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Evidence Builds for Cell-Based Influenza Vaccines

Announcer:
You're listening to ReachMD. This medical industry feature, titled "Evidence Builds for Cell-Based Influenza Vaccines," is sponsored by CSL Seqirus. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I'm your Host, Dr. Jennifer Caudle. When it comes to influenza vaccines, a key discussion has been the difference between traditional egg-based and newer cell-based options.[1-4]

In a previous program, which you can find at ReachMD.com, Dr. Victoria Statler discussed the strategy behind cell-based influenza vaccines and reviewed multi-season data comparing the FLUCELVAX® QUADRIVALENT vaccine against egg-based vaccines.

Announcer:
Data for FLUCELVAX® QUADRIVALENT are relevant to FLUCELVAX® because both vaccines are manufactured using the same process and have overlapping compositions.

Dr. Caudle:
And so for today's discussion, we're building on that conversation and examining the latest real-world evidence from the 2023 to 2024 influenza season in the United States.

Joining me to share these findings is Dr. Wendy Wright. She's a board-certified adult and family nurse practitioner based out of Amherst, New Hampshire, as well as the owner of Wright and Associates Family Healthcare.

Dr. Wright, welcome to the program.

Dr. Wright:
Thank you so much for having me, It is truly a pleasure to be here today.

Dr. Caudle:
Well, let's get right into it, Dr. Wright.

So from Dr. Statler's discussion, we learned that there's already data supporting the safety and efficacy of cell-based influenza vaccines in adults and children from randomized controlled trials.[5-8] And there's also data supporting their effectiveness based on real-world studies.[9-14]

Could you explain why continuing to study cell-based versus egg-based influenza vaccines remains important, and what led to this particular analysis of the 2023 to 2024 flu season?

Dr. Wright:
Absolutely. So you're right, there's already data out there. But one limitation in prior research is that effectiveness studies have historically relied on outcomes based on clinical diagnosis of Influenza-like illness, or ILI, rather than test-confirmed influenza.

Relying on ILI alone to diagnose influenza can complicate research findings due to co-circulating respiratory viruses.[15] Whereas test-confirmed influenza outcomes provide a more specific evaluation of influenza vaccine effectiveness and can help show the clinical differences between cell-based versus egg-based vaccines.[2]

Beyond that, there were a few other key factors driving this latest real-world study. First, the age indication for FLUCELVAX was expanded in October 2021 to include children as young as six months.[5] That expansion opened the door to evaluating influenza vaccine effectiveness in a broader pediatric population. Specifically, it allowed researchers to begin closing a knowledge gap by examining how cell-based technology performs in comparison to egg-based options in adults under 65 years and in very young children. It also presented an opportunity for further analysis of vaccine effectiveness in various pediatric and adult subgroups.[3]

And just so you're aware, adults 65 and older were excluded from this study since that group has preferential recommendations for other influenza vaccines.[3,16]

Now, if we zero in on the 2023–2024 influenza season, all of the egg-based vaccine strains recommended that year showed egg-adapted mutations.[3,17] These changes, which can alter the antigenic properties of the vaccine virus, may impact how well it matches the circulating strain.[1,4] And since one of the advantages of cell-based vaccines is avoiding these egg-adapted mutations, there's ongoing interest in comparing the two vaccination strategies across seasons in cases of test-confirmed influenza.[1-3]

Dr. Caudle:
Interesting. So it sounds like the specific objective of the study was to estimate the relative vaccine effectiveness, or rVE, of quadrivalent cell-based influenza vaccines versus quadrivalent egg-based vaccines in preventing test-confirmed influenza during the 2023-24 season. And this was particularly for individuals six months through 64 years of age in the U.S.[3]

So with that understanding in mind, Dr. Wright, could you tell us a bit more about how the study was designed?

