Transplantation: Year in Review

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University of Colorado
Outline:

• Kidney and Pancreas Transplantation: Outcomes and Trends
• The living donor
• SPK vs living donor transplant for T1DM
• Immunosuppression: the old and the new
• Desensitization and HLA antibodies
The waiting list for kidney transplant continues to grow, with a substantial increase in the number of "inactive" candidates.

- **2002 policy**: Patients gain waiting time when "inactive", now listing of obese, active malignancy, etc more common

The wait list mortality rate remains ~6.5%
Deceased donation:

- Overall growth due to increase in DCD (deceased by cardiac death) donor use.

Living donation:

- Decreasing since 2004.
Kidney: Graft and Patient Survival rates

<table>
<thead>
<tr>
<th></th>
<th>5y Graft Survival</th>
<th>5y Patient Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney (SCD)</td>
<td>70.7</td>
<td>83.3</td>
</tr>
<tr>
<td>Kidney (ECD)</td>
<td>55.3</td>
<td>69.5</td>
</tr>
<tr>
<td>Kidney (LD)</td>
<td><strong>81.1</strong></td>
<td>90.6</td>
</tr>
</tbody>
</table>
SPK: “flat” growth over the last 5 years

Simultaneous Pancreas Kidney (SPK) Transplant Trends 1997-2006

Adapted from SRTR Annual Report 2007 tables 1.3, 1.7, and 8.2

Wiseman AC, ACKD 2009
PAK: reduction in transplants despite growing waiting list

Pancreas After Kidney Transplant (PAK) Trends 1997-2006

Adapted from SRTR Annual Report 2007 tables 1.3, 1.7, and 7.2

Wiseman AC, ACKD 2009
Pancreas:
Patient and Graft Survival rates

**Patient Survival:**

<table>
<thead>
<tr>
<th></th>
<th>1y</th>
<th>10y</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPK</td>
<td>95%</td>
<td>70%</td>
</tr>
<tr>
<td>PAK</td>
<td>98%</td>
<td>65%</td>
</tr>
</tbody>
</table>

**Pancreas Graft Survival:**

<table>
<thead>
<tr>
<th></th>
<th>1y</th>
<th>10y</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPK</td>
<td>86%</td>
<td>53%</td>
</tr>
<tr>
<td>PAK</td>
<td>77%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Transplant trends summary:

- Growing waiting list is driven by an increase in number of patients listed “inactive”
- Deceased donor growth fueled by utilization of DCD kidneys
- Pancreas-after-kidney (PAK) transplant losing favor (worse outcomes than SPK)
- Living donation rates are falling
The living donor
Epidemiologic studies suggest unilateral nephrectomy is safe

WW II US servicemen with NTX compared to military without NTX

Observed vs expected survival in kidney donors-Sweden

KI 1993; 43:110

Transplantation 1997; 64: 976
“Medical Risks in Living Kidney Donors: Absence of Proof is not Proof of Absence”

• All studies retrospective (selection bias)
• Inadequate sample sizes to show differences
• Control group should not be “general population”
• Race and ethnicity must be accounted for
“Long-term consequences of kidney donation”

- 3698 kidney donors at U of Minnesota 1963-2007
- Assessment of mortality based upon SSA Death Master File
- Random selection of donors (at 3 year intervals from donation year) to select 5-10% from each 3y era was initiated in 2003
- 80% successfully contacted, 255 of whom underwent BP, GFR (iohexol) and proteinuria (urine prot/cr ratio) assessment and QOL assessment (SF-36)
- Matched controls were from the NHANES study by age, sex, race, ethnicity, BMI

NEJM 2009; 360: 459
Survival of kidney donors

- 3404 of 3698 were alive at the end of the study
- 268 died (196 prior to study period, 72 after)
- ESRD in 11 donors
- Cr measurements 1-10y prior to death in 232 of the 268, mean 1.2 mg/dl, no history of dialysis or transplantation

NEJM 2009; 360: 459
GFR and Proteinuria following living kidney donation

- 255 donors, mean 12.2 years from donation
- 86% had GFR>60, none with GFR<30
- 11.5% microalbuminuria, 1.2% macroalbuminuria

NEJM 2009; 360: 459
Additional health parameters, donors vs NHANES

- Lower BP
- Similar proteinuria
- Lower FBG
- Lower TG and LDL
- Lower cancer

Due to NHANES smoking???

