Rekombinan Zona Aşısı

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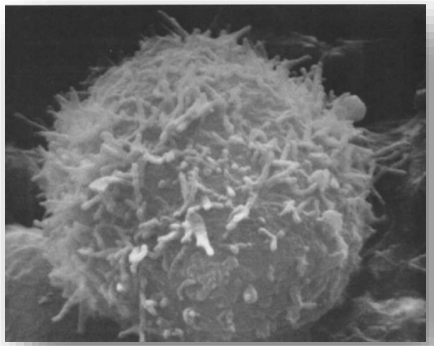
Acıbadem Üniversitesi Maslak Hastanesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

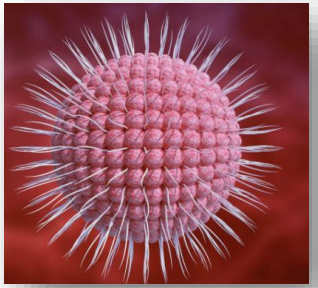
12.Türkiye EKMUD Kongresi, 18-22 Mayıs 2024, Antalya

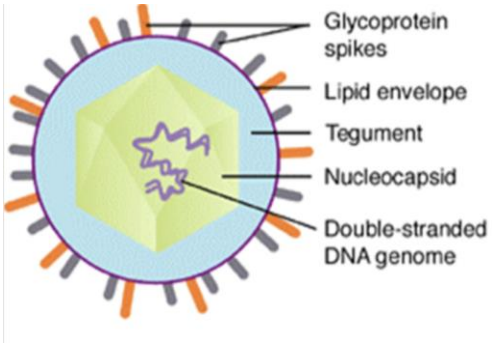
- Hastalık yükü ve risk grupları
- Rekombinan aşının özellikleri
- Etkinlikleri
- Güvenilirliği
- Endikasyonları

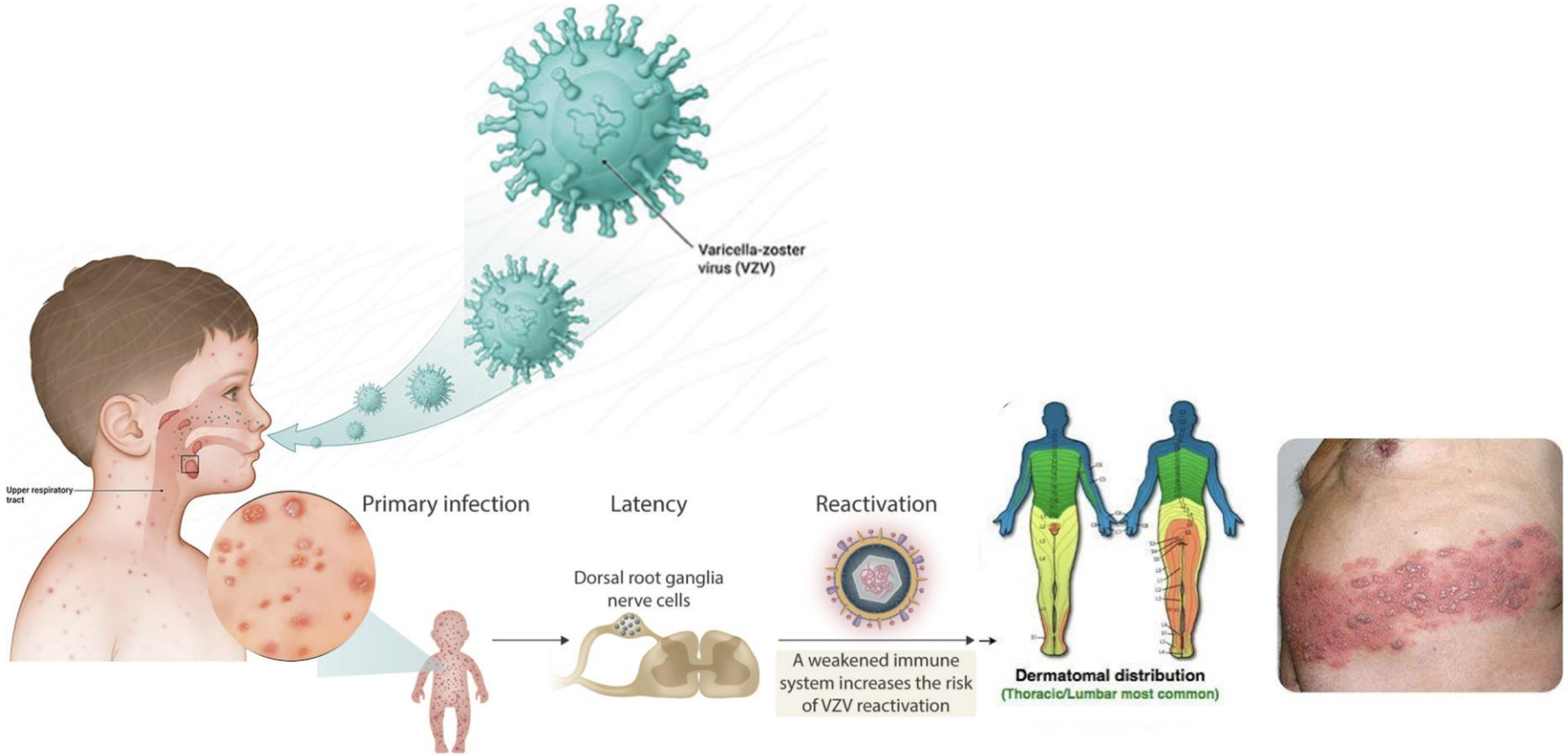
Varicella Zoster Virüsü (VZV)

- Nörotropik alfa herpes virus (HHV-3)
- 180-200 nm çapında, çift sarmallı, sirküler DNA genomundan oluşan zarflı virüsler








Varicella-zoster virus (VZV)
Upper respiratory tract
Primary infection
Latency
Reactivation
Dorsal root ganglia nerve cells
A weakened immune system increases the risk of VZV reactivation
Dermatomal distribution
(Thoracic/Lumbar most common)

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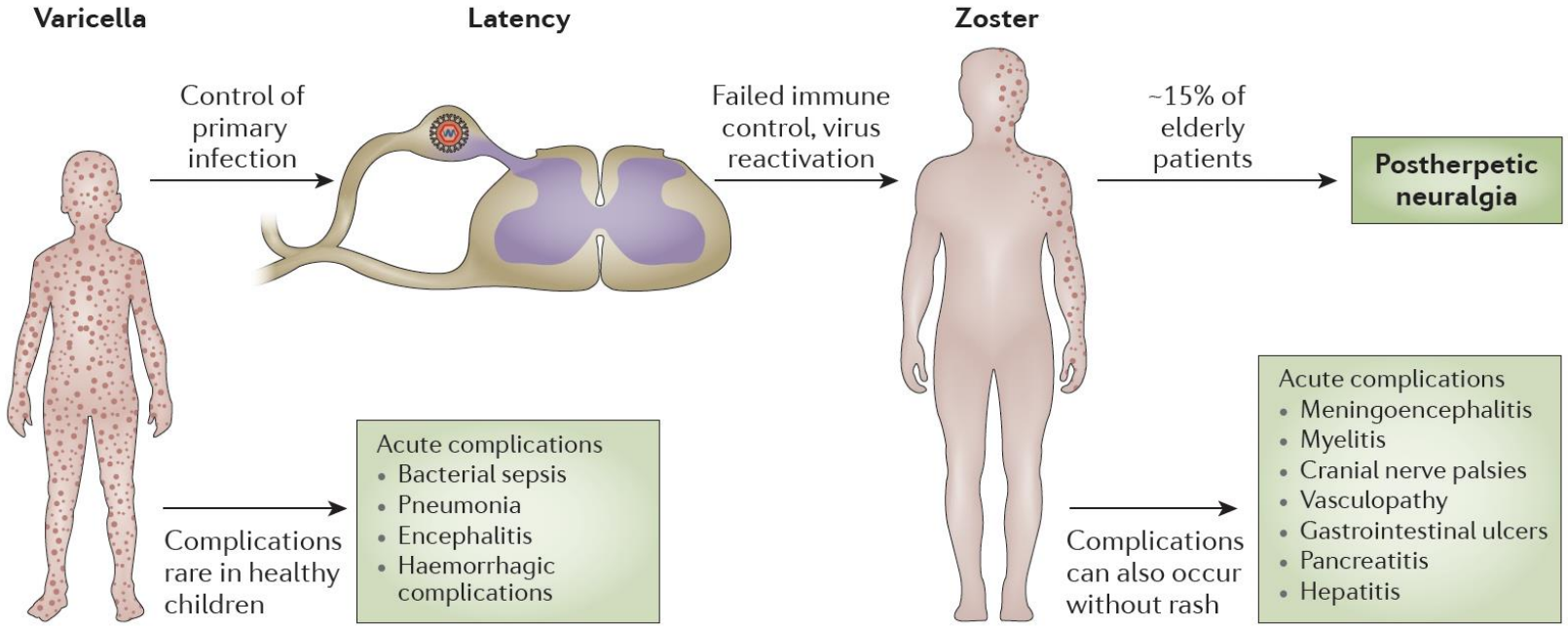


