

Peculiar conditions for implementation of a program of HSCT for AID in Brazil

- **Large experience with allogeneic BMT for hematological autoimmune diseases (aplastic anemia)**
- **Probably worse activity/prognosis of systemic AID due to poor economical and social conditions**
- **High prevalence of tropical autoimmune diseases (rheumatic fever and some forms of pemphigus)**
- **Difficult assess to new technologies (SC selection columns) and therapies (anti-TNF agents for RA)**
- **Universal coverage of health care but highly regulated**
- **Large availability of related HLA-identical donors**

Experience of Brazilian groups with BMT for severe aplastic anemia

- **Un. Federal do Paraná, Curitiba (R. Pasquini)-
≅ 400 cases**
 - ♦ **New conditioning regimen for young (<20 y old) hypertransfused (>15 U) patients (Blood 92: 135a, 1998)**
 - ♦ **Busulfan 3 mg/kg x4 plus Cyclophosphamide (120 mg/kg)**
 - ♦ **N= 43, LTS: 62%, 13 deaths: 4 pre-infec, 3 GVHD, 6 TRM**
 - ♦ **Late graft failure: 5/43 (12%), 2 received IS, 3 received 2nd BMT, all survived**
- **School of Medicine of Ribeirão Preto, Univ. of São Paulo**
 - ♦ **Total allo BMT: 152, 62 CML, 38 SAA (OS= 61%)**

Numbers and causes of death of SLE patients treated with immunosuppressive (IS) therapy (cyclophosphamide pulses) at the University Hospital of Ribeirão Preto- Brazil, from 1995 through 2000

Year	# of pts. on IS	# of deaths	% of deaths	CAUSES OF DEATHS (# of patients)		
				Infection	Disease Activity	Thrombosis
1995	64	7	10.9	2	3	2
1996	70	7	10.0	2	3	2
1997	82	10	12.2	2	4	4
1998	98	12	12.2	2	5	5
1999	112	13	11.6	2	7	4
2000	108	8	7.4	4	4	0
Mean	89	8.8	10.7	2.3	4.3	2.8

Search for HLA-identical donors among sibs of patients candidates to allogeneic BMT at the Immunogenetics Laboratory of the School of Medicine of Ribeirão Preto-Brazil

Year	# of families typed	Mean # of sibs in the family	# of families with at least 1 HLA-id donor	
			Observed	Expected*
1991	28	2,9	19	16
1992	52	2,1	32	24
1993	36	3,4	26	23
1994	50	3,8	32	23
1995	50	3,6	30	33
1996	60	3,6	34	39
1997	70	3,9	49	47
1998	64	2,7	47	35
1999	57	5,0	37	43
2000	70	4,0	48	48
Total	537	3,5 (mean)	354 (66%)	341 (63%)

* $N(1-0,75)^n$ N: number of families typed, n: number of sibs typed

OFFICIAL INDICATIONS FOR HSCT in BRAZIL

(Act No 1217, 13/Oct/99, Ministry of Health)

- **Non-experimental autologous HSCT (<60 y except MM)**
- **Related allogeneic BM transplantation (<55 y)**
- **Non-related allogeneic BM transplantation**
- **Allogeneic peripheral blood HSCT**
- **Cord blood transplantation**
- **OTHER INDICATIONS: For MDS, hereditary or ID diseases, doubtful cases or investigational protocols, approval is needed from a Technical Committee (SBTMO, M/H, INCA) and Institutional Review Board**



INTERNATIONAL WORKSHOP ON HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR AUTOIMMUNE DISEASES

Hotel Shelton Inn- Ribeirão Preto- SP
October 12-14, 2000

SCIENTIFIC COORDINATION: *Richard Burt - Chicago, USA*

Inscrições e reserva de hotel:
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PATROCÍNIOS:



Table 3. Pilot protocols (phases I/II) of hematopoietic stem cell transplantation* for systemic autoimmune diseases in Brazil- a national cooperative study

