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Impact of prior or concomitant seasonal influenza vaccination on MF59-adjuvanted H1N1v vaccine (Focetria™) in adult and elderly subjects

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SUMMARY

Background: When H1N1v vaccines become widely available, most elderly subjects will have already received their seasonal influenza vaccination. Adults seeking H1N1v vaccination may be offered seasonal vaccine as well. We investigated prior seasonal vaccination in adult and elderly subjects, and concomitant vaccination with seasonal vaccine in adults, on the tolerability and immunogenicity of the Novartis MF59-adjuvanted H1N1v vaccine, Focetria®. **Methods:** A total of 264 adult (four groups) and 154 elderly (three groups) subjects were enrolled. The licensure study cohorts for plain (Agrippal®) and MF59-adjuvanted (Fluad®) 2009–2010 seasonal vaccines were invited to receive Focetria 3 months later, with seasonal vaccine–naïve controls, and adults who received Focteria and seasonal vaccine concomitantly. Immunogenicity of all vaccines was assessed by haemagglutination inhibition on Days 1 and 22, safety and reactogenicity were monitored using patient diaries. **Results:** All adult and elderly groups met all the European CHMP licensing criteria for H1N1v, as did adults receiving concomitant seasonal vaccine for the three seasonal strains. Vaccines were generally well tolerated, causing no SAEs, and profiles typical of MF59-adjuvanted vaccines. Reactions were mainly mild or moderate and transient, and unaffected by prior or concomitant seasonal vaccination except for elderly subjects previously given MF59-adjuvanted seasonal vaccine, whose reaction rates to Focetria were about half those seen in groups receiving their first MF59 vaccine. **Conclusion:** One dose of MF59-adjuvanted H1N1v vaccine met the licensure criteria for adult and elderly subjects 3 months after seasonal vaccination, or concomitantly with seasonal vaccine in adults, without impacting the tolerability or immunogenicity of either vaccine, thus facilitating mass influenza immunisation campaigns.

What's known
Initial data suggested one dose of H1N1v is adequate to provide immunity in adults but probably not in elderly.

What's new
- Prior receipt of seasonal influenza vaccine does not interfere with the response to H1N1v vaccine 3 months later.
- Adults can receive both seasonal and H1N1 vaccine concomitantly without affecting tolerability or immunogenicity of either vaccine.
- One dose of MF59-adjuvanted H1N1v vaccine is immunogenic in both adult and elderly populations.

Introduction

The recent declaration of an A/California/7/2009 (H1N1v) pandemic by the WHO (1) has been accompanied by a major effort by all the world's leading vaccine manufacturers to develop H1N1v vaccines, based on lessons learnt from development of H5N1 vaccines. While development and production of H1N1v vaccines was underway, production and distribution of Northern Hemisphere seasonal influenza vaccines at many companies have been anticipated and completed to allow for early seasonal campaigns. As H1N1v vaccines begin to be distributed, it may be anticipated that some recipients, especially those in groups recommended for seasonal vaccination, e.g. the elderly, high-risk groups, will already have received their seasonal vaccination. Furthermore, adults who do not routinely receive seasonal influenza vaccination may now present themselves at healthcare facilities to receive H1N1v vaccine and request or be offered the seasonal influenza vaccination at the same visit. Administering both vaccines at one visit has obvious logistic benefits, both for the recipient and for the administrator, but there are no published data available to show whether concomitant seasonal and H1N1v vaccination, or indeed prior receipt of seasonal vaccine in targeted groups such as the elderly, has any effect on the immunogenicity of either vaccine.

The present study was performed in healthy adults (18–60 years) and 'elderly' adults (≥ 61 years) to

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evaluate vaccination with the Novartis MF59-adjuvanted H1N1v vaccine, Focetria® (Siena, Italy), approximately 3 months after annual seasonal influenza vaccination with either plain seasonal vaccine (Agrippal®, Novartis Vaccines, Siena, Italy), or the MF59-adjuvanted seasonal vaccine (Fluad®, Novartis Vaccines, Siena, Italy). In addition, we studied concomitant vaccination of plain seasonal vaccine with two different dose levels of Focetria in adults.

