IMPORTANCE OF THE TIMING OF CYCLOSPORINE INITIATION IN OKT3 TREATED CARDIAC TRANSPLANT PATIENTS

Maria Rosa Costanzo-Nordin, M.D., F.A.C.C., Maryl R. Johnson, M.D., F.A.C.C., E. Jeanne O'Sullivan, R.N., G. Martin Mullen, M.D., F.A.C.C., Diane Wallis, M.D., F.A.C.C., Roque Pifarre, M.D., Patrick J. Scanlon, M.D., F.A.C.C., John A. Robinson, M.D. Loyola University Medical Center, Maywood, IL.

To determine the importance of the timing of Cyclosporine initiation, we compared the 3 month postoperative course of OKT3 treated (5mg daily x 14 days) cardiac transplant pts who began Cyclosporine preoperatively (CY0), at 4(CY4) or at 11(CY11) days postoperatively. Day 4 was chosen as the earliest day so that stabilization of renal function would minimize Cyclosporine nephrotoxicity. Day 11 was chosen as the latest day to allow achievement of therapeutic Cyclosporine levels before OKT3 termination. Groups were similar in age, sex, type of heart disease, preformed antibodies, hemodynamic support, donor ischemic time and concomitant immunosuppression.

	Cy0(n=11)	Cy4(n=12)	Cy11(n=24)
1 month creatinine (mg/dl)	1.1±0.3	1.0±0.4	1.2±0.6
1 month LV ejection fraction	63±11%	48±6%	50±6%
Infections/pt/3 months	1.6±1.5	2.4±1.8	2.6±2.2
Rejections/pt/3 months	2.8±1.6	1.2±0.9*	2.4±1.6
First rejection (days)	25±20	42±31*	22±8
Deaths	1	2	4

(*P<0.05 Cy4 vs Cy0 and Cy11)

Conclusions: 1) In OKT3 treated pts, Cyclosporine initiation at day 4 provides superior immunosuppression compared to preoperative and day 11 drug initiation. 2) The temporal relationship of Cyclosporine initiation to allografting may affect rejection by producing differential effects on T-cell subsets.

IS AN INTRAVENOUS GLUCOCORTICOID PULSE BETTER THAN ORAL TAPER FOR ASYMPTOMATIC CARDIAC REJECTION? A RANDOMIZED TRIAL.

Jon A. Kobashigawa M.D. F.A.C.C., Lynne W. Stevenson M.D., F.A.C.C., Jaime D. Moriguchi M.D., Nobuyuki Kawata M.D., Amar S. Kapoor M.D., Payam Kamjoo, Lisa Leonard R.N., Roxella Fondrich R.N., Katherine Medkiff R.N. Gaia Magnani, Davis D. Drinkwater M.D., Hillel Laks M.D., F.A.C.C. UCLA School of Medicine, Los Angeles, CA

Intravenous solumedrol pulse therapy (IVS) is frequently given for severe rejection after cardiac transplantation but has not previously been compared to an oral prednisone pulse and taper (OPT) for asymptomatic rejection (RJ) in a randomized trial. For moderate rejection without clinical compromise occurring after initial discharge, 27 consecutive outpatients were randomized to return daily for 3 days of IVS 1000mg (12 pts) or to take OPT 100mg prednisone for 3 days tapering to the previous maintenance dose over 14 days (15 pts). Follow-up biopsies were read at 2 and 4 wks without knowledge of Rx, and infections during the next 3 months were compared for the 2 groups.

	RJ Resolution	Infection
IVS	11/12 (92%)	1/12 (8%)
OPT	13/15 (87%)	3/15 (20%)

OPB is as effective as IVP for resolution of asymptomatic RJ. Further study will be required to determine the relative complication rates. The higher cost and inconvenience of IVP may not be warranted for therapy of asymptomatic moderate RJ after cardiac transplantation.

IMPACT OF PROPHYLACTIC OKT3 ON MILD ACUTE REJECTION OF THE CARDIAC ALLOGRAFT

Tiong Cheat Yeoh, M.D., Hannah Valantine, M.D., Edward Stinson, M.D., Margaret Billingham, M.D., F.A.C.C. Stanford University Medical Center, Stanford, California

The course of mild acute rejection, lymphocytic infiltrate without myocyte necrosis in heart transplant (tx) recipients treated prophylactically with OKT3 is unknown. This study examines the progression of untreated mild rejection during 0-3 mos and 4-12 mos intervals after cardiac tx. The study population consisted of 123 pts, 67 who received prophylactic OKT3 and 56 treated conventionally with Cyclosporine, Azathioprine, and Prednisone (CAP).
During 0-3 mos, the average number of all histologic grades of rejection (mild, moderate, and severe) was less in the OKT3 grp (1.4 vs 2.0 episodes per pt, p<.001); but mild rejection was unchanged (.7 vs .8, p=ns). During the 4-12 mos interval, the average number was not significantly different between the two groups (1.4 and 1.6 per pt for all rejections and .8 vs .9 for mild rejections). Progression of mild episodes to moderate rejection during the two time intervals is compared for each grp using χ^2 tests.

	0-3 months		4-12 months		
	n	Progression to moderate	n	Progression to moderate	p
OKT3	32	14 (44%)	38	11 (29%)	ns
CAP	42	19 (45%)	46	9 (20%)	<.05

Conclusions: 1) OKT3 reduces the average number of rejection episodes during the first 3 months post tx but not that of mild rejection. 2) During 4-12 mos, the frequency of progression from mild rejection is decreased in CAP but not significantly changed in OKT3. These data suggest that in OKT3 treated pts, increased rejection surveillance is required following a mild rejection episode at 4-12 mos post-op.

Tuesday, March 20, 1990
8:30AM–10:00AM, Room 23
Ventricular Ectopy and Late Potentials

LONG-TERM SPONTANEOUS VARIABILITY OF VPD FREQUENCY IN POST-MI PATIENTS

Martin Green MD FACC, William Williams MD FACC, Richard Davies MD PhD FACC, Linda Warriner RN, Donald Beanlands MD FACC, David Salerno MD FACC, Morrison Hodges, MD FACC, and CAST Investigators.

The spontaneous long-term variability of ventricular premature depolarization (VPD) frequency was determined in 521 post-MI patients (pts) enrolled in the Cardiac Arrhythmia Suppression Trial (CAST). We compared the VPD frequency on 24 hr Holter at baseline (CAST qualification), to that following washout of encainide, flecainide or their respective placebos in the same pts. Only pts from CAST sites reporting washout Holters on at least 60% of eligible pts were included to minimize selection bias. The mean interval between baseline and washout Holters was 364 ± 188 days. The mean age was 60.3 ± 9.7 yrs, the mean EF 0.40 ± 0.05. Pts were divided into 2 groups by EF (≤ 0.40 or > 0.40) and VPD frequencies compared using a paired T-test on log(VPDs/hr + 1):

	VPD/hr (mean ± SD) Baseline	Washout	
EF ≤ 0.40 (n= 296)	120.3 ± 258.3	66.1 ± 133.9	p < 0.001
EF > 0.40 (n= 225)	113.3 ± 214.5	89.9 ± 191.2	p < 0.001

Furthermore at washout, 32.3% of pts would not have met CAST VPD qualification criteria (≥ 6 VPDs/hr), and 33.2% would have met CAST suppression criteria (80% VPD suppression, 90% VT suppression) on no therapy. We conclude that significant spontaneous VPD reduction occurs in many post-MI pts. This variability may have important implications to the evaluation of long-term antiarrhythmic therapy.