MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Anticoagulation Therapy in LTC

By: Cynthia Leung,
RPh, BScPhm, PharmD.

Clinical Consultant Pharmacist
MediSystem Pharmacy
Jun 11, 2013

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Agenda

- Stroke and Bleeding Risk Assessment
- Review of Oral Anticoagulation Agents
  - Warfarin, Dabigatran, Rivaroxaban, Apixaban
- Other Relevant Considerations

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

STROKE AND BLEEDING RISK ASSESSMENT

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

CHADS2 SCORE

	Condition	Point
C	CHF	1
H	Blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A	≥75	1
D	Diabetes Mellitus	1
S	Stroke or TIA or Thromboembolism	2

$CHADS_2$ Score	Stroke Risk %	95% CI
0	1.9	1.2–3.0
1	2.8	2.0–3.8
2	4.0	3.1–5.1
3	5.9	4.6–7.3
4	8.5	6.3–11.1
5	12.5	8.2–17.5
6	18.2	10.5–27.4

In CHA2DS2-VASc, three additional risk factors are considered:

- Vascular Disease
- Age 65-74
- Female

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

HAS BLED SCORE

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

HAS-BLED Score	Bleeds/ 100 pts
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.50
Any Score	1.56

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

A typical resident in a long term care facility…

80 yr female with dementia, hypertension, diabetes and atrial fibrillaton.

CHAD2 Score = 3 (Stroke risk = 5.9%)

Has Bled Score = 3 (Bleed/100pts = 1.83)

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Thromboembolic Management

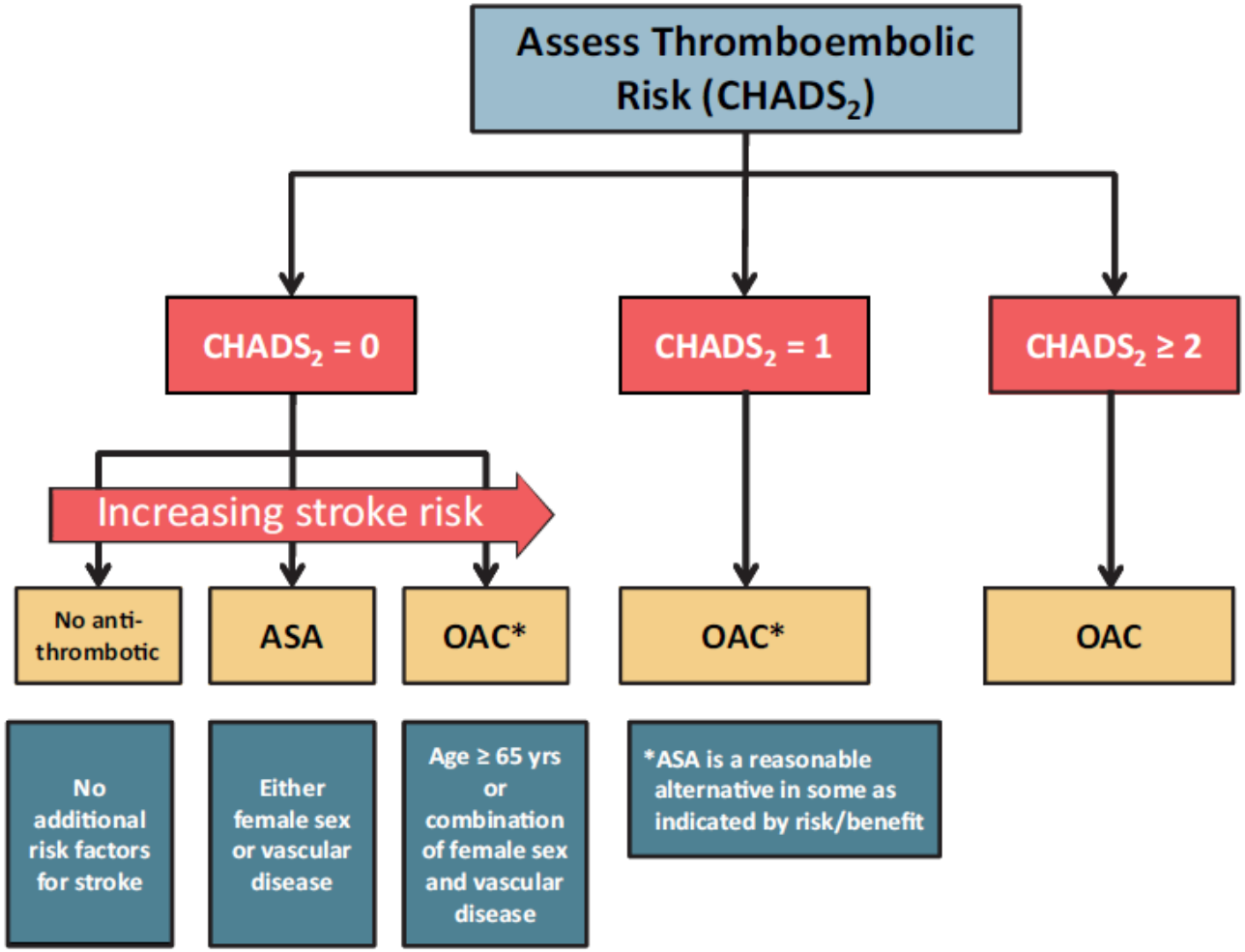


Figure 1. Summary of recommendations for antithrombotic agent use based on Congestive Heart Failure, Hypertension, Age > 75, Diabetes Mellitus, and Prior Stroke or Transient Ischemic Attack ($CHADS_2$) score. Additional risk factors of age > 65, vascular disease, and female sex are integrated to increase granularity at low $CHADS_2$ score ($CHADS_2 = 0$). ASA, acetylsalicylic acid (aspirin); OAC, oral anticoagulant.

