Reply to: "Comment on 'Oral diabetes medications other than dipeptidyl peptidase-4 inhibitors are not associated with bullous pemphigoid: A Finnish nationwide case-control study' and a case report of glucagon-like peptide-1 receptor agonist–induced bullous pemphigoid"

To the Editor: We thank Schwager et al[1] for their interest in our recent publications.[2,3] They comment that the title of our article[3] may mislead the reader into prematurely ruling out oral diabetes medications other than gliptins as a possible aggravating factor for bullous pemphigoid (BP). We agree that our study may have not been able detect an association between the newer diabetes drugs and BP owing to the lack of data on oral diabetes medication used by patients with BP after the year 2013. This limitation is clearly acknowledged in several parts of our article, including the abstract. We agree with the observation that our study included only a small number of patients using glucagon-like peptide-1 receptor agonists (GLP-1RAs). However, because our data were drawn from a nationwide data set, we consider our sample to be representative and do not share the concern of Schwager et al about the small numbers of subjects receiving certain classes of antidiabetic drugs.

Schwager et al[1] present a case in which BP manifested 6 weeks after initiation of treatment with the GLP-1RA dulaglutide. The patient's BP resolved with topical corticosteroids after withdrawal of the dulaglutide. However, Schwager et al do not describe the patient's history of diabetes treatment. We have previously shown that the risk of BP is significantly increased by the use of dipeptidyl peptidase-4 inhibitors (DPP4Is), even when their use is initiated more than a year before BP diagnosis.[2] Other studies of DPP4I-associated BP have described latency periods of more than 6 months between initiation of DPP4I therapy and BP onset.[4,5] Therefore, the argument presented with this case is weakened by the lack of information on prior medication use.

The use of GLP-1RAs is increasing in Europe. However, as of January 2019, the numbers of suspected pemphigoid cases reported by health care professionals to the European database of suspected drug reactions (Eudravigilance [www.adrreports.eu]) are low for exenatide (n = 8), dulaglutide (n = 5), and liraglutide (n = 5). No suspected BP cases have been reported for patients receiving albiglutide or lixisenatide. Suspected cases of BP make up only 0% to 2% of all adverse skin reactions in patients treated with GLP-1RAs. This rate is substantially lower than the rate of suspected BP cases associated with gliptin treatment.

A recent study compared the use of antidiabetic medications in 670 patients with BP and diabetes and 670 controls with diabetes but not BP. There was no difference between the 2 groups in terms of use of antidiabetic agents other than DPP4Is.[6] However, all the antidiabetic drugs aside from DPP4Is were analyzed as a group, and therefore, any potential association between GLP-1RAs could not be examined. Furthermore, to the best of our knowledge, there are no reports in the published English-language literature of GLP-1RA–associated BP. Overall, we agree with the assertion of Schwager et al[1] that more studies are needed to further clarify the potential association between the newer diabetes medications and BP.

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