

The 3rd Scientific Symposium of The WBMT

Haplo-identical HCT: Asian experience

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Preface (1)

So-called “Haplo-identical HCT” (“Haplo”) has been considered an alternate modality for patients who lack HLA genetically identical sibling donors or HLA genotypically/phenotypically identical unrelated donors among adult/cord blood banks. For a patient, the probability to find out such appropriate donors among family members is universally 25% but the probability to find out donors among stem cell banks is varied depending on the donor pool size and the genetic diversity of the people.

Preface (2)

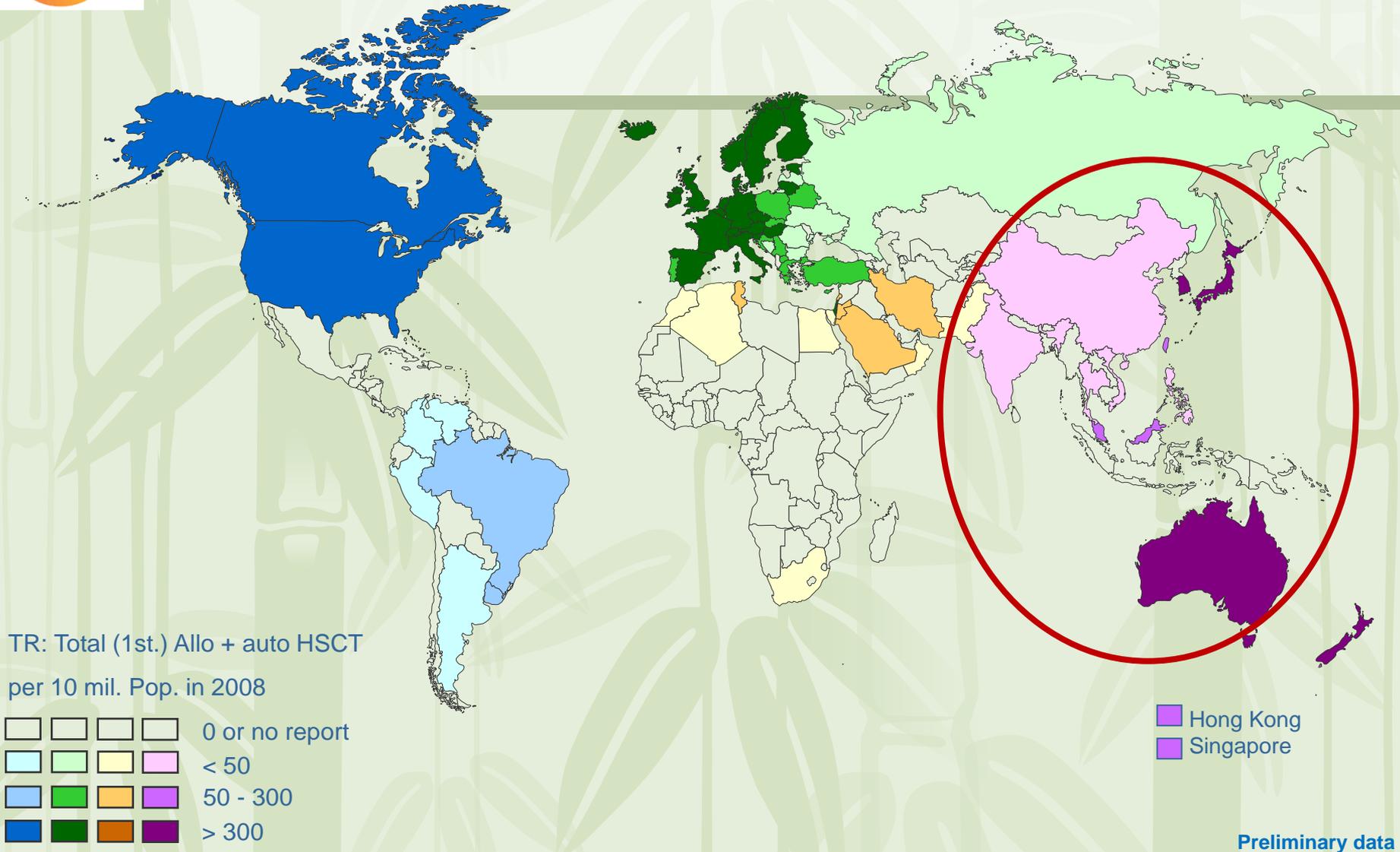
Here I report the experiences of “Haplo” in two Asian countries, Japan and China. The data were obtained from APBMT Annual Survey as well as from several published articles, so well-opened level one data sources.

Data Sources

1. APBMT Annual Survey 2010,2011,2012,2013
2. Ichinohe, T et al: HLA-haploidentical hematopoietic stem cell transplantation between non-inherited maternal antigen (NIMA)-mismatched family members linked with long-term fetomaternal microchimerism. *Blood*. 2004; 104: 3821–3828
3. Koderá Y et al: Human leukocyte antigen haploidentical hemtopoietic stem cell transplantation: indications and tentative outcomes in Japan. *Semin Hematol* 42:112-118, 2005
4. Lu, D.P., et al: Conditioning including antithymocyte globulin followed by un-manipulated HLA-mismatched/haploidentical blood and marrow transplantation can achieve comparable outcomes to HLA-identical sibling transplantation. *Blood*. 2006; 107: 3065–3073



Transplant Rates in the 4 Regions: All HSCT



APBMT (19 countries/regions)

