Use of Valganciclovir in CMV High Risk Liver Transplant Recipients

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Background

1) Patients at highest risk for developing cytomegalovirus (CMV) post transplantation are donor positive, recipient negative.
2) CMV is one of he most common pathogens causing disease during the first 6 months, however, initiation of prophylaxis has altered this timeline.
3) In the absence of prophylaxis, CMV reactivation occurs in approximately 50-60 percent of patients within 6 months.
4) Valganciclovir is the most common agent for prophylaxis.
5) The average valganciclovir cost to the healthcare system is ~$4,000/month.

Study purpose: To better understand the time to CMV seroconversion post-transplant among Oregon Health and Science University liver transplant recipients.

Methods

- Single center, retrospective study at Oregon Health & Science University. Patients >18 years old receiving their first, single organ transplantation and had CMV D+/R- status.
- The primary endpoint was CMV infection or disease at 1 year after transplant.
- Secondary endpoints were leukopenia and use of G-CSF on valganciclovir.
- Univariate analyses were performed using student T test, chi-squared for categorical variables, Fisher's exact for independence nominal variables, and Kaplan-Meier test for time to event. (IRB Number # 21954)

Results

- 438 liver transplants in 426 recipients over an 8-year period (2012-2019) with minimum of one year of follow up.
- A total of 71 D+/R- met inclusion criteria of receiving valganciclovir 900 mg per day for six months and six months of CMV PCR follow up every 2 weeks post transplant as CMV prophylaxis.
- CMV disease occurred in 43 patients (60.5%) by 1 year
- **Average time to CMV infection was 234 days (average of 54 days after discontinuation of valganciclovir therapy for prophylaxis). Figure 1.**
- Two patients experienced CMV infection while on valganciclovir therapy.
- Premature valganciclovir interruption occurred in 3 patients and requiring granulocyte-colony stimulating factor (G-CSF). In addition, 19 patients (27%) of this cohort used granulocyte-colony stimulating factor due to drug toxicity resulting in lymphopenia.

Table 1: Patient demographics

Age (years)	55.62 (49-61)
Gender	
Male	53 (75)
Female	18 (25)
Ethnicity	
white	68 (96%)
Hispanic	2 (3)
Asian	1 (1)
Average MELD	23.5 (18-29)
Original Disease	
HCC	14 (20)
Etoh alone	14 (20)
HCV alone	11 (15)
HCV/Etoh	9 (13)
NAH	8 (11)
PSC	5 (7)
PBC	4 (6)
others	6 (8)

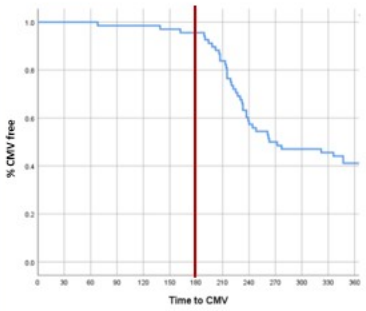
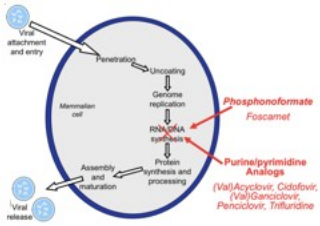


Figure 1: Time to developing positive CMV. As demonstrated, following cessation of CMV prophylaxis, there is a dramatic increase in the number of CMV cases.

Mechanism of Action



Discussion

- During the first 6 months post-transplant, valganciclovir was effective at preventing CMV disease, however, shortly after discontinuing, average time to event was 52 days.
- Opportunistic infections post transplantation are well known to cause graft dysfunction and increase patient morbidity and mortality.
- Toxicity resulting in either interruption or use of granulocyte colony stimulating factor was seen in nearly a third of patients.
- Ultimately, these results necessitate development of a safe, long term, cost effective measures to reduce CMV conversion either after discontinuation of valganciclovir or in place of its use.

References

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2. Santos CA, Delayed- Onset cytomegalovirus disease coded during hospital readmission in a multicenter, retrospective cohort of liver transplant recipients. Liver Transpl. 2015;21(5):581. Epub 2015 Apr 15.
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