RISK FACTORS FOR ACUTE ALLOGRAFT REJECTION IN HIV+ KIDNEY TRANSPLANT RECIPIENTS

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BACKGROUND
Kidney transplantation (KT) of HIV positive patients has transformed the management of end-stage kidney disease in this population. Although favourable outcomes have been reported, patients experience high rates of acute allograft rejection (AR) (1, 2).

AIMS
The aims of the study were:
- To examine if the choice of calcineurin inhibitor (CNI) immunosuppressive therapy had an impact on AR in the first year post-KT
- To examine factors associated with AR in the first year post-KT

METHODS
- The UK HIV/Kidney Transplant Study is an on-going observational cohort study collecting data from 40 Transplant and HIV treatment centres in the UK (1).
- The study was approved by the National Health Service multicentre research committee (MREC).
- Case ascertainment
- Patients were included if HIV+ and ≥18 years of age at time of KT and KT was performed in the UK between 01/01/2005 and 31/12/2013
- For all analyses, patients were a priori stratified by the type of CNI (ciclosporin, CsA or tacrolimus, Tac) received immediately post-KT
- Statistical analysis
- Overall patient and graft survival and cumulative incidence of AR were estimated using Kaplan-Meier methods, patients were censored at the first episode of AR or CNI switch. Log-rank test was used to compare groups.
- Univariable and multivariable Cox proportional hazard regression analyses were used to identify factors associated with acute allograft rejection
- A sensitivity analysis was conducted which examined factors associated with AR during weeks 1-2 and weeks 3-5 post-KT.

RESULTS
- Between January 2005 and December 2013, 78 HIV positive adults underwent KT at the participating centres, with a median follow up of 44.6 (38.5, 51.4) years
- The median age was 45 years, 74% of black ethnicity with a median (IQR) CD4 cell count of 366 (277, 516) cells/mm³ and HIV Viral Load <500copies/mL (Table 1).
- Immunosuppression consisted of induction therapy plus maintenance therapy including CNI + mycophenolate or azathioprine + corticosteroids.

RESULTS (Cont.)

Table 1 Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Ciclosporin</th>
<th>Tacrolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>All Patients</td>
<td>Ciclosporin</td>
<td>Tacrolimus</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>Years</td>
<td>44.6 (36.5, 51.4)</td>
<td>39.0 (35.6, 49.6)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>Male</td>
<td>52 (67)</td>
<td>24 (177)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td>Black</td>
<td>58 (74)</td>
<td>24 (77)</td>
</tr>
<tr>
<td>Cause of ESKD, n (%)</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of pRRT, median (IQR)</td>
<td>Years</td>
<td>4.9 (2.6, 7.1)</td>
<td>4.5 (2.2, 6.4)</td>
</tr>
<tr>
<td>Mode of acquisition, n (%)</td>
<td>Tacrolimus</td>
<td>54 (70)</td>
<td>22 (71)</td>
</tr>
<tr>
<td>CD4 count at KT, median (IQR)</td>
<td>cells/mm³</td>
<td>92 (40, 171)</td>
<td>92 (38, 160)</td>
</tr>
<tr>
<td>Viral load at KT, median (IQR)</td>
<td>log10 copies/ml</td>
<td>1.7 (1.6, 1.7)</td>
<td>1.7 (1.6, 1.7)</td>
</tr>
<tr>
<td>PFe-containing ART, n (%)</td>
<td>30 (36)</td>
<td>15 (48)</td>
<td>15 (33)</td>
</tr>
<tr>
<td>HLA B co-infection, n (%)</td>
<td>5 (13)</td>
<td>5 (13)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>HLA C co-infection, n (%)</td>
<td>4 (5)</td>
<td>3 (10)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Allelograft type, n (%)</td>
<td>Cadaveric</td>
<td>51 (66)</td>
<td>18 (56)</td>
</tr>
<tr>
<td>Donor/Recipient CMV mismatch status, n (%)</td>
<td>2 (4)</td>
<td>2 (4)</td>
<td></td>
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<tr>
<td>Induction therapy, n (%)</td>
<td>Anti-CD3 monoclonal antibody</td>
<td>68 (90)</td>
<td>29 (94)</td>
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</tbody>
</table>

Table 2 Factors Associated with Acute Allograft Rejection

<table>
<thead>
<tr>
<th></th>
<th>Entire follow up (HR, 95% CI)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Age at KT (per year older)</td>
<td>1.02 (0.95, 1.09)</td>
<td>0.99 (0.94, 1.05)</td>
<td>0.89 (0.84, 0.95)</td>
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<tr>
<td>Gender (Male)</td>
<td>1.49 (0.63, 3.35)</td>
<td>1.18 (0.57, 2.44)</td>
<td>0.95 (0.41, 2.27)</td>
</tr>
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<td>Ethnicity (Black)</td>
<td>1.36 (0.55, 3.27)</td>
<td>0.84 (0.36, 2.07)</td>
<td>0.89 (0.49, 1.63)</td>
</tr>
<tr>
<td>Mode of acquisition (Other)</td>
<td>1.24 (0.35, 4.30)</td>
<td>0.61 (0.14, 2.41)</td>
<td>0.80 (0.29, 2.41)</td>
</tr>
<tr>
<td>Transplant year</td>
<td>1.04 (0.86, 1.21)</td>
<td>1.00 (0.84, 1.18)</td>
<td>0.97 (0.82, 1.13)</td>
</tr>
<tr>
<td>CD4 count at KT**</td>
<td>0.98 (0.89, 1.07)</td>
<td>0.93 (0.86, 1.08)</td>
<td>0.84 (0.76, 0.94)</td>
</tr>
</tbody>
</table>

Factors Associated with Acute Allograft Rejection

- In univariable analyses, the only factor that was significantly associated with AR was choice of CNI (HR for Tac vs. CsA 0.25 [95% CI 0.11, 0.57], p=0.001).
- In sensitivity analysis which excluded 8 patients with AR in the first two weeks, post KT, use of Tac (HR 0.16 [0.06, 0.43], abacavir (0.39 [0.16, 0.94]) and PiVr (2.63 [1.08, 6.44]) were associated with AR in univariable analysis; only use of Tac (HR 0.27 [0.12, 0.61]) was associated with AR in multivariable analysis (Table 2).

DISCUSSION
Summary
- Use of Tac was associated with a significantly reduced incidence of AR in the first year post KT.
- Our data suggest that Tac may be the preferred CNI for KT in HIV infection.
- Use of protease inhibitor-sparing antiretroviral therapy may facilitate the safe administration of Tac.

REFERENCES

ACKNOWLEDGMENTS
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