Safety and immunogenicity of mRNA-1345 RSV vaccine coadministered with an influenza or COVID-19 vaccine in adults aged 50 years or older: an observer-blinded, placebo-controlled, randomised, phase 3 trial

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Summary

Background Coadministration of a respiratory syncytial virus (RSV) vaccine with seasonal influenza or SARS-CoV-2 vaccines could reduce health-care visits and increase vaccination uptake in older adults who are at high risk for severe respiratory disease. The RSV mRNA-1345 vaccine demonstrated efficacy against RSV disease with acceptable safety in the ConquerRSV trial in adults aged 60 years and older. We aimed to evaluate the safety and immunogenicity of mRNA-1345 coadministered with a seasonal influenza vaccine or SARS-CoV-2 mRNA vaccine.

Methods We conducted a two-part, phase 3, observer-blinded, placebo-controlled, randomised trial in medically stable adults aged 50 years or older in the USA. In part A, participants were randomly assigned in a 7:10:10 ratio to receive 50 µg mRNA-1345 plus placebo (0·9% sodium chloride) or coadministered with 60 µg of a standard-dose quadrivalent inactivated influenza vaccine (SIIV4), or SIIV4 plus placebo. In part B, participants were randomly assigned in a 1:1:1 ratio to receive 50 µg mRNA-1345 plus placebo or coadministered with 50 µg SARS-CoV-2 mRNA-1273.214 (bivalent [Wuhan-Hu-1 plus omicron BA.1]), or mRNA-1273.214 plus placebo. Random allocation in both parts was stratified by age group (50–59 years, 60–74 years, and ≥75 years) and used interactive response technology. The coprimary objectives in each part were safety in the safety set throughout the study and non-inferiority for six immunogenicity endpoints in the per-protocol set comparing coadministered versus individual vaccines on day 29. Immunogenicity endpoints were geometric mean titre (GMT) ratios (GMRs) of RSV-A neutralising antibodies (nAbs; in parts A and B), GMRs of haemagglutination inhibition (HAI) titres to each of the four influenza strains in SIIV4 (A/Victoria/2570/2019 [H1N1]pdm09-like virus [A/H1N1], A/Cambodia/e0826360/2020 [H3N2]-like virus [A/H3N2], B/Washington/02/2019-like virus [B/Victoria], and B/Phuket/3073/2013-like virus [B/Yamagata]; in part A), GMRs of nAbs against SARS-CoV-2 (ancestral [D614G] and omicron BA.1; part B), and differences in seroresponse rates for nAbs against RSV-A (parts A and B) and SARS-CoV-2 (ancestral [D614G] and omicron BA.1; part B). Non-inferiority was declared when the lower bound of the 95% CI for GMRs was greater than 0·667 and for seroresponse rate differences was greater than –10%. This trial is registered with ClinicalTrials.gov (NCT05330975) and is ongoing.

Findings Between April 1 and June 9, 2022, 1631 participants were randomly allocated in part A and 1623 received vaccinations on day 1 (685 [42%] received mRNA-1345 plus SIIV4, 249 [15%] mRNA-1345 plus placebo, and 689 [42%] SIIV4 plus placebo). Due to an interactive response technology error, the mRNA-1345 plus placebo group was smaller than planned (249 *vs* 420 participants). Of the 1623 participants in the safety set, 877 (54%) were female and 746 (46%) were male. Between July 27 and Sept 28, 2022, 1691 participants were randomly allocated in part B and 1681 received vaccinations on day 1 (564 [34%] received mRNA-1345 plus mRNA-1273.214, 558 [33%] mRNA-1345 plus placebo, and 559 [33%] mRNA-1273.214 plus placebo). Among the 1681 participants in the safety set, 924 (55%) were female and 757 (45%) were male. The reactogenicity profiles of the coadministered regimens were generally similar to the profiles when the vaccines were administered alone. As of the 6-month and 7-month follow-up times for parts A and B, respectively, no serious adverse events, adverse events of special interest, discontinuations due to adverse events, or fatal events considered related to study vaccination were reported. In part A, the GMR of nAbs against RSV-A in the mRNA-1345 plus SIIV4 group versus the mRNA-1345 alone group was 0·81 (95% CI 0·67 to 0·97), and the seroresponse rate difference in nAbs against RSV-A between the groups was –11·2% (95% CI –17·9 to –4·1). GMRs of anti-HAI titres in the mRNA-1345 plus SIIV4 versus SIIV4 alone groups were 0·89 (0·77 to 1·03) for A/H1N1, 0·97 (0·86 to 1·09) for A/H3N2, 0·93 (0·82 to 1·05) for B/Victoria, and 0·91 (0·81 to 1·02) for B/Yamagata. In part B, the GMR of nAbs against RSV-A in the mRNA-1345 plus mRNA-1273.214 versus the mRNA-1345 alone groups was 0·80 (95% CI 0·70 to 0·90), and the seroresponse rate difference was –4·4% (95% CI –9·9 to 1·0). Comparing the mRNA-1345 plus mRNA-1273.214 group with the mRNA-1273.214 alone group, the GMR of nAbs was 0·96 (0·87 to 1·06) for the ancestral (D614G) virus and 1·00 (0·89 to 1·14) for omicron BA.1; seroresponse rate differences were 0·2% (95% CI –6·0 to 6·3) for SARS-CoV-2 ancestral and –0·9% (–6·6 to 4·7) for omicron BA.1.

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See **Online** for appendix

Interpretation Coadministered mRNA-1345 plus SIIV4 or mRNA-1273.214 vaccines had acceptable safety profiles and elicited mostly non-inferior immune responses compared to individual vaccines in adults aged 50 years or older; only the seroresponse rate difference in nAbs against RSV-A in part A did not meet the non-inferiority criterion. Overall, these data support coadministration of mRNA-1345 with these vaccines in this population; longer-term evaluation continues in this study.

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Introduction

Infections with respiratory syncytial virus (RSV), influenza virus, and SARS-CoV-2 can all lead to severe respiratory illness, particularly in older individuals,[1–3] and cause a high burden of disease globally.[4–11] While most adults have been previously infected with, and demonstrate some degree of immunity against, RSV, protective immunity in older adults is not completely understood.[12,13] Decreased serum neutralising activity is a risk factor for RSV, particularly for severe disease, and serum antibodies have been shown to correlate with protection in older individuals.[14,15] The susceptibility of older people to RSV infections is also attributed to waning cellular immunity.[16] Currently licensed RSV vaccines, approved by the US Food and Drug Administration for vaccination of adults aged 60 years and older, including mRNA-1345 (mRESVIA; Moderna), target the stabilised, prefusion conformation of the RSV fusion glycoprotein (pre-F).[17] In clinical trials, these vaccines elicited neutralising antibodies and were efficacious against infections caused by RSV-A and RSV-B, with acceptable safety and tolerability profiles.[18–20]

Research in context

Evidence before this study

Respiratory syncytial virus (RSV), influenza virus, and SARS-CoV-2 infections cause substantial morbidity and mortality in older adults. Seasonal vaccinations are recommended against these viruses in this population. Coadministration of these vaccines could reduce the need for separate vaccination visits and potentially improve uptake; however, concerns over the effects on the immune response to each vaccine and the potential for increased side-effects with coadministration necessitate clinical trials. We searched PubMed for research articles published in English between Jan 5, 2022 and Sept 15, 2023, using the terms ("RSV humoral and cellular immunity"; "RSV, influenza, and SARS-CoV-2 vaccines"; "randomized clinical trials"; AND "observational real-world studies of RSV, influenza and SARS-CoV-2 in older adults worldwide"). In animal models and human studies, the prefusion conformation of the RSV F glycoprotein (pre-F) was shown to be the main antigen of the humoral immune response to RSV, displaying all known neutralising epitopes against both A and B subtypes, and is the target of current RSV vaccine approaches. In previous studies, the mRNA-1345 RSV pre-F vaccine elicited neutralising antibody (nAb) responses and protective efficacy against RSV-A and RSV-B subtypes with an acceptable safety profile. We identified three studies showing that coadministration of different RSV and influenza vaccines had acceptable safety profiles with nAb titre responses that were non-inferior to the individual vaccines.

