**Reviewer’s report**

**Title:** Characteristics of patients initiated on edoxaban in Europe: baseline data from Edoxaban Treatment in routiNe clinical prActice for patients with atrial fibrillation (AF) in Europe (ETNA-AF-Europe)

**Version:** 0  **Date:** 30 Apr 2019

**Reviewer:** Peter Brønnum Nielsen

**Reviewer's report:**

The manuscript by Prof De Caterina et al. reports on the baseline characteristics from the ETNA-Europe prospective registry including data on atrial fibrillation patients using edoxaban for stroke prevention.

The manuscript includes clinically relevant and scientifically interesting insight into the use of the most recent approved NOAC agent. The results are clearly presented and selected subgroup analysis provide meaningful clinically insight. The manuscript is generally well-written, but some overall changes could likely improve the disposition of the text. I have the following suggestions:

**Major comments:**

The structure of the Methods section could be improved: reading a sub-headline with "Objectives" as the last paragraph before the results was confusing. I suggest the following:

1) Remove the last sentence in the Introduction section ("Here, we report..."); page 6, line 1-3.

2) The last sentence from the Objectives section ("The objective of this analysis..."); page 7, line 25-26 and page 8, line 1-2 - this sentence should end the Introduction section.

3) The first paragraph of the Objectives section ("The primary objective..."); page 7, line 20-24 could be moved to page 7, line 9 preceding the sentence starting "Details of the design".

These structural changes to the text would allow the reader to understand the author's purpose of the conducted analysis, and maintain the provided (and necessary) insight in the ETNA-AF registry description.

While the readers are referred to an earlier publication on the design and rationale of the ETNA registry (ref #21), it would be helpful to provide additional information in this manuscript. E.g.
expected number of patients in the registry; how AF was determined; types of previous AF-related therapy collected; assessment/calculation of the CHA2DS2-VASc and HAS-BLED score (rather than providing this additional information in the Results section); and information on number of follow-up visits. Also, specification on subgroup analyses could be described in the Methods section to prime the reader of the Results section.

The Discussion section could preferably begin with a summary of the obtained results, and how these compare with the ENGAGE AF-TIMI 48 trial baseline data. Additionally, in the discussion of limitations of RCTs and the benefits of prospective registries to inform on a use in routine care, it would be fair to also mention the limitations of a prospective registry: That is, patients opt in for enrollment, which causes a selection bias that is difficult to examine, and therefore may hamper the generalizability of the observed results.

Minor comments:

Page 9, line 22: Please avoid using the arbitrary classification of patients as low, intermediate, and high stroke risk based on the CHA2DS2-VASc score; the score level itself is sufficient.

Page 10, line 12: I disagree with the adjective of SmPC adherence of 83.8% is "good". Suggest to report the number as is and avoid interpretation of this result in this section.

Page 10, line 25: A "[" (bracket) typo.

Page 12, line 13-17: Suggest to move this paragraph to the Methods section.

Page 14, line 4: The statement of "commonly observed that NOACs are frequently prescribed at a lower dose" requires a reference.


Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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