Έρπητας ζωστήρας σε δερματολογικούς ασθενείς με ανοσοτροποίηση

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Έρπητας ζωστήρας – Γενικά στοιχεία

- Ο ερπητας ζωστήρας(HZ;) προκαλείται από την αναζωπύρωση του ιού της ανεμευλογιάς – έρπητα ζωστήρα (VZV)
- 20 – 30 % του γενικού πληθυσμού θα εμφανίσει HZ στη διάρκεια της ζωής του
- Ο κίνδυνος αυξάνεται με την ηλικία, λόγω της μειωμένης κυτταρικής ανοσίας
- Η εικόνα είναι τυπική με κατανομή του φυσαλιδώδους εξανθήματος κατά μήκος ενός δερμοτομίου, ενώ παρατηρούνται και περιπτώσεις με πολυδερμοτομιακή ή και διάσπαρτη νόσο
- Η προσβολή των οφθαλμών (σπάνια) μπορεί να οδηγήσει σε μακράς διαρκείας διαταραχή της οράσεως
- Η μεθερπητική νευραλγία παρατηρείται σε ≤30% των ασθενών με HZ και έχει σοβαρές επιπτώσεις στην ποιότητα ζωής των ασθενών

Clinical and Experimental Rheumatology 2022

Έρπητας ζωστήρας σε δερματολογικούς ασθενείς με ανοσοτροποποίηση

- ΄Εχει μελετηθεί κυρίως σε μεγάλο αριθμό ασθενών με ψωρίαση

- Η βιβλιογραφία εμπλουτίζεται ιδιαίτερα με στοιχεία που αφορούν στην επίδραση των βιολογικών παραγόντων και των νέων μικρών μορίων στον κίνδυνο εμφάνισης HZ στους ασθενείς με ψωριασική νόσο (με ή χωρίς συνοσηρότητες)

Και η ίδια η νόσος συνδέεται με αυξημένο κίνδυνο ανάπτυξης ΕΖ

- *Psoriasis patients have higher risk of HZ compared to healthy individuals regardless of which therapies they use*

- *In these patients, it is important to determine whether dermatologic therapies have any effect on risk of HZ*

PLoS One. 2017;12(8):

RESEARCH ARTICLE

Increased risk of herpes zoster in patients with psoriasis: A population-based retrospective cohort study

Shin-Yi Tsai[1,2,3]*, Hsuan-Ju Chen[4,5], Chon-Fu Lio[1,6], Hui-Ping Ho[1], Chien-Feng Kuo[7], Xiaofeng Jia[8,9], Chi Chen[1,10], Yu-Tien Chen[1], Yi-Ting Chou[1], Tse-Yen Yang[11,12], Fang-Ju Sun[13,14], Leiyu Shi[3]*

PLoS One. 2017;12(8):

the risk of HZ was significantly higher in the patients with psoriasis who received immunomodulatory therapy or phototherapy than in those without psoriasis

4077 patients with newly diagnosed psoriasis

The overall incidence density rate of HZ in the psoriasis cohort than in the nonpsoriasis cohort (4.50 vs. 3.44 per 1,000 person-years), with a multivariable Cox proportional hazards model measured adjusted HR of 1.29.
In additional, compared with the nonpsoriasis cohort, **the risk of HZ was higher in the severe psoriasis cohort** than in the nonpsoriasis cohort (adjusted hazard ratio [HR], 1.61)
The comparison between psoriasis and nonpsoriasis cohorts revealed **a greatest magnitude risk of HZ in women** (adjusted HR, 1.36) and study participants in the **age group of 20±39 years** (adjusted HR, 1.77)

Prevention and management of herpes zoster in patients with rheumatoid arthritis and psoriatic arthritis: a clinical review

K.L. Winthrop[1], Y. Tanaka[2], E.B. Lee[3], J. Wollenhaupt[4], A. Al Enizi[5], V.F. Azevedo[6], J.R. Curtis[7]

Και σε ασθενείς με ΨΑ αυξημένος ο σχετικός κίνδυνος ανάπτυξης ΕΖ

- The risk of HZ in patients with auto-immune conditions, such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA), is generally 1.5–2-fold higher *versus* the general population due to disease-associated immune dysregulation and the use of immunosuppressive therapies

- The increased HZ incidence and potential complications in patients with autoimmune conditions highlight a need to raise awareness of the risk and optimise prevention

Clinical and Experimental Rheumatology 2022

Clinical Epidemiology

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ORIGINAL RESEARCH

Herpes Zoster, Hepatitis C, and Tuberculosis Risk with Apremilast Compared to Biologics, DMARDs and Corticosteroids to Treat Psoriasis and Psoriatic Arthritis

a post-marketing safety study

Χαμηλότερος ο σχετικός κίνδυνος με απρεμιλάστη

- The study population included 131,604 patients. For herpes zoster (N=2271), Irs were highest for users of DMARDs+CS (12.5 [9.8–15.7]), CS-only (12.5 [10.4–14.1]), and TNF+DMARDs and/or CS (11.9 [10.6–13.4]), compared with DMARDs only (9.9 [8.7– 11.2]). IRs were lowest for users of IL-only (6.7 [5.8–7.8]) and APR (7.0 [5.8–8.4]). IRs of HepC (N=150) and TB (N=81) were low and between-treatment differences were not significant.
- Conclusion: Rates of herpes zoster varied by treatment: highest among those who received polytherapy, lowest in users of apremilast only. IRs for HepC and TB were low for all exposures.

