# VFA Webinar 2/28/18



# 2018 Adult Immunization Schedule What's New?



## **Disclosures**

- I have no financial interests in immunizations discussed here
- I may discuss off-label use of licensed vaccines



## Herpes Zoster (HZ) and Postherpetic Neuralgia (PHN) epidemiology, United States

- ~1 million cases annually<sup>1,2</sup>
- Incidence of HZ and PHN increase with age, <sup>2,3,4</sup>
- HZ (cases per 1,000 population)
  - Children: <1
  - 80 years and older >15
- PHN
  - -50 years and older: 10-18% of HZ cases develop PHN
- Zoster Vaccine Live (ZVL, zostavax) licensed in U.S. since 2006
  - 33% of individuals 60 years and older report receipt.<sup>5</sup>
- 1. Jumaan et al., JID, 2005, 191:2002-7
- 2. Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9
- 3. Insinga et al., J Gen Intern Med. 2005, 20:748-53
- 4. Harpaz et al, IDWeek 2015
- 5. CDC, provisional unpublished data from NHIS

#### Vaccination Coverage of Zoster Vaccine Live, among adults ≥60 yrs, United States, 2007-2016



\* 2007: National immunization Survey (Lu et al, Vaccine 27:882-7); 2008-13: NHIS (Am J Prev Med 40:e1-6 & MMWR February 5, 2016 / 65(1);1–36), 2016 CDC, unpublished

# **Recombinant Zoster Vaccine - Shingrix**

## **2** components

- Glycoprotein E recombinant protein
- Adjuvant ASO1<sub>B</sub>

# Efficacy & safety evaluated in 2-part, phase III RCT >30,000 subjects

## **FDA licensure on Oct 20, 2017**

https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm

## **Zoster vaccines – Important Differences!**

Zoster vaccine	Storage	Route of injection	Doses in Series
RZV (shingrix)	Refrigerator	IM	2
ZVL (zostavax)	Freezer	SQ	1

Improperly stored vaccine is useless!



ACIP Recommendations Zoster vaccines – General Use

 RZV (shingrix) may be used in adults aged ≥50 years, irrespective of prior receipt of varicella vaccine or ZVL (zostavax), and does not require screening for a history of chickenpox (varicella). ZVL remains a recommended vaccine for prevention of herpes zoster in immunocompetent adults aged  $\geq 60$  years.



## **RZV** is recommended for immunocompetent adults aged ≥50 years.

#### □ Benefits:

- High vaccine efficacy against HZ
  - **97%** (50-69 yrs)
  - **91%** (≥70 yrs)
- High vaccine efficacy against PHN (91% for ≥50 year olds)
- Efficacy ≥ 85% for 4 years following vaccination in ≥ 70 year olds

**Harms**:

- Serious adverse events No differences detected between vaccinated and comparison populations
- Grade 3 reactions more commonly reported in vaccinated groups (17%) compared to placebo (3%) 9

### RZV is preferred over ZVL (but no head-to-head trial)

#### Efficacy

□ Estimates of efficacy against HZ higher across all age groups:

- 60-69 years: 97% vs. 64%
- **70-79 years:** 91% vs. 41%
- >80 years
  91% vs.
  18%

□ Waning apparently slower than ZVL over the first 4 years

Expected to prevent many more cases of HZ and PHN compared to ZVL

#### **Adverse Effects**

Neither vaccine is associated with serious adverse events in immunocompetent persons
 RZV is more reactogenic than ZVL

#### **Economics**

□ Model - RZV prevents more disease, decreases overall costs (vaccine + expected disease)

# HZ - Vaccine efficacy and effectiveness for RZV and ZVL, by age group, during the first 4<sup>‡</sup> years following vaccination



■ RZV (ZOE 50/70)^ ■ ZVL (RCTs\*) ■ ZVL (Baxter 2017) ■ ZVL (Izurieta 2017)

<sup>‡</sup> Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

- ^ ZOE 50/70= 50-59 & 60-69yr: Lal 2015, 70+yrs: Cunningham 2016
- \* RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,

# <u>PHN</u> - Vaccine efficacy and effectiveness for RZV and ZVL, in adults 70 years and older during the first 4 years following vaccination



^ Pooled ZOE 50/70: Cunningham 2016

\* Shingles Prevention Study: Oxman 2005,

#### **<u>HZ</u>** - Vaccine efficacy for ZVL and RZV, by year following vaccination



Note: The Shingles Prevention Study, Short-term Persistence Study, and Long-term Persistence Study followed the same study population over time.

