

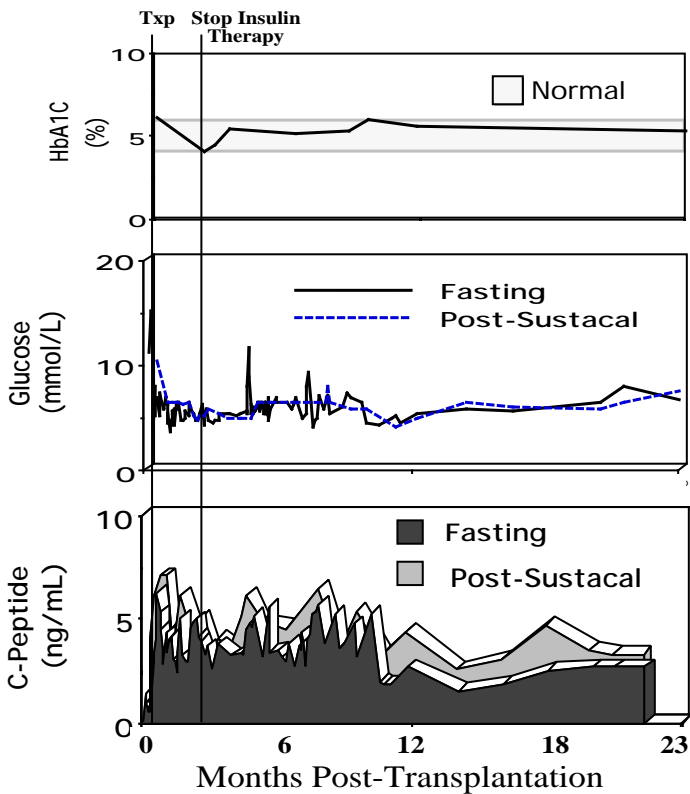
INTERNATIONAL ISLET TRANSPLANT REGISTRY



Edmonton, April 20, 1992

First islet transplant recipient stayed off insulin almost two years after grafting

— Third Edmonton Patient at 23 Months Post-Tx



With kind permission of Dr. G.L. Warnock, Dr. E. Ryan, and Dr. R.V. Rajotte, University of Alberta, Edmonton, Alberta, Canada

Newsletter No. 2

May 1992

In this Newsletter

Results on all adult islet allografts known to be performed through Dec 31, 1991



Publisher

Justus-Liebig-University of Giessen
Department of Medicine

Circulation

The Islet Transplant Registry Newsletter is published regularly and distributed to all interested institutions. It is anticipated that the fourth newsletter will be issued towards the beginning of 1993.

Editorial Board

Konrad Federlin, MD
Professor of Medicine

Reinhard G. Bretzel, MD
Professor of Medicine

Bernhard J. Hering, MD

Registry Staff

Professor Konrad Federlin, MD
Director

Professor Reinhard G. Bretzel, MD
Vice-Director

Bernhard J. Hering, MD
Registry Coordinator

Christian C. Browatzki, MD
Registry Vice-Coordinator

Andreas O. Schultz
Registry Administrator & Programmer

Barbara Watz
Correspondent

Consultants

Professor David E.R. Sutherland, MD, PhD
Director, International Pancreas Transplant Registry

Kay C. Moudry-Munns, RNC, CCRN, BSN
Coordinator, International Pancreas Transplant Registry