Clinical Epidemiology 2020:12

Risk of herpes zoster associated with biological therapies for psoriasis and psoriatic arthritis

A systematic review and meta-analysis

Ailing Zou, MD[a,b], Yongjun Chen, MD[a,b], Nian Shi, BD[a,b], Yu Ye, MD[c,*]

The risk of HZ in biological therapies was higher than that in non-biological (odds ratios [OR]: 1.48; 95% confidence interval [CI]: 1.18–1.86; I2=0%) and non-biological systemic (OR: 1.32; 95% CI: 1.02–1.71; I2=0%) therapies. Furthermore, the risk of HZ associated with tumor necrosis factor-a inhibitors increased significantly (OR: 1.50; 95% CI: 1.11–2.02; I2=0%). Notably, infliximab (OR: 2.43; 95% CI: 1.31–4.50; I2=0%) and etanercept (OR: 1.65; 95% CI: 1.07–2.56; I2=0%) increased the risk of HZ, while adalimumab (OR: 1.21; 95% CI: 0.64–2.30; I2=0%), ustekinumab (OR: 2.20; 95% CI: 0.89–5.44; I2=0%), alefacept (OR: 1.46; 95% CI: 0.20–10.47; I2=0%), and efalizumab (OR: 1.58; 95% CI: 0.22–11.34; I2=0%) did not.

Risk of herpes zoster associated with biological therapies for psoriasis and psoriatic arthritis

A systematic review and meta-analysis

Ailing Zou, MD[a,b], Yongjun Chen, MD[a,b], Nian Shi, BD[a,b], Yu Ye, MD[c,*]

Biological therapies, especially TNF-a inhibitors, may contribute to the risk of HZ in psoriasis and psoriatic arthritis patients. Amongst these agents, infliximab and etanercept have been shown to significantly increase the risk of HZ. Younger age and female sex may also be risk factors.

Zou et al. Medicine (2021) 100:40

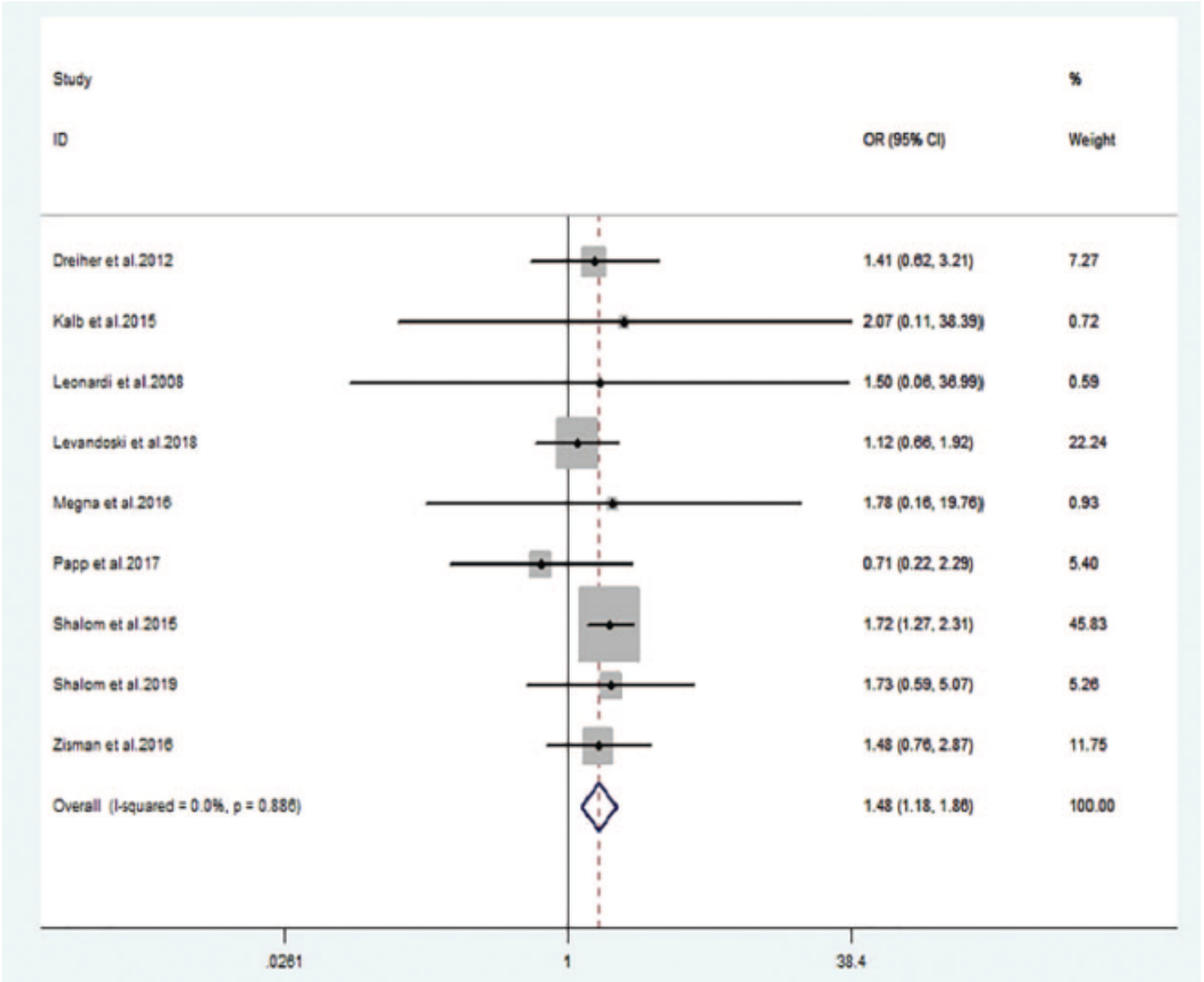


Figure 2. Risk of herpes zoster with biologics compared with non-biological therapies. Compared with non-biological therapies, the risks of HZ increased with the use of biologics (OR: 1.48; 95% CI: 1.18–1.86; $I^2 = 0\%$). CI = confidence interval, HZ = herpes zoster, OR = odds ratio.

