

Shingles Vaccine, Seniors' Joy

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Introduction

Shingles caused by the Varicella Zoster virus (VZV), the same virus that causes chickenpox. VZV infection is highly contagious, producing annual epidemics among susceptible individuals during winter and spring in temperate climates. The virus establishes latency in cells of the dorsal root ganglia during primary infection ¹. It can reappear many years later to cause a case of shingles, which is usually observed in elderly or immunocompromised patients. People can't catch shingles from another person with shingles. Only someone who has had a case of chickenpox or gotten chickenpox vaccine can get shingles. It is estimated that more than 500,000 cases of herpes zoster occur each year in the United States ⁵.

Symptoms

Shingles is a skin rash, often with blisters. It is also called Herpes Zoster. A shingles rash usually appears on one side of the face or body and lasts from 2 to 4 weeks (Fig. 1). Its main symptom is pain, which can be quite severe. Other



Fig. 1 Shingles rash (A) Neck ; (B) Upper back

symptoms of shingles can be fever, headache, chills and upset stomach. Very rarely, a shingles infection can lead to pneumonia, hearing problems, blindness, brain inflammation (encephalitis) or death. For about 1 person in 5, severe pain can continue even after the rash clears up. This is called Post-herpetic neuralgia (PHN) ¹.

Shingles vaccine

Zostavax vaccine (Fig. 2), the vaccine containing live, attenuated VZV (Oka/Merck strain), is indicated for the prevention of herpes zoster (shingles) ². The virus was originally obtained from a child with naturally-occurring varicella and then grown in the laboratory in human diploid cell cultures. Zostavax protects



Fig. 2. Zostavax vaccine product

against the development of zoster by boosting varicella-zoster virus immunity using active immunization. In clinical trials, the vaccine prevented shingles in about half of people 60 years of age and older. It can also reduce the pain associated with shingles. The US Food and Drug Administration approved Zostavax in May 2006. The vaccine costs approximately \$150³. In October 2006, the CDC's Advisory Committee on Immunization Practices recommended that all people age 60 years and older, including those who have a history of herpes zoster, receive a single dose vaccine⁹. Of note, Zostavax is indicated for the prevention of herpes zoster in patients 60 years of age or older. It is not effective in the treatment of shingles or PHN.

Medical significance

Herpes zoster, or shingles, is a common problem, especially in the immunocompromised and elderly people. It is estimated that more than half million cases of herpes zoster occur each year in the United States⁵. Herpes zoster is due to a reactivation of latent varicella-zoster virus within the sensory ganglia. PHN is defined as the persistence of pain 30 days after the onset of rash or after healing of the rash and occurs in 8% to 70% of those affected by herpes zoster, with the prevalence increasing with increasing age. The pain can be debilitating and last for months to years. While antiviral therapy can reduce the duration and severity of herpes zoster, it has not been shown to prevent the development of PHN or other complications. Other complications of herpes zoster include encephalitis,

myelitis, nerve palsies, and hemiparesis. Although rarely fatal, herpes zoster and the resulting PHN often negatively impact quality of life. With the aging population in the United States, the incidence of herpes zoster is expected to increase. Consequently, preventative measures are needed.