Asia-Pacific Blood and Marrow Transplantation Group

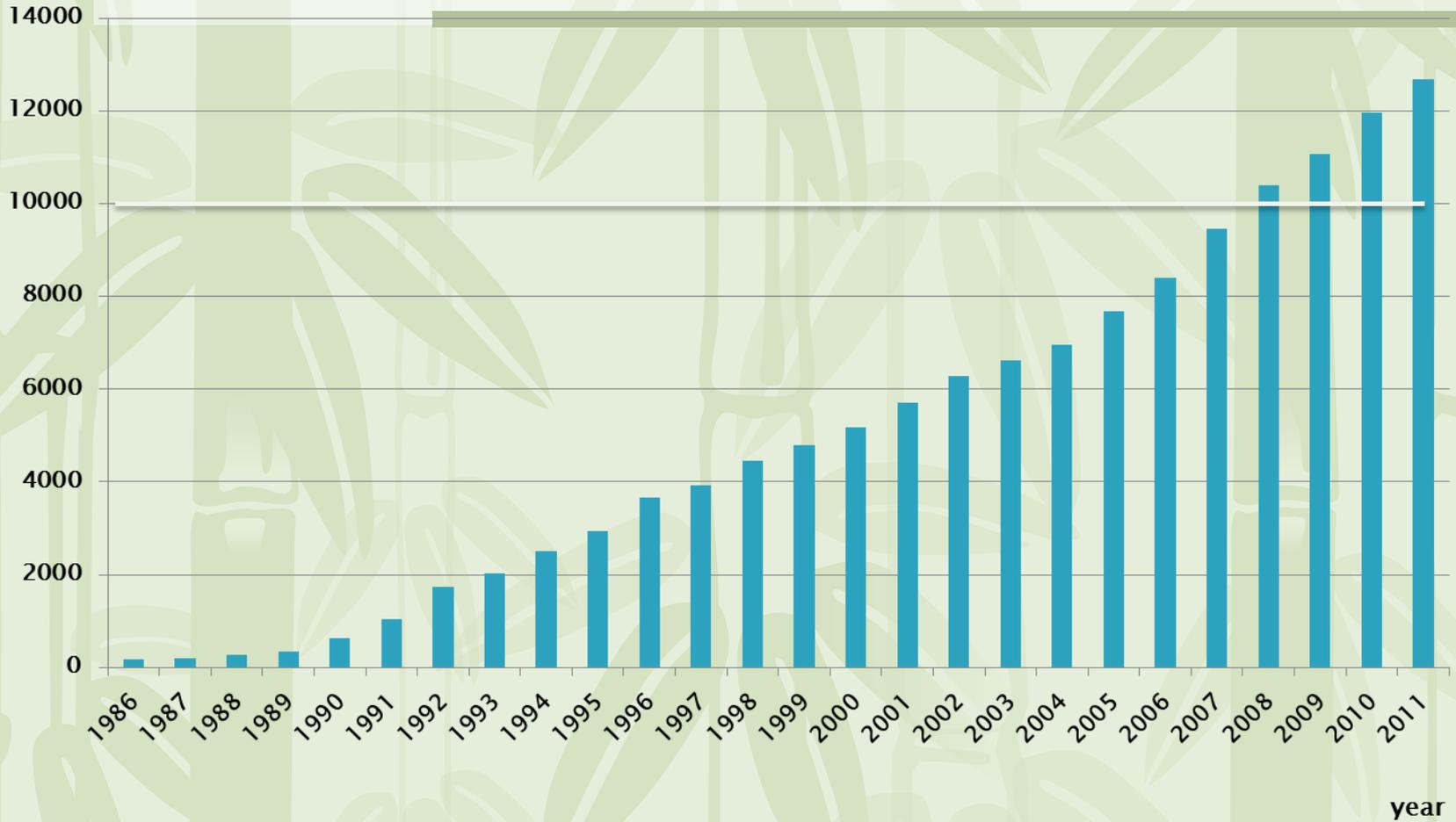


Australia, Bangladesh
Mainland China
Hong Kong, Mongolia
India, Myanmar
Indonesia
Iran
Japan
Korea
Malaysia
New Zealand
Pakistan
Phillipines
Taiwan
Thailand
Singapore
Vietnam



