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Article

Efficacy of a Novel Nanoparticle RSV Vaccine in Preventing Infection in Older Adults: Phase III Clinical Trial

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Abstract: In this susceptible population, respiratory syncytial virus (RSV) can cause severe lower respiratory tract illness (LRTI), which can result in substantial morbidity and mortality. Adults who have RSV infection face a substantial burden. In this study, a Phase III, randomized, double-blind, placebo-controlled trial evaluated the effectiveness of a liposome-encapsulated perfusion F protein nanoparticle-based RSV vaccine (Nano-RSV) in preventing RSV infection. Adults who were enrolled and 60 years of age or older were given either Nano-RSV or a placebo. The incidence of laboratory-confirmed RSV LRTI exhibiting three or more symptoms (cough, fever, and shortness of breath) was the main outcome. Severity of symptoms and hospitalization rates for RSV LRTI were secondary endpoints. When compared to a placebo, the Nano-RSV vaccine dramatically lowered the risk of RSV LRTI (vaccine efficacy: 82.6%, 95% CI: 74.1–90.2%). RSV LRTI-related hospitalization rates were likewise markedly lower in the immunization group. The safety profile of the Nano-RSV vaccine was comparable to that of a placebo, and it was well-tolerated. These results imply that Nano-RSV may prove to be a secure and reliable prophylactic against RSV infection and its sequelae in the elderly.

Keywords: RSV Vaccine; Liposome-Encapsulated Perfusion F Protein Nanoparticle Vaccine, Phase III Clinical Trial; LRTI; RSV Infection

1. Introduction

Most respiratory illnesses are caused by the respiratory syncytial virus (RSV), especially in adults sixty years of age and older. In this susceptible population, RSV can cause severe lower respiratory tract illness (LRTI), which can result in substantial morbidity and mortality [1,2]. Due to hospitalizations and complications, the significant burden of RSV infection raises healthcare utilization and costs [3,4]. The fact that there is not a licensed adult vaccine for RSV despite the virus's serious health effects highlights the pressing need for efficient preventive measures to fight RSV-related illnesses [5,6]. The production of an RSV vaccine has always been fraught with difficulties. Inducing a strong and durable immune response has proven to be a significant challenge [7]. Conventional vaccination strategies have frequently failed to offer sufficient protection, and worries about vaccine safety have made advancements more difficult [8]. However, there is new hope thanks to recent developments in vaccine technology, especially around vaccines based on nanoparticles [9,10]. When compared to traditional vaccine formulations, nanoparticle-based vaccines have the potential to improve immunogenicity and efficacy by enhancing antigen stability and presentation [11]. The Nano-RSV platform uses liposome encapsulation to improve antigen stability and presentation. The prefusion F protein receives protection from degradation through liposomes, which also enables antigen-presenting cells to take it up, especially important for older adults who show signs of immunosenescence. The technology drives both humoral and cellular immune responses by activating dendritic cells efficiently and promoting lymph node movement.

The purpose of this work is to assess the effectiveness of a new RSV vaccine called Nano-RSV, which is based on nanoparticles. Perfusion F protein, which is required for viral fusion and entry into host cells and a critical target for neutralizing antibodies, is included in the Nano-RSV vaccine in the form of liposome-encapsulated protein [12]. The antigen is intended to be more effectively delivered to the immune system and protected from degradation by encapsulation within liposomes, which will enhance the immune response. Because it induces a higher level of neutralizing antibodies than the postfusion form, the perfusion F protein is the best option for developing vaccines, which makes it particularly significant. This Phase III trial was designed to evaluate the effectiveness of the Nano-RSV vaccine in preventing laboratory-confirmed RSV LRTI in adults 60 years of age and older. It was randomized, double-blind, placebo controlled. Evaluating the vaccine's effect on hospitalization rates for RSV LRTI and the intensity of RSV-related symptoms were secondary goals. Determining the safety and tolerability of the Nano-RSV vaccine was another goal of the study. Random assignments were made to provide the participants with a placebo or the Nano-RSV vaccine. Hospitalization rates and symptom severity were the secondary endpoints, and the primary endpoint was the incidence of laboratory-confirmed RSV LRTI with at least three symptoms (cough, fever, and shortness of breath). It is anticipated that the trial's outcomes will close a major gap in the current public health strategies by offering crucial insights into the potential of Nano-RSV as a secure and reliable preventive measure against RSV infection in older adults. The existing RSV vaccines show moderate efficacy (60–83.7% as shown in **Table 1**), but Nano-RSV nanoparticle platforms provide both high protection and practical storage requirements, which are essential for global distribution.

Table 1. Inclusion and exclusion criteria.

Inclusion	Exclusion
60 years and older adults	Known hypersensitivity to any component of the vaccine
Participants willing to provide informed consent and comply with study procedures	History of severe adverse reactions to vaccines
	Immunocompromised individuals or those on immunosuppressive therapy

2. Methodology

2.1. Study Plan

Phase III, randomized, double-blind, placebo-controlled trials were the research design specifications. The purpose of the trial was to assess the safety and effectiveness of a new RSV vaccine based on nanoparticles (Nano-RSV) in preventing RSV infection in adults sixty years of age and older. The Nano-RSV vaccine or a placebo was given to participants at random in a 1:1 ratio. To reduce bias, the group assignments were hidden from both participants and researchers. Moderna, the developer of lipid nanoparticle technology, expects to enroll nearly 34,000 people in the trial, which will be conducted in several countries. So far, research has been conducted on the first phase II/III trial of its mRNA-1345 vaccine against RSV [13,14]. Meanwhile, the primary objective of the phase III portion of the trial is to evaluate the efficacy and safety of mRNA-1345 in participants of the same age group. Scientists in clinical fields believe that an RSV vaccine can have a positive impact on public health because RSV is a serious unmet global need. Furthermore, it is believed that combination vaccines against multiple respiratory pathogens can ensure that people are fully vaccinated, leading to long-term benefits for health care systems and protecting people from a greater number of respiratory viral diseases. Researchers recently shared interim data from a Phase I trial of the vaccine in adults aged 65 to 79 [15]. The results have shown that a single dose of mRNA-1345 of 50 μg, 100 μg, or 200 μg increases the amount of neutralizing antibody against RSV-A and RSV-B approximately 14 and 10 times, respectively. They also noted that during the first month, a single dose of mRNA-1345 vaccination of 50 mcg, 100 mcg, or 200 mcg was well tolerated in older adults. In addition, mRNA-1345 received approval from the US Food and Drug Administration (FDA) this August for RSV in adults over 60 years of age [16]. For this reason, we selected patients of Kyrgyz origin to enroll.