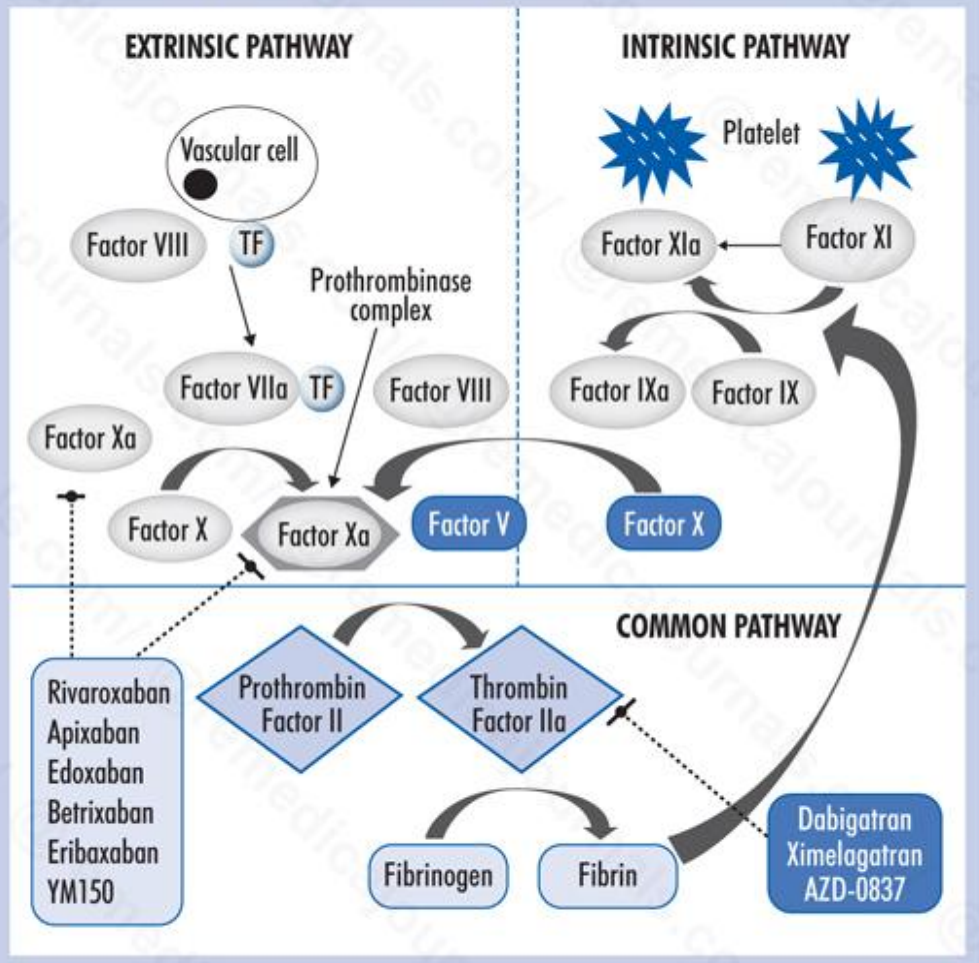
Skanes AC et al. Can J Cardiol 2012;28:125-36

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

REVIEW OF ORAL ANTICOAGULATION AGENTS

Mechanism of Action of Oral Anticoagulants

Figure 1. Coagulation cascade and therapeutic targets. The coagulation cascade is activated via the intrinsic or extrinsic pathway, which ultimately results in the conversion of fibrinogen to fibrin through the common pathway. The new oral anticoagulants act by inhibiting thrombin, or Factor Xa directly [20,26].



TF: tissue factor.

Image courtesy of Remedica Journals
http://www.remedicajournals.com/Advances-in-Venous-Arterial-Thrombosis/BrowseIssues/Volume-1-Issue-3/Article-New-Oral-Anticoagulants-for-Stroke-Prevention-in-AF

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Warfarin

- Indications:
  - Prophylaxis and treatment of venous thrombosis and its extension, pulmonary embolism, atrial fibrillation with embolization
  - Prophylaxis of systemic embolism after myocardial infarction, stroke and reinfarction

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Warfarin - Limitations

- Slow Onset of Action
- Numerous Food and Drug Interactions
- Narrow Therapeutic Range
  - Frequent INR Monitoring & Dose Adjustment
- Genetic Variations
  - Wide Warfarin Dosing
  - Warfarin Resistance
- Average time in therapeutic range is about 50%

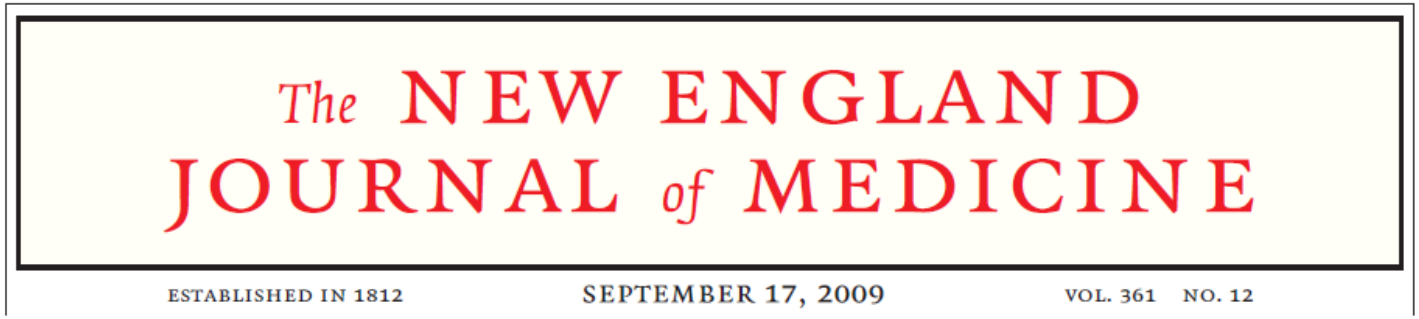
MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran – Drug Profile

Mechanism of Action	Oral Direct Thrombin (IIa) Inhibitors
Indications	Prevention of Stroke in Atrial Fibrillation Thrombo-prophylaxis in knee and hip surgery
Dosing	Knee replacement – 110mg po bid (x10days) Hip replacement – 110mg po bid (x28-35days) Atrial fibrillation - 150mg po bid (If > 80 years old OR >75 with HAS-BLED ≥ 2, 110mg po bid) *Tablet should not be crushed, may drastically increase bioavailability and risk of bleed
Renal Dosing	Same as above if CrCL ≥ 30mL/min. Contraindicated if < 30mL/min.
Side Effects	Bleeding, dyspepsia, anemia, gastritis-like symptoms (GERD, GI ulcer)
Drug Interactions	Amiodarone, quinidine, verapamil, carbamazepine, ketoconazole, PGP inducers and inhibitors
Monitoring	No routine monitoring is necessary. aPTT in specific situations (e.g. rule out excessive anticoagulation)
Drug Coverage	Covered by ODB via LU Code for Stroke Prevention in AF