Added value of this study

This randomised, two-part, phase 3 study evaluated the safety, tolerability, and immunogenicity of the mRNA-1345 RSV vaccine coadministered with a seasonal standard-dose quadrivalent inactivated influenza vaccine (SIIV4; part A) or a bivalent mRNA COVID-19 vaccine (mRNA-1273.214 bivalent [Wuhan-Hu-1 plus omicron BA.1]; part B) in adults aged 50 years and older (NCT05330975). Overall, our results demonstrated that the coadministered vaccine regimens had acceptable safety profiles and elicited immune responses that were generally non-inferior to those elicited by the individual vaccines, including across age, sex, race, and ethnicity subgroups. One coprimary immunogenicity endpoint, the seroresponse rate difference for nAbs against RSV-A in part A, did not meet the prespecified non-inferiority criterion. The clinical relevance of the seroresponse defined in the study as a four-fold rise in nAb following vaccination and the influence of circulating RSV nAb on seroresponse are not completely understood. Previously, lower levels of RSV nAb present before mRNA-1345 vaccination were observed in those who reached seroresponse criteria compared with those who had higher levels of circulating nAb. To our knowledge, this study is the first to demonstrate that two mRNA vaccines can be safely coadministered without a negative effect on immune responses against these viruses.

Implications of all the available evidence

Taken together, the results of this and other trials support coadministration vaccine approaches for these respiratory pathogens, which should improve vaccine uptake and reduce the burden of these respiratory diseases in older adults. Future studies that evaluate the longer-term safety and effectiveness following coadministration of these respiratory vaccines across various population groups are needed, as well as assessment of potential strategies for coadministration of all three vaccines together or given as a single, multicomponent vaccine.

Although SARS-CoV-2 continues to cause disease throughout the year, epidemiological spikes in COVID-19 cases, hospital admissions, and mortality—generally overlapping with seasonal patterns observed for influenza and RSV in the northern hemisphere—have been identified.[2,10,21] Many countries recommend updated seasonal COVID-19 vaccine boosters containing SARS-CoV-2-variant spike sequences to prevent COVID-19, in addition to RSV and influenza immunisations.[22,23] Coadministration of RSV vaccines with influenza and SARS-CoV-2 vaccines could allow individuals to receive these recommended vaccines in one visit, reducing the number of health-care visits and potentially increasing uptake of these vaccines among older people. However, coadministration could lower the immunogenicity of the individual vaccines.[24] In this ongoing study, we aimed to evaluate the safety, tolerability, and immunogenicity of a single dose of mRNA-1345 RSV vaccine coadministered either with a licensed, standard-dose quadrivalent inactivated influenza vaccine (SIIV4) or an mRNA bivalent SARS-CoV-2 vaccine in adults aged 50 years and older.

Methods

Study design and participants

This randomised, observer-blinded, placebo-controlled, phase 3 study was formed of two parts: part A evaluated the safety, tolerability, and immunogenicity of 50 µg RSV mRNA-1345 vaccine coadministered with 60 µg SIIV4 (Afluria Quadrivalent; Seqirus, Parkville, VIC, Australia), and part B assessed the same parameters for the RSV vaccine coadministered with 50 µg SARS-CoV-2 mRNA-1273.214 vaccine (Spikevax bivalent [Wuhan-Hu-1+omicron BA.1]; Moderna, Cambridge, MA, USA; appendix pp 18–19). The trial was conducted in accordance with the International Council for Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice Guidance. The central Institutional Review Board (Advara, Columbia, MD, USA) approved the protocol and consent forms across the study sites in the USA (48 in part A and 58 in part B; appendix pp 3–5). All participants provided written informed consent. Safety was reviewed weekly by an internal safety review team and by an independent data and safety monitoring board on a continual basis. The trial is registered at ClinicalTrials.gov (NCT05330975) and is ongoing.

For both study parts, participants were eligible if they were aged 50 years or older with stable medical conditions, and they were excluded if they had certain immunocompromising conditions. Also excluded from part A were those who had received a seasonal or investigational influenza vaccine within 180 days before random allocation or tested positive for influenza within 180 days before the screening visit (≤14 days before study vaccine administration). In part B, eligible participants had completed an approved primary COVID-19 vaccination series, with the final dose administered 150 days or more before the day of the first trial vaccination (day 1) or if the last dose was a booster, 120 days or more before day 1 (or less per local guidance). Participants were excluded from both parts A and B if they had significant exposure to someone infected with SARS-CoV-2 in the 10 days before screening and day 1, and for part B only, if they had a history of SARS-CoV-2 infection within 90 days before enrolment. Sex data were self-reported at enrolment with the options of female or male. Additional eligibility criteria are provided in the supplementary appendix (pp 6–10).

Randomisation and masking

Part A planned to enrol approximately 1620 adults aged 50 years or older to randomly allocate participants in a 7:10:10 ratio to three groups: 420 participants were to receive mRNA-1345 plus placebo, 600 were to receive mRNA-1345 plus SIIV4, and 600 were to receive SIIV4 plus placebo (appendix pp 18–19). Random allocation used interactive response technology (IRT). Due to an error in the IRT for part A, the actual allocation ratio was 3·6:10:10, with fewer participants than planned in the mRNA-1345 plus placebo group (appendix pp 10, 18). Part B planned to enrol approximately 1680 adults aged 50 years and older, and to randomly allocate them in a 1:1:1 ratio, with 560 participants in each group, to receive mRNA-1345 plus placebo, mRNA-1345 plus mRNA-1273.214, or mRNA-1273.214 plus placebo. Random allocation in both study parts was stratified by age (50–59 years, 60–74 years, and ≥75 years), with the intention that the age cohort aged 50–59 years would make up approximately 20% of participants in part A and approximately 35% in part B. Owing to the IRT error in part A, a higher proportion of participants aged 50–59 years was enrolled in the mRNA-1345 plus placebo group than in the other two groups (44% *vs* 22–23%).

Study vaccine assignment (including injection site [right or left deltoid] and whether the corresponding vaccine or placebo was administered), preparation, administration, and accountability (ie, logging of vaccine and placebo at study sites, including receipt, inventory, dispensing, injections, and return of unused material to the sponsor) were performed by designated unmasked site personnel who did not participate in any clinical study evaluations. The unmasked site personnel prepared study vaccines in a secure location not accessible or visible to participants and other study staff, and opaque sleeves were used to conceal the syringes used for injection. Once injections were complete, only masked study staff performed further assessments and interacted with the participants. Participants, investigators and clinical staff responsible for study assessment and safety were masked. Access to the randomisation code was strictly controlled at the pharmacy; the identity of the study vaccine was not revealed except in case of emergency. Laboratory personnel responsible for immunogenicity testing were masked to the study

vaccine assignment of the samples tested throughout the study.

Procedures

The mRNA-1345 vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine containing 50 µg mRNA that encodes the RSV F-glycoprotein, stabilised in the prefusion conformation. The SIIV4 vaccine is an egg-based influenza vaccine containing 15 µg haemagglutinin for each of the four influenza strains recommended for the 2021–22 influenza season in the northern hemisphere, including A/Victoria/2570/2019 IVR-215 (A/Victoria/2570/2019 [H1N1]pdm09-like virus [A/H1N1]), A/Cambodia/e0826360/2020 IVR-224 (A/Cambodia/e0826360/2020 [H3N2]-like virus [A/H3N2]), B/Victoria/705/2018 BVR-11 (B/Washington/02/2019-like virus [B/Victoria]), and B/Phuket/3073/2013 BVR-1B (B/Phuket/3073/2013-like virus [B/Yamagata]). mRNA-1273.214 is a bivalent vaccine containing 25 µg each of two mRNAs encoding the prefusion-stabilised conformations of spike glycoproteins (S-2P) of SARS-CoV-2 Wuhan-Hu-1 isolate and SARS-CoV-2 omicron B.1.1.529 (BA.1) variant. The placebo was a 0·9% sodium chloride (normal saline) solution (US Pharmacopeia [USP; Frederick, MD, USA], or European Pharmacopeia [Strasbourg, France]).

In both parts, vaccines, placebo, or both were administered as two intramuscular injections into the deltoid muscle, one per arm, on day 1. The mRNA-1345 and mRNA-1273.214 vaccines were each administered as sterile liquids at 0·1 mg/mL in 20 mM Tris buffer containing 87 mg/mL sucrose and 2·2 mM acetate at pH 7·5. The SIIV4 vaccine was given as a 0·5 mL single-dose, pre-filled syringe. On day 29, in part B, one injection of 50 µg mRNA-1273.214 was administered to all study participants who did not receive mRNA-1273.214 at day 1, to allow all participants to receive a COVID-19 booster. Participants in the other two groups received an injection of placebo on day 29 to maintain the study masking.

In both parts, serum samples for immunogenicity assessments were collected on days 1 and 29. Serum neutralising antibodies (nAbs) were measured using different validated assays: a microneutralisation assay for RSV-A and RSV-B; a haemagglutination inhibition (HAI) assay for influenza A and B; and pseudovirus neutralisation assays for ancestral and omicron BA.1 SARS-CoV-2. Immunogenicity assays are described in full in the appendix (p 17).

