P934
Abstract (poster session)

Prophylactic 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 prophylactic therapeutic utility of AVI-7100. Methods. A single 0.1mg intranasal (i.n.) dose of AVI-7100 was administered to female BALB/c mice (n=10/group) at 7 days, 3 days or 4 hours prior to viral challenge with 5 X 105 pfu of A/Port Chalmers/1/73 (H3N2). Lung viral load was determined on day 6 post infection. In a separate study, a single i.n. dose was administered to mice infected with A/PR/8 (H1N1) and plasma and lung oligomer concentrations were determined. Outbred ferrets (Mustela putorius furo; n=7/group) were administered AVI-7100 as a single i.n. dose at 7 days, 5 days, 3 days or 4 hours prior to 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. Results. A single intranasal dose of AVI-7100 (0.1mg/mouse) administered 7 days, 3 days or 4 hours prior to 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. PMOplus concentrations in the lungs of mice following a single insufflation dose follow zero order elimination and tissue concentrations above the AVI-7100 EC50 are maintained for greater than three days. In the ferret, a single i.n. dose of AVI-7100 administered 7 Days, 5 days, 3 days or 4 hours prior to 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. The decrease in viral load in nasal wash samples was directly proportional to the interval of time between prophylactic treatment and viral exposure (a zero order reduction in activity). Conclusions. AVI-7100 is effective against influenza A (H1N1 and H3N2) and in both mouse and ferrets after a single intranasal dose up to seven days prior to viral exposure. Zero order elimination of AVI-7100 from the lung was observed. These observations support the prophylactic use of AVI-7100 in preventing influenza A infection.