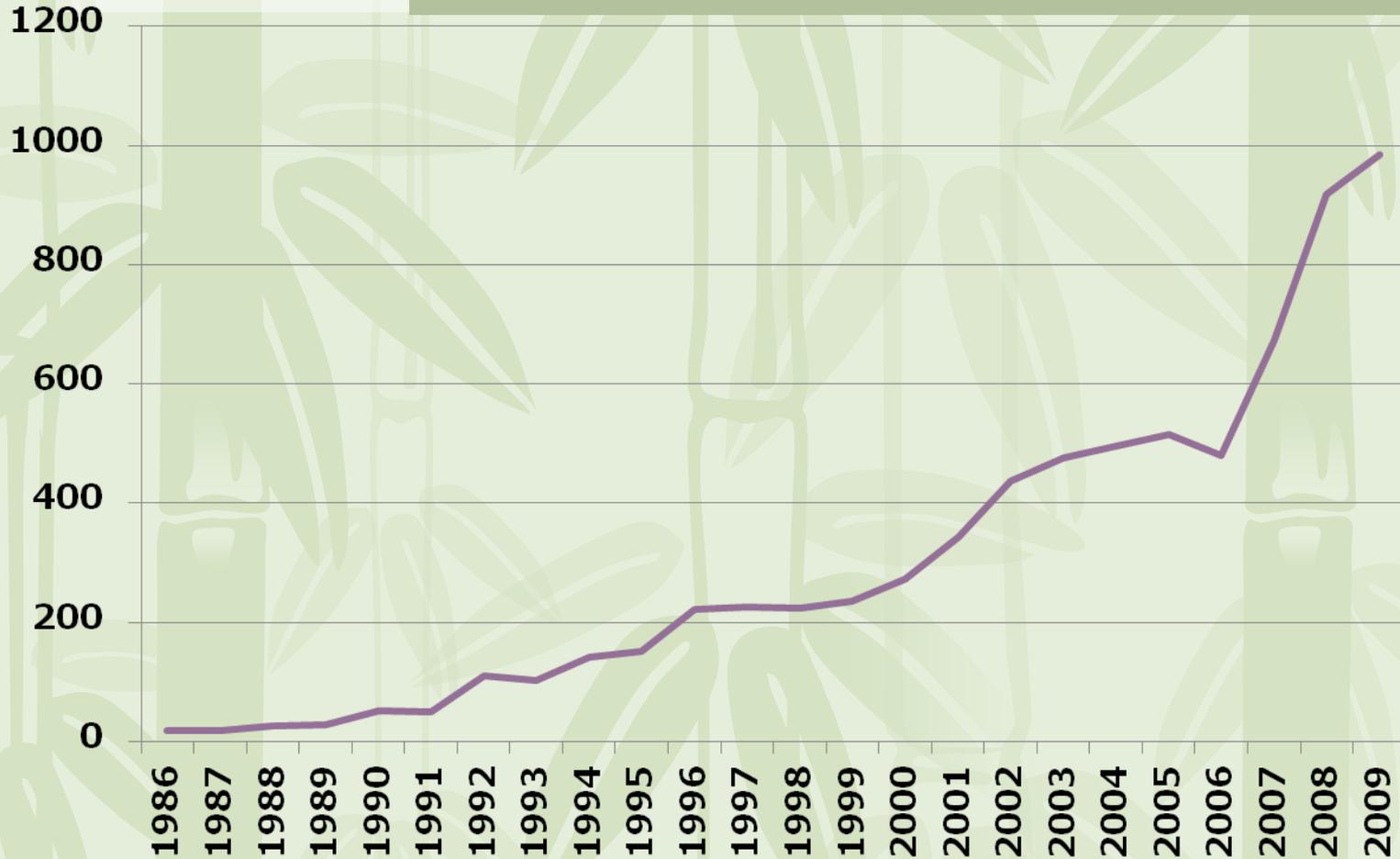
Annual No. of HSCTs in APBMT Region

No. of HSCTs

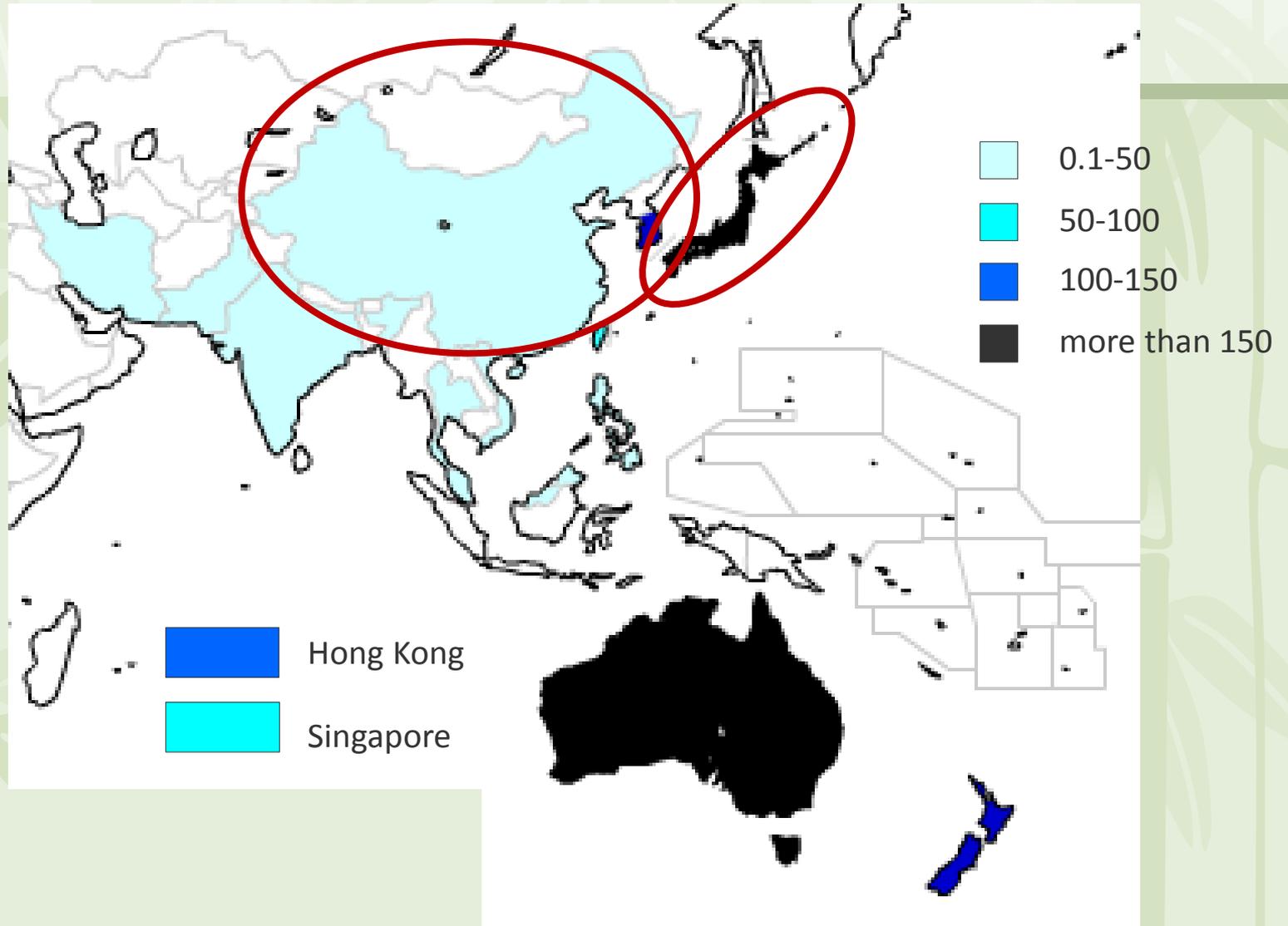


Trends in HLA-Haploidentical HSCT in APBMT Region

No. of HSCTs



No. of Allogeneic Transplants per 10 million population



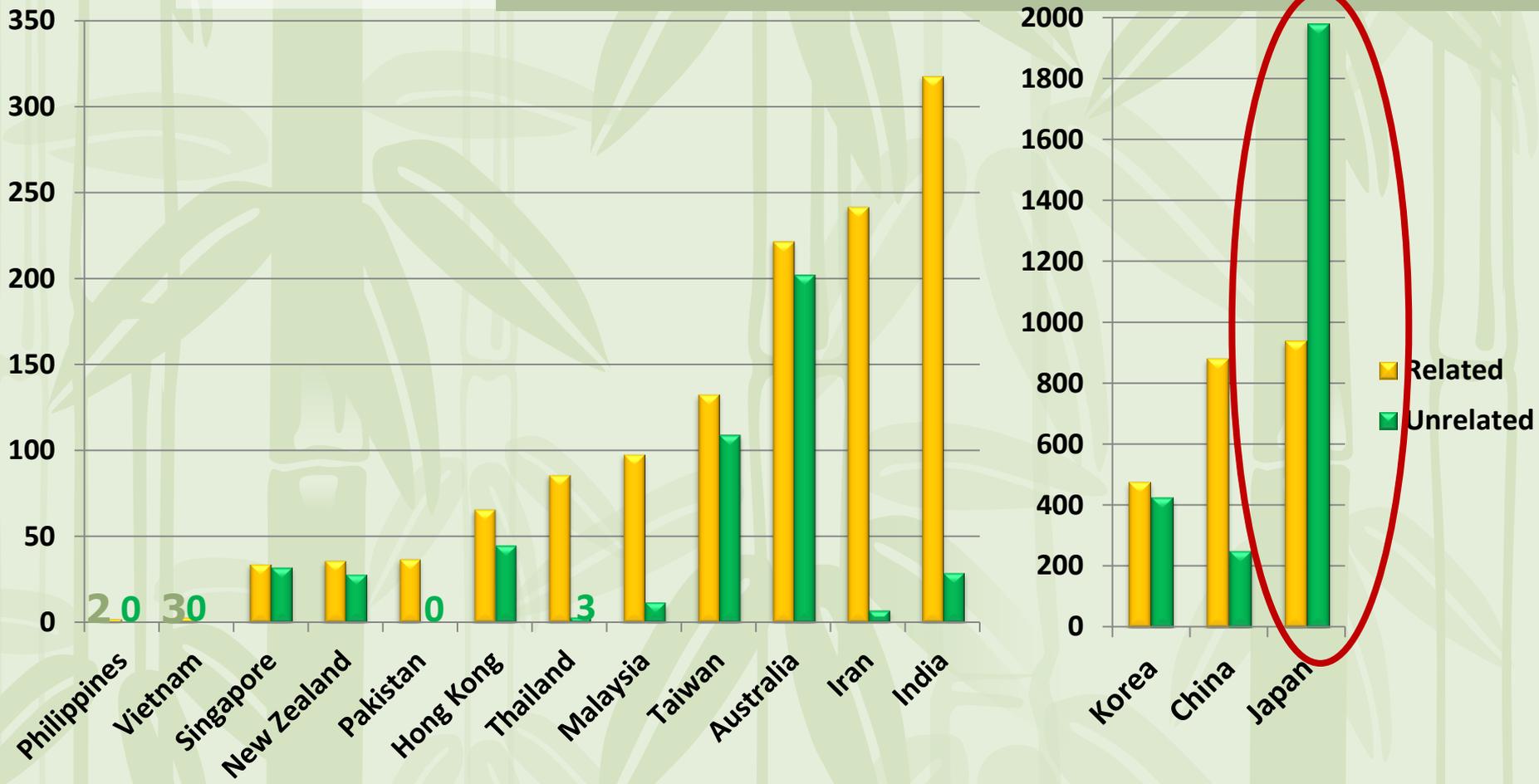
No. of HSCT and Centers

	HSCTs from 1986 to 2009	Centers in 2009	HSCTs in 2009
Australia	17,532	41	1,327
China	6,628	38	1,417
Hong Kong	2,135	2	149
India	1,532	24	562
Iran	2,812	6	366
Japan	51,861	381	4,425
Korea	14,060	43	1,672
Malaysia	1,703	10	213
New Zealand	1,875	6	201
Pakistan	268	2	49
Philippines	29	1	2
Singapore	1,241	5	133
Taiwan	3,341	16	388
Thailand	1,386	5	163
Vietnam	92	3	11
Total	106,495	583	11,078

