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Frequency of UL97 Mutations Related to Ganciclovir Resistance in Clinical CMV Isolates. W.L. Drew, S. Guentzel, K.R. Michels, R.C. Miner, S. Chou, VA Medical Center/Oregon Health Sci Univ., Portland and Mt. Zion Med Center of Univ. of California, San Francisco.

Objective: Determine the frequency of UL97 Phosphotransferase gene mutations in ganciclovir (GCV) resistant isolates of CMV. Methods: 30 CMV isolates from subjects who received GCV therapy were tested for susceptibility to GCV by a plaque reduction assay. Results were correlated with restriction enzyme diagnosis and sequence analysis of the CMV UL97 coding region. Results: 20 of the 30 isolates had one or more mutations in UL97 affecting amino acid encoding at codons 460, 520 or 591-596. All 20 were resistant to GCV with a 50% inhibitory concentration (IC_{50}) of >6 uM (range, 6.7 to 50). The remaining 10 isolates had no mutations at these loci; 8 were susceptible to ganciclovir while the other 2 were borderline resistant (IC_{50} 6.6 and 7.2 uM). None of 40 control CMV isolates from untreated subjects contained any mutations at these loci. Screening for the 3 most common mutations at codons 460, 594 and 595 by restriction digest analysis identified 16 of 20 (80%) of isolates with GCV resistance-related UL97 mutations, or 16 of 22 (73%) of isolates with GCV IC_{50} of >6 uM. Conclusions: A large majority of GCV-resistant clinical CMV isolates contain diagnostically useful mutation in UL97, particularly at codons 460, 594 and 595. The most common mutations have previously been shown in marker transfer studies to confer GCV resistance to strain AD169 (J. Infect. Dis., March 1995).