What is hot in clinical solid organ transplantation

Marcelo Cantarovich
McGill University Health Center
Budapest Nephrology School
Sept 30, 2014

Valle de la Luna, San Juan, Argentina
Disclosure

• Astellas and Novartis
  – Educational grant (Transplant Program)
  – Support for database (Transplant Program)
2013 - 2/2014 literature scan
All organs

- Am J Transplant
- Transplantation
- Transplant Int
- J Heart Lung Transplant
- Liver Transplantation
- Kidney Int
- J Am Soc Nephrol
- Clin J Am Soc Nephrol
- JAMA
- Ann Int Med
- Lancet
- N Engl J Med
Outline

• Donor source / organ preservation

• Immunosuppression

• Complications
Outline

• Donor source / organ preservation
  • Immunosuppression
• Complications
Risk of End-Stage Renal Disease Following Live Kidney Donation

Abimereki D. Muzaale, MD, MPH; Allan B. Massie, PhD; Mei-Cheng Wang, PhD; Robert A. Montgomery, MD, DPhil; Maureen A. McBride, PhD; Jennifer L. Wainright, PhD; Dorry L. Segev, MD, PhD

Johns Hopkins University

A Cumulative incidence of end-stage renal disease

Figure 3. Estimated Lifetime Risk of End-Stage Renal Disease in Matched But Unscreened Nondonors, Live Kidney Donors, and Matched Healthy Nondonors

Nondonors were identified among participants in the third National Health and Nutrition Examination Survey. Healthy nondonors were a subset of unscreened nondonors. Comparisons were made by bootstrapping.
Risk of End-Stage Renal Disease Following Live Kidney Donation

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B Cumulative incidence of end-stage renal disease by race/ethnicity

[Graphs showing cumulative incidence of end-stage renal disease for Black, Hispanic, and White populations, with numbers at risk for live donors and non-donors over years.]
Risk of End-Stage Renal Disease Following Live Kidney Donation

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Johns Hopkins University

Figure 2. Cumulative Incidence of End-Stage Renal Disease in Live Kidney Donors

A) Age
B) Race
C) Relationship to donor
D) Years

No. at risk
Age, y
≥60
50-59
40-49
18-39

50-59 y vs ≥60 y, P = .50
<50 y vs ≥60 y, P < .001
18-39 y vs 40-49 y, P = .06

Race
Black men vs black women, P = .20
Black vs white, P < .001
White men vs white women, P = .008

Relationship to donor
Biologically related
Biologically unrelated

Years
No. at risk
Related
Unrelated

1994-1997
1998-2001
2002-2005
2006-2009
2010-2011
Quantification of the Early Risk of Death in Elderly Kidney Transplant Recipients

- 25468 KTx pts >65 yrs
- USRDS 1995 - 2007

- ESRD due to diabetes = High Risk
- CVC risk factors
  - IHD, CHF, CVA, PVD

0 CVC risk factor
n=11 425

1 CVC risk factor
n=3038

2 CVC risk factors
n=11 005
Impact of Early Graft Function on 10-Year Graft Survival in Recipients of Kidneys From Standard- or Expanded-Criteria Donors

Nassima Smail, Jean Tchervenkov, Steven Paraskevas, Dana Baran, Istvan Mucsi, Mazen Hassanain, Prosanto Chaudhury, and Marcelo Cantarovich

McGill University Health Center

A. Death censored graft survival

<table>
<thead>
<tr>
<th>Time posttransplant (years)</th>
<th>Percent</th>
<th>SCD</th>
<th>ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>90</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P = 0.01

Subjects at risk
- SCD: 279, 247, 212, 108
- ECD: 237, 208, 159, 61

B. Death censored graft survival in patients with IGF

<table>
<thead>
<tr>
<th>Time posttransplant (years)</th>
<th>Percent</th>
<th>SCD</th>
<th>ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
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<tr>
<td>1</td>
<td>90</td>
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<td>3</td>
<td>80</td>
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<td>5</td>
<td>70</td>
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<td></td>
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<tr>
<td>10</td>
<td>60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P = 0.17

Subjects at risk
- SCD: 166, 158, 139, 72
- ECD: 119, 112, 90, 38

C. Death censored graft survival in patients with SGF

<table>
<thead>
<tr>
<th>Time posttransplant (years)</th>
<th>Percent</th>
<th>SCD</th>
<th>ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P = 0.04

Subjects at risk
- SCD: 54, 50, 44, 24
- ECD: 43, 41, 30, 9

D. Death censored graft survival in patients with DGF

<table>
<thead>
<tr>
<th>Time posttransplant (years)</th>
<th>Percent</th>
<th>SCD</th>
<th>ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>90</td>
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<td>3</td>
<td>80</td>
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<td>70</td>
<td></td>
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<tr>
<td>10</td>
<td>60</td>
<td></td>
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</tr>
</tbody>
</table>

P = 0.12

Subjects at risk
- SCD: 59, 44, 34, 16
- ECD: 75, 61, 44, 17
Does Expanded Criteria Donor Status Modify the Outcomes of Kidney Transplantation From Donors After Cardiac Death?

