Korean J Pain 2020;33(3):201-207
https://doi.org/10.3344/kjp.2020.33.3.201
pISSN 2005-9159 eISSN 2093-0569

KJP

Review Article

Check for updates

Recombinant zoster vaccine (Shingrix®): a new option for the prevention of herpes zoster and postherpetic neuralgia

Grisuna Singh[1,2], Sejin Song[2], Eunjoo Choi[2], Pyung-Bok Lee[2,3], and Francis Sahngun Nahm[2,3]

[1]*Department of Anesthesiology and Intensive Care, Nepalgunj Medical College and Teaching Hospital, Nepalgunj, Nepal*
[2]*Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam, Korea*
[3]*Department of Anesthesiology and Pain Medicine, Seoul National University College of Medicine, Seoul, Korea*

Received March 5, 2020
Revised April 15, 2020
Accepted April 16, 2020

Handling Editor: Kyung Hoon Kim

Correspondence
Francis Sahngun Nahm
Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7499
Fax: +82-31-787-4063
E-mail: hiitsme@hanmail.net

Postherpetic neuralgia (PHN) is a challenging condition for pain management specialists. The prevention of herpes zoster (HZ) and subsequent PHN in individuals aged 50 years and older, via the development of new vaccines, is an ongoing research project. The live zoster vaccine (LZV, Zostavax®) was the first proof of concept that vaccination could prevent HZ, but LZV cannot be used in various immune-compromised patients. This led to the development of a new non-live recombinant zoster vaccine (RZV, Shingrix®). This RZV has shown promising results in many clinical trials, with high reactogenicity and similar systemic adverse effects compared to those of LZV. The National Advisory Committee on Immunization has recommended LZV as a standard vaccine for HZ prevention in adults ≥ 50 years of age, but no studies directly comparing the safety and efficacy of RZV and LZV vaccines have been conducted. This article reviews the brief history, efficacy, and safety of the two vaccines and discusses the advantage of RZV over LZV based on the available literature.

Key Words: Herpes Zoster; Herpes Zoster Vaccine; Immunity, Humoral; Neuralgia, Postherpetic; Pain; Vaccines, Attenuated; Vaccines, Subunit; Vaccines, Synthetic.

INTRODUCTION

Postherpetic neuralgia (PHN), a serious complication after varicella zoster virus (VZV) infection, is a challenging neuropathic pain for pain management specialists [1,2]. This peripheral neuropathy can present as any one of three subtypes: continuous burning pain; paroxysmal shooting or electric shock-like pain; or evoked sensations such as mechanical allodynia, mechanical hyperalgesia, or an exaggerated response to light touch [3]. The burden of this illness increases with advancing patient age as a result of declining cell-mediated immunity [4]. This crippling condition can have an enormous negative impact on patient quality of life and their capacity to perform day to day activities. Severe symptoms of PHN cause sleep disturbance, fatigue, and depression, diminish personal satisfaction, and carry a general weight to family and society [3]; therefore, various modalities are used to relieve these symptoms [5]. In the United States (US), 10%-18% of herpes zoster (HZ) patients develop PHN and 68% of HZ and 85% of PHN patients are over 50 years of age and unable to endure the pain of PHN or associated symptoms [6]. The risk of HZ is 8-10 times greater after 50 years of age compared to that of younger ages [2]. A higher occurrence of HZ has been observed in patients with diabetes mellitus [7] and compromised immunity, particularly those with diseases

Author contributions: Grisuna Singh: Writing/manuscript preparation; Sejin Song: Investigation; Eunjoo Choi: Investigation; Pyung-Bok Lee: Investigation; Francis Sahngun Nahm: Writing/manuscript preparation.

affecting the immune system or those taking medications that affect the immune system [8].

Data analysis by the Health Insurance Review and Assessment Service of South Korea [9] showed that the incidence of HZ is 0.25% per year, with a lifetime risk of 23%-30%. More than 50% of HZ patients were older than 60 years, and peak PHN incidence (1.05% per yr) was observed in patients aged 70-79 years. In 2013, the total number of patients with PHN increased by 58% and medical costs increased by 40% compared to 2009. An aging population with an increased prevalence of chronic diseases and immune-compromised states may further add to the burden imposed by HZ and PHN.

