The Clash Of The Titans: Prophylaxis Vs. Preemptive Strategies For CMV Infections After Solid Organ Transplantation. A Meta-analysis

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BACKGROUND

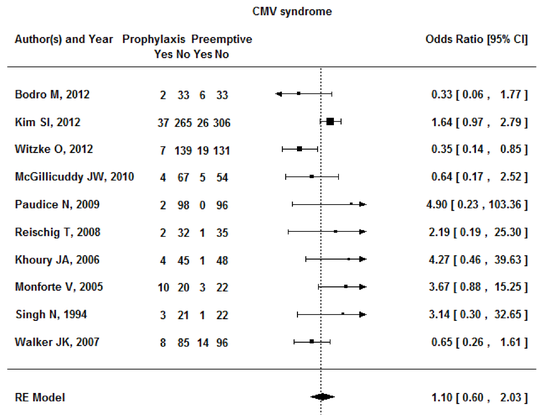
Prophylactic and preemptive strategies are used to prevent cytomegalovirus infections after solid organ transplantation (SOT). Many randomized trials directly comparing these strategies have been published. We assessed the safety and efficacy of both strategies for CMV prevention after SOT.

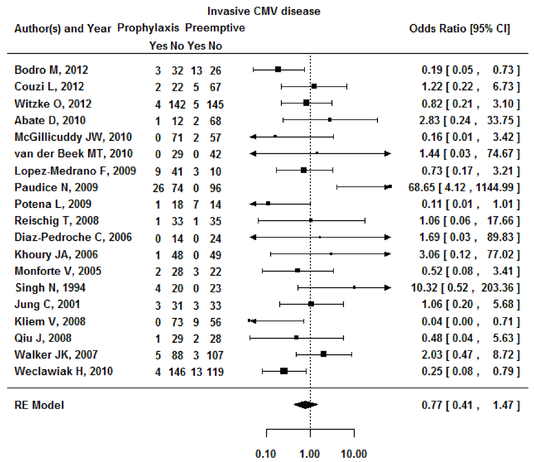
METHODS

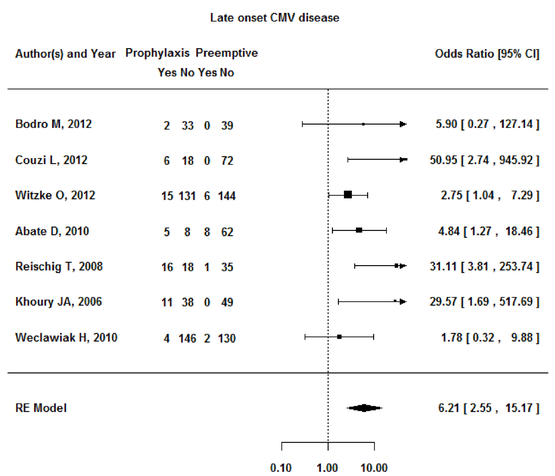
- DerSimonian and Laird random-effects model was used for pooling and Q statistic method and I-squared methods were used to assess statistical heterogeneity.
- 20 studies (2744 patients) were selected.

RESULTS

- The odds of CMV syndrome (**OR=1.10**; 95%CI:0.60-2.03; p=0.76;Q=18.55; I^2=51.49%) and disease (**OR=0.77**; 95%CI:0.41-1.47; p=0.43;Q=32.71;I^2=44.97%.) were not significantly different between strategies.
- The odds of developing late-onset CMV infections were higher for the prophylactic compared to the preemptive strategy (**OR=6.21**; 95%CI:2.55-15.20; p<0.0001; Q=9.66; I^2=37.9%).
- The odds of CMV viremia were lower for prophylaxis (**OR=0.42**;95%CI:0.24-0.74; p=0.003; Q=48.10; I^2=75.1%).
- All drugs caused similar reductions in CMV viremia:
  - acyclovir and valacyclovir (OR=0.37; 0.04-3.70;p=0.40;Q=0.02,I^2=82.51%)
  - ganciclovir (OR=0.45;95%CI:0.12-1.65;p=0.23;Q=0.07,I^2=69.08%)
  - valganciclovir (OR=0.47;95%CI:0.22-0.99;p=0.05;Q<0.0001,I^2=79.80%).







- Compared to preemptive strategy, prophylaxis prevented more CMV viremia when duration was 5.7 -14.3 weeks (OR=0.37; 95%CI:0.20 0.71; p=0.003; Q<0.0001,I^2=78.60%), but not when duration was 17.1-25.7 weeks (OR=0.76; 95%CI:0.31-1.87; p=0.55; Q=0.37,I2=0%).
- No differences between prophylaxis and preemptive strategies were noted for:
  - graft loss (OR=0.88; 95%CI:0.37-2.13; p=0.78; Q=13.03,I^2=38.62%),
  - graft loss censored for death (OR=0.73; 95%CI:0.17-3.21; p=0.68; Q=4.48;I^2=55.32%),
  - acute rejection (OR=0.93; 95%CI:0.70-1.24;p=0.64; Q=12.99;I^2=7.61%)
  - mortality (OR=0.80; 95%CI:0.56-1.14; p=0.22; Q=8.76;I^2=0%).
- More patients on prophylaxis had leukopenia (OR=1.97; 95%CI:1.39-2.79; p=0.0001; Q=7.10;I^2=0%) and neutropenia (OR=2.07;95%CI:1.13-3.78;p=0.02;Q=6.77;I^2=11.40%) compared to patients on preemptive strategy.
- The odds for other infections (HSV, VZV, bacterial and fungal infections) were not significantly different between both strategies.

CONCLUSIONS

The prophylactic and preemptive strategies have similar efficacy in preventing CMV syndrome and disease. Prophylaxis was associated with less viremia early after transplantation, but with significantly more late-onset CMV infections and side effects (leukopenia and neutropenia). Rates of rejection, graft loss, death and other infections were similar.