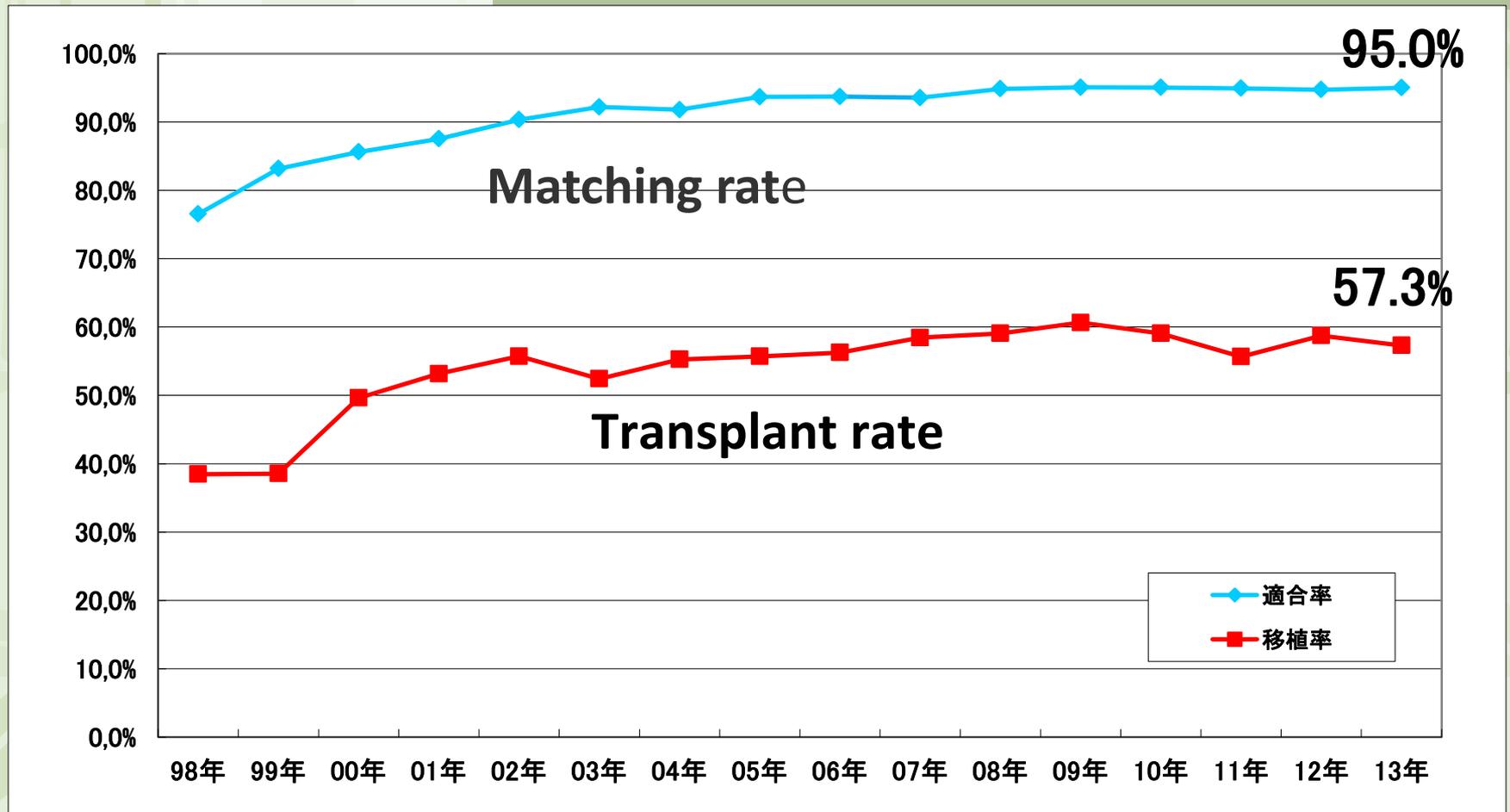
Japanese experience

- ❖ In Japan, 3,300 allogeneic transplants (1,000 transplants from HLA closely matched family donors, 1,300 from adult unrelated donors, 1,000 from cord blood) per year are currently performed and these cover approximately 60% of potential demands of allogeneic transplants. It means, nevertheless, 40% of patients are still remained to receive allografts.

Number of HSCT by country / region : Related vs Unrelated



The rate of HLA Matching and UR Transplant



(2014年3月末現在)

Performance of “Haplo” in Japan

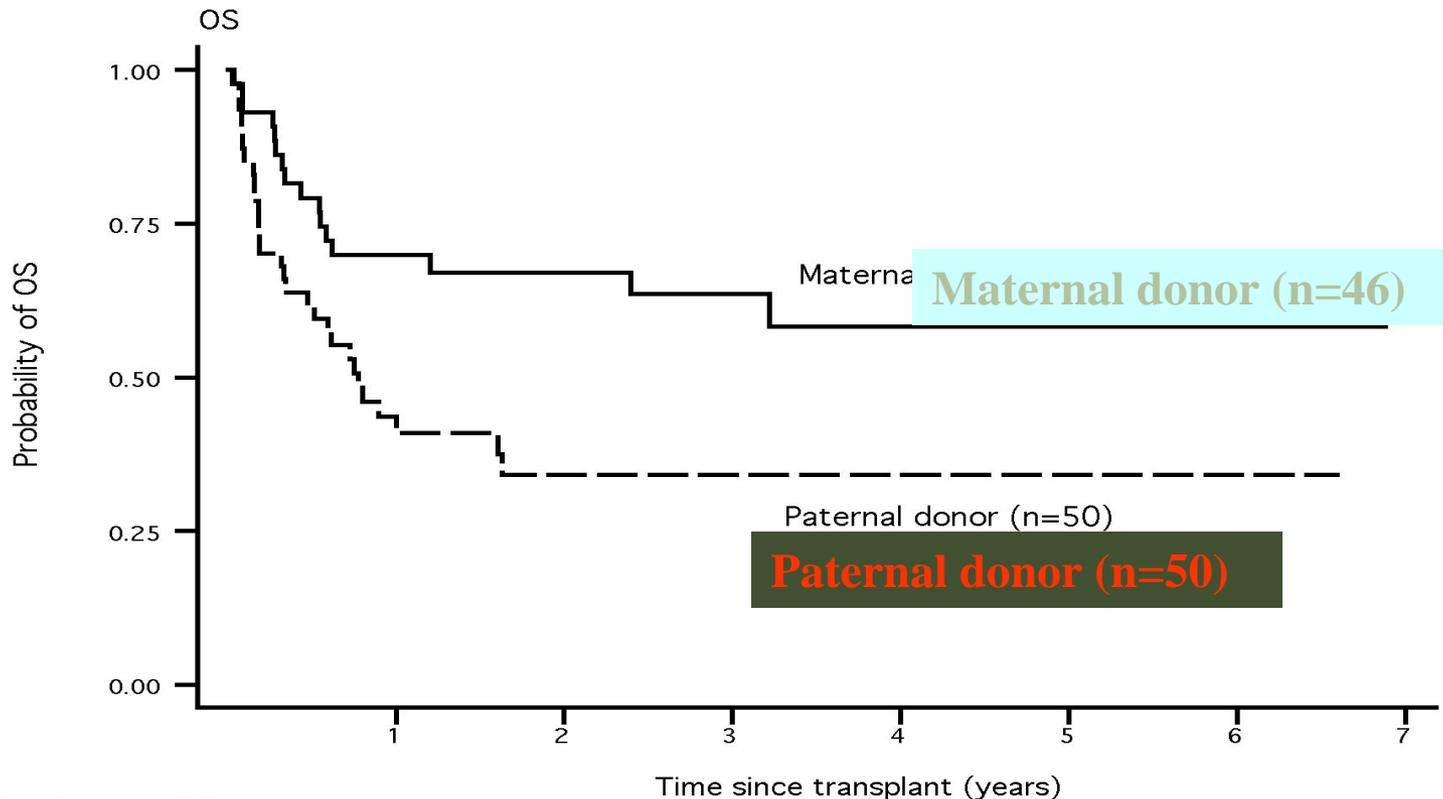
- ❖ To save these patients, transplants from HLA partially mismatched family or unrelated donors as well as from haplo-identical donors have been performed **in step by step fashion** (2), (3) and getting the results that the outcomes of HLA mismatched transplants including haplo is well comparable to that of HLA matched transplants.