The study protocol foresaw two doses of H1N1v vaccine at 21 days' interval, but subsequent data release from other clinical trials indicated that one dose may be adequate in these age groups (1–3). With these data and in view of current clinical use of H1N1v vaccines, we are reporting the data after one dose as a guide for clinicians and healthcare policy makers.

Subjects and methods

This was a phase II, open-label study performed in five centres in Italy in healthy adults from 18 years of age to evaluate the safety, tolerability and immunogenicity of a novel H1N1v vaccine in subjects already vaccinated with seasonal influenza vaccines. The study was performed according to GCP and ICH guidelines, with appropriate ethical approval from all sites, and informed written consent from all participants. Subjects in the licensure studies of the trivalent seasonal vaccines, Agrippal (NCT 00918268) and Fluad (NCT 00956761) who were vaccinated in the second week of June 2009, were invited to enrol in this study, which was performed at the end of August 2009. Additional cohorts of adult and elderly subjects who had not received a 2009–2010 season influenza vaccine were recruited for control groups.

Subjects were adults of either gender, who were healthy at the time of enrolment and did not display any of the exclusion criteria – any known or suspected allergy to a vaccine component or immunosuppressive condition or therapy including chronic use of oral or systemic steroids, any history of influenza disease within 6 months of the study or receipt of any other vaccine within 4 weeks of the study.

Age stratification was in accordance with the European Committee for Medicinal Products for Human Use (CHMP) criteria for licensure (4,5): adults from 18 to 60 years of age and elderly adults aged 61 years or older. All subjects were to receive two doses of the H1N1v vaccine as this was anticipated to be the requirement to provide protective antibody titres against H1N1v disease at the time of protocol preparation. As it became apparent from data released from other clinical studies during the course of this trial that one dose may be adequate, (1–3) this report of the results after one dose of Focetria is being made to help in guiding public policy during the H1N1v immunisation campaigns.

Adults from the seasonal vaccine licensure study were allocated to Group 1, the non-immunised adults being randomly allocated 1 : 1 : 1 to groups 2, 3 and 4. Groups 3 and 4 received seasonal vaccine concomitantly with their first dose of H1N1v vaccine. Elderly subjects who had received plain seasonal or MF59-adjuvanted seasonal vaccines as part of the seasonal licensure studies were allocated to groups 5 or 6, respectively, and non-immunised elderly subjects were assigned to group 7.

Vaccines

All vaccines were manufactured by Novartis Vaccines (Siena, Italy) and supplied in prefilled monodose syringes, containing 0.5 ml of the relevant vaccine formulation. The plain seasonal vaccine originally given to group 1 in adults and group 5 in elderly for the licensure studies, and used for concomitant vaccination in adult groups 3 and 4 was Agrippal S1 (Novartis Vaccines, Siena, Italy) containing 15 μg haemagglutinin antigen (HA) of each of the three

Table 1 Demographics of the study populations

	Adults				Elderly		
	Group 1	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**	**Group 7**
Previous seasonal vaccination	Yes	None	None	None	Yes	Yes + MF59	None
Current vaccination(s)	Focetria	Focetria	Focetria + seasonal	Half-dose Focetria + seasonal	Focetria	Focetria	Focetria
	$n = 50$	$n = 71$	$n = 70$	$n = 69$	$n = 49$	$n = 46$	$n = 59$
Age (years)	46.5 ± 9.7	40.7 ± 12.1	40.6 ± 12.3	38.8 ± 12.2	69.2 ± 7.3	72.8 ± 5.9	70.5 ± 7.5
Female (%)	33 (66)	40 (56)	37 (53)	38 (55)	27 (55)	19 (41)	26 (44)
A/California/04/2009 H1N1v seropositive, ≥ 10 (%)	52	25	29	30	61	65	64
A/California/04/2009 H1N1v seroprotected, ≥ 40 (%)	26	7	11	7	8	15	7