SG-05/24

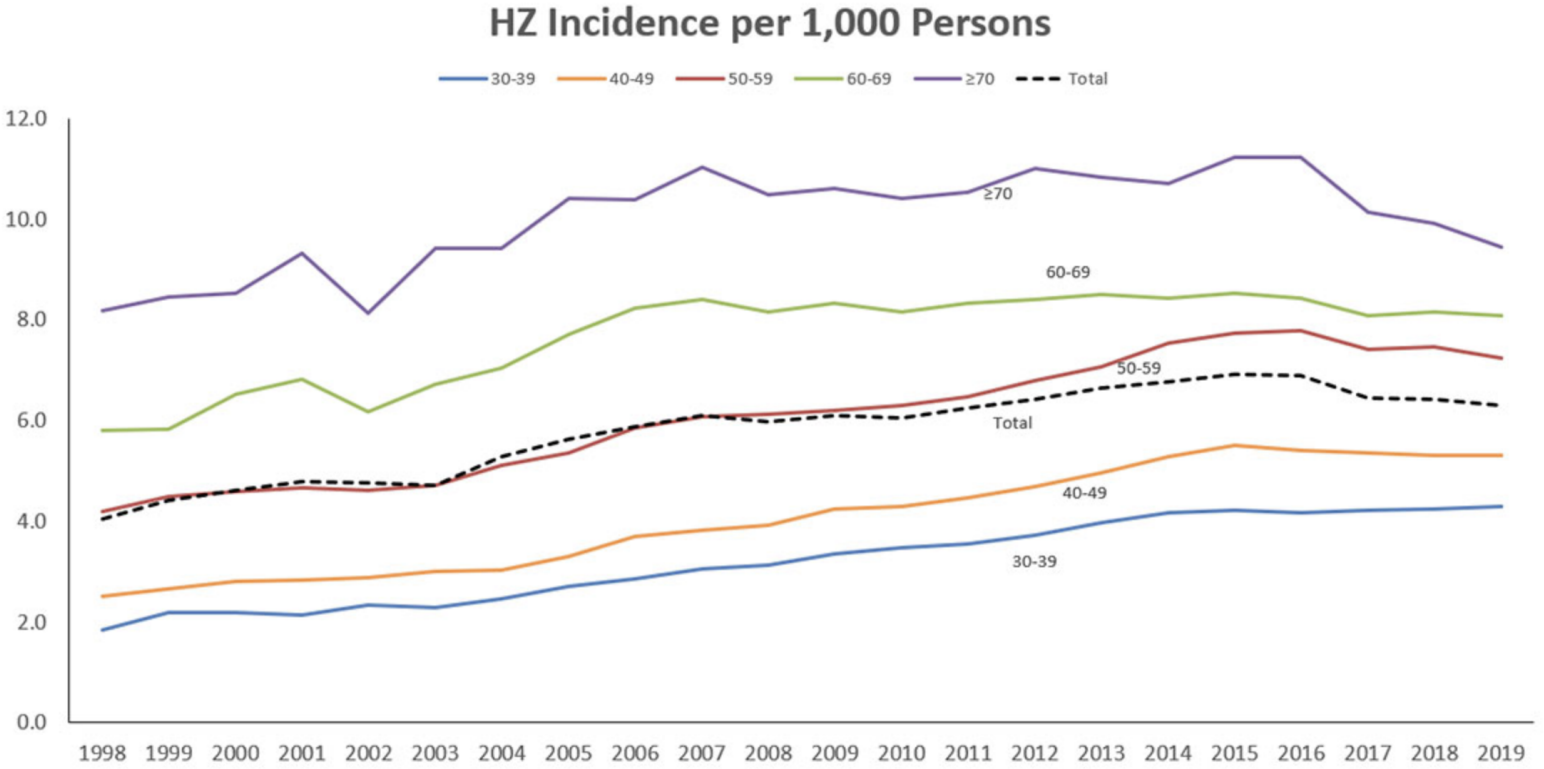
Gershon A., et al. Nat Rev Dis Primers 2015: 15016. https://doi.org/10.1038/nrdp.2015.16

Epidemiyoloji

- ABD'de her 3 kişiden biri yaşamlarında en az bir kez zonaya yakalanmakta.
  - Çoğunluğu bir kez geçiriyor olsa da bazılarında birden çok
- Yaş ve immun zayıflamayla risk artıyor.
  - Çocuklarda insidans 1/1000 iken 80 yaş ve üzerinde >15/1000

Jumaanet al., JID, 2005, 191:2002-7
Yawn, et al., Mayo ClinProc. 2007; 82:1341-9
Insingaet al., J Gen Intern Med. 2005, 20:748-53
Harpaz et al, IDWeek2015

HZ insidansı artıyor



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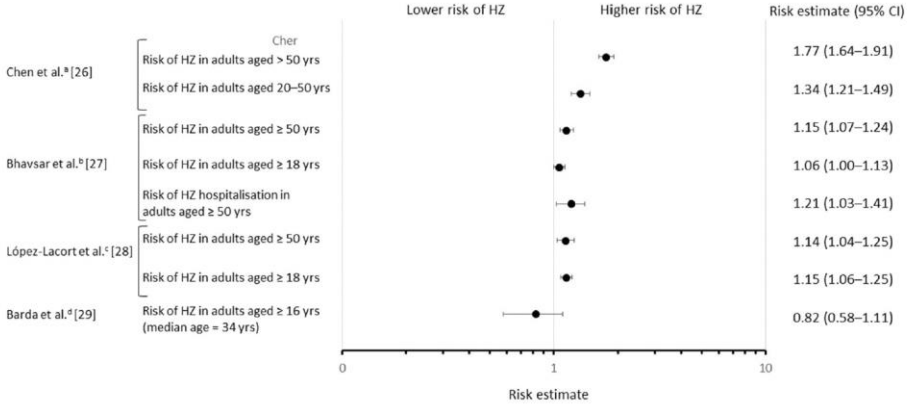
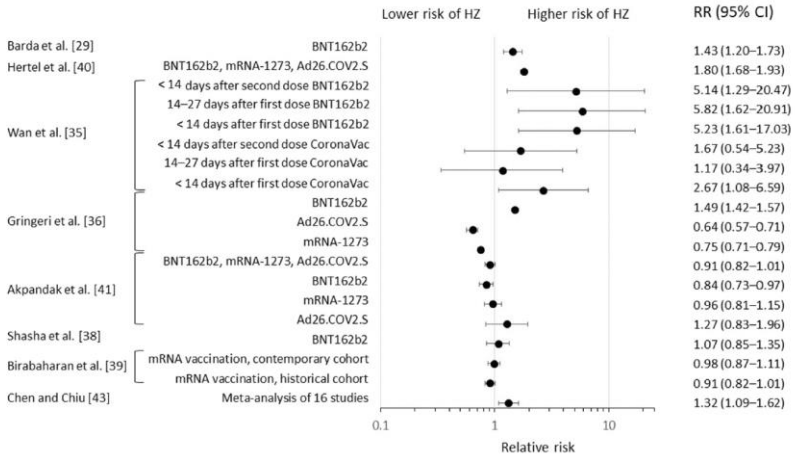
Source: https://academic.oup.com/jid/article/226/Supplement_4/S470/6764830

The Impact of the COVID-19 Pandemic on the Incidence of Herpes Zoster: A Narrative Literature Review

Raunak Parikh · Mitra Yousefi · Desmond Curran · Robyn Widenmaier





Parikh R, et al. Infect Dis Ther 2024;13:447-61.

- Zona ve komplikasyonları yaşam kalitesini olumsuz yönde etkiler.
- En önemli komplikasyonu olan PHN
  - gelişme sıklığı %5-30 arasında değişir
  - en az üçte birinde bir yıldan uzun sürer

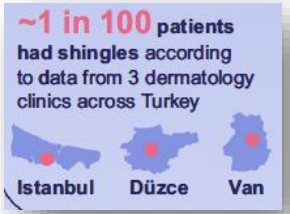
- Yaklaşık %1-4'ü komplikasyonlar nedeniyle hastaneye yatar.
  - Yaşlılar ve immunsuprese hastalar daha çok
  - Hastanede yatanların %30'u immunsuprese

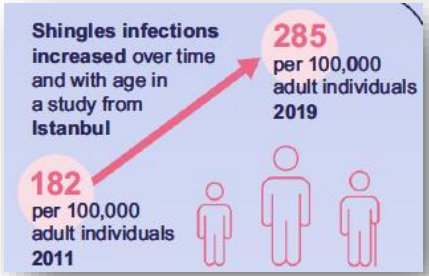
Infect Dis Ther (2023) 12:1937–1954
https://doi.org/10.1007/s40121-023-00849-3

REVIEW

Herpes Zoster Burden of Disease and Clinical Management in Turkey: A Comprehensive Literature Review

Selim Badur · Esin Senol · Alpay Azap · Cihan Yesiloglu · Alev Ozakay · Serdar Ozturk · Adriana Guzman-Holst





Badur S, et al. 2023;12:1937-54.