Vital signs were measured, and full physical examinations were done, at the screening visit and on day 1. Vital sign measurements included systolic and diastolic blood pressure, heart rate, respiratory rate, and body temperature, collected once before and 30 min or more after vaccination. Those signs meeting toxicity grades of 3 or above were monitored until the vital sign reached baseline or stable levels. Follow-up for safety is described in the appendix (pp 12–13).

Outcomes

The primary objectives for both parts were to evaluate the safety, tolerability, and immunogenicity of the coadministered vaccine regimens versus the individual vaccines (appendix pp 28–29). Safety endpoints included solicited local and systemic adverse reactions occurring within 7 days of vaccination; unsolicited adverse events up to 28 days after vaccination; and serious adverse events (SAEs), adverse events of special interest (AESIs; appendix pp 31–32), medically attended adverse events (MAAEs), and adverse events leading to discontinuation from the study up to the data cutoff date or participant withdrawal from the study.

In part A, six coprimary immunogenicity endpoints assessed at day 29 were: geometric mean titre (GMT) ratios (GMRs) and seroresponse rate differences of RSV-A nAbs for mRNA-1345 coadministered with SIIV4 versus mRNA-1345 alone, and GMRs of HAI titres to each of the four influenza strains (A/H1N1, A/H3N2, B/Victoria, and B/Yamagata) for mRNA-1345 coadministered with SIIV4 versus SIIV4 alone. The key secondary objectives, assessed at day 29, were to evaluate the effect of a coadministered influenza vaccine on the immune response to RSV-B based on GMR and seroresponse rate difference, and the effect of a coadministered RSV vaccine on the immune response to influenza (A/H1N1, A/H3N2, B/Victoria, and B/Yamagata) based on seroconversion rate differences. RSV-A rather than RSV-B was chosen for the primary immunogenicity endpoints because mRNA-1345 encodes the membrane-anchored RSV F glycoprotein derived from an RSV-A strain (RSV-A-A2 strain), which is highly conserved across RSV-A and RSV-B subtypes.[12,25] Secondary objectives to evaluate antibody responses to mRNA-1345 with and without SIIV4, and to SIIV4 with and without mRNA-1345, at day 181 and the end-of-study visit will be published at a later date.

In part B, the six coprimary immunogenicity endpoints assessed on day 29 were: GMRs and seroresponse rate differences of nAbs against RSV-A for mRNA-1345 coadministered with mRNA-1273.214 versus mRNA-1345 alone, and GMRs and seroresponse rate differences of nAbs against SARS-CoV-2 (ancestral [D614G] and omicron BA.1) for mRNA-1345 coadministered with mRNA-1273.214 versus mRNA-1273.214 alone. The key secondary objective of part B was to evaluate the effect of coadministered mRNA-1273.214 on the immune response to RSV-B. Secondary objectives to evaluate antibody responses to mRNA-1345 with and without mRNA-1273.214, and to mRNA-1273.214 with and without mRNA-1345, at day 181 and the end-of-study visit will be published at a later date.

Statistical analysis

Non-inferiority of the coprimary immunogenicity endpoints and key secondary endpoints in both parts were tested using a hierarchical testing procedure to

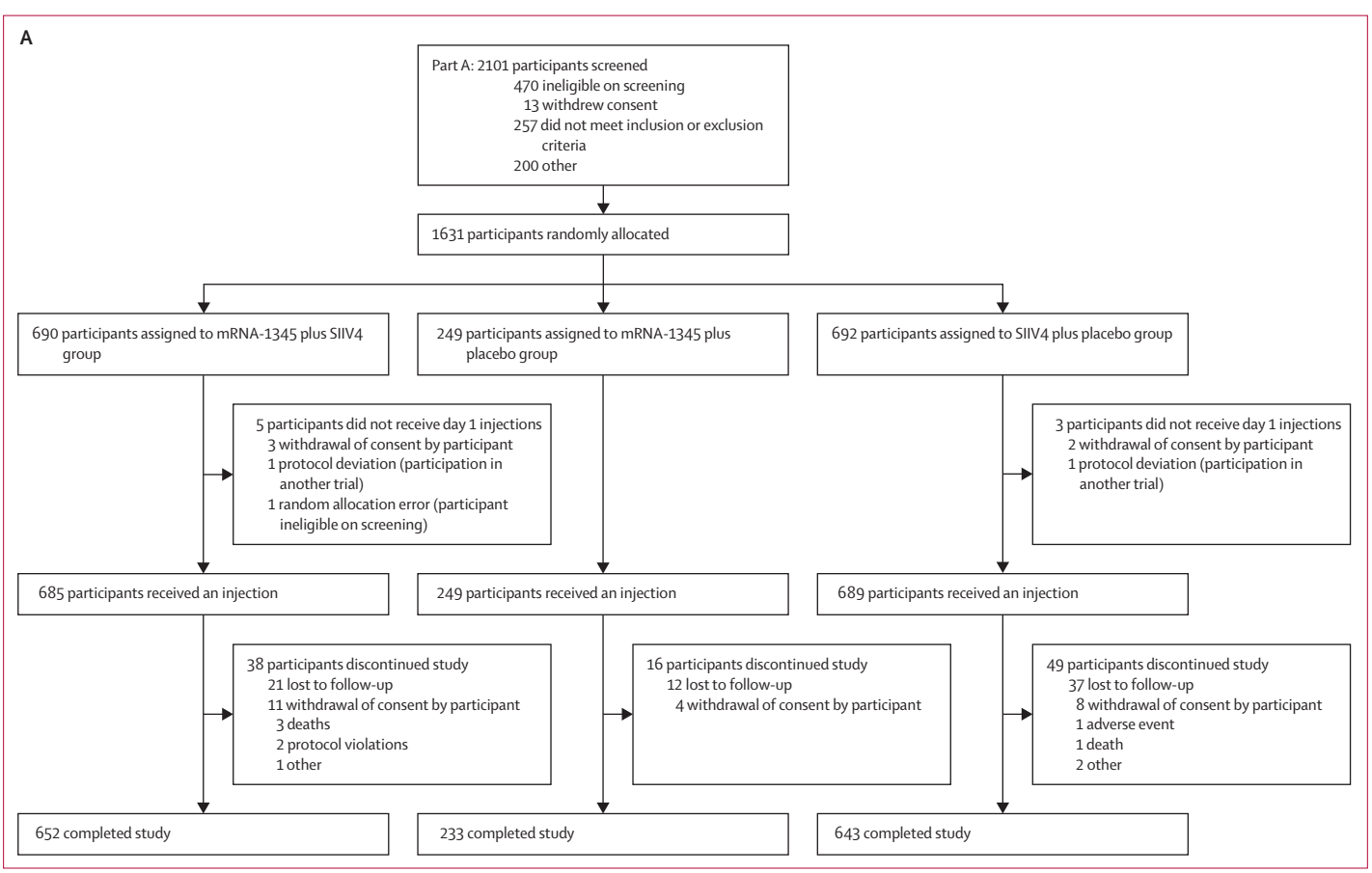
control the overall type 1 error rate at a two-sided α to 0·05 (appendix pp 13–17, 20–21). Non-inferiority hypotheses for the key secondary objectives were only tested if the primary objectives were successfully met. Statistical analysis methods are detailed in the appendix (pp 13–17).

Analysis sets are described in the appendix (p 30). In both parts, the coprimary immunogenicity endpoints were evaluated in the per-protocol set, defined as all participants who received the assigned vaccine dose according to protocol, had baseline and one or more post-injection immunogenicity assessments, and had no major protocol deviations. Participants were evaluated according to the vaccination group to which they were randomly assigned. Safety in both study parts was assessed in the safety set (all participants who received any study vaccination; appendix pp 12–13) and solicited adverse reactions were analysed in the solicited safety set (participants in the safety set who contributed solicited adverse reaction data). Participants in both sets were analysed according to study vaccine received.

Safety endpoints were summarised as numbers and percentages of participants. Since participants received two injections on day 1 in contralateral arms, local solicited adverse reactions were summarised as the highest-grade adverse reaction observed for each injection at left and right arms.

