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Presentation Title:	V-1070 - **In Vivo and In Vitro Activity of DAS181 against NAI-Resistant Influenza Virus**
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Abstract: **Background:** DAS181, a sialidase fusion protein, has been shown effective at treating and preventing infection by seasonal influenza (IFV), highly pathogenic H5N1 avian IFV, and parainfluenza viruses. This study examined the *in vivo* and *in vitro* activity of DAS181 against NAI-resistant strains of IFV. **Methods:** BALB/c mice were infected with 50,000 pfu/mouse of NAI-resistant A/Victoria/3/75(H3N2) and 8 hours later treated with DAS181 or vehicle. Animals were monitored for body weight, viral copies, and survival. The *in vitro* activities of DAS181, zanamivir and oseltamivir were examined against a panel of nine 2009, two 2007 and two 2004 clinical isolates. EC50s were calculated as the concentration of drug reducing plaque number by 50%. Fold resistance values were estimated based on comparison of individual 2007/2009 isolate EC50 to that of 2004 isolate EC50. Each isolate was also sequenced to determine the HA and NA genotypes. **Results:** DAS181-treated

mice had significantly less weight loss (P<0.001), lower viral titers (P<0.001) and increased survival rate (P<0.0001) compared to untreated animals. All of the 2004, 2007 and 2009 clinical isolates were sensitive to DAS181 (avg±SEM EC50 = 0.38±0.12 μM, 0.25±0.05 μM and 0.23±0.08 μM, respectively). In contrast, while the 2004 isolates (2/2) were highly sensitive to oseltamivir, all 2007 (2/2) and 2009 (9/9) isolates exhibited resistance tooseltamivir (avg±SEM EC50 = 3.09±0.17 μM, >342.72±57.28 μM and >380.51±12.96 μM, for 2004, 2007, and 2009 respectively). Most isolates were sensitive to zanamivir (avg±SEM EC50 = 2.99±1.17 μM). All 2007 and 2009 isolates contained the NA mutation H274Y. **Conclusions:** *In vivo* mouse challenge studies with a NAI-resistant strain demonstrated sensitivity to DAS181 treatment. DAS181 *in vitro* was an effective inhibitor of oseltamivir-resistant influenza virus. First in man trials are currently ongoing to test the clinical utility of DAS181 against emerging strains of IFV.