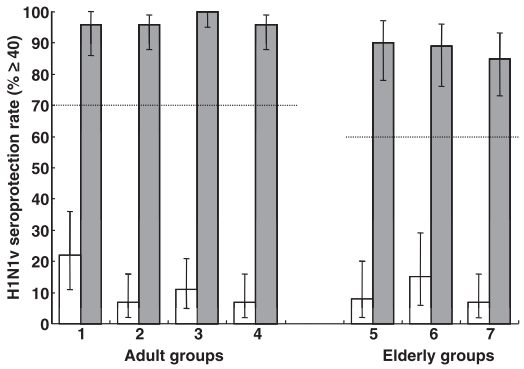

Figure 1 Seroprotection rates (% with H1N1v HI titres ≥ 40) at day 1 (open bars) and day 22 (shaded bars) in the study groups, with 95% confidence intervals. Dotted lines indicate CHMP criteria for adults and elderly, respectively.

strains [A/Brisbane/59/2007(H1N1)-like; A/Brisbane/10/2007(H3N2)-like B/Brisbane/60/2008-like] recommended for the 2009/2010 NH influenza season. The elderly adults in group 6 received the MF59-adjuvanted seasonal influenza vaccine, Fluad®, each dose of which contains the same antigenic components as the plain seasonal vaccine formulated with a full dose of the oil-in water emulsion adjuvant, MF59® (Novartis Vaccines, Marburg, Germany), containing 9.75 mg squalene.

The H1N1v vaccine was the Novartis MF59-adjuvanted H1N1v monovalent influenza vaccine, Focetria®. Each 0.5 ml dose contains 7.5 μg H1N1 HA antigen and the full dose of MF59 adjuvant as found in Fluad. In group 4, only half the dose was administered (using a 0.25 ml mark indicated in the syringe barrel) so recipients received 3.75 μg H1N1 antigen and a half dose of MF59 adjuvant. All subjects received two vaccinations with Focetria, on days 1 and 22, by intramuscular injection in the deltoid in an open fashion, so both study personnel and subject knew which vaccine was being administered.

Reactogenicity

Each subject was monitored after vaccination and reactogenicity was then assessed using patient-completed diaries, in which local and systemic reactions were solicited for 7 days (6). Any other adverse event occurring before the subsequent visit was also to be recorded.

Immunogenicity

Blood samples were drawn on day 1 before the first vaccination, and 21 days thereafter to evaluate antibody titres against the vaccine antigen components using a haemagglutination inhibition (HI) assay (7). Sera obtained from the adults in the plain seasonal vaccine study from June 2009 were also assayed using HI for responses to the vaccine antigens as a historical control group. Geometric mean titres (GMT) and geometric mean ratios (GMR) of day 22 to day 1 titres were calculated for each group. Seroconversion rates were calculated as the percentages of each group that displayed seroconversion in initially seronegative subjects (from HI < 10 prevaccination to ≥ 40 postvaccination) or a significant increase in titre in initially seropositive subjects (a four-fold increase in titre in those ≥ 10 prevaccination). Seroprotection rates were calculated as percentages of each group with HI titres ≥ 40.

Statistical analyses

All observations were to be made descriptively, with no null hypothesis testing. The study was performed in accordance with the European CHMP requirements for influenza vaccine licensure (4,5), for which sample sizes of 60 were chosen in June to ensure 50 evaluable subjects per group, to be compliant with the CHMP guidelines. Sizes of newly recruited subject groups for this study, i.e. with no prior seasonal vaccination, were intended to match those of the seasonal vaccine trials.