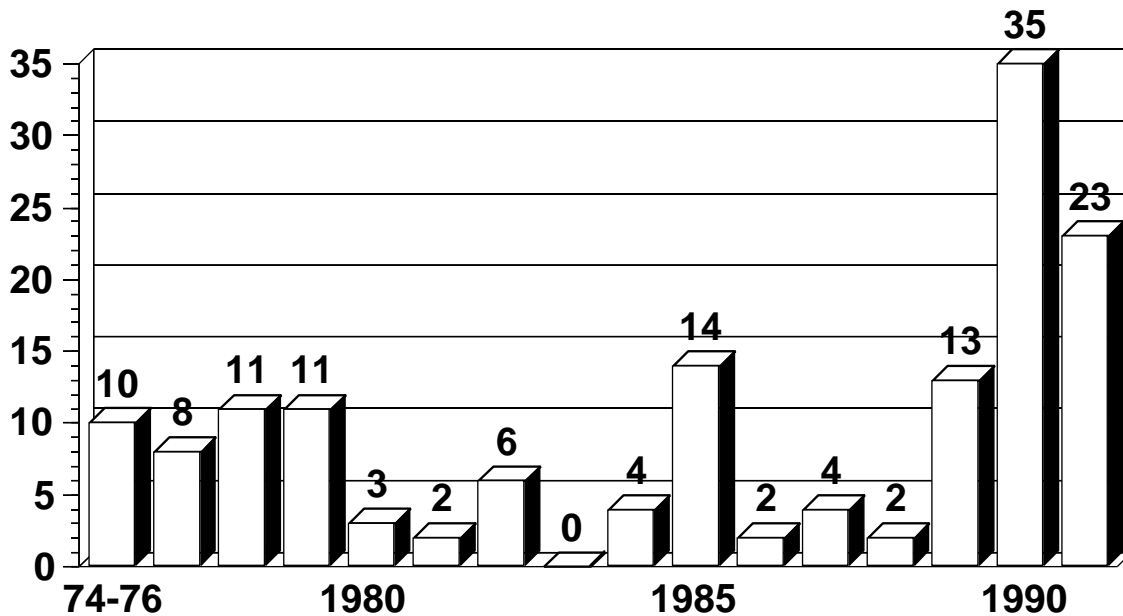
Registry Address

Islet-Transplant-Registry
Contact: Bernhard J. Hering, MD
Department of Medicine
Justus-Liebig-University of Giessen
Rodthohl 6
D-6300 Giessen
Germany
Phone: (49)-641-702-7445/ 3702

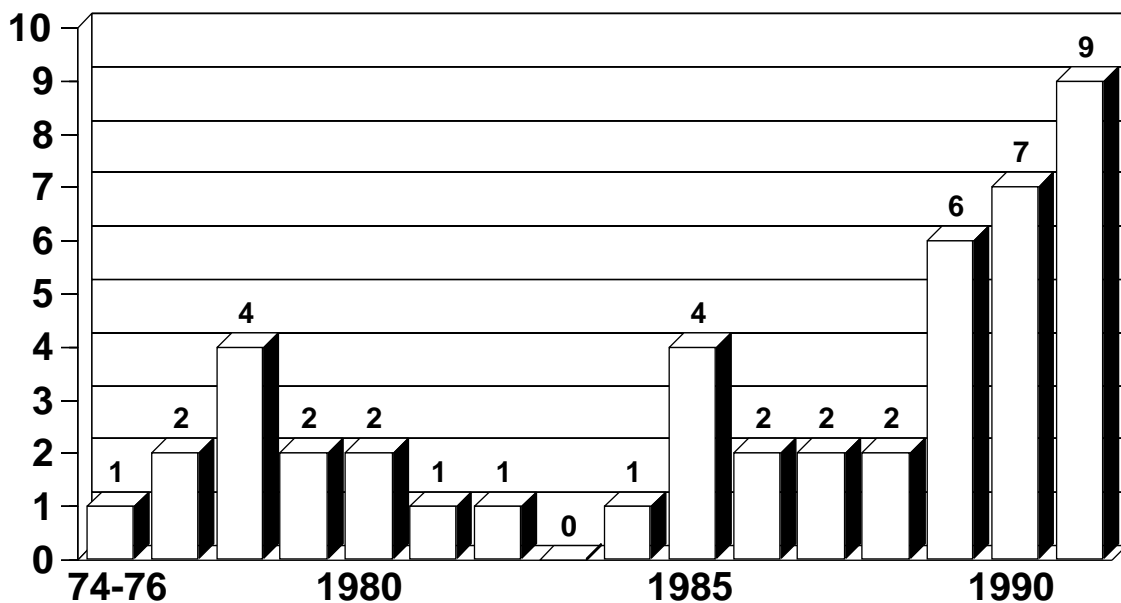
**Summary of
Adult Islet Allografts and Xenografts
according to Institution and Year
through December 1991**

