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Safety and Efficacy Reports on Arexvy Vaccine

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The respiratory syncytial virus (RSV) is a major cause of acute lower respiratory tract infection in children and poses a significant risk to older adults. Developing a vaccine against RSV has been a priorityand the recently approved Arexvy vaccine has shown promise in preventing lower respiratory tract disease (LRTD) caused by RSV in individuals aged 60 years and older.Respiratory syncytial virus vaccine, adjuvanted, contains recombinant glycoprotein F stabilized in the prefusion conformation (RSVPreF3). This antigen is combined with GSK's proprietary $AS01_E$ adjuvant. The vaccine was approved by the US FDA on 3 May 2023 for the prevention of LRTD caused by RSV in individuals 60 years of age and older. In June 2023, the European Commission authorized the vaccine for active immunization for the prevention of LRTD caused by RSV in adults aged 60 years and older. In September 2023, Japan's Ministry of Health, Labor, and Welfare approved the vaccine for the prevention of RSV disease for adults aged 60 years and above. The vaccine has also been approved in the UK and Canada. Regulatory reviews in other countries are ongoing. The proposed trade name remains subject to regulatory approval in other markets.Known as one of the most susceptible populations in getting an RSV disease, ages 60 and older are recommended to get this vaccine. The decision may be informed by the individual's health status, risk factors, healthcare provider recommendation and patient safety. The vaccine is recommended beginning of fall when the disease starts appearing and peaks in winter.AREXVY is given as a single shot through a healthcare provider recommendation or by visiting your local pharmacy.

The efficacy and safety of the vaccine are explored based on phase 3 clinical trial, demonstrating its effectiveness in preventing RSV-associated LRTD. The most common adverse reactions reported include injection site pain, fatigue, myalgia, headache, and arthralgia

Need for booster doses and the long-term impact of the vaccine on reducing the RSV-associated hospitalizations are the ongoing research. A Grading of Recommendations, Assessment, Development and Evaluation (GRADE) review of the evidence for benefits and harms for GSK Respiratory Syncytial Virus (RSV) PreF3 vaccine was presented to the Advisory Committee on Immunization Practices (ACIP) on June 21, 2023. GRADE evidence type indicates the certainty in estimates from the available body of evidence. Evidence certainty ranges from high certainty to very low certainty. The two main policy questions included were "Should vaccination with GSK RSVPreF3 vaccine (120µg antigen + $AS01_E$ adjuvant, 1 dose administered intramuscularly [IM]), rather than no vaccine, be recommended in persons aged ≥65 years?" and "Should vaccination with GSK RSVPreF3 vaccine (120µg antigen + $AS01_E$ adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged 60–64 years?"A systematic review of evidence on the efficacy and safety of GSK RSVPreF3 vaccine among persons aged 60 years and older was also conducted. Efficacy findings were based on analyses of data collected during May 2021–March 2023, which included two complete RSV seasons for Northern Hemisphere participants and one complete RSV season for Southern Hemisphere participants.The quality of evidence from one Phase 3 randomized controlled trial (RCT) and one Phase 1/2 RCT were assessed using the GRADE approach.The benefits chosen by the ACIP RSV Vaccines Work Group (Work Group) as critical or important to policy decisions were prevention of RSV lower respiratory tract illness/disease (LRTI/LRTD) (critical), medically attended RSV LRTI/LRTD (critical), hospitalization for RSV respiratory illness (important), severe RSV respiratory illness requiring supplemental oxygen (O_2) or other respiratory support (important), and death due to RSV respiratory illness (important). The harms chosen by the Work Group as critical or important to policy decisions were serious adverse events (critical), inflammatory neurologic events* (important) and reactogenicity grade ≥3 (important).

RESULTS

A lower risk of RSV LRTD† was observed with vaccination compared to placebo (incident rate ratio [IRR] 0.254, 95% confidence interval [CI]: 0.165, 0.379, evidence certainty: moderate),

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corresponding to a vaccine efficacy of 74.6% (95% CI: 62.1%, 83.5%). A lower risk of medically attended RSV LRTD[¶] was also observed (IRR 0.225; 95% CI: 0.110, 0.421; evidence certainty: moderate), corresponding to a vaccine efficacy of 77.5% (95% CI: 57.9%, 89.0%).The trial was not powered to detect a lower risk of hospitalization for RSV respiratory illness or severe RSV respiratory illness requiring supplemental oxygen or other respiratory support (for both outcomes IRR 0.236; 95% CI: 0.005, 2.112; evidence certainty: very low), corresponding to a vaccine efficacy for both outcomes of 76.4% (95% CI: -111%, 99.5%). No deaths due to RSV respiratory illness were identified among vaccine recipients or placebo recipients.

