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The *in vitro* Activity of Cidofovir against Acyclovir-resistant and Foscarnet-resistant Herpes Simplex Virus (HSV) Isolates. S. Safrin, E. Abarbarchuk, E. Palacios. The Herpes Virus Research Laboratory, San Francisco General Hospital, San Francisco CA.

We tested 40 clinical isolates of HSV for susceptibility against acyclovir, foscarnet, and cidofovir (HPMPC; (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)-cytosine) using the plaque reduction assay. Mean ID_{50} values for cidofovir were significantly lower for 18 acyclovir-resistant than for 22 acyclovir-susceptible strains (7.5 vs. 15.36 ug/ml; $p=.01$). Similarly, mean ID_{50} results for the TK-deficient control strain 11557 were significantly lower for cidofovir than acyclovir in 11 runs (14.39 vs. 54.58 ug/ml; $p<.001$). Mean ID_{50} values for cidofovir were lower than for foscarnet against 40 foscarnet-susceptible clinical isolates (11.8 vs. 22.3 ug/ml; $p<.001$) and were particularly low in 10 runs of the foscarnet-resistant *pol* mutant control strain PAA'5 (2.67 vs. 452 ug/ml; $p=.02$). Although the threshold definition for resistance to cidofovir needs to be further delineated, we find no evidence of cross-resistance between cidofovir and either acyclovir or foscarnet.

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Comparative Evaluation of the Plaque Reduction Assay and a Microplate ELISA Test for Antiviral Susceptibility Testing of Herpes Simplex Virus (HSV) Isolates. S. Safrin, E. Palacios, B. Leahy. San Francisco General Hospital, University of California, San Francisco CA and Royal Perth Hospital, Western Australia.

We evaluated a newly developed microplate in situ ELISA ("MISE") assay for antiviral susceptibility testing of clinical isolates of HSV, using a target sample of 30 collected isolates which were previously characterized using the plaque reduction assay (PRA). Monoclonal anti-HSV antibodies and peroxidase-conjugated rabbit anti-mouse immunoglobulin are sequentially added to virus-infected Vero cell monolayers in 96-well plates, followed by OPD substrate with intervening PBS washes. The concentration of antiviral drug is plotted against absorbance at 490 nm, and the ID_{50} extrapolated. We found concordant results between the MISE and PRA in 17/19 acyclovir-susceptible and 10/11 acyclovir-resistant isolates. All discordant results are to be repeated. Mean ID_{50} values from the MISE and PRA were nearly identical in 22 foscarnet-susceptible isolates (23.9 vs. 24.2 ug/ml) but significantly lower in the MISE for 8 foscarnet-resistant isolates (136.8 vs. 87.1 ug/ml; $p=.02$). The appropriate threshold to define foscarnet resistance in the MISE remains to be determined. The MISE test, which requires only 3 days to derive a susceptibility result, holds promise as a clinically useful and semi-automated assay which has a standardized, objective endpoint.