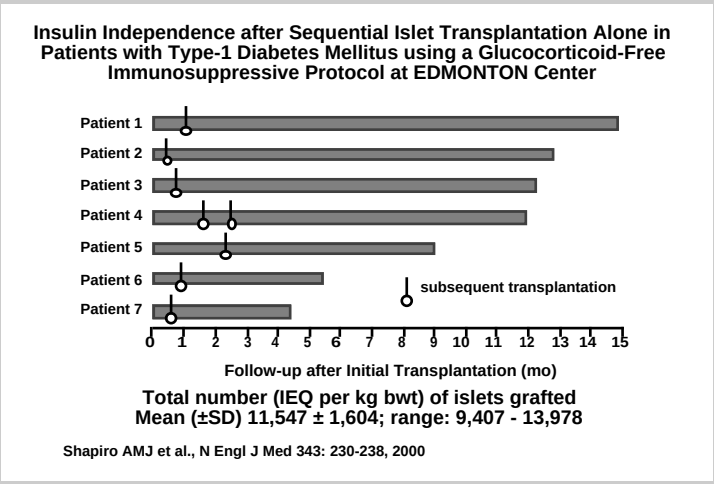
INTERNATIONAL ISLET TRANSPLANT REGISTRY



In a recent milestone achievement, insulin independence and restoration of normoglycemia was established by islet transplantation in seven patients receiving a high islet mass in combination with a novel glucocorticoid-free immunosuppressive regimen. The functional success of this trial is unprecedented in the history of clinical islet transplantation, and impressively confirms, that islet transplantation is a safe and effective strategy for beta cell replacement without additional risks associated with general anesthesia and surgical procedures.

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Third Medical Department
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Announcements

Major breakthrough in clinical islet transplantation introduced by the Edmonton Islet Transplant Center !

In a recent effort reported by the colleagues from the University of Alberta, Edmonton, Canada, islet transplantation led to insulin independence and normal glucose metabolism in seven out of seven consecutive patients with type-1 diabetes mellitus (Shapiro AMJ, Lakey JRT, Ryan EA, Korbutt GS, Toth E, Warnock GL, Kneteman NM, and Rajotte RV: Islet Transplantation in Seven Patients with Type 1 Diabetes Mellitus using a Glucocorticoid-free Immunosuppressive Regimen, New England Journal of Medicine, 343: 230-238, 2000). In this clinical series, recipients without end-stage renal disease received islet grafts alone with no previous or simultaneous transplantation of kidney or other organs. Selection of recipients was based on recurrent severe hypoglycemia or metabolic instability, that did not respond to treatment with exogenous insulin. Key innovations comprised the use of an immunosuppressive regimen combining daclizumab (anti-IL-2 receptor monoclonal antibody), sirolimus and tacrolimus without corticosteroid therapy. In addition, cold ischemia time was kept short, islets were grafted freshly (without incubation in suspension culture), and mass of transplanted islets exceeded 9000 islet equivalents (standardized to the volume of an islet 150 µm in diameter) per kilogram body weight of the recipient. In order to reach this mass, islets were isolated from two (in one case from 4) donor pancreata and transplantated sequentially. Remarkably, the majority of the recipients were discharged from the hospital within 24 hours after islet transplantation. In a subsequent report, these impressive results were confirmed by the Edmonton group with eleven out of twelve consecutive recipients reaching insulin independence, and nine of these patients remaining off-insulin within a follow-up period up to twenty months after islet transplantation (Ryan EA, Lakey RT, Rajotte RV, Korbutt GS, Kin T, Imes S, Rabinovitch A, Elliot JF, Bigam D, Kneteman NM, Warnock GL, Larsen I, and Shapiro AMJ: Clinical Outcomes and Insulin Secretion after Islet Transplantation with the Edmonton Protocol, Diabetes 50: 710-719, 2001).

These clinical data demonstrate for the first time in the history of islet transplantation, that persistant islet function and insulin-independence rates can be reached equivalent to results previously only observed in transplantation of vascularized pancreas. The notion, that immediate and persistent islet function can be drastically improved by increase of viable islet mass and selection of an immunosuppressive regimen protecting from allo- and autoimmune reaction (particularly in light of still lacking markers for islet graft rejection) and less toxic to the islet graft is now impressively confirmed.

As direct consequence of these milestone improvements, the Immune Tolerance Network has implemented a multi-center trial in order to confirm and extend these results at seven North-American and three European Clinical Islet Transplant Centers. For this trial, major efforts are underway in the attempts to standardize procedures of islet isolation and transplantation, and to implement cell processing standards in accordance with clinical good manufacturing practice.

Moreover, substantial amounts of work will be required by the worldwide Islet Transplant Centers in order to adopt the novel immunosuppressive regimen for islet recipients with previous or simultaneous transplantation of kidney or other solid organ. In view of the shortage of available donor organs, further attempts are necessary to both enhance isolation efficacy from single pancreas and to continue exploration of alternative beta cell sources.

Finally, further enhancements to the internet web page of the ITR were implemented. Please note, that this Newsletter with slide set can be accessed and directly downloaded from the ITR-website. In addition, for submission of clinical islet transplant data to the ITR, report forms should be downloaded by the investigator and sent to the ITR.

Our website address is: *http://www.med.uni-giessen.de/itr*

Summary

From 1893 through December 2000, a total of 493 adult islet allograft allotransplantations including historical cases have been performed at 51 institutions worldwide, including 241 at 18 institutions in North America, 246 at 30 institutions in Europe, and six elsewhere. The total number of diabetic patients reported to be insulin independent for ≥ 1, ≥ 3, ≥ 6, ≥ 12, ≥ 24, ≥ 36, ≥ 48, and 60 month(s) through December 31, 2000, is 66, 62, 54, 40, 22, 11, 6, and 2, respectively.

With ongoing improvements in islet isolation and purification methods and continuing exchange between the centers, a further increase of clinical islet transplantations has occurred. The current ITR analysis is focussing on the period between January 1, 1990 and December 31, 2000. In an analysis by era (with one year follow-up), the percentages of pretransplant C-peptide negative patients with type-1 and pancreatectomy-induced diabetes mellitus, who showed basal C-peptide levels ≥ 0.5 ng/ml at ≥ 1 month posttransplant and who became insulin-independent for ≥ 1 week in the 1985-1989 era (n= 28) were 36 % and 7 %, in the 1990-1993 era (n=82) 71 % and 16 %, in the 1994-1997 era (n=118) 68 % and 15 %, and in the 1998-1999 95% and 19%. The further improvement in functional outcome is associated with intensified efforts to improve isolation, establish islet quality control prior to transplantation, eliminate adverse factors in the early engraftment period and refine immunosuppression protocols. In addition, attempts were made to increase number of islets transplantated by utilizing higher islet mass if available from single donor pancreas, or from sequential islet preparations.

A detailed analysis (one year follow-up) was performed on complete datasets of 237 pretransplant C-peptide negative patients with type-1 diabetes mellitus, who received adult islet allografts between 1990 and 1999. This represents an increase of 37 analyzed cases compared to the previous newsletter (no. 8). One year patient and islet allograft survival (as defined by basal C-peptide ≥ 0.5 ng/ml) rates were 96 %, and 41 %, respectively, and 11 % of the recipients were insulin independent at one year posttransplant. As seen in previous analyses, establishment of insulin independence was largely facilitated if 1) islets were isolated from pancreata with a mean preservation time ≤ 8 hours (n=162), 2) if ≥ 6,000 islet equivalents per kg body weight of the recipient were transplanted (n=146), and 3) if induction immunosuppression comprised monoclonal or polyclonal T-cell antibodies (n=192), recently with increasing use of non-depleting antibodies against interleukin-2 receptor epitopes. Additionally, in all analyses islet transplantation into the liver via portal vein injection/infusion (n=220) was shown to be advantageous. In the recent period of analysis, no reports of alternative implantation sites were made.