Disease	Inclusion criteria	Conditioning	Follow-up	References
SLE	Nephritis, vasculitis, cytopenias refractory to IS, catastrophic anti-phospholipid syndrome	CY 200 mg/kg + horse ATG 15 mg/kg x6	SLEDAI, immunorecovery, TRT	Traynor et al, 2000
MS	Progressive forms refractory to IFN & CE, EDSS 3.0-6.5	BEAM + ATG	EDSS, MRI, immunorecovery, TRT	Comi et al, 2000
SS	Duration of disease <4y, pulmonary disease refractory to CY	CY + FLU + ATG	Pulmonary function, CT scan, Rodney score, immunorecovery, TRT	White et al, 2000 Anderlini et al, 2000

HSCT for autoimmune diseases
Brazilian cooperative program
Centers involved*/interested in the study

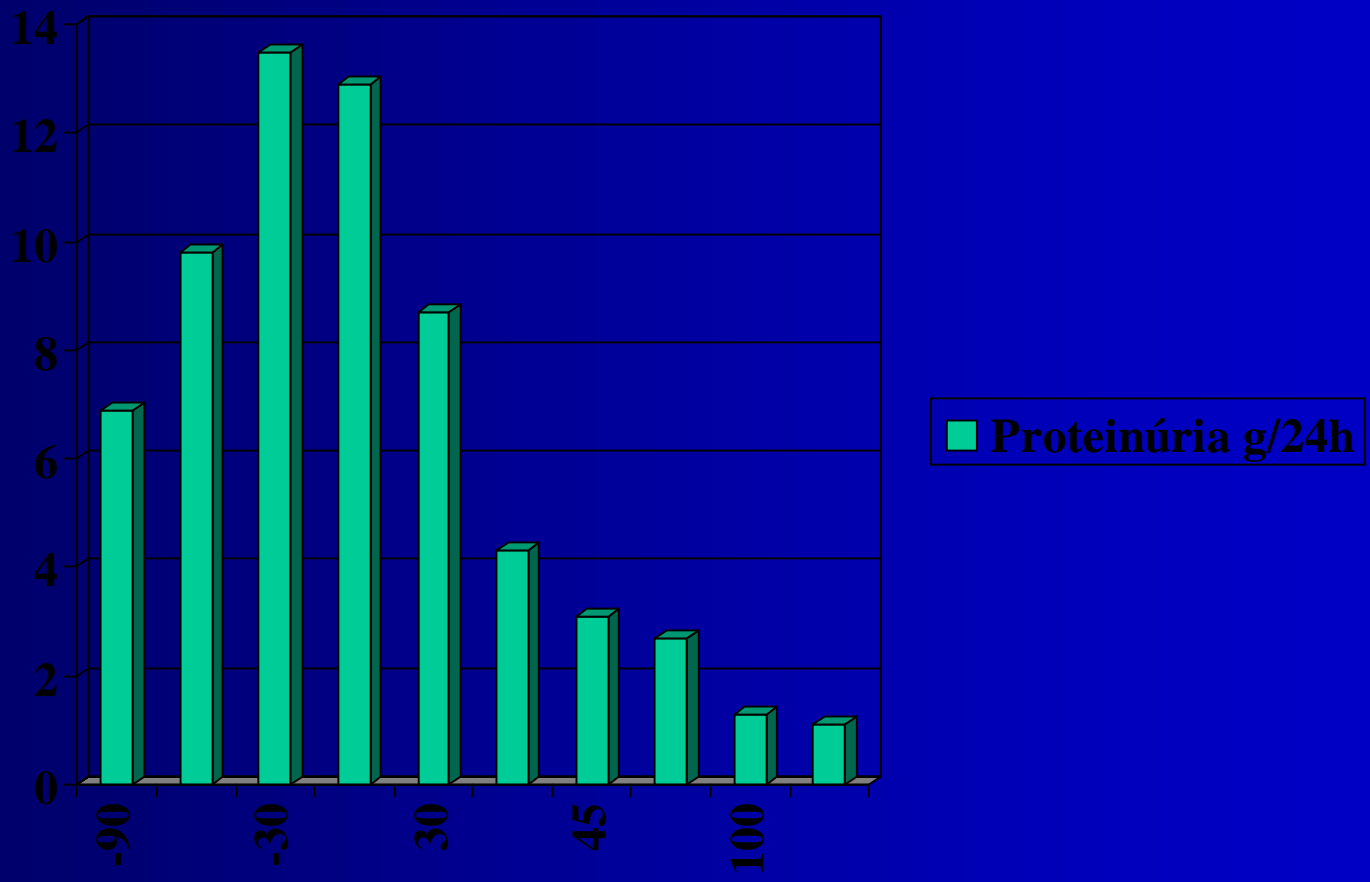
- **Hospital das Clínicas- Ribeirão Preto- SP (Coordination)***
- **Escola Paulista de Medicina- UF São Paulo**
- **Hospital dos Servidores Públicos de SP- São Paulo**
- **Hospital das Clínicas- University of Campinas- SP**
- **Hospital de Base- São José do Rio Preto- SP**
- **Hospital Israelita Albert Einstein- São Paulo***
- **Hospital de Clínicas- Porto Alegre-UFRGS**
- **Hospital São Lucas- Porto Alegre- PUCRGS**
- **Hospital da Universidade Federal da Bahia- Salvador- BA**
- **Hospital das Clínicas- Rio de Janeiro-UFRJ**