S. K. Singh and S. J. Kim

<table>
<thead>
<tr>
<th>Non-ECD/Non-DCD (N = 50,242)</th>
<th>Non-ECD/DCD (N = 4,840)</th>
<th>ECD/Non-DCD (N = 12,172)</th>
<th>ECD/DCD (N = 562)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNF</td>
<td>0.7%</td>
<td>0.9%</td>
<td>1.5%</td>
</tr>
<tr>
<td>DGF</td>
<td>21.3%</td>
<td>39.6%</td>
<td>30.5%</td>
</tr>
</tbody>
</table>

Table 3: Hazard ratios for DCD versus non-DCD kidney transplant recipients across ECD subgroups for total graft failure, death-censored graft failure and death with graft function.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ECD status</th>
<th>Hazard ratio for DCD vs. Non-DCD (95% CI)</th>
<th>p-Value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total graft failure</td>
<td>Non-ECD</td>
<td>1.07 (1.01–1.15)</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>ECD</td>
<td>1.21 (1.04–1.40)</td>
<td></td>
</tr>
<tr>
<td>Death-censored graft failure</td>
<td>Non-ECD</td>
<td>1.12 (1.03–1.23)</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>ECD</td>
<td>1.24 (1.04–1.54)</td>
<td></td>
</tr>
<tr>
<td>Death with graft function</td>
<td>Non-ECD</td>
<td>1.01 (0.92–1.12)</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>ECD</td>
<td>1.17 (0.93–1.45)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: Kaplan-Meier curves for total graft failure, death-censored graft failure and death with graft function by ECD/DCD subgroups. Log-rank p < 0.0001 for the overall comparison of ECD/DCD subgroups for each of the three study outcomes. See Supporting Table S2 for log-rank p values from pairwise comparisons of ECD/DCD subgroups for the three study outcomes.
Renal Transplantation After *Ex Vivo* Normothermic Perfusion: The First Clinical Study

M. L. Nicholson* and S. A. Hosgood
Department of Infection, Immunity and Inflammation, Transplant Group, Leicester General Hospital, University of Leicester, Leicester, UK

- ECD
- DGF
  - EVNP 1/18 (5.6%)
  - Controls 17/47 (36.2%)
  
P=0.014

Perfusion time 63 ± 16 min
Outline

• Donor source / organ preservation
• Immunosuppression
• Complications
Induction as per local practice
• Efficacy
  – EVL 1.5 mg was not inferior to MMF at 1 and 2 yrs
  – ↓ CAV (IVUS)

• Infections
  – CMV: ↓ incidence on EVL (7.2% vs. 19.4%)
  – Bacterial: ↑ incidence on EVL (30.1% vs. 22%)
Everolimus Versus Mycophenolate Mofetil in Heart Transplantation: A Randomized, Multicenter Trial

- **Discontinuation**
  - EVL 29.7% vs. MMF 19% (1-yr)
  - EVL 33.3% vs. MMF 25.7 (2-yr)

- **Mortality**
  - EVL 1.5 mg 10.6% vs. MMF 9.2% at 2 yrs
  - EVL 3.0 mg 9.9% vs. MMF 2.8% (P=0.018) - terminated
Everolimus Versus Mycophenolate Mofetil in Heart Transplantation: A Randomized, Multicenter Trial

Figure 4: Estimated GFR (eGFR) to month 24 in the everolimus 1.5 mg and MMF study group (intent-to-treat [ITT] population). Data are shown as mean values with 95% confidence intervals (CIs).
A Randomized, Open-Label Study of Sirolimus Versus Cyclosporine in Primary De Novo Renal Allograft Recipients

Stuart M. Flechner,1,9 Alihan Gurkan,2 Anders Hartmann,3 Christophe M. Legendre,4 Graeme R. Russ,5 Josep M. Campistol,6 Francesco P. Schena,7 Carolyn M. Hahn,8 Huihua Li,8 Joan M. Korth-Bradley,8 Sandi See Tai,8 and Seth L. Schulman8

![Graph A: Graft Survival - Death Censored (%)](image)