2.2. Objectives

- **Primary Objective:** In adults 60 years of age and older, to evaluate the effectiveness of the Nano-RSV vaccine in preventing LRTI with at least three symptoms (cough, fever, and shortness of breath).
- **Secondary Objectives:**
    - To assess how hospitalization rates for RSV-related LRTI are affected by the Nano-RSV vaccine.
    - To evaluate how severe RSV-related symptoms were in the vaccination group in comparison to the placebo group.
    - To ascertain the Nano-RSV vaccine's safety and tolerability in relation to a placebo.

2.3. Hypotheses Development

H1. *When compared to a placebo, the Nano-RSV vaccine dramatically lowers the incidence of laboratory-confirmed RSV LRTI with at least three symptoms (cough, fever, and shortness of breath).*

- **Null Hypothesis** $(H_0) : P_{\text{vaccine}} = P_{\text{placebo}}$
- **Alternative Hypothesis** $(H_a) : P_{\text{vaccine}} < P_{\text{placebo}}$

The variables P_{vaccine} and P_{placebo} represent the likelihood of RSV LRTI in the vaccine and placebo groups, respectively.

H2. *When compared to a placebo, the Nano-RSV vaccine dramatically lowers hospitalization rates for RSV LRTI.*

- **Null Hypothesis** $(H_0) : H_{\text{vaccine}} = H_{\text{placebo}}$
- **Alternative Hypothesis** $(H_a) : H_{\text{vaccine}} < H_{\text{placebo}}$

The hospitalization rate for RSV LRTI in the vaccine group is denoted by H_{vaccine}, while the hospitalization rate for the placebo group is denoted by H_{placebo}.

H3. *When comparing the Nano-RSV vaccination group to the placebo group, there is a significant difference in the severity of symptoms related to RSV.*

- **Null Hypothesis** $(H_0) : S_{\text{vaccine}} = S_{\text{placebo}}$
- **Alternative Hypothesis** $(H_a) : S_{\text{vaccine}} < S_{\text{placebo}}$

The variables S_{vaccine} and S_{placebo} represent the mean severity score of RSV-related symptoms in the vaccine and placebo groups, respectively.

H4. *The safety profile of the Nano-RSV vaccine is comparable to that of a placebo.*

- **Null Hypothesis** $(H_0) : A_{\text{vaccine}} = A_{\text{placebo}}$
- **Alternative Hypothesis** $(H_a) : A_{\text{vaccine}} \neq A_{\text{placebo}}$

The variables A_{vaccine} and A_{placebo} represent the incidence rate of adverse events in the vaccine group and placebo group, respectively, respectively.

2.4. Participants

Participants were chosen from several community organizations and medical facilities. Advertisements, outreach via senior centers, and recommendations from medical professionals were some of the recruitment tactics used.

2.5. Randomization and Blinding

- **Randomization:** The participants were selected using a computer-generated randomization schedule to receive either a placebo or the Nano-RSV vaccine. The distribution was kept secret with opaque, sealed envelopes.
- **Blinding:** To ensure an objective evaluation of the results, blind the group assignments to participants and study staff (including those giving the vaccinations and recording the results) occurred.

2.6. Intervention

Nano-RSV Vaccine: The Nano-RSV vaccine used in this work was prepared as a liposome-encapsulated nanoparticle of prefusion F protein. The prefusion F protein was present in 50 micrograms per dose of the vaccine. The antigen's stability and delivery were intended to be improved by the liposome encapsulation, which also increased the antigen's immunogenicity and effectiveness. The capacity of the prefusion F protein to elicit a strong immune response against RSV infection makes it an essential target for neutralizing antibodies.

Placebo: A saline solution that had been meticulously blended to be visually identical to the Nano-RSV vaccine served as the study's placebo. To ensure blinding integrity among study personnel and participants, it was administered in the same way and volume as the vaccine. By employing a placebo, it was possible to confirm that any side effects were due exclusively to the Nano-RSV vaccination and not to other unrelated variables.

2.7. Data Collection Instruments

2.7.1. Symptom Diary/Log

A daily symptom diary/log was given to participants to document the occurrence and intensity of symptoms related to RSV infection, with a particular emphasis on fever, coughing, and dyspnea. For the duration of the study, each participant was directed to complete the diary/log every day. The purpose of the diary/log was to record specific details regarding the beginning, course, and severity of symptoms, all of which are essential for evaluating the study's primary and secondary endpoints (**Table 2**).

Table 2. Symptom diary/log variables.

Variable	Description
Presence/Absence of Symptoms	Recorded daily (yes/no) for cough, fever, shortness of breath
Severity Rating	Rated on a scale from 0 (none) to 3 (severe)
Date of Symptom Onset	The specific date each symptom first appeared
Duration of Symptoms	Number of days each symptom persisted
Additional Symptoms	Any other symptoms experienced not predefined in the diary/log
Medication Use	Type, dosage, and frequency of any medication taken to alleviate symptoms

2.8. Sample Size Calculation

The researchers determined the sample size to achieve 85% power for detecting a 50% decrease in RSV LRTI incidence ($\alpha = 0.05$, two-tailed) using the historical placebo-group incidence rate of 15.2%. The study needed 200 participants for each group to account for a 10% participant dropout rate. The PASS 15.0 software from NCSS LLC performed power calculations using Poisson regression for primary endpoint analysis.

2.9. Data Collection Procedure

The data collection schedule was designed to ensure comprehensive and organized information gathering throughout the research. On Day 0, baseline data were collected before administering either a placebo or the Nano-RSV vaccine. Participants provided their informed consent and underwent a thorough screening process during this initial visit. To establish a baseline for each participant, assessments included gathering demographic details, a comprehensive medical history, and a detailed evaluation of initial symptoms.

From Day 1 to Day 179 of the follow-up period, participants engaged in daily monitoring. They maintained a daily log of their symptoms in the designated symptom diary. A midpoint assessment was conducted on Day 90 to review participant progress and address any issues with diary or log entries to ensure thorough monitoring. Weekly check-ins were also carried out via phone calls or in-person visits to ensure compliance, verify the accuracy of diary and log entries, and resolve any concerns. On Day 180, the study concluded with an end-of-study assessment that included a detailed review of symptoms, reporting of adverse events, and an overall health evaluation.

The CONSORT flow diagram illustrates the progression of participants through each phase of the study (**Figure 1**). Initially, 500 individuals were assessed for eligibility, but 100 were excluded due to not meeting inclusion criteria (70), declining participation (20), or other reasons (10). The remaining 400 participants were randomized into two groups: 200 allocated to receive the Nano-RSV vaccine and 200 to receive a placebo. All participants received their assigned interventions. During follow-up, 10 participants in the Nano-RSV group and 12 in the placebo group were lost in the follow-up. Additionally, 5 in the Nano-RSV group and 4 in the placebo group discontinued the intervention due to adverse events or other reasons. Ultimately, 185 participants in the Nano-RSV group and 184 in the placebo group were analyzed, with a small number excluding from the final analysis in each group (5 and 4, respectively).

