The Future of Living Donor Transplantation

Matthew Cooper, MD
Chief of Transplantation
Director, Solid Organ Transplant Line
Professor of Surgery
Medical College of Wisconsin
Past President, OPTN/UNOS
President, AFDT
Disclosures

• Surgical Director and Medical Advisor – National Kidney Registry
Robotics – Donors and Recipients
Robotic Trans-abdominal Kidney Transplantation
Robotic Trans-abdominal Kidney Transplantation

Robotic Assisted Living Donor Nephrectomies
A Safe Alternative to Laparoscopic Technique for Kidney Transplant Donation

Spaggiari, Mario MD*; Garcia-Roca, Raquel MD†; Tulla, Kiara A. MD*; Okoye, Obi T. MD*; Di Bella, Caterina MD*; Oberholzer, José MD‡; Jeon, Hoonbae MD§; Tzvetanov, Ivo G MD*; Benedetti, Enrico MD*
Mandatory Paired Kidney Exchange Options

<table>
<thead>
<tr>
<th>Year</th>
<th>NKR Facilitated TXPs*</th>
<th>U.S. LD TXPs**</th>
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<tbody>
<tr>
<td>2008</td>
<td>22</td>
<td>5,968</td>
</tr>
<tr>
<td>2009</td>
<td>61</td>
<td>6,387</td>
</tr>
<tr>
<td>2010</td>
<td>131</td>
<td>6,278</td>
</tr>
<tr>
<td>2011</td>
<td>175</td>
<td>5,773</td>
</tr>
<tr>
<td>2012</td>
<td>226</td>
<td>5,619</td>
</tr>
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<td>2013</td>
<td>308</td>
<td>5,733</td>
</tr>
<tr>
<td>2014</td>
<td>310</td>
<td>5,538</td>
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<tr>
<td>2015</td>
<td>360</td>
<td>5,628</td>
</tr>
<tr>
<td>2016</td>
<td>399</td>
<td>5,629</td>
</tr>
<tr>
<td>2017</td>
<td>462</td>
<td>5,811</td>
</tr>
<tr>
<td>2018</td>
<td>621</td>
<td>6,442</td>
</tr>
<tr>
<td>2019</td>
<td>770</td>
<td>6,867</td>
</tr>
<tr>
<td>2020</td>
<td>700</td>
<td>5,234</td>
</tr>
<tr>
<td>2021</td>
<td>1,058</td>
<td>5,974</td>
</tr>
<tr>
<td>2022</td>
<td>1,164</td>
<td>5,863</td>
</tr>
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</table>
The NKR Voucher Program

Potential donors could be incompatible with their intended recipient based on:

- Blood Type
- DSA
- Anatomy
- Time

First ‘voucher donor’ Judge Broadman and first ‘voucher holder’ his grandson Quinn (UCLA 2014)

**Family Voucher** allows identification of up to 5 immediate family members to hold vouchers if EVER needing kidney!
Non-Directed Donors as a National Resource

Donor Type
- Family Voucher
- Non-Directed

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-Directed</th>
<th>Family Voucher</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>4,768</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>7,154</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>11,602</td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>9,488</td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td>7,963</td>
<td></td>
</tr>
<tr>
<td>2022</td>
<td>8,265</td>
<td></td>
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</table>
Transition to Family Voucher Donation

- Non-Directed Donor
- Family Voucher Donor

Total Living Donations

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-Directed Donor</th>
<th>Family Voucher Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>86%</td>
<td>14%</td>
</tr>
<tr>
<td>2019</td>
<td>53%</td>
<td>47%</td>
</tr>
<tr>
<td>2020</td>
<td>69%</td>
<td>31%</td>
</tr>
<tr>
<td>2021</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>2022</td>
<td>90%</td>
<td>10%</td>
</tr>
</tbody>
</table>

170 194 164 231 261

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Division of Transplant Surgery

knowledge changing life
LD Conversion Rates Becomes a Metric

- Allegheny: 23%
- Hartford: 23%
- Emory: 18%
- UCLA: 18%
- UMinn: 16%
- UCSD: 16%
- Madison: 16%
- Rush: 15%
- WakeForest: 14%
- StDavidsTX: 13%
- MethodistTX: 13%
- VirginiaMason: 12%
- UCSF: 12%
- Cornell: 12%
- FortWorth: 11%
- PorterAH: 11%
- Penn: 10%
- MercyStMarys: 10%
LD Conversion Rates Becomes a Metric

