

Exhibit A-1. Achievement and Loss of Insulin Independence - All Predictors

CITR 9 th Annual Report Supplemental Exhibit A-1a									
ITA univariate effects of independent predictors (rows) on specified outcomes (columns). Cox proportional hazards; blank entry means NS.	Achieve insulin independence			Lose insulin independence			Complete graft failure		
	N	HR	p	N	HR	p	N	HR	p
Era (1:1999-2002 2:2003-2006 3:2007-2010 4:2011-2014)	.	.		359	0.84	0.03	772	0.74	<0.001
Total infusions (1, 2, 3, 4, 5, 6)		772	0.71	0.001
RECIPIENT CHARACTERISTICS									
Recipient age at Tx1 (1:<35 2:≥35)	772	1.71	0.001	359	0.59	0.01	772	0.45	<0.001
Diabetes duration (1: <21 yrs 2: 21-<37 3:≥37)	.	.		317	0.83	0.09	655	0.69	0.001
Days listed (1: <60 2:6-364 3: ≥365)	
Recipient BMI at Tx1 (1:<21 2:21-<25 3: ≥25)		624	0.77	0.03
Insulin requirement at Tx1 (1: <43 U/day 2: ≥43)	709	0.69	0.005	
Insulin requirement at Tx1 (1: <0.42 U/kg/day 2:26-<0.66 3: ≥0.66)	612	0.85	0.05	
Basal C-peptide at Tx1 (1: <0.3 mg/dL 2:0.3-<0.5 3:≥0.5)		615	1.32	0.05
Fasting blood glucose at Tx1 (1:<100 mg/dL 2:100-<220 3:≥220)	
Recipient HbA1c at Tx1 (1:<6.5% 2:6.5-<8.5 3:≥8.5)	679	0.81	0.02	
Gender (0: F 1: M)	.	.		358	1.31	0.07	.	.	
Severe hypoglycemic events (0:N 1:Y)	
Insulin pump use (0:N 1:Y)	
Baseline IA2 autoantibody (0:Neg 1:Pos)	584	0.54	<0.001	
Baseline GAD autoantibody (0:Neg 1:Pos)	
Baseline Insulin autoantibody (0:Neg 1:Pos)	585	0.79	0.06	
Baseline Microinsulin autoantibody (0:Neg 1:Pos)	585	1.42	0.09	292	0.59	0.05	.	.	
Baseline any autoantibody (0:Neg 1:Pos)	
Baseline Class I PRA (0:Neg 1:Pos)	386	0.69	0.05	
Baseline Class II PRA (0:Neg 1:Pos)	266	0.53	0.04	
Baseline antihyperglycemics (0:N 1:Y)	511	1.31	0.04	.	.		511	0.70	0.07
Baseline hypertension treatment (0:N 1:Y)	524	1.33	0.03	.	.		524	0.69	0.05
Baseline antilipidemics (0:N 1:Y)		522	0.57	0.005
Baseline autonomic neuropathy (0:N 1:Y)	528	1.53	0.005	.	.		528	0.59	0.04
Baseline peripheral neuropathy (0:N 1:Y)	
Baseline retinopathy (0:N 1:Y)	
Baseline macular edema (0:N 1:Y)	
Baseline smoking (0:N 1:Y)	
Serum creatinine (1: <1.0 mg/dL 2:1.0-<1.5 3:≥1.5)	
Total bilirubin (1:<0.8 mg/dL 2:0.8-<1.1 3:≥1.1)	