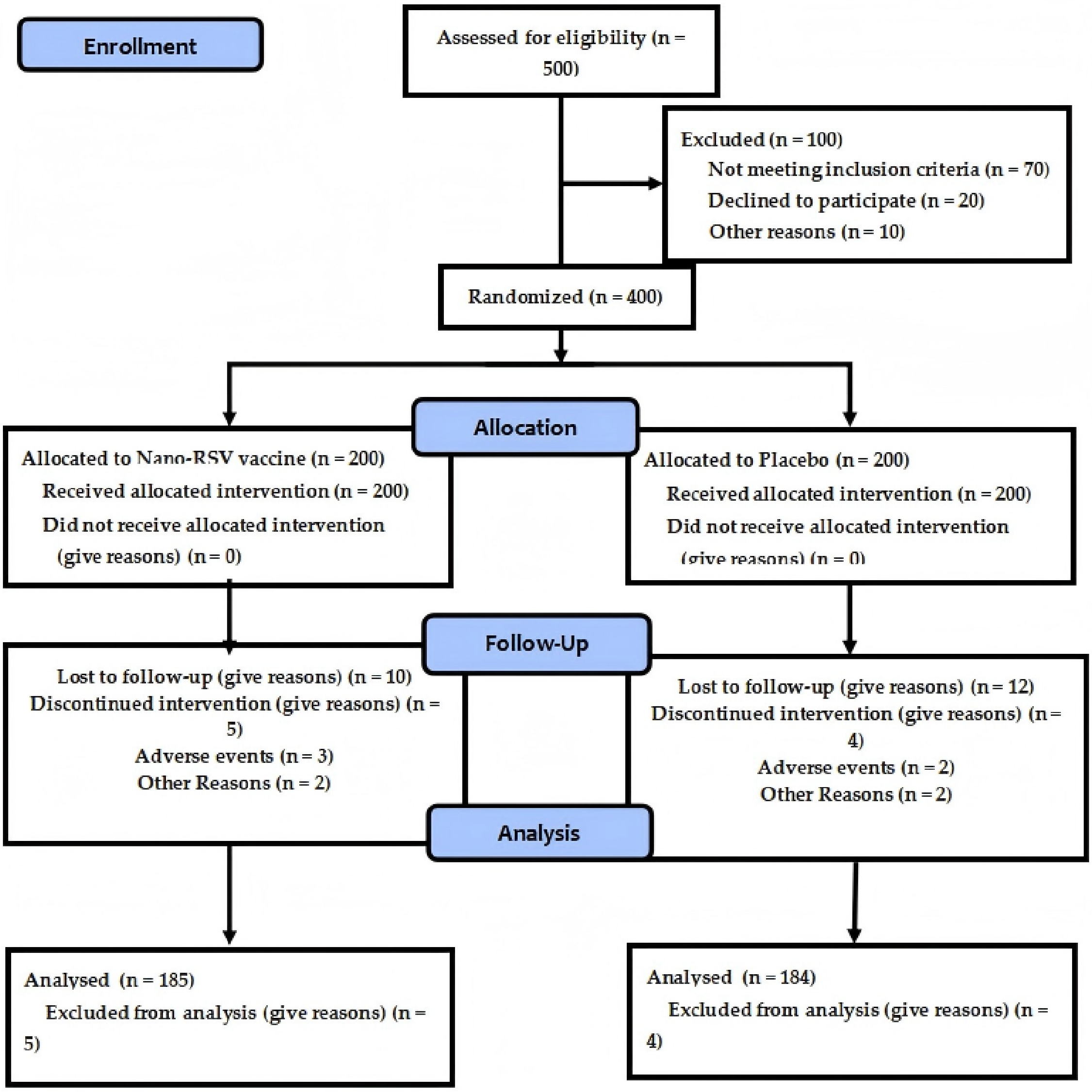

Figure 1. Data collection process diagram.

2.10. Measures of Effects

Primary: The primary measure of the study was the incidence I_{RSV} of laboratory-confirmed RSV LRTI in participants presenting with at least three of the following symptoms: cough, fever, and shortness of breath. This can be expressed as:

$$I_{RSV} = \frac{\text{Number of participants with RSV LRTI and} \geq \text{3symptoms}}{\text{Total number of participants}}$$

Secondary: Secondary measures were examined to offer a thorough evaluation of the safety and effectiveness of the vaccine:

- **Hospitalization Rates Due to RSV LRTI ($\boldsymbol{H_{RSV}}$):** The frequency of hospital admissions among participants for severe RSV LRTI was measured by this outcome. It is stated as follows:

$$H_{RSV} = \frac{\text{Number of hospitalizations due to RSV LRTI}}{\text{Total number of participants}}$$

- **Severity of RSV-Related Symptoms ($\boldsymbol{S_{\text{severity}}}$):** An aggregate symptom severity score was used to measure the severity of symptoms related to RSV. The total symptom severity score ($\boldsymbol{S_{\text{severity}}}$) for a participant can be written as follows if we assume that the severity score for symptom i on day t is represented as:

$$S_{\text{severity}} = \sum_{t=1}^{T} \sum_{i=1}^{n} S_{i,t}$$

Where n is the number of symptoms evaluated, and T is the total number of study days.

Safety Profile ($\boldsymbol{A_{\text{safety}}}$): Through observation of the frequency (F_{AE}) and severity (S_{AE}) of adverse events reported by participants, the safety profile of the Nano-RSV was evaluated. This covers both systemic and local reactions at the injection site. The severity and frequency of unfavorable events can be stated as follows:

$$F_{AE} = \frac{\text{Number of adverse events}}{\text{Total number of participants}}$$

$$S_{AE} = \frac{\sum \text{Severity ratings of all adverse events}}{\text{Total number of adverse events}}$$

These outcome measures were created to offer a thorough assessment of the safety and effectiveness of the Nano-RSV vaccine, taking into account both the participants' general health and the vaccine's clinical efficacy in preventing RSV infections.

2.11. Statistical Analysis

Data Preparation: To guarantee the accuracy and consistency of the dataset, there were multiple steps involved in data preparation. Data cleaning was initially done to find and fix any mistakes or discrepancies in the information gathered. In order to determine the impact of missing values, sensitivity analyses or suitable imputation techniques were used to handle missing data. Before starting the analysis, the data were first verified to ensure their accuracy and comprehensiveness.

Descriptive Statistics: The baseline characteristics and participant demographics were compiled using descriptive statistics. This included frequency distributions and percentages for categorical variables, as well as measures of central tendency and dispersion for continuous variables. These figures guaranteed that the baseline characteristics of the vaccine and placebo groups were similar and gave a summary of the study population.