INSTITUTION	YEAR OF TX	NO. OF CASES
• Bristol	1893	1
• Newcastle-upon-Tyne	1916	2
• Padova	1927	2
• New York	1935	1
• Leiden	1944	1
• Petah Tikva	1968	1
• Minneapolis	1974-1991	28
• Zürich	1977-1988	8
• Genua	1978-1979	13
• Hannover	1978	2
• Detroit	1980-1985	7
• Giessen	1980	1
• Ost-Berlin	1982-1987	8
• St. Louis	1985-1991	21
• Miami	1985-1991	11
• Paris	1988-1991	7
• Perugia	1989	3
• West-Berlin	1989	1
• Edmonton	1989-1990	4
• Mailand	1989-1991	8
• Pittsburgh	1990-1991	22
• Leicester	1991	2
• Oxford	1991	1
• Charlestown	1991	1
TOTAL NO. OF CASES:		156
TOTAL NO. OF INSTITUTIONS:		24

No. of Adult Islet Allografts by Year

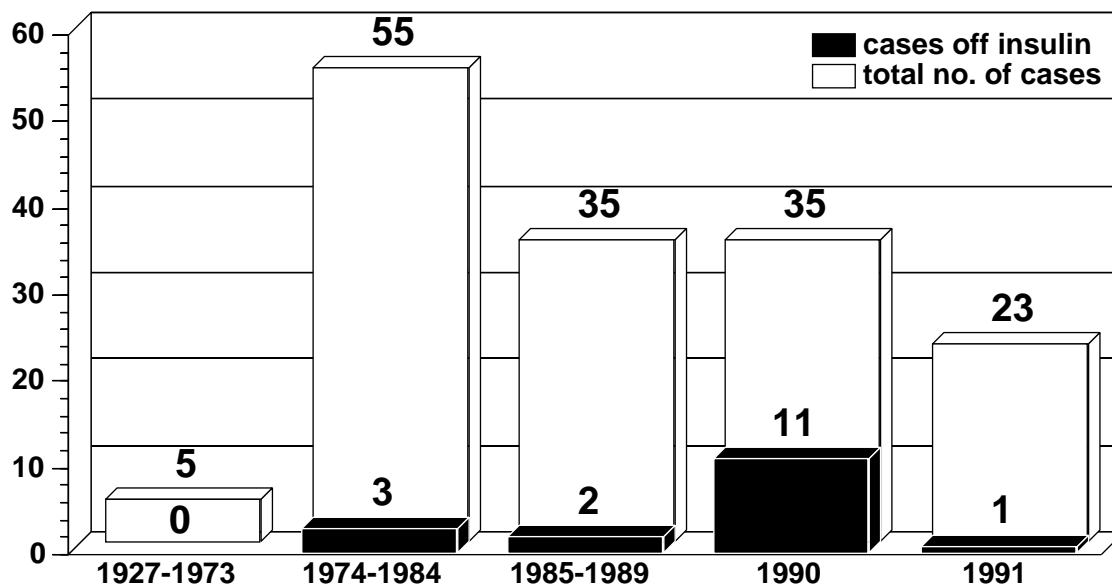


No. of Institutions Reporting Adult Islet Allografts by Year



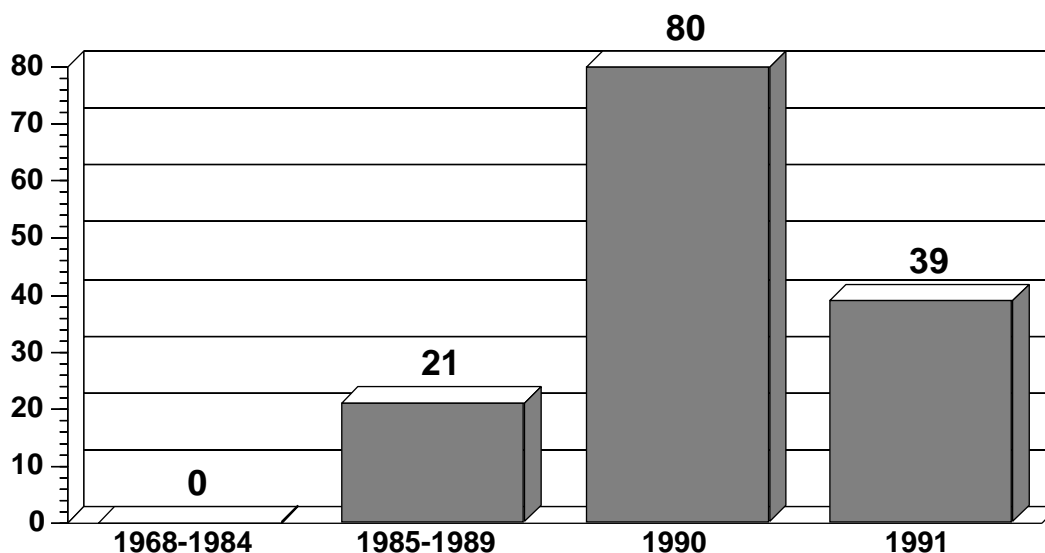
Insulin Independence* after Adult Islet Allografts through December 1991 according to Era

* > 1 week



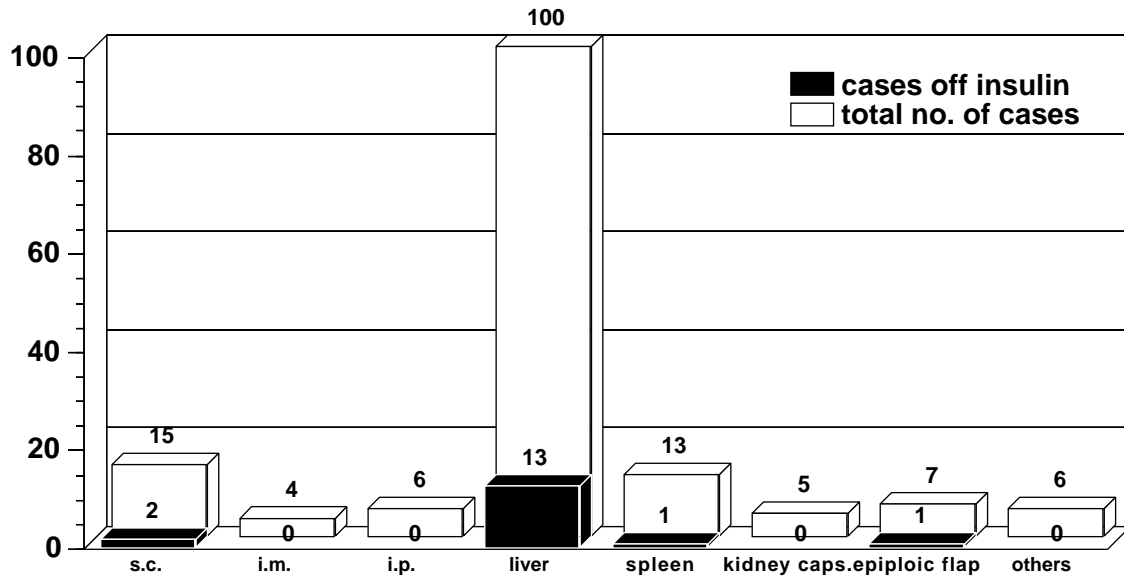
Basal C-Peptide after Adult Islet Allo-Tx according to Era

percentage of patients with basal C-Peptide levels
> 1 ng/ml \geq 1 month posttransplant