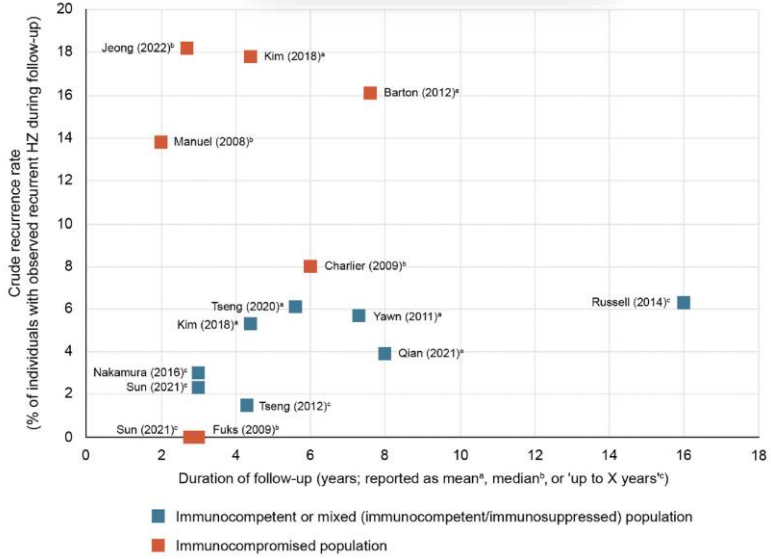
Dermatol Ther (Heidelb) (2024) 14:569–592
https://doi.org/10.1007/s13555-024-01101-7

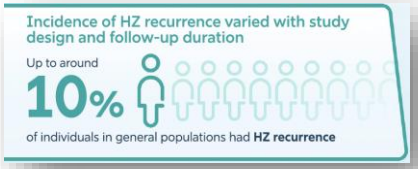
REVIEW

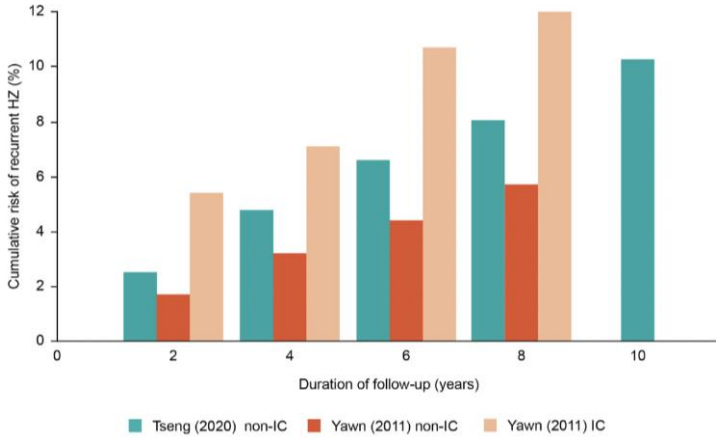
Herpes Zoster Recurrence: A Narrative Review of the Literature

Raunak Parikh · O'Mareen Spence · Nikolaos Giannelos · Iain Kaan

January 2003 — February 2023 PubMed







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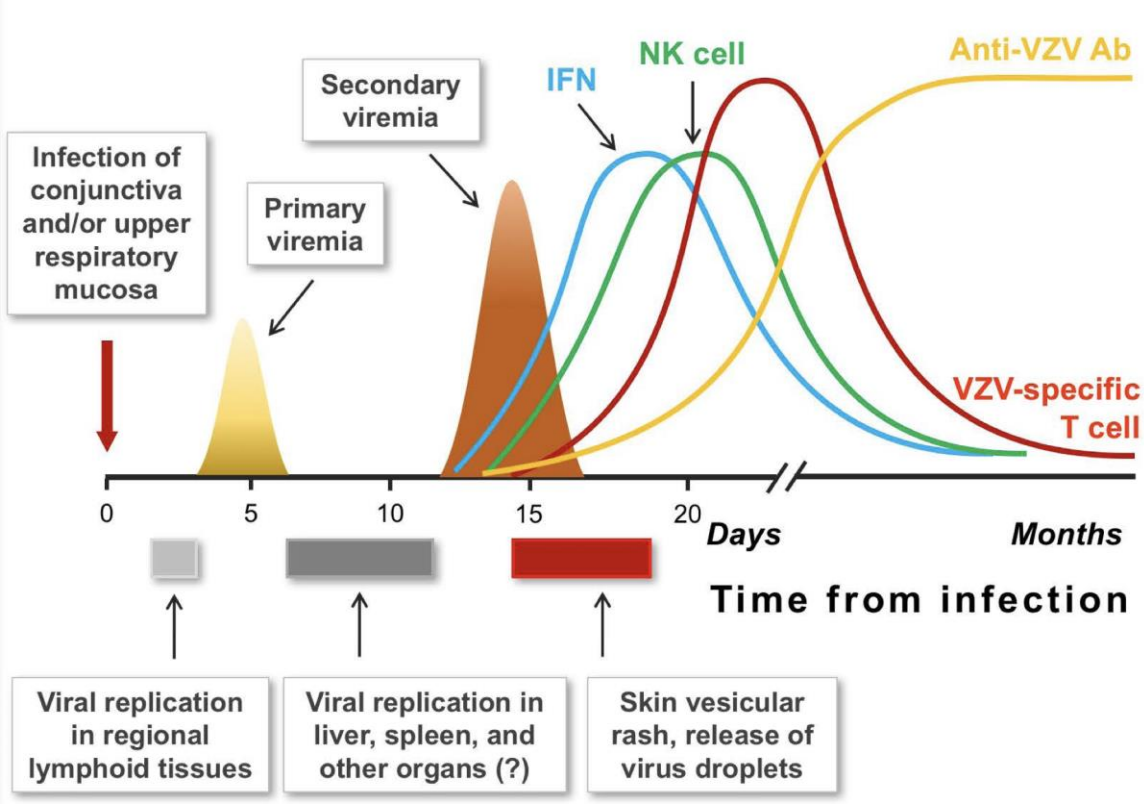
Parikh R, et al. Dermatol Ther 2024;14:569-92.

VZV immünitesi



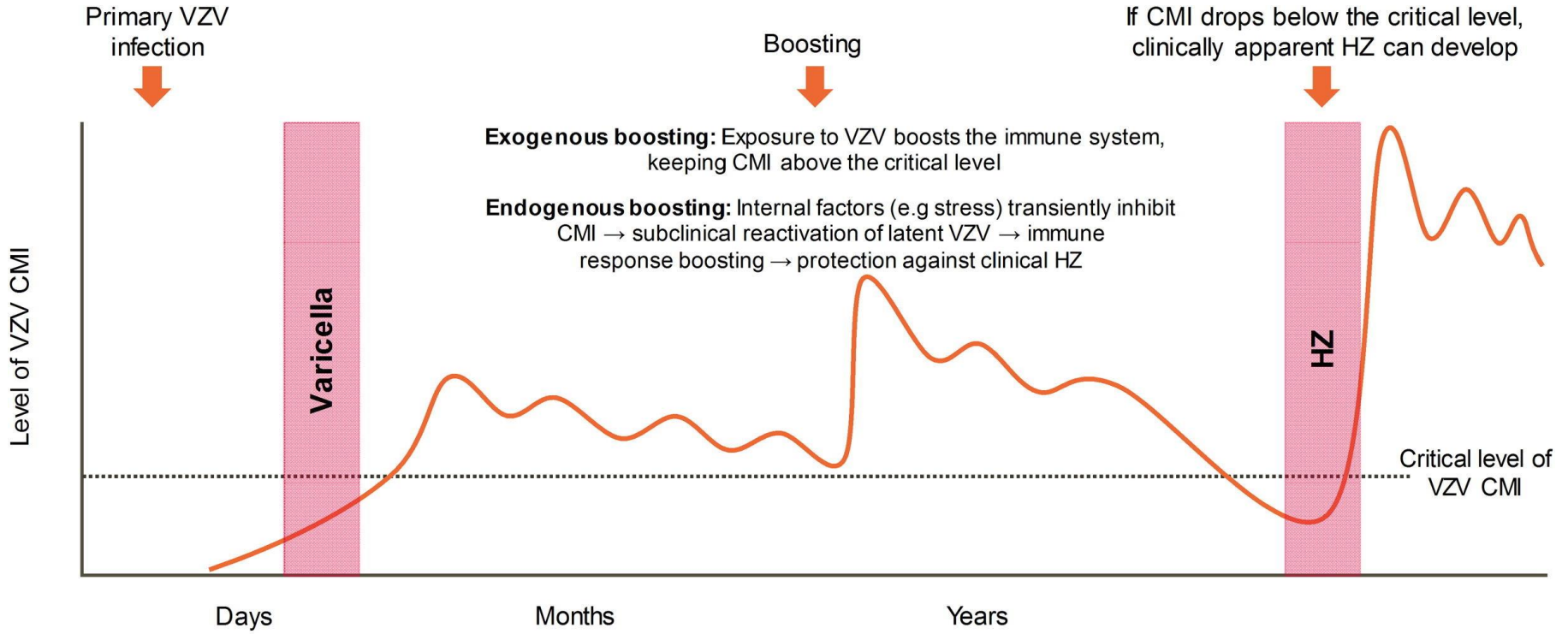
VZV spesifik hücresel immun yanıt zamanla azalır

≥ 55 yaş kişilerin %30-40'ında VZV spesifik T hücre cevabı yok.

Weinberg A, et al. J Infect Dis 2010;201(7):1024-30

Freer G, Pistello M. New Microbiol 2018;41(2):95–105.

Hücresel immünite ve VZV reaktivasyonu



HZ, herpes zoster; VZV, varicella zoster virus; CMI, cell-mediated immunity.

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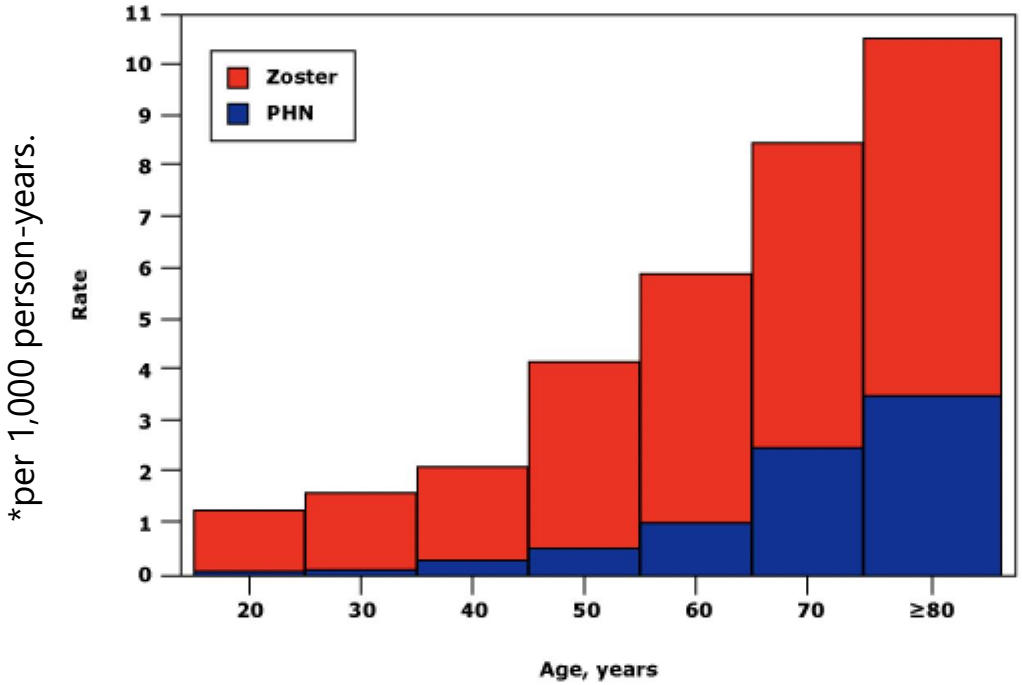
Wutzler P, et al. Vaccine 2018; 36(46): 7072-82.

