Cadrenal Therapeutics, Inc.

NASDAQ: CVKD

May 2024

Caution Concerning Forward-looking Statements

This document contains forward-looking statements. In addition, from time to time, we or our representatives may make forward-looking statements orally or in writing. We base these forward-looking statements on our expectations and projections about future events, which we derive from the information currently available to us. Such forward-looking statements relate to future events or our future performance, including: our financial performance and projections; our growth in revenue and earnings; and our business prospects and opportunities. You can identify forward-looking statements by those that are not historical in nature, particularly those that use terminology such as “may,” “should,” “expects,” “anticipates,” “contemplates,” “estimates,” “believes,” “plans,” “projected,” “predicts,” “potential,” or “hopes” or the negative of these or similar terms.

In evaluating these forward-looking statements, you should consider various factors, including: our ability to successfully develop and commercialize product candidates, our ability to raise capital when needed, and the competitive environment of our business. These and other factors may cause our actual results to differ materially from any forward-looking statement, including those risk factors disclosed in our Annual Report on Form 10-K for the year ended December 31, 2023 filed with the Securities and Exchange Commission on March 11, 2024. Forward-looking statements are only predictions. The forward-looking events discussed in this document and other statements made from time to time by us or our representatives may not occur, and actual events and results may differ materially and are subject to risks, uncertainties, and assumptions about us. We are not obligated to publicly update or revise any forward-looking statement, whether as a result of uncertainties and assumptions, the forward-looking events discussed in this document, and other statements made from time to time by us or our representatives might not occur.

Cadrenal Therapeutics Overview:

Late-stage Drug Company with Multiple Orphan-drug and Fast-track Designations

Developing tecarfarin, a late-stage novel oral and reversible anticoagulant (blood thinner) to prevent heart attacks, strokes and deaths due to blood clots in patients with rare cardiovascular conditions who require chronic anticoagulation

Targeted at conditions where (VKA) Vitamin K antagonist warfarin has failed to achieve sufficiently reliable anticoagulation and Direct Oral AntiCoagulants, or DOACs (Eliquis-class drugs), have not shown benefit

Left Ventricular Assist Devices LVADs

End-stage Kidney Disease (ESKD) + Atrial Fibrillation (AFib)

Thrombotic Antiphospholipid Syndrome (APS)

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Key Investment Highlights for Tecarfarin Opportunity

1	High Level of Unmet Need	NO approved anticoagulation therapies for rare cardiovascular conditions requiring chronic anticoagulation, including LVADs, ESKD with AFib, and APS
2	Proven Mechanism of Action	Tecarfarin is a next-generation VKA that leverages the well-understood mechanism of action and solves the instability issue of legacy VKAs
3	Improved Safety Profile (Less Bleeding)	Extensive safety data from 11 clinical trials in over 1,000 subjects
4	Clear Regulatory Path with No Development Competition	Tecarfarin was granted Orphan Drug Designation and Fast Track Approval by FDA for LVADs and ESKD + AFib, providing 7-year marketing exclusivity, and clarity regarding the pathway to approval
5	Strong Projected Adoption & Pricing	U.S. market potential estimated more than $2 billion combined for the three targeted rare cardiovascular conditions

Experienced management team with opportunistic commercial strategy

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Leadership Team: Clinical to Commercial Expertise

Quang Pham

CEO & Founder, Chairman

Douglas Losordo, MD

Chief Medical Officer

Matthew Szot, CPA

Chief Financial Officer

Jeff Cole

Chief Operating Officer

John R. Murphy

Board Member

Steven Zelenkofske, DO

Board Member

Glynn Wilson, PhD

Board Member

Robert Lisicki

Board Member

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Scientific Advisory Board with Deep Experience in CV and Beyond

Christopher Granger, MD

Professor of Medicine in the Division of Cardiology,
Duke University

Member, Duke Clinical Research Institute (DCRI)

Sean Pokorney, MD, MBA

Electrophysiologist and Assistant
Professor of Medicine,
Duke University

Eloine M. Hylek, MD, MPH

Professor of Medicine,
Boston University School of Medicine

Director of the Thrombosis and Anticoagulation
Service at ***Boston Medical Center (BMC)***

C. Michael Gibson, MD

Professor of Medicine,
Harvard Medical School

Interventional Cardiologist,
Beth Israel Deaconess Medical Center

President & CEO,
Baim Institute for Clinical Research

Wolfgang C. Winkelmayer, MD, MPH

Chief, Section of Nephrology,
Professor of Medicine, ***Baylor University***

Director,
Selzman Institute for Kidney Health

Richard Whitlock, MD

Cardiac Surgeon and Professor of Surgery,
McMaster

University Medical Center Investigator,
Population Health Research Institute

Michael Lincoff, MD

Vice Chairman, Dept. of Cardiovascular Medicine,
Cleveland Clinic

Director of Clinical Research,
Lerner Research Institute

The Problem: Certain Rare Heart Conditions Lack Effective Anticoagulation

Physicians are frustrated with warfarin outcomes and hesitant to prescribe DOACs more broadly, given the negative evidence in clinical trials

