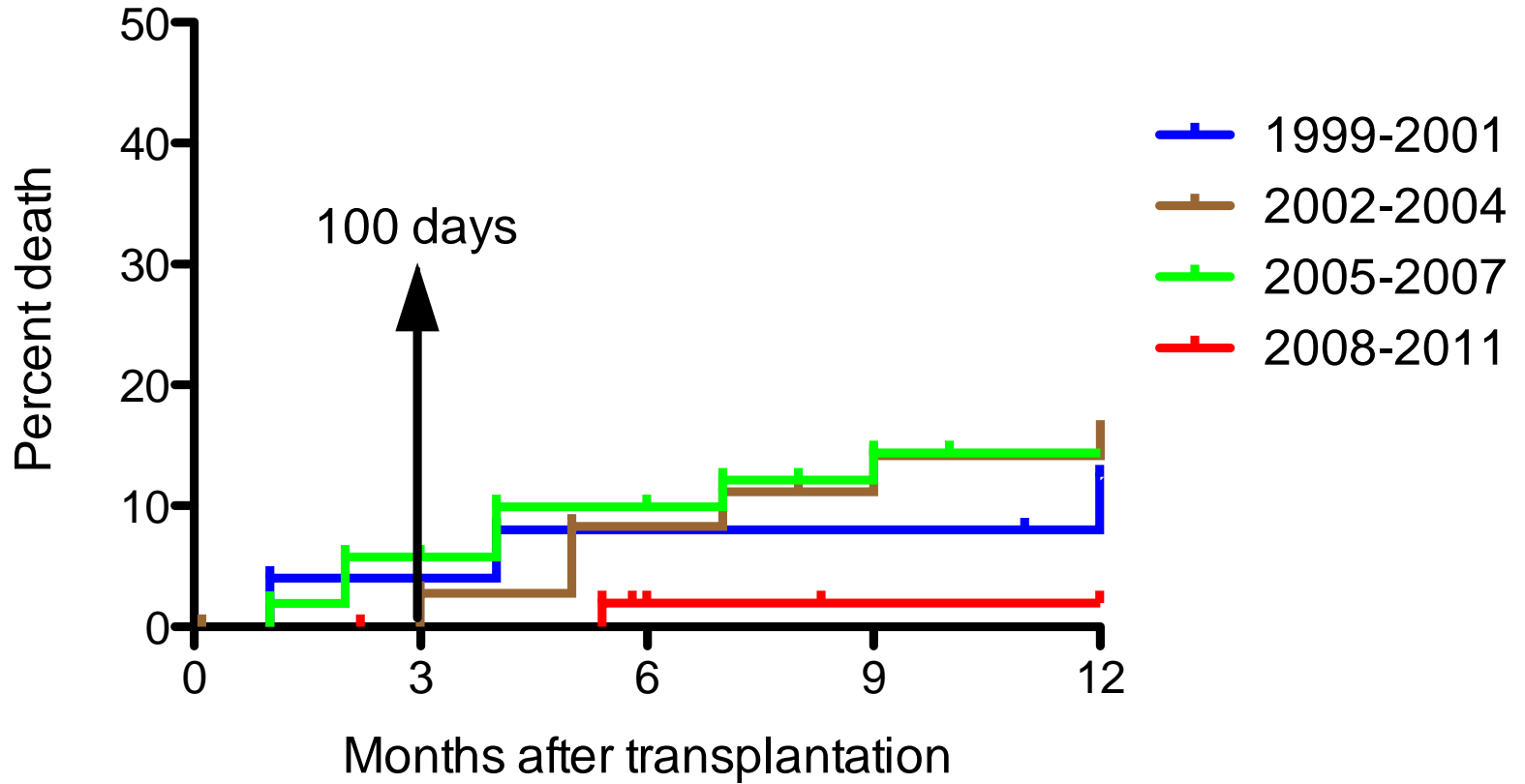


# Overall Survival



% represent estimated 5 years post transplant OS

# TRM



# **Autologous Hematopoietic Stem Cells Transplant**

- **Death by toxicity (Within the first 100 days) has decreased to 0%**
- **One year TRM has decreased to almost 0%**

