EBV Protocol

8.26.14
# Data From UNOS

## Summary Stats 1988-2014 CASU + 2009-2014 CAPC

<table>
<thead>
<tr>
<th>Organ</th>
<th>Total</th>
<th>PTLD</th>
<th>Percent PTLD</th>
<th>Percent PTLD in Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>294</td>
<td>21</td>
<td>7</td>
<td>3-9</td>
</tr>
<tr>
<td>Heart-Lung</td>
<td>34</td>
<td>3</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Intestine</td>
<td>42</td>
<td>7</td>
<td>17</td>
<td>10-45</td>
</tr>
<tr>
<td>Liver</td>
<td>512</td>
<td>12</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Lung</td>
<td>43</td>
<td>5</td>
<td>12</td>
<td>n/a</td>
</tr>
</tbody>
</table>

## Summary Stats 1995-2014 CAPC

<table>
<thead>
<tr>
<th>Organ</th>
<th>Total</th>
<th>PTLD</th>
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<th>Percent PTLD in Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>426</td>
<td>7</td>
<td>2</td>
<td>2-4</td>
</tr>
</tbody>
</table>
PTLD Risk Factors from Literature

• Pre-transplant
  – Seronegative

• Time of transplant
  – Use of T cell suppressive therapy
  – <24 months of age
  – Circulating virus
  – Viral co-infections (?)

• Post-transplant
  – EBV DNAemia
  – Persistent low levels of DNAemia
  – Use of T cell suppressive therapy
  – Use of steroids
  – < 5 years old at time of EBV DNAemia
Screening

• Laboratory pre-transplant
  – EBV serology Viral Capsid IgG and IgM at time of listing and every six months on the list

• Laboratory at time of transplant
  – EBV serology Viral Capsid IgG and IgM for recipient and donor
  – EBV PCR
Risk Stratification

High Risk
- Age < 5 years old
- D+/R-
- D-/+/R+
- D-/R-
- Steroids, ATG, increased immunosuppression
- Small bowel transplant
- Lung transplant

Low Risk
- D-/R- AND ≥ 5 years old
- Kidney transplant
Screening-Post transplant-Low Risk

Year 1

PCR q 3 months → PCR positive

Low Risk
-D-/R- And ≥ 5 years old
-Kidney transplant

Intervention

Asymptomatic
Symptomatic
Screening-Post transplant-High Risk

Year 1
- PCR positive
  - PCR q 2 weeks x 3 months
  - PCR q 1 month x 9 months

Intervention

Asymptomatic
Symptomatic

High Risk
- Age < 5 years old
- D+/R-
- D-/+/R+
- D-/R-
- Steroids, ATG, increased immunosuppression
- Small bowel transplant
- Lung transplant
**Screening - Post transplant**

### Year 1

**High Risk**
- PCR q 2 weeks x 3 months
- PCR q 1 month x 9 months

**Low Risk**
- PCR q 3 months x 12 months

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**High Risk**
- Age <5 years
- Recipient -/Donor+
- Recipient +/Donor+
- Recipient -/Donor-
- Steroids, ATG, enhanced immunosuppression
- Small bowel, lung

**Low Risk**
- Recipient -/Donor- Age >5 years
- Kidney transplant

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**PCR positive**

**Intervention**
Intervention EBV PCR Positive & Asymptomatic

Asymptomatic

If PCR > XX ("high viral load")
- Decrease immunosuppression
- Check PCR q 2 weeks x 4 weeks
  - If PCR decreases by 1 log, continue checking PCR q 2 weeks.
    - Resume normal immunosuppression when PCR negative
  - If PCR is not negative at end of 8 weeks or increases by 1 log at any time

If PCR < XX (threshold)
- Start treatment doses of ganciclovir
- Check PCR q 2 weeks
  - Stop ganciclovir when PCR negative
  - If PCR stable but positive for > 6m or increasing by 2 logs
    - IVIg (dose?)
**Intervention EBV PCR Positive & Asymptomatic**

**Asymptomatic**

- If PCR > XX (“high viral load”)
  - Decrease immunosuppression
- If PCR < XX (threshold)
  - Recheck PCR
- If PCR increases > 2 log
  - Decrease immunosuppression
- If PCR is stable or decreased
  - PCR q 1 month until negative
  - If PCR stable but present >6m or If PCR > XX (“high viral load”)
Intervention EBV PCR Positive & Asymptomatic

Asymptomatic

If PCR > XX (“high viral load”)
- Decrease immunosuppression
- Check PCR q 2 weeks x 4 weeks

If PCR decreases by 1 log, continue checking PCR q 2 weeks.
- Resume normal immunosuppression when PCR negative

If PCR is not negative at end of 8 weeks or increases by 1 log at any time

If PCR increases > 2 log
- Start treatment doses of ganciclovir
- Check PCR q 2 weeks
- Stop ganciclovir when PCR negative

If PCR stable but positive for > 6m or if increasing by 2 logs

If PCR > XX (“high viral load”)
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If PCR < XX (threshold)
- Recheck PCR

If PCR increases > 2 log
- Check PCR q 2 weeks x 4 weeks
- PCR q 1 month until negative

If PCR stable but present >6mo or if increasing by 2 logs
- IVIg (dose?)
- Stop ganciclovir when PCR negative

Resume normal immunosuppression when PCR negative

If PCR increases by 1 log,
- Check PCR q 2 weeks
- Start treatment doses of ganciclovir
Symptomatic EBV - Definition

- EBV viremia or seroconversion AND
  - Fever
  - Leukopenia
  - Atypical lymphocytosis
  - Exudate tonsillitis
  - Adenopathy
  - Hepatitis

- OR tissue diagnosis of EBV infection but not PTLD
Intervention EBV PCR Positive & Symptomatic

Symptomatic

Work up to distinguish SEBV from PTLD

CT scan

Biopsy as indicated

Decrease immunosuppression

Start treatment doses of ganciclovir and IVIg

PCR q 1 week until negative
Data To Extract from STRIDE

- Level of EBV PCR (viral load) that is associated with development of PTLD

- Age range of our patients that have developed PTLD

- Time from transplant for our development of PTLD in our patients.