Probability of grade-3,4 acute GVHD and disease-free survival after HLA allele-mismatched UR-BMT
— cyclosporine vs tacrolimus —

		Probability of Grade-3,4 acute GVHD	3-year DFS
Class-1 DNA 1 mismatch			
cyclosporine	(n: 12)	58%	25%
tacrolimus	(n: 13)	23%	52%
Class-2 DNA 1 mismatch			
cyclosporine	(n: 31)	16%	55%
tacrolimus	(n: 19)	10%	52%

Retrospective study NIMA/ IPA effect

Tamaki S, Ichinohe T et al: BMT (2001)



Number at risk
Paternal donor
Maternal donor

	17	11	10	10	6	2	1
	26	20	14	10	8	3	1

INCIDENCE OF LONG-TERM FETO-MATERNAL CHIMERISM WITH REFERENCE TO DURATION

*Represented by offspring's age at blood sampling.

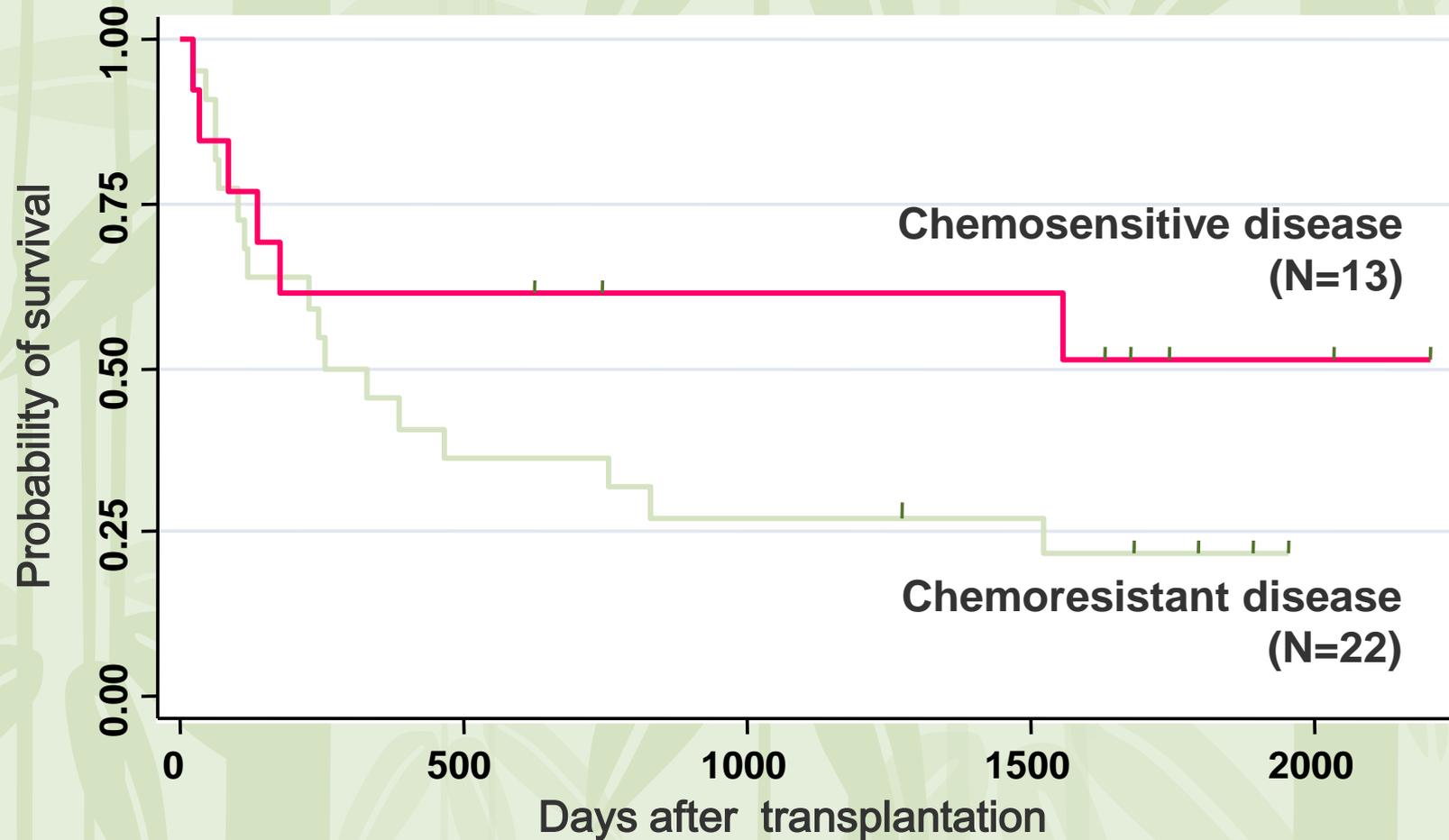
	MATERNAL CELL CHIMERISM in Offspring			OFFSPRING CELL CHIMERISM in Mother		
Duration of chimerism (yr)	No. of Subjects	No. Detected	% Detected	No. of Subjects	No. Detected	% Detected
0-9	39	23	59	42	32	76
10-19	59	46	78	44	35	80
20-29	71	56	79	51	40	78
30-39	39	25	64	17	11	65
40-49	26	13	50	11	8	73
50-59	11	6	55	1	1	100
60-69	1	1	100	0	0	0
total	246	170	69	166	127	77

HLA-haploidentical NIMA-mismatched HSCT a nationwide study 2000-2004: patient characteristics