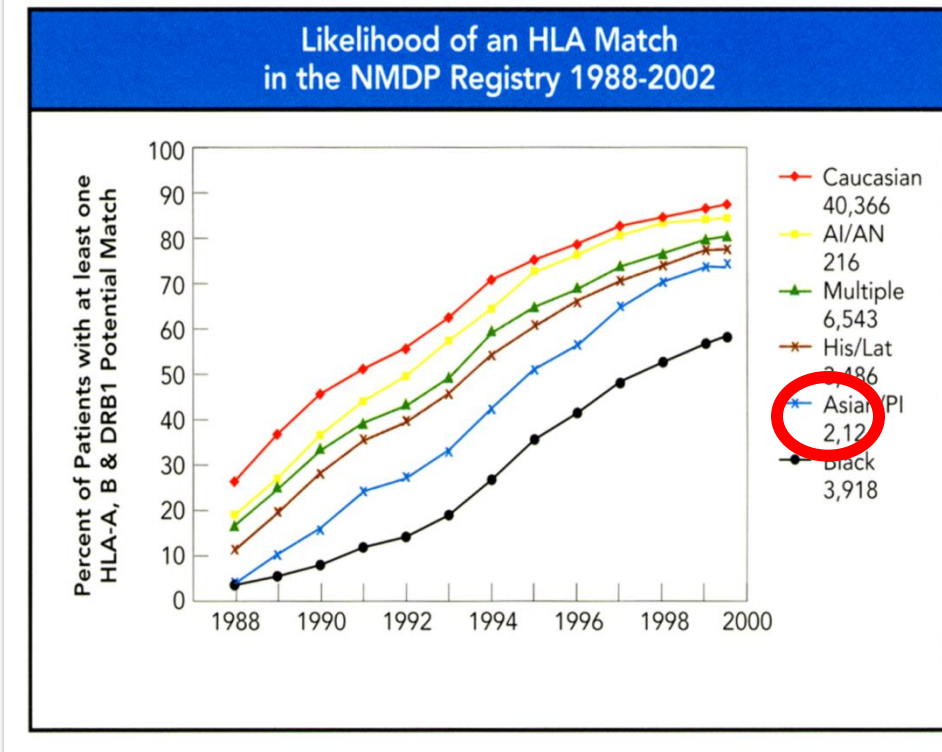


# Allogeneic Hematopoietic Stem Cells Transplant

- **Increased:**  
Number  
Complexity (MMD and UCB)
- **Decreased:**  
TRM

**7 million UBM donors**  
**71000 UCBU**

*Transfusion Medicine, 2008, 18, 250-259*



**Chile: “a mixed population: 64% white, 35% Amerindian, with traces of other admixture and < 4% are foreign born”**



**Aymara**



**Pehuenche**



**Alacaluf**

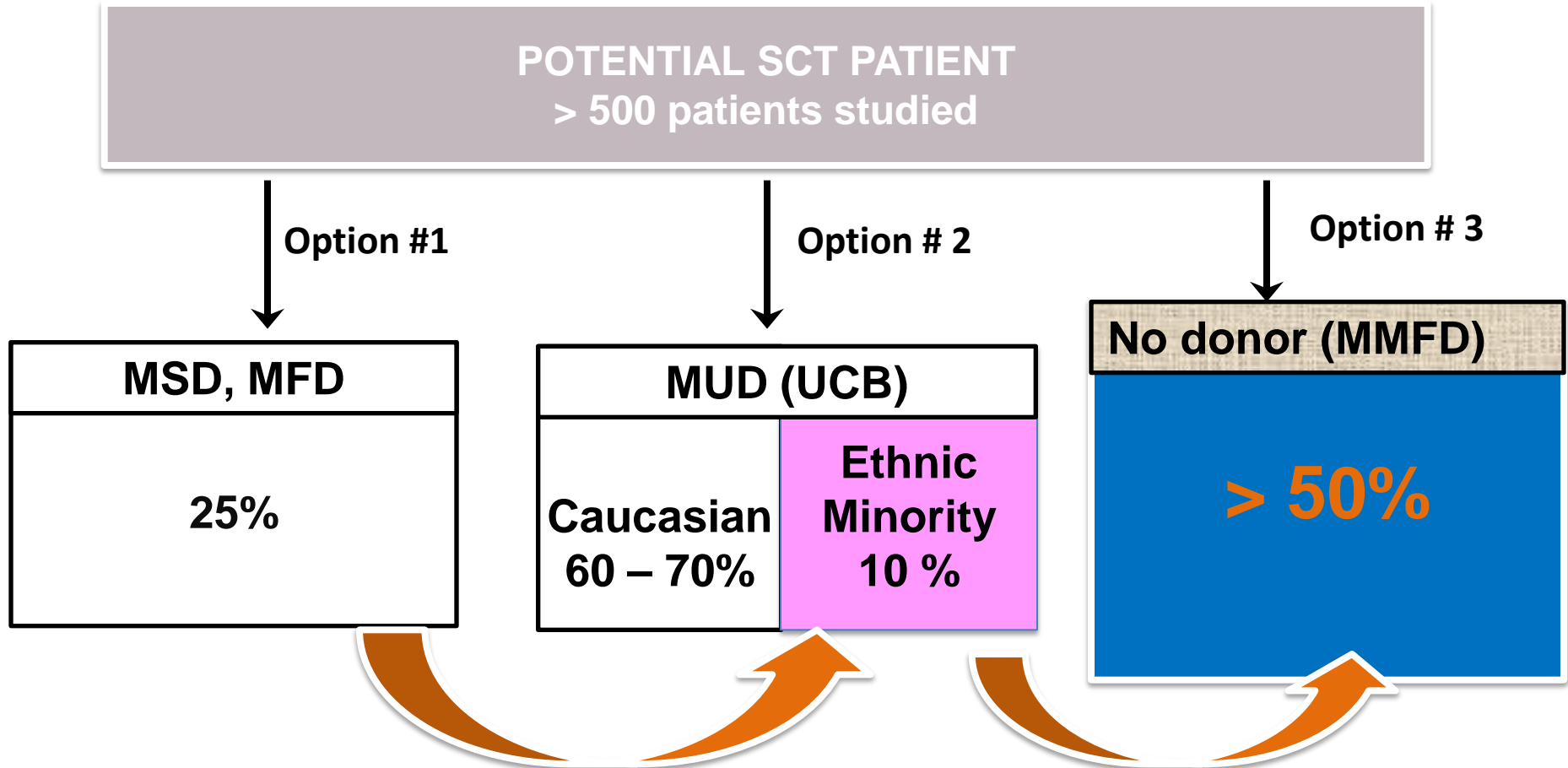


**Atacameño**



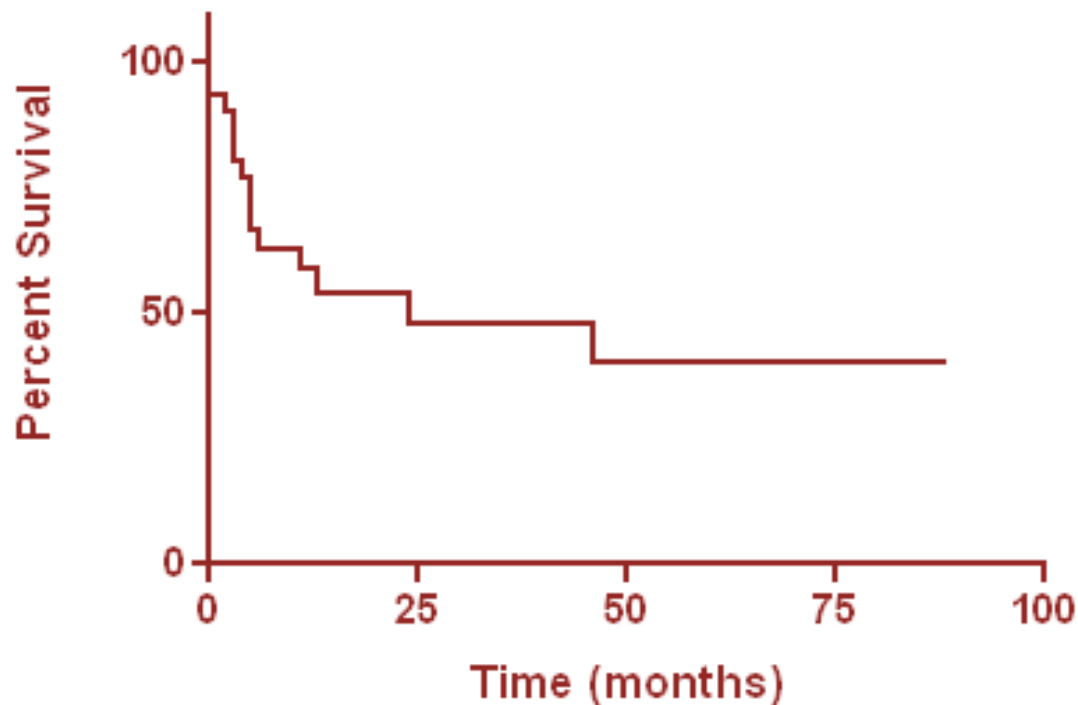
