Clinical trials with direct oral anticoagulants for stroke prevention in atrial fibrillation: are they representative for real life patients?

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1. Background
• Direct oral anticoagulants (DOACs) are increasingly used for stroke prevention in atrial fibrillation (AF), the most common cardiac arrhythmia (prevalence 1.5 to 2.0% in the developed world) [1,2].
• AF patients have a five-fold risk of stroke; about one fifth of all strokes are caused by AF [1,3].

2. Objective
To identify the proportion of real life patients with AF eligible for DOAC therapy*, based on inclusion and exclusion criteria used in the clinical studies, and to 2) on the officially approved indications as mentioned in the Summary of Product Characteristics (SmPC).

3. Methods and setting
• Retrospective cross-sectional study with data extracted from the UZ Brussel Stroke Registry, containing anonymized data of 2,025 patients with a suspected stroke in the period January 2010 – June 2014.
• Patient characteristics with documented AF were compared with the patient characteristics in clinical trials and the approved indications in the SmPC.

4. Main outcome measure
• Proportion of real life patients with AF eligible for DOAC therapy.

5. Results
• Out of 2,025 patients with a suspected stroke, 468 with AF diagnosed before admission were included. All diagnoses of AF were confirmed at hospital admission.
  - Table 1: patients’ demographics, comorbidities and characteristics of patients included in the pivotal trials
  - Table 2: overview of antithrombotic drug use for the included patients
• 156 (33.3%) patients did not receive proper anticoagulation although they had no contraindication and according to the guidelines, anticoagulation was indicated.

Comparison with selection criteria in clinical trials
• Significantly less patients were eligible for treatment with rivaroxaban compared to dabigatran: 39.3% versus 47.6% (p=0.010), but not compared to apixaban 45.5% (p=0.055); see Table 3.

Comparison with SmPC indications and contraindications
• Significantly fewer patients were eligible for apixaban compared to dabigatran and rivaroxaban: 62.0% for apixaban, 72.9% for dabigatran and 75.6% for rivaroxaban; p<0.001 and p<0.001, respectively; see Table 3.

Clinical trials vs. SmPC
• Significantly more patients were eligible for DOAC therapy based on the indications and contraindications in the SmPC compared to the inclusion and exclusion criteria of the clinical trials: 72.9% versus 47.6% for dabigatran (p<0.001); 75.6% versus 39.3% for rivaroxaban (p<0.001) and 62.0% versus 45.5% for apixaban (p<0.001).

6. Conclusions
One third of patients with AF didn’t receive adequate anticoagulation, implying an important undertreatment.

When taking into account the selection criteria from the pivotal clinical trials with DOACs for stroke prevention in AF, less than half of real life patients are eligible for therapy with one of the DOACs. However, the indications mentioned in the SmPCs of these drugs are less strict.

7. References