GMRs of nAbs and HAIs with corresponding two-sided 95% CIs were estimated using an analysis of covariance (ANCOVA) model based on log-transformed titres at day 29, with vaccination group as the fixed variable, log-transformed baseline titres as a fixed covariate, and adjustment for stratified age group used for random allocation. The resulting least square means, difference of least square means, and 95% CIs were back transformed to the original scale for presentation. Non-inferiority of the GMR was demonstrated if the lower bound of the 95% CI was greater than 0·667, with a non-inferiority margin of 1·5 per standard regulatory criteria.[26,27]

Seroresponse rates of RSV-A, RSV-B, and SARS-CoV-2 nAbs were defined as percentages of participants with post-vaccination titres that were four-fold or more above the lower limit of quantification (LLOQ) if baseline titres were less than the LLOQ, or with a four-fold or more rise from baseline if baseline titres were greater than or equal to the LLOQ. Seroconversion rates for influenza HAI antibody titres were defined as percentages of participants with a post-vaccination titre of 1:40 or more if the baseline titre was less than 1:10, or a four-fold or more rise in



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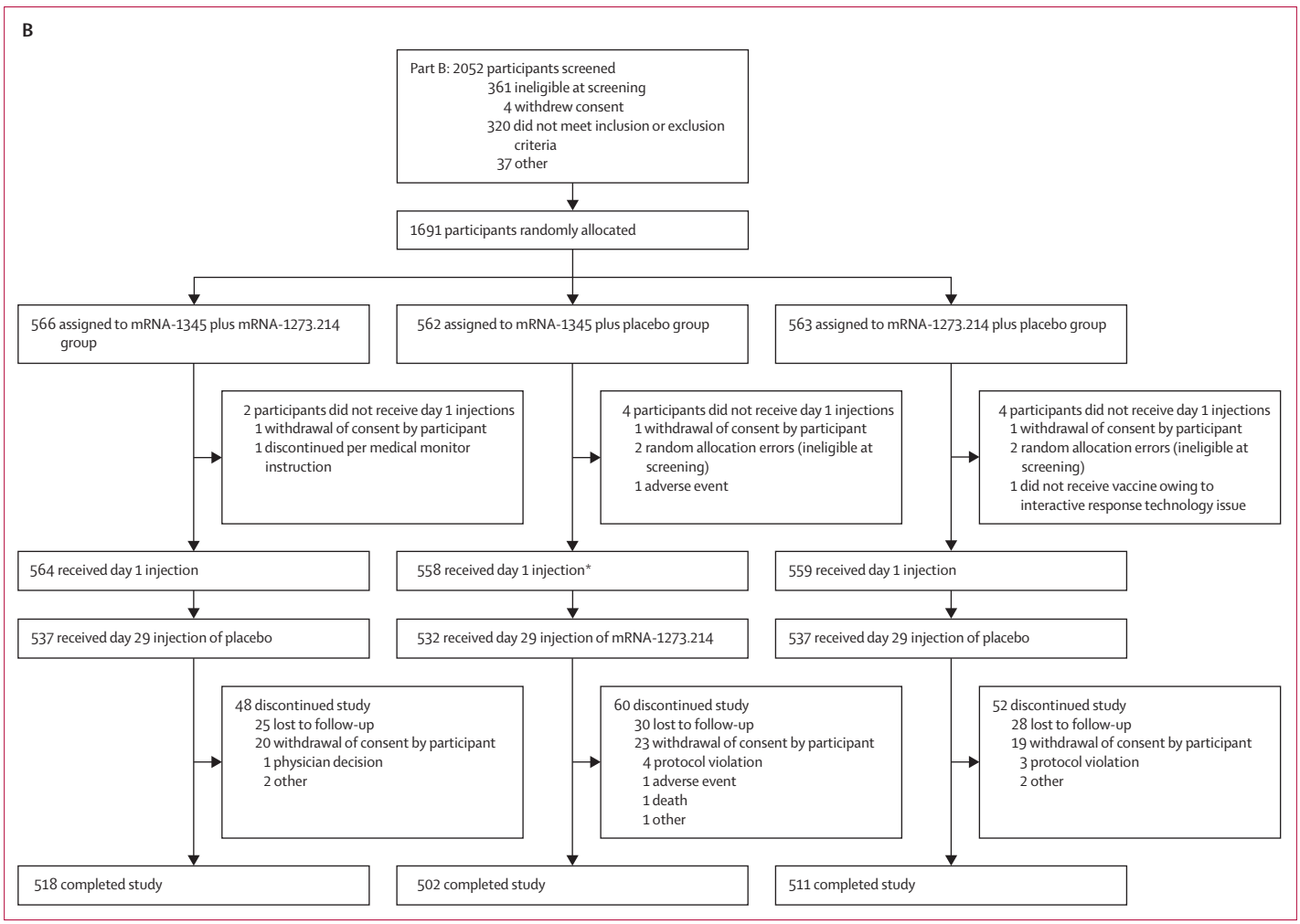

Figure 1: **Trial profile**
In part B, on day 29, participants received an additional injection of mRNA-1273.214 or placebo to allow all study participants to receive an mRNA-1273.214 booster vaccination. Participants who completed the final visits at day 181 (part A) and day 211 (part B) were considered to have completed the study. SIIV4=standard-dose quadrivalent inactivated influenza vaccine. *Two participants assigned to the mRNA-1345 plus placebo group mistakenly received mRNA-1273.214 on day 1.

post-vaccination titres if baseline was 1:10 or greater. The numbers and percentages of participants with a seroresponse or seroconversion at each timepoint post-baseline are provided with two-sided 95% CIs (Clopper–Pearson). The 95% CIs for differences in seroresponse or seroconversion rates at day 29 between vaccination groups were calculated using the Miettinen–Nurminen method. Non-inferiority for seroresponse rates and seroconversion rates was demonstrated if the lower bound of the 95% CI for the seroresponse rate or seroconversion rate difference was greater than –10%.

Primary immunogenicity endpoints were also evaluated in the full analysis set as a sensitivity analysis, using the same methods as used for the per-protocol set. The full analysis set included all participants who were randomly allocated and received any study vaccination, analysed in the vaccination group to which they were assigned. Immunogenicity analyses were also performed in prespecified subgroups of age (50–59 years, 60–64 years, and ≥75 years, or 50–59 years and ≥60 years), sex, race, and ethnicity. A post-hoc subgroup analysis was performed in age groups 50–59 years versus 60 years or older in pooled vaccination groups for parts A and B to further assess the non-inferiority of RSV nAbs in these age groups, per the same above standard success criteria used for the coprimary and key secondary GMR endpoints.

Baseline and day 29 GMTs and geometric mean concentrations (GMCs) and geometric mean fold-rises (GMFRs) in GMTs and GMCs from baseline to day 29 are provided with corresponding 95% CIs (*t*-distribution of log-transformed values, back transformed to original scale for presentation). We also present seroresponse rates at day 29 and percentages of participants with two-fold or greater rises in nAbs from baseline to day 29, with two-sided 95% CIs (Clopper–Pearson).

The database lock dates for safety and immunogenicity analyses were March 8, 2023, for part A, and June 21, 2023, for part B. All analyses were conducted using SAS version 9.4 or higher.

Role of the funding source

The study was funded by the sponsor, Moderna, who was involved in the study design, as well as collection, analysis, and interpretation of the data, writing of the report, and the decision to submit for publication.

Results

In part A of the study, of the 2101 participants assessed for eligibility between April 1 and June 9, 2022, 470 were excluded for not meeting screening criteria, 1631 were randomly allocated, and 1623 received vaccinations on day 1 (685 [42%] in the mRNA-1345 plus SIIV4 group, 249 [15%] in the mRNA-1345 plus placebo group, and 689 [42%] in the SIIV4 plus placebo group; figure 1). The 103 study discontinuations across vaccination groups were mainly due to loss to follow-up. The per-protocol sets included 639 participants in the mRNA-1345 plus SIIV4 group, 232 in the mRNA-1345 plus placebo group, and 626 in the SIIV4 plus placebo group (reasons for exclusion are shown in appendix p 22). The mean age across the three vaccination groups was 63·8 years (SD 7·4). Of the 1623 participants in the safety set, 421 (26%) were aged 50–59 years, 1202 (74%) were aged 60 years or older, 877 (54%) were female, and 746 (46%) were male. 1220 (75%) participants were White, 381 (23%) were Black or African American, and 576 (35%) were of Hispanic or Latino ethnicity (table 1). 299 (18%) participants had pre-existing respiratory diseases, 348 (21%) had type 2 diabetes, and 155 (10%) had cardiac diseases (appendix p 33).

	mRNA-1345 plus SIIV4 (n=685)	mRNA-1345 plus placebo (n=249*)	SIIV4 plus placebo (n=689)
Age at enrolment, years†			
Mean (SD)	64·5 (7·5)	61·3 (7·4)	64·1 (7·1)
Range	50–89	50–80	50–86
Age group 1†			
50–59 years	156 (23%)	110 (44%)	155 (22%)
60–74 years	466 (68%)	125 (50%)	474 (69%)
≥75 years	63 (9%)	14 (6%)	60 (9%)
Age group 2†			
50–59 years	156 (23%)	110 (44%)	155 (22%)
≥60 years	529 (77%)	139 (56%)	534 (78%)
Sex			
Male	322 (47%)	108 (43%)	316 (46%)
Female	363 (53%)	141 (57%)	373 (54%)
Race			
White	520 (76%)	189 (76%)	511 (74%)
Black or African American	156 (23%)	59 (24%)	166 (24%)
Asian	4 (1%)	0	3 (<1%)
Other‡	5 (1%)	1 (<1%)	9 (1%)
Ethnicity			
Hispanic or Latino	238 (35%)	91 (37%)	247 (36%)
Not Hispanic or Latino	442 (65%)	158 (63%)	441 (64%)
Unknown or not reported	5 (1%)	0	1 (<1%)

Data are n (%) unless otherwise specified. Percentages may not total 100% due to rounding. SIIV=standard-dose quadrivalent inactivated influenza vaccine. *Due to an interactive response technology randomisation error in the mRNA-1345 group of part A, the population is smaller than the other two groups and there is a larger percentage of participants aged 50–59 years. †Derived from age collected on electronic case report forms; random allocation was stratified by age (50–59 years, 60–74 years, and ≥75 years). ‡Other race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, other, multiple, or not reported.