Table 2 Adult group H1N1v responses to one dose of Focetria

	Group 1	Group 2	Group 3	Group 4
Previous seasonal vaccination	Yes	None	None	None
Current vaccination	Focetria	Focetria	Focetria + seasonal	Half-dose Focetria + seasonal
	n = 50	*n* = 71	*n* = 70	*n* = 69
GMT				
Day 1 (95% CI)	11 (7.8–17)	8.0 (6.3–10)	9.5 (7.5–12)	8.6 (6.7–11)
Day 22 (95% CI)	441 (259–750)	421 (301–591)	458 (326–643)	264 (188–372)
GMR, day 22 to day 1 (95% CI)	39 (21–70)	52 (36–77)	48 (33–71)	31 (21–45)
Seroconversion rate, % (95% CI)	94 (83–99)	89 (79–95)	99 (92–100)	91 (82–97)

CI, confidence interval; GMT, geometric mean titres; GMR, geometric mean ratios.

Table 3 Elderly group H1N1v responses to one dose of Focetria

	Group 5	Group 6	Group 7
Previous seasonal vaccination	Yes	Yes + MF59	None
Current vaccination	Focetria	Focetria	Focetria
	N = 49	*N* = 46	*N* = 59
GMT			
Day 1 (95% CI)	11 (6.0–19)	14 (7.9–24)	10 (7.2–15)
Day 22 (95% CI)	111 (44–281)	108 (44–266)	98 (53–181)
GMR, day 22 to day 1 (95% CI)	10 (4.5–24)	7.9 (3.5–18)	9.3 (5.3–16)
Seroconversion rate, % (95% CI)	71 (57–83)	70 (54–82)	76 (63–86)

CI, confidence interval; GMT, geometric mean titres; GMR, geometric mean ratios.

Assessment was based on the CHMP criteria: for adults (18–60 years), the three criteria are a seroconversion rate > 40%, a GMR > 2.5 and > 70% having a 'seroprotective' HI titre ≥ 40. For elderly subjects (≥ 61 years), these criteria are seroconversion > 30%, GMR > 2.0 and a seroprotection rate > 60%.

Results

Demographics

Of the 260 adults enrolled, 50 had already participated in the 2009/2010 plain seasonal vaccine study and 210 had no 2009/2010 seasonal vaccination. A total of 154 Elderly subjects included 95 who participated in the 2009/2010 plain seasonal vaccine and MF59-adjuvanted seasonal studies and 59 with no prior 2009/2010 vaccination (Table 1). Demographics were similar in the four adult and three elderly groups.

Immunogenicity: H1N1 vaccine

There were low HI antibody titres against H1N1v on Day 1, with similar GMTs in all groups. However, those adults vaccinated with plain seasonal vaccine 3 months previously (group 1), displayed a higher rate of seropositivity, 52% with a titre ≥ 10, than the three non-vaccinated groups (25–30%) (Table 1). This was reflected in the proportions of the four groups who had protective titres (≥ 40) before vaccination −26% in group 1 vs. 7–11% in groups 2–4 (Table 1 and Figure 1). Proportionally more of the elderly subjects were seropositive, 61–65% in the three groups, with no influence of the previous seasonal vaccination (Table 1), but the proportions with protective titres were similar to that of the adult groups (8–15%; Table 1 and Figure 1).

Three weeks after vaccination with one dose of Focetria, all groups in both age strata displayed anti-H1N1v responses, which comfortably met all the respective CHMP criteria (Tables 2 and 3). There were no differences between the groups on the basis of their prevaccination history or concomitant vaccinations. The only difference between the adult groups was a lower GMT in group 4 (264) compared with the other groups (421–458) consistent with the half dose of vaccine administered to this group. The similar responses in groups 1, 2 and 3 show that seasonal vaccination 3 months previously or concomitantly did not influence the response to H1N1v.