In terms of harms, the pooled available data from the Phase 3 and Phase 1/2 RCTs indicated that serious adverse events (SAEs)[††] were balanced between participants in the vaccine and placebo arms (risk ratio [RR] 1.019; 95% CI: 0.908, 1.145; evidence certainty: high). Reactogenicity grade ≥3[§§] was associated with vaccination (RR 4.099; 95% CI: 1.989, 8.446; evidence certainty: high), with 3.8% of vaccine recipients and 0.9% of placebo recipients reporting any grade ≥3 local or systemic reactions following injection.

Another clinical trial by GSK plc (LSE/NYSE: GSK) announced positive preliminary results from its phase III trial [NCT05590403] evaluating the immune response and safety of Arexvy (respiratory syncytial virus vaccine, adjuvanted) in adults aged 50 to 59, including those at increased risk of respiratory syncytial virus (RSV) lower respiratory tract disease (LRTD) due to certain underlying medical conditions.The vaccine elicited an immune response in adults aged 50 to 59 at increased risk for RSV disease due to select underlying medical conditions that was non-inferior to that observed in adults aged 60 and above, meeting the trial's primary co-endpoint. Vaccine efficacy has previously been demonstrated in adults aged 60 and above. The co-primary endpoint was also met for the broader group of adults aged 50 to 59 also enrolled in the trial. Safety and reactogenicity data were consistent with results from the initial phase III program.NCT05590403 is a phase III, placebo-controlled, observer-blind, randomized, multi-country immunogenicity trial to evaluate the non-inferiority of the immune response and evaluate safety in participants aged 50 to 59 at increased risk of RSV-LRTD compared to older adults aged 60 years and above after a single dose of GSK's RSV vaccine. Immune response in participants aged 50 to 59 with pre-defined stable chronic diseases leading to an increased risk of RSV disease was assessed (n=570). These included participants with chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney disease or chronic liver disease. Immune responses in a broader group of participants aged 50 to 59 without these pre-defined chronic diseases (n=570) was also evaluated compared to adults aged 60 and older. Approximately 1,520 participants were enrolled across eight countries.

RESULTS

The trial's primary endpoints were RSV-A and RSV-B neutralizationtiters of both groups of 50- to 59-year-old at one month after the vaccine administration compared to adults aged 60 and older. There were also safety and immunogenicity secondary and tertiary endpoints. The trial is ongoing to collect further immune data at six months and 12 months after vaccine administration.

SUMMARY

Preliminary results from phase III trial show primary endpoints met, with non-inferior immune responses observed in adults aged 50-59 compared to adults aged 60 and older. Adults aged 50 and above with certain underlying medical conditions are at increased risk for RSV disease[1].GSK is on track to be the first company to submit data in this population to regulators, with decisions on potential label expansion expected in 2024.AREXVY was shown to be effective over 82% in preventing lung and lower airway infection from RSV in people 60 years and older and over 94% effective in preventing lung and lower airway infection from RSV in people aged 60 years and older with asthma, diabetes, COPD, chronic heart failure, advanced liver, or kidney disease or any chronic respiratory or pulmonary disease.The initial GRADE evidence level was type 1 (high) for each outcome because the body of evidence consisted of randomized controlled trials. In terms of critical benefits, the available data indicated that the vaccine was effective for preventing RSV LRTD and medically attended LRTD with moderate certainty. Certainty was downgraded once due to serious concern for indirectness (limited number of adults 80 and older included in the trial and the exclusion of persons with immune compromise).No serious concerns impacted the certainty in the estimate for serious adverse events or reactogenicity (both high certainty). No inflammatory neurologic events were recorded in the phase 3 trial, meaning certainty of this outcome could not be assessed (however, 3 events were

recorded outside of trials included in the GRADE evidence profile).The trial results from [NCT05590403]reinforces confidence in RSV vaccine's ability to help protect adults aged 50 to 59 at increased risk for RSV-LRTD.

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