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Abstract (poster session)

**Post exposure efficacy of AVI-7100 against influenza A in mouse and ferret infection models**

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Objective: AVI-7100 is a phosphorodiamidate morpholino oligomer containing three modified linkages (PMOplus) that is designed to interfere with expression of the M1 and M2 genes of influenza A virus. The objective was to evaluate the therapeutic utility of AVI-7100 up to one day post viral exposure. Methods: A single 0.1mg intranasal (i.n.) dose of AVI-7100 was administered to female BALB/c mice (n=10/group) either 4 hours prior to or 4 hours after viral challenge with with 5 X 105 pfu of A/Port Chalmers/1/73 (H3N2). Lung viral load was determined on day 6 post infection. A similar efficacy study in outbred ferrets (Mustela putorius furo; n=7/group) were administered AVI-7100 as a single i.n. dose 4 hours prior to or 1 day post insufflation viral challenge with 5 X 105 pfu H1N1 A/Hong Kong/2369/09 per ferret. Negative control groups were treated with saline and positive controls were administered oseltamivir at 10 mg/kg p.o. every other day beginning 7 days prior to infection. A plasma pharmacokinetic study with 16 ferrets (4 groups of 4 ferrets/group) in which a 10 mg/kg or 30 mg/kg i.v. dose was evaluated prior to and three days post viral challenge with H1N1 strain A/Mexico/4108/09 or H5N1 strain A/Vietnam/1203/04 . Results: A single intranasal dose of AVI-7100 (0.1mg/mouse) administered either 4 hours prior to or 4 hours after infection with A/Port Chalmers/1/73 (H3N2) significantly ($p<0.05$) reduced lung viral titers in each group compared to vehicle controls and oseltamivir treated mice. In the ferret, a single i.n. dose of AVI-7100 administered 4 hours prior to exposure or 1 day after exposure with A/Hong Kong/2369/09 (an oseltamivir resistant pH1N1) significantly ($p<0.05$) reduced cumulative viral load in nasal wash and in lung bronchiolar lavage compared to saline controls and oseltamivir treated ferrets. A plasma pharmacokinetic study revealed no differences between infected and uninfected ferrets. Conclusions: AVI-7100 is effective against influenza A (H1N1 and H3N2) and in both mouse and ferrets when administered as a single intranasal dose for greater than one day post viral exposure. Post-exposure efficacy data indicate robust antiviral and symptom benefit can be provided by AVI-7100. Infection does not significantly alter plasma pharmacokinetics relative to uninfected ferrets. These data provide a rationale for a therapeutic use of AVI-7100 following influenza exposure.