Numerous researchers have attempted to lower the risk of HZ and subsequent PHN; of these efforts, the development of an adult vaccine for HZ became the most critical turning point. A live zoster vaccine (LZV, Zostavax®; Merck & Co., Inc., Kenilworth, NJ) was the first proof of concept that vaccination could prevent HZ. Many people have benefitted from the use of LZV in reducing the risk of HZ [10]. However, LZV could not be used in certain immune-compromised patients, prompting the advancement for a new recombinant adjuvant subunit vaccine. Recently, a non-live recombinant adjuvant subunit zoster vaccine (RZV) was cultured to overcome the shortcomings of LZV and is commercially available in some countries (*i.e.*, US, Canada, Germany, and Australia). RZV results have been promising in many clinical trials, showing high reactogenicity and similar systemic adverse effects compared to the previous vaccine [11].

In this paper, we review the market-available vaccines for HZ and PHN prevention and compare the efficacy, safety, and advantages of the RZV and LZV vaccines. This review will help pain management specialists better understand the vaccine against HZ and PHN.

MAIN BODY

1. HZ vaccine history

Since 1958, when Weller et al. [12] reported that HZ and childhood chicken pox were caused by the same virus (VZV) [12], significant effort has been made to reduce the risk of this virus. The first live-attenuated vaccine, known as vOka, was manufactured, tested, and successfully used in Japan in 1974 to prevent deadly cases of varicella among immune-compromised children [13]. Since then, varicella vaccines containing the Oka strain have been produced by multiple pharmaceutical companies (*i.e.*, Oka/Merck strain as Varivax® by Merck & Co., Inc. and Oka strain as Varilrix® by GlaxoSmithKline [Brentford, UK]) [14]. In 2006, Merck & Co., Inc. developed a new live attenuated vaccine (Zostavax®) with the Oka/Merck strain to prevent HZ in adults ≥ 60 years of age [15]. Owing to several limitations of Zostavax® in immune-compromised adults, and its waning efficacy over 5-6 years, a new non-live RZV, Shingrix®, was developed and launched by GlaxoSmithKline in 2017 for use in adults ≥ 60 years of age [16]. Several studies have shown the benefit of Shingrix® in immune-compromised adults [16,17] and the National Advisory Committee on Immunization recommends the use of RZV on a case by case basis in immune-compromised adults [18].

Currently, a new inactivated vaccine made from Zostavax® by gamma irradiation was introduced and has been tested. Phase II/III trials have shown that this new inactivated version of LZV is well tolerated, has favorable effects in patients with malignancies, and does not possess significant safety issues [19-21]. In contrast to the single-dose injection required for LZV, this gamma-irradiated vaccine utilizes a four-dose regimen [21]. However, although the new vaccine is not efficacious in patients with hematological malignancies, it is effective for the prevention of HZ in chemotherapy patients with solid tumor malignancies [19]. Thus, though not currently available, this new vaccine is expected to be used in immune-compromised adults and post-transplant recipients.

2. HZ vaccines available on the market

Two types of HZ vaccines are currently in use: the live attenuated vaccine (Zostavax®) and the recombinant adjuvant subunit vaccine (Shingrix®) (**Table 1**). In some articles, the recombinant adjuvant vaccine has been used synonymously with 'inactivated vaccine' [22]. The concept here is that the term 'inactivated vaccine' indicates the vaccine does not contain the active (living) component of the virus and has lost its ability to replicate in the body of

Table 1. Comparison of the Two Types of Zoster Vaccines

Brand name	Zostavax®	Shingrix®
Company	Merck & Co., Inc.	GlaxoSmithKline
Type of vaccine	Live attenuated vaccine	Recombinant adjuvant subunit vaccine
Dosing	Single shot	Two shots (The second dose is given 2-6 mo after the first dose)
Route of administration	Subcutaneous injection	Intramuscular injection
Length of immunity	About 5 yr [27]	About 9 yr [36]

Table 2. Comparison of the ZEST and SPS

Characteristic	ZEST	SPS
Study population	50-59 yr with VZV infection n = 22,439	≥ 60 yr with VZV infection n = 38,546
Median follow-up	1.3 yr (up to 2 yr)	3.12 yr
HZ risk reduction	Overall: 69.8%	Overall: 51.3% 60-69 yr: 63.9% ≥ 70 yr: 37.6%
PHN risk reduction	NA	66.5%
Vaccine-related serious adverse events	n = 1 (*vs.* n = 0 in placebo)	n = 2 (*vs.* n = 3 in placebo)

ZEST: Zoster Vaccine Efficacy and Safety Trial, SPS: Shingles Prevention Study, HZ: herpes zoster, PHN: postherpetic neuralgia, VZV: varicella zoster virus, NA: not assessed.

the host. As such, the recombinant adjuvant subunit and heat-killed vaccine are considered inactivated vaccines.

