

Dear Diego A. Hartasánchez,

Please find below our last responses to comments from reviewer Diego Ayala. The revised manuscript and supplementary files have been deposited on bioRxiv under BIORXIV/2024/587871 – V4 version (<https://doi.org/10.1101/2024.04.03.587871>)

The pdf of this 'V4 revised version' together can be downloaded at <https://www.biorxiv.org/content/10.1101/2024.04.03.587871v4.full.pdf> and the supplementary materials can be downloaded at <https://www.biorxiv.org/content/10.1101/2024.04.03.587871v4.supplementary-material>

Please note that I did not upload a trackchange version as only a single reference was added to the Ms -line 33). tPlease also note that the BioRxiv V4 version has figures embedded within the manuscript. High resolution .tif files are available upon request for further publication in PCI Journal.

We sincerely hope that these last changes will make this study suitable for its recommendation by PCI Evolutionary Biology.

Best wishes,

Jean-Philippe DAVID, on behalf of all co-authors.

Review by Diego Ayala, 29 Oct 2024 13:03

Dear Editor,

I have reviewed the revision of the Manuscript by Bacot et al.,. In the present version, the authors have carried out an extensive revision of the manuscript, including all the remarks and comments done by both reviewers. To my understanding, this new version has gained in clarity and precision. I congratulate to the authors for their work and recommend for its publication

Just few comments :

Line 35. Please include the paper Kamdem et al., 2017 MBE, which as a similar approach in Anopheles

→ This reference was added to the manuscript.

Line 126. According to WHO, the IR13 should be considered as "tolerant" and not as sensible?

→ Though the field-derived IR13 line is slightly less susceptible than the laboratory Bora-Bora line, the resistance status of the IR13 line was set to “susceptible” for more clarity as previously discussed (see previous answers to reviewers).

Line 134. Please provide the dose

→ The dose used for these bioassays is already provided in Table 1 caption.

Line 221-222. Do you mean that the resistant copy is fixed in the Ile-Met ?

→ Yes, as stated in lines 215-216 a 0.5 frequency indicates that the Kdr duplication carrying both the wildtype “Ile” and the “resistant” Met alleles is fixed in the IROF line. However, as stated in lines 224-229, the wildtype “Ile” allele is carried by the partial 3’ copy which is not expressed, meaning that a “Ile-Met” genotype leads to a “Met” resistant phenotype.