Long-Term Care Updates

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RSV Vaccines: Coming Soon to Older Adults Near You?

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Introduction:

Vaccines are constantly in development for prevention of infectious diseases, and in recent years, pharmaceutical companies have been developing vaccines for the prevention of respiratory syncytial virus (RSV) infections, a common respiratory infection that lacks a prophylactic vaccine. Pfizer is one of the frontrunners for RSV vaccine development. Their vaccine candidate, PF-06928316 or RSVpreF, is in an ongoing Phase 3 clinical trial. RSVpreF is a bivalent recombinant vaccine consisting of equal amounts of stabilized perfusion F (preF) antigens from RSV A and RSV B. Recently, Pfizer submitted interim data to the Vaccines and Related Biological Products Advisory Committee (VRB-PAC). On February 28th, 2023, the committee voted in favor of RSVpreF in a 7 to 4 vote, suggesting the vaccine demonstrated adequate safety and efficacy data to date. This vaccine candidate is currently under FDA's review for prevention of acute respiratory disease and lower respiratory tract disease caused by RSV for aged 60 and older. The FDA's decision for approval is expected by in May 2023.[1] This newsletter will review RSV, summarize available clinical data on RSVpreF, and identify other manufacturer's aiming to bring RSV vaccines to market.

Respiratory syncytial virus:

Respiratory syncytial virus or RSV is a common virus that causes respiratory illnesses. Individuals who are infected with RSV may experience mild cold-like symptoms, although some individuals may develop severe complications such as pneumonia and other lung infections. RSV infection is also associated with the exacerbation of asthma, chronic obstructive pulmonary disease (COPD), and congestive heart failure (CHF). According to the Center of Disease Control and Prevention (CDC), RSV infection is the cause of 60,000 to 160,000 hospitalizations and 6,000 to 10,000

deaths of older adults in the United States each year. Individuals 65 years and older, adults with chronic heart or lung disease, and adults with weakened immune systems are more susceptible to RSV infection. There is currently a lack of specific and targeted treatment options for RSV, as well as a lack of prophylactic therapies and vaccines. Individuals infected with RSV are limited to symptomatic relief options such as over the counter antipyretic agents and cold medicines.[2,3]

Clinical Trial Findings:

The RSV vaccine Efficacy study in Older adults Immunized against RSV disease (RENOIR) trial is an ongoing Phase 3 double-blinded, randomized, placebo-controlled trial. This study has not been officially published, but some data are available within the FDA's briefing document of the VRBPAC meeting on February 28th, 2023. The study is being conducted in 240 study sites in Argentina, Canada, Finland, Japan, Netherlands, South Africa, and the United States. RENOIR has a targeted enrollment of 45,000 participants aged 60 and older. Healthy individuals and those with stable chronic conditions (including asthma, COPD and CHF) are being randomized 1:1 to receive an intramuscular injection of RSVpreF (n=17,215) or placebo (n=17,069), with randomization stratified by age group (60-69 years, 70-79 years and ≥ 80 years). RENOIR is designed to continue for two RSV seasons with the primary efficacy analysis assessed during the first RSV season.[4]

Efficacy data:

The efficacy of the vaccine, or vaccine efficacy (VE), is defined as the relative risk reduction in the RSVpreF group compared to the placebo group. The primary efficacy endpoints were VE against laboratory-confirmed RSV associated lower respiratory tract illness (LRTI-RSV) with ≥2 and ≥3 symptoms with onset at least 14 days post vaccination. The VE in prevention of LRTI-RSV ≥2 symptoms was 66.7% (96.66% confidence interval [CI]; 28.8 - 85.8) with 11 cases in the RSVpreF group and 33 cases in the placebo group. The VE in prevention of LRTI-RSV ≥3 symptoms was 85.7% (96.66% CI; 32.0 - 98.7) with two cases in the RSVpreF group and 14 cases in the placebo group. The secondary efficacy endpoint was VE against RSV associated-acute respiratory illness (ARI-RSV). The VE in prevention of ARI-RSV was 62.1% (95% CI 37.1 - 77.9); however, the data were submitted to VRBPAC for review before all swabs were collected from the ARI cases.[4]