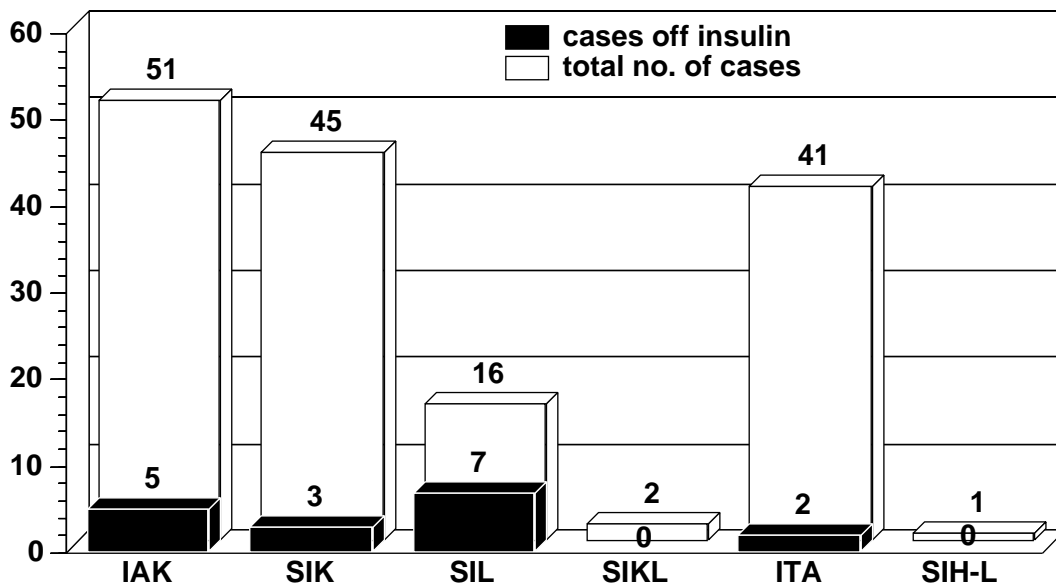
Insulin Independence* after Adult Islet Allografts and Xenografts through December 1991 according to Site of Implantation

* > 1 week



Insulin Independence* after Adult Islet Allografts and Xenografts through December 1991 according to Recipient Category

* > 1 week



ITA: Islet Transplant Alone

IAK: Islet After Kidney

SIK: Simultaneous Islet-Kidney

SIL: Simultaneous Islet-Liver

SIKL: Simultaneous Islet-Kidney-Liver

SIH-L: Simultaneous Islet-Heart-Lung

**Insulin Independence after Adult Islet Allotransplantation
according to
Site of Transplantation**

	1990 - all cases	1990 - off insulin	1991 - all cases	1991 - off insulin
liver	32	11	21	1
spleen	0	0	1	0
epiploic flap	3	0	1	0

**Insulin Independence after Adult Islet Allotransplantation
according to
Induction Immunosuppression**

	1990 - all cases	1990 - off insulin	1991 - all cases	1991 - off insulin
FK 506	17	6	5	0
ATG/ALG	13	3	11	1
OKT3	5	2	7	0

**Insulin Independence after Adult Islet
Allotransplantation according to
No. of Donors**

# of donors	1990 - all cases	1990 - off insulin	1991 - all cases	1991 - off insulin
1	17	3	12	0
2	7	4	3	0
3	7	3	4	1
≥ 4	4	1	4	0