Exhibit A-1. Achievement and Loss of Insulin Independence - All Predictors

CITR 9 th Annual Report Supplemental Exhibit A-1a ITA univariate effects of independent predictors (rows) on specified outcomes (columns). Cox proportional hazards; blank entry means NS.	Achieve insulin independence			Lose insulin independence			Complete graft failure		
	N	HR	p	N	HR	p	N	HR	p
Baseline CKD-eGFR (1: <50 2: ≥50)	
Baseline HDL (1: <50 mg/dL 2:50-74 3:≥75)	
Baseline LDL (1: <75 mg/dL 2:75-109 3:≥110)	563	0.83	0.03	284	1.26	0.05	563	1.30	0.03
Baseline Triglycerides (1:<30 mg/dL 2:30-64 3:≥65)	.	.		304	1.35	0.003	.	.	
Baseline total cholesterol (1:<150 mg/dL 2:150-194 3:≥195)	.	.		304	1.23	0.06	.	.	
<u>DONOR CHARACTERISTICS</u>									
Gender (0: Female 0.5: Mixed 1:Male)	612	0.75	0.06	312	0.55	0.005	.	.	
CMV (0:N 1:Y)	
Blood type A (0:N 1:Y)	
Blood type O (0:N 1:Y)	.	.		322	1.32	0.09	.	.	
Cause of death: trauma (0:N 1:Y)	.	.		313	0.76	0.08	.	.	
Cause of death: CVA (0:N 1:Y)	
Hx hypertension (0:N 1:Y)	.	.		298	1.49	0.01	.	.	
Insulin given (0:N 1:Y)	574	0.73	0.01	.	.		574	0.71	0.05
Steroids given (0:N 1:Y)	
Vasopressors given (0:N 1:Y)	
Intra-operative transfusion (0:N 1:Y)	
Pre-operative transfusion (0:N 1:Y)	
Donor age	578	0.85	0.08	
Donor BMI	
Donor ALT	
Donor AST	
Donor BUN	
Donor maximum blood glucose	505	1.19	0.06	
Donor pre-insulin blood glucose	
Donor serum amylase	
Donor serum creatinine	
Donor serum lipase	
Donor total bilirubin	500	1.23	0.04	

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	Achieve insulin independence			Lose insulin independence			Complete graft failure		
	N	HR	p	N	HR	p	N	HR	p
<u>PROCUREMENT/PROCESSING CHARACTERISTICS</u>									
Gradient type	
Liberase HI	482	1.32	0.05	245	1.45	0.07	482	2.50	<0.001
Collagenase P		482	2.15	0.02
Serva/NB1	482	0.75	0.05	245	0.64	0.04	482	0.46	0.002
Sigmablend	
Thermolysin		482	0.31	0.001
Pulmozyme		482	0.53	<0.001
PRESERVATION: : UW solution	767	1.23	0.05	.	.		767	1.53	0.007
PRESERVATION: : 2-layer	767	1.39	0.006	357	1.30	0.09	.	.	
PRESERVATION: : Celsius		767	2.24	0.010
PRESERVATION: : HTK	767	0.78	0.07	.	.		767	0.45	0.002
PRESERVATION: : Ross	.	.		357	5.19	0.02	.	.	
PRESERVATION: : Eurocollins	.	.		357	2.78	0.04	.	.	
PRESERVATION: : Other	
Processing center related (0:N 1:Y)	471	3.52	0.002	
Procurement center related (0:N 1:Y)	521	0.62	0.003	
Islets cultured (0:N 1:Y)	.	.		238	0.69	0.04	454	0.40	<0.001
Admission to death (hrs)	
Death to crossclamp (hrs)	513	1.26	0.02	
Death to recovery (hrs)	
Death to transplant (hrs)	533	0.72	0.001	.	.		533	0.72	0.01
Recovery to transplant (hrs)	367	0.80	0.03	.	.		367	0.72	0.02
Crossclamp to recovery (hrs)	.	.		203	0.75	0.05	.	.	
Cold storage (hrs)	
Culture (hrs)	454	0.83	0.02	238	0.80	0.02	454	0.60	<0.001
<u>ISLET PRODUCT CHARACTERISTICS</u>									
Viability	486	1.21	0.03	.	.		486	1.23	0.08
Stimulation index	
Purity	.	.		222	0.72	0.03	.	.	
Total beta cells (1000s)	
Total beta cells/kg recipient	

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	N	HR	p	N	HR	p	N	HR	p
Total insulin content	.	.		90	1.51	0.06	.	.	
Trapped islets (%)	
Total particles (1000s)	
Total IEs / islet count	
Packed cell volume	480	1.26	0.02	261	1.27	0.08	.	.	
Total DNA content	
Total endotoxin		368	1.26	0.10
Total endotoxin/kg recipient	.	.		192	1.32	0.04	.	.	
Total IEQs at count	510	1.29	0.06	
IEQs infused (1000s)	590	1.86	<0.001	.	.		590	0.70	0.01
IEQs infused/kg recipient	544	1.37	0.004	
IEQs infused all infusions (1000s)	590	2.13	<0.001	.	.		590	0.65	0.04
<u>IMMUNOSUPPRESSION</u>									
IL2RA	694	1.68	<0.001	326	1.32	0.09	694	1.34	0.07
TCD	694	0.77	0.03	326	0.47	<0.001	.	.	
TNF-a inhibitor	.	.		326	0.65	0.01	694	0.53	0.001
CNI	694	2.78	0.004	.	.		694	0.36	<0.001
mTOR inhibitor	694	1.95	<0.001	.	.		694	1.52	0.03
Belatacept	
DSG_	694	2.68	<0.001	326	0.34	0.07	.	.	
Efalizumab	694	5.00	<0.001	
Steroid	.	.		326	0.58	0.02	.	.	
Induction combinations (cumulated over all infusions)	683	0.72	<0.001	321	0.79	0.04	683	0.63	<0.001
IL2RA only									
TCD and/or TNFInh									
Other									
Maintenance combinations (cumulated over all infusions)	694	2.11	<0.001	
mTORInh+CNI									
Other									