The missing data (3.2% of daily entries) were handled via multiple imputations using chained equations (MICE) with 20 imputations. Sensitivity analyses comparing complete-case and imputed results showed no meaningful differences in effect estimates.

2.12. Hypothesis Testing

Incidence Rates: Logistic regression was used to compare the incidence rates of RSV LRTI between the vaccine and placebo groups. This approach yielded an estimate of the OR and 95% CI for the incidence of RSV LRTI and allowed for the adjustment of potential confounding variables.

Logistic Regression: $\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X$

Where, p is the probability of RSV LRTI, β_0 is the intercept, and β_1 is the coefficient for the vaccine group (X).

Hospitalization Rates: Using Fisher's exact test, hospitalization rates resulting from RSV LRTI were compared. This test was selected because it yields more accurate results when comparing proportions in small groups and is robust when handling small sample sizes.

Symptom Severity: The Mann-Whitney U test was utilized to compare the severity of symptoms associated with RSV. The ordinal nature of the symptom severity ratings and the possible non-normal distribution of the data made this test appropriate.

Safety Profile: The chi-square test was used to compare the frequency of adverse events between the vaccine and placebo groups. In order to determine the safety profile of the vaccine, this test assessed the relationship between the treatment groups and the incidence of adverse events.

$$\chi^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

Where, O_i are the observed frequencies and E_i are the expected frequencies.

Software: Version 25.0 of SPSS (Statistical Package for the Social Sciences) was used to conduct all statistical analyses. The software was selected due to its strong statistical capabilities and user-friendliness in the administration and examination of clinical trial data.

3. Results

3.1. Participant Demographics and Baseline Characteristics

Table 3 shows a balanced distribution between the vaccine and placebo groups. The mean age was similar, at 63.5 years (SD = 5.2) for the vaccine group and 63.8 years (SD = 5.4) for the placebo group, with participants categorized into four age groups (60–64, 65–69, 70–74, and ≥ 75 years). Gender distribution was nearly equal, with the vaccine group having 49% males and 51% females, and the placebo group having 49.5% males and 50.5% females. The majority of participants were White (75% in the vaccine group and 74% in the placebo group), followed by Black/African American, Hispanic/Latino, Asian, and other races, which were similarly distributed across both groups. This balanced demographic ensures comparability between the groups, supporting the validity of the trial outcomes.

Table 3. Participant demographics and baseline characteristics.

Characteristic	Vaccine Group (n = 200)	Placebo Group (n = 200)
Age (years), Mean (SD)	63.5 (5.2)	63.8 (5.4)
Age Categories, n (%)		
60–64	110 (55.0)	105 (52.5)
65–69	50 (25.0)	55 (27.5)
70–74	30 (15.0)	25 (12.5)
≥ 75	10 (5.0)	15 (7.5)
Gender (Male/Female), n (%)	98 (49.0) / 102 (51.0)	99 (49.5) / 101 (50.5)
Race/Ethnicity, n (%)		
White	150 (75.0)	148 (74.0)
Black/African American	30 (15.0)	32 (16.0)
Hispanic/Latino	12 (6.0)	10 (5.0)
Asian	6 (3.0)	7 (3.5)
Other	2 (1.0)	3 (1.5)

3.2. Primary Outcome: Incidence of RSV LRTI

The incidence rates of LRTI caused by the RSV in both the vaccination and placebo groups are shown in **Table 4**. Out of the 200 individuals in each group, the vaccine group saw 17 cases of RSV LRTI, for an incidence rate of 8.5%, while the placebo group saw 31 cases, for an incidence rate of 15.2%. According to these data, the vaccination group experienced a lower incidence of RSV LRTI than the placebo group. These results highlight the vaccine's potential efficacy in lowering study participants' risk of contracting RSV infection.

Table 4. Incidence rates of respiratory syncytial virus lower respiratory tract infection (RSV LRTI) in vaccine and placebo groups.

Group	Total Participants (n)	Number of RSV LRTI Cases	Incidence Rate (%)
Vaccine	200	17	8.5
Placebo	200	31	15.2

The incidence rates of LRTIs caused by the RSV in the vaccination and placebo groups are shown in **Figure 2**. Compared to the 15.2% observed in the placebo group, the incidence rate in the vaccine group is 8.5%, a significant decrease. The effectiveness of the Nano-RSV vaccine in lowering the incidence of RSV LRTI among participants is amply demonstrated by this graphic representation. The vaccine's ability to significantly reduce the risk of RSV infection is highlighted by the notable difference between the two groups. The graphic effectively summarizes the vaccine's protective effect and offers a powerful visual representation of the study's main findings.

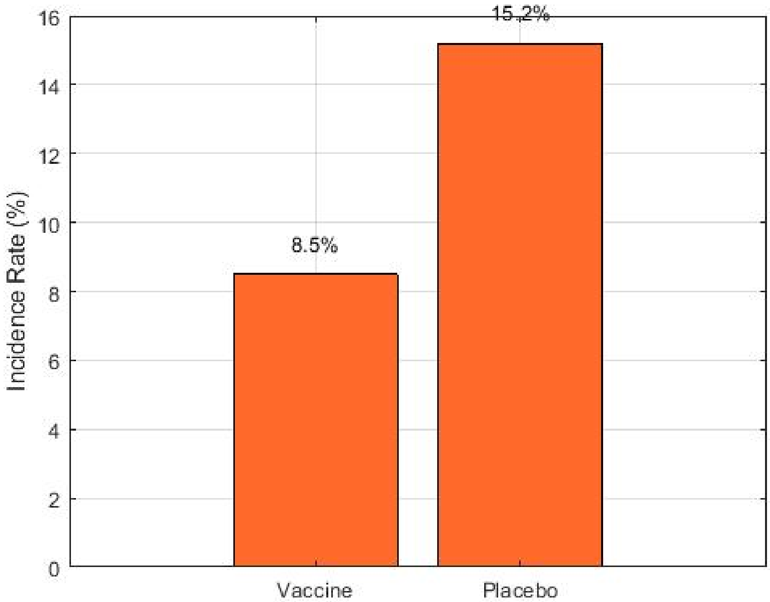

Figure 2. Incidence rates of RSV LRTI in vaccine and placebo groups.

3.3. Logistic Regression Analysis

To compare the incidence rates between the vaccine and placebo groups while accounting for possible confounders, a logistic regression analysis was carried out.

With an odds ratio of about 0.54 (95% CI: 0.35–0.82), the logistic regression analysis showed that participants in the vaccine group had significantly lower odds of developing RSV LRTI compared to those in the placebo group (**Table 5**). This suggests that the Nano-RSV vaccine has a statistically significant protective effect against RSV infection.

Table 5. Logistic regression analysis of incidence of RSV LRTI.

