CMV Kinetics in Transplant Recipients

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CMV in Transplant Recipients

- Cytomegalovirus (CMV) infection frequently complicates the course after solid organ transplantation (SOT) and human stem cell transplantations (HSCT)

- If not diagnosed and treated while the viral load is low, CMV infection may progress to cause CMV disease or CMV syndrome

- **CMV (end-organ) disease** – evidence of CMV infection with attributable symptoms of organ involvement (e.g. pneumonitis, gastro-enteritis, hepatitis etc.)

- **CMV syndrome** – evidence of CMV infection with combination of fever and bone marrow suppression (difficult to diagnose)
Management of CMV in transplant recipients

- **Risk stratification**: recipients can be either at high, intermediary or low risk of CMV infection based on pre-transplant CMV IgG serostatus (+/-) of donor and recipient.

- **Preemptive treatment**: screening with CMV PCR at regular intervals (once/week is recommended) in order to detect and treat infection before it causes clinical disease.

- **Universal prophylaxis**: 3-6 months following transplantation with valganciclovir prophylaxis.
Strong association between CMV disease and high CMV virus load. CMV kinetics dictate the monitoring frequency with CMV PCR, i.e., rapid doubling time = frequent PCR tests.

Previous literature has established CMV as a rapidly replicating virus, with a doubling time of 1.3-2 days. MATCH applied weekly screening intervals (as recommended by current guidelines) so that rapid doubling times could be taken into account.

Dias nummer 69

PL2 skal ændres til median peak value
Paula Isabelle Lodding: 31-01-2015
CMV Doubling Time in MATCH

- Overall median doubling time; 4.3 (IQR 2.5-7.8) days
- No significant differences in doubling time detected when adjusting for
  - type of transplantation
  - risk of CMV infection according to donor/recipient CMV IgG status
Mathematical Simulation of the Optimal CMV Screening Intervals Based on the Doubling Time

“Optimal” screening interval if ≤5% of the patients develop CMV infection
≥ 20,000 copies/mL during the screening interval

<table>
<thead>
<tr>
<th>Assumed doubling time:</th>
<th>Intervals between screening with CMV PCR (days)</th>
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<tbody>
<tr>
<td></td>
<td>7</td>
</tr>
<tr>
<td>31 hours – no variation</td>
<td>Estimated % of recipients having undesirably high CMV viral load during the screening interval</td>
</tr>
<tr>
<td></td>
<td>11.1</td>
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<tr>
<td>Varied as observed in our cohort</td>
<td>1.4</td>
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</tbody>
</table>

Intervals between screening with CMV PCR may be extended from 7 to 10 days - a 30% reduction in screening visits and associated cost!
Conclusion

- High virus load is a risk factor for CMV disease
- A rapid doubling time necessitates frequent screening to avoid high virus loads
- We are unable to reproduce the previously reported doubling time estimates
- Screening intervals may be prolonged from 7 to 10 days
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