**Mapuche**

# SCT Donors

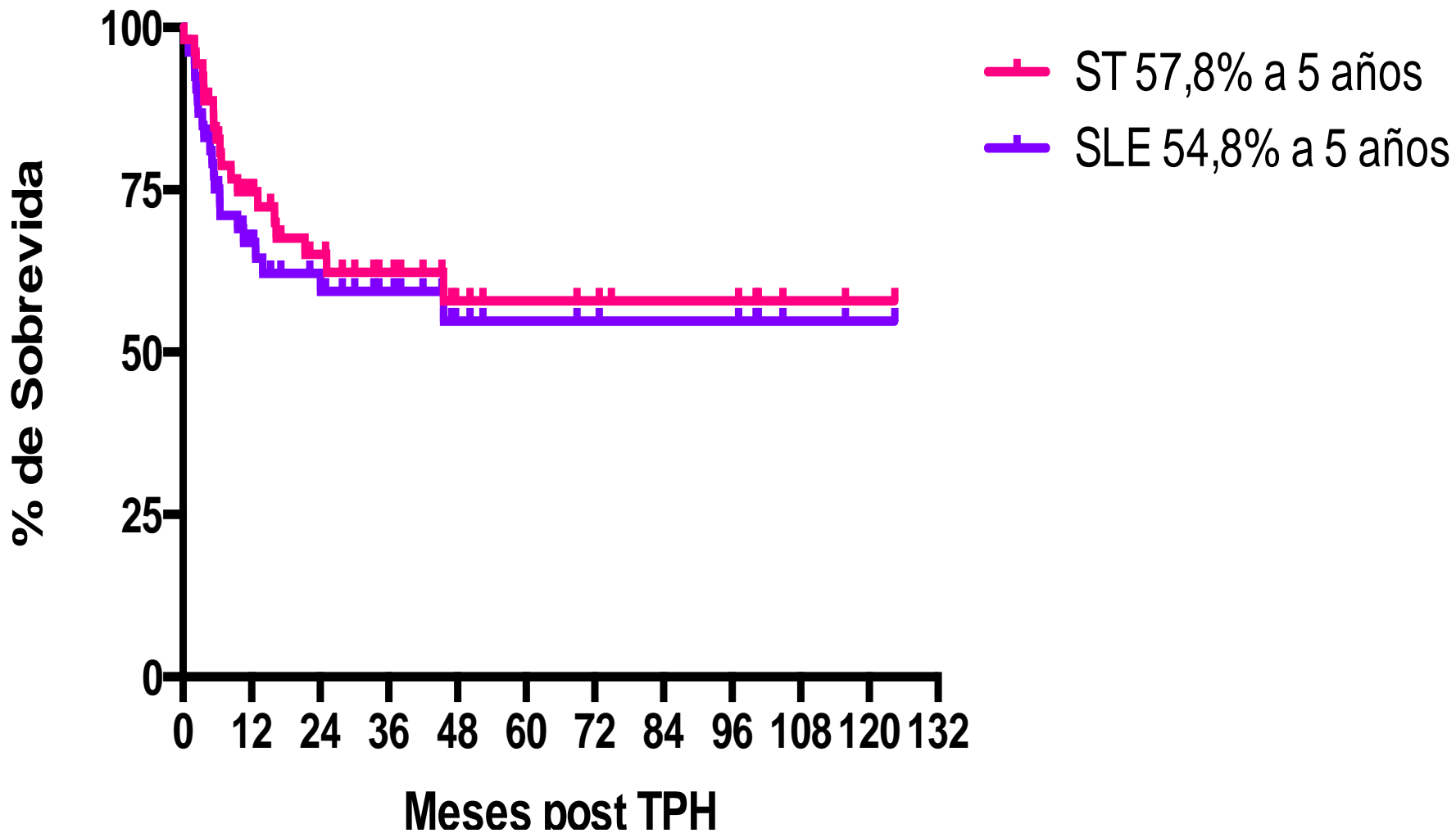


# Pediatric single Unrelated Cord Blood Transplantation (UCBT) for Acute Lymphoblastic Leukemia: Chilean experience

## UCBT Event-free survival



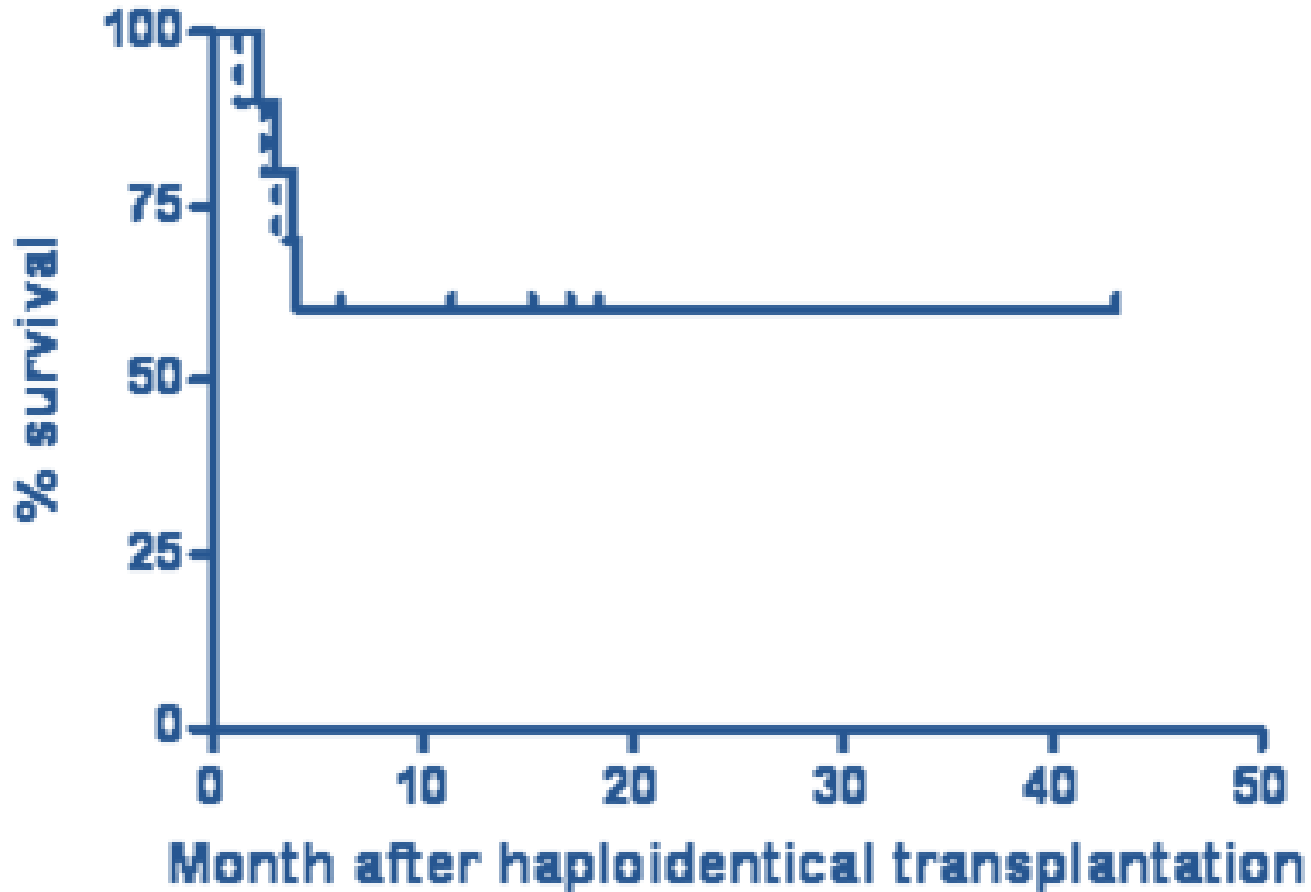
**All UCBT**  
**n = 53**



**ALL: 37 AML: 6 Mixed L: 2 JMML: 1**  
**LAD1:1 BDA:1 SCID: 1 ALD:2 SSCHD: 1 WAS:1**

# Haploidentical Stem Cell Transplantation for Children With High-Risk Leukemia

Julia Palma, MD,<sup>1,2\*</sup> Lucia Salas, MT,<sup>3</sup> Flavio Carrión, PhD,<sup>4</sup> Cristián Sotomayor, MD,<sup>1</sup> Paula Catalán, MD,<sup>1</sup>  
 Claudia Paris, MD,<sup>1</sup> Victoria Turner, PhD,<sup>5</sup> Hugo Jorquera, MT,<sup>6</sup> Rupert Handgretinger, MD,<sup>7</sup>  
 and Gastón K Rivera, MD<sup>5</sup>



— Overall Survival    - - - Event Free Survival

# Conclusions

- **Results are comparable with international literature**
- **Increase life expectancy of children with cancer**
- **UCB and Haplo: HSCT option for ethnical minorities**
- **Increase of HSCT availability**
- **Low TRM: after increasing complexity of HSCT**