Risk grupları

- İleri yaş
- Lenfoproliferatif maligniteler
- Transplant alıcıları
- Belli immunmodülatör tedaviler
- Kemoterapi
- Kortikosteroid
- HIV ile yaşayan bireyler

VZV reaktivasyonunda spesifik hücresel immünitenin azalması esas rolü oynar.

HZ ve PHN oranları* yaşla artar



50 yaş ve üzerinde HZ olanlarda PHN gelişme riski %10-18

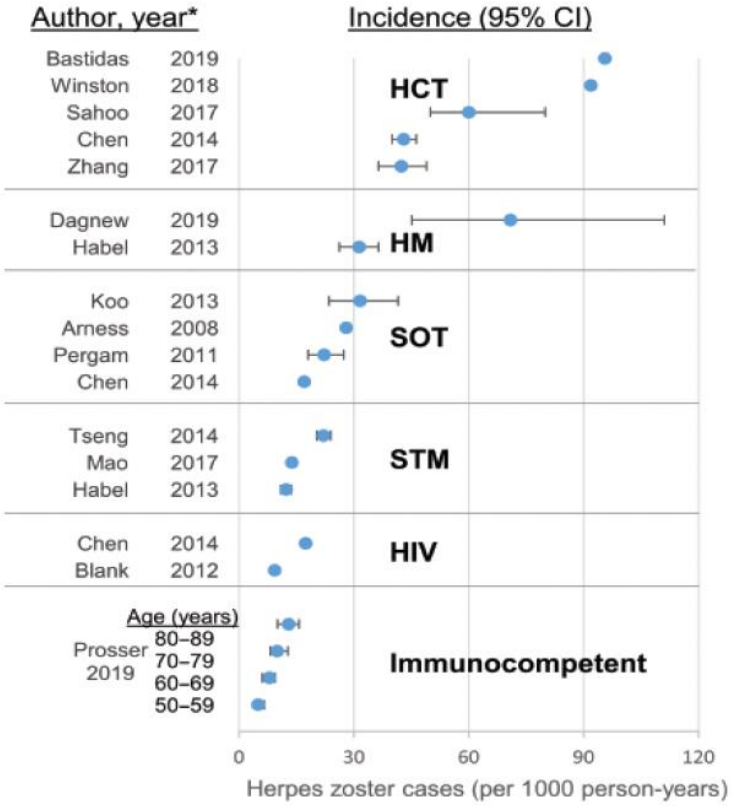
Insingaet al., J Gen Intern Med. 2005, 20:748-53

*PNH: ≥ 30 gün süren ağrı

https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm

Insinga et al. J Gen Intern Med 2005; 20:748-53

HZ ve immunkompromize hastalar



CID 2020;71(7):e125-34.

HZ ve otoimmun hastalıklar

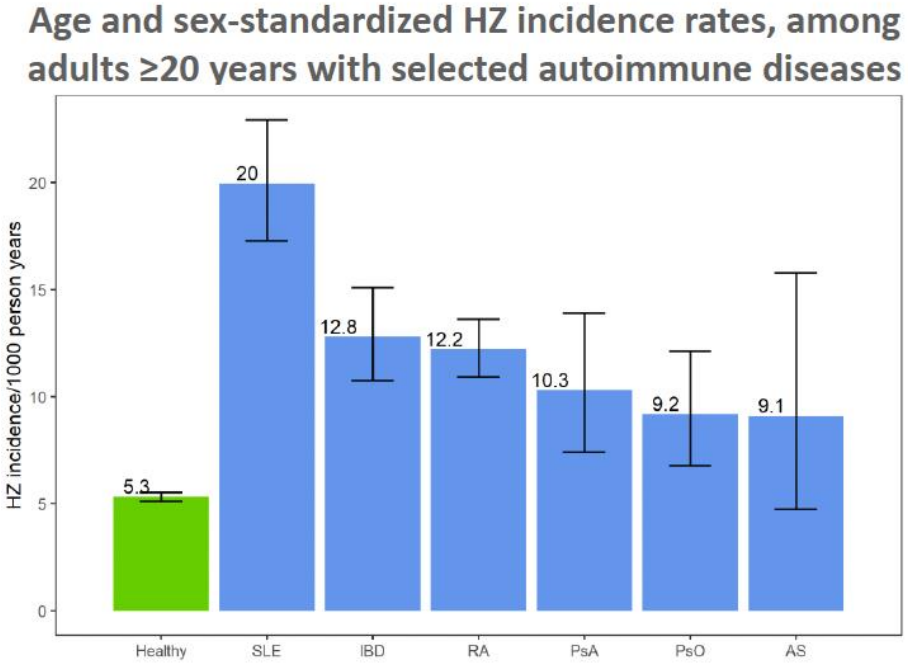


Figure adapted from Yun et al. Bars show the IRs of HZ with 95% confidence intervals. Cohorts of healthy adults without autoimmune diseases or diabetic conditions and adult patients with diabetes were used as controls. SLE=systemic lupus erythematosus; IBD=inflammatory bowel disease; RA=rheumatoid arthritis;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

Arthritis & Rheumatology 2016;68(9):2328-37.
CID 2021;ciab125.

Aşılama

- Zona aşıları, “terapötik aşı” gibi davranır ve VZV spesifik T hücre cevabını arttırarak virüsün reaktivasyonunun önlenmesine veya hafifletilmesine katkı sağlar.

Aşı Tipleri

Rekombinan protein subunit aşısı (Recombinant Zoster Vaccine – RZV)

Canlı zayıflatılmış aşı (Zoster Vaccine Live – ZVL)

Characteristic	ZOSTAVAX (Zoster Vaccine Live; Merck)	SHINGRIX (Recombinant Zoster Vaccine; GlaxoSmithKline)
Vaccine type	Live-attenuated VZV (Oka/Merck); ≥19 400 PFU	Recombinant VZV gE, adjuvanted
Vaccine composition	Two components: 1. lyophilized vaccine 2. sterile diluent	Two components: 1. lyophilized gE antigen 2. AS01B adjuvant suspension
Storage	−50°C to −15°C	+2°C to +8°C
Shelf life	18 months from the date of manufacture of the final filled container when stored at ≤ −15°C	36 months from the date of manufacture when stored at +2°C to +8°C
Dosage and administration	1 dose SQ in deltoid region of upper arm; 0.65 mL/dose	2 doses IM in deltoid region of the upper arm, 2 to 6 months apart; 0.5 mL/dose
Reactogenicity	Low	High
Overall efficacy against incidence of HZ	51.3%	97.2%
Overall efficacy against incidence of PHN	66.5%	91.2%
Persistence of protection against HZ	Up to 8 years	≥10 years (studied up to 10 years)
FDA approval	May 25, 2006 for adults aged ≥60 yoa; March 24, 2011 for adults aged 50–59 yoa	October 20, 2017 for adults aged ≥50 yoa July 23, 2021 for adults ≥18 yoa who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy

50 yaş üzeri onaylı

18 yaş üzeri onaylı

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CIC 2021;224:S429-42

RZV (Shingrix®)

- Rekombinan protein subunit aşısı

VZV glikoprotein E 50 mcg + Adjuvan ($AS01_B$) =

İki-6 ay arayla **2 doz**

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RZV etkinliği

Study Design and Objectives	ZOE-50[1,2] (Zoster-006)	ZOE-70[2,3] (Zoster-022)
Experimental design	Randomized, observer-blind, placebo-controlled, multicenter, multinational (North America, Europe, Latin America, Asia-Pacific)	
Primary objective	HZ efficacy in persons ≥50 years	HZ efficacy in persons ≥70 years
Actual enrolment	**16,160**	**14,816**
Dosing schedule	Vaccine or placebo administered (0.5 mL) intramuscularly at 0 and 2 months	
Primary objectives in pooled analysis	PHN efficacy in ≥70 years of age HZ efficacy in ≥70 years of age	
Total Vaccinated Cohort (pooled analysis)[3]	**17,531** (includes subjects aged ≥70 in ZOE-50 and all ZOE-70 subjects)	

ZOE-50/70 efficacy studies conducted at the same sites.
Subjects ≥70 years of age were randomly assigned to ZOE-50 or ZOE-70.

