Evidence Table 1. Clinical islet transplantation: Patient and transplant characteristics reported in journal articles. All transplants are islet alone unless otherwise indicated.

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/pt	IEq/kg, average of all infusions/pt
University of Alberta	***Protocol: Edmonton immunosuppression[a]; Ricordi chamber islet isolation; +/- 2-layer perfluorocarbon organ storage; +/- islet culture***						
Owen, Ryan, O'Kelly, et al., 2003	34	26		Labile type 1 diabetes, hypoglycemia unawareness resulting in frequent or severe hypoglycemic reactions, or progressive complications (few)			~13,000 required for insulin independence
Ryan, Lakey, Paty, et al., 2002[b]	30	17	≤34	As above	1.8	1.8	
	17		Median 20	As above; 17 who completed transplant protocol, of 30	2.4	2.2	12,330
Paty, Ryan, Shapiro, et al., 2002	7			Subset of patients tested for hypoglycemic counterregulation and symptom recognition			
Johnson, Kotovych, Ryan, et al. (In press)	35			As for Owen, Ryan, O'Kelly, et al., 2003			

[a]Edmonton immunosuppression: Daclizumab; sirolimus; reduced-dose tacrolimus
[b]Includes patients reported by Shapiro, Lakey, Ryan, et al., 2000, and Ryan, Lakey, Rajotte, et al., 2001. Also includes information reported by Casey, Lakey, Ryan, et al., 2002.

Evidence Table 1. Clinical islet transplantation: Patient and transplant characteristics reported in journal articles. All transplants are islet alone unless otherwise indicated. (continued)

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/pt	IEq/kg, average of all infusions/pt
University of Minnesota	***Protocol: Immunosuppression with hOKT3gamma1 (Ala-Ala)/sirolimus/reduced-dose tacrolimus; 2-layer perfluorocarbon organ storage; Ricordi chamber islet isolation; islet culture; single-donor transplantation***						
Hering, Kandaswamy, Harmon, et al., 2004 (In press)	6	6	12	Type 1 diabetes ≥13 years; 5-100 severe episodes per year pretransplant of hypoglycemia unawareness associated with blood glucose <50 mg/dL and requiring the assistance of another person	1	1	10,302
University of Pennsylvania	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation; islet culture***						
Markmann, Deng, Huang 2003[c]	9	7	≤13	Type 1 diabetes ≥5 years; multiple episodes of dangerously severe hypoglycemic unawareness requiring hospitalization despite optimal medical management; C-peptide <0.5 ng/mL	1.7	1.4 (4 of 7 patients, 1 infusion)	8,204 (9,282 for successful single infusions)

[c]Includes results from 1 patient transplanted with islets isolated from a non-heart-beating donor pancreas, as reported by Markmann, Deng, Desai, et al., 2003.

Evidence Table 1. Clinical islet transplantation: Patient and transplant characteristics reported in journal articles. All transplants are islet alone unless otherwise indicated. (continued)

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/pt	IEq/kg, average of all infusions/pt
Baylor College of Medicine and University of Miami	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation***						
Goss, Schock, Brunicardi, et al., 2002	3	2	≤4	Severe recurrent hypoglycemia, coma, or metabolic instability and uncontrolled serum glucose despite maximal exogenous insulin therapy for at least 5 years	1.7	1.7	14,439
Goss, Soltes, Goodpastor, et al., 2003	8	7		As above		2.1	
NIH/NIDDK	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation***						
Hirshberg, Rother, Digon, et al., 2003	6	5	17-22	Type 1 diabetes of 13-50 years; severe, recurrent hypoglycemia events secondary to unawareness and requiring the assistance of others	1.7	1.7	≥10,000
Northwestern University	***Protocol: Edmonton immunosuppression***						
Kaufman, Baker, Chen, et al., 2002	1	1	4	Type 1 diabetes of 40 years with severe recurrent hypoglycemia resulting in multiple visits to the ER or resuscitation by others; successful kidney allograft		1	4,100

Evidence Table 2. Clinical islet transplantation: Outcomes reported in journal articles. All transplants are islet alone unless otherwise indicated.