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran – Clinical Evidence



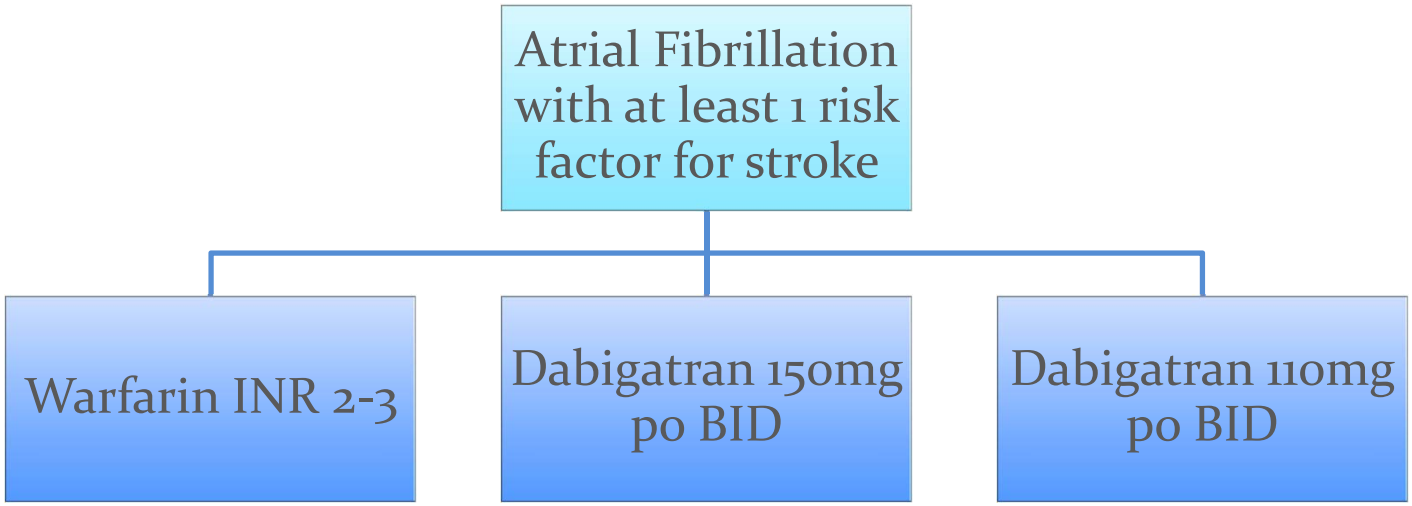
Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Salim Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators*

Connolly SJ el NEJM 2009;361:1139-51

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

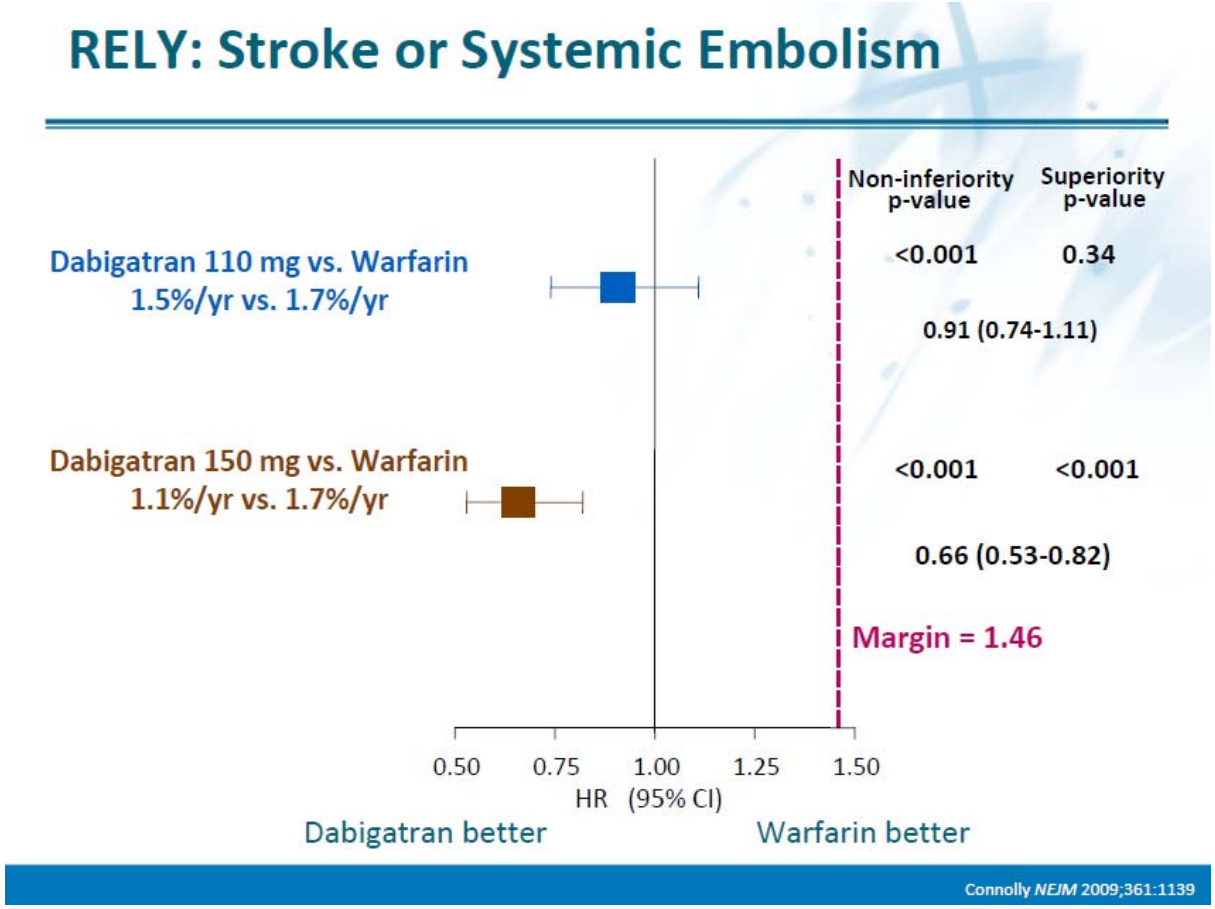
Dabigatran – RE-LY Study Overview



- Study Design: Blinded dabigatran, open label Warfarin
- N = 18 113, mean follow up 2 years
- Mean CHAD2 score = 2.1
- TTR (Time in Therapeutic Range) = 64%