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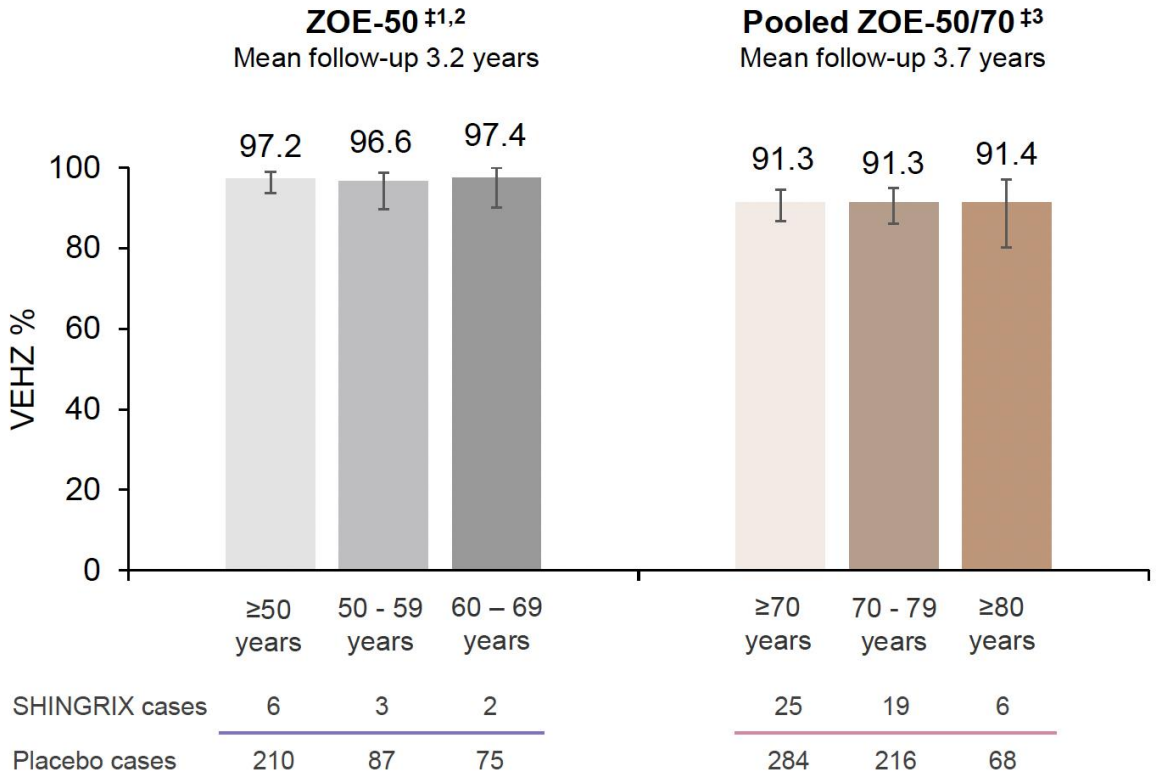
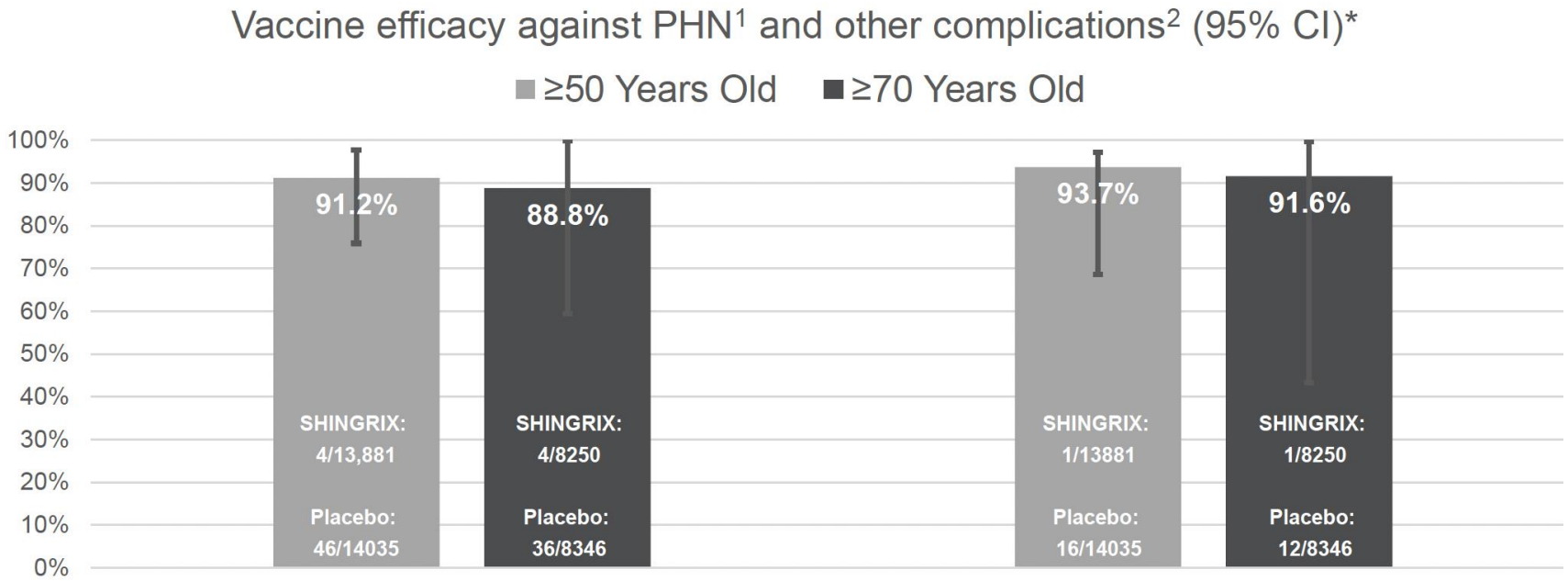
Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med 2015; 372:2087.
Cunningham AL, Lal H, Kovac M, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med 2016; 375:1019.



P<0.001 for all age groups vs. placebo

Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med 2015; 372:2087.
Cunningham AL, Lal H, Kovac M, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med 2016; 375:1019.



Vaccine efficacy against PHN

PHN is defined as HZ-associated pain rated as ≥3 on a 0-10 scale, occurring or persisting for at least 90 days following the onset of rash using the Zoster Brief Pain Inventory questionnaire.[1]

Vaccine efficacy against other HZ-related complications, in a post-hoc pooled analysis

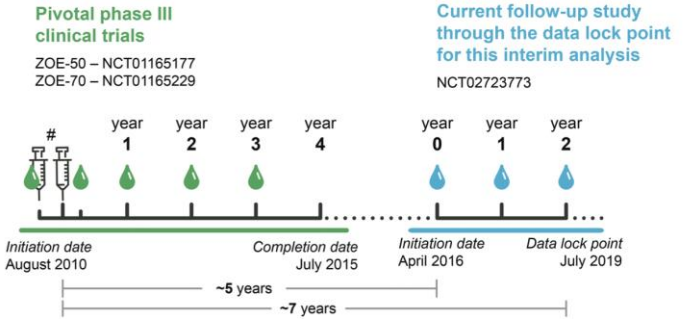
Other complications included HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease, visceral disease, and stroke[1]

Cunningham AL, et al. N EnglJ Med. 2016 Sep;375(11):1019-32.
Kovac M et al. Vaccine;2018;36;1537-1541.

Uzun dönem RZV etkinliği

The Adjuvanted Recombinant Zoster Vaccine Confers Long-Term Protection Against Herpes Zoster: Interim Results of an Extension Study of the Pivotal Phase 3 Clinical Trials ZOE-50 and ZOE-70

Céline Boutry,[1,a] Andrew Hastie,[2] Javier Diez-Domingo,[3] Juan Carlos Tinoco,[4] Chong-Jen Yu,[5] Charles Andrews,[6] Jean Beytout,[7] Covadonga Caso,[8] Huey-Shinn Cheng,[9] Hee Jin Cheong,[10] Eun Ju Choo,[11] Dan Curiac,[12] Emmanuel Di Paolo,[13] Marc Dionne,[14] Tamara Eckermann,[15] Meral Esen,[16] Murdo Ferguson,[17] Wayne Ghesquiere,[18] Shinn-Jang Hwang,[19,20] Thiago Junqueira Avelino-Silva,[21] Pavel Kosina,[22] Chiu-Shong Liu,[23] Jukka Markkula,[24] Beate Moeckesch,[25] Cláudia Murta de Oliveira,[26] Dae Won Park,[27] Karlis Pauksens,[28] Paola Pirrotta,[29] Georg Plassmann,[30] Carol Pretswell,[31] Lars Rombo,[32] Bruno Salaun,[13] Johan Sanmartin Berglund,[33] Isabelle Schenkenberger,[34] Tino Schwarz,[35] Meng Shi,[2] Benita Ukkonen,[36] Toufik Zahaf,[29] Cristiano Zerbini,[37] Anne Schuind,[2,b] and Anthony L. Cunningham[38,39]; on behalf of the Zoster-049 Study Group*



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Boutry C, et al. Clinical Infectious Diseases 2022;74(8):1459–67

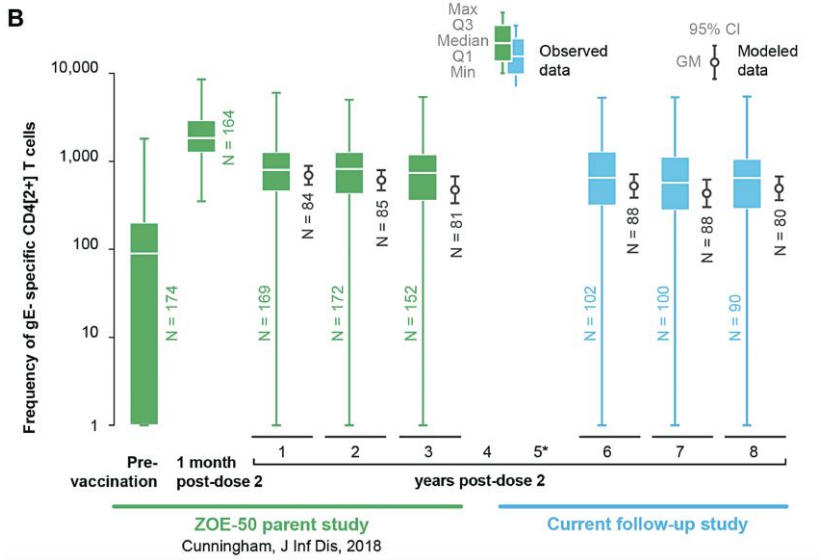
Table 2. Vaccine Efficacy in the ZOE-50 and ZOE-70 Studies and the Current Long-Term Follow-up Study After at Least 2 Additional Years of Follow-up

