Response to: "Missed induced bullous pemphigoid: When the anamnesis is the cure," a comment on "Missed drug-induced bullous pemphigoid leads to longer immunosuppression than recognized cases: A 9-year retrospective review"

To the Editor: We thank Chessa et al[1] for their insightful comments on our recently published research article, "Missed Drug-Induced Bullous Pemphigoid Leads to Longer Immunosuppression than Recognized Cases: A 9-Year Retrospective Review."[1]

Chessa et al raise 2 issues with our definition of missed patients with drug-induced bullous pemphigoid (DIBP) as those "for which any new medication was added within 6 months preceding BP onset and treating dermatologists neither documented the change nor considered the discontinuation." First, the authors indicate that our DIBP cases may have included idiopathic BP that coincided with the recent introduction of a new medication, a possibility and a limitation we had also previously acknowledged in our article[1]; this is a general limitation for most large retrospective studies of this type examining potential drug culprits for BP.[2] We agree with this concern and were careful to describe our missed cases not as definitive DIBP but rather as "potentially drug-related," therefore warranting further examination. Nevertheless, the cases we classified as *missed* were statistically similar to known DIBP cases in timing of onset and distribution of triggering drugs. In fact, the presence among the potential offending medications in our missed DIBP cases of primarily well-documented DIBP drug culprits[3] reassures us that many of these cases may have been true DIBP, although the clinical similarity between the 2 entities makes it difficult to be definitive.[4]

Second, Chessa et al raised the possibility that the six-month cutoff for new drug exposure would miss potential patients with DIBP whose new medications were initiated even earlier. Although we agree with their assessment and acknowledge that there are occasional DIBP cases presenting years after drug initiation, the literature suggests that chronic medications are unlikely to trigger BP.[2] One recent review article affirms that DIBP manifests "up to 3 months after the ingestion of the culprit medication."[3] This is further supported our own multi-institutional experience, where cases of recognized DIBP occurred at a median of 1 month after drug initiation.[1] Our 6-month exposure window was chosen, in accordance with the literature, to optimally capture missed DIBP cases that were plausibly related to a new medication while minimizing the effect on specificity, given that delayed DIBP, although it has been reported, is relatively rare. We favored this conservative approach to avoid biasing the clinical endpoint of patient immunosuppression away from the null hypothesis. Indeed, we may have missed patients with significantly delayed onset, but we believe that these represent a small proportion of likely DIBP cases.

Overall, we are grateful to Chessa et al for their careful consideration of our manuscript and thoughtful analysis of the therapeutic implications of missed DIBP at their institution. We are in strong agreement that, despite differences in case definitions, the consistent, clinically meaningful outcome of both our studies remains: there are significant therapeutic consequences for missing DIBP, such as prolonged multidrug immunosuppression. Therefore, investigating new BP cases as possibly drug-induced is crucial for prompt discontinuation of culprit drugs and avoidance of unnecessary immunosuppression.

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