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	#Pts insulin independent initially/ remaining	Change in Mean HbA1c (SD)		Hypoglycemic reactions	Comment	Complications
					Baseline, %	Current, %			
University of Alberta	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation; +/- 2-layer perfluorocarbon organ storage; +/- islet culture***								
Owen, Ryan, O'Kelly, et al., 2003	34	26		**26/__** **21 at 1 year** post-initial transplant					Serious in 6 of 68 (9%) procedures 2-portal vein thrombosis (hepatic hematoma requiring surgery in 1) 4-hemorrhage (3 transfused)
Ryan, Lakey, Paty, et al., 2002[a]	30	17	≤34	17/11	8.5 (0.49) patients who remained insulin independent	5.8 (0.13) insulin-independent patients	None in patients with C-peptide secretion		Acute: 2-transient bradycardia 5-hemorrhage 2-portal vein thrombosis No deaths, CMV, or PTLD
	17		Median 20	17/11 (**12 of 15 at 1 year** post-initial transplant; **4 of 6 at 2 years**)	8.2 (0.36) all 17 patients	6.08 (0.77) all 17 patients	None in patients with C-peptide secretion	6 pts required insulin at median 10.1 months: 3 are C-peptide-positive and on daily insulin dose 57% of pretransplant dose; 3 are C-peptide negative; urine protein unchanged in 15	From immunosuppression: 15-mouth ulcers 2-recurrent nausea/vomiting requiring rehydration 1-arthralgias 1-rheumatoid arthritis 10-diarrhea 8-anemia From diabetes: 3-retinopathy progression 2-increased serum creatinine 4-increased urine protein 10-increased BP 15-increased cholesterol

Note: Bolded outcomes are of key importance.

[a]Includes patients reported by Shapiro, Lakey, Ryan, et al., 2000, and Ryan, Lakey, Rajotte, et al., 2001. Also includes information reported by Casey, Lakey, Ryan, et al., 2002.

Evidence Table 2. Clinical islet transplantation: Outcomes reported in journal articles. All transplants are islet alone unless otherwise indicated (continued)

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	#Pts insulin independent initially/ remaining	Change in Mean HbA1c (SD)		Hypoglycemic reactions	Comment	Complications
					Baseline, %	Current, %			
University of Alberta (continued)	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation; +/- 2-layer perfluorocarbon organ storage; +/- islet culture***								
Paty, Ryan, Shapiro, et al., 2002	7						No improvement in hypoglycemic symptom recognition	Subset of patients tested for hypoglycemic counterregulation and symptom recognition	(not reported)
Johnson, Kotovych, Ryan, et al. (In press)	35							Fear of hypoglycemia significantly lower in transplant patients compared to transplant-eligible patients (n=46)	
University of Minnesota	***Protocol: Immunosuppression with hOKT3g1 (Ala-Ala)/sirolimus/reduced-dose tacrolimus; 2-layer perfluorocarbon organ storage; Ricordi chamber islet isolation; islet culture; single-donor transplantation***								
Hering, Kandaswamy, Harmon, et al., 2004 (In press)	6	6	12	**4/4 at 1 year post-transplant**	7.2 (1.0) patients who became insulin independent	5.4 (0.6) insulin-independent patients	None (all patients)	1 patient requires 60% of pretransplant insulin; 1 patient early transient reduction in insulin requirement	1 serious: nystatin-related generalized rash; Transient increased liver enzymes, 1 severe, 3 mild to moderate; Transient neutropenia, 3; OKT3-related: low-grade fever, chills, nausea, transient rash. Other, mild to moderate: mouth ulcers, weight loss. No PTLD or increased infections

Note: Bolded outcomes are of key importance.

Evidence Table 2. Clinical islet transplantation: Outcomes reported in journal articles. All transplants are islet alone unless otherwise indicated. (continued)

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	#Pts insulin independent initially/ remaining	Change in Mean HbA1c (SD)		Hypoglycemic reactions	Comment	Complications
					Baseline, %	Current, %			
University of Pennsylvania	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation; islet culture***								
Markmann, Deng, Huang, et al. 2003[b]	9	7	≤13	7/6 1 patient lost function at 8 mos.	7.6 patients who became insulin independent	6.3 insulin-independent patients at 6 mos.	None in insulin-independent patients	At 8 mos. 1 patient requires 50% of original insulin dose; C-peptide 0.5-1.0 ng/mL	None serious
Baylor College of Medicine and University of Miami	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation***								
Goss, Schock, Brunicardi, et al., 2002	3	3	≤4	3/3	9.0 (0.2)	5.8 (mean of 2 patients)	None (all patients)	Islets prepared at distant processing center (U. Miami) and transplanted at Baylor	No complications observed
Goss, Soltes, Goodpastor, et al., 2003	8	7							No sustained portal vein hypertension; no transfusions; no intraparenchymal or intra-abdominal hemorrhage; 71%-moderate abdominal pain 59%-nausea

Note: Bolded outcomes are of key importance.
[b]Includes results from 1 patient transplanted with islets isolated from a non-heart-beating donor pancreas, as reported by Markmann, Deng, Desai, et al., 2003.

