TIME COURSE ANALYSIS OF 25 CASE PATIENTS WITH AVIAN INFLUENZA A (H5N1) VIRUS INFECTION IN CHINA, 2005-2007

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JOHN CHARLES LIDDY : TIME TO VIROLOGICAL SUPPRESSION AND SUBSEQUENT FAILURE IN ARV-NAÏVE SUBJECTS RECEIVING HAART: RESULTS FROM THE HIV-NAT OO6 COHORT. THESIS ADVISOR: ROBERT SEDGWICK CHAPMAN, M.D., M.P.H., 94 pp.

A cohort study of virological suppression (to a plasma viral load [pVL] <50 copies), and subsequent virological failure (pVL rebounding to >50 copies), was conducted in antiretroviral therapy-naive HIV patients in Thailand. Effects of time on highly active antiretroviral therapy (HAART) and of other characteristics on likelihood of suppression and failure were assessed with Kaplan-Meier product-limit curves, person-time logistic and Poisson regression, and Cox proportional hazards regression. Analysis included 404 subjects (221 males and 183 females), all of whom achieved suppression and 69 (17.1%) of whom experienced failure afterwards. The time intervals from starting HAART to suppression, and from suppression to failure or end of study, were examined.

Unstratified Kaplan-Meier curves exhibited two inflection points in the time courses of both suppression and failure (slow initial rise, then steep intermediate, then slow final rise). Thus, the time variable was modeled as the cubic polynomial of time on study in person-time regression models. Regressions were run with only the three terms for the time polynomial, yielding unadjusted time effect estimates. Bivariate analysis was conducted to evaluate effects of other independent variables separately on time to suppression and failure. Variables for which P <0.2 were entered into multivariable regression models, along with the 3 terms for the cubic polynomial of time, yielding adjusted time effect estimates.

Unadjusted and adjusted time effects estimates were highly statistically significant for both suppression and failure (P <0.001). Furthermore, in both logistic and Poisson regressions, differences between unadjusted and adjusted time effects estimates were very small. These observations confirmed the appropriateness and robustness of modeling time with a cubic polynomial. There was no evidence that longer time was associated with increased likelihood of suppression or failure.

Final multivariable analysis identified a baseline regimen including a PI and a baseline pVL <50 000 as predictive of faster suppression (OR 1.87, P<0.0001, OR 0.713, P=0.005 respectively) while a diagnosis of AIDS before baseline showed a trend to slower suppression (OR 0.87, P=0.085) Females were likely to fail more slowly (OR 0.57, P=0.049) while those with a baseline CD4 count >200 cells and those with a baseline pVL >50 000 copies were more likely to fail more quickly (OR 3.13, P<0.0001 and OR 1.94, P=0.015 respectively). A baseline regimen including a PI and suppressing before week 12 showed a trend to slower failure (OR 0.51, P=0.089 and OR 1.93, P=0.058 respectively. Covariate effects were similar in logistic, Poisson and Cox models.

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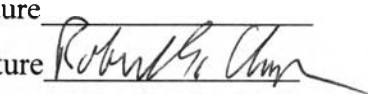
Academic year 2007 _____ Advisor's signature 

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ABBREVIATIONS

CFR	Case Fatality Rate
China CDC	Chinese Centers for Disease Control and Prevention
CI	Confidence Intervals
CRBC	Chicken Red Blood Cells
CRF	Case Report Form
GRBC	Guinea Pig Red Blood Cells
HI	Hemagglutination Inhibition
HCWs	Health Care Workers
HPAI	Highly Pathogenic Avian Influenza
HRBC	Horse Red Blood Cells
ICF	Informed Consent Form
ILI	Influenza Like Illness
IRB	Institutional Review Board
MN	Microneutralization
NIC	National Influenza Center
PI	Principal Investigator
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
SOP	Standard Operating Procedure
WHO	World Health Organization