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran – RE-LY Results



Efficacy:

110mg BID was non-inferior to warfarin
(no different when compared to Warfarin)

150mg po BID was superior to warfarin
(better than warfarin)

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran and its Bleeding Risk

	D 110mg	D 150mg	Warfarin	D 110mg vs. Warfarin		D 150mg vs. Warfarin	
	Annual Rate	Annual Rate	Annual Rate	RR 95% CI	P	RR 95% CI	P
Major Bleeding	2.7%	3.1%	3.4%	0.80 (0.69-0.95)	0.003	0.93 (0.81-1.07)	0.31
Life Threatening Bleed	1.2%	1.5%	1..8%	0.68 (0.55-0.83)	<0.001	0.81 (0.66-0.99)	0.04
Non Life Threatening Bleed	1.7%	1.9%	1.8%	0.94 (0.78-1.15)	0.56	1.07 (0.89-1.29)	0.47
GI Bleed	1.1%	1.5%	1.0%	1.10 (0.86-1.40)	0.43	1.50 (1.19-1.89)	<0.001
Minor Bleed	13.2%	14.8%	16.4%	0.79 (0.74-0.84)	<0.001	0.91 (0.85-0.97)	0.005
Intracranial Bleed	0.23%	0.30%	0.74%	0.31 (0.20-0.47)	<0.001	0.40 (0.27-0.60)	<0.001

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran and its Bleeding Risk

- Dabigatran has an overall lower bleeding risk as compared to warfarin.
- High dose of Dabigatran (150mg po bid) was associated with greater bleeding risks than the low dose of dabigatran (110mg po bid).
- Higher GI Bleed among both Dabigatran groups when compared with Warfarin
  - Also seen in real practice (e.g. main reason for discontinuing Dabigatran)

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

FDA Drug Safety Communication: Update on the risk for serious bleeding events with the anticoagulant Pradaxa

Safety Announcement (Nov 2, 2012)

The results of this Mini-Sentinel assessment indicate that bleeding rates associated with new use of Pradaxa do not appear to be higher than bleeding rates associated with new use of warfarin, which is consistent with observations from the large clinical trial used to approve Pradaxa (the RE-LY trial).

FDA is continuing to evaluate multiple sources of data in the ongoing safety review of this issue.

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran and MI Risk

- The RE-LY trial initially reported a higher incidence of MI with dabigatran 150mg dose vs. warfarin (RR 1.38; 1.00-1.91; p=0.048)*
- A recent meta-analysis (which include both AF and non-AF patients) also found a similar result but noted a reduction in all-cause mortality associated with dabigatran in AF**
- A re-analysis of RE-LY data now suggests the higher incidence not statistically significant.***

*Connoly SJ et al. NEJM 2009;361-1139-51
**Uchino K et al. Arch Intern Med 2012;172(5):397-402
***Hohnloser SH et al. Circulation 2012;125:669-676

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Dabigatran – The Bottom Line

- Dabigatran non-inferior to warfarin
- As Stroke Prevention In AF:
  - Dabigatran 150mg BID appears more effective than warfarin with marginally less bleeding. However there were more (non significant) MI and GI bleeds
  - Dabigatran 110mg BID may be option in older, lower weight, CrCL 30-60mL/min and/or higher rate of bleeding or where INR monitoring is impractical.

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – Drug Profile

Mechanism of Action	Direct Xa inhibitor
Indications	Prevention of Stroke in Atrial Fibrillation Prevention and Treatment of DVT& PE Thrombo-prophylaxis in knee and hip surgery
Dosing	Knee Replacement: 10mg po daily x 14days Hip Replacement: 10mg po daily x 35 days DVT / PE: 20mg po daily or 15mg po bid x 3 weeks, then 20mg po daily Stroke Prevention in AF: 20mg po daily
Renal Dosing	For CrCL 30-49mL/min: 15mg po daily, Avoid if < 30mL/min
Side Effects	Bleeding, elevated liver enzymes, Nausea
Drug Interactions	NSAIDS, salicylates, NHPs, antiplatelets, PGP/CYP3A4 inducers & inhibitors (ketoconazole, clarthromcyin, rifampin, phenytoin, carbamazaepine)
Monitoring	No routine monitoring required. If necessary, PT (prothrombin) time correlates with Rivaroxaban level
Drug Coverage	Covered by ODB via LU Code for Stroke Prevention in AF

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – Clinical Evidence

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 8, 2011 VOL. 365 NO. 10

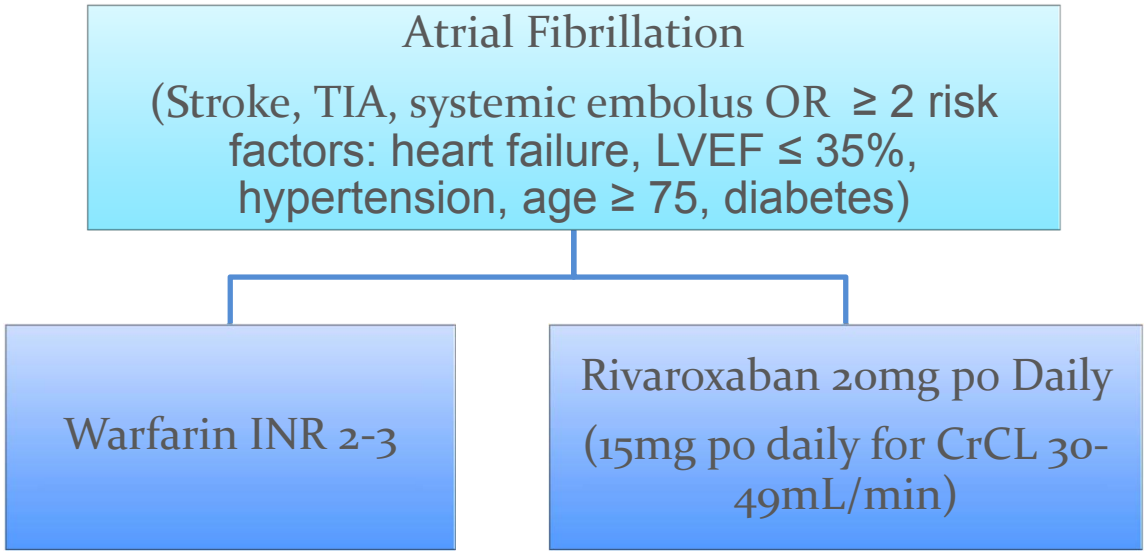
Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation

Manesh R. Patel, M.D., Kenneth W. Mahaffey, M.D., Jyotsna Garg, M.S., Guohua Pan, Ph.D., Daniel E. Singer, M.D., Werner Hacke, M.D., Ph.D., Günter Breithardt, M.D., Jonathan L. Halperin, M.D., Graeme J. Hankey, M.D., Jonathan P. Piccini, M.D., Richard C. Becker, M.D., Christopher C. Nessel, M.D., John F. Paolini, M.D., Ph.D., Scott D. Berkowitz, M.D., Keith A.A. Fox, M.B., Ch.B., Robert M. Califf, M.D., and the ROCKET AF Steering Committee, for the ROCKET AF Investigators*

Patel MR et al. NEJM 2011: 365:883-91

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

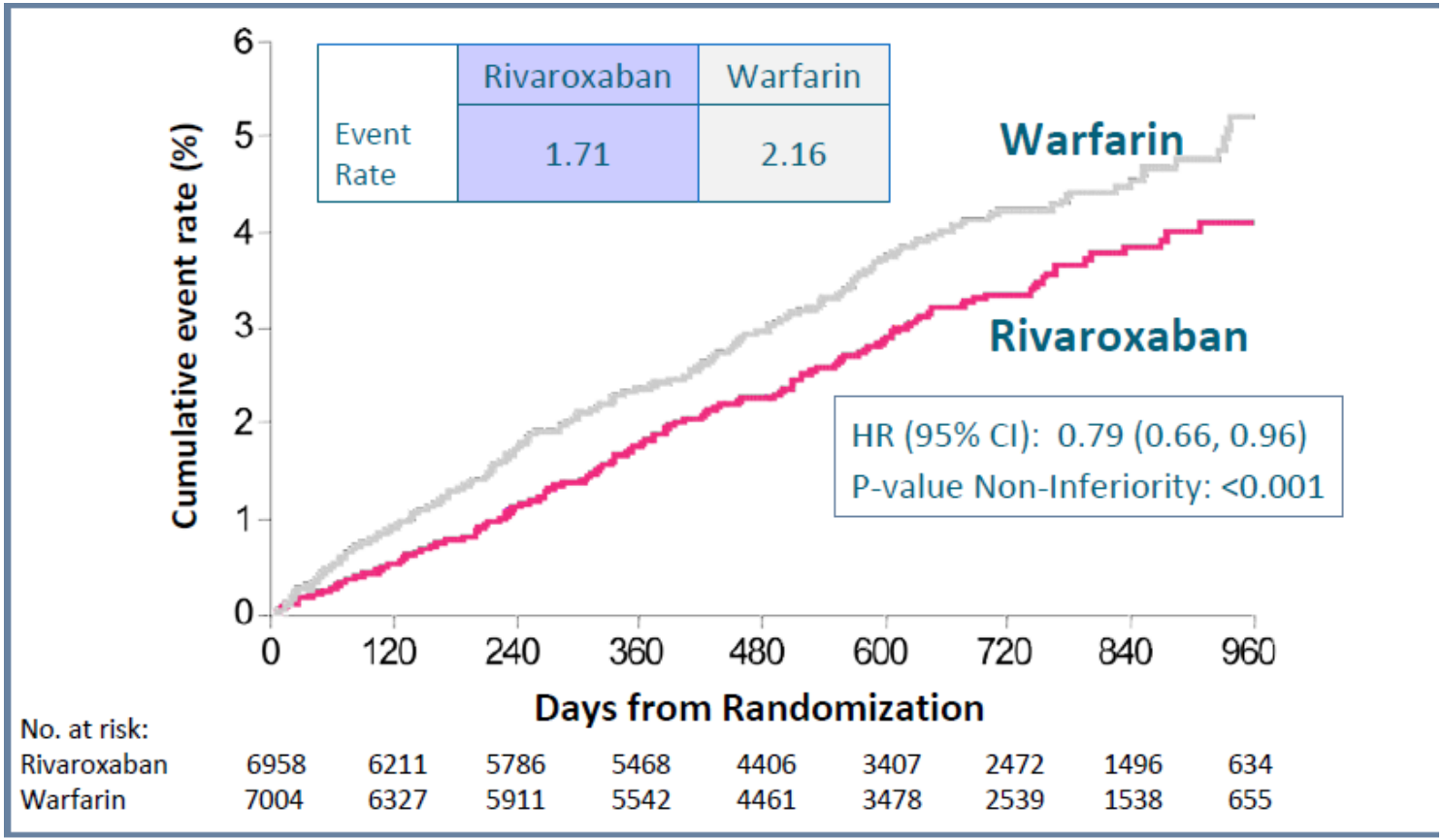
Rivaroxaban – ROCKET-AF Study Summary



Study Design: DB, non-inferiority
CHADS2 mean score 3.5
Median follow up 590 days (1.6 yrs.)
TTR (Time in Therapeutic Range) 55%