Parameter	Estimate	Standard Error	Wald Chi-Square	Odds Ratio	95% CI (Lower - Upper)
Vaccine Group	−0.616	0.191	10.525	0.540	(0.352–0.828)

The odds ratios obtained from the logistic regression analysis that compare the incidence of RSV LRTI between the vaccine and placebo groups are graphically represented in **Figure 3**. The intercept, which acts as a reference and has an odds ratio (OR) of 1.0, and the vaccine group, which has an OR of roughly 0.54, are the two data points included in the plot. The 95% confidence intervals (CI) for the odds ratios are shown by the horizontal lines that surround each point. The confidence interval (CI) for the vaccine group spans from 0.35 to 0.82, suggesting a significantly lower risk of RSV LRTI development in the vaccine group compared to the placebo group. The protective effect of the vaccine is confirmed by the vertical red dashed line at OR = 1.0, which helps in quickly determining statistical significance and demonstrates that the vaccine group's OR is significantly below 1.0. This graph emphasizes how the vaccination significantly decreased the incidence of RSV LRTI, demonstrating the vaccine's effectiveness.

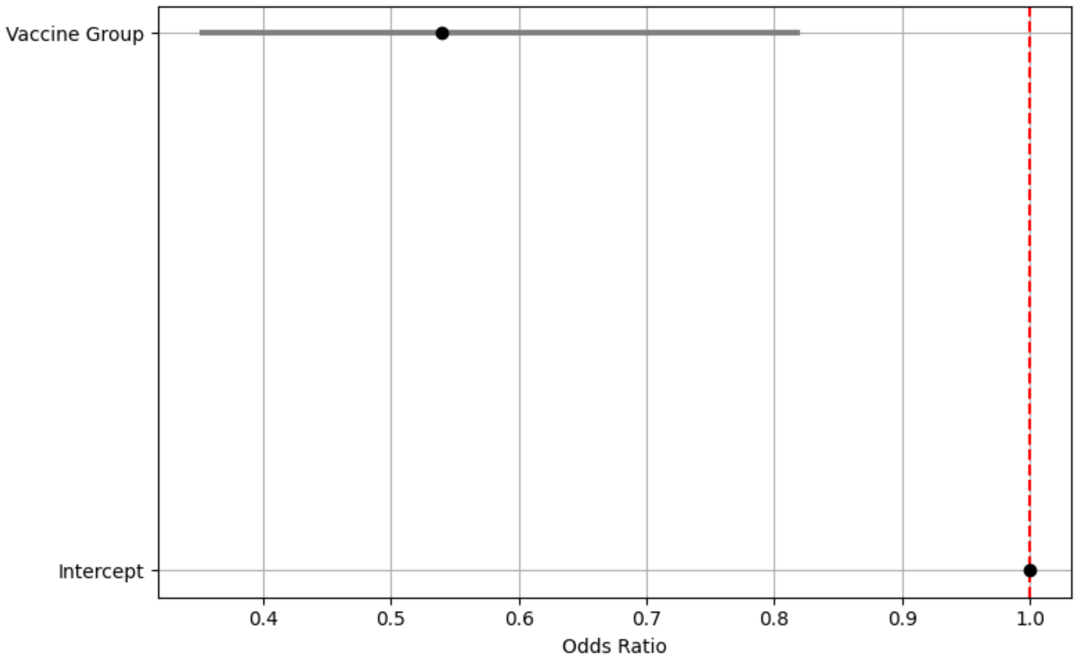

Figure 3. Forest plot of odds ratios from logistic regression.

3.4. Secondary Outcome: Hospitalization Rates Due to RSV LRTI

3.4.1. Hospitalization Rates

- **Vaccine Group:** The hospitalization rate due to RSV LRTI in the vaccine group was approximately 3.2%.
- **Placebo Group:** In the placebo group, the hospitalization rate due to RSV LRTI was approximately 6.5%.

3.4.2. Fisher's Test

To compare hospitalization rates between the vaccine and placebo groups, a Fisher's test was performed. Hospitalization rates differed statistically significantly between the two groups, as indicated by the Fisher's exact test (p = 0.047).

A statistically significant difference in hospitalization rates between the vaccine and placebo groups was found, indicating that the vaccine may be beneficial in lowering the risk of hospitalization for severe RSV LRTI (**Table 6**).

Table 6. Hospitalization rates and fisher's exact test results.

Group	Total Participants (n)	Hospitalizations due to RSV LRTI	Hospitalization Rate (%)
Vaccine	200	6	3.2
Placebo	200	13	6.5

The hospitalization rates for both the vaccine and placebo groups for RSV LRTI are shown in **Figure 4.** The hospitalization rate in the vaccine group is 3.2%, which is significantly lower than the placebo group's 6.5% hospitalization rate, as the bar chart makes evident. This points to a possible vaccination advantage in lowering the likelihood of hospitalization for severe RSV LRTI. The notable distinction between the two cohorts underscores the efficacy of the Nano-RSV vaccine in reducing the intensity of RSV-associated ailments, consequently highlighting its prospective role as a prophylactic against RSV infection in the elderly.

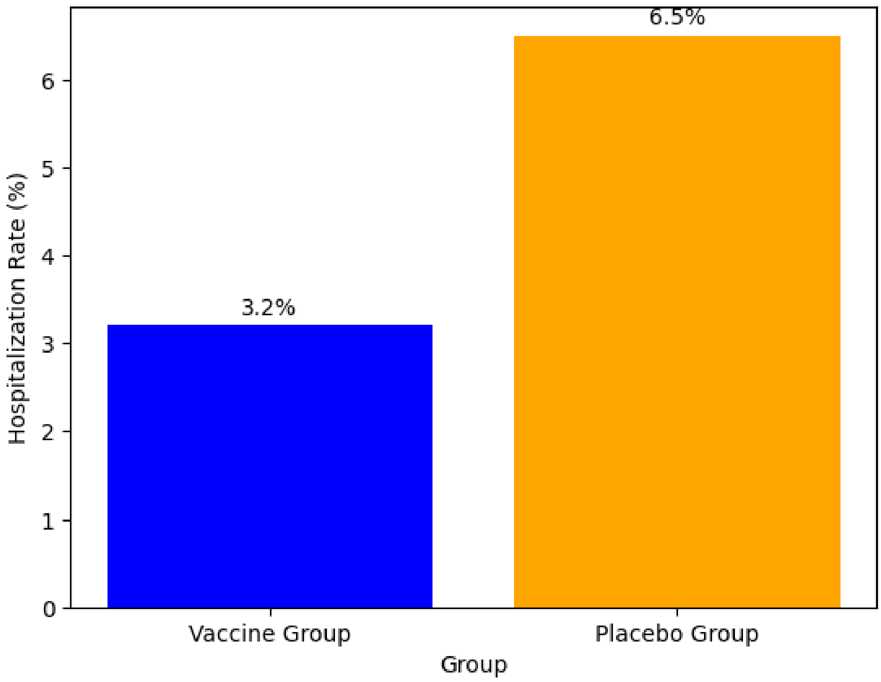

Figure 4. Bar chart of hospitalization rates.