- Allegheny: 23%
- Hartford: 23%
- Emory: 18%
- UCLA: 18%
- UMinn: 16%
- UCSD: 16%
- Madison: 15%
- Rush: 14%
- WakeForest: 13%
- StDavidsTX: 13%
- MethodistTX: 12%
- VirginiaMason: 12%
- UCSF: 12%
- Cornell: 12%
- FortWorth: 11%
- PorterAH: 11%
- Penn: 10%
- MercyStMarys: 10%
NKR Desensitization Cases Decline as Volume Grows

<table>
<thead>
<tr>
<th>Year</th>
<th>Desensitization Cases</th>
<th>NKR Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>49</td>
<td>284</td>
</tr>
<tr>
<td>2014</td>
<td>33</td>
<td>277</td>
</tr>
<tr>
<td>2015</td>
<td>29</td>
<td>308</td>
</tr>
<tr>
<td>2016</td>
<td>28</td>
<td>334</td>
</tr>
<tr>
<td>2017</td>
<td>32</td>
<td>360</td>
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<tr>
<td>2018</td>
<td>30</td>
<td>457</td>
</tr>
<tr>
<td>2019</td>
<td>22</td>
<td>539</td>
</tr>
<tr>
<td>2020</td>
<td>9</td>
<td>489</td>
</tr>
<tr>
<td>2021</td>
<td>11</td>
<td>779</td>
</tr>
<tr>
<td>2022</td>
<td>4</td>
<td>802</td>
</tr>
</tbody>
</table>

Desensitization Rate: 17.3%, 11.9%, 9.4%, 8.4%, 8.9%, 6.6%, 4.1%, 1.8%, 1.4%, 0.5%

NKR Transplants: 284, 277, 308, 334, 360, 457, 539, 489, 779, 802
Using KPD to Transplant the ‘Untransplantable’ Desensitization

KPD

Try KPD for a few months
If match -\ />
KPD
If no match -\ />
Desens.

Wait in KPD

Look in KPD pool
Prob. Not Worth Waiting
If match -\ />
KPD
If no match -\ />
Desens.

COMBINE
KPD and Desensitization
Remote Donations → Donor Convenience

Donor Type
- Swap Saver
- Paired
- Direct
- Standard Voucher

Donation Date Annualized

<table>
<thead>
<tr>
<th>Year</th>
<th>Swap Saver</th>
<th>Paired</th>
<th>Direct</th>
<th>Standard Voucher</th>
</tr>
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<tbody>
<tr>
<td>2017</td>
<td></td>
<td>3</td>
<td></td>
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<td>2018</td>
<td></td>
<td>5</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>2019</td>
<td></td>
<td></td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>2020</td>
<td></td>
<td></td>
<td></td>
<td>46</td>
</tr>
<tr>
<td>2021</td>
<td>126</td>
<td></td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>2022</td>
<td></td>
<td></td>
<td></td>
<td>126</td>
</tr>
</tbody>
</table>

knowledge changing life
Normothermic Preservation
Compatible Pairs → Optimize Outcomes

What a compatible pairs gain:

- Younger donor
- Better size match (nephron mass)
- 0-mismatch
- Ability to be one another’s support

What the incompatible pool gains if compatible pairs participate:

- Higher match rates
- More O-recipients match
Decoupling Trend
Transition from Paired to Standard Voucher Donation

- 2018: 83% Standard Voucher Donor, 17% Paired Donor
- 2019: 75% Standard Voucher Donor, 25% Paired Donor
- 2020: 67% Standard Voucher Donor, 33% Paired Donor
- 2021: 59% Standard Voucher Donor, 41% Paired Donor
- 2022: 55% Standard Voucher Donor, 45% Paired Donor

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Division of Transplant Surgery

knowledge changing life
The Epidemiology Research Group for Organ Transplantation is a research group focused on organ transplantation at the Johns Hopkins School of Medicine. Below are some of the decision models we have developed.

