Zoster Vaccines Session: Introduction of the Evidence to Recommendations Framework for Use of Recombinant Zoster Vaccine in Immunocompromised Adults

ACIP Meeting
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Background

- Risk of herpes zoster (HZ), severe disease, and complications generally higher in immunocompromised (IC) populations
- IC populations are very heterogeneous, both within and across groups
- Zostavax, a live, attenuated HZ vaccine, was contraindicated for persons with IC conditions
- Recombinant zoster vaccine (RZV, Shingrix) can potentially address need in IC populations
How many IC persons in the United States?*

- ~7 million IC adults\(^1\)

- ~3 million among:
  - Hematopoietic stem cell transplant patients\(^2\)
  - Patients with hematologic malignancies\(^3\)
  - Renal or other solid organ transplant recipients\(^4\)
  - Patients with solid tumor malignancies\(^3,5\)
  - Individuals living with HIV\(^6\)

- ~22 million with autoimmune and/or inflammatory (AI) conditions\(^7\)
  - >80 diverse conditions (e.g., systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease)
  - Often have underlying immune defects, but generally not considered frankly IC unless iatrogenic (i.e., on IC treatments)

*References on slide 18
Current ACIP Recommendations

- ACIP recommended RZV in October 2017 for use in immunocompetent adults aged ≥50 years

- Immunocompromised persons:
  - ACIP recommends use of RZV in persons
    - Taking low-dose immunosuppressive therapy
    - Anticipating immunosuppression or who have recovered from an immunocompromising illness
  - Because IC persons and those on moderate to high doses of immunosuppressive therapy were excluded from RZV efficacy studies, ACIP has not made recommendations on use of RZV in these patients

RZV Updates

- European Medicines Agency approved an expanded indication on August 25, 2020
  - Shingrix now approved in the European Union for prevention of herpes zoster (HZ) and postherpetic neuralgia (PHN) in adults 50 years of age or older, and adults 18 years of age or older at increased risk of HZ

- Supplemental biologics license application submitted to FDA to support use in immunocompromised adults 18 years of age or older
  - [https://www.gsk.com/media/6189/q3-2020-results-announcement.pdf](https://www.gsk.com/media/6189/q3-2020-results-announcement.pdf)
Evidence to Recommendations (EtR) Framework: Policy Question

- Plan to split the policy question into two parts

Should vaccination with RZV be recommended for immunocompromised adults 19 years of age and older?

- 19–49 years
- 50+ years
EtR Framework: PICO Question

- **Population:** Immunocompromised adults ≥19 years of age
- **Intervention:** RZV, 2 doses at least 4 weeks apart
- **Comparison:** No vaccine
- **Outcomes**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Harms</th>
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<tr>
<td>Prevent HZ</td>
<td>Serious adverse events</td>
</tr>
<tr>
<td>Prevent PHN</td>
<td>Critical</td>
</tr>
<tr>
<td>Prevent HZ-related</td>
<td>Immune-mediated disease</td>
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<tr>
<td>hospitalization</td>
<td>Reactogenicity (Grade 3)</td>
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- Important

- Critical
Immunocompromised Populations under Consideration

1. Hematopoietic stem cell transplant patients (HCT)
2. Patients with hematologic malignancies (HM)
3. Renal or other solid organ transplant recipients (SOT)
4. Patients with solid tumor malignancies (STM)
5. Individuals living with HIV
6. Patients with primary and acquired immunodeficiencies or immunosuppression not covered in groups 1 through 5 (e.g., AI conditions)
## EtR Framework