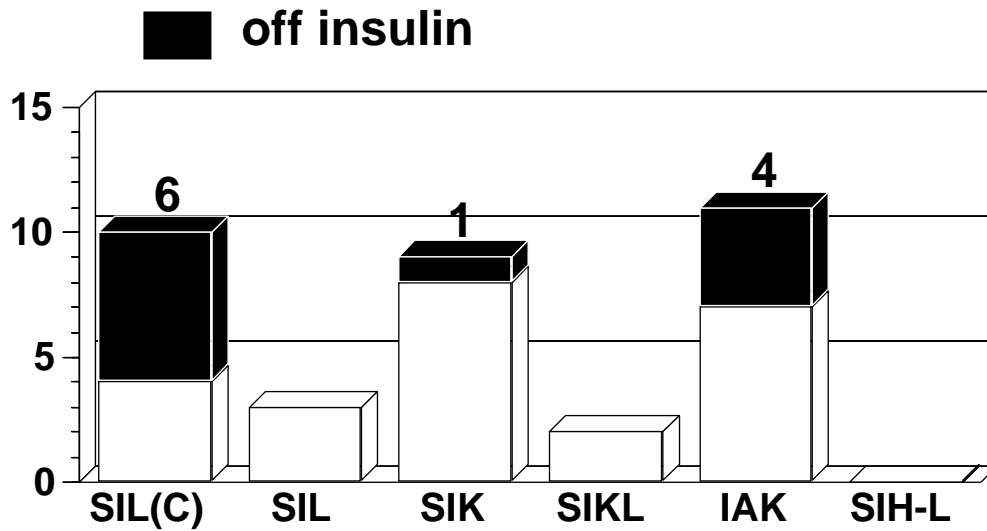
**Insulin Independence after Adult Islet Allotransplantation
according to
Preservation of Islet Tissue**

	1990 - all cases	1990 - off insulin	1991 - all cases	1991 - off insulin
fresh/cultured	30	9	16	0
fresh/cultured and cryopreserved	3	2	6	1
cryopreserved	2	0	1	0

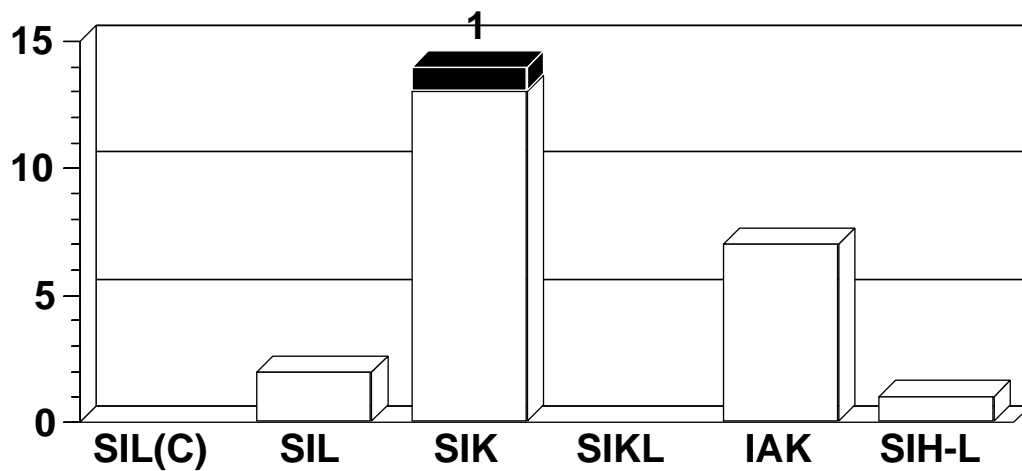
**Insulin Independence after Adult Islet Allotransplantation
according to
Purity of Islet Tissue**

Tx of	1990 - all cases	1990 - off insulin	1991 - all cases	1991 - off insulin
purified islet tissue	34	11	19	1
digest	1	0	4	0

Adult Islet Allotransplantation according to Recipient Category in 1990



Adult Islet Allotransplantation according to Recipient Category in 1991



Summary of Cases reported to be off Insulin after Adult Islet Tissue Transplantation through December 1991

Cases Without Detailed Information

Institution	Year of Tx	No. of Cases	Period of Insulin Independence	Comments
Zurich	1978	1	10th - 20th month post tx	C-peptide not determ.
Minneapolis	1977	1	2nd - 4th day post tx	insulin leakage ?
	1978	1	13th - 17th day post tx	insulin leakage ?
Genova	1979	2	3rd - 10th month post tx	C-peptide data not available
			3rd - 19th month post tx	C-peptide data not available