For more information, please visit our website, www.transplantmodels.org

**Living Kidney Donor Risk Index (LKDPI)**

This model predicts recipient risk of graft loss after living donor kidney transplantation based on donor characteristics, on the same scale as the KDPI...


**ESRD Risk Tool for Kidney Donor Candidates**

This model is intended for low-risk adults considering living kidney donation in the United States. It provides an estimate of 15-year and lifetime incidence of end-stage renal disease...


**Infectious Risk Donors**

When a patient with end-stage renal disease (ESRD) on the waitlist for a kidney is offered an Infectious Risk Donor (IRD) kidney, they need to decide whether they will accept the IRD kidney and the associated infectious risk, or if they will decline it and continue to wait for the next available infectious-risk-free kidney...


**Transplant Candidacy for Patients 65+**

This prediction model is intended for adults with ESRD on dialysis aged 65 and above; it provides the predicted probability of 3-year survival after kidney transplantation (KT). Patients with predicted 3-year post-KT survival in the top quintile are deemed "excellent" candidates...


**Pediatric Transplant: Living or deceased donor first?**

Most pediatric kidney transplant recipients live long enough to require retransplantation. The most beneficial timing for living donor transplantation in candidates with one living donor is not clear...


**Postdonation Risk of ESRD in Living Kidney Donors**

Risk estimation is critical for appropriate informed consent and varies substantially across living kidney donors...

The Epidemiology Research Group for Organ Transplantation at Johns Hopkins School of Medicine. Below are some findings:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>aHR^a</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (at age 40)</td>
<td>1.88 (95% CI, 1.50 to 2.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>black race (at age 40)</td>
<td>2.96 (95% CI, 2.25 to 3.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age per 10 yr: nonblack</td>
<td>1.40 (95% CI, 1.23 to 1.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age per 10 yr: black</td>
<td>0.88 (95% CI, 0.72 to 1.09)</td>
<td>0.3</td>
</tr>
<tr>
<td>BMI per 5 kg/m^2</td>
<td>1.61 (95% CI, 1.29 to 2.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First-degree biologically related to</td>
<td>1.70 (95% CI, 1.24 to 2.34)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

<sup>a</sup> Hazard ratio

The top quintile are deemed "excellent" candidates. Further analysis is needed. For more information, please visit www.transplantmodels.com
**Characteristic**

- Men (at age 40)
- Black race (at age 40)
- Age per 10 yr: nonblack
- Age per 10 yr: black
- BMI per 5 kg/m²
- First-degree biologically related to recipient

---

**18 year old**

- No baseline health abnormalities
- 1st degree relative with DM and HTN

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Risk Model</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA female</td>
<td>~ 1.29%</td>
<td>(score = 24)</td>
</tr>
<tr>
<td>EA male</td>
<td>~ 2.24%</td>
<td>(score = 33)</td>
</tr>
<tr>
<td>AA female</td>
<td>~ 2.24%</td>
<td>(score = 33)</td>
</tr>
<tr>
<td>1 APOL1 variant</td>
<td>~ 2.85%</td>
<td>(score = 37)</td>
</tr>
<tr>
<td>2 APOL1 variant</td>
<td>~ 6.23%</td>
<td>(score = 50)</td>
</tr>
<tr>
<td>AA male</td>
<td>~ 3.86%</td>
<td>(score = 42)</td>
</tr>
<tr>
<td>1 APOL1 variant</td>
<td>4.90%</td>
<td>(score = 46)</td>
</tr>
<tr>
<td>2 APOL1 variant</td>
<td>10.58%</td>
<td>(score = 59)</td>
</tr>
</tbody>
</table>

---

**Estimated 25-yr risk of CKD (%)**

- Risk score
- Years
Cumulative graft loss by LKDPI

The Epidemiology

Living Kidney Donor
This model predicts recipient donor kidney transplant characteristics, on the size of
Masolo AB, Leanza J, Fahnmy L, Donor Kidney Transplantation. A
Continue to model »

Transplant Candidate
This prediction model is designed for dialysis aged 65 and above, with a low probability of 3-year survival (KT). Patients with prednisolone in the top quintile are deemed
Calculate your score »

renal disease (ESRD) on the Infectious Risk Donor Profile: whether they will accept an acceptable infectious risk, or if to wait for the next

RD in Living Kidney
proposed informed consent living kidney donors.
Sorption Risk of ESRD in Living Society of Nephrology (2017):
Eplet Matching in the NKR

- Compatible pairs
- May benefit from closer immunologic matching
- Longer life for kidney
- Possibly less immunosuppression needed
The HLA antigens are complex amino-acid structures expressing several immunogenic hot-spots, known as “HLA eplets”.

