## Non-valvular Atrial Fibrillation: Anticoagulation Colour Comparison Chart

### Landmark AF RCTs Comparing to Warfarin

#### Non-inferiority analysis

<table>
<thead>
<tr>
<th>Drug / BRAND</th>
<th>Vitamin K Antagonist</th>
<th>DOACs</th>
<th>Factor Xa Inhibitors</th>
<th>Thrombin Inhibitor</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
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<tbody>
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<td>Warfarin</td>
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#### Stroke / Systemic Embolism

- **Warfarin**
  - Active comparator; efficacy / safety demonstrated in multiple RCTs. (e.g. ACTIVE-W) & meta-analyses.
  - Note: 75mg dose not studied.

#### Intracranial Hemorrhage

- **Warfarin**
  - Low incidence but ↑ rates in RCTs vs DOACs.

#### Major GI Bleed

- **Warfarin**
  - ↓ rate vs warfarin NNT=116/2yrs. 0.6% (dabi 150mg vs 1.5% warf)

#### Major Bleed

- **Warfarin**
  - ↓ rate vs warfarin NNT=250/1.6yrs. 0.8% riva vs 1.2% warf.

#### Discontinuation Rates

- **Warfarin**
  - 21% rate vs warfarin NNT=25/2yrs.

#### Renal function (CrCl <30mL/min)

- **Warfarin**
  - Contraindicated. Observational data conflicting, benefit may not outweigh harm.

#### Half-life Pros/Cons

- **Warfarin**
  - Half-life of DOACs is shorter than warfarin. Con: nonadherence (missed doses) will result in earlier loss of anticoagulation status vs warfarin. Pro: anticoagulation is achieved faster after starting, & when managing bleeds coagulation status returns to normal faster after stopping.

### Drug Interactions

- Warfarin has ↑↑ drug interactions. However, (1) very few interactions with warfarin are absolutely contraindicated - warfarin dose can be adjusted in response to INR; (2) management on DOACs interactions (esp. 3A4 inducers/inhibitors, P-gp) has expanded over the years.

### Cost per month

- Drug costs:
  - Apixaban: $15
  - Dabigatran: $112
  - Edoxaban: $105
  - Rivaroxaban: $118
  - Warfarin: $107

### Comments

- **There is a positive correlation between warfarin's efficacy/ safety and its time in Therapeutic Range (TTR).** Consider local context.
- **Renal function** (also see row in table): All OAC have limited RCT data with decreased renal function (CrCl <30mL/min). Warfarin: observational data for safety & efficacy is conflicting. Dabigatran is contraindicated (CI) if CrCl <30mL/min; 80-85% renally cleared. Apixaban & rivaroxaban have limited RCT data down to CrCl 15mL/min. Apixaban & warfarin: ongoing studies in ESRD; RENAL-AF: apixaban vs warfarin n=154 (planned for n=760) hemodialysis patients ended early; risk of bleeding & benefit similar. Edoxaban & CrCl >95mL/min: ↑ risk of ischemic stroke; FDA recommends to avoid, but Health Canada does not. NOAC not routinely recommended in Stage 5 CKD (eGFR <15mL/min). CCR AF (under study). 

- **Valvular atrial fibrillation** (e.g. mechanical valves): warfarin is the preferred agent; dabigatran contraindicated (↑ rates of bleeding & thrombotic events in RE-ALIGN trial).

- **Canadian differences:** international trials with few Canadian patients; in general, most Canadian sites would be expected to have better TTR with warfarin than average, & less absolute risk of intracranial hemorrhage. These factors potentially limit DOAC advantages.

- **Importance of dose:** efficacy & bleed risk are both dependent on dose; e.g. dabigatran 110mg BID & edoxaban 30mg daily had less bleeding, but also reduced efficacy, vs dabigatran 150mg BID & edoxaban 60mg daily, respectively.

- **Life-threatening/ fatal bleed was less in dabí / riva trials.**

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**Trials were designed as non-inferiority, with option for superiority analysis. Only direct comparisons of individual DOACs with warfarin have been studied; comparisons above are indirect & have inherent limitations; however, they are the best data available.**

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**RxFiles Q&A**

- **RxFiles Q&A**
  - **An Advantage**
  - **Neutral**
  - **A Disadvantage**
  - **Unknown/Ongoing**
This editorial synthesis was based on interpretation of data from RCTs (RELY, ROCKET-AF, ARISTOTLE, ENGAGE-AF), CADTH reports, product monographs & clinical consultation.

Acknowledgements: Written by Loren Regier and Zack Dumont; reformatted in 2021 by Alex Crawley. Ongoing edits provided by Lynette Kosar. Thanks to our reviewers: Lynette Kosar, Brent Jensen.

Disclosures: No conflicts of interest are reported by the authors.

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<tbody>
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