Beneficial therapeutic effects of delayed intrapulmonary Peramivir administration during severe H1N1 influenza infection in ferrets

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Problem
Most patients with severe influenza disease seek hospital care many days after initial onset of symptoms, limiting the effective use of antivirals. The main goal in the present study was to compare therapeutic effects of delayed intrapulmonary and intramuscular delivery of Peramivir on severe infection outcome.

Materials and Methods
To recapitulate late stage, lower respiratory tract infection, aged ferrets were inoculated intrapulmonary with 106 EID50 influenza A/California/07/2009 H1N1. Peramivir was delivered at 3 and 5 dpi intrapulmonary (PP) or intramuscularly (PM). A group of animals was administrated intrapulmonary with only a vehicle (saline) for control purposes (VP).

Results
All animals in the VP group were euthanized due to severity of the diseases at 8 dpi. Survival in the PP group (75%) was 25% higher than in the PM group (Figure 1). In comparison to the control VP group, intrapulmonary and intramuscular Peramivir administration efficiently reduced viral titers in nasal washes. At 5 dpi, viral titers in lungs from the PP group were lower than in samples from other groups (PP – mean 3.37 TCID50/ml; PM – mean 4.55 TCID50/ml; VP – mean 6.44 TCID50/ml) (Figure 2). Reduced area of lung surfaces with pathology were observed in the PP group (PP – mean 19%; PM – mean 40%; VP – mean 72%) (Figure 3). Microscopic lesions associated with severe disruption of the lung architecture were found only in ferrets from the VP group and one ferret from the PM group (Figure 4).

Conclusions
Delayed intrapulmonary Peramivir administration in aged ferrets has benefits to recovery from severe influenza infection in comparison to delayed intramuscular Peramivir administration.