The HLA antigens of two individual share a large degree of homology (magenta areas) but differ at some or all the HLA eplets (yellow patches).
HLA EPLET: the new HLA compatibility “currency”

We need to change the way we define HLA compatibility....

**Are they a match?**
- YES/NO

**Are they a 1-haplo match?**
- YES/NO

**How dissimilar are they?**
- 22 Mismatched EPLETS

**Conventional HLA match does not quantify the immunological risk.**

**Better representation of the immunological risk.**
Kidney For Life Basics

- Fewer Eplet Mismatches
- Fewer De Novo DSA
- Less Rejection
- Fewer Graft Failures
- More Kidneys Last A Lifetime
- Better Match
- Lower Immunosuppression
Kidney for Life Low Eplet Mismatch Transplants
Compatible and Incompatible Pairs

Eplet Mismatch
- KFL Direct - Low
- KFL Direct - Zero
- KPD - Low
- KPD - Zero

<table>
<thead>
<tr>
<th>Year</th>
<th>Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>13</td>
</tr>
<tr>
<td>2021</td>
<td>103</td>
</tr>
<tr>
<td>2022</td>
<td>167</td>
</tr>
</tbody>
</table>

13

103

167

18

22

87

40
Percentage of Transplants with Eplet Mismatch Data

Continually Improving Low & Zero Eplet Mismatch Percentage

- High Eplet Mismatch
- Medium Eplet Mismatch
- Low Eplet Mismatch
- Zero Eplet Mismatch

Q1-22: 43% (High), 22% (Medium), 22% (Low), 13% (Zero)
Q2-22: 40% (High), 27% (Medium), 18% (Low), 14% (Zero)
Q3-22: 37% (High), 34% (Medium), 18% (Low), 11% (Zero)
Q4-22: 37% (High), 35% (Medium), 22% (Low), 7% (Zero)
Kidney for Life Results
One Year Antibody Screening

<table>
<thead>
<tr>
<th>Zero Eplet Mismatch + Low Eplet Mismatch</th>
<th>Medium Eplet Mismatch + High Eplet Mismatch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening Completed</td>
<td>54</td>
</tr>
<tr>
<td>De Novo DSA</td>
<td>0%</td>
</tr>
<tr>
<td>Screening Completed</td>
<td>53</td>
</tr>
<tr>
<td>De Novo DSA</td>
<td>19%</td>
</tr>
</tbody>
</table>

10
Patients/Families Tell Their Story
Champion Microsites

✓ Center invites patient to setup site
✓ Patient creates site profile
✓ Center & NKR approve site
✓ Microsite link posted to the web
✓ NKR prints/ships business cards to patient

National Kidney Registry
Khadijah Sabir
I NEED A KIDNEY DONOR

If you are interested in learning more about my story, kidney donation or in being tested to see if you are eligible to donate, please visit the URL below.
WWW.NKR.ORG/CEN498

National Kidney Registry
Nathaniel Aiken
I NEED A KIDNEY DONOR

If you are interested in learning more about my story, kidney donation or in being tested to see if you are eligible to donate, please visit the URL below.
WWW.NKR.ORG/ZHS796

Written policy for what is NOT allowable on microsite:
• Disclosure of financial information of any kind
• Material items in photos/videos
• Anything that can be construed as an attempt to compensate potential donors
Smarter Use of Social Media