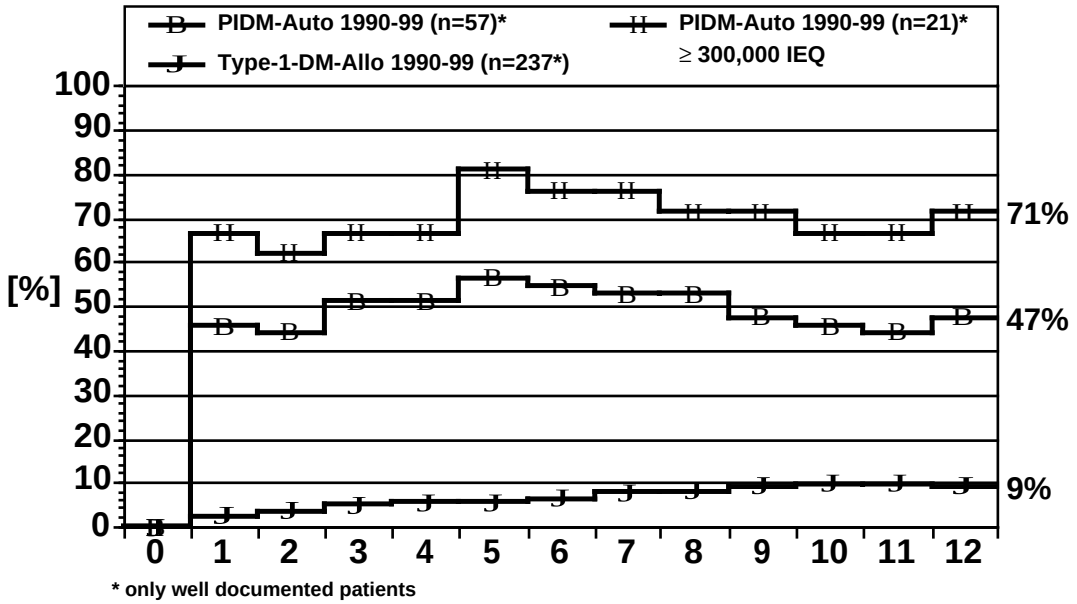
Sixtyseven of the 237 pretransplant C-peptide negative islet allograft recipients with type-1 diabetes mellitus met all of these aforementioned characteristics. 58 of these 67 (87 %) patients showed basal C-peptide levels of ≥ 0.5 ng/ml, 44 of 60 (73 %) had HbA1c levels ≤ 7 %, and 13 of 60 (22 %) were insulin independent at ≥ 1 year follow-up, respectively.

In this preselected group of patients, insulin independent (21 out of 67, 31 %) and dependent recipients (46 out of 67, 69 %) did not differ in regard to age, BMI, diabetes duration, pre-Tx HbA1c, pre-Tx insulin requirements, donor age, cold ischemia time and IEQ/kg body weight. However, the group of insulin independent recipients had higher basal C-peptide levels at both 1 month (2.88 ± 0.45 vs. 1.71 ± 0.22 ng/ml, p=0.0361), and at one year (2.27 ± 0.16 vs. 0.75 ± 0.12, p< 0.0001) posttransplant, respectively. Taken together, in the recent two years significant improvements in outcome of clinical islet transplantation were recorded. As previously delineated, functional islet survival appears to be determined by the integral of characteristics of the islet preparation, effectiveness of engraftment (including resistance against immediate intravascular cellular and humoral inflammatory reaction), susceptibility of islet graft against drug toxicity, metabolic exhaustion, and both allo- and autoimmune reaction. From recent observations utilizing novel immunosuppressive medication (including reduction or omission of corticosteroid therapy), further improvements in islet graft function and insulin independence can be reasonably predicted.

Longest Graft Function of Islet Allografts in Diabetes Mellitus

	graft function	insulin independence
IAK	> 11 yrs 1 mo	4 yrs 2 m
SIK	> 10 yrs 1 mo	5 yrs 10 m
PIDM-Allo	4 yrs 8 m	4 yrs 8 m
PIDM-Auto	> 13 yrs	> 13 yrs

Insulin Independence Following Islet Transplantation in Man
A Comparison of Different Recipient Categories



* only well documented patients

Adult Islet Autografts

Summary of Adult Islet Autografts According to Institution and Year 1990 through December 31, 2000

	Institution	Year of Transplantation											
	(Transplantation/Isolation)	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Σ
1.	Minneapolis	3	1	2	4	12	8	6	6	12	-	-	54
2.	Leicester	-	-	-	-	1	8	7	4	3	6	5	34
3.	Geneva	-	-	2	2	1	4	-	-	3	-	2	14
4.	Indianapolis	-	-	-	-	-	-	-	4	7	-	-	11
5.	Pittsburgh	-	2	1	-	-	1	1	-	-	-	-	5
6.	Rostock	-	-	-	-	-	-	-	-	2	-	1	3
7.	Barcelona	-	-	-	-	-	-	-	2	-	-	-	2
8.	Charlotte	-	-	-	-	-	1	-	-	-	1	-	2
9.	Gent/Brussels	-	-	-	-	-	-	-	-	-	-	1	1
10.	Gent/Giessen	-	-	-	1	-	-	-	-	-	-	-	1
11.	Besancon/Geneva (Gragil)	-	-	-	-	-	-	-	1	-	-	-	1
12.	Kobe	-	-	-	-	-	-	-	-	-	1	-	1
13.	Los Angeles (UCLA-VA)	-	-	-	-	-	1	-	-	-	-	-	1
14.	Paris	-	1	-	-	-	-	-	-	-	-	-	1
15.	Zurich	-	-	-	-	-	-	-	-	-	-	1	1
	Σ	3	4	5	7	14	23	14	17	27	8	10	132
		Total number of Cases through 1990:											108
	2000 data on file incomplete											Σ	240

Islet Autografts from 1990 - 2000

- **Institutions**
  - **Minneapolis 54**
  - **Leicester 34**
  - **Geneva 14**
  - **Indianapolis 11**
  - **11 other Institutions 27**
- **No. of cases 140**
- **Insulin-independent ≥ 7 days (1990-2000): 41 / 64* (64%)**
- **Insulin-independent at ≥ 1 yr (1990-1999 + one year follow-up): 27 / 57* (47%)**
  if more than 300,000 IEQ transplanted: 15 / 21* (71%)
- **Longest insulin-independence follow-up after total pancreatectomy: > 13 yrs**

*** only well documented cases**

2000 data on file incomplete

Adult Islet Allografts

Summary of Adult Islet Allografts According to Institution and Year - 1990 through December 31, 2000