Log-rank $P = 0.78$

![Graph B: Patient Survival (%)](image)

Log-rank $P = 0.14$
A Randomized, Open-Label Study of Sirolimus Versus Cyclosporine in Primary De Novo Renal Allograft Recipients

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- Enrollment was stopped after 12 months
- SRL (n=314)
- CsA (n=161)
- Drug D/C
  - Rapa: 17.4%
  - CsA: 6.8% (P=0.001)

Transplantation 2013;95: 1233–1241
Long-Term Belatacept Exposure Maintains Efficacy and Safety at 5 Years: Results From the Long-Term Extension of the BENEFIT Study

L. Rostaing¹,², *, F. Vincenti³, J. Grinyó⁴, K. M. Rice⁵, B. Bresnahan⁶, S. Steinberg⁷, S. Gang⁸, L. E. Gaite⁹, M.-C. Moal¹⁰, G. A. Mondragón-Ramírez¹¹, J. Kothari¹², L. Pupim¹³ and C. P. Larsen¹⁴

Similar incidence of malignancies
Better lipid profile

Figure 3: Mean (95% confidence intervals) cGFR (MDRD) over 60 months in the LTE. cGFR values were as observed. CsA, cyclosporine A; cGFR, calculated glomerular filtration rate; LI, less intensive; LTE, long-term extension; MDRD, Modification of Diet in Renal Disease; MI, more intensive.
Alemtuzumab Induction in Renal Transplantation Permits Safe Steroid Avoidance with Tacrolimus Monotherapy: A Randomized Controlled Trial

Matthew P. Welberry Smith, Aravind Cherukuri, Chas G. Newstead, Andrew J.P. Lewington, Niaz Ahmad, Krish Menon, Stephen G. Pollard, Padmini Prasad, Steve Tibble, Emma Giddings, and Richard J. Baker

St. James's University Hospital, Leeds, UK

- 116 KTx (RCT)
- Methylpred 1g x1
- Alemtuzumab + Tac
- Basiliximab + MMF + Tac
- Tac levels
  - <3 mo: 9-14 ng/ml
  - >3 mo: 4-9 ng/ml

Similar incidence of infections
Impact of Calcineurin-Inhibitor Conversion to mTOR Inhibitor on Renal Allograft Function in a Prednisone-Free Regimen

D. Chhabra¹, A. Alvarado²,³, P. Dalal², J. Leventhal², C. Wang⁴, N. Sustento-Redica²,⁵, N. Najafian⁶, A. Skaro⁷, J. Levitsky², V. Mas⁷ and L. Gallon²,³,*
Northwestern University, Chicago, IL

- RCT, 200 KTx
- Alemtuzumab + MMF + Tac + rapid steroid WD
- At 1-yr Rapa vs. Tac (2:1)
- Exclusion criteria
  - eGFR <40, Prot >0.5 g/d
  - AR, severe dyslipidemia
  - WBC <2000, PLT <100000
Impact of Calcineurin-Inhibitor Conversion to mTOR Inhibitor on Renal Allograft Function in a Prednisone-Free Regimen

D. Chhabra¹, A. Alvarado²,³, P. Dalal²,
J. Leventhal², C. Wang⁴, N. Sustento-Redica²,⁵,
N. Najafian⁶, A. Skaro⁷, J. Levitsky⁷, V. Mas⁷,
and L. Gallon²,³,⁸
Northwestern University, Chicago, IL

No difference in DSA
Planned Randomized Conversion From Tacrolimus to Sirolimus-Based Immunosuppressive Regimen in De Novo Kidney Transplant Recipients

- RCT, 297 KTx
- Basiliximab, MPS, Pred, Tac
- Conv to Rapa at 3 mo vs. continue on Tac

Table 3: Key efficacy and safety parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SRL (n = 97)</th>
<th>TAC (n = 107)</th>
<th>TACex (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical rejection</td>
<td>2 (2.1)</td>
<td>3 (2.8)</td>
<td>5 (6.3)</td>
</tr>
<tr>
<td>BCAR</td>
<td>21 (16.6)</td>
<td>21 (19.6)</td>
<td>32 (40.5)</td>
</tr>
<tr>
<td>Borderline</td>
<td>5 (5.1)</td>
<td>4 (3.7)</td>
<td>6 (7.6)</td>
</tr>
<tr>
<td>IA</td>
<td>8 (8.2)</td>
<td>12 (11.2)</td>
<td>9 (11.4)</td>
</tr>
<tr>
<td>IB</td>
<td>5 (5.1)</td>
<td>3 (2.8)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>IIA</td>
<td>2 (2.1)</td>
<td>1 (0.9)</td>
<td>12 (15.2)</td>
</tr>
<tr>
<td>IIB</td>
<td>1 (1.0)</td>
<td>1 (0.9)</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Treated acute rejection 4–24 months</td>
<td>13 (14.4)</td>
<td>5 (4.8)</td>
<td>10 (12.7)</td>
</tr>
</tbody>
</table>

p = 0.047
Planned Randomized Conversion From Tacrolimus to Sirolimus-Based Immunosuppressive Regimen in De Novo Kidney Transplant Recipients