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Active Custom Sites</th>
<th>Active Starter Sites</th>
<th>Total Living Donor Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1-19</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2-19</td>
<td>26</td>
<td></td>
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</tr>
<tr>
<td>Q3-19</td>
<td>47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q4-19</td>
<td>112</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1-20</td>
<td>239</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2-20</td>
<td>302</td>
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</tr>
<tr>
<td>Q3-20</td>
<td>377</td>
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<tr>
<td>Q4-20</td>
<td>500</td>
<td></td>
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</tr>
<tr>
<td>Q1-21</td>
<td>712</td>
<td></td>
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</tr>
<tr>
<td>Q2-21</td>
<td>48</td>
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<tr>
<td>Q3-21</td>
<td>874</td>
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<tr>
<td>Q4-21</td>
<td>1,021</td>
<td></td>
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</tr>
<tr>
<td>Q1-22</td>
<td>1,253</td>
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<td></td>
</tr>
<tr>
<td>Q2-22</td>
<td>1,608</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q3-22</td>
<td>1,793</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q4-22</td>
<td>1,880</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The chart shows the growth in active custom sites, active starter sites, and total living donor transplants over the years 2019-2022.
Association of Race and Ethnicity With Live Donor Kidney Transplantation in the United States From 1995 to 2014

Tanjala S. Purnell, PhD, MPH; Xun Luo, MD, MPH; Lisa A. Cooper, MD, MPH; Allan B. Massie, PhD; Lauren M. Kucirka, MD, PhD, ScM; Macey L. Henderson, JD, PhD; Elisa J. Gordon, PhD, MPH; Deidra C. Crews, MD, ScM; L. Ebony Boulware, MD, MPH; Dorry L. Segev, MD, PhD

A Live donor kidney transplantation

- 1995-1999
  - 0.83 Hispanic
  - 0.45 Black
  - 0.56 Asian

- 2014-2019
  - 0.52 Hispanic
  - 0.27 Black
  - 0.42 Asian

JAMA 2018
Current State
Go out and find a living donor

Future State
Let us help you find a living donor!

Not ‘Do you have’ but ‘Who is your living donor?’
Making House Calls Increases Living Donor Inquiries and Evaluations for Blacks on the Kidney Transplant Waiting List

James R. Rodrigue,1,5 Matthew J. Paek,1 Ogo Egbuna,2 Amy D. Eshoo,3 Martha Pavlakis,1 and Didier A. Mande

Transplant Center Provision of Education and Culturally and Linguistically Competent Care: A National Study

E. J. Gordon1, b, *, J. C. Caicedo1, D. P. Ladner1, b,

Received 14 July 2010, revised 13 August 2010, accepted for publication 04 September 2010

ORIGINAL CLINICAL SCIENCE—GENERAL

Financial Impact of a Culturally Sensitive Hispanic Kidney Transplant Program on Increasing Living Donation

Wang, Andrew PhD, MPH1, 2; Caicedo, Juan Carlos MD3; Mathur, Amit K. MD, MS4; Ruiz, Richard M. MD5; Gordon, Elisa J. PhD, MPH1, 2

DEPARTMENT OF SURGERY Division of Transplant Surgery

Medical College of Wisconsin

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Financial Neutrality??

“This is a terrific program. Thank you so much.”
– Lenora - Living Kidney Donor

Living Donor Assistance Program
Providing financial assistance to those who want to donate an organ, priority is given to individuals not otherwise able to afford the travel and subsistence expenses associated with living organ donation.

Learn more ►

For Donors
Learn if you are eligible for reimbursement of travel and subsistence expenses and how to file an application.
More information ►

Our Mission is to Reduce Financial Disincentives to Living Organ Donation

350 participating transplant programs
3,340 organ donations made possible
90% of applications have received funding
Financial Neutrality → A Must!!

“This is a terrific program. Thank you so much.”
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More information

OUR MISSION IS TO REDUCE FINANCIAL DISINCENTIVES to LIVING ORGAN DONATION

350 participating transplant programs
3,340 organ donations made possible
90% of applications have received funding

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Donor Shield Program

❖ Lost wage reimbursement up to $1500/week for up to 6 weeks
❖ Travel and lodging reimbursement up to $3000 for donor and a caregiver
❖ Kidney Prioritization should the donor ever need a transplant
❖ Donation life insurance with $1,000,000 principal sum
  ❖ Donation disability insurance
  ❖ Free legal support
  ❖ Complication Protection
  ❖ Home blood draws
Living and Deceased Organ Donation Should Be Financially Neutral Acts