	Institution (Transplantation/Isolation)	Year of Transplantation 1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Σ
1.	Giessen	-	-	1	5	5	12	11	17	6	4	5	66
2.	Milan	4	3	3	4	4	4	1	-	5	5	10	43
3.	Miami	4	2	1	1	3	9	5	2	3	5	7	42
4.	Pittsburgh	17	6	4	3	4	3	1	-	-	-	-	38
5.	Minneapolis	1	4	5	5	2	10	5	1	-	-	3	36
6.	Edmonton	2	-	1	-	1	1	-	-	-	5	10	20
7.	Geneva	-	-	-	-	1	-	4	2	4	5	4	20
8.	St. Louis	3	3	2	4	2	-	-	-	-	-	-	14
9.	Brussels	-	-	-	-	1	3	3	3	?	?	?	10
10.	Indianapolis	-	-	-	-	-	-	4	5	1	-	-	10
11.	Oxford	-	1	1	1	1	3	-	1	1	-	-	9
12.	Los Angeles (UCLA-VA)	-	-	3	-	-	-	3	2	-	-	-	8
13.	Madrid	-	-	2	1	1	2	2	-	-	-	-	8
14.	San Francisco/LA (UCLA-VA)	-	-	-	1	1	3	-	-	-	2	-	7
15.	Stockholm/Giessen	-	-	-	-	-	-	2	2	1	2	-	7
16.	Grenoble/Geneva (Gragil)	-	-	-	-	-	-	-	-	-	2	3	5
17.	Odense/Milan	-	-	-	-	-	5	-	-	-	-	-	5
18.	Paris	3	1	-	-	-	1	-	-	-	-	-	5
19.	Buenos Aires	-	-	-	-	-	1	1	2	-	-	-	4
20.	London (Ontario)/St. Louis	2	1	1	-	-	-	-	-	-	-	-	4
21.	Perugia	1	1	-	-	2	-	-	-	-	-	-	4
22.	Innsbruck/Milan	-	-	-	-	-	2	1	-	-	-	-	3
23.	Leicester	-	2	1	-	-	-	-	-	-	-	-	3
24.	Lille	-	-	-	-	-	-	-	-	1	1	1	3
25.	Charlestown	-	2	-	-	-	-	-	-	-	-	-	2
26.	Lyon (Gragil)	-	-	-	-	-	-	-	-	-	-	2	2
27.	Nantes	-	-	-	-	-	-	1	-	-	1	-	2
28.	Strasbourg (Gragil)	-	-	-	-	-	-	-	-	-	1	1	2
29.	Berlin RV / Giessen	-	-	-	-	-	-	-	-	-	-	1	1
30.	Bethesda (NIH)	-	-	-	-	-	-	-	-	-	-	1	1
31.	Chicago (NWH)	-	-	-	-	-	-	1	-	-	-	-	1
32.	Chicago University	-	-	-	-	-	-	-	-	-	-	1	1
33.	Harvard	-	-	-	-	-	-	-	-	-	-	1	1
34.	Homburg	-	-	-	1	-	-	-	-	-	-	-	1
35.	Omaha	-	-	-	-	1	-	-	-	-	-	-	1
36.	Padova/Verona	-	-	-	1	-	-	-	-	-	-	-	1
37.	Seoul	-	-	-	-	-	-	-	-	-	1	-	1
38.	Syracuse (NYUM)	-	-	-	-	-	-	-	1	-	-	-	1
39.	Wuerzburg/Giessen	-	-	-	1	-	-	-	-	-	-	-	1
40.	Zurich	-	-	-	-	-	-	-	-	-	-	1	1
	Σ	37	26	25	28	29	59	45	38	22	34	51	394
	Total number of Adult Islet Allografts from 1974 -1989:												99
												Σ	493

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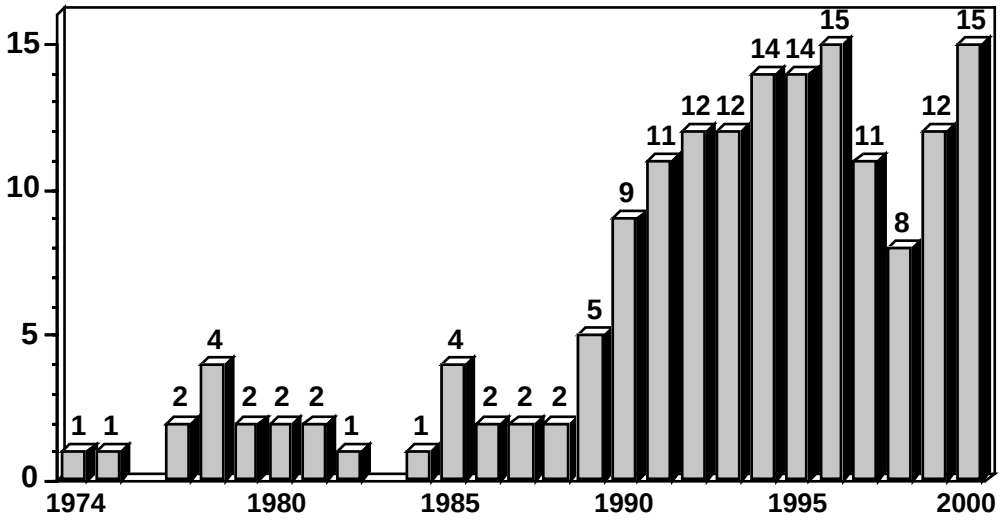
No. of Institutions Reporting Adult Islet Allografts in Patients with Diabetes by Year from 1974 through 2000



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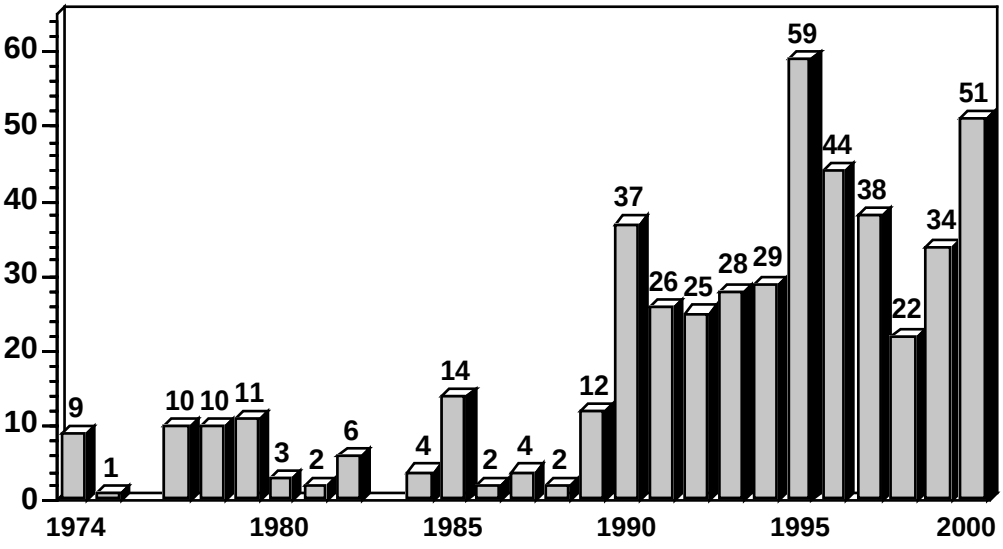
No. of Institutions by Year

No. of Adult Islet Allografts in Patients with Diabetes by Year from 1974 through 2000



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No. of Adult Islet Allografts by Year

Adult Islet Allografts in Type-1 Diabetic Recipients

Summary of Adult Islet Allografts in Type-1 Diabetic Recipients According to Institution and Year - 1990 through Dec. 31, 2000