Zou et al. Medicine (2021) 100:40

Therapeutic Advances in Chronic Disease

Ther Adv Chronic Dis 2022, Vol. 13: 1–11

Comparative risk of herpes zoster in patients with psoriatic disease on systemic treatments: a systematic review and network meta-analysis

Hsien-Yi Chiu*, Yi-Teng Hung*, Shi-Wei Huang and Yu-Huei Huang

Results: This study analyzed 13 studies including 19 treatment arms involving a total of 443,104 patients with psoriatic disease. Corticosteroids (CS) [IRR, 2.56; 95% confidence interval (CI), 1.59–4.13], a Janus kinase inhibitor (JAKi; tofacitinib) (IRR, 2.34; 95% CI, 1.03–5.32), infliximab (IRR, 2.32; 95% CI, 1.27–4.21), conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) + CS (IRR, 2.26; 95% CI, 1.23–4.17), anti-tumor necrosis factor-α (anti-TNF-α) + csDMARDs and/or CS (IRR, 2.13; 95% CI, 1.38–3.31), csDMARDs (IRR, 1.62; 95% CI, 1.18–2.22), and anti-TNF-α except infliximab (IRR, 1.61; 95% CI, 1.13–2.30) were all associated with a significantly higher HZ risk compared to controls. CS treatment possessed the highest HZ risk, followed by infliximab and JAKi (tofacitinib). Phosphodiesterase-4 inhibitor, anti-interleukin-17, -23 or -12/23, phototherapy, and acitretin showed a risk similar to controls without significant differences.

Conclusion: The NMA demonstrated CS, infliximab, and JAKi (tofacitinib), and several combination treatments were associated with higher HZ risk in patients with psoriasis and psoriatic arthritis. Differences in HZ risk should be taken into consideration when considering optimal psoriasis treatment.

Risk of Herpes Zoster Among Psoriasis Patients Taking Biologics: A Network Meta-Analysis of Cohort Studies

Zhenwei Tang[1,2], Minxue Shen[2,3] and Xiang Chen[1,2]**

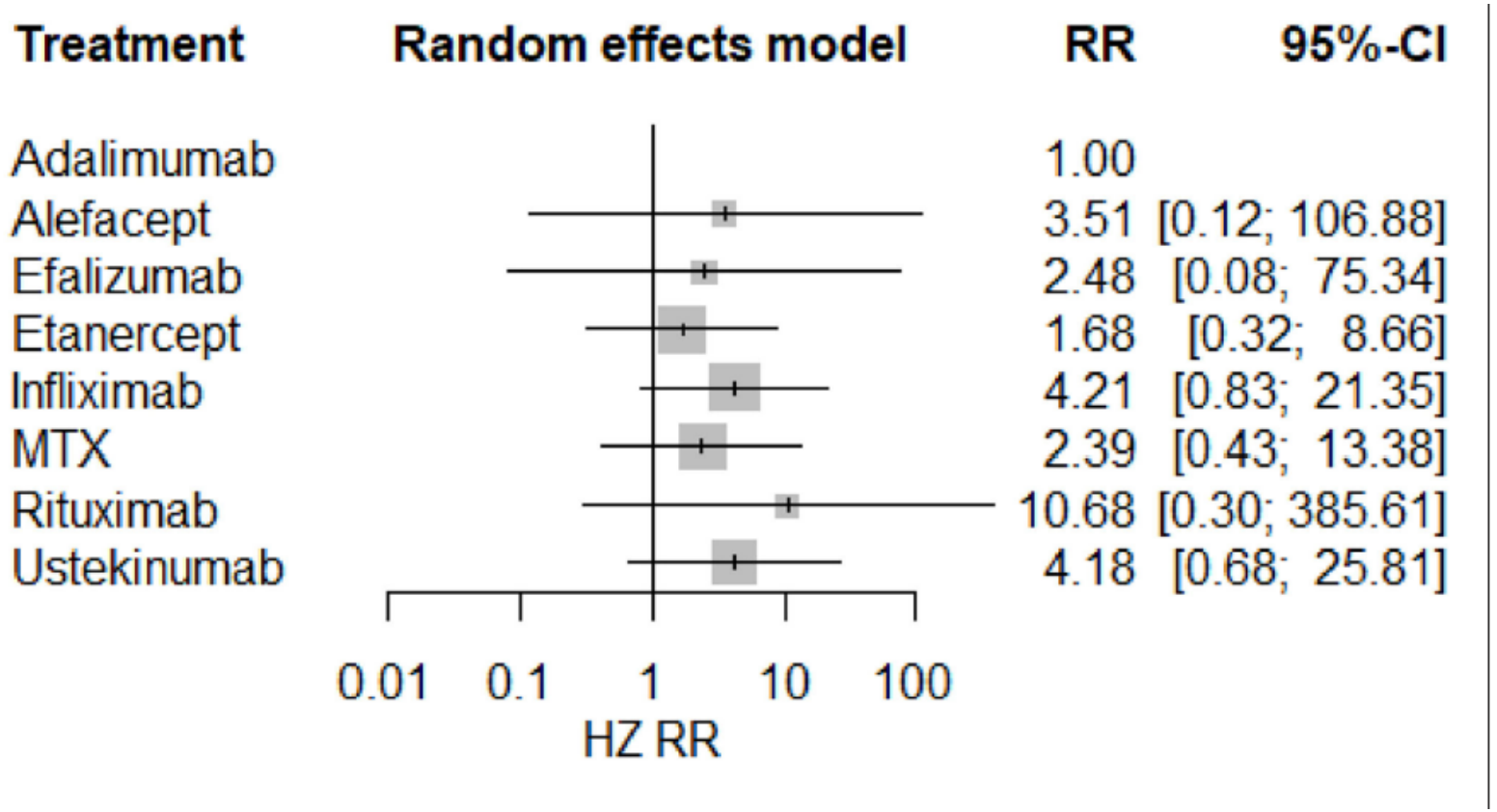
Methods: Herein, we performed a meta-analysis of cohort studies. We included studies referred to seven biologics (adalimumab, alefacept, efalizumab, etanercept, infliximab, rituximab, and ustekinumab) as well as methotrexate for psoriasis. We estimated summary relative risks (RRs) for HZ using pairwise and network meta-analysis.