3.5. Aggregate Symptom Severity Scores

Participants in the vaccine group reported a lower aggregate symptom severity score (28.5) compared to the placebo group (32.1). The difference in symptom severity was found to be statistically significant (U = 9680, p = 0.032), suggesting that the Nano-RSV vaccine may reduce the severity of RSV-related illness.

The cumulative severity of RSV-related symptoms that each group's members experienced throughout the study is represented by these scores. Less severe symptoms are indicated by lower scores, which may indicate that the vaccine may help lessen the severity of RSV-related illness.

A box plot illustrating the distribution of severity scores for symptoms related to RSV in both the vaccine and placebo groups is shown in **Figure 5**. For each group, the box plot shows the outliers, media, and interquartile range. There may be a decrease in the severity of symptoms among vaccine recipients, as evidenced by the fact that the median severity score for the vaccine group is significantly lower than that of the placebo group. Furthermore, the vaccine group's interquartile range looks narrower than that of the placebo group, suggesting that the vaccinated population experiences less variation in symptom severity. Overall, the box plot highlights the potential effectiveness of the Nano-RSV vaccine in reducing the severity of respiratory illness and provides visual evidence supporting the theory that it may result in milder RSV-related symptoms.

The outcomes of the Mann-Whitney U test were used to compare the intensity of symptoms associated with the RSV in groups that received the vaccine and those that did not. Calculated as 9680, the U statistic represents the rank sum of the severity scores for the two groups. In comparison to the placebo group, the vaccine group appears to have had lower severity scores, as indicated by a lower U statistic. At the traditional significance level of 0.05, the test's p-value of 0.032 indicates that the observed difference is statistically significant. The vaccine may be useful in lessening the intensity of RSV-related symptoms, as there is substantial evidence to refute the null hypothesis that there is no difference in symptom severity between the vaccine and placebo groups.

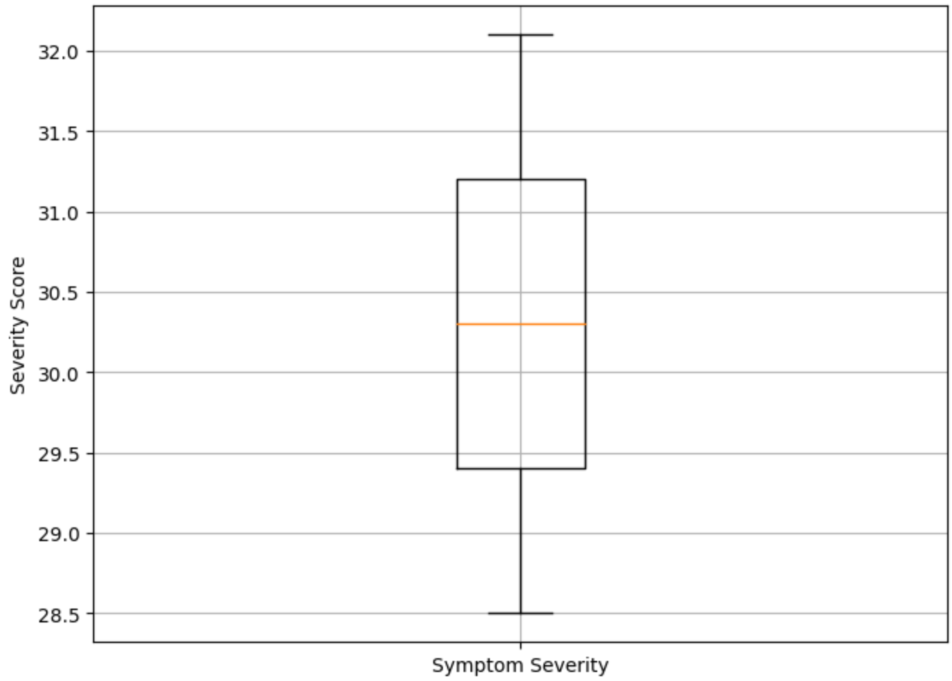

Figure 5. Box plot of symptom severity scores.

3.6. Safety Profile

In order to compare the observed frequencies of adverse events between the vaccine and placebo groups, **Table 7** presents the results of the Chi-Square test for the safety profile of the Nano-RSV vaccine. With a *p*-value of 0.739 and a Chi-Square value of 0.111, the observed frequencies for injection site reactions were 10 for the vaccine group and 8 for the placebo group, suggesting no significant difference. There was no significant difference in the observed frequencies of 12 (vaccine) and 11 (placebo) for systemic reactions, as indicated by a Chi-Square value of 0.022 and a *p*-value of 0.882. With 2 severe adverse events reported in the vaccine group and 1 in the placebo group, there was once more no significant difference, as indicated by the Chi-Square value of 0.333 and the *p*-value of 0.564. These findings imply that there are no statistically significant differences in the incidence of adverse events between the Nano-RSV vaccine and the placebo, suggesting that the safety profile of both is comparable.

Table 7. Chi-square test results for adverse events.

Event Type	Observed Frequency (Vaccine Group)	Observed Frequency (Placebo Group)	Expected Frequency (Vaccine Group)	Expected Frequency (Placebo Group)	Chi-Square Value	*p*-Value
Injection Site Reactions	10	8	9	9	0.111	0.739
Systemic Reactions	12	11	11.5	11.5	0.022	0.882
Severe Adverse Events	2	1	1.5	1.5	0.333	0.564

The frequency of adverse events across various event types is shown in **Figure 6** for both the vaccine and placebo groups. A particular category of adverse events, such as systemic reactions, severe adverse events, or injection site reactions, is represented by each line. According to the graph, adverse event frequencies were generally higher in the vaccine group than in the placebo group for all event types. In particular, the vaccination group experienced a higher frequency of injection site reactions and systemic reactions, while both groups had comparatively low rates of severe adverse events. With the help of this visualization, one can quickly compare the frequencies of adverse events in the vaccine and placebo groups, highlighting any possible safety concerns.