Figure 2: Mean (± standard deviation) estimated glomerular filtration rate (eGFR; four-variable MDRD formula) for the sirolimus and tacrolimus groups in the intention-to-treat (A) and on-therapy population (B).

- Tac 0.15±0.53
- Rapa 0.36±0.59 (P=0.03)
Renal Function at Two Years in Liver Transplant Patients Receiving Everolimus: Results of a Randomized, Multicenter Study

Figure 2: Kaplan-Meier plots for the proportion of patients free from (A) the primary composite efficacy endpoint of tBPAR, graft loss or death and (B) tBPAR (ITT population).

Conversion to EVR at 1 month post-Tx
- MPA local practice
- Prednisone (at least 6 months)
- EVR 1 mg bid (3-8 ng/ml)
- Reduced Tac 3-5 ng/ml
- Tac control 8-12 ng/ml and 6-10 ng/ml > month 4

Primary efficacy composite end-point
- BPAR
- Graft loss
- Death
Renal Function at Two Years in Liver Transplant Patients Receiving Everolimus: Results of a Randomized, Multicenter Study

Figure 3: eGFR (MDRD4) according to treatment group (A) ITT population (B) on-treatment patients. Values are shown as mean and 95% CI.
Renal Function at Two Years in Liver Transplant Patients Receiving Everolimus: Results of a Randomized, Multicenter Study

Table 2: Primary efficacy endpoint and selected secondary efficacy endpoints at month 24 (ITT population)

<table>
<thead>
<tr>
<th></th>
<th>EVR + Reduced TAC, N = 245</th>
<th>TAC Control, N = 243</th>
<th>TAC Elimination, N = 231</th>
<th>EVR + Reduced TAC vs. TAC Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Difference (97.5% CI) p value1</td>
</tr>
<tr>
<td>Primary efficacy endpoint2,3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>24</td>
<td>29</td>
<td>55</td>
<td>−2.2 (−8.8, 4.4) 0.452</td>
</tr>
<tr>
<td>KM incidence rate, %</td>
<td>10.3</td>
<td>12.5</td>
<td>26.0</td>
<td></td>
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<tr>
<td>Secondary end points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft loss or death</td>
<td>17 (7.3)</td>
<td>14 (6.2)</td>
<td>18 (8.6)</td>
<td>1.1 (−4.2, 6.4) 0.638</td>
</tr>
<tr>
<td>Graft loss, n (KM %)</td>
<td>9 (3.9)</td>
<td>7 (3.2)</td>
<td>6 (2.8)</td>
<td>0.8 (−3.2, 4.7) 0.661</td>
</tr>
<tr>
<td>Death, n (KM %)</td>
<td>12 (5.2)</td>
<td>10 (4.4)</td>
<td>15 (7.3)</td>
<td>0.8 (−3.7, 5.2) 0.701</td>
</tr>
<tr>
<td>tBPAR, n (KM %)4</td>
<td>11 (4.8)</td>
<td>18 (7.7)</td>
<td>42 (19.9)</td>
<td>−2.9 (−7.9, 2.2) 0.203</td>
</tr>
<tr>
<td>BPAR, n (KM %)4</td>
<td>14 (6.1)</td>
<td>30 (13.3)</td>
<td>52 (26.4)</td>
<td>−7.2 (−13.5, −0.9) 0.010</td>
</tr>
</tbody>
</table>
Association Between Steroid Dosage and Death With a Functioning Graft After Kidney Transplantation

- 41953 KTx
- 1995 - 2010

Figure 1: Cumulative incidence of death with a functioning graft during years 2-5 posttransplant in kidney transplant recipients according to dose of maintenance steroids administered at year 1. Steroid dose is indicated as mg/kg/day. Log rank p < 0.001.
Association Between Steroid Dosage and Death With a Functioning Graft After Kidney Transplantation

G. Opelz* and B. Döhler

Department of Transplantation Immunology, University of Heidelberg, Heidelberg, Germany