Geometric mean titres were lower in the three elderly groups compared with Adults, as expected

Table 4 Seasonal strain responses to one dose of unadjuvanted seasonal influenza vaccine concomitantly with a full dose (group 3) or half dose (group 4) of Focetria in adults

	H1N1 (A/Brisbane/59/2007)		H3N2 (A/Brisbane/10/2007)		B (B/Brisbane/60/2008)	
Seasonal strain	Group 3 *n* = 70	Group 4 *n* = 69	Group 3 *n* = 70	Group 4 *n* = 69	Group 3 *n* = 70	Group 4 *n* = 69
GMR, day 22 to day 1 (95% CI)	5.8 (4.2–8.0)	5.8 (4.2–8.1)	6.0 (4.2–8.6)	4.5 (3.2–6.5)	4.4 (3.4–5.9)	4.6 (3.5–6.1)
Seroconversion rate, % (95% CI)	57 (45–69)	64 (51–75)	56 (43–68)	51 (38–63)	57 (45–69)	58 (45–70)
Seroprotection rate, % (95% CI)	93 (84–98)	96 (88–99)	84 (74–92)	91 (82–97)	80 (69–89)	81 (70–90)

CI, confidence interval; GMR, geometric mean ratios.

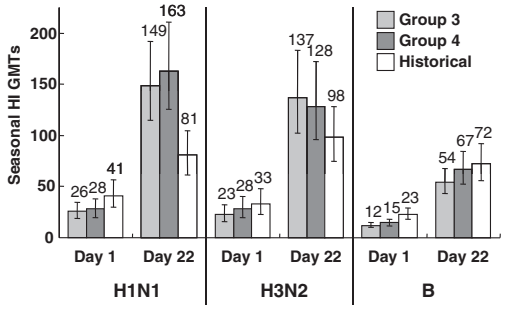

Figure 2 Geometric mean titres of HI antibodies to the three virus strains (H1N1, H3N2 and B) in seasonal vaccine for the 2009–2010 season. Groups 3 ($n = 70$) and 4 ($n = 69$) received seasonal vaccine concomitantly with full and half doses of Focetria respectively. Historical data ($n = 61$) are from sera obtained in the seasonal licensure study 3 months earlier.

with the known lower immune response in this age group, but there was no evidence of any interference of the response because of previous vaccination with plain (group 5) or MF59-adjuvanted (group 6) seasonal vaccines, which displayed similar responses to group 7 (Table 3).

The GMRs and seroconversion rates in adult and elderly groups comfortably surpassed the CHMP criteria, and all groups achieved the required proportions with seroprotective HI titres (≥ 40), respectively 70% and 60% for adult and elderly groups as shown in Figure 1.

Seasonal vaccine

There was no evidence of interference with the response to the seasonal strains in the two adult groups given seasonal vaccine concomitantly with full (group 3) and half (group 4) doses of Focetria (Table 4). GMTs for each of the three seasonal vaccine strains were similar in the two adult groups, when administered concomitantly with a full (7.5 μg) or half dose (3.75 μg) of H1N1v vaccine (Figure 2). The historical data from adults from the seasonal vaccine alone in the licensure study performed 3 months earlier show that the GMTs were not decreased by concomitant H1N1v. For the three seasonal strains, GMRs (4.4–6), seroconversion rates (51–64%), and seroprotection rates (80% to 96%) for the different strains in the two groups met all CHMP criteria for seasonal vaccines (Table 4)

Safety and reactogenicity

One serious adverse event (SAE) was reported – a case of influenza in an adult from group 4 occurring 5 days after vaccination, and lasting 2 days, which was considered not related to the vaccine. There were no drop-outs because of adverse reactions. In adults, overall rates of reported reactions were similar in the four groups, 61–77% reporting some form of solicited reaction, mainly local injection-site reactions. In the Elderly groups, fewer reactions were reported, overall in 43% and 47% of groups 5 and 7, respectively, the two groups having similar profiles. However, only 22% of the subjects in group 6, consisting of elderly subjects vaccinated with MF59-adjuvanted seasonal vaccine 3 months previously, reported any reaction after Focetria vaccination.