Insulin Independence after Simultaneous Liver and Adult Islet Transplantation Summary of Cases Through December 1991

Institution	Year of Tx	No. of Donors	No. of Islets	Site of Tx	Period of Insulin Independence	Comments
Paris	1988	1	150,000	epiploic flap	7th -> 35th month post tx [#]	hemochromatosis simult. islet, liver and kidney tx; CMV inf.
Paris	1990	1	250,000	epiploic flap	1 week [*]	
Pittsburgh	1990	1	470,000	liver	> 24 months [#]	cluster tx/FK 506
Pittsburgh	1990	2	578,000	liver	1st - 13th month [#]	cluster tx/FK 506
Pittsburgh	1990	2	258,000	liver	3rd - 8th and 14th - >22th [#] month ^{**}	
Pittsburgh	1990	1	285,000	liver	1st - 9th months	cluster tx/FK 506
Pittsburgh	1990	2	726,000	liver	1st - >13th months	cluster tx/FK 506
Pittsburgh	1990	2	332,000	liver	1st - 10th months	cluster tx/FK 506

* begin of insulin independency not mentioned

as of Jan 21, 1992

Insulin Independence after Adult Islet Transplantation into Type-I Diabetic Patients^{†‡} Summary of Cases through December 1991

Institution	Year		Site	Type	HLA match		DR	Induction	Period of Insulin Independence	Glucose Control†	
	Fresh	Cryo			ENI* 1000	AB					DR
St. Louis	1989	1/4	-	785	p.v.	IAK*	1/3	2/1	ALG (+M-Pred)	10th -25th day post tx	IV Insulin
	1990	1	+2	550 + 555	p.v.	IAK*	1/2/2	1/1/0	ALG (+M-Pred)	33th -34th day post tx	IV Insulin
Edmonton	1990	1	+4	243 + 368	p.v.	SIK*	4 (fresh) 4 (cryo)	0 (fresh) 0 (cryo)	ALG (+Pred, AZA; CsA at day 10)	69th ->575th‡ day post tx	IV Insulin
Milano	1990	1	-	586	p.v.	IAK*	0	0	ALG (+M-Pred, CsA, AZA)	110th -300th day post tx	IV Insulin
Miami	1990	3	-	1122	p.v.	IAK*	?	?	OKT3 (+M-Pred, CsA, AZA)	42th -78th day post tx	IV Insulin
	1990	3	-	1209	p.v.	IAK*	?	?	OKT3 (+M-Pred, CsA, AZA)	87th -125th day post tx	IV Insulin

* ENI: equivalent no. of islets (number of islets if all were 150 micrometers in diameter)

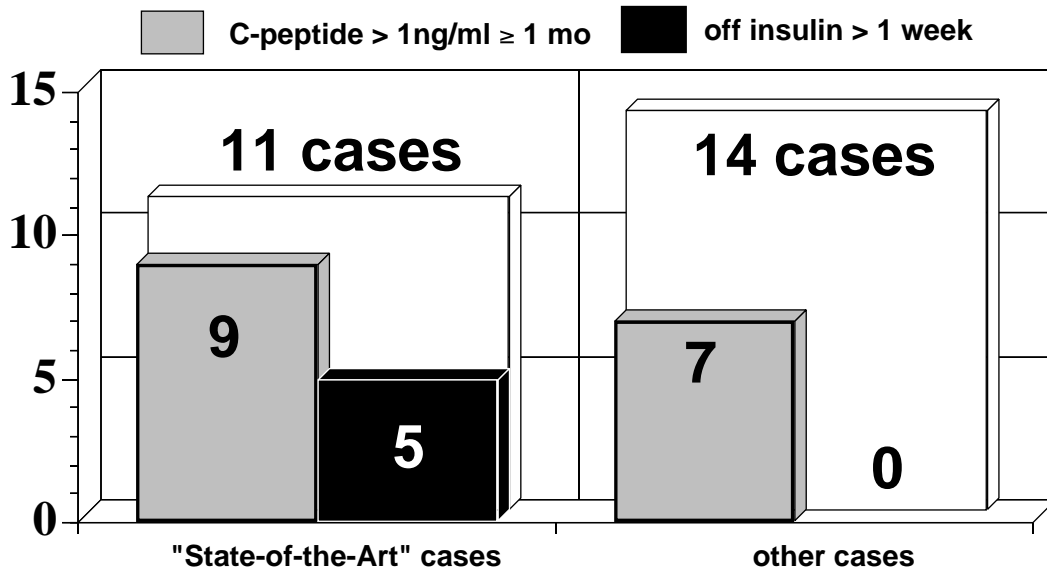
IAK: islet after kidney (islet transplantation in patients with established kidney grafts)