Results: Overall, five studies were included for analysis. A total of 32827.6 patient-years were observed. The result of the meta-analysis showed that the pooled HZ incidence rate of adalimumab, which accounts for the most patient-years in our analysis, is 2.6 per 1,000 patient-years. Our analysis based on several cohorts showed an insignificant difference among the patients receiving adalimumab, alefacept, efalizumab, etanercept, infliximab, rituximab, ustekinumab, and methotrexate.

Conclusions: Based on this analysis, the type of mono-biologic treatment contributes little to the risk of HZ among psoriasis patients. Of note, the negative findings of our study do not mean the unnecessity of vaccination. More efforts must be taken to further determine HZ risk of different therapeutic strategies.

Risk of Herpes Zoster Among Psoriasis Patients Taking Biologics: A Network Meta-Analysis of Cohort Studies

Zhenwei Tang[1,2], Minxue Shen[2,3] and Xiang Chen[1,2]**



Risk of herpes zoster with IL-17 inhibitor therapy for psoriasis and other inflammatory conditions

Kevin K. Wu, Michael P. Lee, Erica B. Lee & Jashin J. Wu

Journal of Dermatological Treatment 2019

- Studies did not detect a higher risk of HZ infections in psoriasis patients treated with IL-17 inhibitors when compared to those treated with placebo or other therapies.
- Studies of IL-17 inhibitors for other indications including psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, and asthma yielded similar results.
- However, IL-17 inhibitors are relatively new medications, and further long-term data may be necessary to confirm whether IL-17 inhibitors increase the risk of HZ.
- Nevertheless, HZ vaccination should be considered on a case-by-case basis prior to initiating IL-17 therapy.

J Am Acad Dermatol
August 2017

Herpes zoster in psoriasis patients treated with tofacitinib

Kevin L. Winthrop, MD, MPH,[a] Mark Lebwohl, MD,[b] Arnon D. Cohen, MD, PhD,[c,d] Jeffrey M. Weinberg, MD,[b] Stephen K. Tyring, MD, PhD,[e] Scott T. Rottinghaus, MD,[f] Pankaj Gupta, PhD,[f] Kaori Ito, PhD,[f] Huaming Tan, PhD,[f] Mandeep Kaur, MD, MS,[g] Alexander Egeberg, MD, PhD,[h] Lotus Mallbris, MD, PhD,[g] and Hernan Valdez, MD[i]

Portland, Oregon; New York, New York; Tel Aviv and Beer-Sheva, Israel; Houston, Texas; Groton, Connecticut; Collegeville, Pennsylvania; and Hellerup, Denmark

Methods: We used phases 2 and 3 and long-term extension (LTE) data from the tofacitinib development program in psoriasis to calculate HZ incidence rates (IR; events per 100 patient-years); potential HZ risk factors were evaluated using Cox-proportional hazard models.

Results: One hundred thirty (3.6%) patients on tofacitinib (IR 2.55), no patients on placebo, and 2 using etanercept (IR 2.68) developed HZ. Nine patients (7%) were hospitalized, and 8 (6%) had multidermatomal HZ; no encephalitis, visceral involvement, or deaths occurred. In total, 121 (93%) patients on tofacitinib continued or resumed use after HZ. HZ risk factors included Asian descent (hazard ratio [HR] 2.92), using tofacitinib 10 mg twice daily (vs 5 mg twice daily; HR 1.72), prior use of biologics (HR 1.72), and older age (HR 1.30).

CAPSULE SUMMARY

- Herpes zoster (HZ) risk is increased in psoriasis patients taking certain immunosuppressive drugs.
- The Janus kinase inhibitor tofacitinib increases HZ risk, particularly among Asians, older individuals, and those with prior biologic use.
- Clinicians can consider vaccination and other preventive strategies for patients who are at increased risk of developing HZ.

Therapeutic Advances in Musculoskeletal Disease Review

Ther Adv Musculoskel Dis2020, Vol. 12: 1–18

JAK inhibitors and infections risk: focus on herpes zoster

Flavia Sunzini, Iain McInnes and Stefan Siebert

Ther Adv Musculoskel Dis
2020, Vol. 12: 1–18
DOI: 10.1177/1759720X20936059

The JAKinibs are promising new treatments for a range of immune-mediated inflammatory diseases. However, the incidence of herpes zoster appears higher than with the current biologic agents and csDMARDs. JAKinibs have a wider pleiotropic biological effect than current biologic agents; compared with the inhibition of one single cytokine or cytokine receptor, JAKinibs are able to simultaneously suppress the action of different cytokines, even if transitorily. This intrinsic characteristic of the JAKinibs can explain the higher risk of zoster compared with other biologic drugs. Although the risk of herpes zoster in phase II/III clinical trials appears similar for the various JAKinibs, further studies are needed to appropriately determine the safety profile of JAKinibs with different selectivities and at various doses. Emerging and pooled data may suggest