Table 1: **Baseline demographics and characteristics of the safety set, part A**

In part B of the study, of the 2052 participants assessed for eligibility between July 27 and Sept 28, 2022, 361 were excluded for not meeting screening criteria, 1691 were randomly allocated, and 1681 received vaccinations on day 1 (564 [34%] in the mRNA-1345 plus mRNA-1273.214 group, 558 [33%] in the mRNA-1345 plus placebo group, and 559 [33%] in the mRNA-1273.214 plus placebo group; figure 1). On day 29, 532 participants in the mRNA-1345 plus placebo group received an injection of mRNA-1273.214, allowing all participants to receive a SARS-CoV-2 booster vaccination; 537 participants in the other two groups received a placebo injection to maintain study masking. Most of the 160 study discontinuations were attributed to loss to follow-up. The safety set included 564 participants in the mRNA-1345 plus mRNA-1273.214 group, 556 in the mRNA-1345 plus placebo group, and 561 in the mRNA-1273.214 plus placebo group; two participants assigned to the mRNA-1345 plus placebo group received mRNA-1273.214 on day 1 (appendix p 22). The per-protocol set included 513 participants in the mRNA-1345 plus placebo group, 514 in the mRNA-1345 plus mRNA-1273.214 group, and 519 in the mRNA-1273.214 plus placebo group (appendix p 22). The mean age of participants in the safety set was 62·5 years (SD 7·6); 624 (37%) of the 1681 participants were aged 50–59 years and 1057 (63%) were aged 60 years or older. 924 (55%) participants were female and 757 (45%) were male; 1291 (77%) were White, 337 (20%) were Black or African American, and 647 (38%) were of Hispanic or Latino ethnicity (table 2). 315 (19%) participants had pre-existing respiratory diseases, 332 (20%) had type 2 diabetes, and 124 (7%) had cardiac diseases (appendix pp 33–34).

The median durations of follow-up were 180 days (IQR 169–183) post-vaccination in part A and 208 days (199–213) in part B. In part A, solicited local and systemic adverse reactions reported within 7 days post-injection were similar in the mRNA-1345 plus SIIV4 and mRNA-1345 plus placebo groups but higher in the coadministration group than in the SIIV4 plus placebo group (figure 2, appendix pp 35–36). In part B, incidences of solicited local adverse reactions were similar across all

	mRNA-1345 plus mRNA-1273.214 (n=564)	mRNA-1345 plus placebo (n=556)	mRNA-1273.214 plus placebo (n=561)
Age at enrolment, years*			
Mean (SD)	62·4 (7·4)	62·6 (7·7)	62·6 (7·8)
Range	50–91	50–89	50–88
Age group 1*			
50–59 years	208 (37%)	207 (37%)	209 (37%)
60–74 years	315 (56%)	309 (56%)	312 (56%)
≥75 years	41 (7%)	40 (7%)	40 (7%)
Age group 2*			
50–59 years	208 (37%)	207 (37%)	209 (37%)
≥60 years	356 (63%)	349 (63%)	352 (63%)
Sex			
Male	246 (44%)	244 (44%)	267 (48%)
Female	318 (56%)	312 (56%)	294 (52%)
Race			
White	428 (76%)	429 (77%)	434 (77%)
Black or African American	113 (20%)	110 (20%)	114 (20%)
Asian	7 (1%)	6 (1%)	1 (<1%)
Other†	16 (3%)	11 (2%)	12 (2%)
Ethnicity			
Hispanic or Latino	214 (38%)	210 (38%)	223 (40%)
Not Hispanic or Latino	349 (62%)	341 (61%)	333 (59%)
Unknown or not reported	1 (<1%)	5 (1%)	5 (1%)

Data are n (%) unless otherwise specified. Percentages may not total 100% due to rounding. *Derived from age collected on electronic case report forms; randomisation was stratified by age (50–59, 60–74, and ≥75 years). †Other race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, other, multiple, or not reported.

Table 2: **Baseline demographics and characteristics of the safety set, part B**

groups, and systemic adverse reactions were numerically higher in the coadministration group than in the other groups (figure 2, appendix pp 37–38). In both parts, the most common local adverse reaction (occurring in ≥20% participants) was injection-site pain, and the most frequent systemic adverse reactions were fatigue, headache, myalgia, and arthralgia (≥20% participants). Solicited adverse reactions were mostly grades 1–2 in severity. In part A, the most frequent solicited grade 3 reaction was fatigue (14 [2%] of 678, three [1%] of 249, and nine [1%] of 683 in the mRNA-1345 plus SIIV4, mRNA-1345 plus placebo, and SIIV4 plus placebo groups, respectively); a grade 4 local event of axillary swelling (one [<1%] of 249) in one participant and fever (one [<1%] of 248) in another participant occurred in the mRNA-1345 plus placebo group. In part B, the small numerical difference in systemic adverse reactions was largely due to a slight increase in the frequencies of fatigue and myalgia reported in the coadministration group versus the individual vaccine groups. No grade 4 local adverse reactions occurred; one grade 4 systemic adverse reaction of fever was observed in the mRNA-1273.214 plus placebo group. In both study parts, the frequencies of local and systemic adverse reactions were similar in participants aged 50–59 years and 60 years and older for the coadministered versus individual vaccines (appendix pp 39–44).

The incidences of unsolicited adverse events, regardless of relationship to vaccination, reported up to 28 days post-injection in part A were similar in the mRNA-1345 plus SIIV4 (57 [8%] of 685), mRNA-1345 plus placebo (21 [8%] of 249), and SIIV4 plus placebo (46 [7%] of 689) groups (appendix p 45). Incidences of SAEs up to 28 days after injection were low and similar across the study groups (five [<1%] of 685 in the combination group, three [1%] of 249 in the mRNA-1345 plus placebo group, and six [1%] of 689 in the SIIV4 plus placebo group); all were considered unrelated to the study vaccination by the investigator (appendix p 46). Six (<1%) of 1623 participants in the part A safety set, involving two participants in each group, had adverse events considered related to vaccination by the investigator; they were mainly respiratory and skin or subcutaneous tissue events (appendix p 47).

In part B, incidences of unsolicited adverse events, regardless of relationship to vaccination, reported within 28 days after vaccination were numerically higher in the mRNA-1345 plus mRNA-1273.214 group (54 [10%] of 564) than in the mRNA-1273.214 plus placebo group (44 [8%] of 561) and mRNA-1345 plus placebo group (41 [7%] of 556; appendix p 48). There were few SAEs in the coadministered vaccine group (four participants [1%] of 564 reporting six events) and mRNA-1345 plus placebo group (one participant [<1%] of 556 reporting one event), and none in the mRNA-1273.214 plus placebo group (appendix p 49); all SAEs were considered unrelated to study vaccination by the investigator. The numbers of participants with adverse events considered related to vaccination by the investigator were similar across the groups (two participants [<1%] of 564 [three events] in the mRNA-1345 plus mRNA-1273.214 group, three [1%] of 556 [three events] in the mRNA-1345 plus placebo group, and five [1%] of 561 [six events] in the mRNA-1273.214 plus placebo group). These events were primarily reactogenicity and were considered non-serious (appendix p 50).

As expected, frequencies of adverse events were generally higher in participants older than 75 years than in those aged 60–74 years and 50–59 years in both parts (appendix pp 53–54). As of the 6-month and 7-month follow-up times for parts A and B, respectively, no SAEs, AESIs, discontinuations due to adverse events, or fatal events considered related to study vaccination were reported (appendix pp 51–52). In both study parts, there were no reported cases of anaphylaxis, Guillan–Barré syndrome, acute disseminated encephalomyelitis, Bell's palsy or facial paralysis, acute myocarditis, or pericarditis.

