IMMUNOGENICITY AND PERSISTENCE OF RESPONSE TO AN ALUM-ADJUVANTED MONOVALENT (H9N2) WHOLE VIRUS INFLUENZA VACCINE IN HEALTHY ADULTS AGED 60 YEARS AND OLDER

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Background: It was previously reported that a low dose whole-virus H9N2 Alum-adjuvanted vaccine is safe and immunogenic in adults. Elderly subjects are known to exhibit a decline in immune responses to vaccine compared to adults. Therefore dose ranging evaluation was needed in the elderly population.

Aims: to evaluate the reactogenicity, immunogenicity and persistence elicited by different formulations of a GlaxoSmithKline Biologicals’ Alum-adjuvanted whole virus H9N2 influenza vaccine in elderly subjects aged 60 years and above.

Methods: A phase III, multicenter, open, randomized (1:1:1:1:1:1:1) study (102499/NCT00306995) was conducted in 385 subjects aged 68.9 ± 5.8 years with parallel groups (55 subjects/group). The candidate vaccines tested contained 15µg, 7.5µg, 3.8µg, 1.9µg haemagglutinin (HA) antigen of H9N2 A/Hong Kong/1073/99 in the presence or absence of Aluminum salts as adjuvant. Two doses were administered intramuscularly, at day 0 and day 21. Blood samples were collected at days 0, 10, 21, 42 and 189 for humoral immune response analysis. Target guidelines set by regulatory agencies (European Authorities, EMEA) for the annual registration of seasonal influenza vaccines and expected for pandemic influenza vaccines were used. Local and general symptoms were recorded using diary cards and serious adverse events (SAEs) were recorded throughout the study period.

Results: On day 42 seroprotection rates (SPR) of 74.5% [95%CI:61.0-85.3] and 64.8% [95%CI:50.6-77.3] were reported in the groups administered with 15µg of unadjuvanted HA or 7.5µg of Alum-adjuvanted HA respectively. This fulfilled the EMEA criterion for influenza SPR (SPR>60%). At day 42, all groups except the one receiving unadjuvanted vaccine containing 1.9µg HA reached the EMEA standard for seroconversion rate (SCR>30%) and seroconversion factor. However, by day 189, only the groups of elderly subjects vaccinated with either 15µg unadjuvanted HA or 7.5µg Alum-adjuvanted HA showed persistent SCR (33.3% [95%CI: 21.1-47.5] for both groups) with rates above the EMEA requirement (i.e. SCR>30%).

All formulations were safe and well-tolerated in the elderly population with only a small trend for higher incidence of localized symptoms after administration of formulations containing Alum. No SAEs related to vaccination occurred during the study period.

Conclusions: In elderly subjects, persistent immunity against H9N2 was only observed following vaccinations with GlaxoSmithKline Biologicals’ monovalent whole virus prototype vaccine containing either 15 µg of unadjuvanted HA or 7.5µg of Alum-adjuvanted HA. These results suggest that an Alum-adjuvanted whole virus vaccine with low HA content can raise persistent protective antibody levels following administration of two vaccine doses to a naïve population associated with a declining immunity. These results support use of adjuvants in dose sparing strategies which endeavor to maximize available vaccine supplies.