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	N	HR	p	N	HR	p	N	HR	p
Era (1:1999-2002 2:2003-2006 3:2007-2010 4:2011-2014)	150	1.45	<0.001	81	0.57	0.002	150	0.48	0.002
Total infusions (1, 2, 3, 4, 5, 6)	.	.		81	0.66	0.08	150	0.45	0.003
RECIPIENT CHARACTERISTICS									
Recipient age at Tx1 (1:<35 2:≥35)	
Diabetes duration (1: <21 yrs 2: 21-<37 3:≥37)	.	.		70	0.53	0.07	.	.	
Days listed (1: <60 2:6-364 3: ≥365)	
Recipient BMI at Tx1 (1:<21 2:21-<25 3: ≥25)	
Insulin requirement at Tx1 (1: <43 U/day 2: ≥43)	142	0.51	0.03	.	.		142	2.66	0.005
Insulin requirement at Tx1 (1: <0.42 U/kg/day 2:26-<0.66 3: ≥0.66)	127	0.63	0.01	.	.		127	1.97	0.01
Basal C-peptide at Tx1 (1: <0.3 mg/dL 2:0.3-<0.5 3:≥0.5)	
Fasting blood glucose at Tx1 (1:<100 mg/dL 2:100-<220 3:≥220)	
Recipient HbA1c at Tx1 (1:<6.5% 2:6.5-<8.5 3:≥8.5)	
Gender (0: F 1: M)	
Severe hypoglycemic events (0:N 1:Y)	
Insulin pump use (0:N 1:Y)	
Baseline IA2 autoantibody (0:Neg 1:Pos)	
Baseline GAD autoantibody (0:Neg 1:Pos)		87	0.24	0.05
Baseline Insulin autoantibody (0:Neg 1:Pos)	
Baseline Microinsulin autoantibody (0:Neg 1:Pos)	
Baseline any autoantibody (0:Neg 1:Pos)	
Baseline Class I PRA (0:Neg 1:Pos)	70	3.29	0.01	
Baseline Class II PRA (0:Neg 1:Pos)	
Baseline antihyperglycemics (0:N 1:Y)	
Baseline hypertension treatment (0:N 1:Y)	
Baseline antilipidemics (0:N 1:Y)		123	0.41	0.03
Baseline autonomic neuropathy (0:N 1:Y)	
Baseline peripheral neuropathy (0:N 1:Y)	
Baseline retinopathy (0:N 1:Y)	
Baseline macular edema (0:N 1:Y)	
Baseline smoking (0:N 1:Y)	76	5.13	0.03	
Serum creatinine (1: <1.0 mg/dL 2:1.0-<1.5 3:≥1.5)	147	0.71	0.02	
Total bilirubin (1:<0.8 mg/dL 2:0.8-<1.1 3:≥1.1)	.	.		65	1.85	0.01	.	.	

