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Susceptibility Profiles of Ganciclovir-resistant HCMV Clinical Isolates to Several Candidate Antiviral Compounds. S. C. Stanat[1], M. T. Gaillard[1], W. L. Drew[2], K. K. Biron[1]. [1]Burroughs Wellcome Co., Research Triangle Park, NC, U.S.A., [2]Mount Zion Hospital and Medical Center, San Francisco, CA, U.S.A.

Recently we reported the isolation of human cytomegalovirus (HCMV) resistant to ganciclovir from several patients with AIDS (NEJM, 320: 289-293. 1989). Others have also reported ganciclovir-resistance of HCMV isolates from AIDS patients receiving extended ganciclovir therapy (29th ICAAC, Abst # 61, 1989). More than 90% of AIDS patients are infected with HCMV. It is now estimated that 15% of AIDS patients with CMV retinitis who receive suppressive ganciclovir therapy will develop ganciclovir-resistant virus. We show here that *in vitro* resistance to ganciclovir of the post-therapy isolates can be attributed to the inability of cells infected with these isolates to phosphorylate ganciclovir. We have also expanded susceptibility profiles of ganciclovir-resistant clinically derived HCMV strains to established antivirals and to several candidate antivirals: acyclovir, ganciclovir, foscarnet, vidarabine, HPMPC, FIAU, and DHPC. The susceptibility patterns of these ganciclovir-resistant isolates correlate with predicted mechanisms of action of these candidate antiviral compounds.

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Pathogenicity for Man of Human Rhinovirus Type 2 Mutants Resistant to or Dependent on Chalcone Ro 09-0410.

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Mutants of human rhinovirus type 2 (HRV-2), resistant to and dependent on the antirhinoviral compound, chalcone Ro 09-0410, have been selected in cell culture under clean laboratory conditions. A total of 42 volunteers were challenged with either the drug resistant mutant [SR2-410(r)] (15 volunteers), drug dependent mutant [SR2-410 (d)] (15 volunteers) or a wild-type HRV-2 which had a similar passage level in vitro as the mutants but without the drug (12 volunteers), Thirty-three percent, 67% and 82% of volunteers challenged with the wild-type HRV-2 developed cold symptoms, shed virus and showed serological evidence of infection, respectively. In contrast only 13%, 27% and 23% of volunteers challenged with the drug resistant mutant developed colds, shed virus or showed serological evidence of infection, respectively. None of the volunteers challenged with the drug dependent mutant became infected or had symptoms of colds. These results demonstrate that a drug resistant rhinovirus was capable of infecting man and producing disease though its infectivity was reduced when compared with the wild-type. In contrast a drug dependent mutant had lost its ability to infect man.