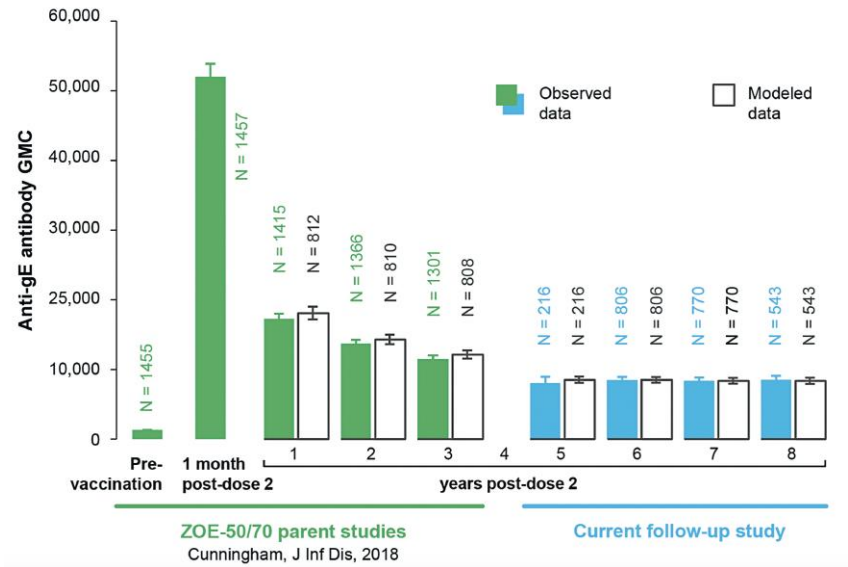
	Adjuvanted Recombinant Zoster Vaccine				Historical Control[a]/Placebo Group in ZOE-50 and ZOE-70[b]				
	N	n	Sum of Follow-up Years	Incidence (per 1000 Person-Years)	N	n	Sum of Follow-up Years	Incidence (per 1000 Person-Years)	Vaccine Efficacy, % (95% Confidence Interval)
Vaccine efficacy in the current follow-up study: primary objective (up to the data lock point for the interim analysis in the current follow-up study)									
Overall[a]	7277	27	19 621.7	1.4	7277	169	19 621.7	8.6	84.0 (75.9–89.8)
Vaccine efficacy from 1 month post-dose 2: secondary objective (up to the data lock point for the interim analysis in the current follow-up study)									
Overall	13 881	59	72 744.6	0.8	13 881	651	72 744.6	8.9	90.9 (88.2–93.2)
Year 1[b]	13 881	3	13 744.5	0.2	14 035	130	13 823.3	9.4	97.7 (93.1–99.5)
Year 2[b]	13 569	10	13 415.6	0.7	13 564	136	13 332.5	10.2	92.7 (86.2–96.6)
Year 3[b]	13 185	9	13 016.1	0.7	13 074	116	12 834.0	9.0	92.4 (85.0–96.6)
Year 4[b]	12 757	10	12 946.7	0.8	12 517	95	12 637.4	7.5	89.8 (80.3–95.2)
Year 6[a]	7277	10	7208.8	1.4	7277	66	7208.8	9.2	84.9 (70.4–93.1)
Year 7[a]	7097	10	6993.1	1.4	7097	68	6993.1	9.7	85.3 (71.3–93.3)
Year 8[a,c]	6876	7	5160.2	1.4	6876	44	5160.2	8.5	84.1 (64.4–94.0)

SG-05/24

Boutry C, et al. Clinical Infectious Diseases 2022;74(8):1459–67

VZV spesifik CD_4 sayısı ve antikor titresi aşı öncesi seviyenin 6 katından yüksek devam ediyor.





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Boutry C, et al. Clinical Infectious Diseases 2022;74(8):1459–67

Persistence of immune response to an adjuvanted varicella-zoster virus subunit vaccine for up to year nine in older adults

Tino F. Schwarz[a], Stephanie Volpe[b], Gregory Catteau[c], Roman Chlibek[d], Marie Pierre David[e], Jan Hendrik Richardus[f], Himal Lal[g], Lidia Oostvogels[b], Karlis Pauksens[h], Stephanie Ravault[i], Lars Rombo[j], Gerard Sonder[k], Jan Smetana[d], Thomas Heineman[l], and Adriana Bastidas[b]

[a]Laboratory Medicine and Vaccination, Klinikum Würzburg Mitte, Standort Juliusspital, Würzburg, Germany; [b]Clinical R&D, GSK, Wavre, Belgium; [c]Biostatistics & Statistical Programming, Clinical Evidence Generation, R&D, GSK, Wavre, Belgium; [d]Department of Epidemiology, Faculty of Military Health Sciences, University of Defense, Hradec Kralove, Czech Republic; [e]Biostatistics & Statistical Programming, Clinical Evidence Generation, R&D, GSK, Rixensart, Belgium; [f]Department of Infectious Disease Control, Municipal Public Health Service Rotterdam-Rijnmond, Rotterdam, The Netherlands; [g]Clinical R&D, Pfizer Inc., Collegeville, PA, USA; [h]Medical Sciences, Section of Infectious Diseases, Uppsala University Hospital, Uppsala, Sweden; [i]Clinical Laboratory Sciences, GSK, Rixensart, Belgium; [j]Department of Medical Biochemistry and Microbiology, Zoonosis Science Center, Uppsala University, Uppsala, Sweden; [k]Department of Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, The Netherlands; [l]Clinical Development, Genocea Biosciences, Cambridge, MA, USA

ABSTRACT

Background: In adults aged ≥60 years, two doses of the herpes zoster subunit vaccine (HZ/su; 50 μg varicella-zoster virus glycoprotein E [gE] and $AS01_B$ Adjuvant System) elicited humoral and cell-mediated immune responses persisting for at least six years. We assessed immunogenicity nine years post-initial vaccination.

Methods: This open extension study (NCT02735915) followed 70 participants who received two HZ/su doses in the initial trial (NCT00434577). Blood samples to assess the cellular (intracellular cytokine staining) and humoral (ELISA) immunity were taken at year nine post-initial vaccination.

Results: Participants' mean age at dose 1 was 72.3 years. The fold increases over pre-vaccination in the mean frequency of gE-specific CD4+ T-cells expressing ≥2 activation markers plateaued from year four post-dose 1 until year nine. Anti-gE antibody geometric mean concentrations plateaued and remained above pre-vaccination levels from year four onwards. Immunogenicity at year nine was similar across age strata (60–69, ≥70 years) and confirmed statistical prediction model results using data for up to year six. Further modeling using all data up to year nine predicted immune responses would remain above the pre-vaccination level up to year 15.

Conclusion: In adults aged ≥60 years, HZ/su-induced immunogenicity remained above pre-vaccination levels for at least nine years post-initial vaccination.

Summary: After vaccination with HZ/su, both cell mediated and humoral immunity remained above pre-vaccination levels up to year 9 regardless of age group. Immune responses are predicted to remain above baseline up to 15 years post initial vaccination.

ARTICLE HISTORY
Received 11 December 2017
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KEYWORDS
herpes zoster (shingles) vaccine; herpes zoster; immunity; persistence; prediction modeling;

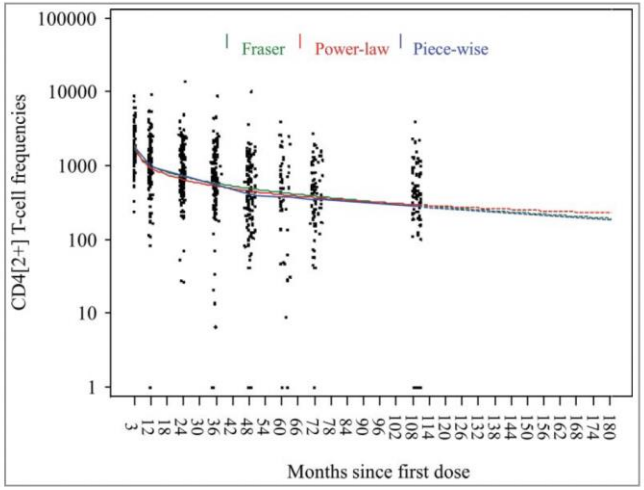

Figure 3. Predicted geometric means of frequencies of gE-specific CD4[2+] T cells based on three statistical prediction models (piece-wise linear, power-law, Fraser).

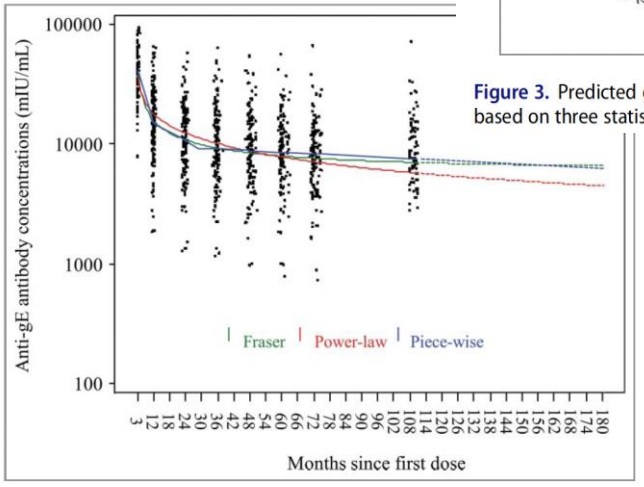

Figure 4. Predictions of anti-gE antibody geometric mean concentrations based on three statistical prediction models (piece-wise linear, power-law, Fraser).