**Autologous**

**Allogeneic**

**First Haplo transplant at HLCM**

**First CB transplant at HLCM**

**First Haplo transplant**

**First CB transplant**

**200 allogeneic transplants**

**1999  
BMTU CHILE  
HLCM/PINDA**



SCT for cancer treatment

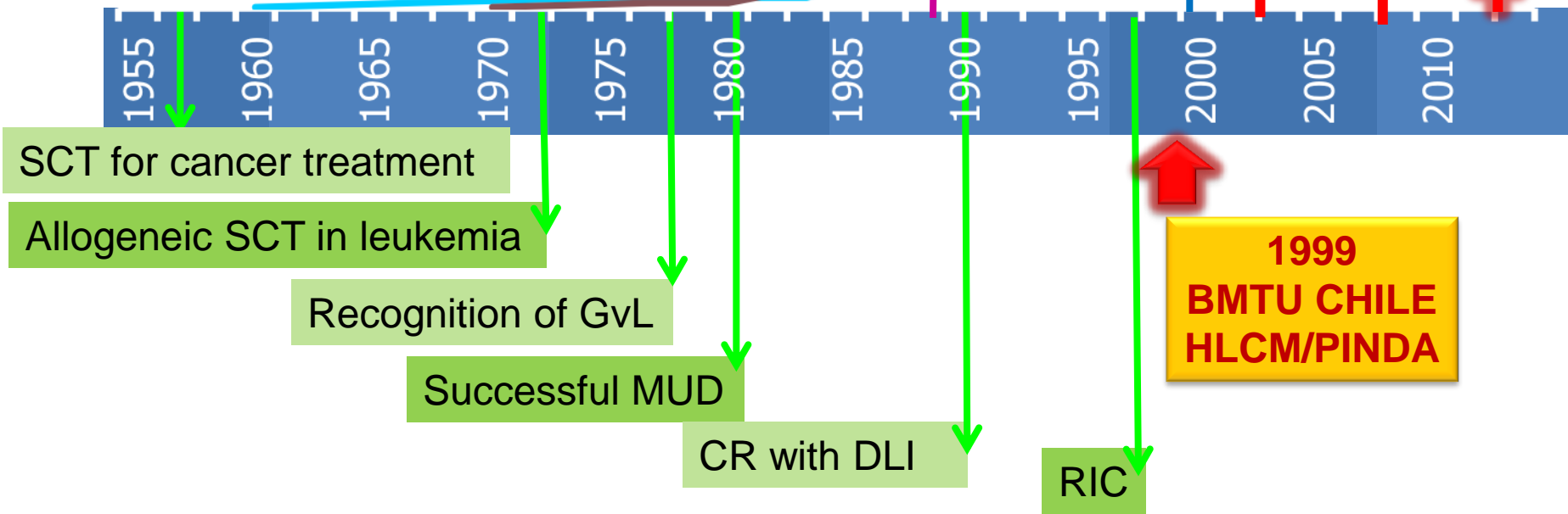
Allogeneic SCT in leukemia

Recognition of GvL

Successful MUD

CR with DLI

RIC





# **BMTU HLCM/PINDA HOT-TOPICS**

- 1. Is it possible to set up a successful public BMTU program at a country with limited resources?**

Report of the establishment of the program *Pediatr Blood Cancer*. 2006, 46:803

- 2. Successful treatment of malignancies in Latin American with common protocol is feasible?**

Collaborative work: Retinoblastoma.

*Bone Marrow Transplant*. 2012 Apr;47(4):522-7

- 3. Are there new, cost effective diagnostic tests, we can perform in house?**

Procalcitonine. *Rev Med Chil*. 2007, Aug;135(8):982-9

CMV PCR. *Rev Chil Infect* 2011; 28(2): 113-117

- 4. How to deal with complex patients in a limited resources setting?**

CMV: *Pediatr Blood Cancer*. 2009 Sep;53(3):453-8

TBC: *Rev Chil Infect*. 2013 Apr;30(2):202-5

# BMTU HLCCM/PINDA HOT-TOPICS

5. **Latin Americans are not well represented at donor registries. How to face the lack of suitable donors?**

Haploidentical. *Pediatr Blood Cancer*. 2012 Nov;59(5):895-901.

6. **As we gain expertise, we were able to developed local/national/regional guidelines.**

EBV *Rev Chilena Infectol*. 2012 Sep;29 Suppl 1:S29-31.

Respiratory Virus *Rev Chilena Infectol*. 2012 Sep;29 Suppl 1:S33-6.

Toxoplasma gondii *Rev Chilena Infectol*. 2012 Sep;29 Suppl 1:S37-9.

Chagas *Rev Chilena Infectol*. 2012 Sep;29Suppl 1:S41-3.

Stem cell harvesting and apheresis. *Transplantation proceedings*, 42, 339-344 (2010)

7. **What happened with survivors health? Non transmissible chronic diseases: present and future pandemics.**

Metabolic Syndrome *PediatrBloodCancer*. 2012 Aug;59(2):306-10.

# **Summary of Practical Guidelines when establishing a new HSCT program**

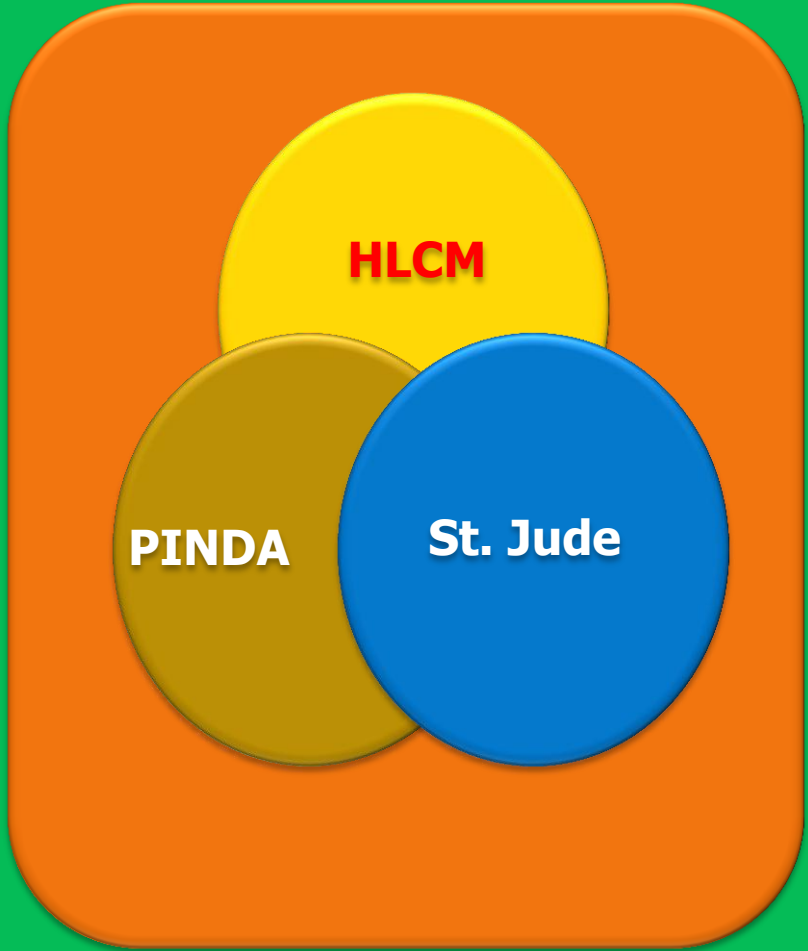
- 1. Pre-established pre transplant treatment protocols within a network**
- 2. Sustainable funding**
- 3. Twinning program or partnership with an experienced HSCT unit**
- 4. Transplantation unit design according to international standards**
- 5. International accreditation requirements**
- 6. Infection prevention measures**
- 7. HSCT committee with regular meetings**

