Transcript Details
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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Cell-Based Option for Seasonal Influenza Prevention in Persons 6 Months & Older

Announcer:
You're listening to ReachMD. This medical industry feature, focusing on "A Cell-Based Option for Seasonal Influenza Prevention in Persons 6 Months and Older" is sponsored by Seqirus. This program is intended for healthcare professionals.

Here's your host, Dr. Charles Turck.

Dr. Turck:
The expansion of a licensed cell culture-based influenza vaccine to include patients as young as 6 months of age offers an important preventive option in pediatric practice. But what are the unique benefits of cell-based vaccines for seasonal influenza prevention and how did the latest safety and immunogenicity data lead to this expanded age indication? These are some of the questions that we'll address on today's program. This is ReachMD and I'm Dr. Charles Turck. Joining me is Dr. Donald Middleton, Professor of Family Medicine at the University of Pittsburgh School of Medicine. Dr. Middleton, welcome to the program.

Dr. Middleton:
Thanks, Charles. Glad to be with you.

Dr. Turck:
Before we dive into the data that led to this expanded age indication, can you give us a frame of reference on the current burden of influenza in children less than 5 years of age?

Dr. Middleton:
Sure. Influenza causes considerable morbidity and mortality in children. In the United States, the CDC estimates that from the 2010-2011 season to the 2019-2020 season, seasonal influenza-related hospitalizations among children younger than 5 years old have ranged from 7,000 to as high as 26,000 every year. And among the reported pediatric influenza-related deaths since 2004, approximately 80% of those children were not fully vaccinated. So, this is a sobering reminder of the pivotal role that vaccination plays in preventing influenza disease. We also need to keep in mind the collateral impacts of influenza in children, which as a patient population have higher influenza infection rates and sheds the virus longer than adults, which makes them a major source of transmission for this disease. So, this information further underscores the importance of vaccinating children against flu.

Dr. Turck:
That's a great level setter for us on influenza risks in children, Dr. Middleton. Thank you.

Let's turn to the vaccines now and focus on the emergence of cell-based influenza technology. What's the rationale for this type of vaccine delivery and influenza prevention?

Dr. Middleton:
Cell-based manufacturing is a different production process compared to traditional egg-based manufacturing. Cell-based influenza vaccines are designed to produce an exact match to the WHO selected strains. In egg-based production, egg adaptation occurs when the vaccine strains selected by the WHO adapts in order to grow in eggs. Importantly, changes to the hemagglutinin or HA protein that help it bind to avian receptors can result in strain mismatch.

But cell-based vaccines avoid egg adaptation by being manufactured in mammalian cells, therefore, they may be an exact match to the annual WHO selected influenza virus strains.

Dr. Turck:
So, with that background then, let's focus on the vaccine option of Flucelvax Quadrivalent, which is currently the only cell-based quadrivalent influenza vaccine licensed in the U.S. and as I'd prefaced earlier was recently approved for use in patients 6 months of age and older. But first, let's review some important safety information.

Announcer:
Indications & Contraindications:
Flucelvax® Quadrivalent is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and types B contained in the vaccine. Flucelvax® Quadrivalent is approved for use in persons 6 months of age and older.

Do not administer Flucelvax® Quadrivalent to anyone with a history of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine.

Additional important safety information will be provided later in this program.

Dr. Turck:
So, Dr. Middleton, let's talk about the study that led to this expanded indication for children at 6 months of age and older. What can you tell us about it?

Dr. Middleton:
So, Charles, this was a phase 3, randomized, observer-blind, multi-centered, non-inferiority study to demonstrate the immunogenicity and safety of Flucelvax Quadrivalent verus the U.S. licensed egg-based quadrivalent influenza vaccine Afluria Quadrivalent in children 6 months through 47 months of age.

The study was conducted in the 2019 to 2020 northern hemisphere flu season in 47 centers across the United States. Immunogenicity was assessed using HA inhibition assays for A/H1N1, B/Yamagata, and B/Victoria Influenza strains and a microneutralization assay for the A/H3N2 strain. The primary objective of this study was to demonstrate non-inferior immunogenicity with endpoints of geometric mean titer or GMT ratio and seroconversion rate or SCR difference.

Secondary objectives included descriptive immunogenicity of Flucelvax Quadrivalent and Afluria Quadrivalent using egg-derived and cell-derived targeted viruses in a subset of participants. Adverse events were collected both local and systemic, as well as solicited and unsolicited.

Dr. Turck:
Can you elaborate on how the study was conducted in terms of treatment schedules for the participants Dr. Middleton?

Dr. Middleton:
Sure, Charles. Participants were randomized to receive Flucelvax Quadrivalent or Afluria Quadrivalent, termed QIVc and QIV, respectively, in a 2 to 1 ratio and were further stratified by prior influenza vaccine status as either previously vaccinated or not previously vaccinated. The not previously vaccinated group was defined as all participants who had not previously received two or more doses of seasonal influenza vaccine prior to the last influenza season, including those with unknown influenza vaccination history. The first dose was given when then enrolled on day 1, followed by the second dose, 29 days later. Meanwhile, the previously vaccinated group included any participant who did previously receive two or more doses of seasonal influenza vaccine, at least 4 weeks apart, prior to the last influenza season. These individuals received a single dose of vaccine.