Clinical trial highlights

The Shingles Prevention Study was a placebo controlled, double-blind, clinical trial, with 38,546 patients who were 60 years of age or older, and was designed to assess the efficacy of herpes zoster vaccine⁶. Patients were randomized to receive either Zostavax (n=19,270) or placebo (n=19,276) and were followed until the development of zoster or until the end of the study. Confirmed cases of herpes zoster occurred in 315 of the vaccine-treated patients and 642 patients in the placebo group. Vaccine virus was not detected in any of the patients who developed herpes zoster, so the vaccine was not responsible for the illness. The overall incidence (per 1000 person-years) was significantly reduced in the vaccine-treated patients (5.42 per 1000 person-years compared with 11.12 per 1000 person-years, $p < 0.001$). The vaccine efficacy with respect to the incidence of herpes zoster was 63.9% among those 60 to 69 years compared with 37.6% in those 70 years or older ($p < 0.001$). After the diagnosis of herpes zoster, the rate of antiviral medication use was similar between the two groups with 87.3% of patients who received the vaccine versus 85.7% of the placebo-treated patients receiving an antiviral medication. The rate of antiviral administration within 72 hours of the appearance of the rash was also similar between the two groups. The duration of time patients experienced pain was significantly lower in patients who received the vaccine compared with those who did not (21 days versus 24 days, $p = 0.03$). Similarly, the severity of illness score was lower in vaccine treated patients. The effect of the vaccine on reducing the severity of the disease was greater in older patients. PHN occurred in 27 patients in the vaccine group and 80 in the placebo group. This translated to a vaccine efficacy for PHN of 66.5% (95% confidence interval 47.5 to 79.2). This rate met the study's prespecified criteria for vaccine efficacy. There was no difference based on sex or age. The investigators concluded that in older adults, the administration of a herpes zoster vaccine markedly reduced the morbidity from herpes zoster and the resulting PHN⁶.

Varivax vs Zostavax

Varivax [Varicella Virus Vaccine Live (Oka/Merck)] is indicated for vaccination against varicella in individuals 12 months of age and older. There have been reports of inadvertent vaccination of adults 60 years or older with Varivax instead of Zostavax. It is important to note that Zostavax is not the same

potency as the vaccine commonly used in children (Varivax). Zostavax has a median potency of 24,600 plaque-forming units (pfu) or about a fourteen times greater dose than that of Varivax (1350 pfu). Higher doses are needed “to elicit a significant increase in the cell-mediated immunity to varicella zoster virus among older adults.” Consequently, Varivax vaccine cannot be interchanged with Zostavax ⁷. Although there are no recommendations on what to do in cases where the vaccines are inadvertently interchanged, it is unknown whether the immune response to Zostavax would be affected by the recent administration of Varivax.

In general, when two live vaccines are to be administered, it is recommended that they be administered on the same day or separated by 28 days. Because of this, experts recommend waiting 28 days between administrations of these two vaccines to ensure an adequate immune response to the Zostavax dose ¹³.

Vaccine development

Zostavax must be kept frozen prior to use. It should be stored at an average temperature of -15 degrees Celsius (+5 degrees Fahrenheit) or colder prior to vaccination ². Following reconstitution, it should be administered immediately, in order to avoid loss of potency ^{2,10}. To expand the patient usage, the storage and handling of the Zostavax vaccine is a big issue. Merck and Company, is currently developing a refrigerator formulation of the vaccine, but the timeline for approval is not known.

A number of questions still exist regarding immunization to protect against herpes zoster. The Shingles Prevention Study showed that the effect of the vaccine on the incidence of herpes zoster was greater in those aged 60 to 69 years compared to those 70 years or older. The degree of efficacy in the very old is unknown and needs to be studied in this population ^{6,7,10}. In addition, the age at which vaccination should be initiated and the exact population that should receive the vaccine are not known ⁸. Merck requested approval for individuals at the ages 50 years to 59 years based on immunogenicity data coupled with efficacy data in the older population, but the FDA felt that the evidence was insufficient to warrant the indication. Merck plans to continue studies in patients between the ages of 50 and 59 years in order to obtain this indication. The duration of protection of the vaccine is also unknown. This information is critical to determine if and at what interval booster doses would be required.

Indications and precautions

Zostavax is administered subcutaneously, as a single dose, in individuals who are 60 years of age or older ². It is not ef-

fective in the treatment of herpes zoster or PHN. It should be avoided in patients who are immunocompromised such as those with primary or acquired immunodeficiency (leukemia, lymphoma, other neoplasms affecting bone marrow or lymphatic system, acquired immunodeficiency syndrome, or HIV) or those receiving immunosuppressive therapy including high doses of corticosteroids ⁴. It is not known if Zostavax interacts with other medications or vaccines, since these interactions have not been studied in clinical trials ⁷.