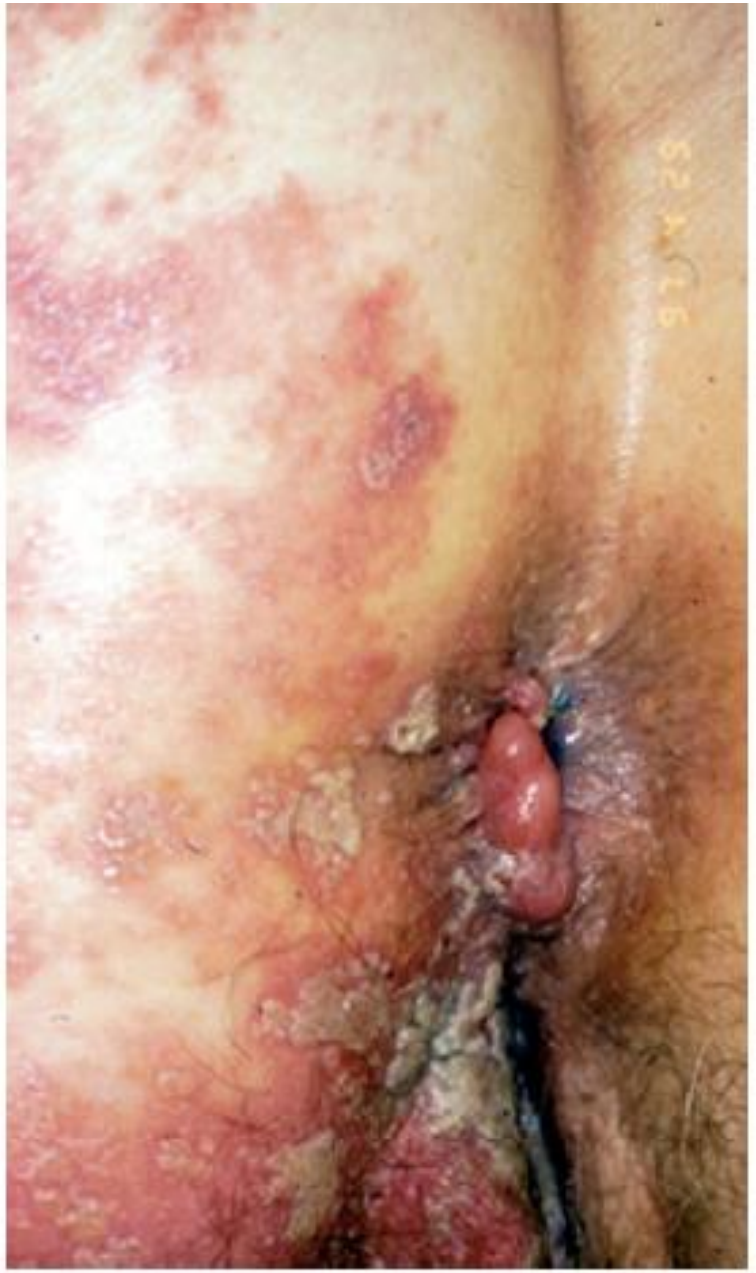
Table 3. Summarised incidence and patients/100years exposure of herpes zoster infections from phase II and III clinical 24 months of treatment.

Inhibitor and dose (+/– MTX and other csDMARDs)	Patients tot n	Zoster cases *n* (%)	Disseminated/serious zoster *n* (%)	Cases/100 patient-years
Tofacitinib 10 mg	713	29 (4.1)	NS	2.6
Tofacitinib 5 mg	1,454	31 (2.1)	4 (0.4)	1.7
PBO	160	0	0	
Methotrexate	186	2 (1.1)	0	0.54
Adalimumab	386	6 (1.6)	2 (0.5)	1.5
Baricitinib 4 mg	1,265	30 (2.4)	1 (<0.1)§	2.6
Baricitinib 2 mg	403	6 (1.5)	0	2.9
PBO	404	0		
Methotrexate	689	4 (0.6)	0	0.8
Adalimumab	330	5 (2)	0	1.4
Upadacitinib 15 mg*	305	5 (1.6)	0	2.9
Upadacitinib 30 mg*	488	9 (1.8)	4 (0.8)	5.4
PBO	219	1 (0.5)	0	1.8

Διαφέρει η πορεία του ΕΖ όταν ο ασθενής λαμβάνει βιολογικό παράγοντα?

Is the severity of HZ increased in psoriasis patients under biological agents?

In the majority of psoriasis patients undergoing biological treatments, the course of HZ will not differ from HZ observed in a normal, nonimmunocompromised, age-matched population in terms of severity. However, the risk and incidence of severe HZ clearly increase in this population. Indeed, some of the patients may present very severe HZ in terms of cutaneous extension inside the involved dermatome(s), multidermatomal involvement in adjacent dermatomes and nonadjacent dermatomes, and increased duration of the HZ skin lesions (Figures 1 and 2).[26–29,38,39,42,43] In a study that identified 86 cases of HZ among 82 patients under biologicals, multidermatomal HZ was observed in 18.3% of patients,



ure 1 Severe and extensive multidermatomal unilateral HZ of the sacral matomes occurring during the use of TNF antagonists for psoriasis.
Note: Photo courtesy of Professor Nikkels.