<table>
<thead>
<tr>
<th>Variable</th>
<th>Kidney Donors (N=255)</th>
<th>Controls† (N=255)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>52.9±9.9</td>
<td>52.9±9.9</td>
<td></td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>62.1</td>
<td>61.8</td>
<td></td>
</tr>
<tr>
<td>White race (%)</td>
<td>99.2</td>
<td>99.2</td>
<td></td>
</tr>
<tr>
<td>Body-mass index &gt;30 (%)‡</td>
<td>29.3</td>
<td>29.3</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic (mm Hg)</td>
<td>121.8±14.6</td>
<td>125.9±19.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Diastolic (mm Hg)</td>
<td>73.0±8.9</td>
<td>71.0±16.5</td>
<td>0.07</td>
</tr>
<tr>
<td>Systolic ≥140 mm Hg or diastolic ≥90 mm Hg (%)</td>
<td>14.4</td>
<td>18.7</td>
<td>0.19</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)§</td>
<td>63.7±11.3</td>
<td>81.6±18.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary albumin-to-creatinine ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural-log–transformed value</td>
<td>1.55±1.2</td>
<td>2.10±1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;0.03 (%)</td>
<td>9.1</td>
<td>8.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.7±1.2</td>
<td>14.5±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>90.9±11.9</td>
<td>102.8±33.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>186.2±33.1</td>
<td>205.2±41.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>124.5±95.6</td>
<td>174.3±182.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (mg/dl)</td>
<td>50.4±16.5</td>
<td>54.5±16.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinical conditions (%)¶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.1</td>
<td>5.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Cancer</td>
<td>8.2</td>
<td>14.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>4.3</td>
<td>3.9</td>
<td>0.81</td>
</tr>
<tr>
<td>Cerebrovascular accident or transient ischemic attack</td>
<td>0.4</td>
<td>1.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Use of antihypertensive drugs (%)¶</td>
<td>24.7</td>
<td>28.8</td>
<td>0.83</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>14.5</td>
<td>21.5</td>
<td>0.03</td>
</tr>
</tbody>
</table>

NEJM 2009; 360: 459
Cardiovascular disease and hypertension risk in living kidney donors: An analysis of health administrative data in Ontario, CA

- 1278 living donors vs 6359 randomly selected controls from 1993-2005
  - Controlled for age, sex, income, no CV/DM/renal history, no overnight hospitalizations, >2 but <10 outpatient primary care visits

- Primary outcome: composite of death + CV event
- Secondary outcome: diagnosis of hypertension

**Results** (Mean f/u 6.2 years):

<table>
<thead>
<tr>
<th></th>
<th>Donors</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome:</td>
<td>1.3%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Dx HTN:</td>
<td>16.3%*</td>
<td>11.9%</td>
</tr>
</tbody>
</table>

*p <0.001*
Paired Donor Exchange and Altruistic Donors

- Evolved as a means to transplant patients with incompatible blood types or +cross matches with otherwise acceptable donors
  - Alliance for Paired Exchange
  - North American Paired Donation Network
  - New England Program for Kidney Exchange

- Altruistic donors can expand paired exchange by providing a “starting point” for transplanting incompatible pairs
"Never-Ending (Nonsimultaneous, Extended) Altruistic-Donor Altruistic Donor Chains"

The difference between conventional and NEAD chain: no harm in “backing out”
"A Nonsimultaneous, Extended, Altruistic-Donor Chain"

10 transplants over 9 months, no backing out…
Live donor kidney or SPK for the patient with Type 1 diabetes?
For T1DM, what to choose: SPK or living donor kidney alone?

• SPK is considered the treatment of choice for patients with type 1 diabetes and kidney dysfunction (DM1), however...