There are additional cautions for patients with unreliable Varicella histories: (1) A few elderly patients who had not had chickenpox in the past; (2) Many patients may have had the disease during childhood but have no records or recollection of the illness. In adults without a reliable history of varicella, it seems to be cost-effective to perform serologic tests and immunize those who are seronegative ¹¹. However, in adults 60 years or older who are to be vaccinated Zostavax, serologic testing may not be necessary. Macalalad et al. reported on the immunogenicity and safety of a high-potency (50,000 pfu) herpes-zoster vaccine in patients either seronegative or weakly seropositive ¹². They concluded that one dose of zoster vaccine appears to be immunogenic and well tolerated in adults, regardless of initial antibody serostatus ¹².

Reimbursement

Zostavax, indicated for the prevention of herpes zoster (shingles) is projected to reach peak annual sales of about \$200 million ¹⁵. There are approximately 44 million US individuals older than 60 years of age, so the eligible patient population for Zostavax is quite large ¹⁶. However, access may be limited because of cost barriers. The acquisition cost of Zostavax is \$150 per dose. Starting January 2007, Medicare begins paying for Zostavax in patients 65 years of age and older. However, it will not be fully covered like most widely used adult vaccines like the flu shot. Zostavax will be treated as a Part D drug with varying co-payments depending on the patient's drug plan ¹⁷. Medicare will not reimburse for administration of Zostavax as a result. Therefore, this administration fee/cost will be passed directly onto the patient or the physician.

Most commercial plans are still waiting for guidance from ACIP regarding vaccination of the senior population before making benefit and coverage decisions for patients over the age of 60 with employer-sponsored plans. In the meantime, patients may have to cover the entire cost of the vaccine or pay higher copayments. The ongoing developments underscore the dynamic and rapidly changing area of vaccine needs and delivery. Healthcare professionals need to stay up to date with new developments in order to serve the growing senior population better ^{14,18}.

Summary

More than 90% of US adults have had chickenpox and thus are at risk for zoster⁵. There is no way to predict when the varicella-zoster virus (VZV) will reactivate or who will develop zoster¹⁹. The incidence and severity of zoster increase with age⁶. Patients diagnosed with zoster or postherpetic neuralgia (PHN) may experience debilitating pain and serious complications.

Zostavax is the first and only vaccine to help prevent zoster. It is a single-dose, subcutaneous vaccine indicated for prevention of herpes zoster (shingles) in individuals 60 years of age or older. Zostavax is not indicated for the treatment of zoster or PHN. Zostavax is not a substitute for Varivax and should not be used in children. As with any vaccine, vaccination with Zostavax may not result in protection of all vaccine recipients

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蘇州·吳中 Pharma Industry

山水蘇州 人文吳中

Landscape of Suzhou Culture of Wuzhong

吳中區地處中國東部沿海長江三角洲中心，位於中國歷史文化名城—蘇州的南部。吳中區歷史悠久、人文薈萃，是中國吳文化的發源地，文明歷史超過了1萬年。吳中區生態優美、景色怡人，濱臨中國第三大淡水湖—太湖，境內有1處國家地質公園，2處國家森林公園，2座中國歷史文化名鎮和7處國家重點文保單位，是國家生態示範區。吳中區經濟發達、產業興旺，有來自全世界40多個國家和地區的1800多家外資企業在吳中區發展，註冊資本超過70億美元，產業涉及電子資訊、新型建材、精密機械、生物醫藥、現代家電等領域。吳中區是中國自然山水最優美、人文景觀最豐富、文化底蘊最深厚的地區之一，實現了最活躍的經濟與最優美的生態的和諧對接。

