Zoster Vaccines Session: Burden of Herpes Zoster in Immunocompromised Adults

ACIP Meeting

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Current ACIP Recommendations

- **ACIP recommended recombinant zoster vaccine (RZV, Shingrix) in Oct 2017 for use in immunocompetent adults age ≥50 years**
- **ACIP recommendations include use of RZV in persons**
  - Taking low-dose immunosuppressive therapy
  - Anticipating immunosuppression or who have recovered from an immunocompromising illness

Dooling et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103–108. DOI: http://dx.doi.org/10.15585/mmwr.mm6703a5.

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
- **RZV can potentially address an unmet need for HZ prevention in IC populations**

How many IC persons in the United States?*

- **~7 million IC adults[1]**
- **~3 million among:**
  - Hematopoietic stem cell transplant recipients[2]
  - Patients with hematologic malignancies[3]
  - Renal or other solid organ transplant recipients[4]
  - Patients with solid tumor malignancies[3,5]
  - People 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 dysfunction, but generally not considered frankly IC unless iatrogenic (i.e., on IC treatments)

*References on slide 20

IC Populations under Consideration

1. **Hematopoietic stem cell transplant (HCT) recipients**
2. **Patients with hematologic malignancies (HM)**
3. **Renal or other solid organ transplant (SOT) recipients**
4. **Patients with solid tumor malignancies (STM)**
5. **People living with HIV**
6. **IC populations at increased risk of HZ not covered in groups 1 through 5** (i.e., patients with primary immunodeficiencies, patients with autoimmune conditions, patients taking immunosuppressive medications)

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	Is the problem of public health importance?
Benefits and Harms	How substantial are the desirable anticipated effects?
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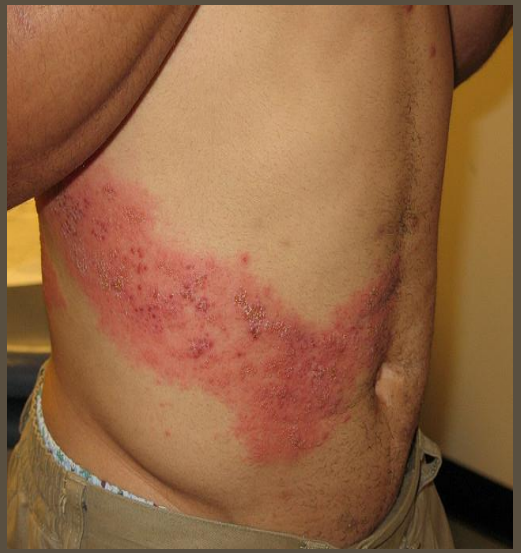
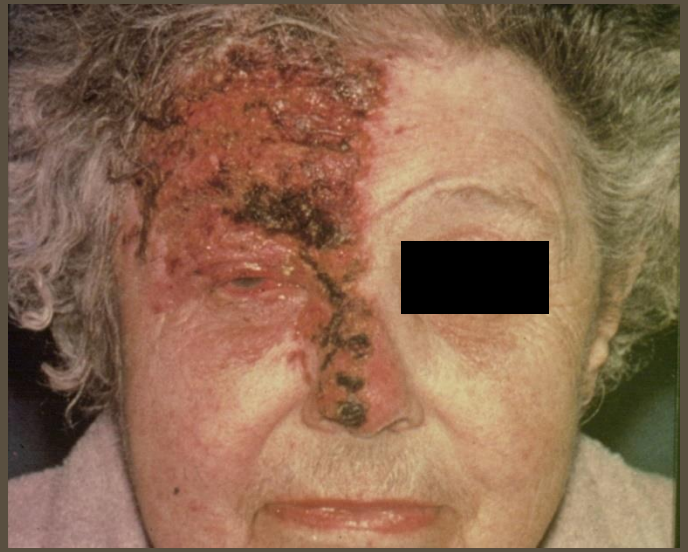
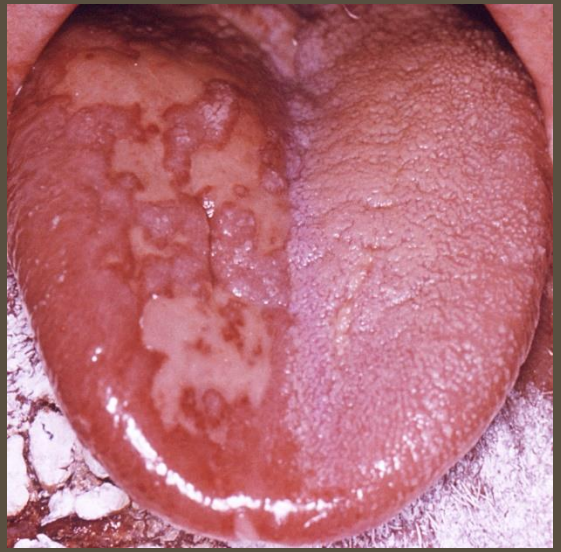
	Do the desirable effects outweigh the undesirable effects?
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?
	Is there important variability in how patients value the outcomes?
Acceptability	Is the intervention acceptable to key stakeholders?
Feasibility	Is the intervention feasible to implement?
Resource Use	Is the intervention a reasonable and efficient allocation of resources?
Equity	What would be the impact of the intervention on health equity?