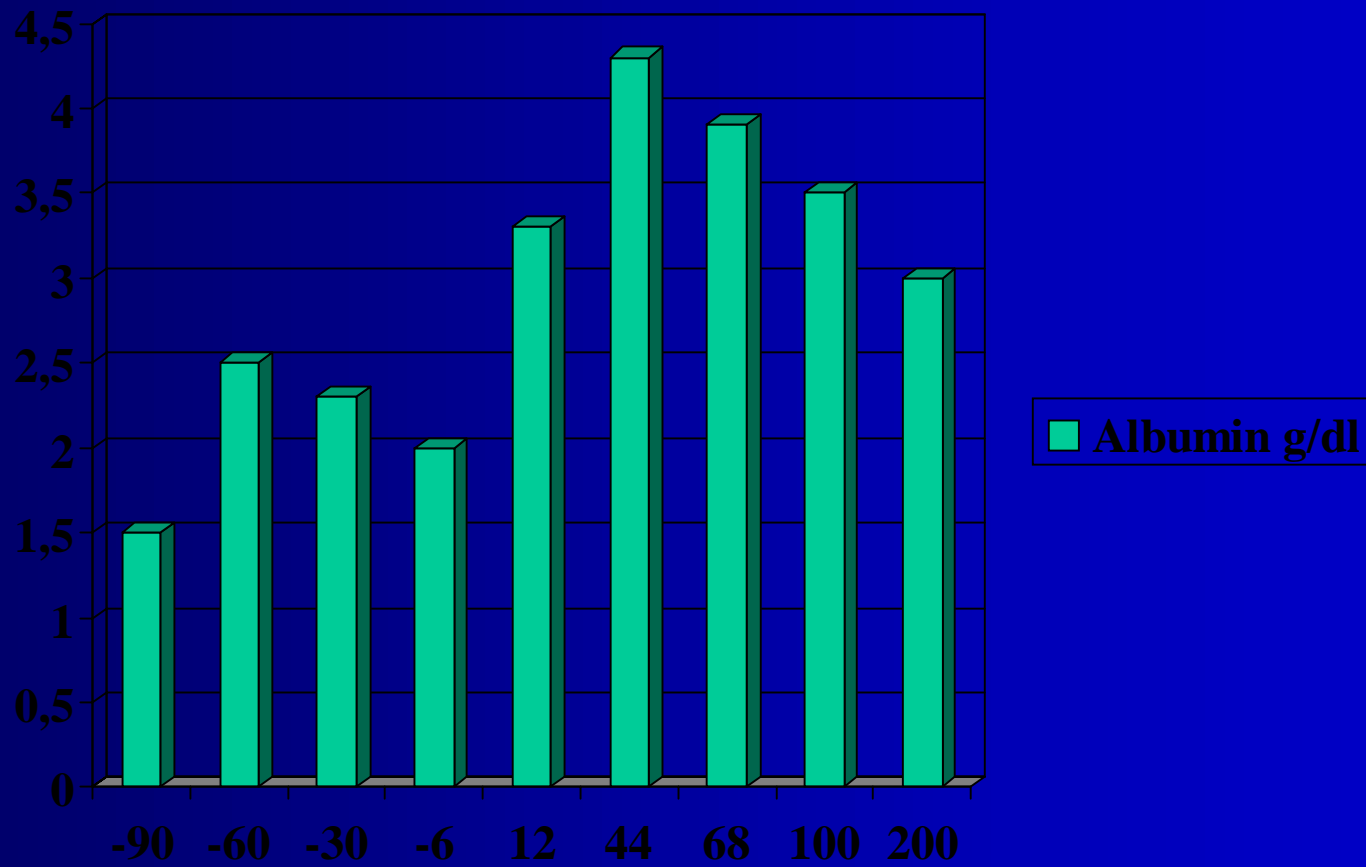
Brazilian cooperative program of HSCT for AID- First case (H. A. Einstein)-SP