Evidence Table 2. Clinical islet transplantation: Outcomes reported in journal articles. All transplants are islet alone unless otherwise indicated. (continued)

Transplant Center; Citation(s)	N	N completed protocol	Follow-up (mos.)	#Pts insulin independent initially/ remaining	Change in Mean HbA1c (SD)		Hypoglycemic reactions	Comment	Complications
					Baseline, %	Current, %			
NIH/NIDDK	***Protocol: Edmonton immunosuppression; Ricordi chamber islet isolation***								
Hirshberg, Rother, Digon, et al., 2003	6	5	17-22	4/2 **3 of 5 at 1 year after second transplant**	8.2 (1.2)	6.0 (0.6) at 1 year	None (all patients)	2 patients who stopped immunosuppression due to adverse events have residual C-peptide production; 3rd patient discontinued when all islet function lost	*Transplantation-related:* 1-portal vein thrombosis, precluded 2nd transplant; 1-intra-abdominal bleeding requiring 4 units *Immunosuppression-related:* All-oral ulcers, diarrhea, leg edema, fatigue, declining over time; 2-transient severe neutropenia treated with G-CSF; 0-CMV 1-Pitisporidium skin infection; 1-recurrent UTI 1-interstitial pneumonitis requiring discontinuation of immunosuppression 1-intolerable fatigue, and renal dysfunction, patient elected to discontinue immunosuppression
Northwestern University	***Protocol: Edmonton immunosuppression***								
Kaufman, Baker, Chen, et al., 2002	1	1	4	1/1	6.9	5.3	No clinically relevant hypoglycemia episodes	Renal allograft function unchanged	(not reported)

Note: Bolded outcomes are of key importance.

norepinephrine, and cortisol, as well as symptom recognition, improved in islet transplanted patients. In contrast, glucagon responses to hypoglycemia and symptom recognition reportedly were fully restored and maintained long-term in whole pancreas transplant patients (Kendall, Rooney, Smets, et al., 1997; Paty, Lanz, Kendall, et al., 2001).

Evidence Table 3. Types of metabolic testing reported by transplant centers.

	Hirshberg, Rother, Digon, et al., 2003	Kaufman, Baker, Chen, et al., 2002	Goss, Schock, Brunicardi, et al., 2002	Markmann, Deng, Huang, et al. 2003	Hering, Kandaswamy, Harmon, et al., 2004 (in press)	Ryan, Lakey, Paty, et al., 2002
N	6	1	1–3	7	4–5	17
IV arginine-stimulated C-peptide	X				X	X
Oral glucose stimulated C-peptide		X				
Oral glucose stimulated plasma glucose					x	X descriptive
Mean amplitude of glycemic excursions, pre- vs. post-treatment			X			X
Mixed meal stimulation, glucose levels			X 1 of 3 patients, descriptive	X descriptive		X
Mixed meal stimulation, C-peptide levels				X descriptive		X
IVGTT: • Acute insulin response to glucose						X
• Glucose disposal						X descriptive
• AUC for insulin						X
• AUC for C-peptide						X descriptive
• Homeostasis model assessment of insulin sensitivity						X descriptive

Quality of Life

No general measures of pre- versus post-islet transplant quality of life have been published; only one publication reports limited data on specific measures. Johnson, Kotovych, Ryan, and co-workers (In press) summarized results of patients in the University of Alberta series who completed the Hypoglycemia Fear Survey (HFS) and other quality of life indices at baseline (pretransplant), between the first and second islet infusions, at 1, 3, 6, and 12 months, and annually thereafter. Forty-six patients completed baseline surveys and 35 transplanted patients completed additional surveys. Results of the last survey for each transplant patient were compared to baseline results. Transplant patients had slightly lower fear of hypoglycemia by HFS at 1 month than pretransplant patients (Evidence Table 4) but a much larger reduction by

month 3. Overall, HFS in pretransplant patients was significantly higher than for post-transplant patients at a median followup of 11.9 months ($p < 0.0001$).

