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An Adjuvanted and Non-Adjuvanted Monovalent Inactivated A/H1N1 Pandemic Influenza Vaccine: Immunogenicity, Safety, and Tolerability in Healthy Adults and Elderly

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Background: Vaccination is the best option to prevent spread of a pandemic influenza virus. Safe and immunogenic vaccines against the swine origin H1N1 influenza virus were developed, registered, and produced in large quantities. Experience with other pandemic influenza candidate vaccines (A/H5N1) indicated that either higher doses of antigen and/or use of an adjuvant was required to generate immune responses in immunologically naive populations comparable to those needed for licensure of seasonal trivalent influenza vaccines. Pandemic influenza vaccines that rapidly induce immune responses are a medical priority; adjuvanted vaccines may offer a solution. Materials and Methods: This randomized, single blind study evaluated the immunogenicity, safety, and tolerability of an MF59®- adjuvanted and non-adjuvanted influenza A/H1N1 swine origin influenza virus (SOIV) vaccine. The inactivated, monovalent subunit A/H1N1 study vaccine was based on the manufacturing method used to make Fluvirin®, a seasonal trivalent subunit influenza vaccine that has been licensed since 1983. A total of 2719 healthy adult subjects were stratified to 18-64 year (N = 1359) and ≥ 65 year (N = 1360) age cohorts and randomized to eight study groups, each given 2 doses of vaccine 3 weeks apart: 3.5 μg HA+half-dose MF59, 7.5 μg + no, half-dose full-dose MF59, 15 μg + no, half-dose full-dose MF59; 30 μg + no MF59. (Half-dose MF59 = 4.88 mg, full-dose = 9.75 mg). Blood was drawn at baseline (day 1, pre-vaccination), day 8, day 22, day 29, and day 43 to determine hemagglutination inhibition (HI) titer against the vaccine antigen. Immune responses in each group, i.e., seroconversion rates and percentage of subjects were compared using 95% confidence intervals (CI). Adverse events were recorded on diary cards. Results: One week after the first vaccination (day 8) all subjects, except those in the ≥ 65 year cohort receiving the 3.75 μg half-MF59, 7.5 μg nonadjuvanted, and 7.5 μg half-MF59 vaccines achieved both CBER seroconversion and HI titer ≥ 1:40 criteria. Three weeks after the first vaccination, 72-91% of subjects 18-64 and 52-73% older than 65 years of age seroconverted; 89-99% of subjects 18-64 and 77-92% of subjects older than 65 years of age achieved an HI antibody titer ≥ 1:40. Three weeks after the second vaccination, seroconversion rates were 75-93% in subjects 18-64 and 51-74% in those ≥ 65 years of age. HI antibody titer ≥ 1:40 were achieved by 94-99% of subjects 18-64 and 79-93% older than 65 years of age. The highest responses were to the 15 μg full-MF59 and 30 μg nonadjuvanted vaccines. In both age cohorts, the CBER criteria were met in all eight study groups from 3 weeks immune responses. However, a single dose of the 3.75 μg half-MF59 vaccine, with the lowest antigen and adjuvant content, met all immunogenicity criteria in both age cohorts. Across all vaccination groups in both age cohorts, the large majority of reported local and systemic reactions were mil. with fewer than 2% of reactions in any group graded as severe. The percentage of subjects reporting solicited reactions was greater in adjuvanted compared with nonadjuvanted vaccination groups. In both age cohorts, there was a tendency toward fewer subjects reporting reactions after the second vaccination, and after each vaccination, fewer subjects 65 years...
and older reported reactions compared with the younger cohort. Conclusion: The MF59 adjuvant allowed a rapid immune response likely to be associated with protection at a lower hemagglutinin dose than required with nonadjuvanted vaccine. A single 3.75 μg half-MF59 vaccination was safe and immunogenic for both the 18-64 and ≥ 65 year age cohorts and provided potential dose-sparing solutions for public health authorities.