The most frequent local reaction was pain at the injection site, reported in 50–61% of the adult groups, 18% and 24% in elderly groups 1 and 3, respectively, and only 4% of elderly group 2 (Table 5). These reports were generally of mild-to-moderate pain, with three reports of severe pain (one case each in adult groups 1, 2 and 3) being the only severe reactions recorded. No elderly subject reported a severe local reaction. All reactions were transient and resolved spontaneously in a few days.

Table 5 Rates of local reactions in the seven study groups, all described as mild or moderate except where indicated

	Study groups						
	Adults				Elderly		
Reaction	1 $n = 50$	2 $n = 71$	3 $n = 71$	4 $n = 72$	5 $n = 49$	6 $n = 46$	7 $n = 59$
Ecchymosis (%)	3 (6)	1 (1)	5 (7)	3 (4)	2 (4)	1 (2)	3 (5)
Erythema (%)	9 (18)	5 (7)	5 (7)	0	3 (6)	3 (7)	1 (2)
Induration (%)	3 (6)	7 (10)	6 (8)	3 (4)	4 (8)	0	2 (3)
Swelling (%)	4 (8)	5 (7)	7 (10)	3 (4)	3 (6)	0	2 (3)
Pain (%)	25 (50)[a]	43 (61)[a]	43 (61)[a]	41 (57)	9 (18)	2 (4)	14 (24)

[a]One case described as severe.

Table 6 Rates of systemic reactions in the seven study groups, described as mild or moderate, except where indicated

	Study groups						
	Adults				Elderly		
Reaction	1 *n* = 50	2 *n* = 71	3 *n* = 71	4 *n* = 72	5 *n* = 49	6 *n* = 46	7 *n* = 59
Chills (%)	3 (6)	5 (7)	4 (6)	4 (6)	3 (6)	0	1 (2)
Malaise (%)	8 (16)	16 (23)[a]	11 (15)	10 (14)	5 (10)[a]	1 (2)	6 (10)
Myalgia (%)	7 (14)	15 (21)	14 (20)	15 (21)	5 (10)	2 (4)	6 (10)
Arthralgia (%)	6 (12)	9 (13)	10 (14)	12 (17)	8 (16)	0	8 (14)
Headache (%)	13 (26)[a]	26 (37)[c]	14 (20)	22 (31)[a]	7 (14)[a]	3 (7)	7 (12)
Sweating (%)	7 (14)	15 (21)	14 (20)	8 (11)	6 (12)	3 (7)	7 (12)
Fatigue (%)	8 (16)	25 (35)[b]	23 (32)	26 (36)[a]	5 (10)	2 (4)	12 (20)[a]
Nausea (%)	6 (12)	12 (17)	3 (4)	7 (10)	1 (2)	0	3 (5)
Fever	0	0	0	0	0	0	0

[a]One case; [b]two cases; [c]four cases described as severe.

Solicited systemic reactions, shown in Table 6, displayed a similar pattern to the solicited local reactions. Adult groups had similar profiles, consisting of mainly mild or moderate transient systemic reactions, although there were 10 systemic reactions described as severe: a single case of severe malaise (group 2), three reports of severe fatigue (two in group 2 and one in group 4), and six reports of severe headache (one in group 1, four in group 2 and one in group 4). In elderly subjects we observed a lower rate of systemic reactions than in adults and noticeably lower rates in group 6, previously vaccinated with Fluad, compared with groups 5 or 7. Three severe systemic reactions (one case each of malaise and headache in group 1) and one case of severe fatigue in group 3 were reported.

Discussion

The MF59-adjuvanted H1N1 vaccine, Focetria™, was generally well tolerated and did not lead to any related SAE when administered to adults or elderly subjects, even when these subjects had previously been vaccinated with seasonal influenza vaccines within the previous 3 months. Surprisingly, this observation included elderly subjects who received a MF59-adjuvanted seasonal vaccine, who displayed consistently lower rates of local or systemic reactions to the H1N1v vaccine than their counterparts who had previously received either plain seasonal vaccine or no previous seasonal vaccination. Local reactogenicity was consistent with previous observations with MF59-containing vaccines (2,8), with an increase in mild-to-moderate, transient injection-site pain. Systemic reactions were also comparable with other studies on MF59-adjuvanted influenza vaccine (9).

