

Drug / BRAND	Vitamin K Antagonist	DOACs			
	Warfarin COUMADIN, g	Thrombin Inhibitor Dabigatran PRADAXA, g	Rivaroxaban XARELTO	Factor Xa Inhibitors Apixaban ELIQUIS	Edoxaban LIXIANA; SAVAYSA
Landmark AF RCTs Comparing to Warfarin non-inferiority analysis; superiority if appropriate	Active comparator; efficacy / safety demonstrated in multiple RCTs (e.g. ACTIVE-W) & meta-analyses.	RE-LY ¹ N=18,113 randomized 1:1:1 dab 110mg or 150mg BID vs warf (TTR 64%) ITT; open-label RCT Note: 75mg dose not studied	ROCKET-AF ² N=14,264 riva 20mg* daily vs warf (TTR 55%) ITT; double-blind, RCT *20% (n=1474) on riva had CrCl 30-49mL/min → 15mg daily	ARISTOTLE ³ N=18,201 apix 5mg* BID vs warf (TTR 62%) ITT; double-blind RCT *4.7% (n=428) on apix had ≥2: ≥80yr, ≤60kg, SCr ≥133 umol/L → 2.5mg BID	ENGAGE-AF ⁴ N=21,105 randomized 1:1:1 edox 30mg* or 60mg daily vs warf (TTR 65%) ITT; double-blind RCT *edox 30mg if CrCl 30-50mL/min, or ≤60kg, or on verapamil or quinidine
↓ Stroke / Systemic Embolism	✓ absolute differences minimal when TTR≥65%	✓✓? NNT=88/2yrs 2.2% dab 150mg vs 3.4% warf; dab 110mg vs warf NS	✓? riva vs warf NS only per-protocol met non-inferiority, not ITT	✓✓? NNT=167/1.8yrs 2.3% apix vs 2.9% warf	✓✓? NNT=141/2.8yrs 2.6% edox 60mg vs 3.3% warf ITT non-infer, mITT superior; edox 30mg vs warf NS
Intracranial Hemorrhage	✗ low incidence but ↑ rates in RCTs vs DOACs	✓ ↓ rate vs warfarin NNT=116/2yrs 0.6% dab 150mg vs 1.5% warf	✓ ↓ rate vs warfarin NNT=250/1.6yrs 0.8% riva vs 1.2% warf	✓ ↓ rate vs warfarin NNT=128/1.8yrs 0.6% apix vs 1.4% warf	✓ ↓ rate vs warfarin NNT=99/2.8yrs 0.9% edox 60mg vs 1.9% warf
Major GI Bleed	✓	✗ NNH=100/2yrs 3.1% dab 150mg vs 2.1% warf; dab 110mg vs warf NNT=77 / 2yrs (but less benefit)	✗ NNH=100/1.6yrs 3.2% riva vs 2.2% warf	✓ no difference vs warfarin 1.2% apix vs 1.3% warf	✗ NNH=166/2.8yrs 3.3% edox 60mg vs 2.7% warf; edox 30mg vs warf NNT=67 / 2.8yrs (but less benefit)
Major Bleed	✓	✓ no difference vs warfarin 6.6% dab 150mg vs 7% warf	✓ no difference vs warfarin 5.6% riva vs 5.4% warf	✓✓ ↓ bleeds vs warfarin NNT=67/1.8yrs 3.6% apix vs 5.1% warf	✓✓ ↓ bleeds vs warfarin NNT=67/2.8yrs 6% edox 60mg vs 7.5% warf
Bleed Management	✓ Vitamin K, PCC	✓ idarucizumab PRAXBIND	✗ FDA'18 antidote: andexanet alfa ANDEXXA		
Discontinuation Rates	-	✗ NNH=25/2yrs 21% dab vs 17% warf	- no difference vs warfarin	✓ NNT=45/1.8yrs 25% apix vs 28% warf	- no difference vs warfarin
Renal function (CrCl <30mL/min)	RCTs ongoing. Observational data conflicting, benefit may not outweigh harm	✗ Contraindicated <30mL/min	very limited data avoid <15mL/min	very limited data avoid <15mL/min	avoid <30mL/min
Half-life Pros/Cons	Half-life of DOACs is shorter than warf. 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.				
Other	INR monitoring ✓ tailor dose re: stroke vs bleed risk ✗ ? inconvenient	✗ ? ↑ MI see RxFiles Q&A ✗ ↑ Dyspepsia NNH=18/2yrs vs warf		↓ All-Cause Mortality NNT=132/1.8yrs 6.6% apix vs 7.4% warf	
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	✓✓ \$15	✗ (\$98 g x ∅) - \$120	✗ \$105	✗ \$118	✗ \$107
	An economic review found new anticoagulants more costly than warfarin even after cost of INR monitoring built in. ⁶ However, "soft" indirect costs (e.g. time/travel to the patient) not included; assess individually with patient.				

✓✓ An Advantage
✓
Neutral
✗
✗✗ A Disadvantage
? Unknown/Ongoing

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. OAC not routinely recommended in Stage 5 CKD (eGFR <15mL/min). [CCS AF WR, LQ](#)
- **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,⁸ & less absolute risk of intracranial hemorrhage.⁷ 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 BID¹ & edoxaban 60mg daily⁴, respectively
- Life-threatening/ fatal bleed was less in dab / riva trials.

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.

apix=apixaban dab=dabigatran edox=edoxaban DOAC=direct oral anticoagulant → apix, dab, edox, or riva PCC=prothrombin complex concentrate riva=rivaroxaban thrombin=aka Factor IIa warf=warfarin wt=weight

Anticoagulation Colour Comparison Chart

This editorial synthesis was based on interpretation of data from RCTs ([RELY](#), [ROCKET-AF](#), [ARISTOTLE](#), ENGAGE-AF), CADTH reports, product monographs & clinical consultation.

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Apixaban	22
Atrial Fibrillation	22
COUMADIN	22
Dabigatran	22
DOACs	22
Edoxaban	22
ELIQUIS	22
LIXIANA	22
PRADAXA	22
Rivaroxaban	22
Warfarin	22
XARELTO	22
Anticoagulant	22

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