1) LZV, Zostavax®

Zostavax® was the first proof of concept vaccine to show that vaccination can prevent HZ. It is a live attenuated vaccine that contains a much higher virus titer than the vaccine for chickenpox; Zostavax® holds at least 19,400 plaque forming units (pfu) per dose of the Oka virus strain compared to 1,350 pfu per dose in the chickenpox vaccine [23]. It is approved by the U.S. Food and Drug Administration (FDA) in adults ≥ 50 years for a one time subcutaneous injection [24]. The FDA recommendation was based on the Zoster Vaccine Efficacy and Safety Trial (ZEST), which showed a 69.8% risk reduction for HZ in patients between 50 and 59 years over 1.3 years of follow-up (**Table 2**) [25]. In another trial conducted by the Shingles Prevention Study (SPS) group, LZV efficacy with respect to the incidence of HZ was lower in subjects ≥ 70 years than in younger subjects (37.6% *vs.* 63.9%). HZ and PHN occurrences were reduced by 51.3% and 66.5%, respectively. Immunization decreased the burden of illness from HZ by 61.1% (**Table 2**) [26].

The short-term persistence sub-study (STPS) was conducted approximately 15 months after the SPS, and followed up for 3.3-7.8 years after vaccination. It was conducted at 12 sites with a study population of 14,270, who were also involved in the SPS group. This study showed that the effect of Zostavax® decreased throughout the 3.3-7.8 years following vaccination. Vaccine efficacy for PHN decreased from 66.5% to 60.1%, and vaccine efficacy for HZ incidence reduction decreased from 51.3% to 39.6% during the same time interval. Therefore, the STPS study concluded that there was a reduced benefit from Zostavax® after 5 years post-vaccination [27].

The long-term persistence sub-study (LTPS) [28] obtained vaccine efficacy information up to 11 years after vaccination. This study enrolled 6,867 vaccinated adults without a placebo group from the SPS study; vaccine efficacy for HZ burden of illness declined and the incidence of HZ and PHN declined from years 7 to 11 after Zostavax® vaccination.

Another study conducted in Kaiser Permanente Southern California (KPSC) followed 704,312 adults (176,078 vaccinated *vs.* 528,234 unvaccinated individuals) aged ≥ 60 years over 8 years and found that vaccine efficacy decreased from 68.7% to 4.2% during this period [29]. Both the SPS study and KPSC study suggested the necessity of a second dose of zoster vaccine [26,29]. Overall vaccine efficacy in the first year post-vaccination was 67.5% but efficacy decreased to 47.2% in the second year and continued to gradually decrease to 30% by year 8. Out of 392,677 total vaccine recipients, 21,665 (5.5%) were immune-compromised. Vaccine efficacy was the same among the immune-competent and immune-compromised recipients [30].

2) RZV, Shingrix®

Despite the promising HZ prevention results of the LZV vaccine in immune-competent adults, there are certain limitations to its use. It cannot be used in pregnant women, patients with active tuberculosis, or those allergic to any of the vaccine components [31]. The uncertain vaccine efficacy after five years post-vaccination, and the unclear recommendation of its use in immune-compromised adults, required the launch of a more efficient vaccine for HZ and PHN protection [26,27], resulting in the introduction of a new, non-live vaccine in 2017.

(1) Shingrix® vaccine efficacy

Shingrix® is a non-live, adjuvant RZV. It contains VZV glycoprotein E (gE) antigen (50 μg) and a liposomal based adjuvant system, $ASO1_B$ (50 μg). $ASO1_B$ is a liposome-based vaccine adjuvant framework that contains two immune-stimulants: 3-O-desacyl-4'-monophosphoryl lipid A and saponin QS-21 [23]. The monophosphoryl lipid activates innate patient immunity and results in cytokine production; QS-21 stimulates CD4+ and CD8+ T cells, and the antigen-specific antibody response leads to a strong cellular and humoral response [32]. Glycoprotein E is the primary target of T cell response because it is the most abundant VZV envelope protein, which assumes a significant role in viral replication and cell to cell virus transfer [33]. Glycoprotein E shows a higher immune response compared to other glycoproteins, is involved in the pathogenesis of skin lesions, and is present in infected cells as HZ is reactivated