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CITR 9 th Annual Report Supplemental Exhibit A-1b <u>IAK</u> univariate effects of independent predictors (rows) on specified outcomes (columns). Cox proportional hazards; blank entry means NS.	Achieve insulin independence			Lose insulin independence			Complete graft failure		
	N	HR	p	N	HR	p	N	HR	p
Baseline CKD-eGFR (1: <50 2: ≥50)	
Baseline HDL (1: <50 mg/dL 2:50-74 3:≥75)	108	0.66	0.02	
Baseline LDL (1: <75 mg/dL 2:75-109 3:≥110)	
Baseline Triglycerides (1:<30 mg/dL 2:30-64 3:≥65)	.	.		70	1.58	0.009	.	.	
Baseline total cholesterol (1:<150 mg/dL 2:150-194 3:≥195)		119	1.83	0.02
<u>DONOR CHARACTERISTICS</u>									
Gender (0: Female 0.5: Mixed 1:Male)	.	.		69	0.44	0.09	.	.	
CMV (0:N 1:Y)	
Blood type A (0:N 1:Y)		128	1.99	0.07
Blood type O (0:N 1:Y)	
Cause of death: trauma (0:N 1:Y)	
Cause of death: CVA (0:N 1:Y)	
Hx hypertension (0:N 1:Y)	
Insulin given (0:N 1:Y)	.	.		52	0.51	0.08	83	0.41	0.08
Steroids given (0:N 1:Y)	70	1.99	0.05	
Vasopressors given (0:N 1:Y)	
Intra-operative transfusion (0:N 1:Y)	
Pre-operative transfusion (0:N 1:Y)	.	.		49	0.29	0.001	.	.	
Donor age	
Donor BMI	
Donor ALT	.	.		62	0.23	0.001	99	0.23	0.003
Donor AST	98	0.64	0.02	62	0.62	0.05	.	.	
Donor BUN	.	.		63	0.51	0.02	.	.	
Donor maximum blood glucose	
Donor pre-insulin blood glucose	
Donor serum amylase	
Donor serum creatinine	
Donor serum lipase	
Donor total bilirubin	.	.		62	1.57	0.09	.	.	

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	N	HR	p	N	HR	p	N	HR	p
<u>PROCUREMENT/PROCESSING CHARACTERISTICS</u>									
Gradient type	
Liberase HI	.	.		55	16.1	0.006	90	5.62	0.09
Collagenase P	
Serva/NB1	.	.		55	0.27	0.008	90	0.29	0.10
Sigmablend	
Thermolysin		90	3.23	0.06
Pulmozyme	
PRESERVATION: : UW solution	
PRESERVATION: : 2-layer	
PRESERVATION: : Celsius	
PRESERVATION: : HTK	
PRESERVATION: : Ross	
PRESERVATION: : Eurocollins		147	25.1	<0.001
PRESERVATION: : Other	
Processing center related (0:N 1:Y)	
Procurement center related (0:N 1:Y)	
Islets cultured (0:N 1:Y)	
Admission to death (hrs)	
Death to crossclamp (hrs)	
Death to recovery (hrs)	
Death to transplant (hrs)	
Recovery to transplant (hrs)	
Crossclamp to recovery (hrs)	
Cold storage (hrs)	
Culture (hrs)	
<u>ISLET PRODUCT CHARACTERISTICS</u>									
Viability	81	1.54	0.04	53	1.60	0.08	.	.	
Stimulation index	
Purity	
Total beta cells (1000s)	
Total beta cells/kg recipient	

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IAK univariate effects of independent predictors (rows) on specified outcomes (columns). Cox proportional hazards; blank entry means NS.	Achieve insulin independence			Lose insulin independence			Complete graft failure		
	N	HR	p	N	HR	p	N	HR	p
Total insulin content	17	0.34	0.04	
Trapped islets (%)	
Total particles (1000s)	85	2.48	0.04	53	0.15	<0.001	.	.	
Total IEs / islet count	
Packed cell volume		74	0.59	0.07
Total DNA content	
Total endotoxin	
Total endotoxin/kg recipient	
Total IEQs at count	80	1.94	0.02	48	0.37	0.02	.	.	
IEQs infused (1000s)	123	1.58	0.08	.	.		123	0.42	<0.001
IEQs infused/kg recipient	120	1.80	0.008	.	.		120	0.54	0.03
IEQs infused all infusions (1000s)		123	0.40	0.02
<u>IMMUNOSUPPRESSION</u>									
IL2RA	134	1.81	0.05	.	.		134	0.41	0.01
TCD	
TNF-a inhibitor	134	1.79	0.04	
CNI	
mTOR inhibitor	134	1.60	0.07	.	.		134	0.38	0.006
Belatacept	
DSG_	
Efalizumab	
Steroid	
Induction combinations (cumulated over all infusions)	134	0.72	0.05	.	.		134	1.66	0.02
IL2RA only									
TCD and/or TNFαInh									
Other									
Maintenance combinations (cumulated over all infusions)	134	1.60	0.07	.	.		134	0.38	0.006
mTORInh+CNI									
Other									