

May 6, 2016

Georg Roeggla
Associate editor
BMJ

RE: Polypharmacy and the effects of apixaban in patients with atrial fibrillation: insights from the ARISTOTLE trial (BMJ.2015.031222.R1)

Dear Georg Roeggla,

On behalf of my co-authors we would like to thank you for complimenting us on the revisions and for the further request for minor revision that strengthens our manuscript.

In this second revision, we have altered the manuscript according to your suggestions:

1) You state in the discussion "In this post-hoc analysis of the ARISTOTLE trial, we demonstrated that polypharmacy is seen in three quarters of AF patients and that the number of concomitant medications is associated with increased comorbidity..." We do not think you can make a conclusion about the prevalence of polypharmacy among ALL AF patients based on the data from this study because the RCT enrolled only select patients who meet strict criteria and may not be representative of the General AF population. We think the second part of the statement is OK.

We have changed our opening sentence of the discussion into: "In this post-hoc analysis of the ARISTOTLE trial, we observed that polypharmacy was present in three quarters of patients and that the number of concomitant medications is associated with increased comorbidity."

We agree that our initial sentence might give the impression that the observed rate of polypharmacy may apply to ALL AF patients, which was not our intention, thank you for your comment. In addition, we added a final sentence to the Limitations section to underscore your point once more.

2) We would like to see more discussion on absolute rather than relative values in the discussion but we acknowledge this may be a matter of style.

We used relative differences in order to better demonstrate the observed treatment interaction, which is based on a difference in relative measures (hazard ratios) across the 3 groups with increasing concomitant medication. We have made some adjustments with more absolute percentages and hope that this fulfills your expectations.

We hope that this is now acceptable for BMJ.

Sincerely,

Christopher B. Granger, MD
Professor of Medicine
Duke University