Table 3. The Efficacy of Recombinant Adjuvant Subunit Vaccine (Shingrix®) in Adults Grouped by Age

Characteristic	ZOE-50	ZOE-70
Study population	n = 14,411 Age: ≥ 50 yr	n = 13,900 Age: ≥ 70 yr
Median follow-up	3.2 yr	3.7 yr
HZ risk reduction (%)	Overall: 97.2 50-59 yr: 96.6 60-69 yr: 97.4 ≥ 70 yr: 97.9	Overall: 89.8
PHN risk reduction (%)	≥ 50 yr: 91.2	≥ 70 yr: 88
Vaccine-related SAE	n = 1 (*vs.* n = 3 in placebo)	n = 12 (*vs.* n = 8 in placebo)

ZOE: study done on the efficacy and safety of the herpes zoster recombinant subunit vaccine, HZ: herpes zoster, PHN: postherpetic neuralgia, SAE: systemic adverse effects.

[23,34]. This vaccine is administered intramuscularly in the deltoid, unlike the subcutaneous administration of Zostavax®. The vaccine does not contain preservatives; therefore, it must be used within 6 hours of reconstitution. It is given in a series of two doses. The second dose is given 2-6 months after the first dose. The efficacy and safety of Shingrix® were studied by two large phase III placebo-controlled randomized studies in 18 countries. The ZOE-50 study was conducted in immune-competent participants or those on low dose steroids aged 50 years or older [35]. The ZOE-70 study was a separate study conducted at the same time in individuals 70 years or older to establish the safety and efficacy of the vaccine in that specific age group (**Table 3**) [11]. A total of 16,160 adults in 18 countries were involved in the ZOE-50 study. A total of 14,759 adults were given two doses of vaccine or placebo, out of which 216 adults (6 cases in the immunization group and 210 cases in the placebo group) were diagnosed with confirmed cases of HZ. Overall vaccine efficacy was 97.2% against HZ [35]. The randomization method, inclusion and exclusion criteria, dosage, and administration of the vaccine in the ZOE-70 study were the same as those in the ZOE-50 study. During the subsequent 3.7 years, 23 cases of HZ occurred in the immunization group and 223 in the placebo group. The overall vaccine efficacy was 89.8%.

In the pooled analysis of data from the ZOE-50 and ZOE-70 studies, the overall efficacy of Shingrix® in decreasing HZ risk was 91.3%. Vaccine efficacy was 97.6% in the first year, 92% in the second year, 84.7% in the third year, and 87.9% in the fourth year. PHN did not develop in individuals below 70 years of age. Vaccine efficacy against PHN was 88.8% in adults ≥ 70 years old [11].

Persistent immunity against HZ after Shingrix® vaccination was shown in a study by Schwarz et al. [36]. Irrespective of age, both the cellular and humoral resistance stayed above the pre-vaccination level up to 9-years post-vaccination. Immune response was anticipated to stay over the benchmark up to 15 years post-initial vaccination.

(2) Safety and reactogenicity of RZV (Shingrix®)

In the reactogenicity subgroup of the ZOE-50 and ZOE-70 studies, localized injection site reactions (pain, redness, and swelling) and systemic reactions (fatigue, fever, gastrointestinal discomforts, headache, myalgia, and shivering) were recorded. Adverse reactions (84.4% and 37.8% in the RZV and placebo groups, respectively) were recorded within seven days after vaccination. The most common localized reaction was injection site pain (79.1% in RZV group and 11.2% in the placebo group). Myalgia was the most widely recognized fundamental response (46.3% in the RZV group and 12.1% in the placebo group). A severe reaction was recorded in one patient in the RZV group and in three patients in the placebo group [11,35].