	Institution (Transplantation/Isolation)	Year of Transplantation											
		1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	Σ
1.	Giessen	-	-	1	5	5	12	11	17	6	4	5	66
2.	Milan	4	3	2	4	4	4	1	-	5	5	10	42
3.	Minneapolis	1	3	5	5	2	10	5	1	-	-	3	35
4.	Miami	4	2	1	1	1	6	2	-	3	5	7	32
5.	Pittsburgh	7	5	3	3	4	3	1	-	-	-	-	26
6.	Edmonton	2	-	1	-	1	1	-	-	-	5	10	20
7.	Geneva	-	-	-	-	-	-	4	2	4	5	4	19
8.	St. Louis	3	3	2	4	2	-	-	-	-	-	-	14
9.	Brussels	-	-	-	-	1	3	3	3	?	?	?	10
10.	Indianapolis	-	-	-	-	-	-	4	5	1	-	-	10
11.	Madrid	-	-	2	1	1	2	2	-	-	-	-	8
12.	Oxford	-	1	1	1	1	2	-	1	1	-	-	8
13.	Stockholm/Giessen	-	-	-	-	-	-	2	2	1	2	-	7
14.	Grenoble/Geneva (Gragil)	-	-	-	-	-	-	-	-	-	2	3	5
15.	Odense/Milan	-	-	-	-	-	5	-	-	-	-	-	5
16.	San Francisco/LA (UCLA-VA)	-	-	-	1	1	1	-	-	-	2	-	5
17.	Buenos Aires	-	-	-	-	-	1	1	2	-	-	-	4
18.	London (Ontario)/St. Louis	2	1	1	-	-	-	-	-	-	-	-	4
19.	Perugia	1	1	-	-	2	-	-	-	-	-	-	4
20.	Innsbruck/Milano	-	-	-	-	-	2	1	-	-	-	-	3
21.	Leicester	-	2	1	-	-	-	-	-	-	-	-	3
22.	Lille	-	-	-	-	-	-	-	-	1	1	1	3
23.	Los Angeles (UCLA-VA)	-	-	2	-	-	-	1	-	-	-	-	3
24.	Paris	3	-	-	-	-	-	-	-	-	-	-	3
25.	Lyon (Gragil)	-	-	-	-	-	-	-	-	-	-	2	2
26.	Nantes	-	-	-	-	-	-	1	-	-	1	-	2
27.	Strasbourg/Geneva (Gragil)	-	-	-	-	-	-	-	-	-	1	1	2
28.	Berlin	-	-	-	-	-	-	-	-	-	-	1	1
29.	Bethesda (NIH)	-	-	-	-	-	-	-	-	-	-	1	1
30.	Charlestown	-	1	-	-	-	-	-	-	-	-	-	1
31.	Chicago (NWH)	-	-	-	-	-	-	1	-	-	-	-	1
32.	Chicago University	-	-	-	-	-	-	-	-	-	-	1	1
33.	Harvard	-	-	-	-	-	-	-	-	-	-	1	1
34.	Homburg (Saar)	-	-	-	1	-	-	-	-	-	-	-	1
35.	Omaha	-	-	-	-	1	-	-	-	-	-	-	1
36.	Seoul	-	-	-	-	-	-	-	-	-	1	-	1
37.	Zurich	-	-	-	-	-	-	-	-	-	-	1	1
	Σ	27	22	22	26	26	52	40	33	22	34	51	355
	Total number of Adult Islet Allografts from 1974 -1989:												90
												Σ	445

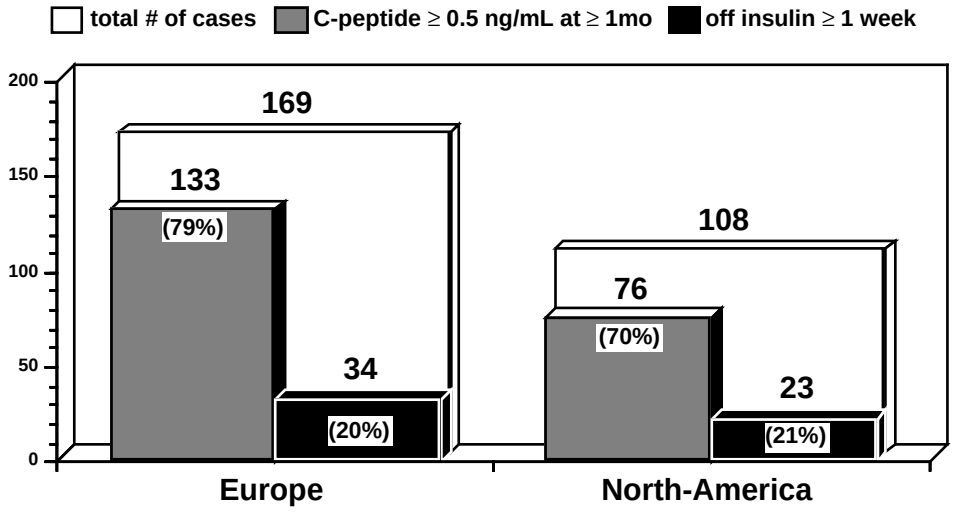
2000 data on file incomplete

Adult Islet Allografts in Type-1 Diabetic Recipients 1990 - 2000

• No. of cases:		355
• Institutions:	Giessen	66
	Milan	42
	Minneapolis	35
	Miami	32
	Pittsburgh	26
	Edmonton	20
	Geneva	19
	St. Louis	14
	29 additional institutions (≤ 10 cases)	99
• Insulin-independent ≥ 7 days (1990-2000):		52 / 281 (19%)*
• Insulin-independent at ≥ 1 yr (1990-1999 + one year follow-up):		27 / 237 (11%)*
• Insulin-independent after 1:1 tx ≥ 7 days (1990-2000):		21 / 151 (14%)*
• Insulin-independent after 1:1 tx at ≥ 1 yr (1990-1999+ one year follow-up):		13 / 140 (9%)*
• Longest insulin-indepence follow-up:		70 months

*** only well documented cases**

Insulin Independence and Basal C-Peptide after Adult Islet Allotransplantation in 281 Type-1 Diabetic Recipients from 1990 - 2000 according to Continent



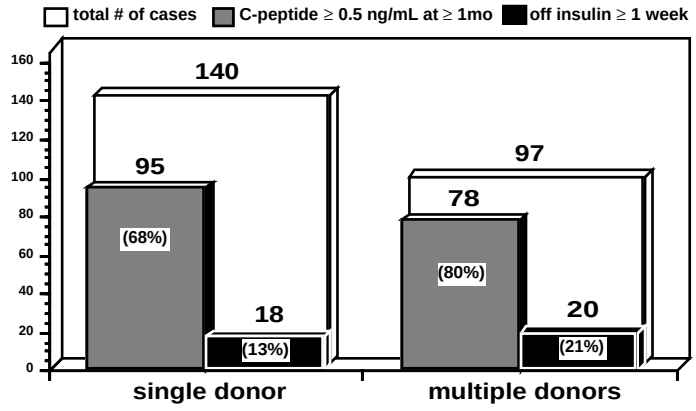
Four transplantations performed elsewhere

THE 1990-1999 CASES - One Year Follow-Up

DETAILED DATA ON 237 C-PEPTIDE NEGATIVE TYPE-1 DIABETIC ADULT ISLET ALLOGRAFT RECIPIENTS TRANSPLANTED FROM 1990 TO 1999

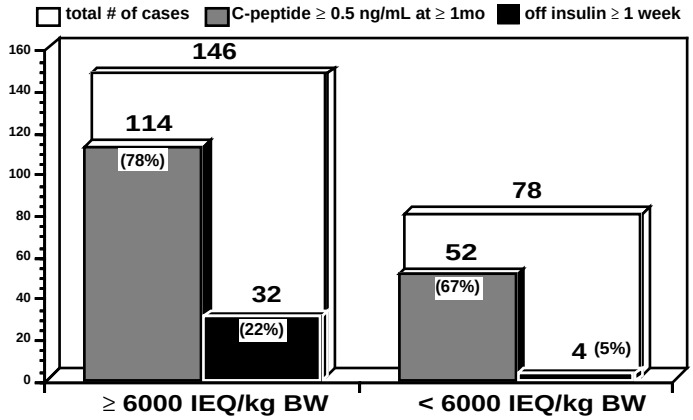
Two hundred thirty seven type-1 diabetic patients with complete data records, and no residual C-peptide secretion pretransplant who received an islet allograft between 1990 and 1999 were taken into the analysis. Assuming that the vast majority of islet allografts performed worldwide during this period were reported to the Registry, the following analysis should reflect the current status of islet allotransplantation in patients with type-1 diabetes mellitus.
The overall outcome assessed at one year after islet transplantation for patient survival was 96 %, for graft survival (basal C-peptide ≥ 0.5 ng/mL) 41 % and for insulin independence 11 %.