• Morbidity associated with pancreas transplantation leads many patients to select kidney alone (KA) rather than SPK
“Living donor kidney versus simultaneous pancreas-kidney transplant in type I diabetics: an analysis of the OPTN/UNOS database”

2000-2007: T1DM receiving first transplant were studied (SPK, LDKA, DDKA)

Multivariate Analysis: Lower risk of graft loss (HR 0.71) or death (HR 0.78) with LDK

Conclusion: LDKT utilization should be considered in all T1DM with an available donor

Young et al. CJASN 2009; 4: 845-852
“Metabolic control improves long-term renal allograft and patient survival in type 1 diabetes”

In patients with T1DM and kidney function at 10 years post-transplant: Those with SPK had the greatest survival from years 10-18, dependent upon pancreas function

Morath C et al, JASN 2008; 19: 1558
“12 Month Pancreas Graft Function Significantly Influences Survival Following Simultaneous Pancreas-Kidney Transplantation (SPK)”

Retrospective analysis of all patients transplanted from the SPK waitlist from 1997-2005

9630
SPK Waitlisted Patients Transplanted 1997-2005

7952
SPK

616
DD KA

1062
LD KA

12 month survivors with functioning kidney grafts*
SPK =86%
DD KA=84%  LD KA= 85%

6486
SPK, P+ Functioning Panc

371
SPK, P- Failed Pancreas

520
DD KA

904
LD KA

*Excluded death, kidney graft loss, LTFU, <12mo FU

Weiss AS et al, CJASN 2009; 4: 988
84 Month Survival

SPK, P+: 72.0%
LD KA: 63.6%
SPK, P-: 59.8%
DD KA: 49.7%

84 Month Survival
P-value for Log-rank test of equality over strata < 0.0001

Weiss AS et al, CJASN 2009; 4: 988
84 Month Survival

SPK, P+: 88.6%
LD KA: 80.0%
SPK, P-: 73.9%
DD KA: 64.8%

P-value for Log-rank test of equality over strata < .0001

Weiss AS et al, CJASN 2009; 4: 988
Conclusions: SPK or LD KA for T1DM?

• SPK: Early mortality followed by a “Catch up”:
  – LD KA and SPK survival differences of 1-2% in the first year due to excess mortality with SPK, but similar outcomes by 6 years

• A functional pancreas leads to better outcomes with SPK vs LD KA
  – For SPK recipients with functioning pancreas at 12 months, or 10 years: significantly better patient survival than LD KA

• To your patient: go for SPK if you can accept the ~1-2% increased mortality at 1 year and the 15% risk of early pancreas failure
Immunosuppression: What’s new?
The Symphony Trial: Defining today’s “Gold Standard”

• 12-month randomized open-label multicenter trial of 1645 KTX
• 4 Treatment arms: all receive Basiliximab induction, MMF/Prednisone
  – CSA 150-300 ng/ml x 3 months, then 100-200 ng/ml
  – CSA 50-100 ng/ml
  – TAC 3-7 ng/ml
  – SRL 4-8 ng/ml

At 12 months:

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Acute Rejection (%)</th>
<th>Graft Survival (%)</th>
<th>GFR (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSA “standard”</td>
<td>25.8</td>
<td>89.3</td>
<td>57.1</td>
</tr>
<tr>
<td>CSA “low”</td>
<td>24.0</td>
<td>93.1</td>
<td>59.4</td>
</tr>
<tr>
<td>TAC “low”</td>
<td>12.3*</td>
<td>94.2*</td>
<td>65.4*</td>
</tr>
<tr>
<td>SRL “low”</td>
<td>37.2</td>
<td>89.3</td>
<td>56.7</td>
</tr>
</tbody>
</table>

NEJM 2007; 357: 2562-75
Current maintenance immunosuppression trends
Hazards of Immunosuppression

- Hypertension
- Glucose intolerance
- Bone disease
- Infection
- Hyperlipidemia
- Cosmetic
- Nephrotoxicity
- Malignancy
- Eye disorders
- Weight gain

CNI nephrotoxicity (%)

Years after transplant:


Patient preference- discontinue:

Prasad GV et al, Clin Transplant 2003: 17: 135
How often are medications eliminated?

