Abstract: P4746

Worsening of renal function in atrial fibrillation patients with stage 3 or 4 chronic kidney disease treated with warfarin or rivaroxaban - evidence from the real-world CALLIPER study in the US claims

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Background: Anticoagulation therapy with vitamin K antagonists (e.g. warfarin) has recently been shown to contribute to the accelerated vascular calcification and worsening of renal function. Therefore, it is compelling to investigate the impact of different oral anticoagulants (OACs) on kidney function in non-valvular atrial fibrillation (NVAF) patients. Common co-morbidities in these patients are chronic kidney disease (CKD) and type 2 diabetes mellitus (T2DM), which might be presented at the OAC therapy initiation.

Purpose: The overall objective of the CALLIPER study was to evaluate the effectiveness and safety of the reduced dose rivaroxaban (15 mg once daily) as compared to warfarin in NVAF patients with renal dysfunction in real-world setting. In particular, we evaluated the risk of worsening of renal function in NVAF patients with CKD stage 3 and 4 at baseline (1 year prior to the cohort entry). Additionally, a sub-group analysis of patients with T2DM was performed. We defined worsening of renal function as progression to CKD stage 5, kidney failure or need for dialysis.

Methods: Individual level data of warfarin- and rivaroxaban-naïve NVAF patients from the MarketScan database for the years 2012 through 2017 were used. Patients with moderate-to-severe CKD (stage 3 and 4) were included in the study cohort and were followed until progression to CKD 5, kidney failure or dialysis, OAC discontinuation/switch, insurance disenrollment or end of data availability. A comparative analysis evaluating the hazard ratios (HRs) with the corresponding 95% confidence intervals (CIs) under warfarin or rivaroxaban treatment was performed using Cox regression. A stabilized inverse probability of treatment weighting was used to adjust for imbalances in baseline patient characteristics.

Results: We identified 5,906 warfarin- and 1,466 rivaroxaban-naïve patients with NVAF and CKD stage 3 and 4, of which 60% were male, median (25-75% range) age=79 (71- 84) years, CHADS2 score=2.67 (2.00-3.50), CHA2DS2-VASc score=4.43 (3.40-5.62), modified HAS-BLED score=3.00 (2.40 - 3.65). T2DM was present in more than 50% of patients (Table), namely, in 3,160 warfarin- and 746 rivaroxaban-users. Hazard ratios and 95%CI for worsening of renal function were evaluated at 0.53 (0.35; 0.83) in the main cohort and 0.50 (0.30; 0.83) in the T2DM sub-group, meaning that rivaroxaban was associated with a significant 47% and 50% risk reduction of this outcome in NVAF patients with CKD stage 3 and 4 with and without T2DM, respectively.

Conclusion: The reduced dose of rivaroxaban has appeared to lower significantly the risk of worsening of renal function versus warfarin in NVAF patients with CKD stage 3 and 4 present at the OAC therapy initiation. The conclusion holds true for the patients with the co-morbid T2DM. This evidence was generated by the CALLIPER study using one of the largest US administrative claims database.
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