The authors note that these data are limited by the small sample size and their cross-sectional nature. They represent the beginning of longitudinal data collection on a growing population of patients. As presented at the Annenberg Second Annual Symposium (Johnson, 2002), Johnson and colleagues are collecting data from both general and disease-specific quality of life instruments for eventual analysis of quality of life trends over time.

Evidence Table 4. Results of Hypoglycemia Fear Survey post-islet transplant compared to baseline.

	Pretransplant	1 month	3 months	Median 11.9 months
Median Hypoglycemia Fear Survey score	47	30	6.5	5

Long-Term Diabetic Complications

Only Ryan, Lakey, Paty, and colleagues (2002) reported on long-term diabetic complications. Of 17 subjects who had completed the transplant protocol at the time of this publication and were followed for 3 years or less, three patients had progression of their retinopathy requiring laser photocoagulation. Nine patients either started or increased antihypertensive therapy. Cholesterol rose in 15 patients and in 11 required statin therapy. There were no major changes in neuropathy. Serum creatinine and urine protein did not change significantly except for two patients with pre-existing renal impairment who suffered serious deterioration in renal function; both patients' renal dysfunction was stabilized by withdrawing potentially nephrotoxic tacrolimus.

Adverse Events

Portal vein hypertension, thrombosis and hemorrhage. One center reported branched portal vein thrombosis (main portal veins remained patent in all patients) in two of 34 transplanted patients (Ryan, Lakey, Paty, et al., 2002; Casey, Lakey, Ryan, et al., 2002; Owen, Ryan, O'Kelly, et al., 2003). One of these patients also developed a hepatic hematoma requiring surgery, but without other long-term consequences. Four additional patients transplanted early in this series experienced hemorrhage from percutaneous portal vein access (Ryan, Lakey, Paty, et al., 2002). Of six patients described in the initial experience at the U. S. National Institutes of Health (NIH) between December, 2000 and June, 2001, symptomatic portal vein thrombosis occurred in one and intra-abdominal hemorrhage requiring transfusion occurred in another (Hirshberg, Rother, Digon, et al., 2003). Various measures have been adopted to minimize risks of these complications (Goss, Soltes, Goodpastor, et al., 2003; Owen, Ryan, O'Kelly, et al., 2003; Baidal, Froud, Ferreira, et al., 2003; Froud, Yrizarry, Alejandro, et al., [In press]). Four other groups did not encounter portal vein thrombosis or hemorrhage among 24 transplanted patients (Evidence Table 2; Hering, Kandaswamy, Harmon, et al., 2004 [In press]; Markmann, Deng, Huang, et al., 2003; Goss, Soltes, Goodpastor, et al., 2003; Kaufman, Baker, Chen, et al., 2002).

Nearly all of 26 patients evaluated for pressure changes during the procedure experienced transient moderate increases of portal venous pressure that correlated with the volume and number of islets transfused (Casey, Lakey, Ryan, et al., 2002). However, only one of the two

Evidence Table 5. Clinical islet transplantation: Patient and transplant characteristics reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003.

Study	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/ pt	IEq/kg, average of all infusions/pt
Islet-alone transplantation, combined results from multicenter trials							
Shapiro, Hering, Ricordi, et al., 2003 (ATC #3) Multicenter ITN trial	32	17		Metabolic lability, severe recurrent hypoglycemia, or progressive complications	1.5		
Shapiro, 2003 1st Islet Transplant Congress Combined data from U Alberta, U MN, U Miami	75	75	12–36	Metabolic lability, severe recurrent hypoglycemia			
Islet-alone transplantation, single-center reports							
Shapiro, Lakey, Paty, et al., 2003 (ADA #284-OR) U Alberta	48	30	≤36	Type 1 diabetes mellitus			
Shapiro, 2003 1st Islet Transplant Congress Data from U Alberta only	59		≤48				

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Study	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/ pt	IEq/kg, average of all infusions/pt
Islet-alone transplantation, single-center reports (continued)							
Goss, Brunicardi, Feliciano, et al., 2003 (IPITA #011) Baylor College	9	5	mean 6	Type 1 diabetes mellitus w/ history of severe hypoglycemia and metabolic instability	2	2	>10,000
Alejandro, Ferreira, Froud, et al., 2003 (ATC #568)	15	13	<18	Type 1 diabetes mellitus		1.8	13,667
Alejandro 2003 1st Islet Transplant Congress U Miami	16	16		Type 1 diabetes mellitus	2 + 5 supplemental in 5 patients	2 + 5 supplemental in 5 patients	13,007 for 1st+ 2nd infusions; 8,713 for 3rd
Hering, Kandaswamy, Parkey, et al., (submitted for ATC 2004) U Minnesota	20	20	Mean 23 (2-40)	Type 1 diabetes mellitus with hypoglycemic unawareness	18 single donor; 2, 2 donors	18-1 2-2	8,300 for single-donor recipients