Safety Data:

Safety of the vaccine was analyzed using reported local and systemic solicited adverse reactions within 7 days following vaccination; unsolicited adverse events through 1 month post vaccination and through data cutoff were also recorded. The safety data submitted for review includes 34,284 vaccinated individuals (17,215 RSVpreF and 17,069 placebo). Local and systemic solicited adverse reactions were collected from a subset of study participants (N=7,196), and unsolicited adverse events were collected from all participants (N=34,284). Table 1 lists adverse reactions reported in ≥2% of individuals receiving RSVpreF at a rate higher than those receiving placebo within 7 days following vaccination. The most common adverse reactions in the RSVpreF group were fatigue (15.5%), headache (12.8%), injection site pain (10.6%), and muscle pain (10.1%). These adverse reactions were reportedly mild to moderate and more common in individuals 60-69 years of age when compared to other age groups. Most adverse reactions were resolved within 1 to 2 days following vaccination.[4]

Table 1. Solicited systemic and local adverse reactions reported within 7 days of vaccination.[4]

Solicited Adverse Reactions	RSVpreF N=3621	Placebo N=3539
Fatigue	15.50%	14.40%
Headache	12.80%	11.70%
Injection Site Pain	10.60%	6.00%
Muscle Pain	10.10%	8.40%
Joint Pain	7.50%	6.90%
Diarrhea	5.90%	5.20%
Injection Site Erythema	2.70%	0.70%
Injection Site Swelling	2.50%	0.50%

Unsolicited adverse events reported within 1 month post vaccination were similar between the RSVpreF group and the placebo group (8.9% and 8.5%, respectively). Additionally, unsolicited adverse events reported within 30 minutes of vaccination were reported similar between the RSVpreF group and the placebo group (0.2% for both groups). These events were mainly injection site reactions, and no anaphylaxis was reported. The percentages of RSVpreF and placebo recipients who reported severe adverse events within 1 month were 0.4% and 0.3%, respectively, and 0.1% of individuals in each group reported life threatening adverse events. The rates of non-fatal serious adverse events through data cutoff (July 2022) were the same in both groups (2.3%). Vaccine related serious adverse events were only observed in the RSVpreF group (<0.1%, n=3). These included hypersensitivity, Miller Fisher Syndrome, and Guillain-Barre Syndrome (GBS). No deaths were considered related to the vaccination (52 [0.3%] RSVpreF and 49 [0.3%] placebo). Overall, there were similar safety data, and no subgroups were identified to be more susceptible to the adverse events. Post VRBPAC meeting, the FDA requested that Pfizer propose a postmarketing safety evaluation to assess the risk of GBS and other immune-mediated conditions. The vaccine candidate will undergo further review by the FDA prior to the decision for approval.[4]

Other companies:

While RSVpreF by Pfizer is undergoing FDA review for approval, other pharmaceutical companies are also developing a vaccine for RSV. Moderna, GSK, Johnson and Johnson, and Bavarian Nordic's investigational RSV vaccine candidates are all in an ongoing Phase 3 clinical trial. Interim analysis of all trials showed that the vaccine candidates were efficacious.[5-8]

Conclusion:

RSV is a contagious respiratory virus with a lack of specific and targeted treatment, vaccines, or preventative therapies. Pfizer's vaccine candidate (RSVpreF) was recently reviewed by VRBPAC and deemed adequate in safety and efficacy. Interim results from the RENOIR Phase 3 clinical trial show that the RSVpreF is efficacious when compared to placebo in reducing LRTI-RSV ≥2 or ≥3 symptoms and ARI-RSV in adults 60 years and older. RSVpreF was also well-tolerated in adults aged 60 years and older. RSVpreF by Pfizer will undergo further evaluation by the FDA and the decision for approval is expected soon.

References:

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