RZV is recommended for immunocompetent adults who previously received zoster vaccine live (ZVL)

- ~20 million people have been vaccinated with ZVL and potentially eligible for RZV<sup>1</sup>
- In a small study, vaccination with RZV 5 yrs following ZVL did not alter the safety or immunogenicity of RZV.
- Cost-effectiveness ratio of revaccination at a minimal interval (~8 weeks\* post ZVL) is similar to or lower than other adult vaccines:
  - \$15,000 /QALY (80-89 yrs) to \$117,000 /QALY (50-59 yrs)

<sup>1.</sup> Source: IMS

<sup>\*</sup> Revaccination at 8 weeks was approximated in the CEA model by revaccination immediately following ZVL

- Following dose #1 of RZV, dose #2 should be given 2–6 months later.
  - If dose #2 of RZV is given <4 weeks after #1, repeat dose #2.
  - 2 doses of RZV are necessary regardless of prior history of herpes zoster or prior receipt of ZVL.
  - Based on expert opinion, RZV should not be given <2 months after prior receipt of ZVL.



## ACIP Recommendations Zoster vaccines – History of Zoster

- Persons with a history of zoster should receive shingles vaccine.
- If a patient is experiencing an episode of herpes zoster, vaccination should be delayed until the acute stage of the illness is over and symptoms abate.



## ACIP Recommendations Zoster vaccines – Co-morbidity

- Persons with <u>chronic medical conditions</u> (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) should receive RZV.
- Immunocompromised persons. No recommendations yet
   To be discussed as additional data become available.



**ACIP Recommendations Zoster vaccines – Recap** 

- Age 50 years and older
- Administer 2 doses of RZV 2–6 months apart regardless of
  - past episode of herpes zoster, or
  - receipt of past doses of ZVL
    - wait at least 2 months after ZVL before dose of RZV.

## Age 60 years or older

- Administer either RZV (preferred) or ZVL
  - wait at least 2 months after ZVL before dose of RZV



# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

### CONTRAINDICATION

History of severe allergic reaction, such as anaphylaxis, to any component of RZV

### PRECAUTIONS

Current herpes zoster infectionPregnancy and breastfeeding

# Shingrix- Recombinant Zoster Vaccine (RZV) Reactogenicity

### Before vaccination, counsel about expected reactogenicity

- pain (78%)
- myalgia (45%)
- fatigue (45%)

**□** Reactions to 1st dose didn't predict reactions to 2nd dose

□ Vaccine recipients should be encouraged to complete the series even if they experienced a grade 1–3 reaction to the first dose.

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

## **RZV** may be co-administred with other vaccines

- RZV+ QIV (Fluarix) -- no interference or safety problems
- RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix)— studies ongoing
- RZV+ Fluad– have not been studied
- https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm

## Improperly stored vaccine is useless!

Zoster vaccine	Storage	Route of injection	Doses in Series
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# Mumps

- Outbreaks in 2016 and 2017
  - Mostly in young adults in college settings.
  - Also, >3,000 cases in Arkansas outbreak
  - Intensity of exposure to the virus in close-contact settings (such as a college campus)



\* Case count is preliminary and subject to change.

\*\*Cases as of January 27, 2018. Case count is preliminary and subject to change.

Source: Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables

https://www.cdc.gov/mumps/outbreaks.html

#### Mumps Cases in U.S., by Year



## **Other Changes to Schedule - Mumps**

 Persons ≥12 months who previously received ≤2 doses of mumps-containing vaccine and are identified by public health authorities to be at increased risk during a mumps outbreak should receive a dose of mumps-virus containing vaccine.



# **ACIP Updates – Adult Hepatitis B Prevention**

Reminder to vaccinate persons with chronic liver disease

- Hepatitis C virus [HCV] infection
- Cirrhosis
- Fatty liver disease
- Alcoholic liver disease
- Autoimmune hepatitis
- ALT or AST level greater than twice the upper limit of normal



## Low coverage rates, HAV + HBV vaccines

2014 and 2015 National Health Interview Surveys Adults aged ≥ 18 years self-reporting receipt of vaccines

HAV

- 19% ≥1 dose 12% ≥2 doses Chronic Liver Disease (CLD)
- 15% ≥1 dose
   9% ≥2 doses
   No CLD

HBV

- 36% ≥1 dose 29% ≥3 doses CLD
- 30% ≥1 dose 25% ≥3 doses No CLD



## Hepatitis A Outbreak Cases as of 11/10/17 Hospitalization or Death for Persons with CLD

	San Diego	Santa Cruz	Los Angeles
Start of outbreak	11/2016	4/2017	9/2017
Cases	546	76	11
Deaths	20	1	0
Homeless or illicit drug use (%)	69%	81%	55%
Hospitalized (%)	68%	43%	73%
HCV or HBV coinfection (%)	19%	39%	_
Male (%)	68%	63%	91%
Median age (years)	43	37	40