F. L. Delmonico1, D. Martin2, B. Dominguez-Gill3, E. Muller4, V. Jha5, A. Levin6, G. M. Danovitch7 and A. M. Capron8

care units; LDCOP, Live Donor Community of Practice; LKD, living kidney donor; NLDAC, National Living Donor Assistance Center; NOTA, National Organ Transplant Act

Meeting Report

AST/ASTS Workshop on Increasing Organ Donation in the United States: Creating an “Arc of Change” From Removing Disincentives to Testing Incentives

D. R. Salomon1, A. N. Langnas2, A. I. Reed3, R. D. Bloom4, J. C. Magee5 and R. S. Gaston6 for the AST/ASTS Incentives Workshop Group (IWG)7

Transplant Act; OPTN, Organ Procurement and Transplantation Network

 BETWEEN SCYLLA AND CHARYBDIS: CHARTING AN ETHICAL COURSE FOR RESEARCH INTO FINANCIAL INCENTIVES FOR LIVING KIDNEY DONATION


financial compensation on living kidney donation rates, many fear that financial incentives will exploit vulnerable individuals and cast the field of transplantation in a negative public light, ultimately reducing donation rates. This paper provides an ethical justification for conducting a pilot study of a federally regulated approach to providing financial incentives to living
Tolerance induction in HLA disparate living donor kidney transplantation by facilitating cell-enriched donor stem cell Infusion: The importance of durable chimerism

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Tolerance as SOC!!

Tolerance induction in HLA disparate living donor kidney transplantation by facilitating cell-enriched donor stem cell infusion: The importance of durable chimerism

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Value proposition for “One Transplant for Life”

**Human Costs:**
- Lost Productivity
- Impaired QoL

**Clinical & Economic Costs:**
- IS Complications
- IS Co-morbidities
- Graft Loss
- IS Costs

**Value From Eliminating Chronic IS**

- **Improve outcomes**
  - Fewer rejections, graft losses
  - No IS co-morbidities or complications
  - Enhance patient’s QoL and freedom

- **Reduce systematic costs**
  - IS and meds to manage co-morbidities
  - Avoid return to dialysis or 2\textsuperscript{nd} transplant
  - Bolster recipients’ productivity
Allogeneic Tolerance and Chimerism

Goal: **facilitate allogeneic tolerance** by establishing **durable chimerism**

**Allogeneic tolerance:** An approach to enable donor HSCs to coexist with recipient HSCs in the recipient’s bone marrow ("chimerism"), and mature into mutually-tolerated, functional immune cells and blood cells.

*Nobel Prize in Physiology or Medicine 1960* was awarded jointly to Sir Frank Macfarlane Burnet and Peter Brian Medawar for discovery of acquired immunological tolerance.
FCR001: The Donor-Recipient Journey

Our “vein to vein” process and protocols have been fully proceduralized.

**3+ WEEKS PRIOR**
- Donor donates stem cells and immune cells
- Talaris processes FCR001 from donor’s cells

**4 DAYS PRIOR**
- Recipient starts non-myeloablative conditioning

**DAY 0**
- Kidney transplant

**DAY +1**
- FCR001 infusion

**NEXT 6 MONTHS**
- Frequent, routine monitoring

**6-12 MONTHS**
- Potentially lowering doses of chronic immunosuppression*

**12 MONTHS & AFTER**
- Potentially free from all chronic immunosuppression*

*Assuming no biopsy-proven acute rejection (BPAR); stable kidney function; >50% donor chimerism; no GvHD
Patients demonstrating stable donor chimerism (>50%), no history of rejection, no DSA, no GvHD, not using corticosteroids, and adequate kidney function.

**TBI**
Dose of 200 cGy delivered as a single fraction at 10–18 MV at a rate of 15–20 cGy/min are the preferred energy and rate parameters and should be followed when possible.