Insulin Independence and Basal C-Peptide One Year after Adult Islet Allotransplantationin 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Number of Donors*



*** Only well documented cases**

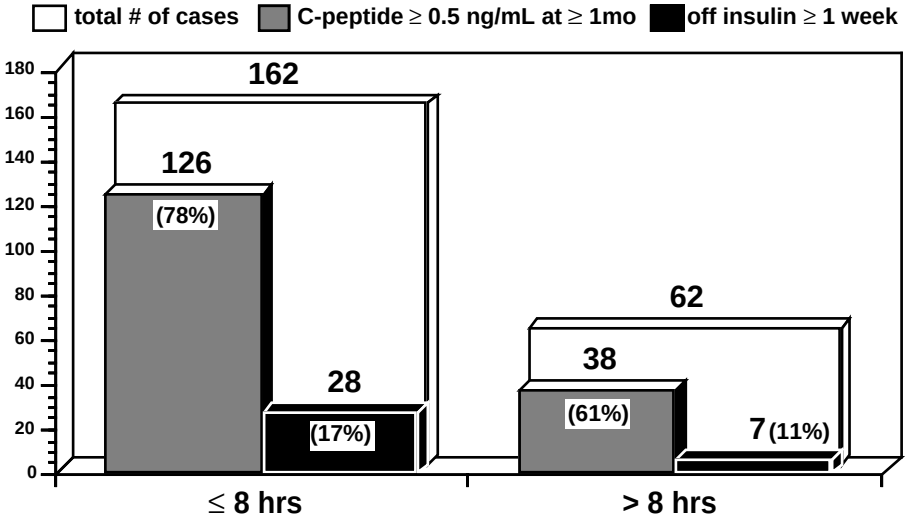
Insulin Independence and Basal C-Peptide One Year after Adult Islet Allotransplantation in 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Number of Islet Equivalents per kg Body Weight*



*** Only well documented cases**

no data available in 13 cases

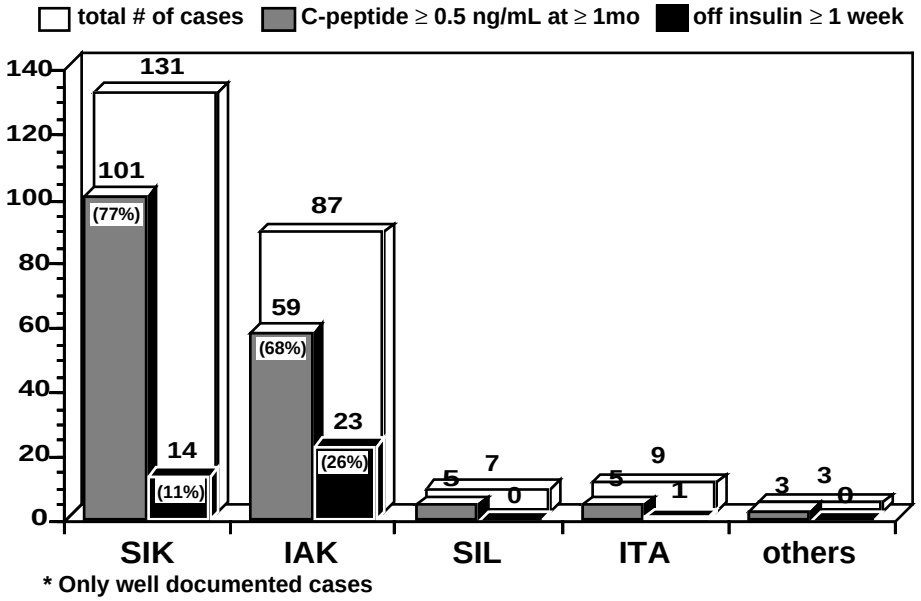
Insulin Independence and Basal C-Peptide One Year after Adult Islet Allotransplantation in 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Cold Ischemia Time*



* Only well documented cases

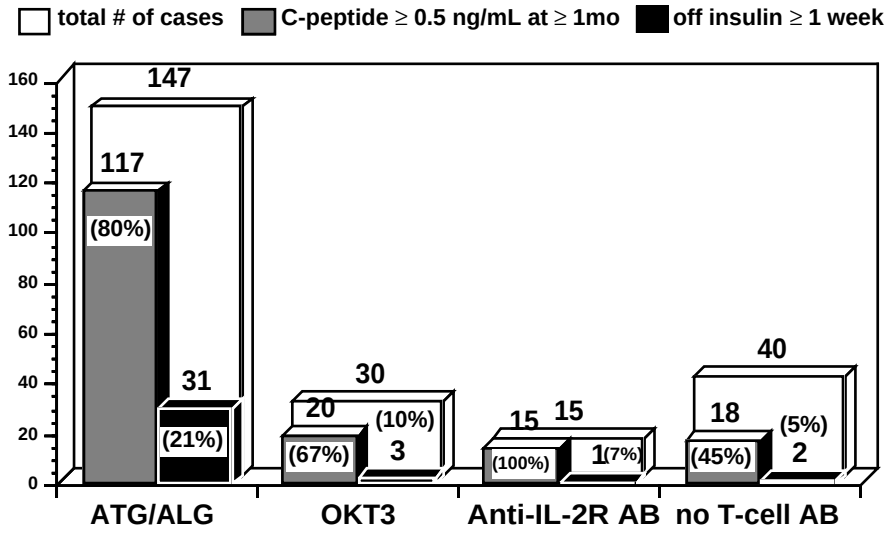
no data available in 13 cases

Insulin Independence and Basal C-Peptide One Year after Adult Islet Allotransplantation in 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Recipient Category*



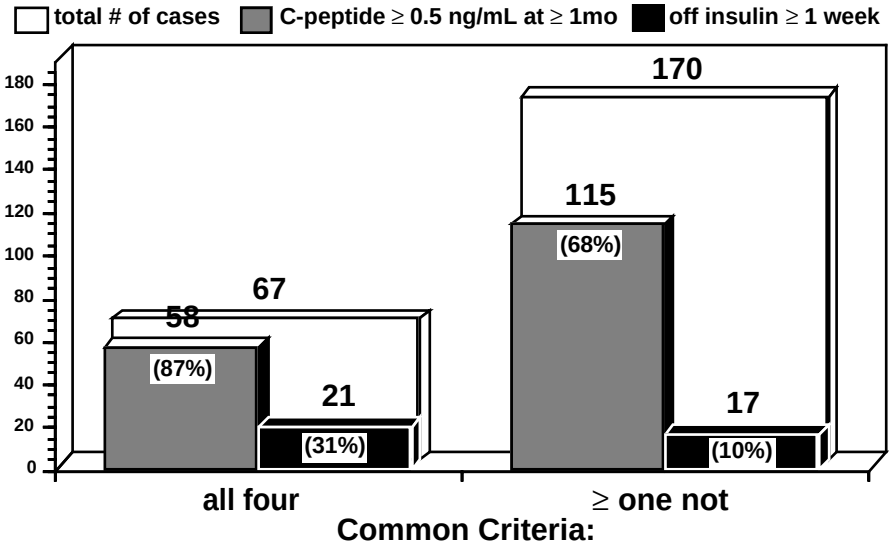
* Only well documented cases

Insulin Independence and Basal C-Peptide after One Year Adult Islet Allotransplantation in 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Induction Immunosuppression*



*** Only well documented cases (Five additional cases with Anti-CD4 not depicted)**

Insulin Independence and Basal C-Peptide One Year after Adult Islet Allotransplantation in 237* pre Tx C-Peptide negative Type-1 Diabetic Recipients from 1990 - 1999 according to *Common Criteria*