SIK: simultaneous islet and kidney transplantation

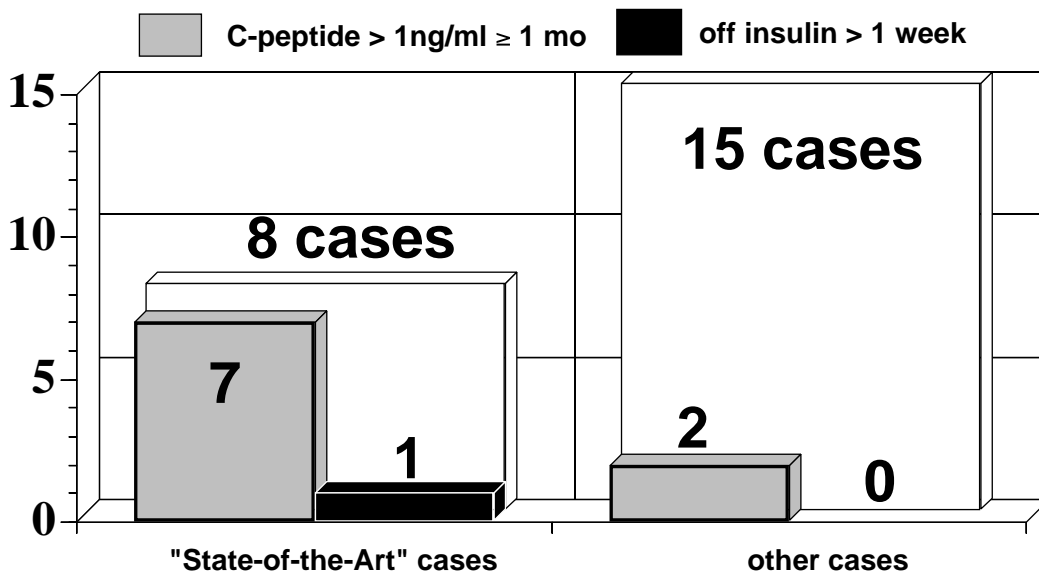
† as of Jan 20, 1992

‡ in the early posttransplant period

"State-of-the-Art" cases vs other cases in 1990
 (Type I diabetes mell., ≥ 8000 IEQ/kg; $\geq 50\%$ pure; liver; ATG, ALG or OKT3)



"State-of-the-Art" cases vs other cases in 1991
 (Type I diabetes mell., ≥ 8000 IEQ/kg; $\geq 50\%$ pure; liver; ATG, ALG or OKT3)



Prerequisites for Successful Clinical Islet Transplantation

Lessons from the Clinical Trials in 1990

- **8,000 - 10,000 purified islet equivalents (fresh or cryo)/kg (multiple donors)**
- **portal vein**
- **IAK or SIK (or SIL)**
- **HLA compatibility ?!**
- **ALG/OKT3**
- **strict blood glucose control with IV insulin in the early posttransplant period**

Accomplished in Man

- ✓ • **Insulin Independence**
- (✓) • **Prevent Rejection**
 - **Prevent Rejection in Non-Uremic Patients**
 - **Prevent Rejection in Non-Uremic Patients without Chronic Immunosuppression**
 - **Avoid Recurrence of Autoimmunity**
 - **Prevent Diabetic Complications**