Wuzhong District is located in the center of the Yangtze River Delta in eastern China, and is situated in the south of Suzhou, The Famous Cities of Chinese History and Culture. It has a long history and a galaxy of talent, and is the cradle of Wu Culture in China, with a history over 10,000 years. Close to the 3rd biggest freshwater lake Taihu Lake, Wuzhong District has beautiful ecological environment and sceneries and possesses 1 national geographic park, 2 national forest parks, 2 historic towns of China and 7 cultural relics under special protection of the state. It is the national-class ecological demonstrative district. Wuzhong District has developed economy and prosperous industries. Over 1800 foreign enterprises from more than 40 countries and areas have started their business in Wuzhong District, in industries such as electronics and information, new construction materials, precise machinery, biological pharmacy, modern electric appliances, etc. The total registration capital has exceeded \$7 billion. Wuzhong District is one of the regions that have the most beautiful landscape, richest historic sceneries and the most profound culture in China. It integrates the active economy with the beautiful ecology harmoniously.





Pharma Industry

吴中醫藥產業基地

Wuzhong Pharma Industry Base

吴中區是中國醫藥產業最為發達的縣（市、區）之一。2001年經國家科技部批准，建立了國家火炬計劃一吳中醫藥產業基地。區內現有蘇州東瑞制藥有限公司、惠氏制藥有限公司、蘇州中凱生物藥業有限公司、蘇州長征-欣凱制藥有限公司、蘇州天吉生物醫藥有限公司等9家藥品生產骨干企業。產品涉及化學合成、生物合成、基因醫藥、營養補充劑、中藥制劑、醫療器械等領域。區內的江蘇省西山動物實驗開放服務中心，是中國綜合條件最好的靈長類實驗動物基地之一，與美國、加拿大、日本等多個國家的動物實驗機構和製藥企業建立了合作關係。位于吴中經濟開發區的吴中科技城擁有經國家科技部認定的國家級科技創業園，以生命科學、生物醫藥等科技型企業為主體，將為醫藥產業投資提供最佳的創業載體。2006年，中國領先的醫藥研發服務公司一藥明康德簽約吴中區，在此投資建立頗具規模并完全符合美國FDA、AAALAC標準的藥物安全評價中心。至此，吴中區的醫藥產業已經初步形成了一條從研發、中試、測評，到成藥的完整產業鏈。

Wuzhong District is one of the most developed county (city/district) in pharmacy industry in China. In 2001, it established Wuzhong Pharmacy Industry Base planned by the National Torch Project with the approval of the Ministry of Science and Technology. The Pharmacy Industry Base has 9 backbone enterprises such as Suzhou Dawnrays Pharmaceutical Co., Ltd., Wyeth Pharmaceutical Co., Ltd., Suzhou Zhongkai Biopharmaceutical Co., Ltd., Suzhou Chang Zheng Cinkate Pharmaceutical Co., Ltd., Suzhou Tianji Biopharmaceutical Co., Ltd., etc. The products cover fields such as chemosynthesis, biosynthesis, gene pharmacy, nutrition supplement, Chinese traditional medicine, medical treatment, etc. As one of the best Primates experimental bases in China, Jiangsu Xishan Animal Experimental Open Service Center, located inside the district, has established cooperative relationships with many animal experimental institutions and pharmaceutical enterprises of USA, Canada, Japan, etc. Located in Suzhou Wuzhong Economic Development Zone, Wuzhong Sci-tech City, boasting the national-class Sci-tech Incubation Park graded by the Ministry of Science and Technology, relies on sci-tech enterprises engaged in life science, bio-pharmacy, etc, and is producing the best incubation platform for pharmacy industry. In 2006, WuXi Pharma Tech Co., Ltd., a leading pharmaceutical R&D service company in China, signed an agreement with the Wuzhong District of the Jiangsu Province to build one of the largest, state-of-the-art GLP Safety Assessment Center. When completed, the center will provide comprehensive drug safety testing which comply with FDA, AAALAC and EMEA standards. The pharmacy industry in Wuzhong District has established a complete industrial chain, from R&D, testing, evaluation to the finished medicine.