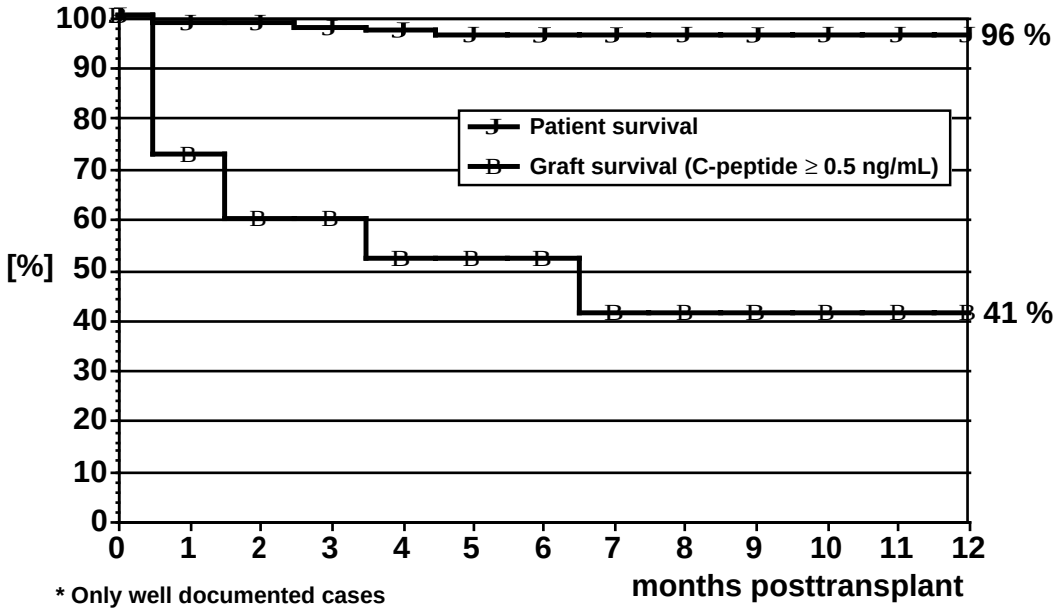


Common Criteria:

a) IEQ/kg BW ≥ 6,000; b) CIT ≤ 8 hrs; c) ALG/ATG; d) Implantation Site: Liver (via portal vein)

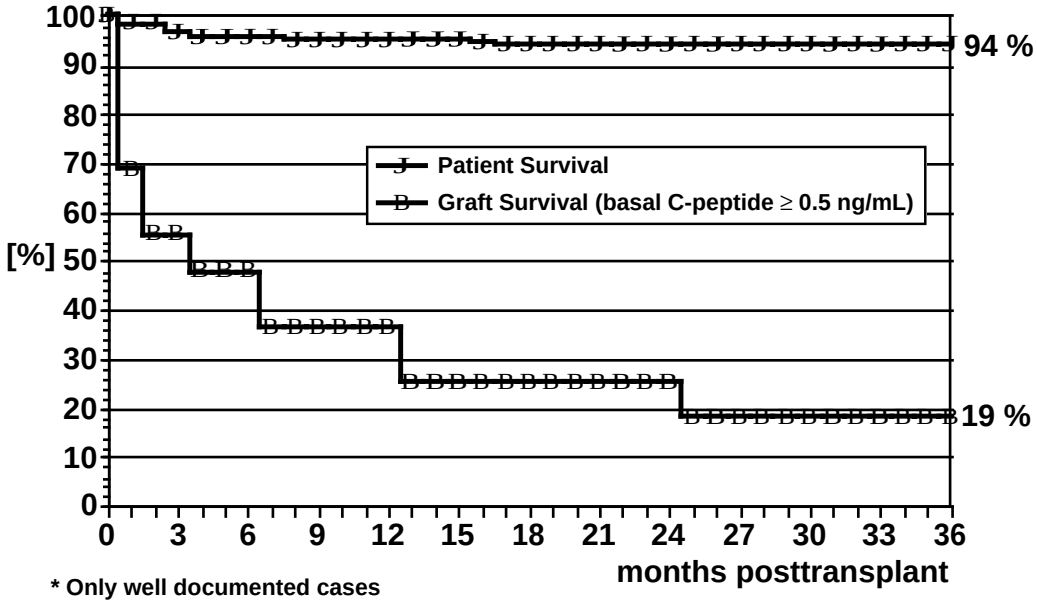
*** Only well documented cases**

Cumulative One-Year Patient and Graft Survival in 237* pre Tx C-Peptide Negative Type-1 Diabetic Recipients (1990-1999)



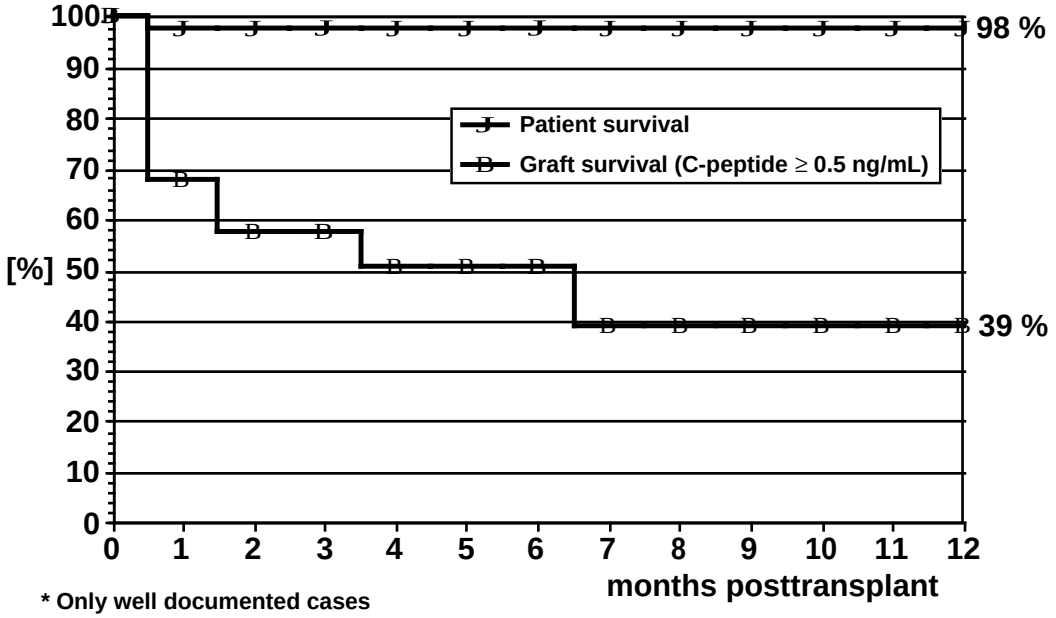
* Only well documented cases

Cumulative Three-Year Patient and Graft Survival in C-Peptide Negative Type-1 Diabetic Recipients; 1990-1997; n=200*



