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Maximizing Flu Protection: The Clinical Value of Cell-Based Vaccines

ReachMD Announcer:
Welcome to ReachMD. This medical industry feature, titled “Maximizing Flu Protection: The Clinical Value of Cell-Based Vaccines” is sponsored by CSL Seqirus. Here’s your host, Dr. Jennifer Caudle.

Dr. Caudle:
We all know that clinicians play a fundamental role in safeguarding public health, especially when it comes to influenza. And it’s imperative for all healthcare professionals to grasp the clinical significance and underlying rationale that cell-based influenza vaccines bring to the table—as alternatives to traditional egg-based counterparts—to help combat the seasonal flu. But what studies can we look to for confirmation of vaccine effectiveness?

This is ReachMD, and I’m your host Dr. Jennifer Caudle. Joining me to discuss a retrospective test negative study titled “Superior effectiveness of cell-based versus egg-based quadrivalent influenza vaccines against outpatient test-confirmed influenza over three consecutive seasons in the US”, is Dr. Victoria Statler, Associate Professor of Pediatrics at the University of Louisville. Dr. Statler, welcome to the program.

Dr. Statler:
Thank you for having me.

Dr. Caudle:
Well we’re excited that you’re here and before we dig into our study, I’d like to start off with an overview of the differences between egg-based and cell-based influenza vaccine manufacturing. Dr. Statler, what are those differences and how does each affect vaccine effectiveness, or VE?

Dr. Statler:
Well, after the reference strains are selected based on what the WHO believes will cause the most illness in an upcoming flu season,[1] those differences you mentioned start to come into play.

The traditional manufacturing process for influenza vaccines relies on fertilized chicken eggs. And while vaccine seed viruses adapt to avian receptors found within eggs, a process known as egg adaptation, not all human influenza strains grow well in eggs.[2]

So, egg adaptation describes the mutations that occur in the receptor-binding region of hemagglutinin, allowing influenza viruses to infect avian cells more efficiently. But because this adaptation occurs in the dominant antigenic region of the virus, it can include changes to key viral antigens that may alter the vaccine’s antigenicity and therefore reduce vaccine effectiveness.[3-11]

On the other hand, manufacturing influenza vaccines in cell culture from mammalian-cell-derived seed viruses eliminates the potential for egg-adapted changes. And as a result, cell-culture technology may improve the match between the vaccine virus strain and the candidate vaccine virus selected by the WHO. So cell-based vaccine viruses are more likely to be antigenically similar to viruses circulating within the community and thus, these vaccines may demonstrate improved vaccine effectiveness against influenza infection.[12,13]

Dr. Caudle:
Thanks for that background, Dr. Statler. So what kind of data do we have to support improved vaccine effectiveness in cell-based flu

vaccines versus egg-based vaccines?

Dr. Statler:
Well we do have several studies demonstrating efficacy and effectiveness in adults and children in both randomized controlled trials and real-world settings.[2-11] But the problem is there have been limited data using *test-confirmed* influenza outcomes. And these data are key.

Effectiveness studies have historically relied on outcomes based on clinical diagnosis of Influenza-like illness, or ILI, due to limited routine testing. And relying solely on ILI to diagnose influenza is complicated because of the recent co-circulation of other major respiratory viruses, like COVID-19 and respiratory syncytial virus, or RSV.[14]

But test-confirmed influenza outcomes provide a more specific evaluation of influenza vaccine effectiveness and can help to illustrate the benefit of cell-based versus egg-based vaccines.[15]

Now fortunately, there was a study presented at the Nineth Influenza Conference of the European Scientific Working Group on Influenza, or ESWI for short, that provides us a better sense of vaccine effectiveness of a cell-based vaccine called Flucelvax® (Influenza Vaccine).

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

Dr. Caudle:
So, yes, let's dive in deeper here. Can you tell us about this study's objective and design?

