HIV and Prevention of Herpes Zoster

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Case

37-year-old man with Stage 3 HIV, initial CD4 count 76 and HIV RNA 170,000, presents 3 weeks after starting dolutegravir and tenofovir/emtricitabine with a painful rash.
Case

He is prescribed valacyclovir 1g tid x 10 days for this infection. He asks how can this be prevented in the future. Which of the following would you offer?

1. Nothing – it cannot be prevented
2. Acyclovir 400mg po bid for prophylaxis
3. Zoster vaccine
Zoster and HIV

- HIV+ individuals have higher rates of herpes zoster (12-17 fold higher incidence)
- Even with ART, zoster incidence 2-3 fold higher than in HIV- persons
- Higher rates noted immediately after ART initiation (immune reconstitution)
Acyclovir Prophylaxis Reduces the Incidence of Herpes Zoster Among HIV-Infected Individuals: Results of a Randomized Clinical Trial

Ruanne V. Barnabas,1,2,3,6 Jared M. Baeten,1,2,3 Jairam R. Lingappa,1,2 Katherine K. Thomas,1 James P. Hughes,4,5 Nelly R. Mugo,1 Sinead Delany-Morettwe,7 Glenda Gray,9 Helen Rees,7 Andrew Mujugira,1,3 Allan Ronald,10 Wendy Stevens,8 Saidi Kapiga,11 Anna Wald,1,2,5,8 and Connie Celum1,2,3, for the Partners in Prevention HSV/HIV Transmission Study Team

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Acyclovir for VZV Prophylaxis


• Acyclovir 400 bid for HIV/HSV co-infected men and women

• Outcome – incident VZV reactivation (by exam or self-report) in pts not on ART with CD4 counts >250, no ADIs

Barnabas RV et al. J Infect Dis 2015
Acyclovir for VZV Prophylaxis

• 1693 acyclovir and 1688 placebo
• 2/3 participants women, median age 32, median CD4 count 462

• 4% incidence in year prior to enrollment in both groups
• 1% had VZV on baseline exam at time of enrollment

• Adherence to acyclovir was high (96% by pill count and self report)
Acyclovir for VZV Prophylaxis

- 95 incident cases of herpes zoster during study
  - 26 events in 22 patients in acyclovir arm
    - 1.00 case/100 person-yrs
  - 69 events in 64 patients in placebo arm
    - 2.68 case/100 person-yrs

- Acyclovir prophylaxis decreased incidence of herpes zoster by 62%
Acyclovir for VZV Prophylaxis

Barnabas RV et al. J Infect Dis 2015
Acyclovir for VZV Prophylaxis

• Caveats:
  - Acyclovir did not prevent herpes zoster in patients with prior episodes
    • Possibly related to specific VZV T cell immune deficits
    • Authors suggest pts may need higher doses of acyclovir for prevention
  - No patients with low CD4 counts included in study
Zoster Vaccine:
2008 ACIP Recommendations

Study Design
N = 38,546
Adults ≥ 60
Randomized, double-blind
Followed for mean 3.1 yrs
Single dose vaccine vs placebo

Decreased Herpes Zoster by 51.3%
Decreased PHN by 66.5%

Oxman MN et al. NEJM 2005;352:2271-84
Age Specific Recommendations:

All persons $\geq 60$ years*
- Excludes those with contraindications to live vaccine
- Includes those with history of zoster or have chronic medical conditions

Dose:
Single dose
HIV and Zoster Vaccine

- Contraindicated for patients with CD4 counts < 200
- Safe and immunogenic in adults with CD4 counts > 200 and viral load < 75 copies/mL (Benson C et al. Abstr #96. CROI 2012)
- No recommendations in patients with CD4 counts > 200, except Primary Care Guidelines recommend considering for age >60 with CD4 >200
• October 2008: the ACIP recommended a dose of HZV for all adults $\geq 60$ years unless they have contraindications.

• March 2011: FDA approved use of Zostavax in adults aged 50-59 years.

• **Should we be administering HZV at ages 50-59 years?**
HZ Incidence by Age:
Olmsted County, MN, 1996-2001

Source: Yawn 2007
Proportion of HZ Progressing to PHN*, by Age: Olmsted County, MN, 1996-2001

*PHN defined as ≥ 90 days of pain

Source: Yawn 2007
Rate of HZ-Related Hospitalization by Age: Connecticut, 1986-1995

74% of HZ-related hospitalizations in persons ≥60 years

Source: Lin 2000
Herpes Zoster (Shingles) Vaccine Coverage Among US Adults National Health Interview Survey, 2008-2012

National Immunization Survey (NIS), 2007; National Health Interview Survey (NHIS), 2008-2012
Cumulative Number of PHN* Cases by Vaccination Strategy

* PHN = moderate to severe pain lasting >90 days  Ortega-Sanchez. ACIP OCT 2013
## Cost-Effectiveness Summary by Strategy (Societal Perspective)

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<tr>
<th>Vaccinate at</th>
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<td>50</td>
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<tr>
<th>Metric</th>
<th>Vaccinate at 50</th>
<th>Vaccinate at 60</th>
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<tr>
<td>Net cost*</td>
<td>$178.5 Million</td>
<td>$169.0 Million</td>
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<tr>
<td>Cost per HZ prevented</td>
<td>$11,255</td>
<td>$8,455</td>
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<td>Cost per PHN prevented</td>
<td>$61,084</td>
<td>$19,761</td>
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<td>Cost per QALY saved **</td>
<td>$271,713</td>
<td>$79,967</td>
<td>$38,191</td>
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* NC = Cost of Vaccination Program - Savings in Cost-of-Illness from Vaccination

** Does not including indirect cost savings
ACIP Recommendations

- Affirms existing recommendation for routine vaccination of persons 60 years of age and older
  - Burden of HZ disease increases with age
  - HZ vaccine administration should be timed to achieve the greatest reduction in burden of HZ and its complications
  - There is insufficient evidence for long term protection offered by the HZ vaccine
  - Providers should counsel persons who are vaccinated at 50-59 years of age that the duration of protection offered by the vaccine is uncertain; therefore they may not be protected when the incidence of HZ and its complications are highest.
VZV & HIV

• Higher VZV incidence in patients with HIV

• There may be a role for acyclovir prophylaxis but perhaps not in patients with prior disease

• Vaccine efficacy unclear but likely safe in patients with CD4 counts >200
Questions?
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