Courtesy of NIAID



Courtesy of MN Oxman UCSD/San Diego VAMC



Courtesy of CDC/Robert Sumpter

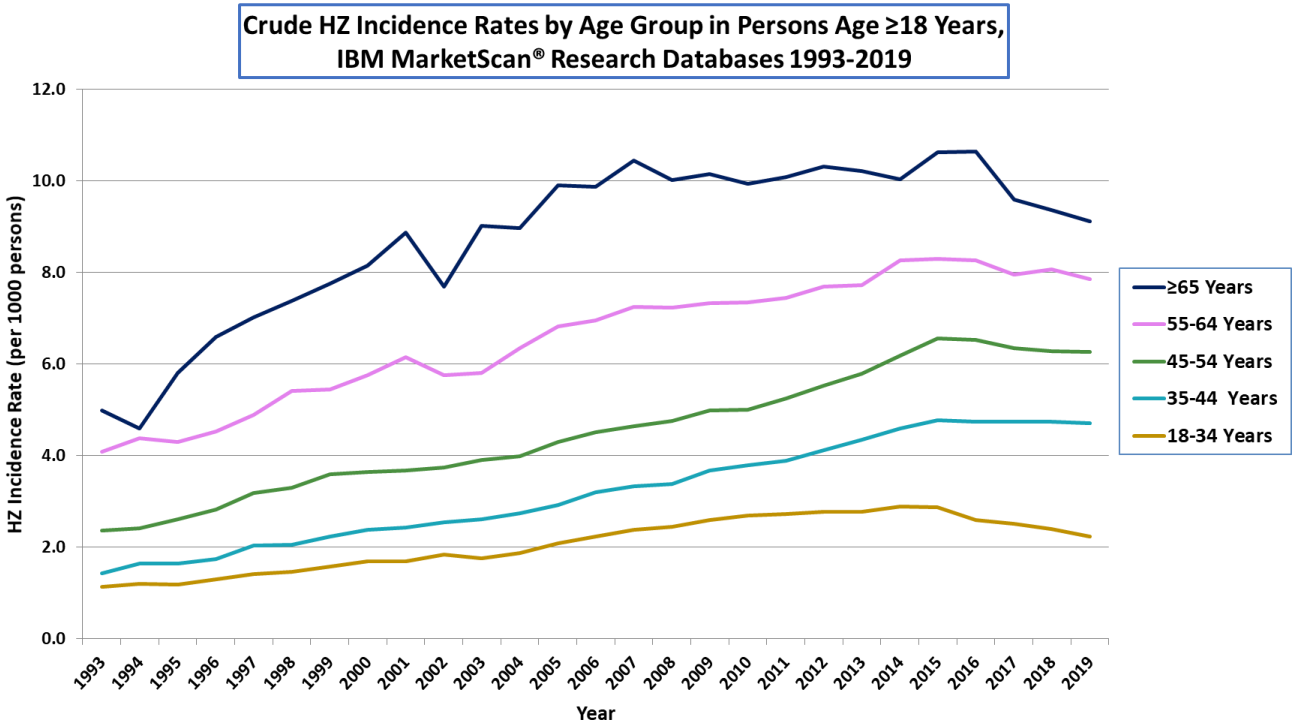
Clinical Presentations of Herpes Zoster

“Five years later, I still take prescription medication for pain. My shingles rash quickly developed into open, oozing sores that in only a few days required me to be hospitalized. I could not eat, sleep, or perform even the most minor tasks. It was totally debilitating. The pain still limits my activity levels to this day.”

—A 63-year-old harpist who was unable to continue playing due to shingles
https://www.cdc.gov/shingles/about/complications.html