# **Summary of Practical Guidelines when establishing a new HSCT program**

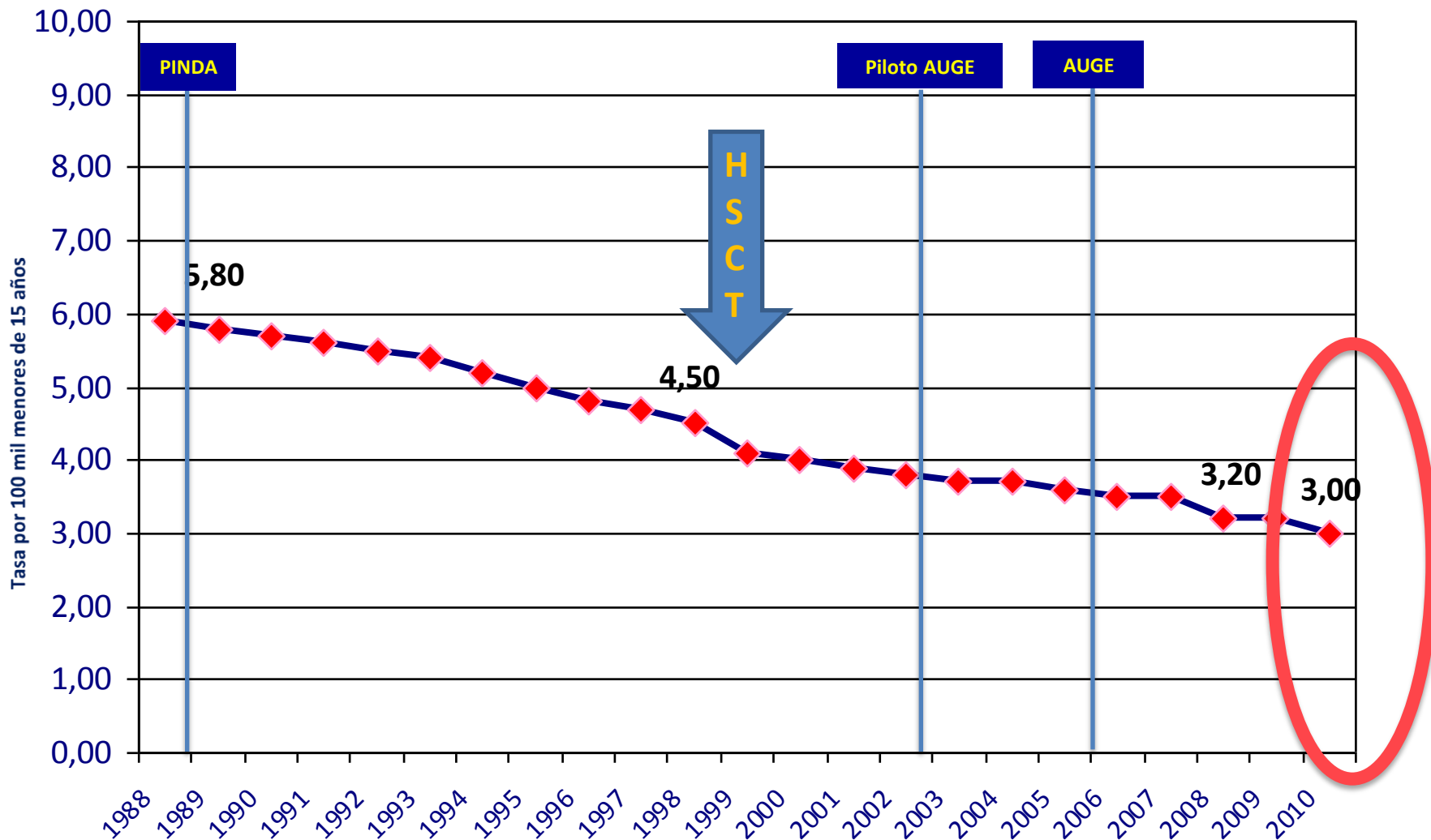
- 8. Availability of pediatric subspecialist services and ICU**
- 9. Working relationship with local laboratories**
- 10. Comprehensive pre-transplant evaluations**
- 11. Availability of all pharmacological agents and radiotherapy**
- 12. Long term follow-up HSCT clinic**
- 13. Regular critical review of results and progress**
- 14. Once standard HSCT has been mastered, endeavour to also master more complex HSCT**