Dr. Wright:
Sure. So the researchers used a retrospective test-negative design to compare the FLUCELVAX QUADRIVALENT cell-based vaccine with quadrivalent egg-based vaccines.[3]

Patients were included if they were tested for influenza within seven days of a documented acute respiratory or febrile illness and at least 14 days had passed since their last influenza vaccination. And so those who tested positive were classified as cases, while those who tested negative served as controls.[3] The analysis drew on data from HealthVerity, which linked electronic health records with medical and pharmacy claims as well as laboratory results nationwide.[3]

Now, what really stands out is the scale. More than 106,000 patients were included, making this the largest retrospective test-negative study of its kind for this comparison. Additionally, 57 percent of the study population was pediatric, and 16 percent of the overall study population received the cell-based vaccine. Altogether, this allowed for meaningful evaluation across pediatric and adult subgroups.[3]

Dr. Caudle:
With so many patients included, how did the investigators make sure the results weren't biased by differences in who received which vaccine?

Dr. Wright:
I'm glad you brought that up because that's an important thing to note here. From a statistical standpoint, the study applied a doubly robust approach, combining inverse probability of treatment weighting and multivariable adjustment to balance covariates. *A priori* covariates included:

- age,

- sex,

- geographic region,

- calendar time,

- and recent COVID-19 vaccination status within the past six months.[3,17]

Other covariates, such as:

- week of vaccination,

- Charlson Comorbidity Index score,

- high risk conditions,

- health care resource use,

- payer,

- and test type,

were also adjusted if they were imbalanced.[3]

And finally, to further address potential bias, the investigators conducted prespecified sensitivity analyses. One adjusted for the propensity to be tested, and another matched cases and controls by the week of influenza testing as an additional way to account for calendar time and seasonality.[3]

Dr. Caudle:
Thank you for breaking all of that down for us, Dr. Wright. Now, if we turn to the study findings, what was observed in the 2023-2024 analysis, and how does that compare to previous influenza seasons?

Dr. Wright:
Well, in the 2023–24 season, the analysis showed that FLUCELVAX QUADRIVALENT had an rVE of nearly 20 percent compared to egg-based vaccines, with a 95 percent confidence interval above zero. Also, the results from the sensitivity analyses were very similar to the main analysis, suggesting that there was minimal bias due to testing practices or epidemic timing. So overall, the results were significant and demonstrated a meaningful advantage in real-world practice.[3]

And when we place that in the context of earlier seasons, the consistency becomes clear. In retrospective test-negative studies of individuals aged four through 64, the rVE was:

- about 15 percent in 2017-2018,

- nearly 13 percent in 2018-2019,

- and 10 percent in 2019-2020,

with confidence intervals that excluded zero in each case.[2] More recently, in the 2022 to 2023 season, when the age range was expanded down to six months, the rVE was just under eight percent, again with a confidence interval excluding zero.[18]

So across multiple influenza seasons, these results continue to support the use of cell-based vaccines as an effective option compared with traditional egg-based vaccines.[2,3]

Dr. Caudle:
For those just tuning in, you're listening to ReachMD. I'm Dr. Jennifer Caudle, and today I'm speaking with Dr. Wendy Wright about real-world evidence on the cell-based influenza vaccine in individuals six months through 64 years of age during the 2023 to 2024 influenza season.

So, Dr. Wright, we've covered the overall findings from this analysis showing how the rVE of the cell-based influenza vaccine compares with the egg-based option. But as I understand it, subgroup analyses were also conducted by age and included a closer look at different pediatric age ranges. So could you walk us through those results?

Dr. Wright:
Yes, absolutely. Looking first at adults 18 to 64 years of age, the adjusted rVE was around 19 percent. And turning to the pediatric population, which included patients aged six months to 17 years, the adjusted rVE was about 20 percent.[3]

And when we break down the pediatric findings further, the benefit remained consistent across age groups: around 18 percent for children six months to 8 years, and just over 24 percent for those 9 to 17 years of age.[3]

And within that pediatric group, when the analysis was restricted to children tested in the outpatient setting, the adjusted rVE was about 20 percent, again showing consistent findings.[3,17] All of these results favored the cell-based vaccine over the egg-based option, as the confidence intervals excluded zero.[3,17]

Dr. Caudle:
And how about when the analysis was expanded to the broader outpatient population? What were the findings there and in other subgroups that were evaluated in this study?

