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CHARACTERIZATION OF INFLUENZA VIRUS CLINICAL ISOLATES OBTAINED DURING UMIFENOVIR CLINICAL STUDY "ARBITR"

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Abstract: Oral drug umifenovir (Arbidol) is licensed and widely used in Russia for treatment and prophylaxis of influenza A and B infections. We investigated susceptibility of influenza viruses isolated from patients pre- and during administration of umifenovir in phase IV clinical trial ARBITR. In addition, we examined the susceptibility of a panel of reference and NA inhibitor-resistant viruses and their sensitive counterparts to umifenovir. Umifenovir inhibited replication of all reference human influenza A and B viruses that circulated in 2012-2014 seasons. The wild-type influenza viruses and their oseltamivir-resistant mutants were susceptible to umifenovir at similar levels. All 18 isolates obtained before and during therapy with umifenovir in ELISA-cell assay were equally sensitive to umifenovir with IC50 falling in the range of 7.0 to 12,5 ug/ml and similar to IC50 previously observed for laboratory and clinical isolates. Matched isolates of two patients from whom we were able to obtain day 3, 5 and 7 samples were chosen for sequence analysis. No amino acid changes in HA that had previously been identified in vitro as being involved with reduction of susceptibility to umifenovir were observed. None of the viruses isolated before and during therapy with umifenovir displayed reduced susceptibility to NA inhibitors and no mutations that led to an amino acid substitution in the NA were found in studied samples. Umifenovir is effective against influenza viruses of 2012-2014 season and oseltamivir-resistant influenza viruses. No umifenovir-resistance has emerged during therapy of acute influenza infection. Umifenovir administration did not affect the susceptibility of influenza viruses to NA inhibitors.