HZ Incidence Common in Adults and Increases with Age

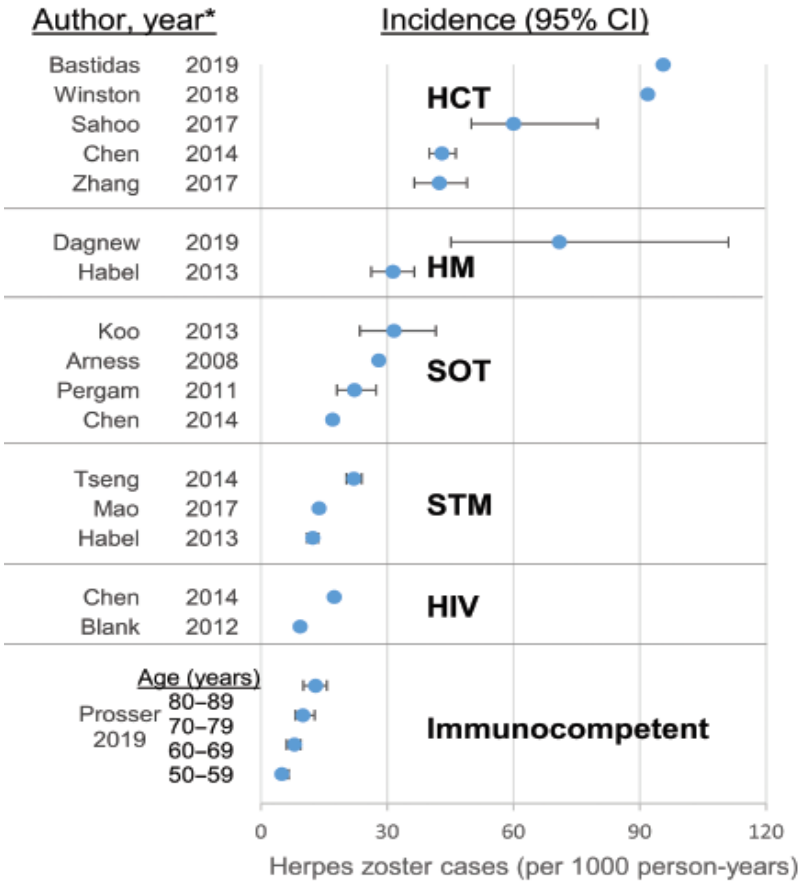
~1 million HZ cases per year in U.S. during pre- HZ vaccine era[1]



1. Harpaz et al. Prevention of Herpes Zoster, *MMWR*, June 6, 2008, Vol 57, #5
2. CDC, unpublished data; Updated from Harpaz et al. *Clinical Infectious Diseases*, Volume 69, Issue 2, 15 July 2019, Pages 341–344, https://doi.org/10.1093/cid/ciy953

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 >50 years**



McKay et al. Herpes zoster risk in immunocompromised adults in the United States: A systematic review. CID 2020;71(7):e125–34.

