

Message from FLU Co-chairs

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Colleagues:

The current 2012-2013 influenza season in the Northern Hemisphere is shaping up to be perhaps one of the more serious that we have seen over the past decade. Despite likely reporting delays associated with the recent holidays, the number of new cases of respiratory illness being diagnosed in both Northern Europe and North America continue to rise, with a sizeable percentage of those cases being confirmed as due to influenza A or B.

In U.S. states where influenza activity was high, the number of outpatient visits already recorded this season far exceed the past several years combined. A heavy volume of new cases flooding hospital emergency rooms in some regions or cities (e.g., Boston) has prompted some public health authorities to declare local states of emergency. The number of pediatric deaths attributable to influenza in the United States (currently recorded as 20) has also risen this season from prior low levels. As a result, despite an adequate nationwide supply overall, the increased demand for influenza immunization has caused temporary vaccine shortages in some of the hardest hit regions of North America.

While data are still limited, the distribution of influenza isolates between Europe and North America is showing some early discordance, with the A(H1N1)pdm09 subtype having "re-emerged" and co-circulating in Europe at higher frequency than is presently being seen in the United States and Canada, where H3N2 and influenza B continue to be the predominant subtypes isolated to date. If persistent, it will be important to learn whether this relative resurgence of A(H1N1)pdm09 in some areas represents a degree of antigenic drift within that subtype, or perhaps reflects instead just differential host susceptibility within populations having different degrees of vaccine uptake since 2009. One of the many strengths of our INSIGHT FLU 002 and 003 studies is that we capture prior vaccination histories and other pertinent demographic information at enrollment that we can then correlate with the in-depth sequencing of viral isolates obtained from our study participants, thus facilitating this type of causal analysis.

We appreciate that a robust influenza season may result in an unexpected influx of clinical responsibilities that could push active participation in observational research studies to a lower priority. Unfortunately, with the unpredictability that influenza so frequently manifests, a flu season that comes on early and heavily can also begin to wane with equal rapidity. Hence, we strongly encourage site investigators not to delay aggressive enrollment of new flu cases into the two main studies so that those data are not lost, but rather can add meaningfully to the subsequent analyses of the many host and viral factors that contribute to the dynamics of the current season. As always, we thank you for your diligence and participation in these important studies.

Project Updates

The current status of manuscripts associated with the FLU 002 and 003 studies is summarized below:

Accepted at Plos One: *The Association Between Serum Biomarkers and Disease Outcome in Influenza A(H1N1)pdm09 Virus Infection: Results of Two International Observational Cohort Studies.*

Submission planned for this month: *Sequence Analysis of in vivo defective-interfering (DI)-like RNA of Influenza A H1N1 pandemic virus.*

Manuscript preparation targeted for spring 2013:

- Bacterial and Viral Co-Infection in A(H1N1)pdm09 Patients
- Serologic Analysis of A(H1N1)pdm09 Patients

To track influenza activity in your area and worldwide:

-Contact your local public health agencies

-INSIGHT website www.insight-trials.org > Influenza Links

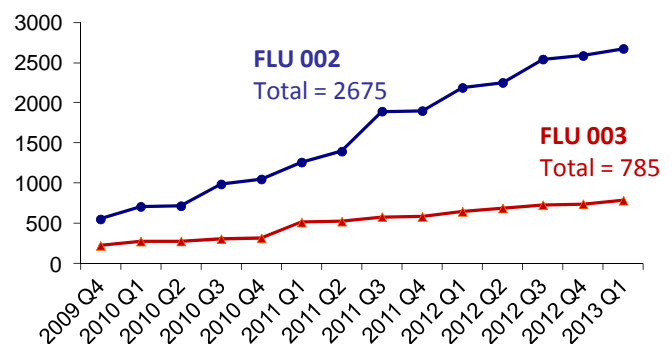
Influenza Activity (as of 05 January 2013)

According to the European Center for Disease Prevention and Control, increased flu activity was reported by 16 countries, compared to only nine of 20 countries in the last week of 2012. Twelve countries report medium or high intensity ILI activity, with the majority of them indicating widespread geographic spread. Countries in northern and western Europe were most affected. Of 734 sentinel specimens tested across 20 countries, 44% were positive for influenza virus. Of those, 44% were type A (of those, 51% A(H3N2) and 49% A(H1N1)pdm09) and 56% type B.

In the U.S., the percentage of respiratory specimens testing positive for influenza viruses for the week ending in 05 January decreased from 35.2% in the previous week to 32.8%, according to the CDC. Twenty-four states (down from 29 states last week) and New York City are reporting high ILI activity. Forty-seven states reported widespread geographic influenza activity (up from 41 states the previous week).

Of the isolates that have been subtyped in the U.S. in the week ending 05 January, 79.8% have been influenza A (of influenza A, 98% were H3 viruses and 2% A(H1N1)pdm09) and 20.2% have been influenza B. Ninety-nine percent of the H3N2 influenza virus isolates tested have been characterized as A/Victoria/361/2011-like, and 67% of the influenza B viruses belonged to the B/Yamagata lineage of viruses. This is important because those two viruses comprise the H3N2 and B virus components of the 2012-2013 Northern Hemisphere influenza vaccine. On 11 January, CDC published an early seasonal influenza vaccine effectiveness of 62% (95% CI: 51%-71%) for medically attended acute respiratory infection [MMWR, 2013;62(Early Release)1-4. CDC has tested 70 A(H1N1)pdm09, 600 A(H3N2) and 230 influenza B isolates for neuraminidase inhibitor resistance; all of the isolates tested were susceptible to oseltamivir and zanamivir.

Cumulative Enrollment



Enrollment by Country (01 JAN 2012 to present)