A pooled analysis of the ZOE-50 and ZOE-70 studies [11] included 14,645 adults in the RZV group and 14,660 adults in the placebo group. Injection site pain was the most widely recognized localized reaction (68.1% in the RZV group, 6.9% in the placebo group). Grade 3 pain (significant pain at rest, preventing normal daily activities) at the injection site was reported in 3.8% of the RZV group and 0.2% of the placebo group. Similarly, the most common general symptoms were myalgia and fatigue, which were observed in 32.9% of the RZV group and 32.2% of the placebo group. Grade 3 fatigue (preventing normal daily activities) was reported in 3% of the RZV group and 0.5% of the placebo group. These reactions occurred within 1-3 days post-vaccination. Unsolicited reactions occurred more often in the RZV group (50.5%) than in the placebo group (32.0%), with a relative risk of 1.58 (95% confidence interval, 1.52-1.64). These reactions occurred within 30 days post-vaccination and occurred irrespective of age, sex, and race. Most of the unsolicited reactions occurred within the first week after vaccination. The occurrence of serious adverse events such as cardiac disorders, pneumonia, and neoplasms was comparable between the two groups within 30 days post-second dose vaccination (2.3% in the RZV group and 2.2% in the placebo group). Similarly, the occurrence of fatal adverse reactions such as neoplasms, cardiac failure, and myocardial infarction were comparable between the two groups (4.3% in the RZV group and 4.6% in the placebo group). Of these, only one was considered to be vaccine-related and occurred in a previously thrombocytopenic 90-year-old patient [37].

3. Comparison of Zostavax® *vs.* Shingrix®; which vaccine has a higher efficacy in preventing HZ and PHN?

There has been no head-to-head study that directly compares LZV and RZV vaccine efficacy and safety; only an indirect comparison between RZV and LZV is available. One such study is a network meta-analysis performed by GlaxoSmithKline in which RZV was compared to LZV in terms of efficacy and safety for HZ and PHN prevention [38]. In this study, RZV showed significantly higher efficacy compared to LZV in HZ prevention in adults ≥ 60 years (92% for RZV *vs.* 51% for LZV). Similarly, the vaccine efficacy of RZV for reducing PHN in adults ≥ 60 years was 89%, and that of LZV was 66%. However, there were more injection site reactions in the RZV group than the LZV group.

4. Will an additional vaccination with Shingrix® be advisable for patients that previously received the Zostavax® vaccination?

In the open-label, multicenter study performed by Grupping et al. [39], which involved 822 adults ≥ 65 years of age, who were vaccinated with LZV ≥ 5 years previously, immunogenicity was assessed after re-vaccination with RZV. Humoral and cellular immune markers of adults previously vaccinated with LZV and group-mated LZV naïve adults were compared. The anti-gE antibody response of adults in both groups was comparable. The RZV vaccine was well tolerated, and cellular immunity, safety, and reactogenicity were comparable between the two groups. This comparison indicated that revaccination with RZV in adults previously vaccinated with LZV was highly beneficial because RZV efficacy was significantly higher in decreasing HZ and PHN incidence. It also provided sustained humoral and cellular immunity compared to LZV. Therefore, a booster vaccination with RZV may be advisable, regardless of previous vaccination with LZV.

5. National recommendation for RZV use by country

The US Advisory Committee on Immunization Practices recommended RZV as the standard vaccine for HZ and PHN prevention in adults ≥ 50 years [40]. The German Standing Committee on Vaccination did not recommend LZV as a standard vaccination for the elderly [41], but did recommend RZV for HZ and PHN prevention in adults ≥ 60 years of age [42]. The national immunization guides of Austria and Canada recommend RZV for HZ prevention in individuals ≥ 50 years [43].

CONCLUSIONS

LZV and RZV vaccines for HZ and PHN prevention are readily available on the market. Although the efficacy and safety of LZV has been proven in many studies, major drawbacks to its use include limited use in immune-compromised adults, waning cell-mediated immunity, and lower efficacy compared to RZV in reducing HZ and PHN incidence. RZV (Shingrix®), a non-live vaccine containing recombinant glycoprotein E with a new adjuvant ($ASO1_B$), is preferable to LZV and has been increasingly used since its launch in 2017, mainly because of its higher efficacy. The new RZV vaccine showed favorable outcomes in various population subgroups, including different races, adults with a history of HZ, individuals previously vaccinated with Zostavax®, and even immune-compromised individuals and transplant recipients. This new vaccine will protect many people from the risk of HZ and subsequent PHN.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

FUNDING

No funding to declare.

ORCID

Grisuna Singh, https://orcid.org/0000-0002-6320-361X
Sejin Song, https://orcid.org/0000-0002-8596-4655
Eunjoo Choi, https://orcid.org/0000-0002-7002-3932
Pyung-Bok Lee, https://orcid.org/0000-0003-0325-3356
Francis Sahngun Nahm, https://orcid.org/0000-0002-5900-7851

REFERENCES

1. Jeon YH. Herpes zoster and postherpetic neuralgia: practical consideration for prevention and treatment. Korean J Pain 2015; 28: 177-84.
2. Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of varicella-zoster virus. N Engl J Med 2000; 342: 635-45.
3. Johnson RW, Rice AS. Clinical practice. Postherpetic neuralgia. N Engl J Med 2014; 371: 1526-33.