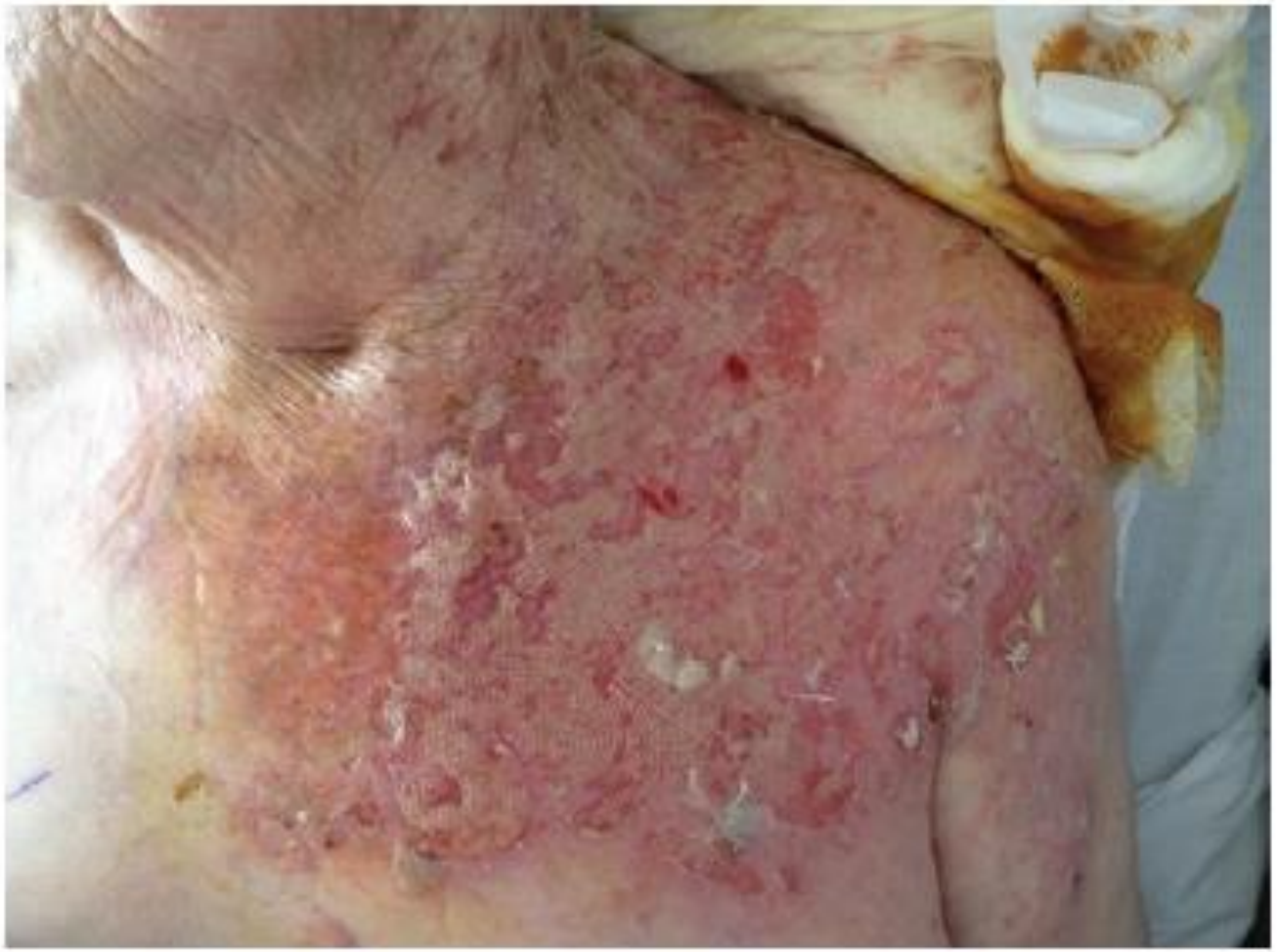


Figure 2 Severe multisegmental HZ in an elderly woman using TNF antagonists for psoriasis.
Note: Photo courtesy of Professor Nikkels.

Herpes zoster in psoriasis patients undergoing treatment with biological agents: prevalence, impact, and management challenges

Πότε θα χορηγήσουμε ενδοφλεβίως αντιική αγωγή?

Table 2 Indications of intravenous administration of ACV as suggested for patients with complicated HZ or who are at a high risk of complicated HZ

HZ of the head and/or neck area, particularly in elderly patients
HZ with hemorrhagic/necrotizing lesions, multisegmental involvement, abnormal vesicles/satellite lesions, or involvement of mucous membranes or generalized HZ
HZ in immunocompromised patients
HZ with signs of visceral or central nervous system involvement

Abbreviations: ACV, acyclovir; HZ, herpes zoster.

Psoriasis: Targets and Therapy 2016:6

HZ vaccination recommendations in patients receiving immuno-suppressive therapy for RA and PsA

- Two vaccines are available for the prevention of HZ and postherpetic neuralgia in patients aged ≥50 years. An attenuated live zoster vaccine (Zostavax®; referred to as LZV) became available in 2006, and an adjuvant recombinant subunit vaccine (Shingrix®; referred to as HZ/su) administered as two injections 2–6 months apart, became available in 2017.
- The findings of a recent systematic literature review and network meta-analysis suggest that **HZ/su is superior to LZV for HZ prevention in patients aged >50 years,** but is associated with a significantly higher risk of injection-site reactions
- However, the relative efficacy and safety of the vaccines in patients with autoimmune conditions have not been established and **LZV is contraindicated in immunosuppressed patients**

Clinical and Experimental Rheumatology 2022

Ποιες χρόνιες δερματολογικές παθήσεις ανευρίσκονται σε ασθενείς με ΕΖ που χρήζουν νοσηλείας?