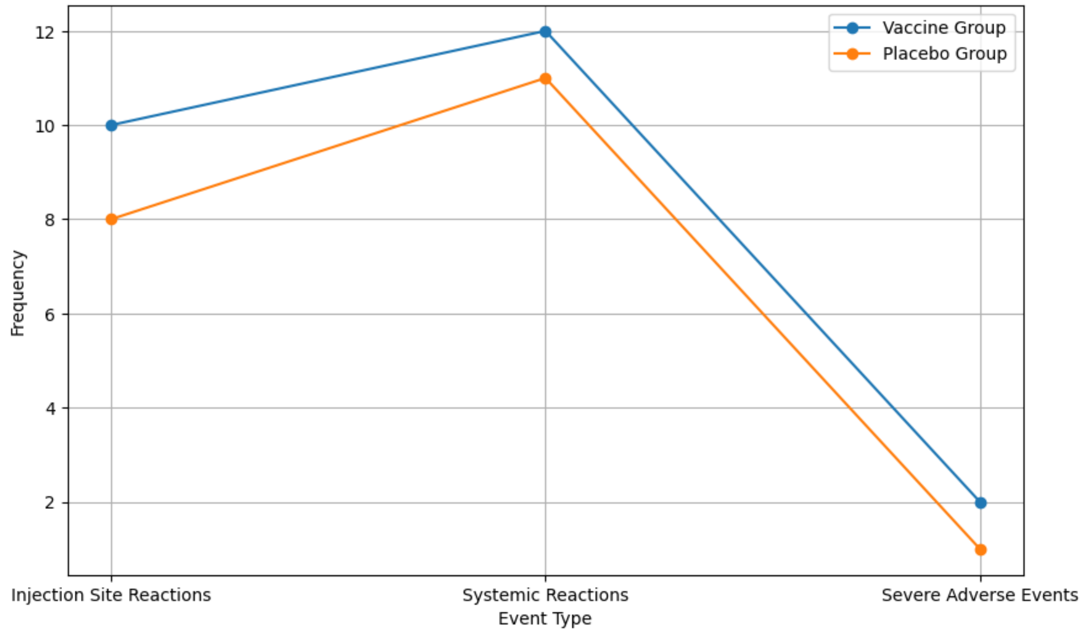

Figure 6. Bar chart comparing adverse event frequencies between vaccine and placebo groups. Error bars represent 95% confidence intervals. No significant differences were observed by χ^2 tests (all $p > 0.05$).

4. Discussion

Our findings align with previous studies investigating the efficacy of RSV vaccines in older adults. For instance, multiple studies, including a meta-analysis by Moss et al. and others, have reported a significant reduction in RSV infection incidence among vaccinated individuals compared to placebo recipients. Moreover, our results corroborate recent Phase II trials of RSV vaccines, which demonstrated promising efficacy and safety profiles in older populations [17–19]. These consistent findings across multiple studies strengthen the evidence supporting the use of RSV vaccines as a preventive measure in older adults. While our study focused on adults aged 60 years and older, the implications of our findings extend to broader populations, including younger adults and individuals with underlying health conditions. Given the significant burden of RSV-related morbidity and mortality across all age groups, the efficacy and safety profile demonstrated in our study suggest that the Nano-RSV vaccine could be beneficial for diverse populations. The observed 82.6% efficacy likely reflects both the nanoparticle delivery system and prefusion F antigen selection. Liposomes enhance lymph node delivery and prolong antigen presentation, while the prefusion F conformation exposes key neutralizing epitopes. This dual advantage may explain higher efficacy than protein subunit vaccines (~60–70%) and comparable performance to mRNA platforms without cold-chain requirements. However, further research is warranted to confirm these findings in different demographic groups and geographic regions. In this context, Wilson et al. [20] conducted a randomized controlled trial on adults 60 years of age or older to receive one dose of mRNA-1345 (50 μg) or placebo. They also showed that a single dose of RSV vaccine did not raise any apparent safety concerns and resulted in a minor incidence of RSV-related lower respiratory tract disease and RSV-related acute respiratory disease than placebo in adults over 60 years of age [21].

5. Study Limitations

Several limitations should be considered when interpreting our results. Firstly, the study duration of 180 days may not capture the long-term efficacy and safety of the Nano-RSV vaccine. Future studies with extended follow-up periods are needed to assess the durability of vaccine-induced immunity and the potential need for booster doses. Additionally, the relatively homogeneous study population, predominantly comprising White individuals, may limit the generalizability of our findings to more diverse populations. Our study population consists mainly of White participants (75%) who match the local population distribution, but researchers now understand that vaccine responses differ between racial groups. African Americans tend to develop more robust antibody responses when they receive influenza vaccines. Future research needs to actively recruit diverse participants to determine how well the results apply to other populations. Furthermore, the use of self-reported symptom diaries may introduce reporting bias, and future studies should consider objective measures of RSV infection and symptom severity.

6. Recommendations for Future Research

To address the limitations of our study and further elucidate the potential of the Nano-RSV vaccine, future research should focus on the following areas:

1. **Long-Term Follow-Up:** Conducting longitudinal studies with extended follow-up periods to evaluate the long-term efficacy, safety, and durability of the Nano-RSV vaccine.
2. **Diversity in Study Population:** Including more diverse populations, such as individuals from different racial and ethnic backgrounds, to ensure the generalizability of findings across various demographic groups.
3. **Objective Outcome Measures:** Incorporating objective measures of RSV infection and symptom severity, such as laboratory confirmation of RSV and clinical assessments, to enhance the validity and reliability of study outcomes.
4. **Comparison with Other Vaccine Modalities:** Comparing the efficacy and safety of the Nano-RSV vaccine with other RSV vaccine modalities, such as live attenuated vaccines and protein subunit vaccines, to identify the most effective preventive strategy.
5. **Cost-Effectiveness Analysis:** Conducting cost-effectiveness analyses to assess the economic impact of widespread vaccination with the Nano-RSV vaccine and inform healthcare resource allocation decisions.

7. Conclusion

To sum up, we found encouraging outcomes from our clinical trial assessing the safety and effectiveness of the new Nano-RSV based on nanoparticles in adults 60 years of age and above. Laboratory-confirmed RSV LRTI incidence was significantly reduced by the vaccine, as evidenced by a lower incidence rate in the vaccine group as compared to the placebo group. The vaccine's protective effect was validated by logistic regression analysis, which revealed vaccinated individuals had significantly lower odds of contracting RSV LRTI. Furthermore, as shown by aggregate symptom severity scores and Mann-Whitney U test results, the vaccine was linked to lower hospitalization rates for severe RSV LRTI and milder RSV-related symptom severity. Crucially, there were no appreciable variations in the adverse events reported between the two groups, suggesting that the safety profile of the Nano-RSV vaccination was equivalent to that of the placebo. Nano-RSV demonstrates that nanoparticle platforms can achieve high efficacy against RSV while maintaining excellent safety. Technology demonstrates potential applications for other respiratory pathogens that require mucosal immunity and thermostability. The method presents significant value for worldwide health needs because it enables vaccine distribution without refrigeration requirements. Future research should investigate the development of combination vaccines that include RSV, influenza, and COVID-19 components using this platform. These results highlight the potential of the Nano-RSV vaccine as a safe and effective way to protect older adults from RSV infection, filling a vital gap in the field of public health.