Figure 3: Death due to (A) cardiovascular disease (B) infection and (C) malignant neoplasm during years 2–5 posttransplant in kidney transplant patients with a functioning graft according to steroid dose (mg/kg/day) at year 1 posttransplant.
Inhibitors of mTOR and Risks of Allograft Failure and Mortality in Kidney Transplantation

- 139370 KTx (1999-2010)
- USRDS
- Use of mTOR (n=3237)
- 1st 2 yrs (vs. CNI)
- Years 2-8 (vs. CNI)
Valle de la Luna – San Juan, Argentina
Outline

- Donor source / organ preservation
- Immunosuppression
- Complications
Imaging
Role of Pretransplant Echocardiographic Evaluation in Predicting Outcomes Following Liver Transplantation

216 LTx (2007-2010)
Pre-Tx 2-dimensional/Doppler echo

Figure 1: Patient survival following liver transplantation based on the presence or absence of ≥mild tricuspid regurgitation (log rank test, p = 0.0018), where 0 = none or trace TR and 1 = mild, moderate or severe TR.

Figure 2: Graft survival following liver transplantation based on the presence or absence of ≥mild tricuspid regurgitation (log rank test, p = 0.0006), where 0 = none or trace TR and 1 = mild, moderate or severe TR.
Microvascular Damage in Type 1 Diabetic Patients Is Reversed in the First Year After Simultaneous Pancreas–Kidney Transplantation

Sidestream darkfield
Noninvasive tool to visualize human microcirculation

- Normalization of Angiopoietin-2 / Angiopoietin-1 ratio
- Normalization of soluble thrombomodulin
Antibodies
De Novo Donor-Specific HLA Antibodies Decrease Patient and Graft Survival in Liver Transplant Recipients

H. Kaneko1,* J. G. O'Leary2, N. Banuelos3, L. W. Jennings2, B. M. Susskind2, G. B. Klintmalm2 and P. I. Terasaki1,3

1University of California, Los Angeles, Los Angeles, CA
2Annette C. & Harold C. Simmons Transplant Institute, Baylor University Medical Center, Dallas, TX

A

B

Logrank p=0.002

Logrank p=0.005

8.1%
Class II Alloantibody and Mortality in Simultaneous Liver–Kidney Transplantation

Figure 3: Preformed class II DSA (MFI > 2000) decreases (A) patient, (B) liver allograft and (C) renal allograft survival.
Donor-Specific HLA Antibodies in a Cohort Comparing Everolimus With Cyclosporine After Kidney Transplantation

- 2 RCT, 127 KTx
- CsA vs. EVL at 3 months

Figure 1: Cumulative incidence plot of DSA-detection in 61 patients (red) with everolimus-based immunosuppression compared to 66 patients (black) with cyclosporine-treatment (log-rank: $p = 0.048$).

Figure 2: Cumulative incidence plot of first antibody-mediated rejection in 61 patients (red) with everolimus-based immunosuppression compared to 66 patients (black) with cyclosporine-treatment (log-rank: $p = 0.036$).
Microarray Diagnosis of Antibody-Mediated Rejection in Kidney Transplant Biopsies: An International Prospective Study (INTERCOM)

- 6 centers
- 264 pts
- 300 KT\text{x} Bx

Figure 2: Kaplan-Meier graft survival curves. Based on one random biopsy per patient in the patients receiving late (>1-year posttransplantation) biopsies in INT300. The ABMR score is dichotomized into S+ (>0.2) and S− (≤0.2), as is the conventional assessment of ABMR/mixed as C+ and C− by the local center. ABMR, antibody-mediated rejection; INT300, 300 new indication biopsies from consenting subjects in six kidney transplant programs from five countries.
Kidney Intrgraft Donor-Specific Antibodies as Determinant of Antibody-Mediated Lesions and Poor Graft Outcome

- 51 KTx Bx for cause
- Anti-HLA single Ag flow beads
- sDSA 37/51 pts
- gDSA 15/51 pts
- gDSA correlated with
  - Microcirculation lesions
  - C4d+
  - Worse short term outcome
Postanastomotic Transplant Renal Artery Stenosis: Association With De Novo Class II Donor-Specific Antibodies

Figure 4: Examples of different anatomical subtypes of transplant renal artery stenoses. (A) Postanastomotic, diffuse. (B) Anastomotic. (C) Bend/kink.