Association of herpes zoster and chronic inflammatory skin disease in US inpatients

Raj Chovatiya, MD, PhD,[a] and Jonathan I. Silverberg, MD, PhD, MPH[b]
Chicago, Illinois and Washington, DC

J Am Acad Dermatol
December 2021

Results: In multivariable logistic regression models including age, sex, race/ethnicity, insurance, household income, and long-term systemic corticosteroid use, hospitalization for HZ was associated with atopic dermatitis (adjusted odds ratio [95% confidence interval], 1.38 [1.14-1.68]), psoriasis (4.78 [2.83-8.08]), pemphigus (1.77 [1.01-3.12]), bullous pemphigoid (1.77 [1.01-3.12]), mycosis fungoides (3.79 [2.55-5.65]), dermatomyositis (7.31 [5.27-10.12]), systemic sclerosis (1.92 [1.47-2.53]), cutaneous lupus erythematosus (1.94 [1.10-3.44]), vitiligo (2.00 [1.04-3.85]), and sarcoidosis (1.52 [1.22-1.90]). Only lichen planus (crude odds ratio [95% confidence interval], 3.01 [1.36-6.67]), Sézary syndrome (12.14 [5.20-28.31]), morphea (2.74 [1.36-5.51]), and pyoderma gangrenosum (2.44 [1.16-5.13]) showed increased odds in bivariable models. Sensitivity analyses among those younger than 60 and younger than 50 years showed similar results. Predictors of HZ in CISD included female sex, fewer chronic conditions, and long-term systemic corticosteroid use.

Limitations: Cross-sectional study.

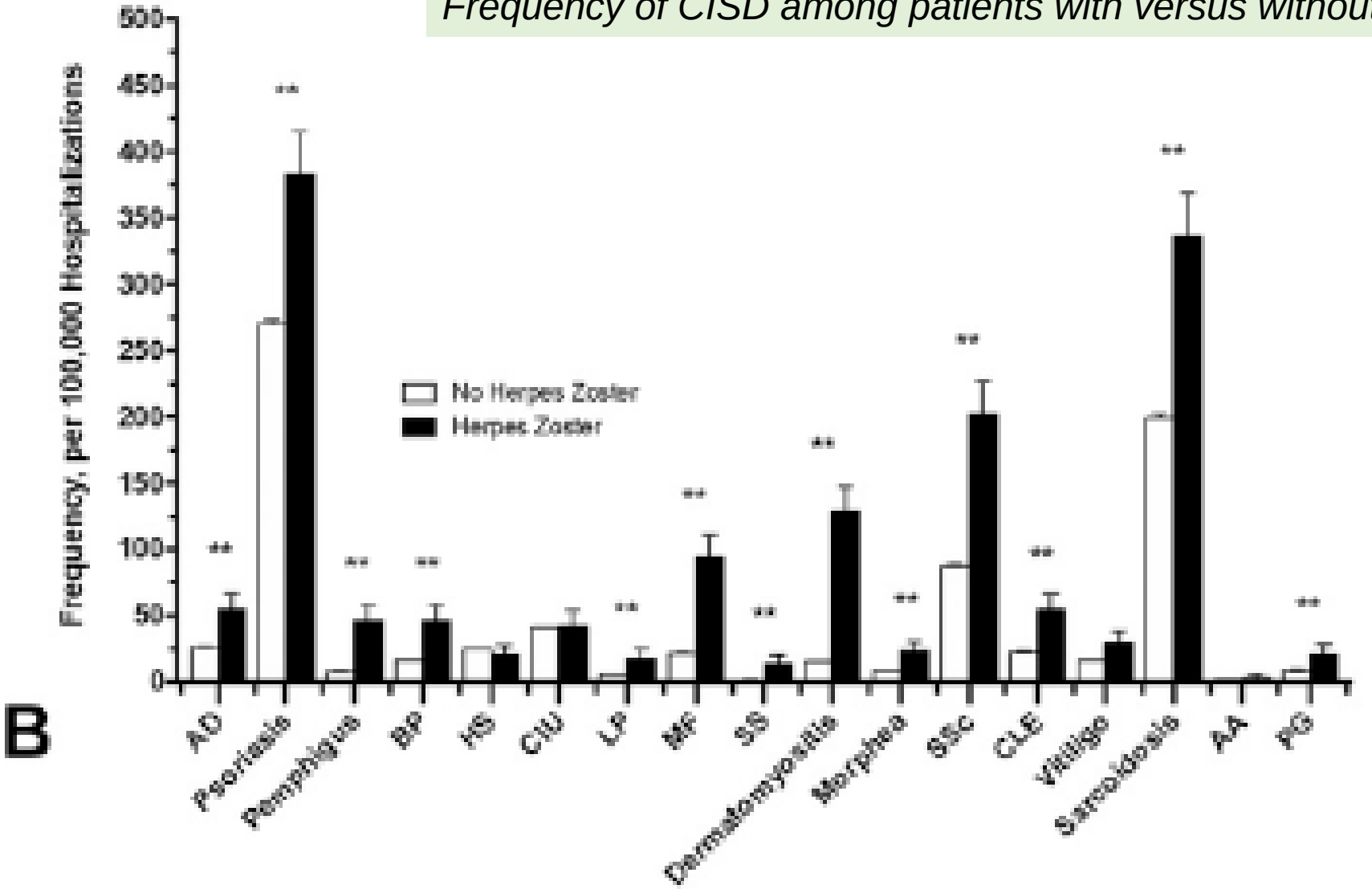
Conclusions: Many CISDs are associated with increased hospitalization for HZ, even below the ages recommended for HZ vaccination. Additional studies are needed to establish CISD-specific vaccination guidelines. (J Am Acad Dermatol 2021;85:1437-45.)

CAPSULE SUMMARY

- Patients with a variety of chronic inflammatory skin disease had higher odds of hospitalization for herpes zoster, even at ages below current vaccination guidelines, as well as prolonged inpatient length of stay and increased cost of hospital care.
- Dermatologists should consider disease-specific risk factors in these patients and encourage enhanced vaccination coverage.