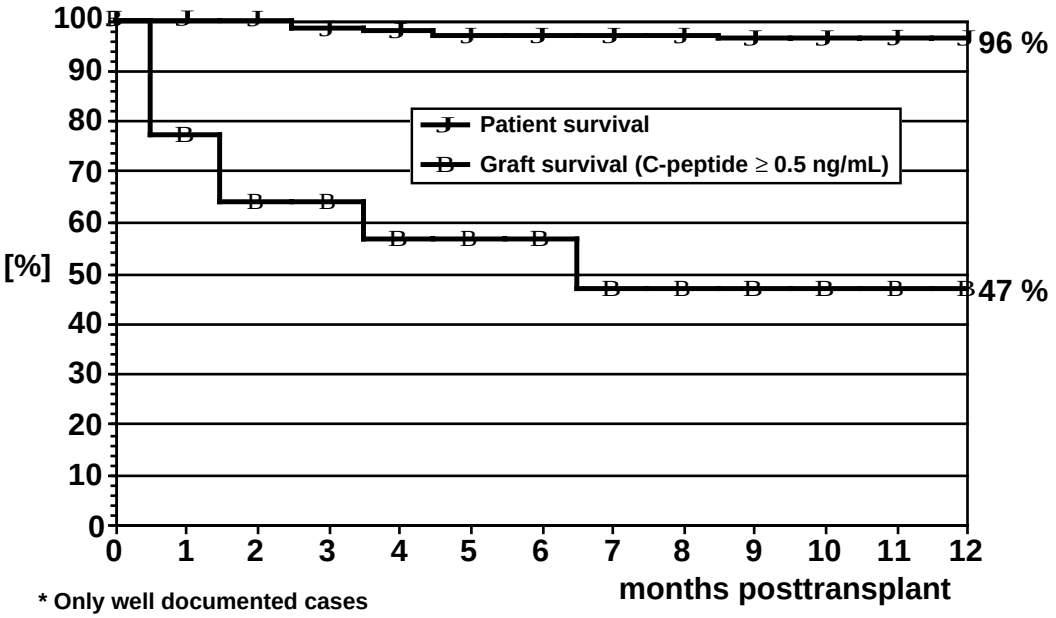
* Only well documented cases

Cumulative One-Year Patient and Graft Survival in
87* pre Tx C-Peptide Negative Type -1 Diabetic Recipients (1990-1999)
Islet After Kidney (IAK) Transplantation



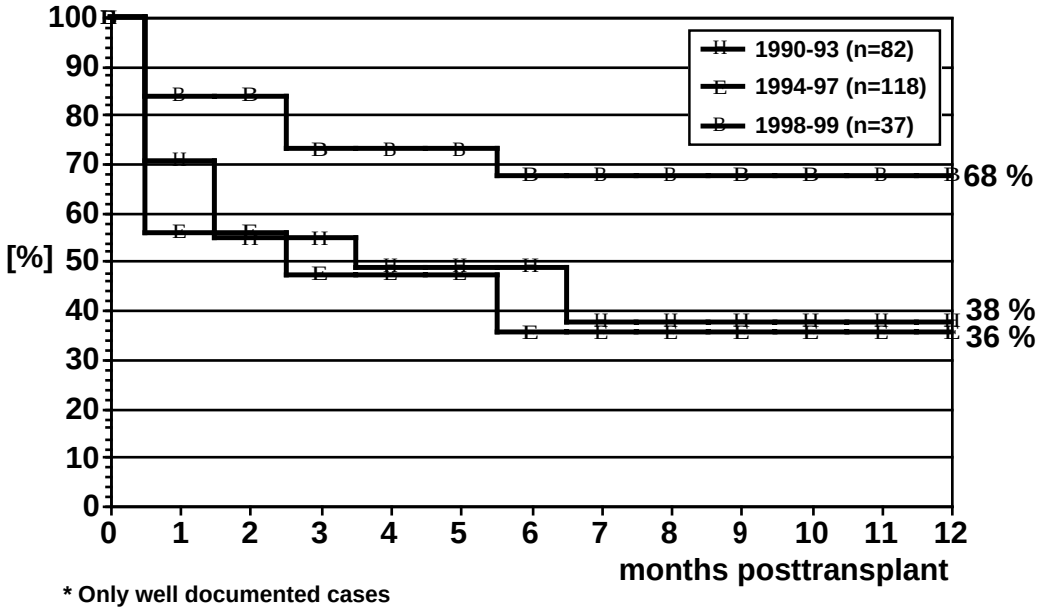
* Only well documented cases

Cumulative One-Year Patient and Graft Survival in
131* pre Tx C-Peptide Negative Type-1 Diabetic Recipients (1990-1999)
Simultaneous Islet Kidney (SIK) Transplantation



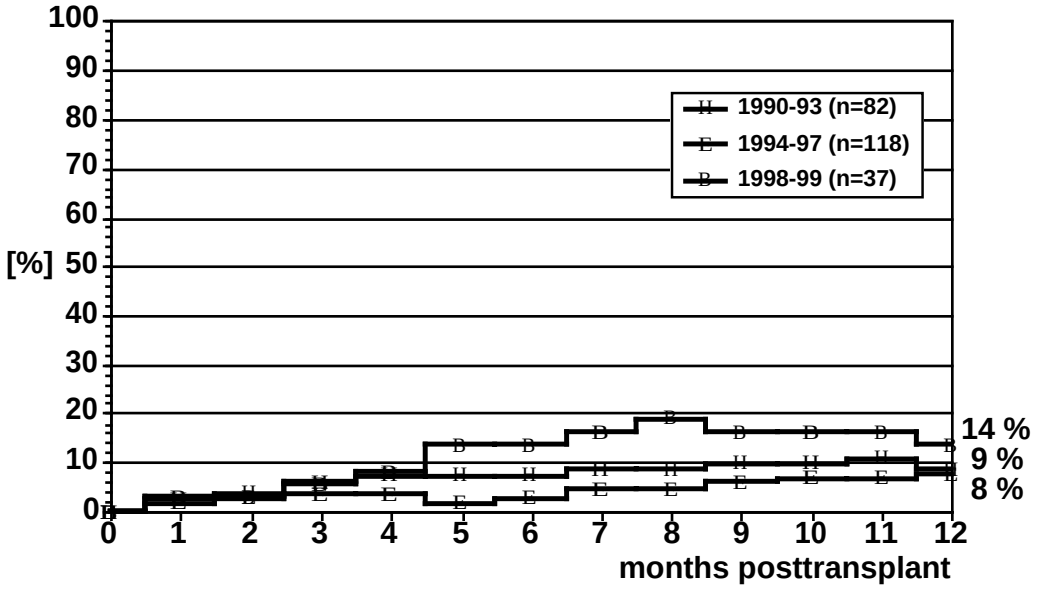
* Only well documented cases

Cumulative One-Year Graft Survival by ERA
C-Peptide Negative Type-1 Diabetic Recipients; 1990-1999; n=237*



* Only well documented cases

One-Year Insulin Indepence by ERA
C-Peptide Negative Type-1 Diabetic Recipients; 1990-1999; n=237*



* Only well documented cases

Adult Islet Allograft Survival in 237# Type-1 Diabetic Recipients with Complete Data Records (1990-1999 Cases)

