

The Prudent Prescriber

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Pharm Reps \neq Rational Prescribing

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Shingrix: Shangri-La ? Zostavax, Dead in the Water?

At the end of their October, 2017 meeting, the Advisory Council on Immunization Practices (ACIP) voted to recommend use of the recently FDA approved Shingrix, subunit (HZ/su) shingles vaccine.

ACIP proposes that:

- HZ/su is recommended for immunocompetent adults aged 50 and over.
- HZ/su is recommended for immunocompetent adults aged 50 and over who have previously received Zostavax.
- HZ/su is preferred over Zostavax (this vote 8-7).

Do we really need a New and Better shingles vaccine?

Zostavax was approved in 2006 based on a phase 3 trial showing 51% efficacy in preventing the disease and about 67% efficacy in preventing postherpetic neuralgia. This spring a study by Izurieta (*Clin Infect Dis* 64(6), March 15, 2017) using data from 2 million Medicare beneficiaries found Zostavax protection effectiveness of 33% within three years after vaccination and only 22% at 4 years or longer. Schmader *et al* (*Clin Infect Dis* 2102; 54:922-8) showed that Zostavax efficacy against herpes zoster decreased with age (from 70% in adults between 50 and 59 years and 38% in those greater than 70 years of age).

Antibiotics do
NOT

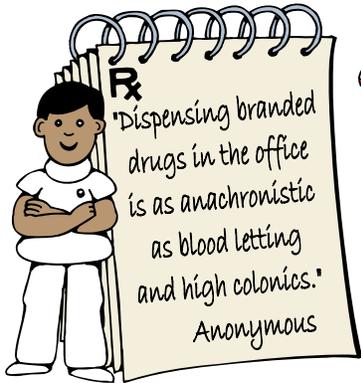


help
acute bronchitis

**β -blockers in
post-MI
save
lives**



Pill splitters save
BIG



CHE?

Think:

Ace
Aldactone
B-blocker
Dig
Diuretic



Avoid these expensive
"me-too" drugs:

Intermezzo
Vimovo
Livalo
Pristiq
Viibryd
Edarbi
Daliresp



Treat patients
> 60 years to 150/90



NOW AVAILABLE
ON THE
GENERIC MARQUEE

Frova \rightarrow frovatriptan
Voltaren gel \rightarrow diclofenac Na 1% gel
Crestor \rightarrow rosuvastatin
Nuvigil \rightarrow armodafinil
Jalyn \rightarrow dutasteride/tamsulosin
Ortho Tri-Cyclen Lo \rightarrow Tri-Lo-Marzia,
Tri-Lo-Sprintec, & others

The evidence for Shingrix

GlaxoSmithKline paid for and published two randomized controlled studies involving 15,411 participants (NEJM May 28, 2015) and 13,900 participants (NEJM September 15, 2016) to bring Shingrix to market. Exclusion criteria in both studies: immunocompromised patients and those with a history of herpes zoster or immunization with Zostavax or varicella vaccines.

Results:

In the first study, during a mean follow-up of 3.2 years, herpes zoster was confirmed in 9 participants in the vaccine group (received at least one Shingrix injection) and in 235 participants in the placebo group (incident rate, 0.4 versus 9.1 per 1000 person-years). Vaccine efficacy = 96.2%. Number Needed to Immunize (NNI) with Shingrix rather than placebo to prevent one case of zoster = 115. Vaccine efficacy was between 94.1% and 98.3% in all three age groups (50-59, 60-69 and >70).

In the second study, with a mean follow-up of 3.7 years, herpes zoster occurred in 23 Shingrix recipients and in 223 placebo recipients (0.9 versus 9.2 per 1000 person-years). NNI = 120. Vaccine efficacy against zoster was 89.8% and was similar in participants 70-79 years of age (90.0%) and in participants 80 years of age or older (89.1%). Vaccine efficacy was 88.8% in preventing postherpetic neuralgia. Protection against postherpetic neuralgia appears to be driven by the lower incidence of herpes zoster. There is no evidence for additional efficacy against postherpetic neuralgia among Shingrix recipients with breakthrough herpes zoster.

In both studies, participants who received Shingrix vaccine had more local and systemic reactions (myalgias, fever, fatigue, headache) than the placebo (saline) group. Grade 3 reactions (preventing normal everyday activities, but not life threatening) occurred in 11.9% to 15.6% in the Shingrix group vs. 1.9%- 2% in the placebo group.

Shingrix in patients who previously received Zostavax

In a small study (J Infect Dis. September 26, 2017) with 430 participants, Gruppung *et al* demonstrated that HZ/su induces a strong immune response, irrespective of prior vaccination with Zostavax.

What's unique about Shingrix?

- Recombinant vaccines, like HZ/su, may be suitable for persons who are immunosuppressed because the risk of disease resulting from replication of the vaccine virus is nil.
- The relatively new AS01 adjuvant utilized in this vaccine has effects that are rapid and transient, being limited to the injected muscle and draining lymph nodes. It is the same adjuvant that is a constituent of a malaria vaccine that is being field tested in children.
- It is recommended that Shingrix be given as two intramuscular injections, two - six months apart.
- It is anticipated that Shingrix will be given final approval by the FDA after the first of the year.
- GlaxoSmithKline says its new vaccine will cost about \$280 for two doses.

My Take:

- The efficacy data for Shingrix do look better than those for Zostavax, with downsides of increased local and systemic reactions.
- We only have documented evidence for 3+ years of duration of effect. Will Shingrix efficacy fade, like Zostavax, particularly in those over 70 years of age?
- With the close vote by the ACIP to prefer Shingrix over Zostavax, should we continue to peddle the older vaccine?

- Perhaps the biggest stumbling blocks to promoting Zostavax have been its price and Medicare Part D status. We are stuck with another expensive immunization. Wouldn't it be a more effective public health strategy to make it a Part B benefit?
- In the face of the relatively small N (<30,000) in the studies that brought Shingrix to market, the relatively large Number Needed to Immunize (115-120) to prevent one case of zoster and a brand spanking new adjuvant, I'm going to hold off for a while in taking this vaccine or in recommending it to others.

Thank you

I send my ongoing appreciation to Mark and Linda at the St. Mary's Hospital and Medical Center Medical Library whose expertise save me hours of research time each month.

Steve and Zach, the Rocky Mountain Health Plans Pharm Ds are generous with their ideas and work. On multiple occasions, they have kept me out of harm's way.

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