COMPARATIVE SAFETY AND EFFECTIVENESS OF NON-VITAMIN-K ORAL ANTICOAGULANTS VS PHENPROCOUMON IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION AND DIABETES - RESULTS FROM THE RELOADED STUDY

Bonnemeier H¹, Kreutz R², Kloss S³, Enders D⁴, Häckl D⁵, Schmedt N⁴

¹ University Medical Center of Schleswig-Holstein, Department of Electrophysiology and Rhythmology, Kiel, Germany.
² Campus Charité Mitte, Institute of Clinical Pharmacology and Toxicology
³ Bayer AG, Berlin, Germany.
⁴ InGef – Institute for Applied Health Research Berlin, Berlin, Germany
⁵ WIG2 GmbH, Leipzig, Germany

BACKGROUND

Evidence regarding the effectiveness and safety of Factor-Xa non-vitamin-K oral anticoagulants (NOACs) in patients with non-valvular atrial fibrillation (NVAF) and specific high-risk subgroups is scarce. This analysis of the RELOADED study aimed to compare the risk of effectiveness and safety outcomes of individual NOACs vs. phenprocoumon in German patients with diabetes.

OBJECTIVES

The objective of this subgroup analysis was to describe the risk of ischemic stroke (IS)/ systemic embolism (SE), intracranial hemorrhage (ICH), end-stage renal disease (ESRD) or dialysis, acute kidney injury (AKI) and fatal bleeding in patients with NVAF and diabetes initiating treatment with individual NOACs (rivaroxaban, apixaban and edoxaban) compared to phenprocoumon.

METHODS

A new-user cohort study was conducted in patients with non-valvular atrial fibrillation and diabetes based on German claims data between January 1st, 2013 and June 30th, 2017[1]. A multiple Cox-regression was performed to calculate on-treatment confounder-adjusted hazard ratios (HRs) and related 95% confidence intervals. Treatment naïve users of each NOAC (rivaroxaban, apixaban and edoxaban) were compared to treatment naïve users of phenprocoumon. As a sensitivity analysis a stockpiling approach was used to address uncertainty in exposure time calculation for remaining tablets regarding the endpoints IS/SE and ICH.

RESULTS

	Event rates , % per year (95% confidence interval) On Treatment Analysis			
	Phenprocoumon N=8545	Rivaroxaban N=6997	Apixaban N=5438	Edoxaban N=865
IS/SE	1.50 (1.28- 1.75)	1.29 (1.05- 1.56)	2.11 (1.75- 2.53)	1.15 (0.5- 2.27)
ICH	0.48 (0.36- 0.64)	0.38 (0.25- 0.54)	0.25 (0.14- 0.42)	N<5
Fatal Bleed	0.51 (0.39- 0.67)	0.46 (0.33- 0.64)	0.39 (0.24- 0.59)	N<5
ESRD/Dialysis	0.93 (0.76- 1.14)	0.23 (0.13- 0.36)	0.60 (0.42- 0.84)	N<5
AKI	1.22 (1.02- 1.45)	0.86 (0.66- 1.08)	1.62 (1.31- 1.99)	0.72 (0.23- 1.68)

	Event rates , % per year (95% confidence interval) On Treatment Analysis (Stockpiling)			
	Phenprocoumon N=8545	Rivaroxaban N=6997	Apixaban N=5438	Edoxaban N=865
IS/SE	1.52 (1.31- 1.75)	1.22 (1.01- 1.45)	2.00 (1.67- 2.38)	1.68 (0.9- 2.88)
ICH	0.51 (0.39- 0.65)	0.39 (0.28- 0.53)	0.31 (0.19- 0.47)	N<5

Confounder-adjusted hazard ratios and related 95% confidence intervals:

	On Treatment Analysis			
	Phenprocoumon N=8545	Rivaroxaban N=6997	Apixaban N=5438	Edoxaban N=865
IS/SE	1.00 (ref.)	0.83 (0.65- 1.07)	1.03 (0.80- 1.32)	0.64 (0.31- 1.30)
ICH	1.00 (ref.)	0.77 (0.49- 1.21)	0.41 (0.22- 0.74)	N<5
Fatal Bleed	1.00 (ref.)	0.96 (0.63- 1.48)	0.68 (0.40- 1.15)	N<5
ESRD/Dialysis	1.00 (ref.)	0.32 (0.19- 0.53)	0.60 (0.40- 0.89)	N<5
AKI	1.00 (ref.)	0.72 (0.53- 0.97)	1.07 (0.82- 1.41)	0.56 (0.23- 1.37)

	On Treatment Analysis (Stockpiling)			
	Phenprocoumon N=8545	Rivaroxaban N=6997	Apixaban N=5438	Edoxaban N=865
IS/SE	1.00 (ref.)	0.70 (0.63- 1.00)	0.96 (0.76- 1.22)	0.96 (0.55- 1.70)
ICH	1.00 (ref.)	0.77 (0.52- 1.15)	0.48 (0.28- 0.81)	N<5

CONCLUSION

This study adds evidence for NOACs vs. VKA in a diabetes population. In the confounder-adjusted analysis, a comparable risk of IS/SE was observed for each NOAC compared to phenprocoumon with a trend towards better effectiveness for rivaroxaban. This trend was confirmed by the stockpiling approach, taking into account remaining tablets. Despite a general increased bleeding risk in this diabetic subgroup, we observed a numerical benefit for NOACs over phenprocoumon related to bleeding outcomes and significant risk reductions related to end stage renal disease for rivaroxaban (68%) and apixaban (40%). For the risk of acute kidney injury, only rivaroxaban showed a risk reduction (28%). This study underlines a beneficial effect of NOACs on renal preservation over time when compared to phenprocoumon. Further studies are warranted to consolidate these findings.

REFERENCES

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DISCLAIMER

This study was sponsored by Bayer AG and S. Kloss is employee of Bayer AG. All authors contributed to the study design and interpretation of the results. Data analyses were conducted independently by WIG2 and InGef.