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Study	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/ pt	IEq/kg, average of all infusions/pt
Islet-alone transplantation, single-center reports (continued)							
Zavala, Hanaway, Peddi, et al., 2003 (ATC #1452) U Cincinnati	6		3	Type 1 diabetes mellitus with hypoglycemic unawareness	1	1	
Maffi, Bertuzzi, De Taddeo, et al., 2003 (IPITA #063) San Raffaele Scientific Institute, Milan	10		18	Type 1 diabetes mellitus, "brittle," with hypoglycemia unawareness and chronic complications		1.7	5,200/ infusion
Larsen, 2003 1st Islet Transplant Congress Emory U	4	3	1-9	Type 1 diabetes mellitus >5 years with hypoglycemic unawareness	2 (n=2) 1 (n=1) 1 awaiting 2nd transplant	2 (n=2) 1 (n=1)	12,100 for completed protocols

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Study	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/ pt	IEq/kg, average of all infusions/pt
Islet and kidney transplantation							
Berney, Bucher, Mathe, et al. 2003b (ATC #401) Berney, Bucher, Mathe, et al. 2003a (IPITA #014) U Geneva	4 2 1		3	islet alone islet-kidney islet after kidney			≥5,000/infusion
	5 2 3			islet alone islet-kidney islet after kidney			
Berney, Bucher, Kessler, et al., 2003 (IPITA #013) GRAGIL IB Multicenter trial	9	7	3-12	Type 1 diabetes mellitus with prior kidney transplant; tapered off corticosteroids			target 10,000+
Froud, Ferreira, Hafiz, et al., 2003 (IPITA #061) U Miami	3		0.5-4.5	islet after kidney	1	1	8,511

Evidence Table 5. Clinical islet transplantation: Patient and transplant characteristics reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003. (continued)

Study	N	N completed protocol	Follow-up (mos.)	Patient description	Donor organs/pt	Infusions/ pt	IEq/kg, average of all infusions/pt
Islet and kidney transplantation (continued)							
Lehmann, Weber, Zuellig, et al., 2003 (ADA #285-OR) U Hosp Zurich	8	6	mean 15	Type 1 diabetes mellitus of 40 +/- 9-year duration; Islet-kidney transplant			
Cagliero, 2003 1st Islet Transplant Congress Harvard-Mass Gen	5 5	5 3	3-23	Islet after kidney Islet alone	~2 (1-IAK,1 donor; 2-IAK, 3 donors)	~2 (1-1 infusion, 2-3 infusions)	mean 13-14,000 (mean 19,546 for 3 combined infusions, n=2)

Evidence Table 6. Clinical islet transplantation: Outcomes reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003.

Study	N	N completed protocol	Follow -up (mos.)	#Pts insulin independent initially/ remaining	HbA1c, most current (%)	Hypo-glycemic reactions	#Pts withdrawn	Comment	Complications
Islet-alone transplantation, combined results from multicenter trials									
Shapiro, Hering, Ricordi, et al. 2003 (ATC #3) Multicenter ITN trial	32	17	?	__/14 of 17 completing protocol			2	30 of 32 (94%) C-peptide positive UPDATE: after median 9.4 mos., 52% insulin-free[a]	15-severe adverse event 4-hemorrhage 2- severe neutropenia 40%-statin therapy for new-onset hypercholesterolemia
Shapiro, 2003 1st Islet Transplant Congress Combined data from U Alberta, U MN, U Miami	75	75	12-36	__/64 of 75 (85%) at 1 year	6.1 1yr n=34 6.2 2yr n=18 6.5 3yr n=10			All patients receiving cultured cells; ~same protocols for all; 99% demonstrated primary function; 96% C-peptide positive at 1 year	3 left branch thrombus (U Alberta); 0 main portal thrombosis; 0 deaths; 0 cancer, PTLD; 0 CMV, EBV
Islet-alone transplantation, single-center reports									
Shapiro, Lakey, Paty, et al., 2003 (ADA #284-OR)	48	?	≤36	1 year-84% (30 pts with 1+ year data) 2 year-64% (15 pts with 2+ year data) by Kaplan-Meier analysis	6 in insulin-indep pts			4 patients became C-peptide negative due to recurrent autoimmunity, rejection, or islet exhaustion	0-deaths, malignancy, PTLD or CMV 11% liver bleeds w/ transfusion 2% hemobilia 5% severe neutropenia 2% portal thrombosis