Figure 3. Herpes zoster incidence rates among patients with selected immunocompromising conditions. *Studies with low or medium risk of bias.

Public Health Importance
Severity of HZ in IC Groups 1–5

- **Postherpetic neuralgia (PHN)**
  - **~6–10%** vs ~4% overall in administrative claims databases[1]
  - Between **6% and 45%** across IC conditions and studies[2]
- **Disseminated HZ:**
  - **~3%**[2] of IC, but exceedingly uncommon in healthy persons
  - **10–17%** mortality associated with disseminated HZ among renal transplant recipients[3,4]
- **Hospitalization: 8%** of HCT recipients with HZ[5] vs ~<1% of overall Medicare beneficiaries with HZ[6]

[1]**Chen et al.** Incidence of herpes zoster in patients with altered immune function. Infection 2014; 42(2): 325–34; [2]**McKay et al.** Herpes zoster risk in immunocompromised adults in the United States: A systematic review. CID 2020;71(7):e125–34; [3]**Rommelaere et al.** Disseminated varicella zoster virus infection in adult renal transplant recipients: Outcome and risk factors. Transplantation Proceedings. 2012; 44(9): 2814-2817; [4]**Kirnap et al.** Prevalence and outcome of herpes zoster infection in renal transplant recipients. Exp Clin Transplant. 2015; Apr;13 Suppl 1:280-3; [5]**Winston et al**. Inactivated varicella zoster vaccine in autologous haemopoietic stem-cell transplant recipients: an international, multicentre, randomised, doubleblind, placebo-controlled trial. Lancet (London, England) 2018; 391(10135): 2116–27; [6]**Izurieta et al.** Effectiveness and duration of protection provided by the live-attenuated herpes zoster vaccine in the Medicare population ages 65 years and older. CID 2017;64(6):785–93.

Antiviral Prophylaxis

- Antiviral prophylaxis is recommended post-transplant
  - **No universal standard prophylactic regimen for transplant recipients, and antiviral drug, duration, and dosage vary**
  - Studies of patients post HCT with follow up >2 years revealed that **HZ incidence increases once prophylaxis is discontinued**
- ACIP General Best Practice Guidelines, Altered Immunocompetence
  - Most inactivated vaccines should be initiated 6 months after HCT

https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html

IC Populations under Consideration

1. Hematopoietic stem cell transplant (HCT) recipients
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3. Renal or other solid organ transplant (SOT) recipients
4. Patients with solid tumor malignancies (STM)
5. People living with HIV
6. **IC populations at increased risk of HZ not covered in groups 1 through 5**
   - Patients with primary immunodeficiencies
   - Patients with autoimmune (AI) conditions
   - Patients taking immunosuppressive medications

Public Health Importance

Risk of HZ in IC Group 6

- **~2 to 4-fold higher risk** in patients with AI conditions than in healthy individuals[1]
- **~1.5-fold higher risk** for unvaccinated Medicare beneficiaries with AI conditions vs not IC[2]

Age and sex-standardized HZ incidence rates, among adults ≥20 years with selected autoimmune diseases