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

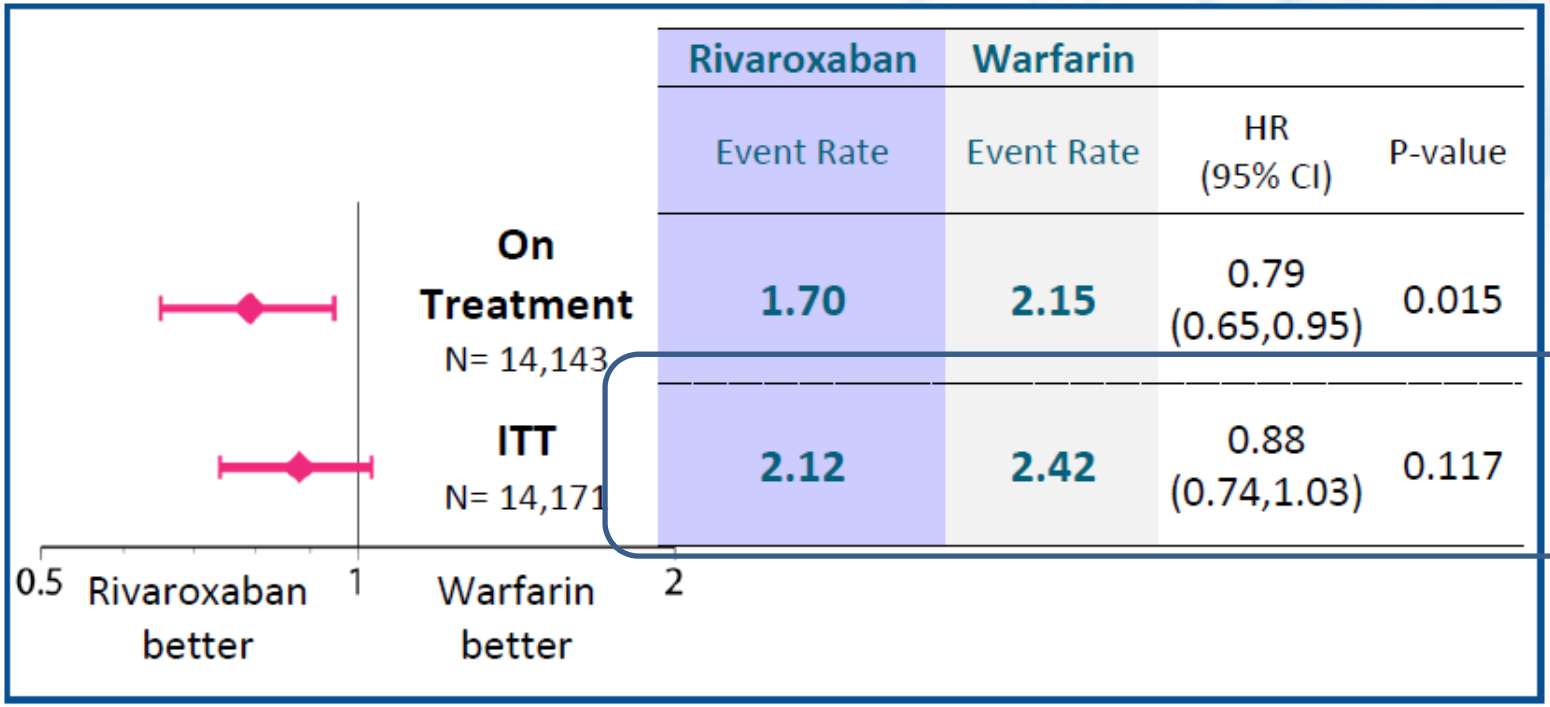
Rivaroxaban – ROCKET AF Results



Event Rates are per 100 patient-years

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – ROCKET AF Results (Cont`d)



	Rivaroxaban	Warfarin		
	Event Rate	Event Rate	HR (95% CI)	P-value
On Treatment N= 14,143	**1.70**	**2.15**	0.79 (0.65,0.95)	0.015
ITT N= 14,171	**2.12**	**2.42**	0.88 (0.74,1.03)	0.117

Event Rates are per 100 patient-years

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – Rocket AF Results (Cont'd)

	Rivaroxaban Event Rate	Warfarin Event Rate	HR (95% CI)	P-value
Stroke Type				
Hemorrhagic	0.26	0.44	0.59 (0.37, 0.93)	0.024
Ischemic	1.34	1.42	0.94 (0.75, 1.17)	0.581
Unknown Type	0.06	0.10	0.65 (0.25, 1.67)	0.366
Non-CNS Embolism	0.04	0.19	0.23 (0.09, 0.61)	0.003
Myocardial Infarction	0.91	1.12	0.81 (0.63, 1.06)	0.121
All Cause Mortality	1.87	2.21	0.85 (0.70, 1.02)	0.073

Event Rates are per 100 patient-years

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – Bleeding Risks

	Rivaroxaban	Warfarin		
	Event Rate %	Event Rate %	HR (95% CI)	P-value
Major	3.60	3.45	1.04 (0.90, 1.20)	0.576
≥2 g/dL Hgb drop	2.77	2.26	1.22 (1.03, 1.44)	0.019
Transfusion (> 2 unit)	1.65	1.32	1.25 (1.01, 1.55)	0.044
Critical organ bleed	0.82	1.18	0.69 (0.53, 0.91)	0.007
Fatal	0.24	0.48	0.50 (0.31, 0.79)	0.003
Intracranial Hemorrhage	0.49	0.74	0.67 (0.47, 0.94)	0.019

- Warfarin rates of life-threatening, intracranial/critical/fatal bleed were higher than Rivaroxaban
- More transfusion or drop in Hgb with rivaroxaban
- More GI bleed, epistaxis & hematuria with rivaroxaban

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Rivaroxaban – The Bottom Line

- Rivaroxaban non-inferior to warfarin
- Stroke Prevention In AF:
  - Rivaroxaban significantly reduced risk of hemorrhagic stroke and systemic embolism compared to warfarin (secondary outcome)
  - Warfarin had more intracranial/critical bleeding than rivaroxaban
  - Rivaroxaban had more transfusion, drop in hemoglobin, GI bleed, epistaxis and hematuria.

