**1063. Estimating Health Outcomes of Antiviral Use in Influenza (flu) Outbreaks by Linking PK/PD and Epidemiology via Transmission Dynamic Model: A Novel Approach**

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***Background.*** Whilst the potential for pharmacokinetic/pharmacodynamic (PK/PD) optimisation of anti-influenza therapy to improve individual patient outcomes has been published, the indirect benefits of reducing disease transmission has not been described. We explored the latter using a novel approach to link oseltamivir (OS) PK/PD to epidemiological models of influenza (flu) transmission. With this linked PK/PD-Epi model, we examined the impact of high and low doses of OS on flu attack rates (AR) under different levels of infectiousness and percentages of patients receiving OS.

***Methods.*** OS active metabolite (OC) AUC distributions were simulated for 75 and 150mg po BID via a published population PK model. In the model, flu viral shedding duration ($T_{shed}$) is impacted by OC exposure according to published PK/PD breakpoints. The effect of treatment with OS on $T_{shed}$ was linked to an SEIR (Susceptible, Exposed, Infected, Recovered) compartmental model incorporating OS treatment. Using Monte Carlo simulation (including sampling relevant OC AUC and $T_{shed}$ distributions), populations of 100,000 were simulated over one flu season. One thousand flu seasons were then simulated for scenarios including OS 75mg and 150mg bid assuming treatment of 25, 50, and 80% of the infected population, for viruses of low and high infectiousness.

***Results.*** The AR/1,000 patients infected generated from the model by OS dose, percentage of patients receiving treatment, and infectiousness are shown in the table.

The proportion of simulated Flu seasons that had AR >5% tended to be lower as the percentage of patients receiving treatment and/or dose was increased.

| Infectiousness | Percentage of patients receiving OS | 75mg bid | 150mg bid |
|---|---|---|---|
| High (Reference AR 675) | 25% | 593.29 | 530.32 |
| | 50% | 413.31 | 317 |
| | 80% | 209.41 | 128.81 |
| Low (Reference AR 371) | 25% | 51.33 | 32.55 |
| | 50% | 10.6 | 4.81 |
| | 80% | 4.67 | 0.85 |

***Conclusion.*** This is the first study utilising PK/PD modelling to inform a compartmental epidemiological model to estimate the potential impact of OS dose on influenza infection rates. The novel approach suggests that antiviral PK/PD optimised treatment may have direct and indirect benefits reducing societal burden of flu, including containment strategies. Linking PK/PD and epidemiological models may have utility for other antivirals and for other infections.

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