Increasing number of HSCT: >200 Allo

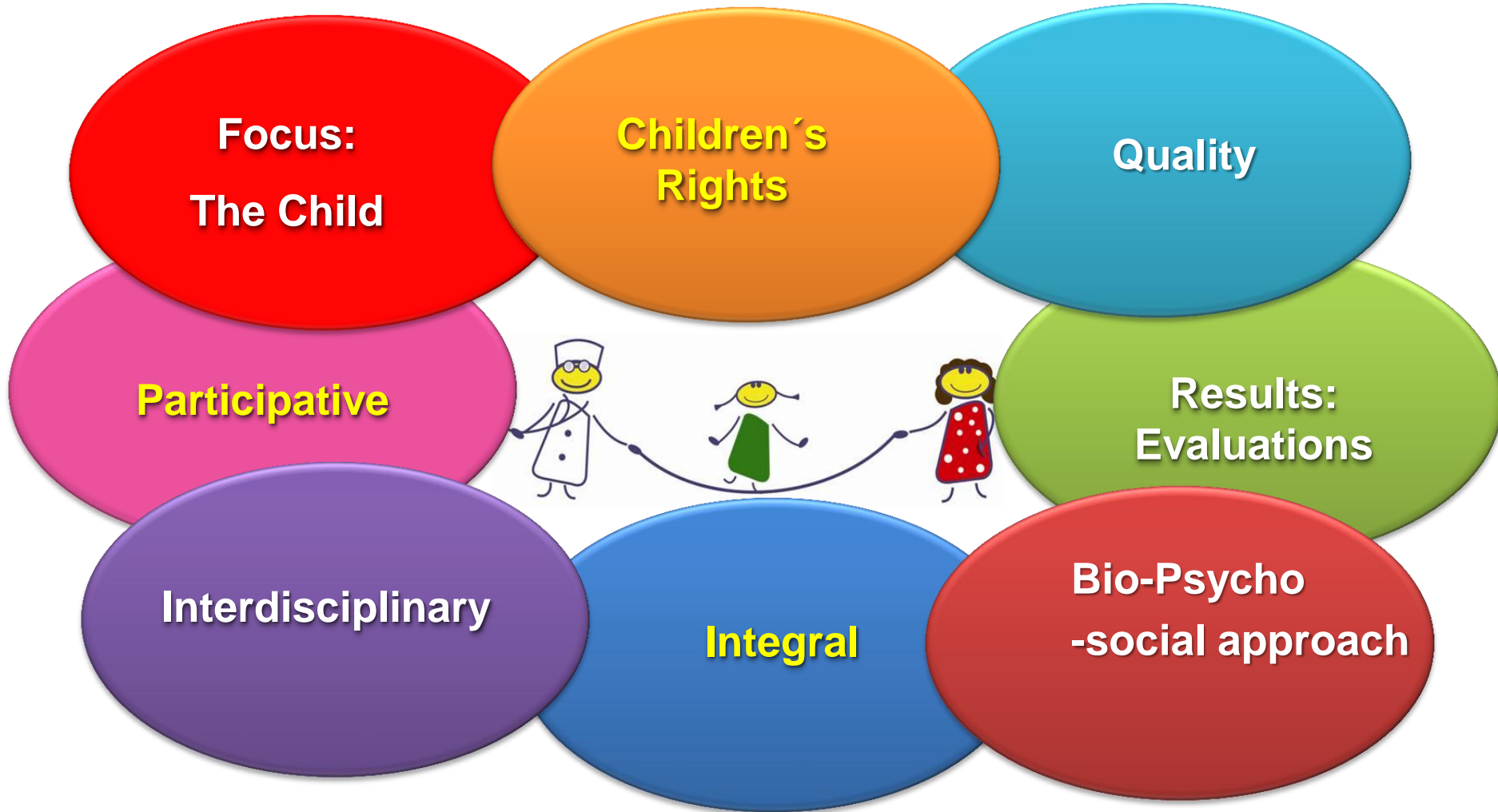
# Quality



# TASA DE MORTALIDAD POR CÁNCER INFANTIL PINDA, 1988 al 2010



# Friendly health care attention model



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**ST. JUDE CHILDREN'S RESEARCH HOSPITAL**  
**DANNY THOMAS - FOUNDER**

