CMV Treatment and Prevention in Transplantation

Clinical Trial Design Issues
HSCT Recipients:

Proposed primary endpoint is CMV viremia (DNAemia) or CMV tissue-invasive disease.

- At what virologic threshold should prophylaxis be considered a failure?
  - Should the threshold differ depending on baseline risk factors for CMV?
  - Should any clinical considerations be taken into account, in addition to virologic threshold, in assessing primary endpoint?
CMV Prophylaxis Trials

SOT Recipients:
Proposed primary endpoint is CMV disease (CMV syndrome or tissue-invasive disease).
– What is the virologic threshold for defining CMV syndrome?
Preemptive Therapy Trials

HSCT Recipients:
Proposed primary endpoint is undetectable CMV DNAemia and prevention of CMV tissue-invasive disease.

- What is appropriate duration of preemptive therapy?
- At what time point after initiation of preemptive therapy should primary endpoint be assessed given that most patients will be switched to maintenance/suppressive therapy?
Preemptive Therapy Trials

SOT Recipients:
Proposed primary endpoint is undetectable CMV DNAemia and prevention of CMV disease (including tissue-invasive disease and CMV syndrome in SOT recipients).

• What is appropriate virologic threshold for initiation of preemptive therapy?
• What is appropriate duration of preemptive therapy?
• At what time point after initiation of preemptive therapy should primary endpoint be assessed given that most patients will be switched to maintenance/suppressive therapy?
Trials for Treatment of CMV Disease

How long should patients with CMV tissue-invasive disease be treated?

• Is duration of therapy the same for tissue-invasive disease and CMV syndrome in SOT recipients?
• Does duration of therapy depend on specific end-organ involvement?
• When should primary endpoint (clinical improvement/resolution of signs and symptoms, plus undetectable CMV DNAemia) be assessed?