Vaccines are the main prophylactic measures against pandemic influenza and have an important role in pandemic preparedness plans worldwide. The ability to rapidly develop and produce a specific monovalent vaccine targeted to a new circulating pandemic strain is paramount. The pathogenicity and direct transmission of avian viruses to humans suggest that H5N1 has important pandemic potential with a high case fatality. Influenza vaccine manufacturing has relied on embryonated chicken eggs to produce antigens for over 50 years. During a highly pathogenic avian influenza outbreak/pandemic both egg quantity and quality may be compromised. Rapid production of a vaccine specific against an emerging pandemic influenza strain is critical to controlling its spread.

Allocated US Department of Health and Human Services funds have assisted Seqirus’ development of an MF59-adjuvanted cell culture-derived monovalent pandemic influenza vaccine. The MF59-adjuvanted cell culture-derived H5N1 (aH5N1c) vaccine is not subject to the potential limitations of egg-based production (e.g., requires large quantities of fertilized eggs, potential for egg-adaption of seed virus and antigenic mismatch), and helps address the medical need for a safe and effective pandemic vaccine.

STUDY AIM

To evaluate immunogenicity and lot-to-lot consistency of 3 consecutively produced lots of aH5N1c vaccine produced by HSNI haemagglutination inhibition (HI) antibody responses in healthy subjects ≥18 years of age, and to assess safety.

METHODS

- 316% subjects were randomized to 4 groups of equal size to receive one of 3 consecutively produced lots of aH5N1c virus vaccine by HSNI haemagglutination inhibition (HI) antibody responses in healthy subjects ≥18 years of age, and to assess safety.
- 2 doses of vaccine (7.5 μg HA of H5N1 + 0.25 mL MF59 adjuvant, each dose) were administered 3 weeks apart, on Day 1 and Day 22. The co-primary immunogenicity analysis was based on HI antibody titers collected 3 weeks after the second vaccination administration, on Day 43.
- Geometric mean titers (GMTs) and geometric mean ratio (GMR) were analysed.
- Subjects were stratified into 2 age groups, 18 to <65 and ≥65 years of age.
- Solicited local and systemic safety events were monitored for 7 days after each dose. Key unsolicited safety events, such as SAEs, Medically Attended Adverse Events, New Onset of Chronic Diseases (NOCD) and Adverse Events of Special Interest (AESI) were measured through Day 387.

RESULTS

The age-appropriate Center for Biologics Evaluation and Research (CBER) immunogenicity criteria at Day 43 were met, as the lower bound of the 2-sided 95% CI for the percentage of subjects achieving an HI antibody titer ≥20:40 exceeded the predefined limits of 70% (for subjects 18 to <65 years of age) and 50% (for subjects ≥65 years of age) for the active treatment groups (Table 2). Seroconversion rates were similarly met after aH5N1c at Day 43 for age-appropriate CBER criteria for both age groups (data not shown).

The baseline HI GMTs were similar among the active treatment and placebo groups, for both age groups, and was responsible for the majority of the treatment difference. The most commonly reported solicited systemic AE was fatigue. Overall, the solicited AEs in both groups were predominantly either mild or moderate in severity. The frequency of the most commonly reported unsolicited AE was pain (49.9% of aH5N1c treated subjects compared with 41.7% of placebo treated subjects), and was responsible for the majority of the treatment difference. The proportion of subjects for whom unsolicited AEs were reported was similar for the treatment groups from Day 1 through study termination (53.1% vs. 52.3%). The same pattern was also observed for all categories of unsolicited AEs. The majority of the reported unsolicited AEs were of mild or moderate intensity (Figure 2).

CONCLUSION

The MF59-adjuvanted, cell culture-derived H5N1 influenza vaccine aH5N1c elicited high levels of antibodies and met CBER immunogenicity criteria at Day 43 for both adult and elderly subjects. The safety profile was clinically acceptable and consistent with prior reported trials of MF59-adjuvanted influenza vaccines. Lot-to-lot manufacturing consistency was demonstrated by equivalence of HI GMTs.

REFERENCES


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