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In Vitro Exposure of Cytomegalovirus (CMV)-Infected Cells to High Concentrations of Acyclovir (ACV) Induces Resistance to Ganciclovir (GCV). Dworkin RJ*, Miner RC, Drew WL. Biskind Pathology Research Laboratory, Mt. Zion Hospital and Medical Center, San Francisco, CA.

ACV is frequently given to patients with HIV infection for the treatment of herpes simplex (HSV) and varicella zoster virus infections and for prophylaxis or suppression of CMV infections. The molecular structure of ACV differs from GCV by only a single hydroxyl side chain. ACV is activated by phosphorylation in HSV-infected cells. Its lack of significant antiviral activity against CMV is attributed to lack of phosphorylation in CMV-infected cells. Nevertheless, it was intriguing that one of the original three patients described with GCV-resistant CMV had been on long-term therapy with ACV¹. We hypothesized that ACV exposure might induce cross-resistance to GCV. Three clinical isolates of CMV known to be highly sensitive to GCV were exposed to increasing concentrations of ACV. As controls, the same cultures were serially passaged in MEM. Viral isolates obtained at the final concentration of ACV were tested against ganciclovir by plaque reduction assay. Isolate #1 was passed up to a final concentration of ACV of 150 uM, while #2 and 3 were passed up to 100 uM.

ED50/90 vs ganciclovir

Isolate	#1	#2	#3
Control (no ACV)	3.9/8.9	3.4/8.2	1.4/4.8
Post-ACV	7.7/21	2.7/7.6	7.1/15.2

The results suggest that isolate #1 and #3 became more resistant to GCV when exposed to increasing concentrations of ACV. If similar increases in GCV resistance occur in vivo as a result of exposure to ACV, GCV resistant CMV may become a frequent clinical problem even prior to GCV therapy.

Reference: 1. Erice A et al. Progressive disease due to GCV-resistance CMV in immunocompromised patients. *N Engl J Med* 1989;320:289-293.

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Activity of Foscarnet versus Ganciclovir-resistant Cytomegalovirus (CMV). W.L. DREW, D. MINER, D. PARENTI. Mount Zion Hospital and Medical Center of U.C. San Francisco and George Washington University Medical Center, Washington D.C.

We have tested 6 Ganciclovir (GCV) sensitive and 10 GCV resistant strains of Cytomegalovirus (CMV) against Foscarnet. Plaque reduction assays were used to determine all antiviral susceptibilities and each isolate was from a different patient. Results are as follows:

	GCV (uM)		Foscarnet (uM)	
	mean		mean	
GCV sensitive strains (6)	ED50	ED90	ED50	ED90
	4.8	12.5	222	466
GCV resistant strains (10)	23.6	49.0	373	741

Only 1 of 6 GCV sensitive strains had a Foscarnet ED90 >500 uM while 7 of 10 GCV resistant strains had ED90 >750uM. We conclude that GCV resistant strains of CMV are less sensitive to Foscarnet than GCV sensitive strains. The clinical significance of these findings remains to be determined.