

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	PATIENT-REPORTED WELL-BEING IN VALUE-BASED CARE USING TILDRAKIZUMAB IN A REAL WORLD SETTING: PROTOCOL OF A MULTI-NATIONAL, PHASE IV, 1 COHORT PROSPECTIVE OBSERVATIONAL STUDY (THE POSITIVE STUDY)
AUTHORS	Augustin, Matthias; Sommer, Rachel; Dauden, E.; Laws, Philip; de Jong, Elke; Fabbrocini, Gabriella; Naldi, Luigi; Navarini, Alexander; Lambert, Jo; Reguiai, Ziad; Gerdes, Sascha; Massana, Eric; Obis, Teresa; Kasujee, Ismail; Mrowietz, Ulrich

VERSION 1 – REVIEW

REVIEWER	Lada, Georgia The University of Manchester, Dermatopharmacology Unit I declare that I have received speaker honoraria from Janssen, Lilly, Leo, and Novartis in the last 3 years.
REVIEW RETURNED	09-Mar-2022

GENERAL COMMENTS	<p>The protocol is well presented. The introduction contains a comprehensive review of the literature, and the study rationale and objectives are clear. The study addresses an important gap in the psoriasis literature and its clinical relevance is also clearly outlined in the protocol. I have some comments for further clarification in the methods. Could you please elaborate in some more detail about the following:</p> <p>a) in surveys about psychological outcomes there is sometimes potential for distress or identifying participants who are unwell; could you please elaborate regarding any intended plan of action or protocol provision if there is such (e.g. signposting, follow-up), for participants with low/very low wellbeing scores, particularly since 75% of psoriasis patients are expected by the researchers to meet the less stringent/specific WHO-5 cut-off criterion (≤ 50) used for a depression screening diagnosis (Reference 43)</p> <p>b) the outcome measure “Heat map”; as this term may be confusing on its own for readers, please consider adding “Skin manifestations distribution” or similar in Table 3 along with the “heat map/patient’s grid” term; also please add a brief comment on the outcome measure and how it will be scored/used in the analysis (as described for questionnaires)</p> <p>c) the statistical analysis methods which are expected to be used. Although I appreciate the issues before data collection, the data analysis section is very vague; I believe some more detail is warranted for the primary objective (how effects of tildrakizumab on the overall well-being of patients will be tested); also consider a comment on if or how multiple comparisons will be addressed, given</p>
-------------------------	---

	<p>the use of several questionnaires and multiple study objectives mentioned.</p> <p>d) please consider including in the limitations potential time-related maturation/history effects, especially post-pandemic, on the primary outcome measure (general wellbeing), given the long observational period and lack of control group.</p>
--	--

VERSION 1 – AUTHOR RESPONSE

- Reviewer 1: “a) in surveys about psychological outcomes there is sometimes potential for distress or identifying participants who are unwell; could you please elaborate regarding any intended plan of action or protocol provision if there is such (e.g. signposting, follow-up), for participants with low/very low wellbeing scores, particularly since 75% of psoriasis patients are expected by the researchers to meet the less stringent/specific WHO-5 cut-off criterion (≤ 50) used for a depression screening diagnosis (Reference 43)”.

R: Thank you very much for your comment. We really appreciate the time and effort that you dedicated during your review. However, in the current study the intended plan of action and follow-up is planned to be the same for all included patients, regardless their wellbeing score. The study was designed to evaluate the effect of tildrakizumab in real-world conditions, following the routine clinical practice on each participant country. There is no specification in the protocol for patients with a low/very low wellbeing score. We understand that doctors will follow the best practices with all patients.

- Reviewer 1: “b) the outcome measure “Heat map”; as this term may be confusing on its own for readers, please consider adding “Skin manifestations distribution” or similar in Table 3 along with the “heat map/patient’s grid” term; also please add a brief comment on the outcome measure and how it will be scored/used in the analysis (as described for questionnaires)”.

R: Thank you very much for this excellent suggestion. Based on your feedback, we have slightly modified the wording in Table 3 in order to facilitate readers’ understanding. Moreover, we have added a brief comment on how this outcome will be assessed and used in the analyses. Please see revised manuscript with track changes.

- Reviewer 1: “c) the statistical analysis methods which are expected to be used. Although I appreciate the issues before data collection, the data analysis section is very vague; I believe some more detail is warranted for the primary objective (how effects of tildrakizumab on the overall wellbeing of patients will be tested); also consider a comment on if or how multiple comparisons will be addressed, given the use of several questionnaires and multiple study objectives mentioned”.

R: Thank you very much for highlighting this issue. Based on your suggestion, we have presented in more detail how the primary objective will be analysed. Moreover, we have also further detailed the statistical analysis methods for secondary outcomes. Please see revised manuscript with track changes.

- Reviewer 1: “d) please consider including in the limitations potential time-related maturation/history effects, especially post-pandemic, on the primary outcome measure (general wellbeing), given the long observational period and lack of control group”.

R: Thank you very much for this excellent suggestion. We have included this limitation in the discussion section of the paper. Please see revised manuscript with track changes.

VERSION 2 – REVIEW

REVIEWER	Lada, Georgia The University of Manchester, Dermatopharmacology Unit I declare that I have received speaker honoraria from Janssen, Lilly, Leo, and Novartis in the last 3 years.
REVIEW RETURNED	23-Nov-2022
GENERAL COMMENTS	No further comments.