<table>
<thead>
<tr>
<th>EtR Domain</th>
<th>Question</th>
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<tbody>
<tr>
<td><strong>Public Health Problem</strong></td>
<td>Is the problem of public health importance?</td>
</tr>
<tr>
<td><strong>Benefits and Harms</strong></td>
<td>How substantial are the desirable anticipated effects?</td>
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<tr>
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<tr>
<td></td>
<td>Do the desirable effects outweigh the undesirable effects?</td>
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<tr>
<td><strong>Values</strong></td>
<td>Does the target population feel the desirable effects are large relative to the undesirable effects?</td>
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<td>Is there important variability in how patients value the outcomes?</td>
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<td><strong>Acceptability</strong></td>
<td>Is the intervention acceptable to key stakeholders?</td>
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<tr>
<td><strong>Feasibility</strong></td>
<td>Is the intervention feasible to implement?</td>
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<tr>
<td><strong>Resource Use</strong></td>
<td>Is the intervention a reasonable and efficient allocation of resources?</td>
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<tr>
<td><strong>Equity</strong></td>
<td>What would be the impact of the intervention on health equity?</td>
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Public Health Importance: Risk of HZ in IC Groups 1–5

- Median HZ incidence estimates for these IC groups exceeded those reported for immunocompetent adults aged >50 years
  - Variation in study estimates for cumulative incidence and incidence of HZ within each IC group
- HZ complications and severe disease
  - Increased in IC populations
  - Data insufficient to assess risk by group


Figure 3. Herpes zoster incidence rates among patients with selected immunocompromising conditions. *Studies with low or medium risk of bias.
Public Health Importance: Risk of HZ in IC Group 6 (Figure: AI Conditions)

- ~1.5 to 2.0-fold higher risk in patients with AI conditions than in healthy individuals
- Risk varied across conditions and by age groups
- Age-standardized HZ incidence rates varied
  - 19.9 per 1,000 person-years (SLE)
  - 6.8 per 1,000 person-years (gout)

Figure 3. Age- and sex-standardized incidence rates (IRs) of HZ per 1,000 person-years, standardized to the values in the 2010 US Census population, among adults ages ≥20 years. Bars show the IRs of HZ with 95% confidence intervals. Cohorts of healthy adults without autoimmune diseases or diabetic conditions and adult patients with diabetes were used as controls. SLE = systemic lupus erythematosus; IBD = inflammatory bowel disease; RA = rheumatoid arthritis; PsA = psoriatic arthritis; PsO = psoriasis; AS = ankylosing spondylitis.

Work Group Interpretation

- Are HZ and HZ complications in IC adults of public health importance?
  - Yes

- Summary of work group discussions
  - IC populations are very heterogeneous, both across and within groups
  - Risk of HZ and HZ complications generally higher in IC populations, although there is variability across and within IC groups
  - Not feasible to define every possible IC condition/medication combination
  - Important to consider broad recommendations and appropriate guidance for IC populations
EtR Framework: Next Steps

- Presentation on HZ in IC adults planned for next ACIP meeting
- Review available evidence regarding use of RZV in IC adults to address remaining EtR domains
  - Benefits and Harms
  - Values
  - Acceptability
  - Feasibility
  - Resource Use
  - Equity
EtR Framework: Next Steps, cont.

- Review knowledge, attitudes, and practices
- GRADE analysis
- Cost effectiveness analysis of use of RZV in IC populations
- Update EtR Framework
Question for ACIP

- Do ACIP members have any questions or feedback regarding the initial EtR Framework for use of RZV in IC adults?
Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Backup slides
## IC Populations: Groups 1–5

<table>
<thead>
<tr>
<th>IC Condition</th>
<th>Incident Cases (New cases per year)</th>
<th>Prevalent Cases</th>
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<tbody>
<tr>
<td>Hematopoietic stem cell transplant(^1)</td>
<td>23,379</td>
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<tr>
<td>Hematologic malignancy(^2)</td>
<td>~176,200</td>
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<tr>
<td>Solid organ (including renal) transplant(^3)</td>
<td>58,532</td>
<td>~591,000</td>
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<td>Solid tumor on chemotherapy(^2,4)</td>
<td>~1,200,000</td>
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<tr>
<td>HIV infection(^5)</td>
<td>38,739</td>
<td>1,008,929</td>
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<tr>
<td><strong>Total</strong></td>
<td>~1,496,850</td>
<td>~1,599,929</td>
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