[a]Ault, 2003

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Study	N	N completed protocol	Follow -up (mos.)	#Pts insulin independent initially/ remaining	HbA1c, most current (%)	Hypo-glycemic reactions	#Pts withdrawn	Comment	Complications
Islet-alone transplantation, single-center reports (continued)									
Shapiro, 2003 1st Islet Transplant Congress Data from U Alberta only	59		≤48	1 year-90% cultured islets, 95% non-cultured; 2 year-79% cultured islets; 4 year-2 of 3; all by Kaplan-Meier analysis				88% C-peptide positive, 16-48 months liver bleeds early, preventable complication; protocols have been modified to avoid	14% liver bleeds 5% gallbladder problem 2% hemobilia 3% severe neutropenia 3% pneumonia 3% ileal ulcer 2% sensitization various mild to moderate adverse events of immunosuppression in 23-87% of patients
Alejandro, Ferreira, Froud, et al., 2003 (ATC #568)	15	13	≤18	13/8	6 (all pts)	None in insulin-independent pts		69% of initially insulin-free pts remained so at 1 year; pts on insulin (31%) still had significant islet function	(Not reported)
Alejandro 2003 1st Islet Transplant Congress U Miami	16	16		14/10; 1 year: 80%				5 required supplemental 3rd infusion at 1 yr or later; of these, 3 are insulin indep	1-severe gastroparesis 1-parvovirus both discontinued immunosuppression 1-tacrolimus toxicity, changed to MMF
Goss, Brunicardi, Feliciano, et al., 2003 (IPITA #011) Baylor College	9	5	mean 6	5/5	Normal (all pts)	None (all pts)		4 awaiting 2nd tx reduced insulin by >75%	no technical complications from procedure or unexpected adverse effects from immunosuppression

Evidence Table 6. Clinical islet transplantation: Outcomes reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003. (continued)

Study	N	N completed protocol	Follow -up (mos.)	#Pts insulin independent initially/ remaining	HbA1c, most current (%)	Hypo-glycemic reactions	#Pts withdrawn	Comment	Complications
Islet-alone transplantation, single-center reports (continued)									
Hering, Kandaswamy, Parkey, et al. (submitted for ATC 2004) U Minnesota	20	20	Mean 23 (2-40)	1 year: 85% of 20 of 18 single donor recipients, 16 initially insulin independent; 11 >1 year	of 11 insulin-indep: 1 yr-5.5 2 yr-5.1 (n=7) 3 yr-5.5 (n=3)			Recipients participated in 4 pilot clinical trials	Of 20: 0-portal vein thrombosis 0-bleeding 0-opportunistic infections 0-malignancies 7-severe transient neutropenia 1-transient anemia 1-acute cholecystitis
Zavala, Hanaway, Peddi, et al., 2003 (ATC #1452) U Cincinnati	6	1	3	1/1		None in insulin-independent pts; improvement with 50% insulin reduction		3-50% insulin reduction 2-25% insulin reduction	1-portal vein thrombosis and later re-admission for rectal ulcer
Maffi, Bertuzzi, De Taddeo, et al., 2003 (IPITA #063) San Raffaele Scientific Institute, Milan	10		18	_/5	6.8 at 1 year (all pts)			8 pts reduced insulin by >50%; 3 pts lost islet function by 3 mos.	1-portal thrombosis 2-deteriorating renal function 10-mouth ulceration 6-acne-like lesions controlled by decreased sirolimus dose no hypertension, dyslipidemia or severe neutropenia/leukopenia

Evidence Table 6. Clinical islet transplantation: Outcomes reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003. (continued)