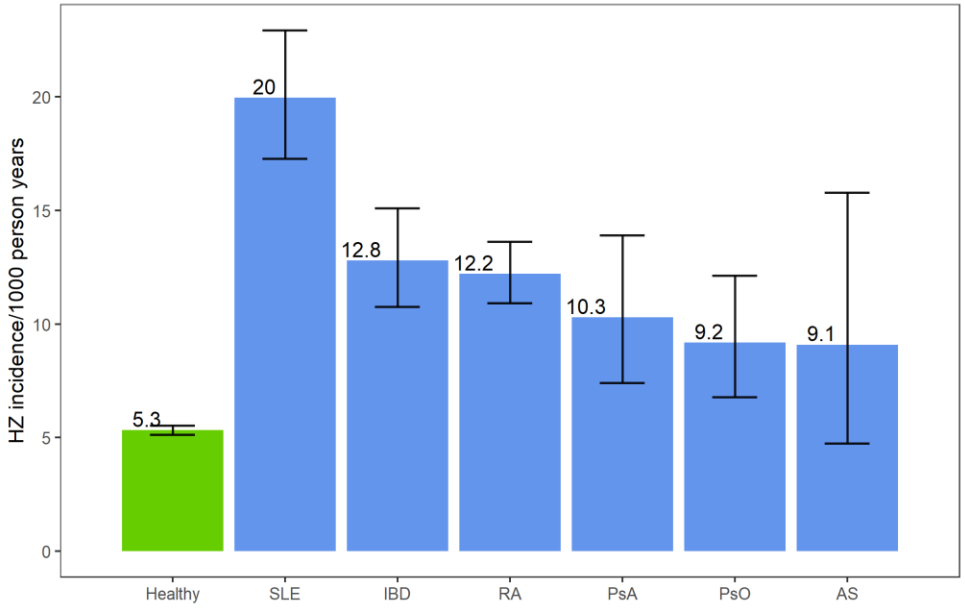


Figure adapted from Yun et al. Bars show the IRs of HZ with 95% confidence intervals. Cohorts of healthy adults without autoimmune diseases or diabetic conditions and adult patients with diabetes were used as controls. SLE=systemic lupus erythematosus; IBD=inflammatory bowel disease; RA=rheumatoid arthritis; PsA=psoriatic arthritis; PsO=psoriasis; AS=ankylosing spondylitis.

1. **Yun et al.** Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases. Arthritis & Rheumatology 2016;68(9):2328-2337.
2. **Izurieta et al.** Recombinant Zoster Vaccine (Shingrix) real-world effectiveness in the first two years post-licensure. Clinical Infectious Diseases, 2021;, ciab125, https://doi.org/10.1093/cid/ciab125

Group 6 Examples: SLE, IBD, and RA

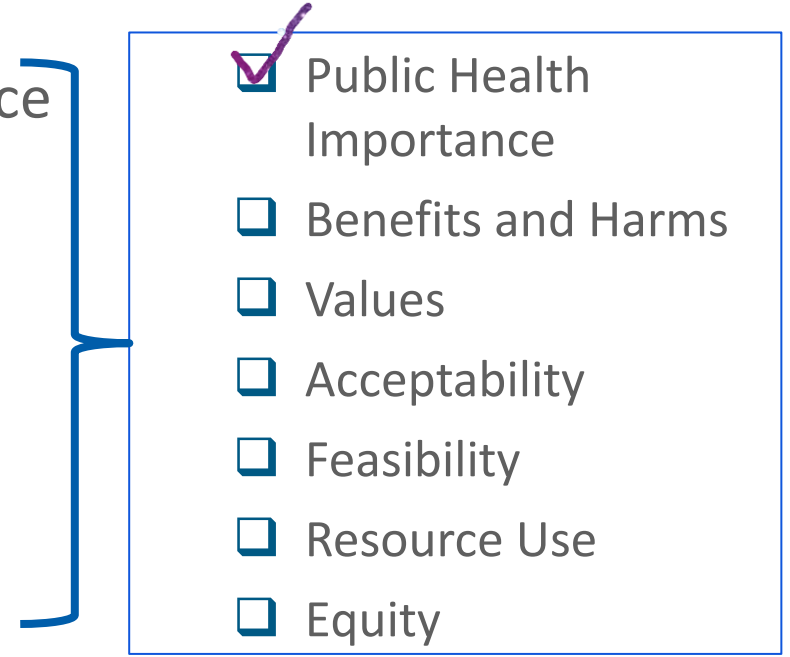
- **Disease burden**
  - HZ risk ~2 to 4-fold higher
  - Age-specific incidence rates among 21–50-year-olds comparable or substantially higher than corresponding rates in healthy adults >60 years
- **Impact of immunosuppressive treatments**
  - Standard of care for patients to be on ≥1 IC drugs
  - Not possible to define high risk subgroups based on anticipated drugs
    - Disease modifying antirheumatic drugs, or DMARDs (e.g., methotrexate)
    - Glucocorticoids
    - Biologics (e.g., Janus Kinase inhibitors)