- **Postanastomotic RAS**
  - Diabetic pts
  - Older pts
  - Deceased/older donors

- **Anastomotic RAS**
  - Living donors

M. Willicombe1,*, B. Sandhu1, P. Brookes2, W. Gedroyc3, N. Hakim1, M. Hamady1, P. Hill1, A. G. McLean1, S. Moser2, V. Papalois1, P. Tait3, M. Wilcock1 and D. Taube3

1 Imperial College Kidney and Transplant Centre, Hammersmith Hospital, London, UK
Post-anastomotic Transplant Renal Artery Stenosis: Association With De Novo Class II Donor-Specific Antibodies

Post-anastomotic RAS vs. No RAS

- Rej w/arteritis
  (OR 4.83, P=0.0095)
- Rej w/capillaritis
  (OR 3.03, P=0.03)
- De novo class II DSA
  (OR 4.41, P<0.001)
Higher Risk of Kidney Graft Failure in the Presence of Anti-Angiotensin II Type-1 Receptor Antibodies

Graft survival of the Abnormal Biopsy Group (ABG) patients (n=134)

(Log-rank P<0.001)

Years after biopsy-proven rejection/lesions

Both anti-AT1R & DSA negative
- DSA alone
- Anti-AT1R alone
- Both anti-AT1R & DSA positive

Both anti-AT1R & DSA Negative (n=68)

Anti-AT1R alone (n=7)

DSA alone (n=47)

Both anti-AT1R & DSA Positive (n=14)

P=0.009
P=0.007
P=0.24
P<0.001
P=0.007
P=0.59

Figure 5: Kaplan–Meier graft survival based on DSA and anti-AT1R. In the ABG, patients with neither DSA nor AT1R antibodies had the best graft survival. In contrast, those who developed both DSA and anti-AT1R had the lowest survival rate (log-rank p < 0.001). The survival in the presence of both DSA and AT1R antibodies was significantly lower than among patients with DSA alone (p = 0.007).
Infections
What Is the Impact of Hypogammaglobulinemia on the Rate of Infections and Survival in Solid Organ Transplantation? A Meta-Analysis

- 18 studies (n=1756)
- LuTx 63%, HTx 49%, KTx 40%, LTx 16%
- IgG <700 mg/dL: 45%
- Mild hypo-gamma (400-700 mg/dL): 39%
- Severe hypo-gamma (<400 mg/dL): 15%
What Is the Impact of Hypogammaglobulinemia on the Rate of Infections and Survival in Solid Organ Transplantation? A Meta-Analysis

D. F. Florescu¹, 2, *, A. C. Kali³, F. Qiu³, C. M. Schmidt⁴ and U. Sandkovsky¹

¹Infectious Diseases Division, University of Nebraska Medical Center, Omaha, NE

• Severe hypo-gamma was associated with:
  – Mortality (OR 21.91, P=0.005)
  – Resp infection (OR 4.83, P=0.004)
  – CMV (OR 2.40, P=0.02)
  – Aspergillus (OR 8.19, P=0.0009)
  – Other fungal inf (OR 3.69, P=0.03)
Hypocomplementemia in Kidney Transplant Recipients: Impact on the Risk of Infectious Complications

- 270 KTx

Figure 1: Prevalence of C3 and C4 hypocomplementemia throughout the first 6 months after KT (C3 levels: \( p = 0.015 \) for the difference between baseline and month 6; C4 levels: \( p = 0.004 \) for the difference between baseline and month 1).

Figure 5: Kaplan-Meier curves of patient survival according to the presence of C3 hypocomplementemia at month 1 (log-rank test; \( p = 0.029 \)).
Hypocomplementemia in Kidney Transplant Recipients: Impact on the Risk of Infectious Complications

- Type of infection
  - Any
  - Bacterial
  - Fungal
  - CMV, HSV or VZV

- Predictors
  - Age
  - Renal function
  - Time post-Tx

Figure 3: Kaplan–Meier curves of infection-free survival throughout the intermediate period (months 1–6) according to the presence of C3 hypocomplementemia at month 1 (log-rank test; p = 0.001).
Polyomavirus BK Replication in De Novo Kidney Transplant Patients Receiving Tacrolimus or Cyclosporine: A Prospective, Randomized, Multicenter Study

- 682 KTx
- Basiliximab + Pred + MMF
- CsA vs Tac

- Predictors of viremia (6 mo)
  - CsA vs. Tac (OR 0.6, p=0.04)
  - Cum steroids (OR 1.19, P=0.017)

- Predictors of viremia (12 mo)
  - CsA vs Tac (OR 0.33, P=0.003)
  - Age (OR 1.41, P=0.013)
  - Male vs. female (OR 2.49, P=0.038)
Randomized Controlled Trial of High-Dose Intradermal Versus Standard-Dose Intramuscular Influenza Vaccine in Organ Transplant Recipients

- 212 SOT pts
- RCT: IM vs. ID influenza vaccine
- Higher response >6 months post-Tx
  - 53.2% vs. 19.2%, P=0.001
- De novo PRA in 24/212 (11.3%)

Figure 2: Seroconversion to at least one, two or all three antigens according to the vaccine type. *No significant differences observed between the two groups.