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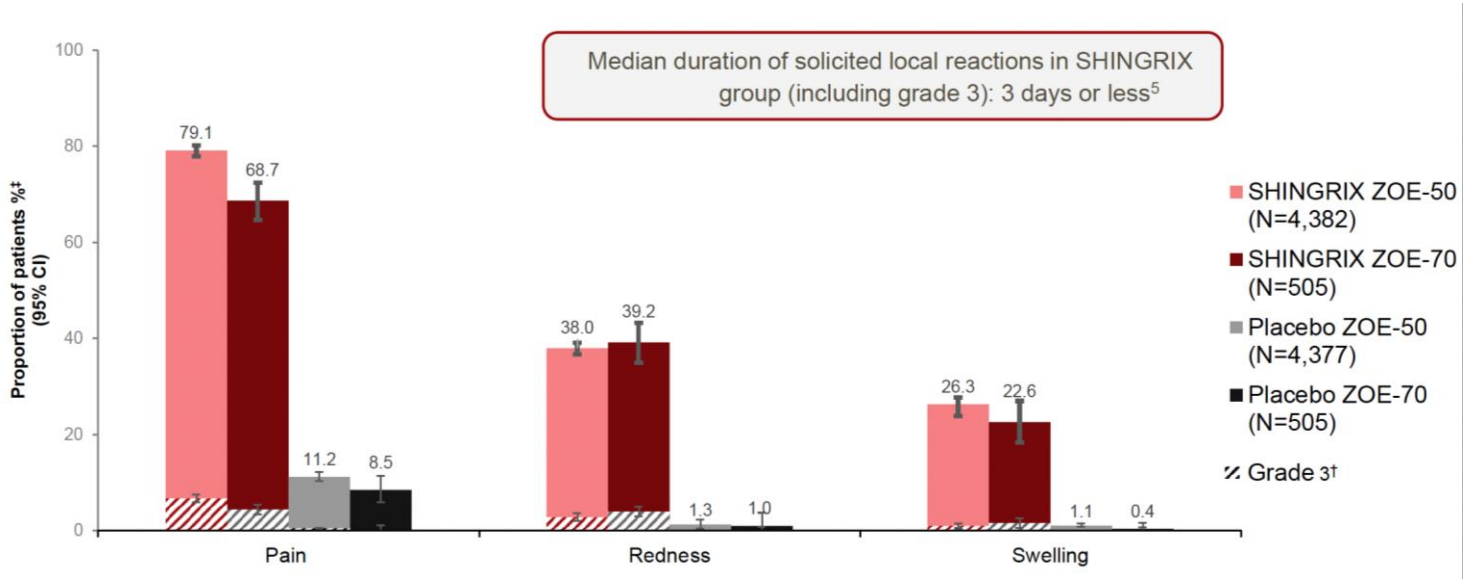
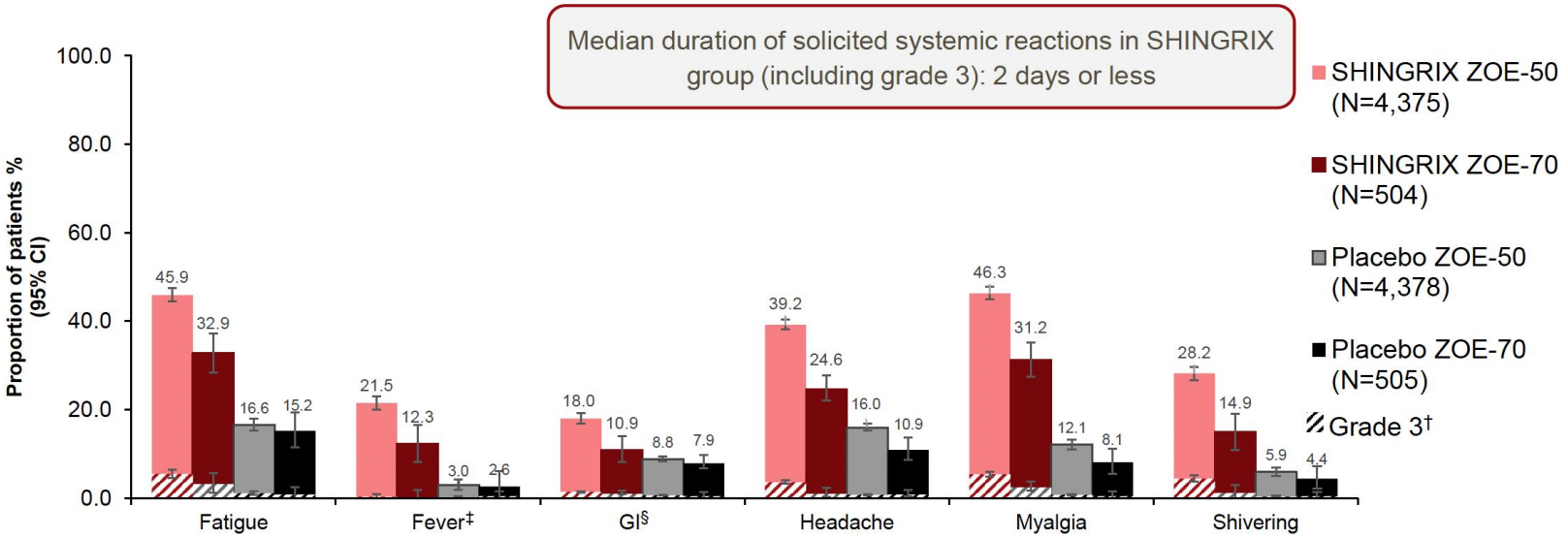
Schwartz TF, et al. Hum Vacc Immunother 2018;14(6):1370-7.

Lokal yan etkiler (ilk 7 gün)



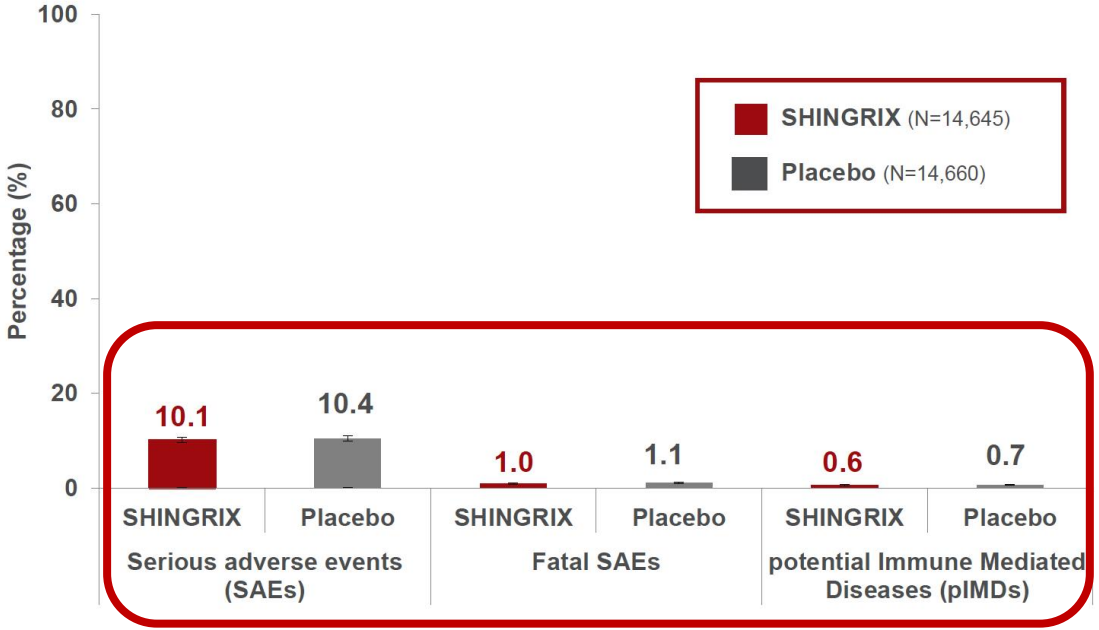
Lal H, *et al. N EnglJ Med* 2015;372:2087–96.
Cunningham AL, *et al. N EnglJ Med* 2016;75:1019–32.
Lopez-Fauqued, M et al. Vaccine 2019;37:2482-2493.26

Sistemik yan etkiler (ilk 7 gün)



Lal H, *et al. N Engl J Med* 2015;372:2087–96.
Cunningham AL, *et al. N Engl J Med* 2016;75:1019–32.
Lopez-Fauqued, M et al. Vaccine 2019;37:2482-2493.26

Ciddi yan etkiler açısından aşı ve plasebo grubu arasında fark yok



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Lopez-FauquedM, et al. Vaccine 37 (2019) 2482–2493.
StrezovaA, et al. Open Forum Infect Dis. 2022; ofac485,https://doi.org/10.1093/ofid/ofac485.

Post hoc analysis of reactogenicity trends between dose 1 and dose 2 of the adjuvanted recombinant zoster vaccine in two parallel randomized trials

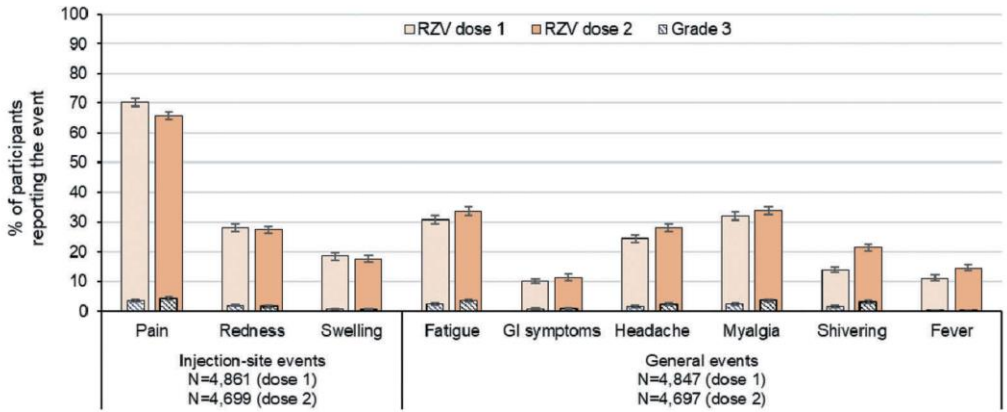

Figure 1. Incidence of solicited injection site and general events reported during the 7-day post-vaccination period following each dose among RZV recipients (TVC reactogenicity).