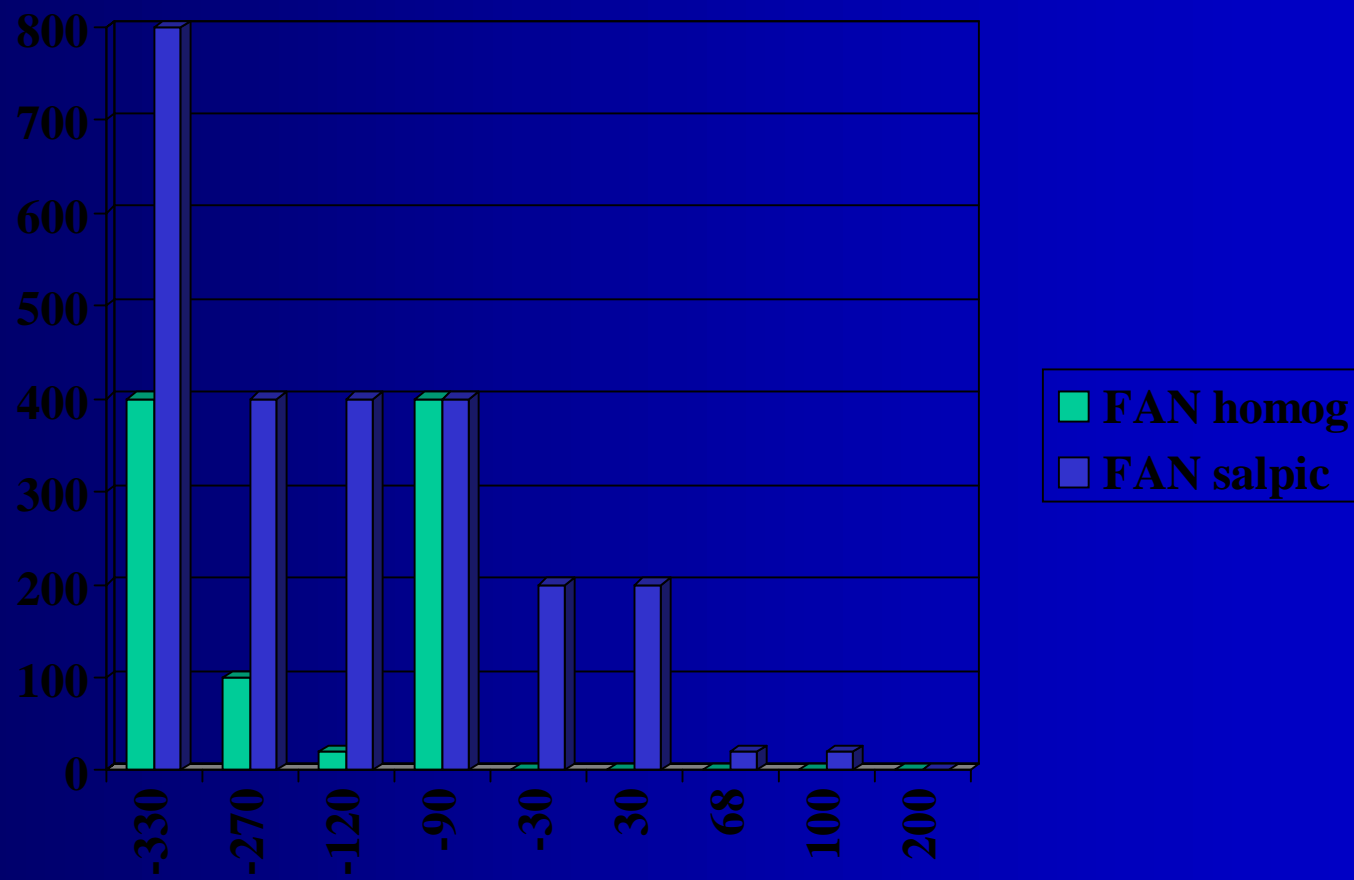
- **CSG, female, MS diagnosed in April/96**
- **Progressive relapsing form, treated w/ corticosteroids (low-dose & pulses) and β -IFN**
- **Six episodes of relapses in the 2 y previous to mobilization**
- **EDSS- 6.0, SNRS- 61, walking with assistance (walker)**
- **MRI: No gadolinium-enhancing lesions, but other criteria present**
- **Infusion (June/26/01): 8.9×10^6 CD34/kg**
- **Engraftment: Neutrophils: D+9, Platelets: D+8**
- **TRT: mucositis, neutropenic fever, edema, diarrhea. Discharged, on physical therapy, no more relapses, off steroids, $\uparrow\uparrow$ muscle strength.**