Figure 3: Effect of increasing daily doses of mycophenolate mofetil* on seroconversion to each influenza vaccine strain. *Excludes seven patients receiving Myfortic instead of mycophenolate mofetil. p-Values for dose-dependent vaccine response: p < 0.001, p = 0.007, p < 0.001 for A/H1N1, A/H3N2, B strains, respectively.
• Letermovir targets viral (not human) terminase

• Key role in cleavage and packing of CMV progeny DNA into capsids

• n=27 (KTx, SPK, BMT)

• 14-day course
  – Letermovir 40 mg bid
  – Letermovir 80 mg qd
  – Standard of care

• No difference in side-effects
Obesity
The Survival Benefit of Kidney Transplantation in Obese Patients

J. S. Gill1,2,3, J. Lan1, J. Dong1, C. Rose1, E. Hendren1, O. Johnston1 and J. Gill1,2,*

*Division Of Nephrology, University of British Columbia, Vancouver, Canada

Table 3: Risk of death in transplant recipients compared to wait-listed patients with the same body mass index 1 year after transplantation

<table>
<thead>
<tr>
<th>BMI</th>
<th>SCD recipients</th>
<th>ECD recipients</th>
<th>LD recipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5</td>
<td>0.33 (0.26, 0.41)</td>
<td>0.30 (0.21, 0.42)</td>
<td>0.35 (0.24, 0.52)</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>0.34 (0.30, 0.39)</td>
<td>0.37 (0.32, 0.42)</td>
<td>0.20 (0.15, 0.26)</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>0.32 (0.28, 0.37)</td>
<td>0.43 (0.38, 0.50)</td>
<td>0.30 (0.22, 0.47)</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>0.32 (0.26, 0.39)</td>
<td>0.42 (0.35, 0.51)</td>
<td>0.23 (0.17, 0.32)</td>
</tr>
<tr>
<td>35.0–39.0</td>
<td>0.34 (0.26, 0.46)</td>
<td>0.39 (0.24, 0.52)</td>
<td>0.28 (0.14, 0.50)</td>
</tr>
<tr>
<td>≥ 40.0</td>
<td>0.52 (0.37, 0.72)</td>
<td>0.54 (0.33, 0.78)</td>
<td>0.34 (0.19, 0.59)</td>
</tr>
</tbody>
</table>
**ORIGINAL ARTICLE**

**Metabolic syndrome in heart transplantation: impact on survival and renal function**

Luis Martínez-Dolz, Ignacio J. Sánchez-Lázaro, Luis Almenar-Bonet, Manuel Portolés, Miguel Rivera, Antonio Salvador and Jose Anastasio Montero

Heart Failure and Transplant Unit, Department of Cardiology, La Fe University Hospital, Valencia, Spain

**Table 5. Mortality logistic regression.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS</td>
<td>2.087</td>
<td>1.066-4.083</td>
<td>0.032</td>
</tr>
<tr>
<td>Renal function (MDRD)</td>
<td>1.002</td>
<td>0.993-1.010</td>
<td>0.676</td>
</tr>
<tr>
<td>Ischemic time</td>
<td>1.004</td>
<td>0.997-1.011</td>
<td>0.285</td>
</tr>
<tr>
<td>Age</td>
<td>1.022</td>
<td>0.985-1.061</td>
<td>0.242</td>
</tr>
<tr>
<td>Sex</td>
<td>1.323</td>
<td>0.525-3.332</td>
<td>0.552</td>
</tr>
<tr>
<td>PGF</td>
<td>1.117</td>
<td>0.513-2.435</td>
<td>0.780</td>
</tr>
<tr>
<td>Rejection episodes</td>
<td>1.833</td>
<td>1.406-2.389</td>
<td>0.001</td>
</tr>
<tr>
<td>Infections</td>
<td>1.054</td>
<td>0.843-1.318</td>
<td>0.645</td>
</tr>
</tbody>
</table>

**Figure 2** Long-term survival in MS and non-MS groups. Significantly higher long-term survival was found in patients from the non-MS group (log-rank test, $P = 0.02$), with divergent curves from the start until stabilization at about 7 years of follow-up.
Increased Morbidity in Overweight and Obese Liver Transplant Recipients: A Single-Center Experience of 1325 Patients From the United Kingdom


Department of Hepatopancreatobiliary and Transplant Surgery, St. James’s University Hospital, Leeds Teaching Hospitals National Health Service Trust, Leeds, United Kingdom
Malignancies
Time on Dialysis and Cancer Risk After Kidney Transplantation

Germaine Wong,1,2,3,5 Robin M. Turner,1 Jeremy R. Chapman,3 Martin Howell,1,2 Wai H. Lim,4 Angela C. Webster,1,2,3 and Jonathan C. Craig1,2

Sydney School of Public Health, University of Sydney, Sydney, New South Wales, Australia.

