

Shady Grove Office 15215 Shady Grove Road Suite 306 Rockville Maryland 20850

Keith M. Lindgren, M.D., Dennis J. Donohue, M.D., Robert DiBianco, M.D.

Louis J. Larca, M.D., David M. Brill, M.D., James L. Cockrell, Jr. M.D., Laurence R. Kelley, M.D.

Daniel J. Fernicola, M.D., Maureen C. Fennell, M.D.

**If you are taking the "blood thinner" warfarin (Coumadin™ anticoagulant) for atrial fibrillation, a new FDA-approved alternative that does not require blood testing may be appropriate for you!**

**- My views: Robert DiBianco, MD**

For many decades, warfarin (Coumadin™) has been the only effective "blood thinner" (anti-coagulant) in tablet form for preventing blood clots that can clog arteries or veins and lead to serious medical problems including:

- obstructed leg veins (thrombophlebitis or deep vein thrombosis, DVT)
- obstructed arteries to brain causing stroke in patients with carotid artery disease, atrial fibrillation or artificial heart valves
- obstructed arteries to lung, so-called pulmonary embolism or PE.

The benefits of warfarin (Coumadin™) are truly remarkable and come at a bargain price since it is now available as generic drug. Warfarin (Coumadin™) can

- Reduce strokes by 64% in patients with atrial fibrillation
- Prevent over 50% of the leg clots in high risk patients such as after surgery
- Prevent 74% of deaths in patients with pulmonary emboli
- In heart attack victims:
  - reduce 24% of the deaths
  - reduce 38% of new heart attacks
  - reduce 55% of the strokes

Problems however exist with all medications and especially anticoagulants, since they reduce clotting and can increase bruising, minor and major bleeding (hemorrhage). Sometimes major disability follows a fall, head injury or as a result of internal bleeding from an ulcer or tumor. Warfarin has unique additional problems that make it difficult to use. These include:

- Requirement for frequent blood testing to confirm that daily dosage is correct
- Necessary dietary restrictions of green leafy vegetables and other sources of that contain Vitamin K that can lessen or block warfarin's action
- Many drug interactions that can change the effect of any daily dose, potentially leading to
  - overdosing (increased risk of bleeding)
  - underdosing (lack of adequate protection from clotting)

So what's new? Dabigatran (Pradaxa™) is a new anticoagulant pill approved to prevent stroke and blood clots in patients with atrial fibrillation. Unlike warfarin (Coumadin™) dabigatran does not require regular blood testing or dietary restrictions; although certain drugs (verapamil, amiodarone and quinidine) interfere with dabigatran's effectiveness, drug interactions are much fewer than with warfarin. Unfortunately for now, and since dabigatran is a trade name drug, it undoubtedly will be expensive.

Dabigatran has been compared to warfarin in a 2 year study of 18,113 patients with atrial fibrillation published in the New England Journal of Medicine September 17, 2009. Dabigatran 150mg twice a day was found to prevent 34% more strokes and blood clots than warfarin while it was less likely to cause bleeding problems. Patients with severe liver disease, kidney disease or those who were not reliable at taking medicine were prevented from taking part in the study.

# Dabigatran versus Warfarin in Patients With Atrial Fibrillation

New England Journal of Medicine (Vol.361 pages 1139-1151)

Published: September 17, 2009,

By: Connolly SJ, Ezekowitz MD, Yusuf S and others.

## Background:

Warfarin reduces the risk of stroke in patients with atrial fibrillation but increases the risk of hemorrhage and is difficult to use. Dabigatran is a new oral direct thrombin inhibitor.

The study is designed to compare the effectiveness of both therapies, the prevention of strokes and other blood clotting problems and the safety or risk of new bleeding problems.

18,113 patients

Average age 71 years, 64% men, 36% women

Risk of stroke: 1/3 low, 1/3 moderate and 1/3 of patients at high risk of stroke

All had atrial fibrillation – (types: 1/3 persistent, 1/3 paroxysmal, 1/3 permanent)

- 1) **Paroxysmal:** recurrent, intermittent, stops without specific therapy.  
Paroxysmal atrial fibrillation is self-limited.
- 2) **Persistent:** recurrent, sustained stopped by therapeutic intervention (cardioversion with meds or electric pacing or shock).  
Persistent atrial fibrillation is not self-limited, but may be converted to sinus rhythm by medical or electrical intervention.
- 3) **Permanent:** Continuous atrial fibrillation which cannot be converted to normal sinus rhythm by pharmacologic or electrical techniques.

All had at least one of the following:

Prior stroke or TIA (transient ischemic attack or small stroke)

Heart failure or weakened heart muscle (LVEF <40%)

Age 64 to 75 with diabetes, hypertension or coronary disease

None had recent or severe stroke, severe kidney or liver disease or were pregnant.

## Results:

These are the annual rates results for the recently FDA approved dose of Dabigatran 150 mg twice a day and warfarin, regulated to keep the prothrombin INR between 2.0 and 3.0 are shown.

|                                | Results   | Dabigatran 150 mg | Warfarin | Statistical significance |
|--------------------------------|-----------|-------------------|----------|--------------------------|
| Stroke and clotting (embolism) | ↓ 34%     | 1.11 %            | 1.69 %   | p<.001                   |
| Major bleeding                 | no change | 3.11 %            | 3.36 %   | No difference            |
| Stroke from bleeding           | ↓ 64 %    | .10 %             | .38 %    | P<.001                   |
| Death rate                     | ↓ 12 %    | 3.64 %            | 4.13 %   | P<.051                   |

## Conclusions:

In patients with atrial fibrillation, “Dabigatran given at a dose of 150 mg twice a day, compared to warfarin, “was associated with lower rates of stroke and systemic embolism” (blood clotting problems) “but similar rates of major hemorrhage.”