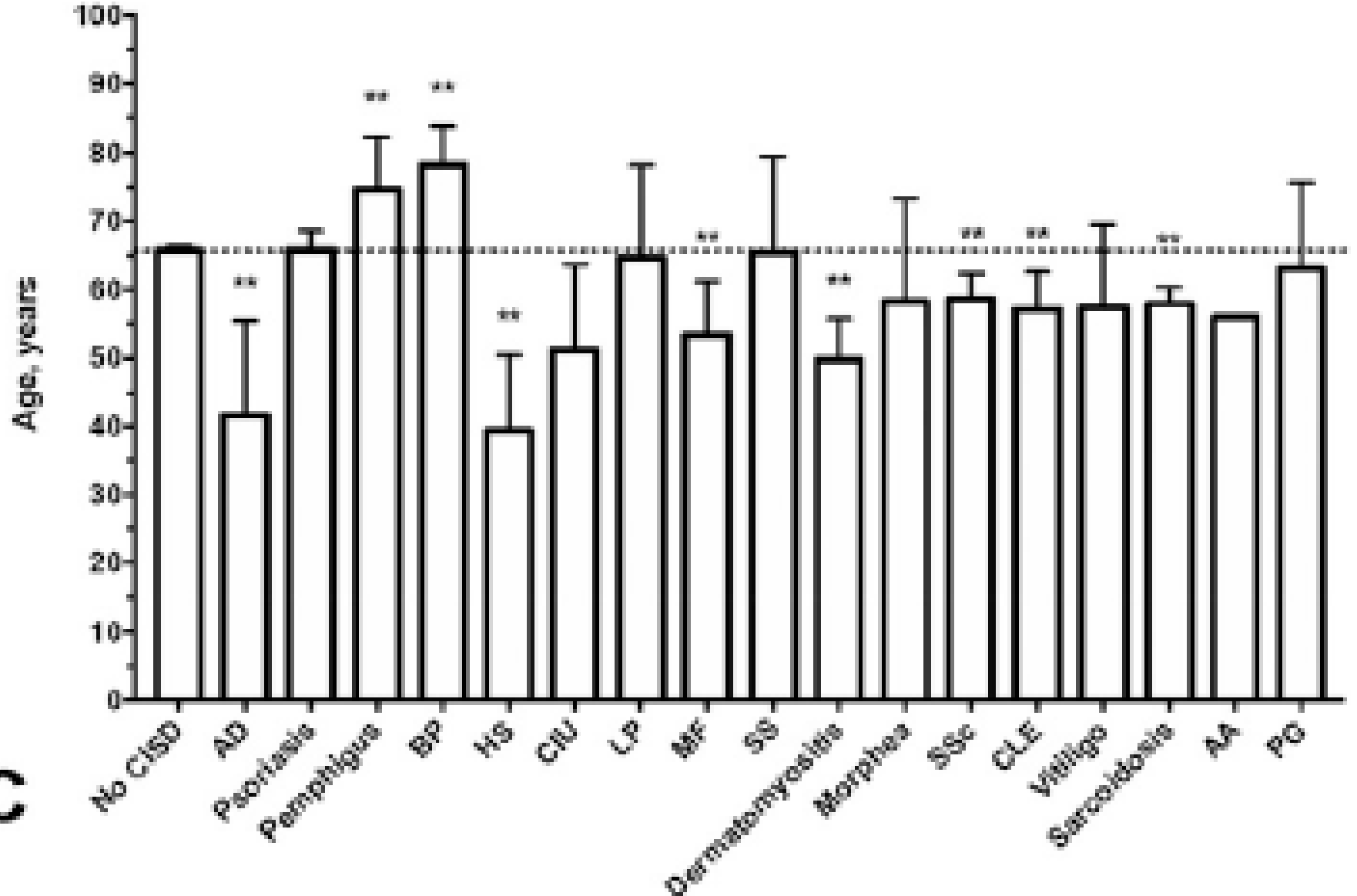
J Am Acad Dermatol
December 2021

Frequency of CISD among patients with versus without HZ.



Mean age of inpatients with HZ with versus without CISD. The dashed line represents the mean for inpatients with HZ without CISD.

J Am Acad Dermatol
December 2021



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Περί εμβολιασμού κατά του ΕΖ..

Shingles Vaccination

What Everyone Should Know about the Shingles Vaccine (Shingrix)

Shingles vaccination is the only way to protect against shingles and postherpetic neuralgia (PHN), the most common complication from shingles.

Shingrix provides strong protection against shingles and PHN. In adults 50 years and older who have healthy immune systems, Shingrix is more than 90% effective at preventing shingles and PHN. Immunity stays strong for at least the first 7 years after vaccination. In adults with weakened immune systems, studies show that Shingrix is 68%-91% effective in preventing shingles, depending on the condition that affects the immune system.

Who Should Get Shingrix?

Adults 50 years and older should get two doses of Shingrix, separated by 2 to 6 months. Adults 19 years and older who have or will have weakened immune systems because of disease or therapy should also get two doses of Shingrix. If needed, people with weakened immune systems can get the second dose 1 to 2 months after the first.

You should get Shingrix even if in the past you:

- Had shingles
- Received Zostavax*
- Received varicella (chickenpox) vaccine

There is no maximum age for getting Shingrix.

Έρπητας ζωστήρας σε δερματολογικούς ασθενείς με ανοσοτροποίηση

- Η ψωρίαση, η ατοπική δερματίτιδα, και άλλα χρόνια δερματικά νοσήματα που απαιτούν ανοσοτροποποίηση αυξάνουν τον κίνδυνο εμφάνισης έρπητα ζωστήρα
- Οι αντι - TNF παράγοντες και οι Jak αναστολείς συνδέονται περισσότερο με αυξημένο κίνδυνο εμφάνισης έρπητα ζωστήρα
- Ο εμβολιασμός προτείνεται σε όλους τους ασθενείς >50 ετών υπό ανοσοτροποποιητική αγωγή

Σας ευχαριστώ