Birinci doz ile karşılaştırıldığında ikinci doz sonrası lokal yan etkiler daha az, sistemik yan etkiler daha fazla

Colindres R, Wascotte V, Brecx A, et al. Hum Vaccin Immunother 2020; 16:2628.

Postlicensure Safety Surveillance of Recombinant Zoster Vaccine (Shingrix) — United States, October 2017–June 2018

TABLE 2. Most commonly reported symptoms* after receipt of recombinant zoster vaccine (RZV) in reports submitted to VAERS (N = 4,381)† — United States, October 2017–June 2018

Sign/Symptom	Total RZV reports, no. (%)	RZV given in combination with other vaccines, no. (%)
Pyrexia	1,034 (23.6)	57 (26.6)
Injection site pain	985 (22.5)	49 (22.9)
Injection site erythema	880 (20.1)	50 (23.4)
Pain	853 (19.5)	45 (21.0)
Chills	847 (19.3)	32 (15.0)
Headache	730 (16.7)	30 (14.0)
Fatigue	703 (16.0)	23 (10.7)
Pain in extremity	691 (15.8)	37 (17.3)
Injection site swelling	588 (13.4)	29 (13.6)
Myalgia	530 (12.1)	19 (8.9)

Abbreviation: VAERS = Vaccine Adverse Event Reporting System.

* According to Medical Dictionary for Regulatory Activities Preferred Terms, a single report may be assigned more than one Preferred Term (i.e., terms are not mutually exclusive).

† Includes reports for RZV given alone (95.1%) and concomitantly with other vaccines.

50–69 yaş aralığında sistemik bulgu ve belirtiler daha fazla:

Ateş %29.1
Titreme %24.6
Başağrısı %21.3

≥70 yaş grubunda lokal semptomlar daha fazla:

Eritem %22.5
Ağrı %21.5

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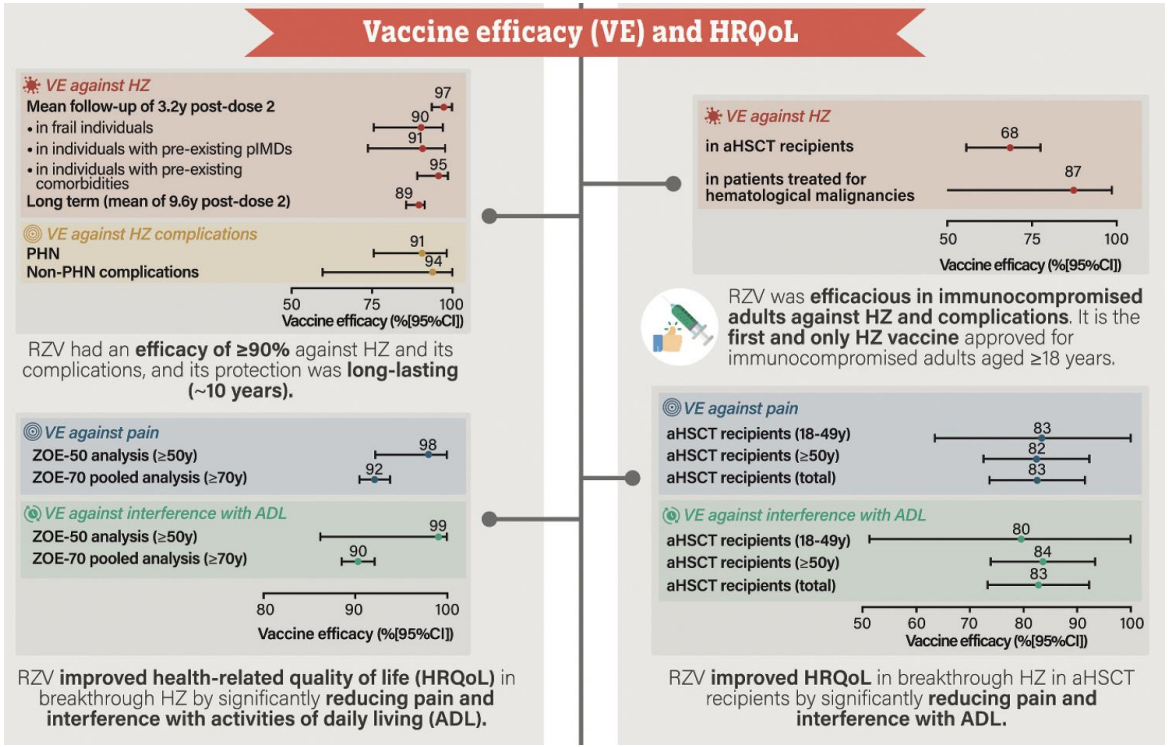
Hesse EM, Shimabukuro TT, Su JR, et al. MMWR Morb Mortal Wkly Rep 2019; 68:91.

Recombinant zoster vaccine in immunocompetent and immunocompromised adults: A review of clinical studies

Agnes Mwakingwe-Omari[a], Nicolas Lecrenier[b], Abdi Naficy[a], Desmond Curran[c], and Inga Posiuniene[b]

[a]Clinical Sciences, GSK, Rockville, MD, USA; [b]Medical Affairs Department, GSK, Wavre, Belgium; [c]Evidence and Outcome Department, GSK, Wavre, Belgium



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Mwakingwe-Omari A, et al. Hum Vaccin Immunother 2023;19(3):2278362.

Endikasyonlar

- ≥ 50 yaş immunkompetan yetişkinler
- ≥ 18 yaş immunkompromize hastalar

Kontraendikasyonlar

- Aşı içeriğindeki bir bileşene karşı anafilaksi öyküsü
- GBS öyküsü
  - Gözlemsel çalışmaların sonuçları RZV ile GBS arasında bir ilgi olduğunu gösterdi (???)
- Gebelik
  - Emzirme kontraendike değil
- Bazı transplant alıcılarında RZV adjuvanının immun cevabı uyarmasına bağlı olarak rejeksiyon riski var!

Aşı öncesi serolojik test isteyelim mi?

Önceden VZV enfeksiyonu veya aşılama olmasının önemi yok !

- Ancak bazı hasta gruplarında (transplant gibi) rutin serolojik test yapılabilir
  - ✓Bağışıklık yoksa
    - Immunsupresyon geciktirilecekse varicella aşısı önerilir.

Ne zaman aşılayalım?

- İdeal olarak immunsupresyon öncesi aşılama yapılmalı
  - ✓İmmunsupresif tedaviden en az 14 gün önce ikinci doz yapılmış olmalı
    - Gerektiğinde iki doz arasındaki süre bir-iki aya inebilir.
      - mümkün değilse en az 4 hafta önce ZVL (alternatif)
- Bu yapılamadıysa bireysel karar
  - ✓Aşının etkinliği? Hastalık riski? Aşılama riski?
  - ✓Immunsupresyon riskinin azaldığı ve stabil hastalık döneminde

Düşük doz immunsupresif tedavi alan hastalarda

- Düşük doz prednizon (<2 mg/kg; ≤20 mg/gün) veya eşdeğeri
- Metotreksat (≤0.4 mg/kg/gün)
- Azatioprine (≤0.3 mg/kg/gün)
- 6-merkaptourine (≤1.5 mg/kg/gün)

- Her hangi bir zaman aşılama yapılabilir

✓etkinliği??

Daha önce HZ geçirenler

- Öykü dikkate alınmaz !!!

- Ne zaman ??
  - Bir yıl beklenebilir ?? yada lezyonlar geçene kadar beklenebilir.

Tablo 19. Erişkinlerde yaş gruplarına göre 2024 aşı önerileri ve dozları

Aşı	19-26 yaş	27-49 yaş	50-64 yaş	≥65 yaş
Tetanoz, difteri (Td)[1]	Her 10 yılda bir rapel doz			
Tetanoz, difteri, boğmaca (TdaB)[1,2]	1 doz			
İnfluenza	Her sonbaharda 1 doz			
Konjuge Pnömokok (PCV13)[3,4]	1 doz[4]			1 doz[3]
Polisakkarit Pnömokok (PPSV23)[3,4]	2 doz (5 yıl arayla)[4]			1 doz[3]
Hepatit B[5]	3 doz (0, 1, 6. ay)			
Hepatit A[6]	2 doz (0, 6. ay)			
Rekombinant Zoster[7]	2 doz		2 doz (2-6 ay arayla)	
Suçiçeği[8]	2 doz (1 ay arayla)			
Kızamık, kızamıkçık, kabakulak (KKK)[9]	1 veya 2 doz			
Meningokok ACWY[10]	1 veya 2 doz (0, 2. ay)			
Meningokok B[11]	2 veya 3 doz			
Haemophilus influenzae tip b (Hib)[12]	1 veya 3 doz (0, 1, 2. ay)			
Human papilloma virus (HPV)[13]	3 doz (0, 2, 6. ay)			
COVID-19	2 veya 3 doz, ardından rapeller (güncel önerilere göre)			

Tüm erişkinlere uygulanması önerilir.
Risk faktörü veya belirli endikasyonu olan erişkinlere uygulanması önerilir.

Tesekkürler