Dr. Statler:
So the objective of this large, robust, real-world study was to estimate the relative vaccine effectiveness, or rVE, of Flucelvax Quadrivalent versus egg-based vaccines in preventing test-confirmed influenza among people four to 64 years of age. And it was conducted in the outpatient care setting during the last three influenza seasons prior to the COVID-19 pandemic in the United States, so the 2017-2018, 2018-2019, and the 2019-2020 seasons.[15]

Now I'd like to point out that the population was restricted to ages four to 64 because different vaccines are recommended for people 65 and older, and because Flucelvax Quadrivalent wasn't yet registered for children younger than four years old during the years looked at for the study.[15]

Now the study used a retrospective test-negative design of patients vaccinated with either Flucelvax Quadrivalent or an egg-based vaccine and who were tested for influenza within seven days of a documented acute respiratory or febrile illness. Data were collected from outpatient electronic health records linked to pharmacy and medical claims.[15]

Now in this case-control study, season-specific rVE was estimated by comparing a logistic regression model used to obtain odds ratios comparing the odds of testing positive for influenza among Flucelvax Quadrivalent recipients with the odds among egg-based vaccine recipients for each season. And the odds ratio was then adjusted to combine inverse probability of treatment weighting with multivariate adjustment by age, sex, geographic region, calendar time, and influenza risk factors.[15]

Finally, prespecified sensitivity analyses included additional adjustments for the propensity to be tested, an analysis restricted to the peak season to avoid potential misclassification of outcome in periods of low influenza activity, and an analysis matched on the test index week, as a different way to adjust for calendar time and seasonality.[15]

Dr. Caudle:
Thank you for that, and for those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Victoria Statler about cell-based versus egg-based vaccine effectiveness using a retrospective case-control study with test-confirmed outcomes data.

So, Dr. Statler, now that we've reviewed the objective and design, what were the results of this study?

Dr. Statler:
Well after weighting for imbalances, like age, geographic region, and differences in high-risk conditions among patients in the test-negative control group,[15]and multivariable adjustment, the rVE results were quite notable for Flucelvax Quadrivalent.

The main analysis showed *consistently* notable results of the effectiveness of Flucelvax Quadrivalent over egg-based vaccines across all

three seasons in the study, with an estimated rVE of 14.8% in the 2017-2018 season, 12.5% in the 2018-2019 season, and 10% in the 2019-2020 season. The 95% confidence intervals were quite tight, and in all cases excluded zero, showing a statistical difference.[15]

Overall, these results confirm effectiveness of cell-based influenza vaccines that we've seen in the other real-world and randomized control trials.[2-11]

Now as far as sensitivity analyses for each season, these results confirm the robustness of the main analysis. In each season, the analyses were adjusted for propensity to be tested, limited to the peak season or matched on test index week. And this shows that results were highly consistent with the main analysis, with overlapping confidence intervals, and showed a statistical difference.[15]

Dr. Caudle:
Thank you so much for that, Dr. Statler. And as we come to a close for today, and given these study results, what do you hope your fellow clinicians will take away from this study?

Dr. Statler:
Yeah, so I think the most valuable thing clinicians need to take away is that this study showed across three different seasons that vaccination with Flucelvax Quadrivalent showed a statistical difference and thus, lower rates of test-confirmed influenza when compared with egg-based vaccines.[15]

And I believe that in order to better combat the flu year over year, we need to see a change in behavior in embracing alternative influenza vaccine options, such as cell-based vaccines.

Dr. Caudle:
These are great insights to think on as we come to the end of today's program. I'd like to thank my guest, Dr. Victoria Statler, for helping us better understand the relative vaccine effectiveness that Flucelvax provides. Dr. Statler, it was great speaking with you today.

Dr. Statler:
It was a pleasure to be here.

Dr. Caudle:
I'm your host Dr. Jennifer Caudle and please stay tuned to hear some Important Safety Information.

ReachMD 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 FLECELVAX.

ReachMD Announcer:
This program was sponsored by CSL Seqirus. If you missed any part of this discussion, visit *Industry Feature* on ReachMD.com/IndustryFeature. This is ReachMD. Be Part of the Knowledge.

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