Murine study for BSL-2 virus

Influenza
Animal: BALB/c mouse or another adequate murine model
Virus: Influenza
Experimental design: Mice are divided in groups of 10 (n=10), and infected with the influenza strain of choice. One group is kept as uninfected control. A time after the infection is determined to treat the animals with the test compounds: for example, 8h, 24h, 48h or another interval to be determined. The mice are anesthetized using an IP injection of ketamine/xylazine (50/5 mg/kg) and the test-compound is given intranasally (IN) at the adequate doses (e.g., 11.25, 7.5, or 3.75 mg/kg/day, etc.), and an infected control group that receives the vehicle under identical conditions (adequate vehicle, for example PBS): same volume as the compound (e.g., 0.05 ml) via the same route (IN) starting at an adequate time after the viral challenge, for example 8- or 24- or 48- hours. A positive control, preferably using a clinically accepted pharmaceutical such as Oseltamivir at the recommended dose (e.g., 30 mg/kg/day regimen for Oseltamivir) administered via the recommended route (orally - PO - for the Oseltamivir example), for the recommended duration (twice daily for 5 days in the Oseltamivir example) starting at the same time as the test-compounds (8-, 24- or 48 hours post-infection). An additional group treated with the positive control that uses a different administration route can be created to receive the same intranasal vehicle once daily to mimic the test-compound conditions. Individual weights recorded every day beginning on the day of virus challenge and mice were observed daily for survival. Other measurables such as viral titer in a tissue of interest (e.g., Lungs, trachea, nasal conchae), harvesting of organs and tissues for histopathological analysis to be considered according to need.

A study can resemble the example in the table below. More than one test compound can be envisioned.

<table>
<tr><th>No./group</th><th>Group No.</th><th>Compound</th><th>Dose</th><th>Treatment Route & schedule</th><th>Observations/testing</th></tr>
<tr><td>3</td><td>1</td><td>Untreated</td><td></td><td></td><td rowspan="7">Daily body weight measurement and mortality observation. Other measurables such as viral titer in tissues of interest, histopathological analysis to be evaluated according to need.</td></tr>
<tr><td>10</td><td>2</td><td>PBS-vehicle</td><td></td><td rowspan="4">Intranasal administration (50ul in both nostrils) daily for 2 to 5 days, beginning, for example 8h or 24h post-infection</td></tr>
<tr><td>10</td><td>3</td><td rowspan="3">Compound</td><td>Dose 1</td></tr>
<tr><td>10</td><td>4</td><td>Dose 2</td></tr>
<tr><td>10</td><td>5</td><td>Dose 3</td></tr>
<tr><td>10</td><td>6</td><td>Positive control Oseltamivir</td><td>30mg/kg/day</td><td>Oral administration twice daily for 5 days, beginning 8h or 24h post-infection</td></tr>
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