No. (Percentage) of Cases Functioning

Category	n	at ≥ 1 Month: Basal C-Peptide ≥0.5 ng/mL	at ≥ 1 Month: Insulin Indep. (≥7 days)	at ≥ 1 Year: Basal C-Peptide ≥0.5 ng/mL	P Values	at ≥ 1 Year: Insulin Indep. (≥7 days)	P Values
All cases	237	173 (73%)	37 (16%)	98 (41%)		25 (11%)	
A. Continent							
1. North America	88	57 (65%)	9 (10%)	23 (26%)	p=0.0001***	4 (5%)	p=0.0170*
2. Europe	145	116 (80%)	28 (19%)	75 (52%)	1 vs. 2	21 (14%)	
3. others	4						
B. Recipient Gender							
1. male	148	105 (71%)	14 (9%)	54 (36%)	p=0.0571	8 (5%)	p=0.0017**
2. female	89	68 (76%)	23 (26%)	44 (49%)		17 (19%)	
C. Recipient Age							
1. ≤ 40 y	135	96 (71%)	21 (16%)	52 (39%)	p=0.3472	13 (10%)	p=0.6691
2. > 40 y	99	76 (77%)	16 (16%)	45 (45%)	1 vs. 2	12 (12%)	
3. no data	3						
D. Duration of Diabetes							
1. ≤ 20 y	64	45 (70%)	8 (13%)	22 (34%)	p=0.1826	3 (5%)	p=0.0937
2. > 20 y	167	125 (75%)	28 (17%)	74 (44%)	1 vs. 2	21 (13%)	
3. no data	6						
E. Average CIT							
1. ≤ 480 min	162	126 (78%)	28 (17%)	73 (45%)	p=0.0201*	21 (13%)	p=0.0583
2. > 480 min	62	38 (61%)	7 (11%)	18 (29%)	1 vs. 2	3 (5%)	
3. no data	13						
F. No. of Donors							
1. 1	140	95 (68%)	17 (12%)	52 (37%)	p=0.1401	13 (9%)	p=0.5206
2. > 1	97	78 (80%)	20 (21%)	46 (47%)		12 (12%)	
G. IEQ / kg BW							
1. < 6,000	87	52 (67%)	4 (5%)	30 (38%)	p=0.2966	0 (0%)	p<0.0001***
2. ≥ 6,000	146	114 (78%)	32 (22%)	63 (43%)	1 vs. 2	25 (17%)	
3. no data	13						
H. Pre Tx Viab. Tests							
1. yes	143	105 (73%)	22 (15%)	62 (43%)	p=0.0325*	15 (10%)	p=1.0000
2. no	54	40 (74%)	9 (17%)	14 (26%)	1 vs. 2	5 (9%)	
3. ND	40						
I. Islet Purity (%)							
1. < 90	179	132 (74%)	28 (16%)	72 (40%)	p=0.0802	18 (10%)	p=0.1839
2. ≥ 90	43	33 (77%)	9 (21%)	23 (53%)	1 vs. 2	7 (16%)	
3. no data	15						
J. Recipient Category							
1. IAK	87	59 (68%)	23 (26%)	34 (39%)	p=0.3292	13 (15%)	p=0.2000
2. SIK	131	101 (77%)	14 (11%)	61 (47%)	1 vs. 2	12 (9%)	
3. others	19						
K. Induction Immunosupp.							
1. ATG/ALG/IL-2R	162	132 (81%)	32 (20%)	80 (49%)	p= 0.0016**	23 (14%)	p=0.0274*
2. OKT3	30	20 (67%)	3 (10%)	9 (30%)	1 vs. 3	1 (3%)	1 vs. 3
3. no T-cell antibody	40	18 (45%)	2 (5%)	9 (23%)		1 (3%)	
4. others	5						
L. Site of Tx							
1. liver	220	168 (76%)	37 (17%)	95 (43%)	p=0.0317*	25 (11%)	p=0.1400
2. others	17	5 (29%)	0 (0%)	3 (18%)		0 (0%)	
M. Common Charact.## of Ins. Indep. Cases							
1. all four fulfilled	67	58 (87%)	21 (31%)	35 (52%)	p=0.0236*	16 (24%)	p<0.0001***
2. ≥ 1 not fulfilled	170	115 (68%)	16 (9%)	63 (37%)		9 (5%)	

P values comparing islet graft survival rates between groups at ≥ one year after transplantation were calculated by the one-sided (categories E, G, I, K, L, M) and by the two-sided (categories A, B, C, D, F, H, J) Fisher´s exact test.
* p<0.05 significant, ** p<0.01 very significant, *** p<0.001 highly significant.
CIT: Cold Ischemia Time; IEQ: Islet Equivalents (no. of islets if all had a diameter of 150 µm)
Common Characteristics: a) IEQ/kg Bw ≥ 6,000; b) Cold Ischemia Time ≤ 8 hrs; c) ALG/ATG; d) Implantation Site: Liver
Only well documented cases

Type-1 Diabetic Recipients of Adult Islet Allografts (One Year Follow-Up)
Insulin-Independent Cases (n=50) through December 31, 1999

Case	Institution	Year of Tx	No. of IEQ/kg	No. of Donors	Purity (%)	Immunosuppressior
1.	Zurich	1978	3,864	1	1	ALG, S, A, CPM
2.	Paris	1988	2,143	1	80	ALG, S, C, A
3.	St. Louis	1989	12,582	2	95	ALG, C, A
4.	St. Louis	1990	14,735	3	91	ALG, S, A
5.	St. Louis	1993	22,055	8	93	OKT3, S, C, A
6.	St. Louis	1993	26,494	5	88	ALG, S, C, A
7.	Edmonton	1990	9,692	5	70	ALG, S, C, A
8.	Edmonton	1992	9,866	6	59	ALG, S, C, A
9.	Edmonton	1999	9,407	2	60	aIL2-R, T, Si
10.	Edmonton	1999	11,138	2	60	aIL2-R, T, Si
11.	Edmonton	1999	13,225	2	60	aIL2-R, T, Si
12.	Edmonton	1999	11,800	4	60	aIL2-R, T, Si
13.	Edmonton	1999	13,987	2	60	aIL2-R, T, Si
14.	Milan	1990	10,773	1	95	ALG, S, C, A
15.	Milan	1990	8,610	2	75	ALG, S, C, A
16.	Milan	1991	16,859	3	80	ALG, S, C
17.	Milan	1992	11,557	2	80	ALG, S, C, A
18.	Milan	1994	28,995	3	63	ALG, S, C, A
19.	Milan	1994	14,489	1	60	ALG, S, C, A
20.	Milan	1995	9,601	1	50	ALG, C, A
21.	Milan	1998	13,750	2	65	ALG, C, MMF
22.	Milan	1998	NA	2	75	ALG, S, C
23.	Milan	1999	12,948	2	50	ALG, S, C, MMF
24.	Milan	1999	7,413	1	90	ALG, S, C, MMF
25.	Milan	1999	NA	2	65	ALG, S, C, MMF
26.	Miami	1990	18,669	3	47	OKT3, S, C, A
27.	Miami	1990	18,884	3	50	OKT3, S, C, A
28.	Miami	1995	15,691	1	85	ATG, S, T, MMF
29.	Giessen	1992	6,156	1	92	ATG, S, C
30.	Giessen	1995	7,246	1	95	aIL2-R, S, C
31.	Giessen	1995	12,031	1	90	ATG, S, C, A
32.	Giessen	1995	8,251	1	90	ATG, S, C, A
33.	Giessen	1995	6,379	1	85	ALG, S, C, A
34.	Giessen	1996	5,475	1	90	ALG, S, C, A
35.	Giessen	1996	7,777	1	98	ATG, S, C, A
36.	Giessen	1996	5,472	1	85	ATG, S, C, A, MMF
37.	Giessen	1997	6,548	1	85	ALG, S, C, A
38.	Giessen	1997	7,896	1	90	ATG, S, C, A
39.	Giessen	1997	12,636	1	70	ATG, S, C, A
40.	Minneapolis	1992	7,882	1	5	ALG, S, C, A, D
41.	Minneapolis	1992	13,319	1	5	ALG, S, C, A, D
42.	Minneapolis	1995	9,004	1	5	S, C, A
43.	Pittsburgh	1994	8,137	1	80	S, T
44.	Brussels	1995	4,400	6	70	S, C, A
45.	Brussels	1996	2,600	8	59	S, C, A
46.	Odense/ Milan	1995	9,360	2	80	ATG, C
47.	Geneva	1996	8,800	2	28	ATG, S, C, A
48.	Geneva	1999	19,135	1	50	aIL2-R, S, C, MMF
49.	Los Angeles VA	1996	NA	4	NA	S, T, MMF
50.	Nantes	1999	9,467	2	50	ALG, S, C, MMF
	Mean ± SEM		11,217±822	2.24±0.25	67.5±3.6	

S=Steroids, C=Cyclosporine, T=Tacrolimus, Si=Sirolimus, D=Deoxyspergualin, A=Azathioprin, MMF=Mycophenolate Mofetil, aIL2R=Anti IL-2 Rec Ab, CPM=Cyclophosphamide, NA=Not Available
Insulin independence for ≥ 7 days at any time after I-Tx

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