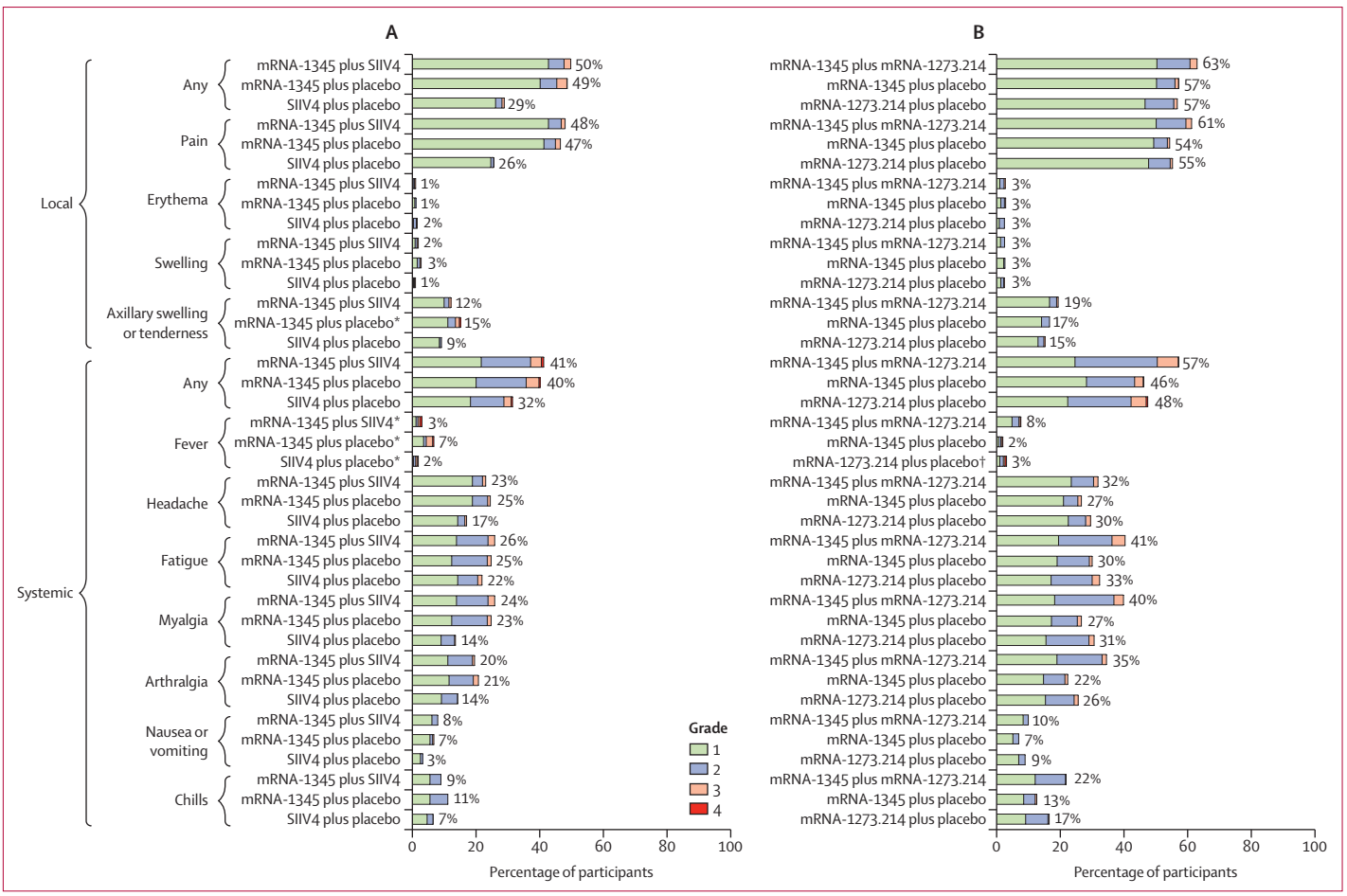

Figure 2: **Solicited local and systemic adverse reactions within 7 days after injection in the solicited safety sets**
Absolute numbers are provided in the appendix (pp 35–38). Local adverse reactions are summarised based on the highest grade of the adverse reaction observed from both injection sites (left and right arms). Percentages represent all grades for each adverse reaction; for details by grade see the appendix (pp 35–38). SIIV4=standard-dose quadrivalent inactivated influenza vaccine. *Grade 4 fever events were eDiary data entry errors in the mRNA-1345 plus SIIV4 and SIIV4 plus placebo groups; one true grade 4 fever event and one true grade 4 event of axillary swelling or tenderness occurred in the mRNA-1345 plus placebo group. †One true grade 4 event of fever occurred in the mRNA-1273.214 plus placebo group; all other grade 4 fevers were eDiary data entry errors.

In part A, baseline nAb GMTs were similar for RSV-A and RSV-B in the mRNA-1345 plus SIIV4 and mRNA-1345 plus placebo groups (figure 3A, appendix p 55), and baseline levels of anti-HAI antibody GMTs against the four influenza strains were similar in the mRNA-1345 plus SIIV4 and SIIV4 plus placebo groups (figure 3A, appendix pp 56–57). Five of the six coprimary immunogenicity endpoints met the prespecified non-inferiority criterion of the study (lower bound of 95% CI >0·667; figure 4A, appendix pp 55–57): GMRs of nAbs against RSV-A (0·81 [95% CI 0·67 to 0·97]) and of anti-HAI titres against the four influenza strains—A/H1N1 (0·89 [0·77 to 1·03]), A/H3N2 (0·97 [0·86 to 1·09]), B/Victoria (0·93 [0·82 to 1·05]), and B/Yamagata (0·91 [0·81 to 1·02]). The coprimary endpoint of seroresponse rate difference for nAbs against RSV-A (–11·2% [95% CI –17·9 to –4·1]) following mRNA-1345 plus SIIV4 versus mRNA-1345 plus placebo did not meet the non-inferiority criterion (lower bound of 95% CI ≥–10%), and so key secondary endpoints—GMR and seroresponse rate difference against RSV-B and seroconversion rate differences for the influenza strains—were not formally assessed for statistical non-inferiority per the testing strategy, although the data are shown in figure 4A.

In part B, baseline GMTs or GMCs and day 29 GMFRs for nAbs against RSV-A, RSV-B, and SARS-CoV-2 (ancestral [D614G] and omicron BA.1) were generally similar in the coadministration and individual vaccine groups (figure 3B, appendix pp 58–59). The coprimary endpoints of GMRs of nAbs against RSV-A (0·80 [95% CI 0·70 to 0·90]) and SARS-CoV-2 ancestral (0·96 [0·87 to 1·06]) and omicron BA.1 (1·00 [0·89 to 1·14]) all met the prespecified non-inferiority criterion (lower bound of 95% CI >0·667; figure 4B, appendix pp 58–59). The coprimary endpoints of seroresponse rate differences of nAbs against RSV-A (–4·4% [95% CI –9·9 to 1·0]) and SARS-CoV-2 ancestral (0·2% [–6·0 to 6·3]) and omicron BA.1 (–0·9% [–6·6 to 4·7]) also met the prespecified non-inferiority criterion (lower bound of 95% CI ≥–10%). The key secondary endpoint of GMR of nAbs against RSV-B met

