Efficacy, Immunogenicity, and Safety Evaluation of an MF59 Adjuvanted Quadrivalent Influenza Virus Vaccine Compared to Non-adjuvanted Influenza Vaccine in Children

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BACKGROUND
Children are at increased risk for influenza virus–induced morbidity.1 Young children, particularly those younger than 2 years, have immature immune systems, which respond poorly to standard influenza vaccines. Enhanced influenza vaccines may help address this need in this most vulnerable population.

STUDY AIM
This phase III study evaluated the relative vaccine efficacy (rVE) of MF59 adjuvanted quadrivalent inactivated influenza vaccine (aIIV4) with a non–adjuvanted influenza vaccine comparator against influenza disease in children 6 months to 5 years of age.

METHODS
In this phase III, observer-blind, active-controlled, relative efficacy study, children aged 6 months to 5 years were randomized 1:1 to receive 1 or 2 doses of aIIV4 or non-adjuvanted comparator vaccine (Fluzone®) (see Figure 1 for design). As comparator, trivalent inactivated influenza vaccine [IIV3] was used in Season 1 and quadrivalent inactivated influenza vaccine [IIV4] in Season 2. For both efficacy and immunogenicity, results from B/Victoria from Season 1 were not included in the analyses in view of this strain lacking in the comparator vaccine in Season 1.

Endpoints included reverse transcriptase polymerase chain reaction (RT-PCR)-confirmed, culture-confirmed, and antigendispatched matched influenza A and/or B and immunogenicity against homologous and heterologous strains.

All endpoints were prespecified for the overall age group and for the subgroup of children aged 6 to 23 months.

The study was conducted during the 2013/2014 and 2014/2015 seasons in 9 countries; Finland, United States, and Canada in Seasons 1 and 2, and Italy, Poland, Spain, Philippines, Thailand, and Taiwan in Season 2.

RESULTS
Significantly greater rVE was demonstrated in the 6- to 23-month age group [rVE 31.4% [95% CI: 3.1, 51.4%], although not in the overall study population (overall rVE 0.7% [95% CI: -19.8, 15.4%]) (Table 1).

In vaccine-naïve subjects aged 6 months to 5 years, rVE was 54.7% [95% CI: 18.1, 74.9%] and 70.6% (95% CI 65.2, (86.0%) 7% and 14 days after the first dose until vaccination, respectively, demonstrating benefit of aIIV4 in preventing early cases of influenza (Table 2).

In all ages, aIIV4 elicited a superior immune response relative to comparator vaccine for all vaccine strains (Figure 3). In addition, aIIV4 elicited a superior immune response against 3 heterologous strains, including A/Hong Kong/4801/2014 (H3N2) (data not shown).

The highest ratios of geometric mean titres (GMT) were observed in children 6 to 23 months of age, consistent with higher relative efficacy observed in this age group (Figure 3).

SAFETY
The overall vaccine safety profiles were similar except for the expected higher incidence of solicited adverse events (AEs) for aIIV4 (Figure 4).

The proportion of subjects with any unsolicited AE was similar for the aIIV4 and comparator vaccine groups (68.2% vs 68.6%). The same pattern was observed for related to related AEs, any unsolicited serious AEs, adverse events of special interest, unsolicited AEs leading to death, unsolicited AEs leading to withdrawal from study or vaccine, hospitalisation, and new-onset chronic disease for subjects 6 months to 5 years of age.

CONCLUSION
In this study, aIIV4 provided additional clinical benefit over non-adjuvanted influenza vaccine, with significantly greater efficacy in children aged 6 to 23 months. In addition, aIIV4 resulted in greater early efficacy in vaccine-naïve children after the first up to the second vaccination. Relative to comparator vaccine, aIIV4 was associated with superior immunogenicity and a similar safety profile in all children.

REFERENCES

FIGURE 2. Enrolment and Subject Disposition.

FIGURE 3. Geometric Mean Titres and Vaccine Group Ratios Against Homologous Vaccine Strains 21 Days After Last Vaccination.

FIGURE 4. Overview of Adverse Events Occurring Within 7 Days After Any Vaccination in Subjects 6 Months to 5 Years of Age.

TABLE 1. First-occurrence RT-PCR-confirmed and Culture-confirmed Influenza and Relative Vaccine Efficacy in Subjects 6 Months to 5 Years of Age.

TABLE 2. First-occurrence RT-PCR-confirmed Influenza and Relative Vaccine Efficacy in Subjects 6 Months to 5 Years Within 21 Days After Last Vaccination.

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