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Letter

The Incidence of Herpes Zoster Is Increased in the Population of Patients With Rheumatoid Arthritis

To the Editor:

We read with interest the recent retrospective cohort study by Singer and colleagues on the incidence of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) in the United States.[1] After analyzing age and treatment regimens in both cohorts, the authors concluded that the incidence of HZ was increased in patients with RA.[1] We support and appreciate the authors' work and agree with their conclusions but have some concerns about some of the details in the article.

First, this retrospective longitudinal cohort study used data from an administrative claims database, which included both commercial and Medicare Advantage Part D data from October 2015 to February 2020.[1] However, there are limitations to relying on retrospective analyses based on an administrative claims database as it may not accurately determine the nature of individual events, and using diagnostic codes to define events may increase the likelihood of misclassifying RA and HZ. We suggest that the authors combine the administrative claims database with diagnosis and treatment prescription data.

Second, the average age of patients in the RA cohort was higher than that of the non-RA cohort (64.8 [SD 12.7] yrs vs 53.5 [SD 19.0] yrs; standardized difference 70.1%).[1] In addition, the RA cohort had a higher burden of comorbidities (0.7 [1.2] vs 0.4 [1.0]; standardized difference 32.8%), particularly in terms of chronic pulmonary disease (18.9% vs 7.5%; standardized difference 33.8%), peripheral vascular disease (9% vs 4%; standardized difference 20.4%) and moderate or severe kidney disease (9.4% vs 4.2%; standardized difference 20.8%), which may indicate poorer immune function among patients in the RA cohort and a greater need for medication.[1] The authors also found that the incidence rate (IR) of HZ was higher in the RA cohort compared to the non-RA cohort (21.5 vs 7.6/1000 person-years). The IR of HZ remained higher in the RA cohort compared to the non-RA cohort when stratified by age group and compared using adjusted IR ratios.[1] Immunosenescence, the natural decline in immune function with age, as well as immunosuppression caused by disease or treatment, are associated with an increased risk of HZ.[1,2] This indicates that age and underlying comorbidities are important confounding factors. Therefore, additional sensitivity analyses should be performed to explore the effect of these confounding factors on the study and the robustness of the study results. Further, studies have shown that female sex is a risk factor for reactivation of the varicella zoster virus (VZV)[3]; therefore, additional subgroup analyses, such as sex and distribution of HZ, could provide more information for clinical physicians.

Finally, although the authors included comorbidities such as chronic pulmonary disease, peripheral vascular disease, and moderate or severe renal disease in the study, additional risk factors that can lead to reactivation of the VZV, such as HIV infection, lymphoma, leukemia, bone marrow transplantation, solid organ transplantation, and other immunocompromised states, should be considered and included in this study. These potential diseases are more commonly associated with VZV-specific cell-mediated immunosuppression.[3,4] Therefore, these potential uncategorized diseases may have interfered with the study results.

In conclusion, before these issues are clarified, this study's findings should be interpreted cautiously.

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The authors declare no conflicts of interest relevant to this article.

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