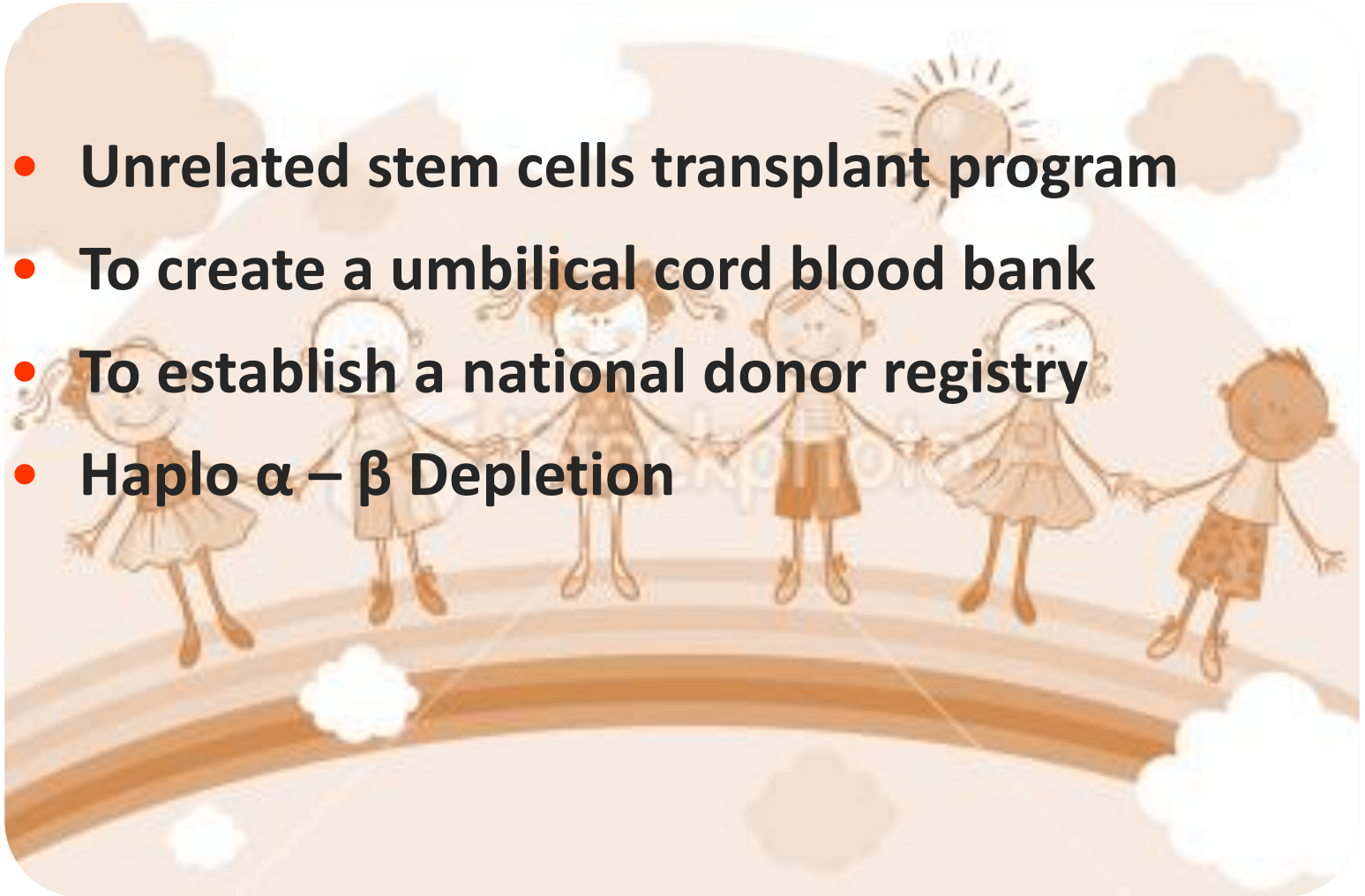
**HLA Laboratory**

**2012**

**HR HLA typing v**

# Goals: Long-term (Near future)

- Unrelated stem cells transplant program
- To create a umbilical cord blood bank
- To establish a national donor registry
- Haplo  $\alpha - \beta$  Depletion





# PINDA Network and BMT Unit HLCM thanks to:



Memphis

G.K Rivera  
G.Hale  
W.Leung  
P. Wooddard  
R.Barfield  
K. Kasow  
E. Horwitz  
M.Otto  
and many others

R. Ribeiro

V. Turner



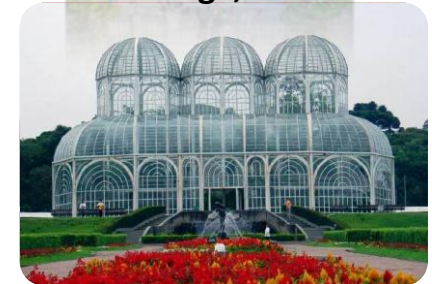
R. Handgretinger



A. Madrigal  
P. Veys  
M. Contreras  
C. Navarrete



J.J Ortega, T. Olive



R. Pasquini  
Noemi F.  
Euza

# Papers

## (2012-2013)

1. **Haploidentical stem cell transplantation for Children with high-risk.** Palma J, Salas L, Carrión F, Sotomayor C, Catalán P, Paris C, Turner V, Jorquera H, Handgretinger R, Rivera GK. *Pediatr Blood Cancer.* 2012 Nov;59(5):895-901.
2. **Successful treatment of metastatic retinoblastoma with high-dose chemotherapy and autologous stem cell rescue in South America.** Palma J., Sasso DF., Dufort G., Koop K., Díez B., Richard L., Castillo L., Chantada GL. *Bone Marrow Transplant.* 2012 Apr;47(4):522-7.
3. **Evaluation of metabolic syndrome after hematopoietic stem cell transplantation in children and adolescents.** Paris C, Yates L, Lama P, Zepeda AJ, Gutiérrez D, Palma J. *Pediatr Blood Cancer.* 2012 Aug;59(2):306-10.
4. **Omission of in vivo T cell depletion promotes rapid expansion of naïve CD4+ cord blood lymphocytes and restores immunity within 2 months after unrelated cord blood transplant.** Chiesa R, Gilmour K, Qasim W, Adams S, Worth AJ, Zhan H, Montiel-Equihua CA, Derniame S, Cale C, Rao K, Hiwarkar P, Hough R, Saudemont A, Fahrenkrog CS, Goulden N, Amrolia PJ, Veys P. *Br J Haematol.* 2012 Mar;156(5):656-66..
5. **Profilaxis de enfermedad por virus de Epstein Barr en niños y adultos receptores de trasplante de órganos sólidos y de precursores hematopoyéticos.** Paula Catalán y Andrea Alba.. *Rev Chilena Infectol* 2012; 29 (Supl 1): 29-31
6. **Profilaxis de infección por virus respiratorios en niños y adultos sometidos a trasplante de órganos sólidos y precursores hematopoyéticos** Ana M. Álvarez, Paula Catalán, Andrea Alba y Marcela Zuleta. *Rev Chilena Infectol* 2012; 29 (Supl 1): 33-36
7. **Profilaxis de toxoplasmosis en niños y adultos sometidos a trasplante de órganos sólidos y precursores hematopoyéticos** Ernesto Payá, Isabel Noemí, Renzo Tassara, Paula Catalán y Carmen L. Avilés.. *Rev Chilena Infectol* 2012; 29 (Supl 1): 37-39
8. **Profilaxis de enfermedad de Chagas en niños y adultos sometidos a trasplante de órganos sólidos y de precursores hematopoyéticos.** Rosana Benítez, Isabel Noemí, Renzo Tassara, Paula Catalán y Carmen L. Avilés. *Rev Chilena Infectol* 2012; 29 (Supl 1): 41-43
9. **Infección por *Mycobacterium tuberculosis* en una niña sometida a trasplante de progenitores hematopoyéticos.** Julia Palma, Paula Catalán, Patricia Mardones y M. Elena Santolaya. *Rev. chil. infectol.* [online]. 2013, vol.30, n.2, pp. 202-205. ISSN 0716-1018.