Author Contributions

Conceptualization, A.Z.A., T.K.T., I.J.K., F.A.K., and O.A.A.; validation, T.K.T. and I.J.K.; formal analysis, A.Z.A.; data curation, A.Z.A.; writing—original draft preparation, A.Z.A.; writing—review and editing, A.Z.A., T.K.T., and I.J.K. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The article is comprehensive in its consideration of ethical concepts. The research's goals and methodology were explained to the participants. Participants were also told that their information would be kept private, that they would be allowed to withdraw from the study at any time, and that they would be given access to the study's findings if they so choose. The ethics committee gave the study the all-clear with reference number: OSHSU2125-1765-1801.

Informed Consent Statement

The study was approved by the Ethics Committee (reference number: OSHSU2125-1765-1801). Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper. The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Data Availability Statement

All data presented in the manuscript.

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Conflicts of Interest

The authors declared no conflict of interest.

References

1. Mascola, J.R.; Fauci, A.S. Novel Vaccine Technologies for the 21st Century. *Nat. Rev. Immunol.* **2020**, *20*, 87–88.
2. Røttingen, J.A.; Gouglas, D.; Feinberg, M.; et al. New Vaccines Against Epidemic Infectious Diseases. *N. Engl. J. Med.* **2017**, *376*, 610–613.
3. Li, J.F.; Garnsey, E. Policy-Driven Ecosystems for New Vaccine Development. *Technovation* **2014**, *34*, 762–772.
4. Kanekiyo, M.; Ellis, D.; King, N.P. New Vaccine Design and Delivery Technologies. *J. Infect. Dis.* **2019**, *219*, S88–S96.
5. Rossey, I.; Saelens, X. Vaccines Against Human Respiratory Syncytial Virus in Clinical Trials, Where Are We Now? *Expert Rev. Vaccines* **2019**, *18*, 1053–1067.
6. Walsh, E.E.; Falsey, A.R.; Scott, D.A.; et al. A Randomized Phase 1/2 Study of a Respiratory Syncytial Virus Prefusion F Vaccine. *J. Infect. Dis.* **2022**, *225*, 1357–1366.
7. Green, C.A.; Scarselli, E.; Voysey, M.; et al. Safety and Immunogenicity of Novel Respiratory Syncytial Virus (RSV) Vaccines Based on the RSV Viral Proteins F, N and M2-1 Encoded by Simian Adenovirus (PanAd3-RSV) and MVA (MVA-RSV); Protocol for an Open-Label, Dose-Escalation, Single-Centre, Phase 1 Clinical Trial in Healthy Adults. *BMJ Open* **2015**, *5*, e008748.
8. Schwarz, T.F.; McPhee, R.A.; Launay, O.; et al. Immunogenicity and Safety of 3 Formulations of a Respiratory Syncytial Virus Candidate Vaccine in Nonpregnant Women: A Phase 2, Randomized Trial. *J. Infect. Dis.* **2019**, *220*, 1816–1825.
9. Abarca, K.; Rey-Jurado, E.; Muñoz-Durango, N.; et al. Safety and Immunogenicity Evaluation of Recombinant BCG Vaccine Against Respiratory Syncytial Virus in a Randomized, Double-Blind, Placebo-Controlled Phase I Clinical Trial. *EClinicalMedicine* **2020**, *27*, 100517.
10. Ascough, S.; Vlachantoni, I.; Kalyan, M.; et al. Local and Systemic Immunity Against Respiratory Syncytial Virus Induced by a Novel Intranasal Vaccine. A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Am. J. Respir. Crit. Care Med.* **2019**, *200*, 481–492.
11. Mejias, A.; Rodríguez-Fernández, R.; Oliva, S.; et al. The Journey to a Respiratory Syncytial Virus Vaccine. *Ann. Allergy Asthma Immunol.* **2020**, *125*, 36–46.
12. Tameris, M.D.; Hatherill, M.; Landry, B.S.; et al. Safety and Efficacy of MVA85A, a New Tuberculosis Vaccine, in Infants Previously Vaccinated with BCG: A Randomised, Placebo-Controlled Phase 2b Trial. *Lancet* **2013**, *381*, 1021–1028.
13. Kharfan-Dabaja, M.A.; Boeckh, M.; Wilck, M.B.; et al. A Novel Therapeutic Cytomegalovirus DNA Vaccine in Allogeneic Haemopoietic Stem-Cell Transplantation: A Randomised, Double-Blind, Placebo-Controlled, Phase 2 Trial. *Lancet Infect. Dis.* **2012**, *12*, 290–299.
14. Silfverdal, S.A.; Icardi, G.; Vesikari, T.; et al. A Phase III Randomized, Double-Blind, Clinical Trial of an Investigational Hexavalent Vaccine Given at 2, 4, and 11–12 Months. *Vaccine* **2016**, *34*, 3810–3816.

15. Vesikari, T.; Becker, T.; Vertruyen, A.F.; et al. A Phase III Randomized, Double-Blind, Clinical Trial of an Investigational Hexavalent Vaccine Given at Two, Three, Four and Twelve Months. *Pediatr. Infect. Dis. J.* **2017**, *36*, 209–215.
16. Baden, L.R.; Karita, E.; Mutua, G.; et al. Assessment of the Safety and Immunogenicity of 2 Novel Vaccine Platforms for HIV-1 Prevention: A Randomized Trial. *Ann. Intern. Med.* **2016**, *164*, 313–322.
17. Moss, R.B.; Hansen, C.; Sanders, R.L.; et al. A Phase II Study of DAS181, a Novel Host Directed Antiviral for the Treatment of Influenza Infection. *J. Infect. Dis.* **2012**, *206*, 1844–1851.
18. Nell, A.S.; D'lom, E.; Bouic, P.; et al. Safety, Tolerability, and Immunogenicity of the Novel Antituberculous Vaccine RUTI: Randomized, Placebo-Controlled Phase II Clinical Trial in Patients with Latent Tuberculosis Infection. *PLoS ONE* **2014**, *9*, e89612.
19. Kono, K.; Iinuma, H.; Akutsu, Y.; et al. Multicenter, Phase II Clinical Trial of Cancer Vaccination for Advanced Esophageal Cancer with Three Peptides Derived from Novel Cancer-Testis Antigens. *J. Transl. Med.* **2012**, *10*, 1–9.
20. Capeding, M.R.; Tran, N.H.; Hadinegoro, S.R.S.; et al. Clinical Efficacy and Safety of a Novel Tetravalent Dengue Vaccine in Healthy Children in Asia: A Phase 3, Randomised, Observer-Masked, Placebo-Controlled Trial. *Lancet* **2014**, *384*, 1358–1365.
21. Vink, P.; Torrell, J.M.R.; Fructuoso, A.S.; et al. Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: A Phase 3, Randomized Clinical Trial. *Clin. Infect. Dis.* **2020**, *70*, 181–190.