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Letter to the Editor

Comment on: Comparative short-term risks of infection and serious infection in patients receiving biologic and small-molecule therapies for psoriasis and psoriatic arthritis: a systemic review and network meta-analysis of randomized controlled trials

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Dear Editor,

We read with great interest the article by Chiu et al.[1] The authors present a systematic review and network meta-analysis of randomized controlled trials in psoriasis and psoriatic arthritis, focusing specifically on short-term risks of infection and serious infection in patients receiving biologic treatments. We had a particular interest in the relative risk (RR) of infection and serious infection in psoriatic arthritis, by treatment (reported in Figure 3(b) and Supplemental Figure S2 of Chiu et al.). The reported methodology was to quantify the risk of infection and serious infections for treatments during the placebo-controlled periods of randomized-controlled trials.

Bimekizumab treatment in psoriatic arthritis was reported for BE ACTIVE, a 48-week phase IIb dose-ranging study.[2] BE ACTIVE was double-blind and placebo-controlled to Week 12, and dose-blind to Week 48. After Week 12, patients receiving placebo or bimekizumab 16 mg were re-randomized to receive bimekizumab 160 mg or 320 mg. Therefore, no patients remained on placebo after Week 12.

Within the Chiu et al. article, the RR presented for bimekizumab in psoriatic arthritis compared with placebo appears to have been incorrectly calculated as 14.23 (Figure 3(b) of Chiu et al.), a value that is approximately 10-fold greater than any other drug, as well as over 10-fold greater than the RR of 1.36 calculated for bimekizumab in psoriasis (Figure 3(a)). To the best of our deductions, the authors used the reported BE ACTIVE psoriatic arthritis study infection rates for the full 68-week study period (48 weeks + 20 weeks safety follow-up) for bimekizumab and the 12-week infection rates for placebo to calculate the RR, instead of the initial 12-week placebo-controlled phase for bimekizumab. With this methodological error, the authors would have overestimated and seriously misrepresented the infection risk of bimekizumab in the treatment of psoriatic arthritis. Rates of serious infections can be found in Table 4 of the paper by Ritchlin et al.[2] and Supplemental Table S1 of the paper by Coates et al.[3] Rates of the most frequently reported treatment-emergent adverse events (where incidence was ⩾5% in any treatment arm), including infections, can also be found in Supplemental Table S1 of the

Table 1. Incidence of infection and infestation TEAEs reported by ⩾3% of patients in any treatment group up to Week 12 in the BE ACTIVE study.

MeDRA (Version 19.0) SOC PT	Placebo *n* = 42 *n* (%) [#]	BKZ 16 mg *n* = 39 *n* (%) [#]	BKZ 160 mg *n* = 43 *n* (%) [#]	BKZ 160 mg w/LD *n* = 41 *n* (%) [#]	BKZ 320 mg *n* = 41 *n* (%) [#]
Any TEAE	24 (57.1)	13 (33.3)	19 (44.2)	16 (39.0)	20 (48.8)
Infections and infestations	3 (7.1) [3]	7 (17.9) [9]	10 (23.3) [11]	8 (19.5) [11]	10 (24.4) [13]
Ear infection	0	2 (5.1) [2]	1 (2.3) [1]	0	0
Respiratory tract infection	0	2 (5.1) [2]	2 (4.7) [2]	0	0
Nasopharyngitis	0	3 (7.7) [3]	1 (2.3) [1]	1 (2.4) [1]	1 (2.4) [1]
Pharyngitis	0	0	0	0	2 (4.9) [2]
Sinusitis	0	0	0	1 (2.4) [1]	2 (4.9) [2]
Urinary tract infections	0	0	2 (4.7) [2]	0	0

Source: Safety Set; data on file.[4]
Number of events reported for infection and infestation TEAEs.
#, number of events; BKZ, bimekizumab; LD, loading dose; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SOC, System Organ Class; TEAE, treatment-emergent adverse event.

paper by Coates et al.[3] (Of note, within this table the results for patients randomized to 160 mg are combined with the results from patients randomized to 160 mg with a 320 mg loading dose.) These data have been summarized in Supplemental Table S1 of our supplement.

Furthermore, we would like to provide relevant data on file from the BE ACTIVE clinical study report (Table 1),[4] showing the total number of infections to Week 12 in all treatment arms including placebo. Overall infection data have not previously been published to Week 12, but are provided below for reference and to allow the calculations to be re-run accurately.

We also wish to note a series of additional errors in the reported findings for bimekizumab and certolizumab pegol in the supplement of the Chiu et al. article.

- In Supplemental Table S4 of Chiu et al., authors have mistakenly reported the loading dose data (41 patients, 2 serious infections) under the bimekizumab 160 mg heading, and data for the bimekizumab 160 mg group (43 patients, 0 serious infections) under the loading dose heading. The correct data for these outcomes may be found in the Ritchlin et al.[2] paper, and are also summarized in Supplemental Table S1 of our supplement.
- Also in Supplemental Table S4 of Chiu et al., and marked up in Supplemental Table S2 of our supplement, there are a number of potential calculation errors for infection data reported from bimekizumab in psoriasis studies.
- In Supplemental Table S3 of Chiu et al., there are a number of minor errors in the study characteristics data for studies of certolizumab pegol and bimekizumab, also marked up in Supplemental Table S2 of our supplement.
- Certolizumab (pegol) is misspelled as "cetrolizumab" throughout the Supplemental Material.

We would respectfully ask the Editors to direct authors to the values reported in Ritchlin et al.[2] and Coates et al.,[3] as well as in Table 1 of this letter, so they may recalculate the RR for infections with bimekizumab treatment in psoriatic arthritis, recheck this for serious infections, and update the serious infection data in the supplement. Upon author confirmation of the correct values and updated RRs, we would politely ask that the authors are instructed and assisted to publish a correction. Given the degree of misrepresentation in the data, we would sincerely appreciate this being carried out in an expedited manner.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Author contributions
Barbara Ink: Conceptualization; Writing – review & editing.

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Competing interests
B.I.: Employee of UCB, shareholder of AbbVie, GSK, and UCB. R.B.: Employee and shareholder of UCB. V.S.: Employee of UCB.

Availability of data and materials
All relevant data and material are either included within this letter from data on file, or part of already-published literature.

Supplemental material
Supplemental material for this article is available online.

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