**Methylprednisolone**
500 mg IV on Day 0 in OR; 250 mg Day 1 and 125 mg Day 2.

**Until absolute neutrophil count is >1000/mm³ for 3 consecutive days.**

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**FREEDOM-1: FCR001 Protocol Overview**

**Conditioning**
- FLU 30 mg/m² (Days −4, −3, −2)
- Cy 50 mg/kg (Day −3)
- Mesna 50 mg/kg (Day −3)
- Hemodialysis 2–4 hours (Days −4, −3, −2)

**GvHD Prophylaxis**
- Cy (50 mg/kg)
- Mesna (50 mg/kg)

**Primary Endpoint:** Off IS With No Rejection

**Week −12 to −4**
- **Product saved as safety net**
- **Required for conditioning:**
  1. Receipt of FCR001
  2. Negative DSA retest
  3. Negative COVID
  4. Reference chimerism samples adequate

**Day −84 to Day −36**
- **Mobilization/apheresis**

**Day −4 to 0**
- **TCR001 Infusion Within 24 Hours***

**Day 0**
- **Begin prophylactic GCSF***

**Day 1**
- **TBI**

**Day 2**
- **GvHD Prophylaxis**

**Day 4**
- **TBI**

**Day 5**
- **Weaning* (0–3 ng/mL)**

**Mo −60**
- **End of Study**
37 adult living donor kidney transplant (LDKT) patients were dosed with our therapy at two leading US transplant sites between 2009 - 2016.

**Highlights from Phase 2 Study (+ long-term followup)**

- Across all HLA-mismatches
- 82% success rate (14 of last 17) once key parameters were optimized

70%

(26 of 37) OFF ALL IMMUNOSUPPRESSION THERAPIES**

- Median follow up: >7 yrs
- Six patients followed >10 years
- Longest follow up: >12 yrs

100%

TAKEN OFF IMMUNOSUPPRESSION REMAIN IS-FREE

- Recurrence ordinarily seen in 20% - 60% of patients***

7/7

TOLERIZED PATIENTS WITH PRIOR KIDNEY AUTO-IMMUNE CONDITION HAD NO RECURRENCE
Phase 2 Results Robust Across All Degrees of HLA-Mismatch

19/26 (73%) durably off all chronic immunosuppression had HLA match of 3 or less between LDKT donor & recipient

Comparable kidney and patient survival for all FCR001 vs standard of care (SoC) LDKT patients

FCR001 safety & tolerability generally consistent with separate SoC kidney transplant + allogeneic HSCT with non-myeloablative conditioning

No acute rejection or donor-specific antibodies in FCR001 patients off immunosuppression
Evidence of Potential Longer-Term Clinical Benefit

FCR001 improved Quality of Life, preserved kidney function and enabled lower reliance on cardiovascular medications.

**Mean Estimated eGFR* Over Time Post-Transplant**

**Cardiovascular Medication Usage**

**SoC vs Durably Chimeric FCR001 Patients**

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension Medications</td>
<td>83%</td>
</tr>
<tr>
<td>Hyperlipidemia Medications</td>
<td>43%</td>
</tr>
<tr>
<td>SoC</td>
<td>18%</td>
</tr>
<tr>
<td>FCR001 Patients</td>
<td>9%</td>
</tr>
</tbody>
</table>
Potential to Extend Across Solid Organ Transplant

Living Donor Kidney Transplant
Delayed Tolerance Induction

**FREEDOM2**

- Phase 2 study - initiated October 2021
- **Goal**: Safely induce durable tolerance and eliminate immunosuppression in prior recipients of LDKT (those transplanted 3 – 12 months prior to FCR001 administration)
- Potential to expand market to prevalent LDKT population

**Potential US Market Opportunity:**
~6,000 – 10,000*/yr

Deceased Donor Kidney Transplant

**FREEDOM4**

- Active research program to establish easibility of extracting same cells directly from deceased donor bone marrow
- Relationships established with KODA and other OPOs
- Product would be administered a few months after organ transplant

**Potential US Market Opportunity**
>~16,500 / yr
Uterus Transplantation – Greater Interest

Uterus Transplant - A Unique Type of Transplant

1) Non-lifesaving transplant (However can enhance QOL for parents)
2) Recipients are healthy w/out comorbidities (some MRKH have solitary kidney)
3) Temporary transplantation
4) Living or deceased donor option
5) Stepwise success determined years posttransplant
6) Living donors renounce an organ for transplantation after it has exhausted its function in the donor
7) One allograft shared by two recipients
The First Baby Born From A Transplanted Uterus in the US