Study	N	N completed protocol	Follow -up (mos.)	#Pts insulin independent initially/ remaining	HbA1c, most current (%)	Hypo-glycemic reactions	#Pts withdrawn	Comment	Complications
Islet-alone transplantation, single-center reports (continued)									
Larsen, 2003 1st Islet Transplant Congress Emory U	4	3	1-9	3/2				1 pt resumed insulin meal boluses at 9 weeks, awaiting 3rd transplant; Edmonton immunosuppression	of 4: 3-mild anemia 3-grade I-II leukopenia mild ulcers, diarrhea, elevated LFT common
Islet and kidney transplantation									
Berney, Bucher, Mathe, et al. 2003b (ATC #401)	4 2 1		3	_/5	6.3 (?all pts)			All pts C-peptide positive; pts received 2nd infusion if not insulin-independent by 3 mos.; 1 pt scheduled for a third infusion	1-died 2° to OKT3 2-acute rejection episodes 1-bleeding after portal access 1-acute pyelonephritis 1-severe tubulopathy 3-mouth ulcerations 6-dyslipidemia, statin therapy
Berney, Bucher, Mathe, et al. 2003a (IPITA #014) U Geneva	5 2 3			_/6					1-died 2° to OKT3 2-acute rejection episodes 2-bleeding after portal access 1-severe tubulopathy 6-mouth ulcerations 8-dyslipidemia 7- leukopenia

Evidence Table 6. Clinical islet transplantation: Outcomes reported in meeting abstracts from the American Transplant Congress (ATC), June, 2003; the 63rd Scientific Sessions of the American Diabetes Association (ADA), June, 2003; and the 9th Congress of the International Pancreas and Islet Transplant Association (IPITA), July, 2003 and the 1st Islet Transplant Congress, November, 2003. (continued)

Study	N	N completed protocol	Follow -up (mos.)	#Pts insulin independent initially/ remaining	HbA1c, most current (%)	Hypo-glycemic reactions	#Pts withdrawn	Comment	Complications
Islet and kidney transplantation									
Berney, Bucher, Kessler, et al., 2003 (IPITA #013) GRAGIL IB trial	9	7	3-12	6/1				4 retain graft function; 3 lost graft function; no corticosteroids, but not Edmonton protocol; islets shipped	1 death: severe pneumonopathy 1-intraperitoneal hemorrhage 1-partial, reversible portal thrombosis 1-severe mouth ulcerations
Froud, Ferreira, Hafiz, et al., 2003 (IPITA #061) U Miami	3		0.5-4.5	1/1[b]	5 (1 pt)			85% mean insulin reduction; mild deterioration in renal function	mild deterioration of renal function in all patients (0.13 mg/dL mean elevation of serum creatinine)
Lehmann, Weber, Zuellig, et al., 2003 (ADA #285-OR) U Hospital Zurich	8	6	mean 15	5/5	5.8 (n=8)			treated with continuous subcutaneous insulin infusion initial 2 mos.	1 kidney rejection resolved with reinstitution of immunosuppression rejection rate no different than for SPK
Cagliero, 2003 1st Islet Transplant Congress Harvard-Mass Gen	5 5	5 3	3-23	3 IAK insulin independent 1 IA insulin independent	6.8 (n=8)		1 graft failure	2-IAK, 25-30% of pretransplant insulin, awaiting 3rd transplant; 1-IA weaning off insulin after 3rd transplant	

[b] In presentation, information updated to 3 of 3 completing protocol were insulin independent, one with a single donor (Alejandro R, personal communication).

Evidence Table 7. 2nd Annenberg Islet Symposium: Transplant Center Results as of December, 2002.

Center	#Infusions	#Patients	#Completed	#Insulin-free by 3 mos., 1 infusion	#Insulin-free by 3 mos., 2 infusions	#Using insulin but free of hypoglycemia and with normal HbA1c 1 infusion	#Using insulin but free of hypoglycemia and with normal HbA1c 2 infusions
Boston	9	6	4	1	4	3	0
Cincinnati	6	6	1	1		4	0
Edmonton	85	43	33	4	28	26	15
Geneva	28	16	12	1	8	1	3
Houston	16	7	5	3	0	0	0
London	3	1	0	0	0	0	1
Memphis	6	3	3	1	2	2	1
Miami	35	21	17	1	12	0	4
Minneapolis	19	18	16	15	1	1	0
NIH	10	6	6		3		2
Philadelphia	12	9	7	5	2	0	0
Seattle	8	6	0	0	0	2	1
St. Louis	12	7	4	0	2	0	0
Uppsala	14	6	5	0	3	0	3
Total	**263**	**155**	**113**	**32**	**65**	**39**	**30**