Herpes Zoster Rates in a Large Cohort of Patients With Systemically Treated Psoriasis

Herpes zoster (HZ) is caused by reactivation of latent varicella zoster virus (VZV). Risk increases with waning cell-mediated immunity secondary to advanced age and immunosuppression. Some of the systemic agents used in moderate-to-severe psoriasis may be associated with increased HZ risk, though studies are conflicting, and data among patients with psoriasis is lacking.1 In patients with systemically treated psoriasis, the association between medication use and HZ risk remains poorly characterized, especially with regard to biologic vs nonbiologic therapy. This study aimed to estimate HZ incidence rates (IR) among systemically treated patients with psoriasis, comparing patients treated with biologic vs nonbiologic agents, in a community-based health care delivery setting.

Methods | We examined a cohort of adult health plan members with systemically treated psoriasis diagnosed 1998 to 2011 at Kaiser Permanente Northern California (KPNC), an integrated health care delivery system serving more than 4 million members in Northern California. Study cohort details have been reported previously.2 Medication use was extracted from pharmacy databases for biologic agents (ie, adalimumab, etanercept, infliximab, ustekinumab, golimumab, certolizumab, tocilizumab, abatacept, anakinra, and rituximab) and nonbiologic agents (ie, methotrexate, retinoids, cyclosporine, hydroxyurea, mycophenolate mofetil, sulfasalazine, and thioguanine). Participants were followed through December 31, 2012 for incident HZ, defined by provider-rendered diagnosis codes (International Classification of Diseases, Ninth Revision [ICD–9] codes 053.2, 053.20, 053.21, 053.22, and 053.29). Systemic treatment was handled as a time-dependent covariate, capturing whether the patient was currently exposed to biologics only, nonbiologics only, combination of biologic and nonbiologic, or no systemic medication on each day of follow-up. Crude HZ IRs and age- and sex-adjusted IRs (aIR; direct method, 2000 US Census as standard population) were calculated per 1000 person-years of follow-up with 95% confidence intervals (CIs). The Kaiser Permanente Northern California institutional review board approved this study and written informed consent was waived.

Results | Cohort members were followed for a mean of 5.3 person-years. Nonbiologic users were older than biologic users, and women were less likely to have used biologics (Table 1). Of the 5889 participants with systemically treated psoriasis, 291 had HZ diagnosed during follow-up. Crude IRs showed that, compared with those on no systemic therapy at the time of HZ diagnosis (IR, 8.6; 95% CI, 7.1–10.0), those on systemic therapy had a statistically nonsignificant increased HZ risk (IR, 10.2; 95% CI, 8.6–11.8; P = .14) (Table 2). After adjusting for age and sex, there were no significant differences between those receiving no systemic therapy (aIR, 6.1; 95% CI, 4.1–8.1), any systemic therapy (aIR, 8.1; 95% CI, 5.3–11.0), biologics only (aIR, 7.8; 95% CI, 4.1–11.5), nonbiologics only (aIR, 8.9; 95% CI, 4.1–13.6), or a combination therapy (aIR, 5.6; 95% CI, 1.2–10.0).

Discussion | Few studies have examined the association between systemic medication use and HZ risk in patients with
psoriasis. Crude point estimates did not suggest an increased HZ risk in systemically treated patients with psoriasis, and we found no significant differences in HZ risk among those exposed to biologic vs nonbiologic therapy after adjusting for age and sex.

**Limitations.** Limitations of the study include lack of data on disease severity and potentially limited generalizability to other healthcare settings.

**Conclusions** Among a cohort of patients with moderate-to-severe psoriasis who were treated with a systemic agent on cohort entry, we found no significant differences in HZ risk at time of HZ diagnosis among those treated with systemic therapy vs no systemic therapy, and among systemically treated patients, among those treated with biologics versus no biologic agents. Our results are similar to those of a recently published retrospective cohort study that found no significant association between biologics as single agents and adjusted HZ risk in patients with psoriasis. We previously reported an increased risk of bacterial skin and soft tissue infections among those treated with biologics compared with those treated with nonbiologics in this cohort. Biologics block the activity of cytokines such as TNF-α, which plays a role in protecting against bacterial infections and inhibiting reactivation of latent viruses. Incident rates of HZ were increased in systemically treated patients with psoriasis as compared with the general population. However, we found no significant differences in HZ risk among those exposed to biologic vs nonbiologic therapy after adjusting for age and sex. Our results suggest that among systemically treated psoriasis patients, biologics may preferentially inhibit immune mechanisms specific for bacterial defense while sparing cell-mediated immune responses specific for maintaining VZV latency.

Katherine A. Levandoski, BS
Charles P. Quesenberry, PhD
Ai-Lin Tsai, MA
Maryam M. Asgari, MD, MPH

**Author Affiliations:** Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston (Levandoski, Asgari); Division of Research, Kaiser Permanente Northern California, Oakland (Quesenberry, Tsai, Asgari).

**Corresponding Author:** Maryam M. Asgari, MD, MPH, Department of Dermatology, Massachusetts General Hospital, 50 Staniford St, Ste 230A, Boston, MA 02114 (harvardskinstudies@mgh.harvard.edu).

**Accepted for Publication:** September 26, 2017.

**Published Online:** December 20, 2017. doi:10.1001/jamadermatol.2017.4840

**Author Contributions:** Dr Quesenberry and Ms. Tsai had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Levandoski, Asgari.

**Acquisition, analysis, or interpretation of data:** All authors.

**Drafting of the manuscript:** Levandoski, Asgari.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Quesenberry, Tsai.

**Obtained funding:** Asgari.

**Administrative, technical, or material support:** Levandoski.

**Study supervision:** Asgari.

**Conflict of Interest Disclosures:** Drs Asgari and Quesenberry have received research funding from Pfizer Inc and Valeant Pharmaceuticals. The authors have no other potential conflicts of interest to disclose.

**Funding/Support:** This study was supported in part by grants from the National Institutes of Health (K24AR069760 to Asgari) and Pfizer Inc.

**Role of the Funder/Sponsor:** National Institutes of Health and Pfizer Inc had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.


**Firefighter Skin Cancer and Sun Protection Practices: Evidence From the Florida Firefighter Cancer Initiative**

Firefighters serve in a hazardous occupation and face unique dermal exposures. Recent epidemiologic studies have found an elevated risk for skin cancer among firefighters compared with the general population. Firefighter exposure studies have detected carcinogenic chemicals on firefighter skin and gear following fire-incident response. There is limited research on risk factors and occupational hazards related to skin cancer in the firefighter workforce. We examine skin cancer history, skin cancer screening, and sun protection habits among active Florida firefighters.

**Methods** The Annual Cancer Survey (ACS) research project of the Firefighter Cancer Initiative launched with a 127-item comprehensive cancer questionnaire administered via REDCap to a nonprobabilistic sample of firefighters and/or paramedics.