Prior seasonal influenza vaccination of adults or elderly did not interfere with the immune response to the A/California/7/2009 (H1N1)-like strain in Focetria, assessed by HI assay, and all study groups satisfied all three CHMP criteria for licensure in adult and elderly age groups, respectively. Although a large proportion of the elderly subjects displayed some immune response to H1N1v, attested by seropositivity rates (≥ 10) of 61–65% before H1N1v vaccination, they had low antibody levels such that only 8–15% displayed seroprotective titres (≥ 40) against the novel viral strain. The number of subjects was too small to draw any conclusion from the slightly higher rate (15%) in subjects previously exposed to MF59-adjuvanted seasonal vaccine. However, those adults vaccinated with the plain seasonal influenza vaccine 3 months previously had higher levels of antibodies to H1N1v, 52% being seropositive and 26% having seroprotective titres, compared with 25–30% seropositivity and 7–11% seroprotection in the non-vaccinated adults. This 22% difference in seropositivity following seasonal vaccination is consistent with the observation that 12–22% of 18–64 year olds displayed significant increases in cross-reactive antibodies to H1N1v following vaccination with trivalent seasonal vaccine, while only 5% of elderly subjects displayed such a response (10). This indicates the existence of shared antigens among previously circulating seasonal H1N1 and other A subtype viruses with the pandemic strain, that have allowed for a single dose of the pandemic vaccine to be immunogenic. However, epidemiological studies have shown that recent seasonal vaccination neither protected against nor increased risk of illness because of the pandemic virus (11), suggesting that the common antigens, while priming the antibody response,

are not associated with protection. Similar increases in cross-reactive responses to H1N1v after seasonal vaccine in adults and in those > 60 years have been observed, but at levels that suggest that seasonal vaccination itself is unlikely to provide protection against the novel H1N1v strain (12).

We also observed that in the two adult groups who received respectively a full or half dose of Focetria concomitantly with the plain trivalent seasonal vaccine, there was no interference by either dose with the response to seasonal vaccine, which met all three CHMP criteria for all three strains in both groups. The response to seasonal vaccine was similar in both groups, and consistent with the responses observed in adults when they received the vaccine in the seasonal licensure study (group 1). In fact, the GMT HI response to the seasonal H1N1 strain was twofold higher when Focetria and seasonal vaccine were co-administered compared with the response of the historical control group that received seasonal vaccine alone (Figure 2). As the mechanism of action of MF59 is local (13), requiring the administration of adjuvant and antigen at the same site, and the two vaccines were administered at different sites, the slightly elevated titre is further evidence of a cross-reactive response from the pandemic vaccine specifically against the seasonal H1N1 strain (as there was no increased response against the B strain and a smaller increase against the other A subtype, H3N2, virus). However, other studies of Focetria given alone showed no cross-reactivity to the seasonal A/Brisbane/59/2007(H1N1) strain (Novartis data on file).

Other reports of H1N1v vaccines have shown protective responses with one 15 μg dose of H1N1v HA without adjuvant in 96.7% (1) and 97.1% (3) of adults, and in 80% with a 7.5 μg dose with MF59 adjuvant (2). The present data show that 7.5 μg with MF59, or even a lower dose of 3.75 μg with a half dose of MF59, will provide protection for the majority of adults and elderly subjects and can be given concomitantly or subsequently to vaccination against seasonal influenza. Furthermore, prior immunisation with an MF59-containing vaccine appears to diminish, rather than increase the reactions to this adjuvanted vaccine. As supplies of H1N1v increase, the logistics of vaccine administration will be facilitated by concomitant vaccination of adults with Focetria and seasonal vaccine at the same visit.

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