Dr. Turck:
I think that background on the study's methods is so helpful for providing context for the study's results. So, with that said what were the findings from this study?

Dr. Middleton:
Coming back to the eight co-primary endpoints that were used to assess immunogenicity, starting with the GMT ratio endpoints, Flucelvax Quadrivalent met the pre-specified, non-inferiority criteria for GMT ratio in children 6 through 47 months of age for all four strains using cell-derived target viruses. The pre-specified success criterion was that the upper bound of the two-sided 95% confidence interval for GMT ratios did not exceed 1.5. Looking at the seroconversion rate differences as the other co-primary endpoints, Flucelvax Quadrivalent also met the pre-specified non-inferiority criteria for SCR difference for all four strains evaluated in the study. The pre-specified success criterion in this case was that the upper bound of the two-sided 95% confidence interval for SCR differences did not exceed 10%. So, Charles, in meeting the pre-specified non-inferiority criteria for all eight co-primary endpoints, the primary immunogenicity objective was also met.

Dr. Turck:
That's a great synopsis, but what about the side effect profiles observed in this study? Anything we should take away from those findings?

Dr. Middleton:
The most commonly reported solicited local adverse events in both the Flucelvax Quadrivalent and the comparator groups for tenderness at 27.9% versus 30% of participants respectively and erythema in 25.8% versus 24.6% of participants. For solicited systemic adverse events, the most frequently reported in both Flucelvax Quadrivalent and comparator groups were irritability at about 28% versus 30% of participants, respectively and sleepiness in approximately 27% versus 26% of participants. It's important to note that following vaccination, there were no notable differences in rates of solicited systemic adverse events between the Flucelvax Quadrivalent and comparator groups. And the majority of solicited local and systemic adverse events after any vaccination were mild or moderate in severity.

The rates of unsolicited adverse events assessed as related to the study vaccine were low and similar between the two comparator groups at 4.4% for Flucelvax Quadrivalent and 4.5% for the U.S. licensed egg-based comparator Afluria Quadrivalent. Severe adverse events were reported in 0.9% of both vaccine groups but none in either group were determined to be related to the study vaccine. So, those results are actually comparable.

Dr. Turck:
Looking over these findings in aggregate, Dr. Middleton, what can our audience take away from this clinical trial and the expanded age indication that followed for Flucelvax Quadrivalent?

Dr. Middleton:
In a nutshell, Flucelvax Quadrivalent met all eight pre-defined, co-primary endpoints. The immunogenicity data was consistent across all four strains of influenza that were tested and Flucelvax Quadrivalent was well-tolerated when comparing adverse events among both vaccine groups. And an important point to add here is that this data is consistent with previously reported data in older children. From a clinical perspective, for the 2021-2022 flu season, five vaccines are currently indicated for persons 6 months of age and older; four of them are egg-based, while Flucelvax Quadrivalent represents the only cell-based vaccine.

So, this means that with the expanded age indication for children as young as 6 months of age, we now have an opportunity to opt for a differentiated influenza vaccine.

Dr. Turck:
I want to thank my guest, Dr. Donald Middleton for helping us better understand the data behind the expanded age indication for Flucelvax Quadrivalent to include patients as young as 6 months of age. Dr. Middleton, it was great speaking with you today.

Dr. Middleton:
Charles, it was great to be with you and everyone should keep on vaccinating.

Dr. Turck:
I'm Dr. Charles Turck. Before we go, let's take a moment to review some important safety information.

Announcer:
Warnings and Precautions
If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUCELVAX QUADRIVALENT should be based on careful consideration of the potential benefits and risks.

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

Syncope (fainting) can occur in association with administration of injectable vaccines, including FLUCELVAX QUADRIVALENT. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope by maintaining a supine or Trendelenburg position.

After vaccination with FLUCELVAX QUADRIVALENT, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response.

Vaccination with FLUCELVAX QUADRIVALENT may not protect all vaccine recipients against influenza disease.

Adverse Reactions

In children 6 months through 3 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (27.9%), erythema (25.8%), induration (17.3%) and ecchymosis (10.7%). The most common systemic adverse reactions were irritability (27.9%), sleepiness (26.9%), diarrhea (17.9%) and change of eating habits (17.4%).

In children 2 through 8 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (28.7%), pain (27.9%) and erythema (21.3%), induration (14.9%) and ecchymosis (10.0%). The most common systemic adverse reactions were sleepiness (14.9%), headache (13.8%), fatigue (13.8%), irritability (13.8%) and loss of appetite (10.6%).

In children and adolescents 9 through 17 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were injection site pain (21.7%), erythema (17.2%) and induration (10.5%). The most common systemic adverse events were headache (18.1%) and fatigue (17.0%).

In adults 18 through 64 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (45.4%), erythema (13.4%) and induration (11.6%). The most common systemic adverse reactions were headache (18.7%), fatigue (17.8%) and myalgia (15.4%).

In adults ≥65 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (21.6%) and erythema (11.9%).

To report SUSPECTED ADVERSE REACTIONS, contact Seqirus at 1-855-358-8966 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

Before administration, please see the full US Prescribing Information for FLUCELVAX QUADRIVALENT.

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