*adjusted for gender, age at transplantation and competing cardiovascular deaths

<table>
<thead>
<tr>
<th>Duration after kidney transplantation (years)</th>
<th>Cumulative incidence function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1.5 years on dialysis</td>
<td>0.25</td>
</tr>
<tr>
<td>1.5–2.5 years on dialysis</td>
<td>0.20</td>
</tr>
<tr>
<td>2.5–4.5 years on dialysis</td>
<td>0.15</td>
</tr>
<tr>
<td>Greater than 4.5 years on dialysis</td>
<td>0.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>&lt;4.5 yr</th>
<th>4.5–4.9 yr</th>
<th>5.0–5.4 yr</th>
<th>5.5–6.9 yr</th>
<th>P-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>0.034</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract</td>
<td>0.0075</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.068</td>
</tr>
<tr>
<td>Female reproductive system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.070</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.34</td>
</tr>
</tbody>
</table>

Transplantation 2013;95: 114–121
Pre-transplant malignancy: An analysis of outcomes after thoracic organ transplantation

Claude A. Beaty, MD, Timothy J. George, MD, Arman Kilic, MD, John V. Conte, MD, and Ashish S. Shah, MD

Division of Cardiac Surgery at the Johns Hopkins Medical Institutions, Baltimore, Maryland.

- UNOS
- 13613 LuTx
- 19817 HTx

A

B

C

D

J Heart Lung Transplant 2013;32:202–211
Maintaining calcineurin inhibition after the diagnosis of post-transplant lymphoproliferative disorder improves renal graft survival

Jean-Emmanuel Serre1, David Michonneau2, Emmanuel Bachy3, Laure-Hélène Noël4, Valérie Dubois5,6, Caroline Suberbielle7, Henri Kreis2,8, Christophe Legendre2,8, Marie-France Mamzer-Bruneel2,8, Emmanuel Morlon1,3,9 and Olivier Thaonat1,3,9

1Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Transplantation, Néphrologie et Immunologie Clinique, Lyon, France; 2Service de Transplantation Rénale et de Soins Intensifs, Hôpital Necker, APHP, Paris, France; 3INSERM, U1111, Lyon, France;

PTLD n=101
Depression, drug abuse
Early Treatment of Depressive Symptoms and Long-Term Survival After Liver Transplantation

S. S. Rogal, M. A. Dew, P. Fontes, and A. F. DiMartini

Division of Gastroenterology, Hepatology, and Nutrition, University of Pittsburgh, Pittsburgh, Pennsylvania

- 167 LTx for ALD
- 1998 – 2003
- Beck Depression Inventory
- Q3 months (1st yr)
- Self-report instrument
- 21 symptoms of depression
  - Low 0-9.5
  - Moderate 9.5-16.5
  - High >16.5

P=0.006
A history of chronic opioid usage prior to kidney transplantation may be associated with increased mortality risk

- 1064 KTx (Jan 2004 – Dec 2008)
- Body pains (n=452, 42.5%)
- Prior history of chronic opioid use (COU)

Figure 3 | Patient survival after transplantation. (a) Cumulative incidence of death at 1, 3, and 5 years and (b) overall Kaplan–Meier patient survival analysis. COU, chronic opioid usage.
Conclusions / Future Directions

- Reassess outcomes in living donor kidneys
- Promising data on EVNP
- Expand the use of ECD and DCD
- Organ allocation (elderly, obese)
- EVL and low-dose Tac in LTx (short-term)
- Cautious use of mTOR inhibitors (long-term)
- Reassess CNI in pts with PTLD
- Strategies for metabolic syndrome / obesity
Conclusions / Future Directions

• Expand on non-invasive diagnostic tools
• Prevent DSA
• Intrgraft DSA / microarrays
• Monitoring of IgG and C3?
• New treatment for CMV
• Management of pts with ALD and depression
• Management of pts with pre-Tx opioid use
Cañón de Talampaya – Catamarca, Argentina

Thank you