	Total	Type of donor		<i>P</i>
		Mother	Offspring/sibling	
	N=35	N=15	N=20	
Median age (range)	28 (2-58)	18 (3-33)	42 (2-58)	.007
Sex [M/F]	17/18	10/5	7/13	NS
Diagnosis, n (%)				
AML	12 (34)	3 (20)	9 (45)	
ALL	12 (34)	7 (47)	5 (25)	
CML	7 (20)	3 (20)	4 (20)	NS
DLBCL	3 (9)	2 (13)	1 (5)	
ATL	1 (3)	0 (0)	1 (5)	
Disease status, n(%)				
In remission	13 (37)	4 (27)	13 (37)	NS
Chemorefractory	22 (63)	11 (73)	22 (63)	

HLA-haploidentical NIMA-mismatched SCT: Survival

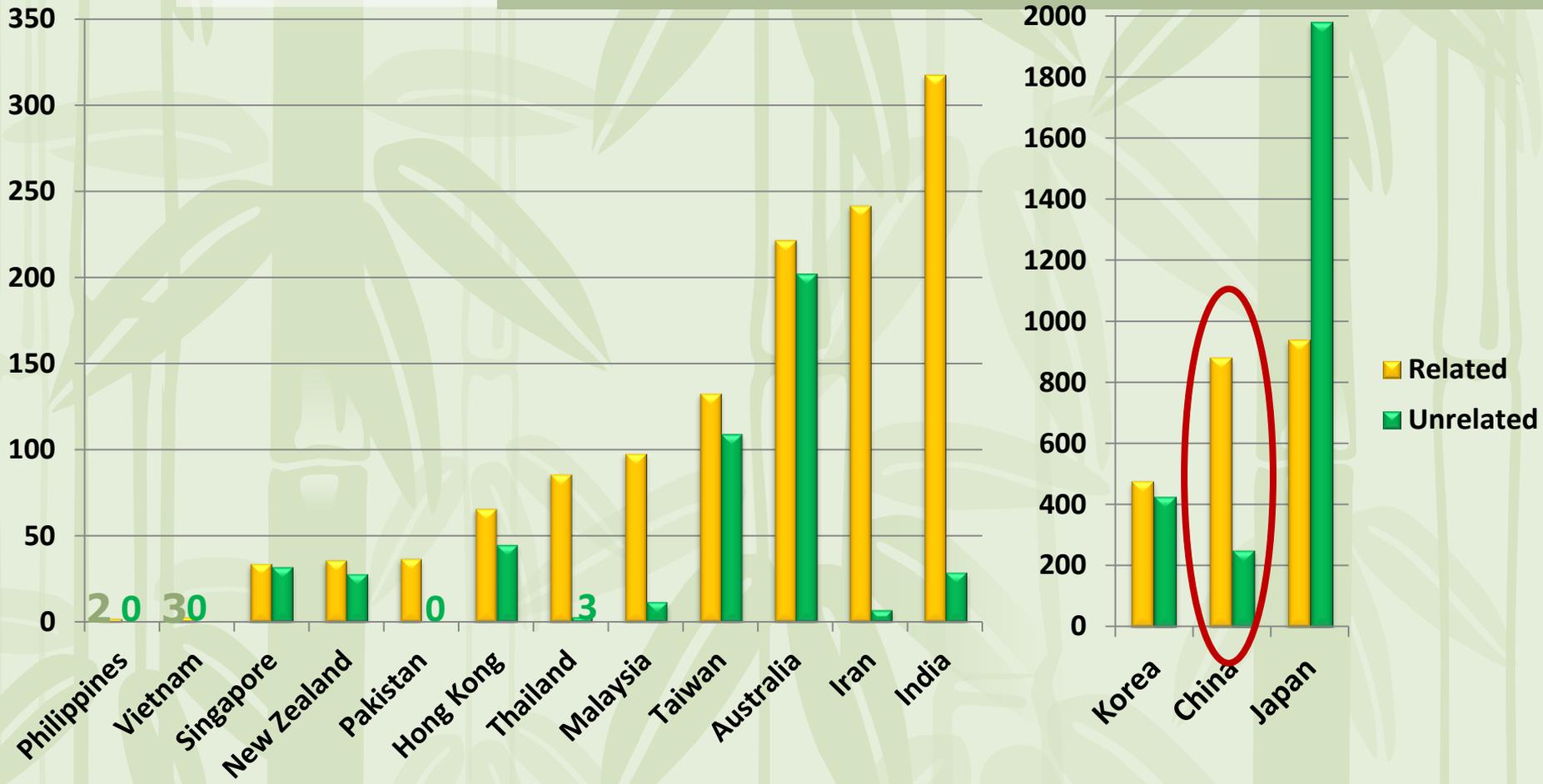
06/2007 update of a nationwide registry study 2000-2004



Chainese experience

- ❖ In China, despite of the presence of relatively large donor pool size of their adult donor bank, it is still short to cover their big population and the big genetic diversity. Also the “single child policy” makes it difficult to find out genetically HLA matched sibling donors. To solve these problems, they have intensively performed haplo transplants by using various regimens, resulting also well comparable results of HLA matched transplants (4).

