Comparing Rivaroxaban and Apixaban in GARFIELD-AF according to ROCKET AF and ARISTOTLE trial selection criteria

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Background

- Inclusion and exclusion criteria for the landmark trials on rivaroxaban (ROCKET AF) and apixaban (ARISTOTLE) for use in non-valvular atrial fibrillation (AF) were substantially different
- The extent to which differences in selection criteria and outcome definitions influenced their differences in outcomes relative to vitamin K antagonists (VKAs) is debated

Purpose

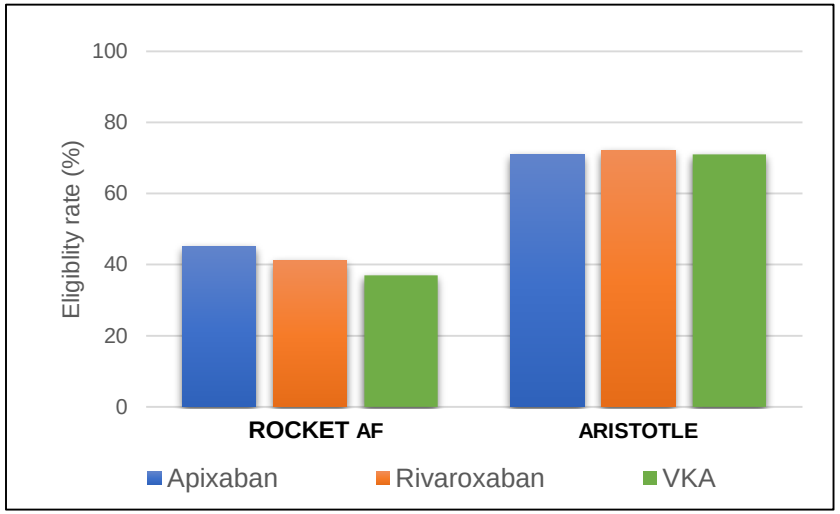
- To assess the influence of the ROCKET AF and ARISTOTLE inclusion and exclusion criteria on results for safety and efficacy of apixaban and rivaroxaban versus VKA using uniform endpoints in the world's largest prospective registry of newly diagnosed AF patients: GARFIELD-AF

Methods

- We included patients from GARFIELD-AF Cohorts 3-5 (recruited April 2013-August 2016) for the analysis, as NOACs had not yet been introduced into many countries prior to 2013
- We replicated inclusion criteria for ROCKET AF and ARISTOTLE and derived those eligible for each trial among AF patients on apixaban, rivaroxaban or VKA
- We obtained hazard ratios (HRs) for each NOAC versus VKA through Cox models using the propensity method of overlap weighting to balance covariates in the population
- We presented estimates for the endpoints stroke or systemic embolism (SE), major bleeding, and all-cause mortality, selecting first according to ROCKET AF criteria, followed by selection according to ARISTOTLE criteria

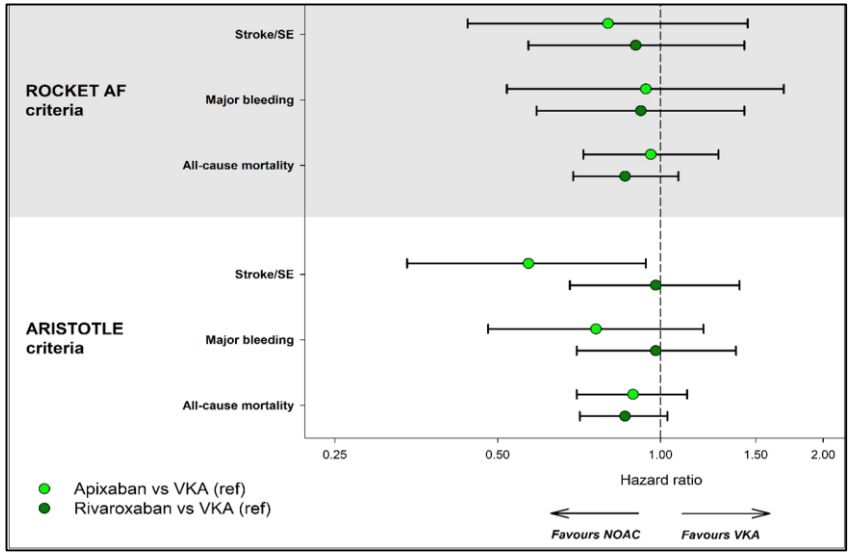
Results

Figure 1. Eligibility rates of patients on apixaban, rivaroxaban and VKA in GARFIELD-AF Cohorts 3-5 for ROCKET AF (left) and ARISTOTLE (right)



- Cardiovascular co-morbidity was greater in those eligible for ROCKET AF than in those eligible for ARISTOTLE
- Selecting using the more restrictive ROCKET AF criteria showed similar results when compared the NOACs with VKA (Fig 2, top)

Figure 2. HRs (95%CI) of NOAC vs VKA (ref) for 2-year outcomes in apixaban, rivaroxaban and VKA users eligible for ROCKET AF (top) and ARISTOTLE (bottom)



- The two sets of comparisons remained non-significant when applying the less restrictive ARISTOTLE criteria, but there were trends for less similarity (Fig 2, bottom)

Conclusion

- Apixaban vs VKA showed similar results to rivaroxaban vs VKA when selecting for higher-risk patients using the ROCKET AF criteria. In patients selected using ARISTOTLE criteria the similarity was less pronounced
- Our results underline the problems faced in comparing treatments across rather than within clinical trials. For instance, co-morbidities were substantially different for patients recruited into the original ARISTOTLE and ROCKET AF trials
- The current work points to the need for high-quality observational data for assessment of relative drug performance in absence of direct drug comparisons through randomized trials

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