4. Gershon AA, Breuer J, Cohen JI, Cohrs RJ, Gershon MD, Gilden D, et al. Varicella zoster virus infection. Nat Rev Dis Primers 2015; 1: 15016.
5. Shrestha M, Chen A. Modalities in managing postherpetic neuralgia. Korean J Pain 2018; 31: 235-43.
6. Leung J, Harpaz R, Molinari NA, Jumaan A, Zhou F. Herpes zoster incidence among insured persons in the United States, 1993-2006: evaluation of impact of varicella vaccination. Clin Infect Dis 2011; 52: 332-40.
7. Chernev I, Gomez E. Herpes zoster and diabetes mellitus. Korean J Pain 2014; 27: 92.
8. Kimberlin DW, Whitley RJ. Varicella-zoster vaccine for the prevention of herpes zoster. N Engl J Med 2007; 356: 1338-43.
9. Hong MJ, Kim YD, Cheong YK, Park SJ, Choi SW, Hong HJ. Epidemiology of postherpetic neuralgia in Korea: an electronic population health insurance system based study. Medicine (Baltimore) 2016; 95: e3304.
10. Kim KH. Herpes zoster vaccination. Korean J Pain 2013; 26: 242-8.
11. Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, Díez-Domingo J, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Engl J Med 2016; 375: 1019-32.
12. Weller TH, Witton HM, Bell EJ. The etiologic agents of varicella and herpes zoster; isolation, propagation, and cultural characteristics in vitro. J Exp Med 1958; 108: 843-68.
13. Takahashi M, Otsuka T, Okuno Y, Asano Y, Yazaki T. Live vaccine used to prevent the spread of varicella in children in hospital. Lancet 1974; 2: 1288-90.
14. Wang L, Zhu L, Zhu H. Efficacy of varicella (VZV) vaccination: an update for the clinician. Ther Adv Vaccines 2016; 4: 20-31.
15. Sanford M, Keating GM. Zoster vaccine (Zostavax): a review of its use in preventing herpes zoster and postherpetic neuralgia in older adults. Drugs Aging 2010; 27: 159-76.
16. Syed YY. Recombinant zoster vaccine (Shingrix®): a review in herpes zoster. Drugs Aging 2018; 35: 1031-40.
17. Dagnew AF, Ilhan O, Lee WS, Woszczyk D, Kwak JY, Bowcock S, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. Lancet Infect Dis 2019; 19: 988-1000.
18. Warrington R, Ismail S; National Advisory Committee on Immunization (NACI). Summary of the NACI update on herpes zoster vaccines. Can Commun Dis Rep 2018; 44: 220-5.
19. Mullane KM, Morrison VA, Camacho LH, Arvin A, McNeil SA, Durrand J, et al. Safety and efficacy of inactivated varicella zoster virus vaccine in immunocompromised patients with malignancies: a two-arm, randomised, double-blind, phase 3 trial. Lancet Infect Dis 2019; 19: 1001-12.
20. Eberhardson M, Hall S, Papp KA, Sterling TM, Stek JE, Pang L, et al. Safety and immunogenicity of inactivated varicella-zoster virus vaccine in adults with autoimmune disease: a phase 2, randomized, double-blind, placebo-controlled clinical trial. Clin Infect Dis 2017; 65: 1174-82.
21. Parrino J, McNeil SA, Lawrence SJ, Kimby E, Pagnoni MF, Stek JE, et al. Safety and immunogenicity of inactivated varicella-zoster virus vaccine in adults with hematologic malignancies receiving treatment with anti-CD20 monoclonal antibodies. Vaccine 2017; 35: 1764-9.
22. Cohen JI. Strategies for herpes zoster vaccination of immunocompromised patients. J Infect Dis 2008; 197(Suppl 2): S237-41.
23. Lecrenier N, Beukelaers P, Colindres R, Curran D, De Kesel C, De Saegher JP, et al. Development of adjuvanted recombinant zoster vaccine and its implications for shingles prevention. Expert Rev Vaccines 2018; 17: 619-34.
24. Choi WS. Herpes zoster vaccine in Korea. Clin Exp Vaccine Res 2013; 2: 92-6.
25. Schmader KE, Levin MJ, Gnann JW Jr, McNeil SA, Vesikari T, Betts RF, et al. Efficacy, safety, and tolerability of herpes zoster vaccine in persons aged 50-59 years. Clin Infect Dis 2012; 54: 922-8.
26. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005; 352: 2271-84.
27. Schmader KE, Oxman MN, Levin MJ, Johnson G, Zhang JH, Betts R, et al. Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy. Clin Infect Dis 2012; 55: 1320-8.
28. Morrison VA, Johnson GR, Schmader KE, Levin MJ, Zhang JH, Looney DJ, et al. Long-term persistence of zoster vaccine efficacy. Clin Infect Dis 2015; 60: 900-9.
29. Tseng HF, Harpaz R, Luo Y, Hales CM, Sy LS, Tartof SY, et al. Declining effectiveness of herpes zoster vaccine in adults aged ≥60 years. J Infect Dis 2016; 213: 1872-5.
30. Baxter R, Bartlett J, Fireman B, Marks M, Hansen J, Lewis E, et al. Long-term effectiveness of the live zoster vaccine in preventing shingles: a cohort study. Am J Epidemiol 2018; 187: 161-9.
31. Zussman J, Young L. Zoster vaccine live for the prevention of shingles in the elderly patient. Clin Interv Aging 2008; 3: 241-50.
32. Didierlaurent AM, Laupèze B, Di Pasquale A, Hergli N, Collignon C, Garçon N. Adjuvant system AS01: helping to overcome the challenges of modern vaccines. Expert Rev Vaccines 2017; 16: 55-63.
33. Berarducci B, Ikoma M, Stamatis S, Sommer M, Grose C, Arvin AM. Essential functions of the unique N-terminal region of the varicella-zoster virus glycoprotein E ectodomain in viral replication and in the pathogenesis of skin infection. J Virol 2006; 80: 9481-96.
34. Symoniak MR, Farrokh P, Gandhi MA, Slish JC. Herpes zos-

