



<b>Title</b>	<b>Harvesting Convalescent Plasma for Hyperimmune Intravenous Globulin Production: A Multicentre Randomised Double-Blind Controlled Trial for Treatment of Patients with Serious S-OIV H1N1 Infection</b>
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## P107-Ab0089

### Harvesting Convalescent Plasma for Hyperimmune Intravenous Globulin Production: A Multicentre, Randomised Double-Blind Controlled Trial for Treatment of Patients with Serious S-OIV H1N1 Infection

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**Background:** Experience from influenza pandemics suggested that convalescent plasma treatment given within 4 to 5 days of symptom onset might be beneficial. However, robust treatment data is lacking.

**Methods:** This is a multicentre prospective double-blind randomized controlled trial. Convalescent plasma from patients who recovered from the 2009 pandemic influenza [A(H1N1)pdm09] infection was fractionated to hyperimmune intravenous immunoglobulin (H-IVIG) by CSL Biotherapies, Australia. Patients with severe A(H1N1)pdm09 infection on standard antiviral treatment requiring intensive care and ventilatory support were randomized to receive H-IVIG or normal IVIG manufactured before 2009 as control. Clinical outcome and adverse effects were compared.

**Results:** Between 2010 and 2011, thirty-five patients were randomized to receive H-IVIG (17 patients) or IVIG (18 patients). One defaulted patient was excluded from analysis. No adverse event related to treatment was reported. Baseline demographics and viral load before treatment were similar between the two groups. Serial respiratory viral load demonstrated that H-IVIG treatment was associated with significantly lower day 5 and 7 post-treatment viral load when compared to the control ( $p=0.04$  and  $p=0.02$  respectively). The initial serum cytokine level was significantly higher in the H-IVIG group but fell to similar level 3 days after treatment. Subgroup multivariate analysis of the 22 patients who received treatment within 5 days of symptom onset demonstrated that H-IVIG treatment was the only factor which independently reduced mortality [OR:0.14, 95% CI, 0.02-0.92;  $p=0.04$ ].

**Conclusions:** Treatment of severe A(H1N1)pdm09 infection with H-IVIG within 5 days of symptom onset was associated with a lower viral load and reduced mortality.

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## P108-Ab0090

### In Silico Structure-based Screening and Characterization of Inhibitors for Influenza A Virus Nucleoprotein

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The trend of drug resistance developed in different strains of influenza viruses is worrying, and it is of utmost importance and urgency to develop new drugs against this virus. The viral nucleoprotein (NP) is a major component of the ribonucleoprotein (RNP) complex for the transcription and replication of the virus. In order to maintain a stable RNP structure, NP forms homooligomers by inserting its tail-loop to the tail-loop insertion site of another NP. In this study, we have employed structure-based virtual screening on the influenza A NP tail loop insertion site and found two hit compounds number 7 and 16 that can subdue influenza RNP activities. Subsequently, two analogs from compound 16 were identified which inhibit RNP activities of various influenza A subtypes and viral growth at micromolar levels. These analogs were also shown to directly interact with NP at  $12.0 \pm 1.25$  and  $41.6 \pm 1.93$   $\mu\text{M}$  respectively by surface plasmon resonance assay. These novel anti-influenza compounds would provide a template for designing drug candidates with higher potency.

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## P109-Ab0091

### A Detailed Longitudinal Study of Infection Attack Rates among Healthy Adults in Hong Kong during the Epidemic of the Human Swine Influenza A/H1N1 Virus in 2009

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**Background:** In an emerging influenza pandemic, estimating severity (the probability of a severe outcome, such as hospitalization, if infected) is a public health priority. As many influenza infections are subclinical, sero-surveillance is needed to allow reliable real-time estimates of infection attack rate (IAR) and severity.

**Methods and Results:** We tested 14,766 sera collected during the first wave of the 2009 pandemic in Hong Kong using viral microneutralization. We estimated IAR and infection-hospitalization probability (IHP) from the serial cross-sectional serologic data and hospitalization data. Had our serologic data been available weekly in real time, we would have obtained reliable IHP estimates 1 wk after, 1-2 wk before, and 3 wk after epidemic peak for individuals aged 5-14 y, 15-29 y, and 30-59 y. The ratio of IAR to pre-existing seroprevalence, which decreased with age, was a major determinant for the timeliness of reliable estimates. If we began sero-surveillance 3 wk after community transmission was confirmed, with 150, 350, and 500 specimens per week for individuals aged 5-14 y, 15-19 y, and 20-29 y, respectively, we would have obtained reliable IHP estimates for these age groups 4 wk before the peak. For 30-59 y olds, even 800 specimens per week would not have generated reliable estimates until the peak because the ratio of IAR to pre-existing