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixaban – Drug Profile

Mechanism of Action	Direct Xa inhibitor
Indications	Thrombo-prophylaxis in knee and hip surgery Prevention of stroke and systemic embolic in AF
Dosing	Knee Replacement: 2.5mg po daily x 10-14days Hip Replacement: 2.5mg po daily x 28-35 days Stroke Prevention in AF: 5mg po BID
Renal Dosing	No dosage adjustment needed for Hip/Knee Replacement (For AF pts who are > 80 yr, < 60kg or SCr > 133umol/L : 2.5mg po BID Avoid if < 25mL/min
Side Effects	Nausea, anemia, hemorrhage and contusion
Drug Interactions	CYP 3A4 or P-glycoprotein mediated (Ketoconazole, Rifampin)
Monitoring	None Recommended, AntiFXa assay may be helpful in selected situations
Drug Coverage	Not covered by ODB; for 5mg po BID, it costs approximately $ 160/month

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixaban: Clinical Evidence

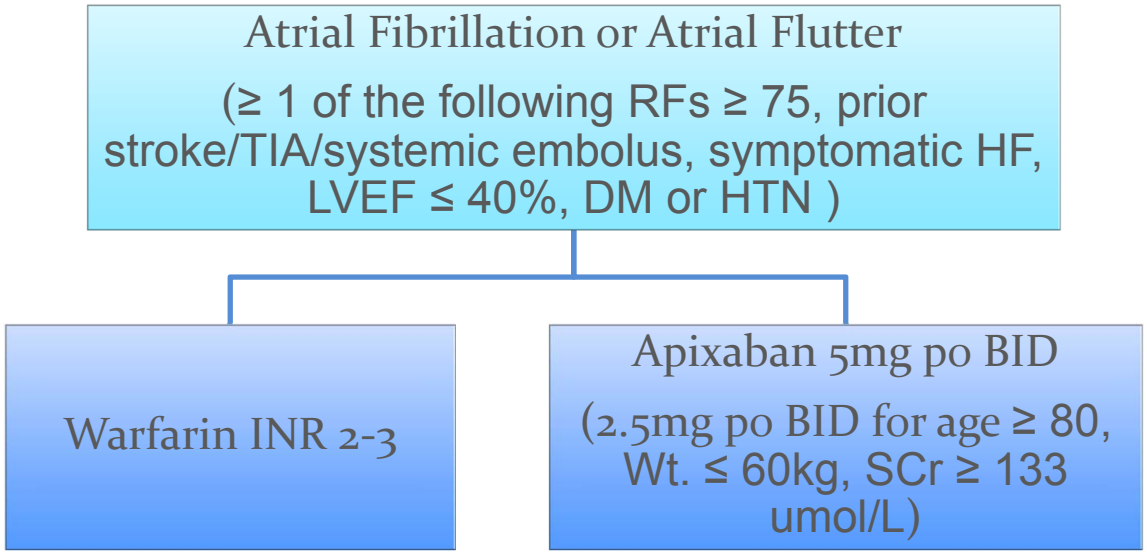
Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S., John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H., Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Atar, M.D., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D., David Garcia, M.D., Margarida Geraldes, Ph.D., Bernard J. Gersh, M.D., Sergey Golitsyn, M.D., Ph.D., Shinya Goto, M.D., Antonio G. Hermosillo, M.D., Stefan H. Hohnloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D., Petr Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators*

Granger GB et al. NEJM 2011;365:981-92

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixiban: ARISTOTLE Study Overview



Study Design: DB, non-inferiority
CHADS2 mean score 2.1
Median follow up 1.8 yrs.
TTR 62%

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixaban: ARISTOTLE Results

Outcome	Apixaban (N=9120) Event Rate (%/yr)	Warfarin (N=9081) Event Rate (%/yr)	HR (95% CI)	P Value
Stroke or systemic embolism*	1.27	1.60	0.79 (0.66, 0.95)	0.011
Stroke	1.19	1.51	0.79 (0.65, 0.95)	0.012
Ischemic or uncertain	0.97	1.05	0.92 (0.74, 1.13)	0.42
Hemorrhagic	0.24	0.47	0.51 (0.35, 0.75)	<0.001
Systemic embolism (SE)	0.09	0.10	0.87 (0.44, 1.75)	0.70
All-cause death*	3.52	3.94	0.89 (0.80, 0.998)	0.047
Myocardial infarction	0.53	0.61	0.88 (0.66, 1.17)	0.37

- Non-inferior/superior to warfarin for the primary outcome
- Stroke/hemorrhagic stroke rates lower with apixaban
- All-cause mortality lower with apixaban

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixaban: Bleeding Risks

Outcome	Apixaban (N=9088) Event Rate (%/yr)	Warfarin (N=9052) Event Rate (%/yr)	HR (95% CI)	P Value
Primary safety outcome: ISTH major bleeding*	2.13	3.09	0.69 (0.60, 0.80)	<0.001
Intracranial	0.33	0.80	0.42 (0.30, 0.58)	<0.001
Gastrointestinal	0.76	0.86	0.89 (0.70, 1.15)	0.37
Major or clinically relevant non-major bleeding	4.07	6.01	0.68 (0.61, 0.75)	<0.001
GUSTO severe bleeding	0.52	1.13	0.46 (0.35, 0.60)	<0.001
TIMI major bleeding	0.96	1.69	0.57 (0.46, 0.70)	<0.001

Overall lower bleeding risks compared to warfarin

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Apixaban – The Bottom Line

- Apixaban superior to warfarin
- In AF:
  - Apixaban reduced stroke or systemic embolism
  - Apixaban reduced all-cause mortality compared to warfarin
  - Apixaban had less major bleeding compared to warfarin
  - Net clinical outcomes of stroke, systemic embolism, major bleeding or death from any cause favours apixaban vs. warfarin

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Compared to warfarin, which one is better?

	Dabigatran 150mg po BID	Dabigatran 110mg po BID	Rivaroxaban 20mg po daily (or 15mg po daily if CrCL between 30-49mL/min)	Apixaban 5mg po BID (or 2.5-5mg po BID if CrCL between 30-49ml/min)
Stroke Prevention in AF	Better than Warfarin	No different than warfarin	No different than warfarin	Better than Warfarin

Limitations of the new oral anticoagulants:

- No antidote available
- Renally excreted (If CrCL < 30mL/min, warfarin is preferred)
- Limited post marketing experience

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

OTHER CONSIDERATIONS

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Coronary Artery Disease

- The 2010 CCS Consensus recommend that warfarin be used in preference to dabigatran in those patients with AF and CAD requiring oral anticoagulant (OAC) therapy.

- The new updates in 2012 suggests that one of the new OAC could be used in preference to warfarin when OAC is indicated for stroke prevention with concomitant AF and CAD.