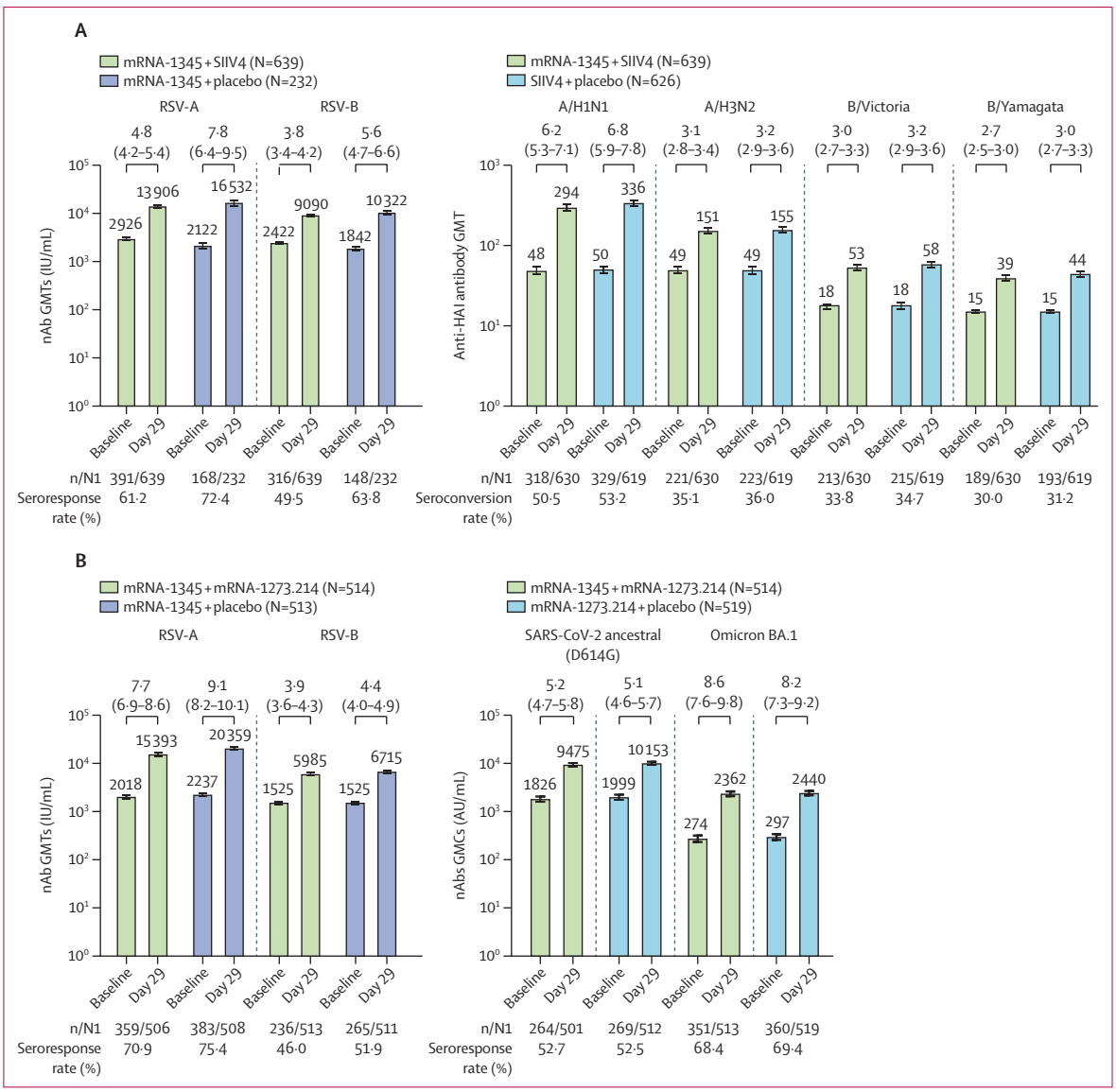

Figure 3: **Antibody titres to RSV-A, RSV-B, and influenza or SARS-CoV-2 after coadministration of mRNA-1345 with SIIV4 or mRNA-1273.214 versus individual vaccines**

Antibody values reported as below the LLOQ are replaced by 0·5 × LLOQ; values greater than the ULOQ are replaced by the ULOQ. Geometric mean fold-rises (95% CIs) at day 29 versus baseline are shown with 95% CIs above the graphs. Error bars on the graphs indicate 95% CIs. A/H1N1=A/Victoria/2570/2019 [H1N1]pdm09-like virus. A/H3N2=A/Cambodia/e0826360/2020 [H3N2]-like virus. B/Victoria=B/Washington/02/2019-like virus. B/Yamagata=B/Phuket/3073/2013-like virus. GMC=geometric mean concentration. GMT=geometric mean titre. HAI=haemagglutination inhibition. IU=international units. LLOQ=lower limit of quantification. N=number of participants in the per-protocol set. n=number of participants with a seroresponse or seroconversion. N1=number of participants with data at baseline and day 29. nAb=neutralising antibody. RSV=respiratory syncytial virus. SIIV4=standard-dose quadrivalent inactivated influenza vaccine. ULOQ=upper limit of quantification.

non-inferiority, but non-inferiority for the seroresponse rate difference against RSV-B was not met. Similar results were observed in a sensitivity analysis performed in the full analysis set for both parts A and B (appendix pp 60–62).

The GMRs of antibody responses across age, sex, race, and ethnicity subgroups for coadministered vaccines compared with the respective individual vaccines were generally similar to those of the overall study cohort (appendix pp 23–27, 63–84), with the exception of the lower GMRs against RSV-A and wide 95% CIs against RSV-B observed in the smaller age group of 75 years and older. The seroresponse rates and seroconversion rates in the older age groups (≥60 years and ≥75 years) in part A were generally numerically lower than those of the overall cohort, whereas those in the younger age groups (50–59 years) were more similar to the overall cohort, noting that the baseline GMTs were higher in the older age groups. An analysis of GMRs of nAb responses

against RSV-A and RSV-B for the pooled mRNA-1345 groups and pooled coadministered mRNA-1345 plus SIIV4 and mRNA-1345 plus mRNA-1273.214 groups in parts A and B showed generally higher GMTs in those aged 50–59 years than in those aged 60 years or older, with GMRs and corresponding lower bounds of 95% CIs over 1·0, regardless of vaccination group (appendix p 85).

Discussion

In this phase 3 trial in adults aged 50 years or older, coadministration of the RSV mRNA-1345 vaccine with SIIV4 or mRNA-1273.214 vaccines elicited antibody responses that were non-inferior to those of the vaccines administered alone, at least on the basis of GMTs. Both coadministered vaccines had acceptable safety profiles similar to those of mRNA-1345, SIIV4, and mRNA-1273.214 alone, with no new safety concerns identified.[28,29] To our knowledge, this trial is the first to demonstrate the safety and immunogenicity of coadministered RSV and COVID-19 vaccines and that two different mRNA vaccines can be coadministered without a negative effect on the immune response to either vaccine.

In both study parts, per the testing strategy, the non-inferiority success criteria of immune responses for the coadministered vaccines for each of six coprimary endpoints had to be met to assess non-inferiority for the secondary endpoints. Coadministration of mRNA-1345 with SIIV4 in part A met success for five of the six coprimary endpoints of GMRs at day 29 against RSV-A and influenza, which were all non-inferior to those of the comparator groups; however, the seroresponse rate difference of nAbs against RSV-A for mRNA-1345 plus SIIV4 versus mRNA-1345 plus placebo did not meet the prespecified non-inferiority criterion. Thus, non-inferiority of the part A key secondary endpoints was not formally assessed, although the lower bounds of the 95% CIs for these endpoints satisfied the specified success criteria. In part B, all six coprimary endpoints met the prespecified criteria for non-inferiority, and testing of the non-inferiority hypotheses for the key secondary endpoints found non-inferiority was met for the GMR of nAbs against RSV-B induced by mRNA-1345 plus mRNA-1273.214 versus mRNA-1345 alone. By contrast, non-inferiority was not met for the seroresponse rate difference in nAbs to RSV-B for the coadministered vaccine versus mRNA-1345 alone. In the absence of a threshold of protection, and in a population previously exposed to RSV, the clinical relevance of the seroresponse definition in this study is not completely understood. In the ConquerRSV efficacy study, lower baseline GMTs were observed among participants meeting the seroresponse criterion compared with those who did not, for both RSV-A and RSV-B subtypes,[25] indicating that baseline antibody levels influence the fold-rise following vaccination, and that participants not meeting the specified seroresponse criterion have higher circulating levels of nAbs available at the time of vaccination. It is also noted that while the point estimates of the coadministered vaccines were numerically lower than the comparator individual vaccines, the five coprimary GMR endpoints in part A and all six in part B were met; the clinical implications of this are not known in the absence of an established threshold of protection.