% of patients taking prednisone or CNI at discharge from transplant and at 12 months.
The CONVERT study: Can CNIs be withdrawn later after transplant to preserve renal function?

CNI* (n=830) 6 months to 120 months posttransplant

Randomization
Mean of 3.2 years after kidney transplantation

CNI*
(n=275)
Baseline GFR
STRATUM 1: 20-40 mL/min: n=29
STRATUM 2: >40 mL/min: n=246

Sirolimus*
(n=555)
Baseline GFR
STRATUM 1: 20-40 mL/min: n=58
STRATUM 2: >40 mL/min: n=497

*Concomitant medications included mycophenolate mofetil (MMF) or azathioprine (AZA), and corticosteroids.

The CONVERT study: Late conversion to a sirolimus-based regimen showed no renal function benefit in the overall population (ITT Analysis)

### Baseline GFR 20–40 mL/min

<table>
<thead>
<tr>
<th></th>
<th>SRL conversion</th>
<th>CNI continuation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12 month Nankivell GFR (mL/min)</strong></td>
<td>24.56±2.42</td>
<td>27.24±3.71</td>
<td>0.575</td>
</tr>
<tr>
<td><strong>24 month Nankivell GFR (mL/min)</strong></td>
<td>21.73±3.15</td>
<td>17.88±4.84</td>
<td>0.538</td>
</tr>
</tbody>
</table>

### Baseline GFR > 40 mL/min

<table>
<thead>
<tr>
<th></th>
<th>SRL conversion</th>
<th>CNI continuation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12 month Nankivell GFR (mL/min)</strong></td>
<td>59.04±0.89</td>
<td>57.73±1.1</td>
<td>0.278</td>
</tr>
<tr>
<td><strong>24 month Nankivell GFR (mL/min)</strong></td>
<td>53.73±1.13</td>
<td>52.14±1.41</td>
<td>0.301</td>
</tr>
</tbody>
</table>

**U_{Pr/Cr} in patients with baseline GFR >40 mL/min**

The CONVERT study

Baseline GFR >40 mL/min

Baseline GFR >40 mL/min and \( U_{Pr/Cr} < 0.11 \)

* \( P < 0.001 \)

Proteinuria – potential mechanisms

• The mechanism of proteinuria observed with sirolimus use is unknown:
  – Release of CsA-induced afferent arteriolar vasoconstriction may play a role\(^1\)
  – Glomerular injury occurring following acute rejection may further contribute to glomerular proteinuria\(^1\)
  – Sirolimus may induce proteinuria through podocyte injury and antagonism of VEGF\(^2\)

Steroid use in solid organ transplant has declined significantly

Early Corticosteroid Withdrawal:
Results of the ONLY long-term, randomized, double-blind, multi-center trial

Low immunologic risk, first kidney transplant

Induction therapy*, TAC/MMF maintenance, Corticosteroids for 7 days
(n=397)

Corticosteroid Withdrawal
(n=197-191)

Thymoglobulin: 65.4%
IL-2Ra: 34.5%

Corticosteroid Maintenance#
(n=200-195)

Thymoglobulin: 69.7%
IL-2Ra: 30.3%

7 days after kidney transplantation

*Induction therapy was left to the investigator and could include Thymoglobulin 1.5 mg/kg x 4d or IL-2Ra (Simulect/Daclizumab)

#Corticosteroid maintenance: Day 8-14: 0.4 mg/kg, Day 15-29: 0.3 mg/kg, Day 30-89: 0.2 mg/kg, Day 90-119: 0.15 mg/kg, Day 120-180: 0.1 mg/kg, Day>180: 5 mg/d

Prednisone-free immunosuppression in Kidney Transplant

- 5y follow-up:
  - Similar graft/patient survival rates with or without prednisone
  - Similar CrCl at 5 years when assessed by quartiles

Impact of Steroid Withdrawal on Incidence of Acute Rejection

- Higher acute rejection rate, particularly with IL-2ra induction
- Higher incidence of chronic allograft injury in “withdrawal” cohort

Additional Outcomes

No difference in incidence of infections (including CMV, BKV), HTN, cholesterol, Framingham risk score, cataract formation.