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Coronary Artery Disease

Antithrombotic Management of AF/AFL in CAD

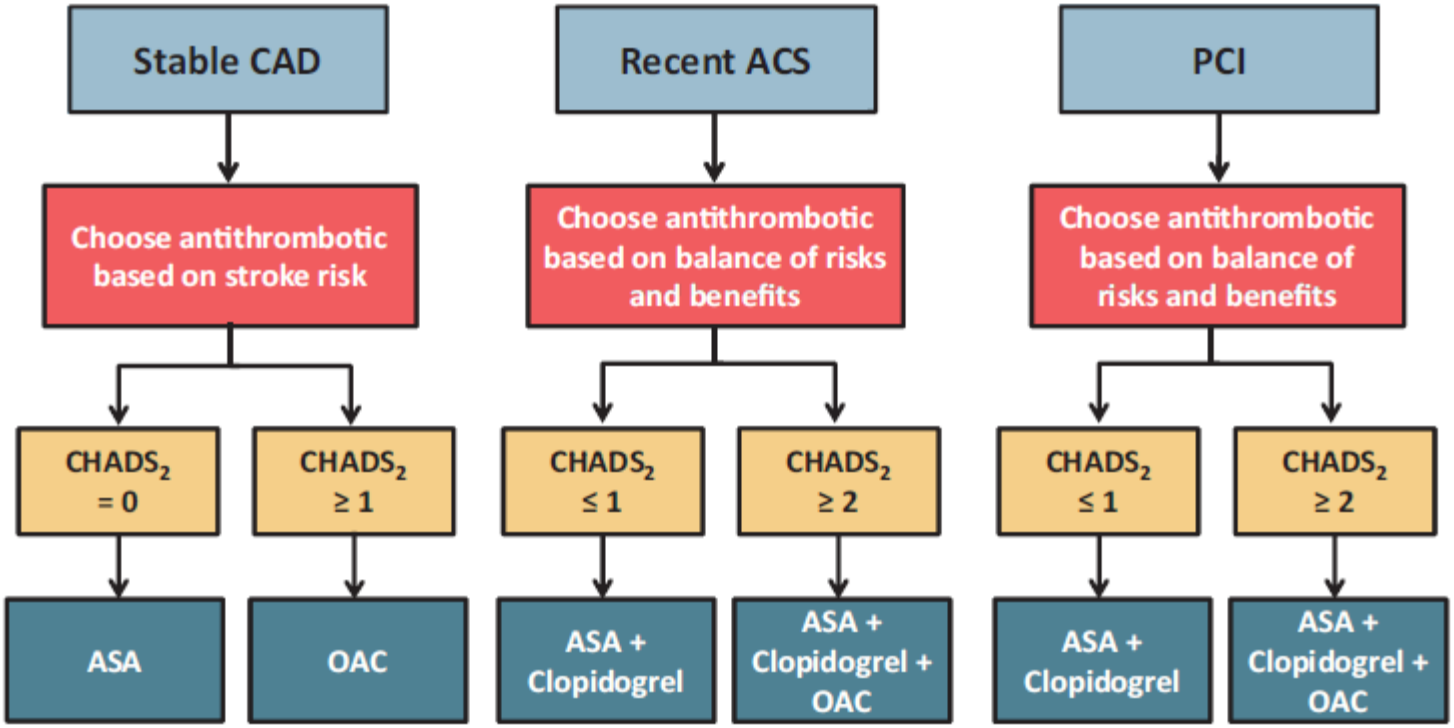


Figure 2. A summary of our recommendations for antithrombotic management in settings of CAD. ACS, acute coronary syndrome; AF, atrial fibrillation; AFL, atrial flutter; ASA, acetylsalicylic acid (aspirin); CAD, coronary artery disease; $CHADS_2$, Congestive Heart Failure, Hypertension, Age > 75, Diabetes Mellitus, and Prior Stroke or Transient Ischemic Attack; OAC, oral anticoagulant; PCI, percutaneous coronary intervention.

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Renal Impairment in the Elderly

- All new oral anticoagulants are eliminated renally to various degrees.
- Prior to starting the new OAC, a CrCL should be done. (repeat CrCL at least annually and may be more frequently in selected cases)
- Different Formulas available for renal function:
  - Cockcroft and Gault (may under-estimate CrCL)
  - eGFR (Modified Diet Renal Disease formula) (may over-estimate CrCL)

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Risk of GI bleeds with Dabigatran

- GI bleed is higher with Dabigatran use
  - Whether the cause is excessive anticoagulation or local irritant with tartaric acid remains unclear
  - For people with history of GI bleed or other GI conditions (Crohn`s, Hiatus Hernia, IBS), may want to consider warfarin or avoid dabigatran

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Potential Candidates to Switch…

- What is the patient`s warfarin TTR ? Also is INR monitoring impractical?
- What is the patient`s renal function?
  - Consider stability
  - Comparison between eGFR and Cockcroft and Gault
  - Clinical status (e.g. recent fall, hospitalization etc.)
- Any recent ACS or MI: prefer warfarin (& avoid dabigatran?) Apixaban may increase risk of bleed when used with antiplatelets
- If there is a history of GI disease, consider staying with warfarin or switch to Apixaban (if approved in Canada) over Dabigatran or Rivaroxaban
- Apixaban is not covered by ODB but looks to be a promising agent based on preliminary clinical evidence

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Switching from warfarin to the new oral anticoagulants

Dabigatran / Apixaban

- Start dabigatran / Apixaban after warfarin has been discontinued and patient's INR is below 2.0

Rivoraxaban

- Start rivaroxaban after stopping warfarin and INR is ≤ 2.5
- If INR is > 2.5, delay start of rivaroxaban until INR is ≤ 2.5

Refer to the Product Monograph if switching from Dabigatran / Rivoraxaban / Apixaban to warfarin

MediSystem Pharmacy
A SHOPPERS DRUG MART COMPANY

Timing of Discontinuation* for Surgery or Invasive Procedures

Creatinine Clearance	Timing of discontinuation after last dose before surgery	
	Standard risk of bleeding	High risk of bleeding
Dabigatran		
> 50mL/min	24 hours	2 days
>30mL/min ≤ 50mL/min	2 days	4 days
≤ 30mL/min	4 days	6 days
Rivaroxaban		
>30mL/min	24 hours	2 days
≤ 30mL/min	2 days	4 days

*After Last dose before surgery or invasive procedures

MediSystem™
Pharmacy
A SHOPPERS DRUG MART® COMPANY

QUESTIONS?