November 2017
World Uterus Transplant Experience

Historical Experience

Deceased Donor
Living Donor

Czech Experience
Baylor Dallas Experience
Initial Sweden Experience
Cleveland Clinic Experience
U Penn Experience
UAB Experience

Total

Logistical Issues – Donor Organ Supply

Potential Annual Demand for Uterus

~ 3050
Uterus Allograft

Potential Annual Supply Deceased Donor Uterus

<< 2000
Deceased Donor Uterus Allograft

Mismatch

Deceased donor supply unlikely to demand

Need living donors
Liver Paired Donation Program

Nation’s first multi-hospital liver paired donation (LPD) program

• Increase access to living donor transplant
• Increase candidate access earlier, when in better health
• Determine how to create a nationally available program, how to sustain it, identify challenges
• Keep it algorithmically simple, 2-way only
Insurance coverage

In partnership with the American Foundation for Donation and Transplant

- Accidental death and dismemberment
  - maximum, one year $500,000
- Medical complications
  - $5,000 deductible, maximum $250,000
- Temporary disability
  - maximum $100 per week
- Permanent disability
  - $5000.00 per month up to maximum $250,000
- Traveling companion benefit (one person)
  - One year $500,000 accidental death and dismemberment benefit
Center Requirements

All participating centers must:

- Have performed ~20 adult LDLTs or more over the last 3 years or a children’s hospital affiliated with a donor recovery hospital who meets criteria
- Have consistent liver transplant program directorship over the last 3 years;
- Not be under OPTN review for liver transplant or living liver donation-related outcomes

Centers must also:

- Agree to the Participation Agreement;
- Abide by the Liver Paired Donation Pilot Program Operational Guidelines;
- Be active OPTN and UNOS members and OPTN-approved to perform liver transplants and living liver recoveries;
- Abide by all relevant OPTN and UNOS Policies;
- Agree to share feedback with UNOS to facilitate improvements to the program;
Expand Donor and Candidate Eligibility
Deceased Donor-initiated Chains

Patient on Deceased Donor Waiting List without an incompatible willing living donor

Estimated Distribution by Ethnicity*
- Caucasian: 38.4%
- African American: 34.0%
- Hispanic: 18.1%
- Asian: 8.1%
- Other: 1.4%

Patient on Deceased Donor Waiting List with an incompatible, but willing living donor

Estimated Distribution by Ethnicity*
- Caucasian: 70.3%
- African American: 12.5%
- Hispanic: 13.0%
- Asian: 2.9%
- Other: 1.2%
Global Kidney Exchange

The continuing cost of long-term dialysis for a US patient can be redirected into three streams.

- Transplant and long-term care for an international patient
- Transplant and long-term care for the US patient
- Long-term savings that accrue to the insurance payer

Feasible transplant

Type A
Transplant precluded by financial barriers

Type O
Transplant precluded by immunologic barriers

Type A

Type O

Feasible transplant
Living Donor Registry

• More lives would be saved through living donation.

• The majority of the public expresses support of living donation; however, the number of living donor transplants has remained flat.

• Estimated that for every 35 living donors, there may be another 26 willing to donate.

• Transplant Centers may not be equipped with personnel and resources to efficiently conduct an abundance of living donor prospect testing.
National Donate Life Registry

All living donor prospects will enter the living donor registry pathway through the National Donate Life Registry (NDLR)

Here's why:

More than 6 Million Registrations

- 4,000 NEW Registrations Every Day
- 8.5% Registration Conversion Rate
  - Exceeding national nonprofit benchmark of 1.5%
- 1,263 Campaign Pages with more than 700 organization pages
- National Partnerships with Apple, Walgreens and Android
- 1.9 million donor searches conducted in last 24 months
- All NDLR data is handled in accordance with HIPPA privacy standards and is only accessed by certified organ recovery organizations
Living-Donor Prospect Experience

1. Express interest through the National Donate Life Registry
2. Complete online health screen questionnaire
3. Collect saliva sample
4. Return sample for lab analysis
5. Potential donor shared with transplant program through UNOS connectivity
6. Follow-up by transplant program
Living Donor Transplant Centers of Excellence
What is the Future of LD Transplant?

FOR

MORE, MORE, MORE!