The GMRs for RSV, influenza, and SARS-CoV-2 induced by the coadministered versus individual vaccines were similar to those of the overall cohort when subgroups of age, sex, race, and ethnicity were evaluated, although with some differences and wider CIs. The seroresponse rates in part A were generally numerically lower in the older age groups (60–74 years and ≥75 years) than in the overall cohort, although as described

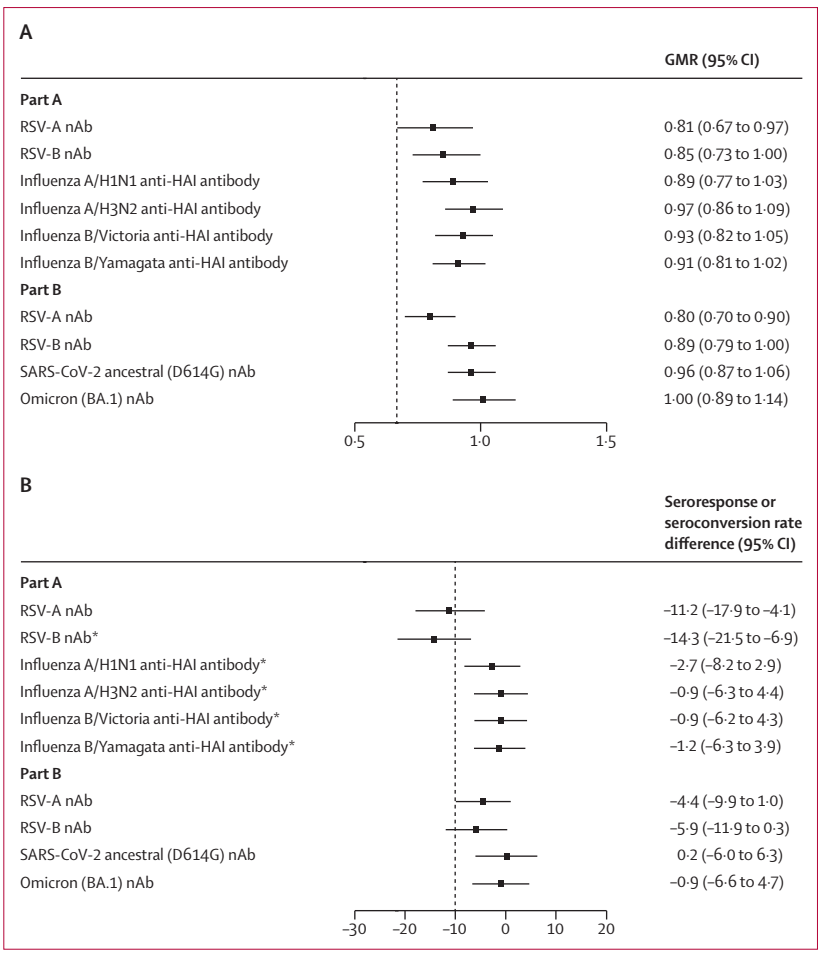

Figure 4: **GMRs of antibody responses (A) and seroresponse or seroconversion differences (B) after coadministration of mRNA-1345 with SIIV4 (part A) or mRNA-1273.214 (part B) versus individual vaccines**
Seroresponses for nAbs to RSV and SARS-CoV-2 ancestral (D614G) and omicron BA.1 were defined at the participant level as a change from below the LLOQ to equal or above 4 × LLOQ, or at least a four-fold rise if baseline titres were equal to or above the LLOQ. Seroconversion for anti-HAI titres to each of the influenza viruses was defined at the participant level as a titre equal to or greater than 1:40 if baseline titres were lower than 1:10 or a four-fold or greater rise from baseline in titres if baseline was equal to 1:10 or greater. The dotted lines represent a GMR of 0·667 (A) or a seroresponse or a seroconversion difference of −10% (B), corresponding to the non-inferiority margins. GMR=geometric mean ratio. HAI=haemagglutination inhibition. LLOQ=lower limit of quantification. nAb=neutralising antibody. RSV=respiratory syncytial virus. SIIV4=standard-dose quadrivalent inactivated influenza vaccine. *Not formally assessed for statistical non-inferiority, per the testing strategy.

previously, higher baseline levels observed in the older age groups could influence the seroresponse rate.[25] Overall, the immune responses elicited against RSV-A and RSV-B in the older age groups when mRNA-1345 was coadministered with influenza or COVID-19 vaccines were consistent with the immunogenicity and efficacy findings reported across age groups in previous studies of mRNA-1345 vaccination.[25,28,30]

The coadministered vaccine regimens were well tolerated. During the median follow-up of approximately 6–7 months from the day 1 injection, no SAEs, AESIs, study discontinuations due to adverse events, or fatal events considered related to vaccination were reported for any of the vaccine groups. In addition, there were no cases of anaphylaxis, Guillan–Barré syndrome, acute disseminated encephalomyelitis, or acute myocarditis or pericarditis. The overall safety, tolerability, and reactogenicity profiles of mRNA-1345 coadministered with SIIV4 or the mRNA-1273.214 vaccine support the favourable benefit–risk profile previously demonstrated for mRNA-1345 in older adults.[25]

Seasonal vaccination of older adults against RSV, influenza, and COVID-19 is recommended to prevent associated respiratory illnesses, which can be severe in this population.[2,8,11,23] Coadministration of RSV and influenza or COVID-19 vaccines might help to increase the uptake of these vaccines by reducing vaccination visits and so reduce the burden of severe respiratory disease in older adults. The evidence for non-inferior immune responses and acceptable safety in this trial is consistent with previous studies demonstrating non-inferiority of GMRs of immune responses elicited by pre-F RSV vaccines when coadministered with seasonal influenza vaccines compared to pre-F RSV vaccines administered alone, and adds to the evidence by showing that two mRNA vaccines can be safely coadministered without having a detrimental effect on the immune response to either vaccine, including for coadministration with COVID-19 vaccine.[31–33] Taken together, the findings of this and other studies[31,33] support a coadministration approach for these vaccines against the specified respiratory pathogens in older adults and should encourage setting of relevant policies by regulatory agencies. Future studies will need to demonstrate the efficacy and effectiveness of coadministration strategies in protecting against these respiratory pathogens. Future strategies could assess coadministration of all three vaccines together or a single, multicomponent vaccine for RSV, influenza, and SARS-CoV-2; the mRNA platform has the flexibility to evaluate a multicomponent vaccine, if the need arises.

Strengths of this study include its randomised, observer-blinded design and the fact that the majority of participants were aged 60 years or older and the study included individuals with pre-existing respiratory, endocrine, and cardiac conditions—known risk factors for severe RSV disease.[1–3,9] This study also included individuals aged 50–59 years who had risk factors for severe RSV disease (or severe respiratory disease more generally) and would potentially be eligible for RSV vaccinations in real-world settings. Together with an ongoing trial in participants aged 18–59 years (ClinicalTrials.gov NCT06067230), these data could potentially form the basis for extension of the use of RSV vaccines to other vulnerable adult populations. The immune responses observed in older age groups, another group at risk of severe RSV disease, were generally consistent with the immune responses reported in the overall study population.[20] While older age groups and individuals at risk of RSV were evaluated in our study, additional, larger studies that evaluate various population groups, including in low-income and middle-income countries, are needed.

Study limitations include a lower number of participants than anticipated in the mRNA-1345 group in part A due to an IRT randomisation error, which could have affected statistical power for endpoint assessment. While a standard-dose inactivated influenza virus vaccine was used in part A, high-dose or adjuvanted inactivated influenza virus vaccines are recommended for adults aged 65 years and older in many countries;[10] coadministration of mRNA-1345 with a high-dose inactivated influenza virus vaccine is being evaluated in a different clinical study (ClinicalTrials.gov NCT06060457). We decided to use the mRNA-1273.214 vaccine as it was approved at the time for SARS-CoV-2 vaccination by regulatory authorities; study and real-world data indicate that these findings will be applicable to other variants as updated SARS-CoV-2 variant vaccines become available.

In conclusion, these data support coadministration of the RSV mRNA-1345 vaccine with influenza SIIV4 or mRNA-1273.214 COVID-19 vaccines. Longer-term safety and immunogenicity, and durability of immune responses to mRNA-1345, are being further evaluated in this and other ongoing phase 3 studies (ClinicalTrials.gov NCT05127434 and NCT05127434).

Contributors

JG, EW, AK, RDh, CAS, SKS, LL, and HZ contributed to the design of the study. JG, DCH, AC, VR, and AKS contributed to study oversight. JG, DCH, JFC, AK, VR, and AC contributed to data collection. XW, LL, JD, and HZ conducted statistical analyses. AK was responsible for immunogenicity assays and CR, RDh, and LW were responsible for safety data and oversight. JG, XW, LL, AKS, JD, HZ, SKS, EW, RDa, JMM, and JET interpreted the data, results, or both, and JET and JG drafted the manuscript. JG, JFC, JET, and XW have directly accessed and verified the underlying data reported in the manuscript. All authors contributed to the review and editing of the manuscript and approved the final version for submission. The authors vouch for the completeness and accuracy of the data and for the fidelity of the study to the protocol. JG verifies that all authors had full access to the study data and accept responsibility to submit for publication.

Declaration of interests

JFC declares no competing interest. JG, DCH, AKS, AK, LW, RDa, XW, AC, VR, LL, JD, HZ, SKS, CAS, CR, EW, JMM, and RDh are employees of Moderna, and may hold stock or stock options in the company as part of their employment. JET is a consultant for Moderna.

Data sharing

As the trial is ongoing, access to patient-level data and supporting clinical documents with qualified external researchers will be made available upon request and subject to review after the trial completion date. A materials transferor data access agreement with the sponsor will be required to access shared data. Requests can be made to Jaya Goswami at jaya.goswami@modernatx.com.

Acknowledgments

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