ter subunit vaccine for the prevention of herpes zoster. Am J Health Syst Pharm 2018; 75: 861-9.
35. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med 2015; 372: 2087-96.
36. Schwarz TF, Volpe S, Catteau G, Chlibek R, David MP, Richardus JH, et al. Persistence of immune response to an adjuvanted varicella-zoster virus subunit vaccine for up to year nine in older adults. Hum Vaccin Immunother 2018; 14: 1370-7.
37. López-Fauqued M, Campora L, Delannois F, El Idrissi M, Oostvogels L, De Looze FJ, et al. Safety profile of the adjuvanted recombinant zoster vaccine: pooled analysis of two large randomised phase 3 trials. Vaccine 2019; 37: 2482-93.
38. McGirr A, Widenmaier R, Curran D, Espié E, Mrkvan T, Oostvogels L, et al. The comparative efficacy and safety of herpes zoster vaccines: a network meta-analysis. Vaccine 2019; 37: 2896-909.
39. Grupping K, Campora L, Douha M, Heineman TC, Klein NP, Lal H, et al. Immunogenicity and safety of the HZ/su adjuvanted herpes zoster subunit vaccine in adults previously vaccinated with a live attenuated herpes zoster vaccine. J Infect Dis 2017; 216: 1343-51.
40. Dooling KL, Guo A, Patel M, Lee GM, Moore K, Belongia EA, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. MMWR Morb Mortal Wkly Rep 2018; 67: 103-8.
41. German Standing Committee on Vaccination (STIKO) at the Robert Koch Institute (RKI). Background paper to the decision not to recommend a standard vaccination with the live attenuated herpes zoster vaccine for the elderly in Germany: statement of the German Standing Committee on Vaccination (STIKO) at the Robert Koch Institute (RKI). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2017; 60: 1162-79.
42. Siedler A, Koch J, Garbe E, Hengel H, von Kries R, Ledig T, et al. Background paper to the decision to recommend the vaccination with the inactivated herpes zoster subunit vaccine: statement of the German Standing Committee on Vaccination (STIKO) at the Robert Koch Institute. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2019; 62: 352-76.
43. Gabutti G, Bolognesi N, Sandri F, Florescu C, Stefanati A. Varicella zoster virus vaccines: an update. Immunotargets Ther 2019; 8: 15-28.