Dr. Wright:
Of course. In the broader outpatient population covering ages six months through 64 years, the adjusted rVE was nearly identical to the

main analysis, with both coming in just under 20 percent.[3]

The study also evaluated individuals with high-risk conditions, such as chronic lung disease, cardiovascular disease, and immunocompromising states. In this subgroup, the adjusted rVE was just below 15 percent for the overall population aged six months to 64 years.[3]

So whether we look at outpatients overall or patients with high-risk conditions, the findings are consistent with the age-based analyses, showing improved effectiveness of the cell-based vaccine compared with the egg-based option.[3]

Dr. Caudle:
Well, we've certainly covered a lot today, but just to bring this all together before we close, Dr. Wright, what are the main lessons from this study both in terms of what it adds to the evidence base and what it means for everyday vaccination strategy?

Dr. Wright:
So this study reinforces a consistent pattern we've now seen across five influenza seasons.[2,3] In the 2023 to 2024 season, the FLUCELVAX QUADRIVALENT cell-based vaccine demonstrated an rVE of nearly 20 percent compared with quadrivalent egg-based vaccines in individuals six months through 64 years of age.[3]

What stands out here is that this is the first demonstration of improved influenza vaccine effectiveness in the pediatric population as young as six months through 17 years.[3] And when you add to that the consistency of benefit across adult and pediatric subgroups, high-risk patients, and even in the outpatient setting,[3] it helps strengthen confidence in the role of cell-based technology as part of our vaccination strategy.

From a public health perspective, these results add to the growing body of evidence supporting the use of cell-based influenza vaccines.[2,3,9-11,19-28] By avoiding egg-adapted mutations, they may help maintain antigenic match.[1,2] And with circulating influenza strains continuing to evolve year after year,[1,4,29] having real-world evidence across the broader population could help guide both day-to-day clinical decision-making and broader vaccine policy.

Dr. Caudle:
Those are some great takeaways. As those final comments bring us to the end of today's discussion, I'd like to thank my guest, Dr. Wendy Wright, for helping us better understand the real-world evidence on influenza vaccine effectiveness during the 2023 to 2024 season.

Dr. Wright, thanks so much for being here today; I really enjoyed our conversation.

Dr. Wright:
Thank you so much, and it's my pleasure. And again thank you for having me here today.

Dr. Caudle:
Of course, and for ReachMD, I'm your host Dr. Jennifer Caudle. Please stay tuned to hear some Important Safety Information.

Announcer:
FLUCELVAX® (Influenza Vaccine)
INDICATION AND IMPORTANT SAFETY INFORMATION
INDICATION AND USAGE
FLUCELVAX is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUCELVAX is approved for use in persons 6 months of age and older.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
Do not administer FLUCELVAX to anyone with a history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine.

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

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of FLUCELVAX.

Syncope (fainting) has been reported following vaccination with FLUCELVAX. Procedures should be in place to avoid injury from

fainting.

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

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

ADVERSE REACTIONS
Data for FLUCELVAX QUADRIVALENT are relevant to FLUCELVAX because both vaccines are manufactured using the same process and have overlapping compositions.

In children 6 months through 3 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (28%), erythema (26%), induration (17%) and ecchymosis (11%). The most common systemic adverse reactions were irritability (28%), sleepiness (27%), diarrhea (18%) and change of eating habits (17%).

In children 4 through 8 years of age who received FLUCELVAX, the most commonly reported local injection-site adverse reactions were pain (29%) and erythema (11%). The most common systemic adverse reaction was fatigue (10%).

In children and adolescents 9 through 17 years of age who received FLUCELVAX, the most commonly reported injection-site adverse reactions were pain (34%) and erythema (14%). The most common systemic adverse reactions were myalgia (15%) and headache (14%).

In adults 18 through 64 years of age who received FLUCELVAX, the most commonly reported injection-site adverse reactions were pain (28%) and erythema (13%). The most common systemic adverse reactions were headache (16%), fatigue (12%), myalgia (11%) and malaise (10%).

In adults ≥65 years who received FLUCELVAX the most commonly reported injection-site reaction was erythema (10%). The most common systemic adverse reactions were fatigue (11%), headache (10%) and malaise (10%).

Other adverse events may occur.

To report SUSPECTED ADVERSE REACTIONS, contact CSL 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.

Announcer:
This medical industry feature was sponsored by CSL Seqirus. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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