**ANTIBODY RESPONSES AGAINST HETEROLOGOUS H5N1 STRAINS FOR AN MF59-ADJUVANTED CELL CULTURE-DERIVED H5N1 (aH5N1c) INFLUENZA VACCINE IN ADULTS AND THE ELDERLY**

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**BACKGROUND**

The risk of influenza-associated morbidity and mortality is potentially greater with pandemic influenza than with seasonal influenza because of little or no pre-existing immunity to the virus in the human population. Unlike with seasonal influenza, healthy adults might be at similar risk of severe influenza-associated complications and death as are young children and older adults in a pandemic. Vaccines are the main prophylactic measure against pandemic influenza and have an important role in pandemic preparedness plans worldwide.

Rapid production of a vaccine specific to an emerging pandemic influenza strain is critical to the public health response. A vaccine supply system solely dependent on an egg-based manufacturing process is at risk of being easily overwhelmed by highly-pathogenic avian influenza virus that may compromise egg production or viability. To avoid egg supply dependence, Seqirus has applied a cell culture method using mammalian MDCK cells to pandemic vaccine manufacturing.

The ability of MF59-adjuvanted vaccines, such as the cell-culture-derived MF59 adjuvanted aH5N1c vaccine, to generate cross-reactive immune responses is especially relevant during the early phase of a pandemic, when stockpiled vaccines may need to be used while strain-matched vaccines are being made and in later days of a pandemic when protection against pandemic virus strains that have undergone antigenic drift may be needed.1-3

**STUDY AIM**

To measure antibody responses against heterologous influenza strain(s) by hemagglutination inhibition (HI) and microneutralization (MN) assays following two vaccinations with a MF59-adjuvanted, cell-derived H5N1 virus against the set criteria by the Center for Biological Evaluation and Research (CBER), and the former Committee for Medicinal Products (CHMP) criteria, in adult and elderly populations.

**METHODS**

- In separate but similar studies, a total of 975 subjects 18 to <65 years of age (adults), and 1388 subjects ≥65 years of age (elderly), were randomized to receive two full (7.5 μg HA of H5N1 per dose) or half (3.75 μg HA of H5N1 per dose) doses of the MF59-adjuvanted, cell-derived H5N1 vaccine, aH5N1c, on day 1 and day 22.

- In a predefined exploratory analysis, HI and MN antibody responses against five H5N1 homologous influenza strains were evaluated in a subset of subjects from the full dose treatment arms in trials VBV 04 and VBV 13 (Table 1).

- Homologous antibody responses for all subjects at days 1, 22 and 43 were previously reported.1

**RESULTS**

For 5 heterologous strains, the geometric mean titer (GMT) on Day 43 in the adult and elderly subjects significantly increased from baseline (Table 2).

- Depending on the heterologous strain, HI≥1:40 was achieved by 17% to 64% of subjects on Day 43 (Figure 1). MN assay responses against these heterologous strains were generally higher compared with the HI assay (Figure 2).

- Notably, the Day 43 seroconversion (SC) rate for HI in adults 18-64 years of age for 3 heterologous strains (H5N1 Egypt, Hubei and Vietnam) had a lower bound of 95% CI at 240%, which exceeded the corresponding homologous strain serum response rate (Figure 3).

- For the elderly ≥65 years of age, 17% to 46% of subjects on Day 43 achieved SC.

**RESULTS (CONT’D)**

In adults and the elderly, two 7.5 μg doses of an MF59-adjuvanted H5N1 cell cultured vaccine (aH5N1c), administered three weeks apart, demonstrated increased immunogenicity from baseline against multiple heterologous H5N1 strains, of five separate genetic clades. These findings illustrate the potential for the aH5N1c vaccine to provide cross-protection against other H5N1 strains.

**TABLE 1. KEY STUDY ELEMENTS FOR POPULATIONS TESTED.**

**TABLE 2. GEOMETRIC MEAN TITERS (95% CI) FOR HOMOLOGOUS AND HETEROLOGOUS STRAINS—HI AND MN ASSAYS.**

**REFERENCES**

1. Fedson DS. Pandemic influenza and the global vaccine supply. CID. 2005;36:1552-1561


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