Drug Use Evaluation: Ganciclovir and Valganciclovir for Treatment of Cytomegalovirus in Bone Marrow Transplant Patients

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Background

Cytomegalovirus (CMV) is often reactivated in bone marrow transplant (BMT) patients and is an important contributor to morbidity and mortality (e.g., colitis, retinitis). Prior to development of these symptoms, it is often detected in the blood, giving an opportunity to provide pre-emptive therapy to prevent these more serious events (1, 2).

Treatment includes the use of either IV ganciclovir (CrCl and weight-based dosing) or oral valganciclovir (CrCl based dosing). Both require close monitoring and review with twice a week full blood counts (FBC) to aid in monitoring for common side effects such as neutropenia, anaemia, and thrombocytopenia (3, 4).

Valganciclovir is non-inferior to ganciclovir as pre-emptive therapy in CMV in other populations (2). Valganciclovir is also devoid of adverse events related to intravenous (IV) or indwelling catheter access. Cancer Care Services received approval for the use of valganciclovir within its haematology and post BMT population for CMV pre-emptive therapy in place of ganciclovir.

Aim

To compare cost effectiveness, drug use and clinical outcomes between valganciclovir and ganciclovir use to evaluate the impact of the practice change.

Methods

Audit design: A single centre retrospective audit

Inclusion: Post-BMT outpatients who commenced on ganciclovir in 2019 and who commenced on valganciclovir in 2021.

Exclusion: Patients who were admitted to hospital during the course of their pre-emptive treatment

Data collection: electronic medical records, pharmacy dispensing record and pathology results.

The data collected includes gender, age, weight, creatinine, blood counts, CMV viral load, drug dosage.

Data analysis: Fishers Exact test & Mann-Whitney U test were used to analyse data

Results

	Ganciclovir	Valganciclovir	Statistics
Total patients	27	24	
Drug cost (includes inpatient use)	$48,401	$19,901	
Median length of treatment	21	29.5	*P = 0.002*
Neutropenia	3	9	*P*=0.049
Thrombocytopenia	11	10	*P*=0.79 (NS)
Number of patients with overdosing	4	7	*P*=0.32 (NS)
Number of patients with underdosing	6	0	*P*=0.02
Unclear dosing due to obesity	3	3	N/A

Discussion

The treatment duration was longer in valganciclovir compared to ganciclovir despite non-inferiority. A possible reason for this is reduced monitoring, as this cohort of patients are not attending day therapy unit (DTU) as they would if they were being treated with ganciclovir. Although the duration is significantly longer, the patient benefits by not requiring IV access, ability to access telehealth and not requiring DTU admission.

A significantly larger number of patients experienced neutropenia when being treated with valganciclovir. Similar data has been reported in solid organ transplants, valganciclovir 8.2%, vs ganciclovir 3.2%, although this didn't appear to impact the proportion of patients discontinuing therapy, as this remained similar in both groups (5).

Despite closer monitoring, more patients received lower than recommended doses when treated with ganciclovir ((N=6/27 vs N=0/24) (P+0.02)). Although, this does not account for the potential inter- and intra- patient variability of ganciclovir serum concentration that can be seen in the extremes of renal function (6).

This change in standard therapy was a significant cost saving exercise with valganciclovir being substantially cheaper than ganciclovir. It also saved 55 hours of DTU chair time, which frees up nursing time potentially allowing more patients to be treated.

Conclusion

The significant findings relating to increased duration of treatment and increased adverse effects in patients being treated with valganciclovir, suggest that improved monitoring and clinical considerations are required to optimise treatment of CMV with valganciclovir. Although, it should be acknowledged that this change in standard practice has been a cost saving exercise benefitting the hospital and the patient

References

1. Azevedo LS, Pierrotti LC, Abdala E, Costa SF, Strabelli TMV, Campos SV, et al. Cytomegalovirus infection in transplant recipients. Clinics (Sao Paulo). 2015;70(7):515-23.
2. RBWH BMT Guidelines.
3. Australian Medicines Handbook: Valganciclovir. Adelaide SA: Australian Medicines Handbook Pty Ltd 2022.
4. Australian Medicines Handbook: Ganciclovir. Adelaide SA: Australian Medicines Handbook Pty Ltd 2022.
5. Vaziri S, Pezhman Z, Sayyad B, Mansouri F, Janbakhsh A, Afsharian M, et al. Efficacy of valganciclovir and ganciclovir for cytomegalovirus disease in solid organ transplants: A meta-analysis. J Res Med Sci.
6. Märtson A-G, Edwina AE, Burgerhof JGM, Berger SP, de Joode A, Damman K, et al. Ganciclovir therapeutic drug monitoring in transplant recipients. Journal of Antimicrobial Chemotherapy. 2021;76(9):2356-63.