Brazilian cooperative program of HSCT for AID- 2nd case (Ribeirão Preto- USP)

- **RSS, 25 y-old, male, admitted in Oct/2000 with nephrotic syndrome (urinary protein- 6.4 g/24 h, serum albumin- 1.5, ANA 1:400/>1:800, anti-DNA: neg, low C3/C4, Cr 1.1 → 7.8**
- **Kidney biopsy: class IV GN, 12/24 activity, 0/12 chronicity**
- **Nov/2000: start pulses of CY/6/MP x7**
- **June/01: Urinary protein: 6.9 g/24 h, sAlb: 1.5, Cr: 1.1,**
- **ANA: 1:400, anti-DNA:+, low C, SLEDAI: 20**
- **Mobilization and collection (2 apheresis): 3.25×10^6 CD34/kg**
- **Complications: neutropenia, sinusitis and fluid overload**
- **Sept/01: CY 200 mg/m², ATG (horse, 30 mg/kg), cell infusion**
- **Complications: renal failure post-ATG, H/cystitis, pancytopenia, cardiac tamponade *Pseudomonas sensis* discharge on D+32**







Brazilian cooperative trial of HSCT for AID- 3rd case (Ribeirão Preto)

- 12 y old boy with 3y history of SLE + extensive skin and pulmonary SS refractory to 11 pulses of Cytoxan
- Pre-transplant evaluation: lupus nephritis VI + VI, 4/24 activity, 4/12 chronicity, lung & GI +, heart-
- 6.3 mi SC/kg mobilized w/ Cy 2 g/m² + G-CSF in 11/01
- Pericarditis in 12/01, controled w/ steroids
- After 1st dose of Cy (50 mg/kg) in 01/02, acute thoracic syndrome and pericardial effusion, conditioning stopped
- +48 h: repeated and severe seizures, cardiac arrest, death
- CNS NRM: vasculitis; kidney necropsy: nephrosclerosis

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMIZED TRIAL WITH HIGH DOSE CYCLOPHOSPHAMIDE

PATIENT SELECTION

Stem cell mobilization: cyclophosphamide 2g/m² + G-CSF 5 µg/Kg/d

Autologous HSCT

HD cytoxan

Cytoxan 200 mg/kg
+
selected
CD34⁺ autologous Tx

Freeze HSC for back-up Cytoxan
200mg/Kg

*Inject HSC if no
graft by day
+21*

SUPPORTIVE TREATMENT

CLINICAL & LABORATORY FOLLOW-UP

Brazilian cooperative program of HSCT for AID- Future randomized studies

- **Autologous x mini-allo**
- **Autologous unmanipulated x selected cells**
- **TBI or busulfan x standard conditioning**
- **Transplant x conventional therapies
(international protocols)**