Work Group Interpretation

- **Are HZ and HZ complications in IC adults ≥19 years of public health importance?**
  - Yes
- **Summary of work group discussions**
  - IC populations are very heterogeneous, both across and within groups and among individuals over time
  - 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

- GRADE analysis of existing evidence of RZV benefits and harms
- Review knowledge, attitudes, and current practices for RZV in IC populations
- Cost effectiveness analyses of use of RZV in IC populations



Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Backup Slides

Slide 4 References

1. Harpaz R, Dahl RM, Dooling KL, JAMA, 2016, 316(23):2547-8.
2. D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018. Available at https://www.cibmtr.org.
3. American Cancer Society, https://cancerstatisticscenter.cancer.org; 2019 incidence estimates.
4. United Network for Organ Sharing, https://unos.org/data/transplant-trends/#transplants_by_organ_type+year; 2018, Renal= Kidney + Kidney/Pancreas, Solid organ = all listed.
5. Halpern MT, Yabroff KR, Cancer Invest, 2008, 26(6):647-51; Derived from Halpern and Yabroff 2000-2004 data on chemo/radiotherapy among all patients with cancers, adjusted based on proportion of all cancers in 2007 due to solid organ cancers, further adjusted by projections that solid cancers increased by 20% between 2007 and 2018 (data from American Cancer Society website).
6. CDC, https://www.cdc.gov/hiv/statistics/overview/ataglance.html; 2017 incidence, 2016 prevalence of diagnosed HIV infections.
7. Derived from Hayter SM. Autoimmun Rev. 2012 Aug;11(10):754-65 (prevalence 4.5% for all conditions excluding psoriasis) and Rachakonda TD. J Am Acad Dermatol. 2014 Mar;70(3):512-6 (prevalence of 3.2% for psoriasis alone), applied to projected adult US population in 2020 (US Census: 289.6 million).

IC Populations: Groups 1–5

IC Condition	Incident Cases (New cases per year)	Prevalent Cases
Hematopoietic stem cell transplant[1]	23,379	
Hematologic malignancy[2]	~176,200	
Solid organ (including renal) transplant[3]	58,532	~591,000
Solid tumor on chemotherapy[2,4]	~1,200,000	
HIV infection[5]	38,739	1,008,929
Total	~1,496,850	~1,599,929

1. D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018. Available at https://www.cibmtr.org.
2. American Cancer Society, https://cancerstatisticscenter.cancer.org; 2019 incidence estimates.
3. United Network for Organ Sharing, https://unos.org/data/transplant-trends/#transplants_by_organ_type+year; 2018, Renal= Kidney + Kidney/Pancreas, Solid organ = all listed.
4. Halpern MT, Yabroff KR, Cancer Invest, 2008, 26(6):647-51; Derived from Halpern and Yabroff 2000-2004 data on chemo/radiotherapy among all patients with cancers, adjusted based on proportion of all cancers in 2007 due to solid organ cancers, further adjusted by projections that solid cancers increased by 20% between 2007 and 2018 (data from American Cancer Society website).
5. CDC, https://www.cdc.gov/hiv/statistics/overview/ataglance.html; 2017 incidence, 2016 prevalence of diagnosed HIV infections.

Policy question: “Should vaccination with RZV be recommended for immunocompromised adults 19 years of age and older?”

- **Population:** IC adults ≥19 years of age; split into two parts (19–49 years, ≥50 years)
- **Intervention:** RZV, 2 doses at least 4 weeks apart
- **Comparison:** No vaccine
- **Outcomes**

	Benefits	Harms
Critical	**Prevent HZ**	**Serious adverse events**
Important	Prevent PHN Prevent HZ-related hospitalization	Immune-mediated disease Reactogenicity (Grade 3) Graft versus host disease (HCT) Graft rejection (SOT)