Bone disease

Weight Gain

Conclusions

The best study we will ever have examining steroid withdrawal
- 5 year data, randomized, prospective, double blind

- 5 year outcomes (“primary endpoint”) comparable
  - Overall GFR comparable
  - No difference in HTN, weight gain, LDL/total cholesterol, Framingham CV risk scores, malignancy

- Some differences in “secondary analyses”:
  - Triglycerides, bone disease, insulin use vs acute rejection, chronic allograft nephropathy incidence
  - Does 5 mg of prednisone account for these differences?
Current thoughts on CNI withdrawal, Prednisone withdrawal

**CNI withdrawal:**
- At outset of transplant (avoidance):  
  - Acute rejection higher, large trials do not support  
  - New agents (belatacept?) may make this possible
- Within 3-12 months after transplant:  
  - Improved GFR despite increased risk of acute rejection in small and interim trials
- “Late” after transplant:  
  - No benefit, large trials do not support

**Early Steroid Withdrawal:**
- 5 year outcomes (“primary endpoint”) comparable, higher acute rejection, no difference in HTN, weight gain, LDL/total cholesterol, Framingham CV risk, malignancy  
- “We believe the benefits of corticosteroid withdrawal in kidney recipients to be overstated. The recent study by Woodle and colleagues demonstrates only a modest impact of CSWD on corticosteroid-associated side effects along with a potential downside of CSWD in terms of a modestly higher rate of CAN. A more cautious conclusion would be that CSWD is marginally beneficial at best, and potentially harmful compared with long-term, low-dose CCS use.”  
Pre-transplant desensitization for positive crossmatch/donor specific HLA antibodies

<table>
<thead>
<tr>
<th>Cedars Sinai</th>
<th>Mayo Clinic</th>
<th>Johns Hopkins</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients are screened for IVIG inhibition in</td>
<td>• Pre-transplant: TPE/IVIg x ≥4, +Rituxan x 1,</td>
<td>• Pre-transplant: Rituxan x 1-4, then TPE/CMVIg x</td>
</tr>
<tr>
<td>vitro…if successful…</td>
<td>+Thymoglobulin</td>
<td>2-20, TAC/MMF, +/- Splenectomy</td>
</tr>
<tr>
<td>• IVIG given 2g/kg monthly x 4 pre-transplant</td>
<td>• Post-transplant DSA monitoring and repeat</td>
<td>• Post-transplant DSA monitoring and repeat</td>
</tr>
<tr>
<td>• Induction + 3-drug therapy</td>
<td>TPE/IVIg</td>
<td>TPE/IVIg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Induction + 3-drug therapy</td>
</tr>
</tbody>
</table>

IVIg + Rituximab for desensitization

- IVIg 2g/kg x2: d 0, 30
- Rituxan 1g x2: d 7, 20

- 20 patients (on waiting list for 5-27 years), 16 ultimately transplanted within 6 months of therapy

- 8 with AR
- 3 with C4d+ AHR
- 1 graft loss

Vo A et al, NEJM 2008; 359 :242
“Positive cross-match living donor kidney transplantation: Longer term outcomes”

41 XM+ patients from 1999-2006 underwent desensitization with TPE/IVIg then LD KT{x, compared to 41 age/sex/era/race-matched controls:

Graft survival: 1y 5y
XM+  89%  69%
Controls  98%  81%

“ABO incompatible renal transplantation: A paradigm ready for broad implementation”

- 60 ABOi kidney transplants at JHH 1999-2007, with a planned TPE/IVIg preconditioning regimen and quadruple immunosuppression

No cases of hyperacute rejection, 11 cases of AMR in 10 patients

**TABLE 1.** The number of planned pre- and posttransplant PP/IVIg treatments correlate with the starting isohemagglutinin titer