Number of HSCT by country / region : Related vs Unrelated



Detailed information of mixture transplantation (1)

Type	Number
BM+PB	671
BM+CB	14
PB+CB	21
BM+PB+CB	3
Total	709

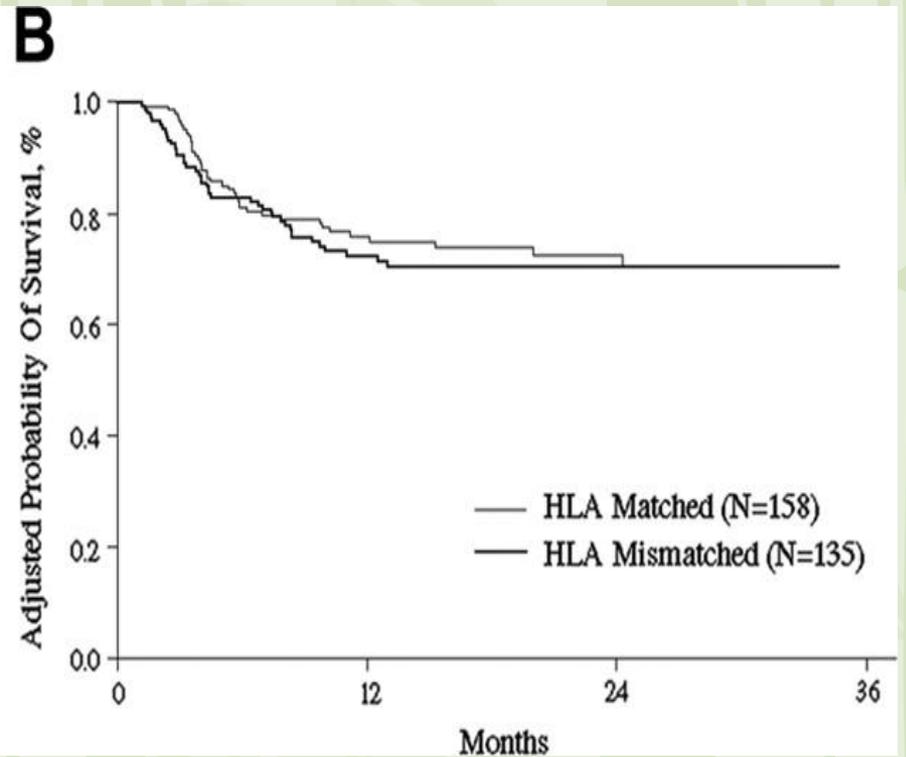
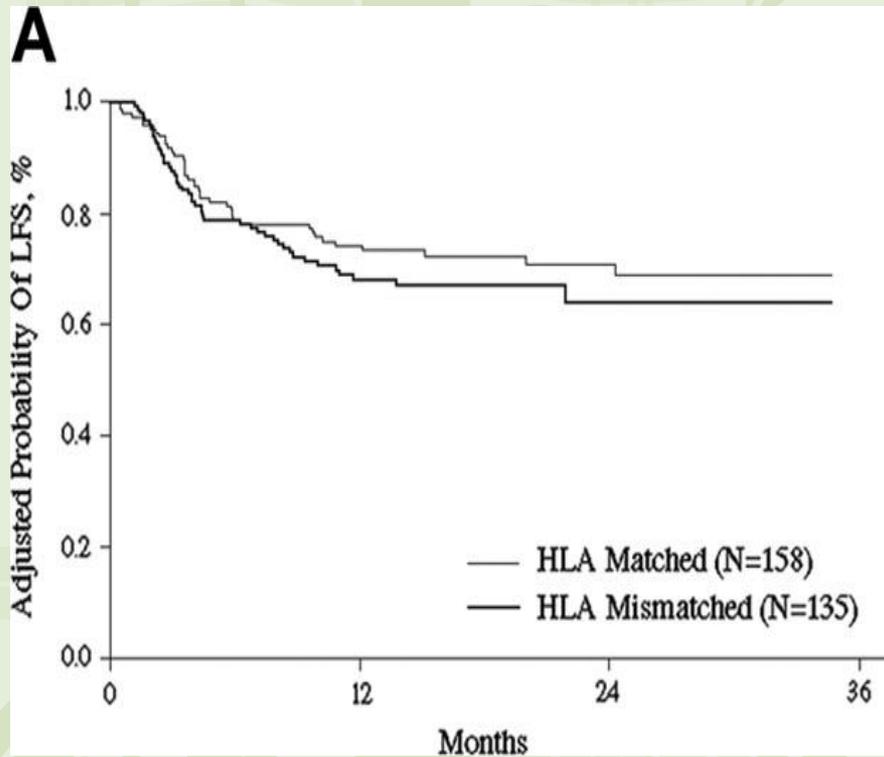
Country	Number
Australia	5
China	667
Hong Kong	0
India	7
Iran	0
Japan	13
Korea	10
Malaysia	-
New Zealand	1
Pakistan	4
Philippines	0
Singapore	1
Taiwan	1
Thailand	0
Vietnam	0
Total	709

Detailed information of mixture transplantation (2)

			Total HSCTs	No. of Mixture Transplants	% of Mixture Transplants
Allogeneic	Related	HLA - id sibling	2560	239	9.3
		non - id	985	384	39.0
		twin	29	2	6.9
	Unrelated		3127	13	0.4
Autologous			4377	22	0.5

Variable	HLA-identical sibling HCT	Related mismatched HCT	P
Donor-patient sex match, no. (%)			0.38
MM	54 (34)	37 (27)	
MF	30 (19)	21 (16)	
FM	54 (34)	55 (41)	
FF	20 (13)	22 (16)	
ABO match, no. (%)			0.12
Matched	85 (54)	68 (50)	
Minor mismatched	23 (15)	32 (24)	
Major mismatched	50 (32)	35 (26)	
Donor-patient relationship, no. (%)			—
Mother to child	0 (0)	60 (44)	
Father to child	0 (0)	21 (16)	
Child to parent	0 (0)	13 (10)	
Sibling	158 (100)	37 (27)	
Cousin	0 (0)	4 (3)	
Graft type, no. (%)			< .001
BM + PB	103 (65)	130 (96)	
BM alone	31 (20)	4 (3)	
PB alone	24 (15)	1 (1)	
G-CSF use after HCT, no. (%)	85 (54)	132 (98)	< .001

LFS and OS after transplantation.



Lu, D.P., et al, *Blood*. 2006; 107: 3065–3073

Summary

- ❖ These Asian experiences would encourage the promotion of haplo transplants in certain countries where stem cell banking system has not been established. **Nevertheless, it must be mentioned that these promising results were obtained by institutes which have enough experiences of HLA matched transplants. Because of that, quick training to experience the standard transplants is recommended before full operation of haplo transplant in emerging countries.**