# **New Hepatitis B Vaccine for Adults**

- Single-antigen HepB (HEPLISAV-B, Dynavax Technologies Corp.)
- 11/2017: Licensed by FDA for persons ≥ 18y years of age
- 2/2018: ACIP voted to recommend published recommendations to follow
- Joins other inactivated HBV vaccines in U.S
  - Engerix-B, Recombivax HB, Pediarix, Twinrix
- Yeast-derived recombinant HBsAg
- 1018 adjuvant
  - 22-mer oligonucleotide sequence containing CpG that binds Toll-like receptor 9 to stimulate directed immune response
- <u>2 doses</u> given at least 1 month apart



## Heplisav-B – Seroprotection and Safety

#### Immunogenicity

- Healthy: 90%–100% vs. 71%–90% (3 doses Engerix-B)
- Diabetes Type II: 90% vs. 65% (3 doses Engerix-B)
- Chronic kidney disease: 90% (3 doses) vs.

#### Safety and reactogenicity

- Mild adverse events
   46% vs.
   46% (Engerix-B)
- Serious adverse events 5% vs. 6% (Engerix-B)
- Cardiovascular events 0.27% vs. 0.14% (Engerix-B)
- Potentially immune-mediated events (e.g., granulomatosis + polyangiitis, Grave's disease)

0.1%–0.2% vs. 0%–0.7% (Engerix-B)

81% (4 double doses Engerix-B)

Jackson S, Lentino J, Kopp J, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. Vaccine 2017; 36:668-74

Janssen R, Bennett S, Namini H, et al. Immunogenicity and Safety of Two Doses of Investigational Heplisav Compared to Three Doses of Licensed Hepatitis B Vaccine (Engerix-1) in Two Phase 3 Trials. Journal of Hepatology 2013; 58(Suppl 1):S574

HEPLISAV-B™ [Hepatitis B Vaccine (Recombinant), Adjuvanted] package insert. https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UC

# Influenza – 2/18 ACIP Meeting

- Live attenuated influenza vaccine returns as an one of many vaccine options for 2018-2019 influenza season
- 2017-18 (A/Slovenia) vs. 2015-16 (A/Bolivia) H1N1 strains
  - Increased reproduction in human cells, more immunogenic
  - No effectiveness data yet

• License indication unchanged: healthy, 2-49 years of age



# Influenza vaccine 2018-2019 season

 WHO recommends that vaccines for use in the 2018-2019 northern hemisphere influenza season contain:

## Trivalent

- A/Michigan/45/2015 (H1N1)pdm09-like virus;
- A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus CHANGE
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage) CHANGE

#### Quadrivalent - above +

B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)



# **Hepatitis A Post-exposure Prophylaxis**

ACIP vote February 22, 2018 – not final until published

- Ages 12 months and older Hep A vaccine
- Ages 40 years and older
  - Hep A vaccine
  - +/- Immune globulin, "depending on the provider's risk assessment."
- Age 6-12 months travelling internationally
  - Early Hep A vaccine dose
  - + regular 2-dose series on or after 1<sup>st</sup> birthday



## **Thank you - Questions?**

Many thanks to following CDC staff for sharing their slides:

- Kathleen Dooling, MD MPH
- David Kim, MD

ZosterHepatitis B



# Shingrix Rollout for VFA Providers

- Availability of vaccine
  - Timeline uncertain at this time but vaccine should be available in Q2 or Q3 ordering period
  - Reminder it is a 2 dose series licensed down to 50 yrs of age
- Letter describing vaccine recommendations and availability will be released in upcoming weeks
- VFA providers should continue to offer Zostervax until Shingrix is available—do not miss opportunities to vaccinate VFA-eligible patients

## Key Differences Between Zoster IZs

	Shingrix (RZV)	Zostavax (ZVL)
Storage	Refrigerator (between 36°F and 46°F) - Store both vials together in refrigerator before reconstitution. DO NOT FREEZE.	Freezer (between -58°F and +5°F) for powder containing vial. Diluent should be stored at room temperature or refrigerator.
Vaccine Type	Recombinant, adjuvanted (non-live)	Live
Route of Administration	Intramuscular (IM) – 0.5ml / dose	Subcutaneous (SQ) – 0.65ml / dose
Dose Interval	2 dose series, spaced 2 to 6 months apart*	Single dose
Recommended Age	≥ 50 years**	≥ 60 years (FDA licensure is ≥ 50 years)

\*Minimum interval for Shingrix immunization after Zostavax is 8 weeks.

\*\*Even people who have had shingles or previously got Zostavax can be vaccinated with Shingrix.

**Thank you - Questions?** 

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