<table>
<thead>
<tr>
<th>Starting isohagglutinin AHG titer</th>
<th>Pretransplant PP/IVIg treatments</th>
<th>Posttransplant PP/IVIg treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>16–32</td>
<td>3</td>
<td>2–3</td>
</tr>
<tr>
<td>64</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>128</td>
<td>5–6</td>
<td>4</td>
</tr>
<tr>
<td>256</td>
<td>7–8</td>
<td>4</td>
</tr>
<tr>
<td>512</td>
<td>9–10</td>
<td>5</td>
</tr>
<tr>
<td>&gt;512</td>
<td>&gt;10</td>
<td>6</td>
</tr>
</tbody>
</table>

PP, plasmapheresis; AHG, anti-human globulin.

**TABLE 4.** Patient and graft survival among 60 ABOi kidney transplant recipients transplanted at the Johns Hopkins Hospital between 1999 and 2007

<table>
<thead>
<tr>
<th>ABOi cohort</th>
<th>Years posttransplant</th>
<th>Graft survival (%)</th>
<th>Patient survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>98.3</td>
<td>96.3</td>
<td></td>
</tr>
<tr>
<td>3 yr</td>
<td>92.9</td>
<td>96.3</td>
<td></td>
</tr>
<tr>
<td>5 yr</td>
<td>88.7</td>
<td>89.4</td>
<td></td>
</tr>
</tbody>
</table>

Montgomery RA et al, Transplantation 2009; 87: 1246
Bortezomib (Velcade): A proteosome inhibitor with a unique ability to inhibit plasma cells

- Pro-apoptotic actions upon plasma cells, T cells
- Approved for treatment of multiple myeloma
Bortezomib in the treatment of acute humoral rejection

- 6 patients with cellular and humoral rejection (C4d+, donor-specific antibodies) refractory to TPE/Rituxan/Thymoglobulin

- Bortezomib 1.3 mg/m² x 4 doses reversed rejection and reduced DSA levels

Everly M et al, Transplantation 2008; 86: 1754
Bortezomib for the treatment of De-Novo Donor-Specific Antibody (DSA) formation

11 patients with de-novo anti-HLA Ab formation, detected within 4 months post- tx:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr), Gender</th>
<th>Antigen MM</th>
<th>Post-Txp baseline Scr</th>
<th>Scr at Ab appearance</th>
<th>Scr at FU</th>
<th>Primary Ab*</th>
<th>Secondary Ab*</th>
<th>POD of primary Ab appearance</th>
<th>Pre-Bortezomib Ab MFI</th>
<th>Peak Ab MFI</th>
<th>Post-Bortezomib Ab MFI</th>
<th>Ab MFI at last FU</th>
<th>Number of Bortezomib cycles</th>
<th>Time to resolution (d)</th>
<th>Days of Post-Bortezomib FU</th>
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* Number in parentheses is the broad antibody specificity (serologic equivalent).

b MFI of Primary antibody (other antibodies may have higher peak levels that occurred after primary antibody appearance). All MFIs are rounded to the nearest 100.

Txp, transplant; M, Male; MM, mismatch; Ab, antibody; Scr, serum creatinine; POD, postoperative day; MFI, mean fluorescence intensity; FU, follow-up.

Trivedi H et al, Transplantation 2009; 87: 1555
Successful DSA Abrogation following 1 cycle of Bortezomib

Trivedi H et al, Transplantation 2009; 87: 1555
Failure to Suppress DSA with Bortezomib

Trivedi H et al, Transplantation 2009; 87: 1555
Conclusions:

• Living donation: decreasing rates despite safety, innovative strategies

• SPK vs LD KA: Pancreas is protective if you make it through the first year

• Immunosuppression: CNI withdrawal in established grafts of little benefit, steroid withdrawal is of questionable benefit/potential harm

• +Crossmatch Transplants: desenstization works, but plenty of treatments, rejection, and graft outcomes similar to deceased donors
  – Bortezomib may play future role in elimination/treatment of HLA antibody