SIGNIFICANT **ISSUES** WITH CURRENT THERAPIES FOR THESE PATIENTS

	Warfarin	DOACs (Pradaxa, Xarelto, Eliquis & Savaysa)
LVAD 	⊖ High frequency of hemorrhagic events despite warfarin therapy ⊖ Unstable metabolism due to drug-drug interactions, genetic variability of elimination pathway	⊖ No ability to monitor the level of anticoagulation ⊖ Cost and time of reversal compared to vitamin K is not acceptable for patients at high risk of bleeding or intervention ⊖ LVAD patients excluded from approval studies ⊖ DOACs not in guidelines for LVAD patients
ESKD+AFib 	⊖ Higher risk of bleeding in dialysis patients with AFib compared to DOACs ⊖ Multiple dose adjustments to keep patients within International Normalized Ratio (INR) range ⊖ Drug interaction in patients with multiple comorbidities	⊖ Limited head-to-head evidence; existing data fails to demonstrate benefit in thromboembolism and reveals stroke risk ⊖ Not included in ESKD treatment guidelines ⊖ Ambiguity in dosing recommendations

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The Solution: Tecarfarin Aims to Solve Warfarin's Major Problems and Fill Significant Market Void

Warfarin: Unreliable metabolism
MAJOR PROBLEM
for patients with certain orphan diseases

Variable/Unreliable anticoagulation
in patients at high risk for thrombotic events

Challenging to control
despite nearly 70 years of use

Metabolism via the
cytochrome P450 pathway
potential drug-drug interactions

Significant variability in PK due to genetic variants and competition with other drugs

SOLUTION: Tecarfarin

SPECIFICALLY DESIGNED TO
solve the warfarin metabolism problem, thereby
DECREASING RISK OF STROKE & BLEEDING

Metabolized via an alternate pathway that is abundant and essentially insaturable

Reliable, stable PK profile

STABLE ANTICOAGULATION
with proven mechanism of action
including patients with certain orphan diseases

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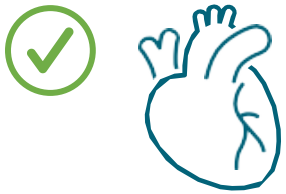
Attractive Addressable Market Opportunities

U.S. market potential estimated more than $2 billion for three targeted rare indications

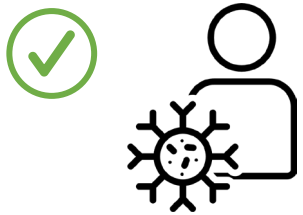


Left Ventricular Assist Devices

+

End-stage Kidney Disease with AFib

+



Thrombotic Antiphospholipid Syndrome

Approximately

>$2 Billion

Combined Peak Annual Market Potential*

(if approved by the FDA)

*Based on management's market analysis studies and expected adoption rates.

Financial Summary

Cap Table

Cash (at 3/31/24)	$6.6 million
Debt	NONE
Common Shares Outstanding	16,008,469
Warrants – Investors (avg. $1.75)	4,285,715
Warrants - Underwriter & Placement Agt. Warrants (avg. $2.68)	389,071
Stock Options Outstanding (avg. $0.90)	2,195,000

Q1 2024 Financial Results

Operating Expenses (excluding non-cash items)	$1.6 million
Cash used in operating activities	$1.8 million

Market Capitalization

As of 5/14/24	$7 million

Insider Ownership (Common Stock)

Insider Ownership as Percent of Shares Outstanding	47%

Tecarfarin Clinical Development Pipeline

Potential 2024 catalysts for future milestones to build enterprise value

Program	Prioritized Target Indications	Regulatory Strategy/Status
Tecarfarin	Left Ventricular Assist Devices (LVADs)	FDA Orphan Drug Designation Granted Developing Trial Protocol
	End Stage Kidney Disease with AFib	FDA Orphan Drug Designation Granted FDA Fast Track Designation Granted EMA Orphan Drug Application In Process
	Thrombotic Antiphospholipid Syndrome (APS)	FDA Orphan Drug Application Pending Review Developing Trial Protocol

Future milestones this year may include Ph 3 trial enrollment, anticipated data readouts and progress with strategic partnerships

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Why Cadrenal Now?

Tecarfarin is targeted for indications where it is NOW CLEAR FROM DATA that warfarin FAILS to achieve sufficiently stable anticoagulation and DOACs have clinically NOT shown benefit

Unmet Need

Certain rare cardiovascular conditions requiring chronic anticoagulation where warfarin has been unreliable, and DOACs (Eliquis-class drugs) are not FDA-approved

Proven Mechanism of Action

Tecarfarin is a VKA with a well-understood mechanism of action; Phase 1 and 2/3 clinical data supports that tecarfarin is an effective and safe anticoagulant

Improved Safety Profile

Tecarfarin is metabolized via a different metabolic pathway than warfarin – thus providing more stable anticoagulation than warfarin, thereby decreasing the risk of stroke and bleeding

Regulatory Pathway

Tecarfarin has been granted two Orphan Drug Designations and a Fast-track designation by FDA providing potential seven-year marketing exclusivity post-approval.

Large Commercial Market & Opportunistic Strategy

Marketed drugs for certain rare CV diseases command significant price premiums that value the tecarfarin addressable market at over $2B; right team to execute commercial strategy

Contact Us

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CFO
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APPENDIX

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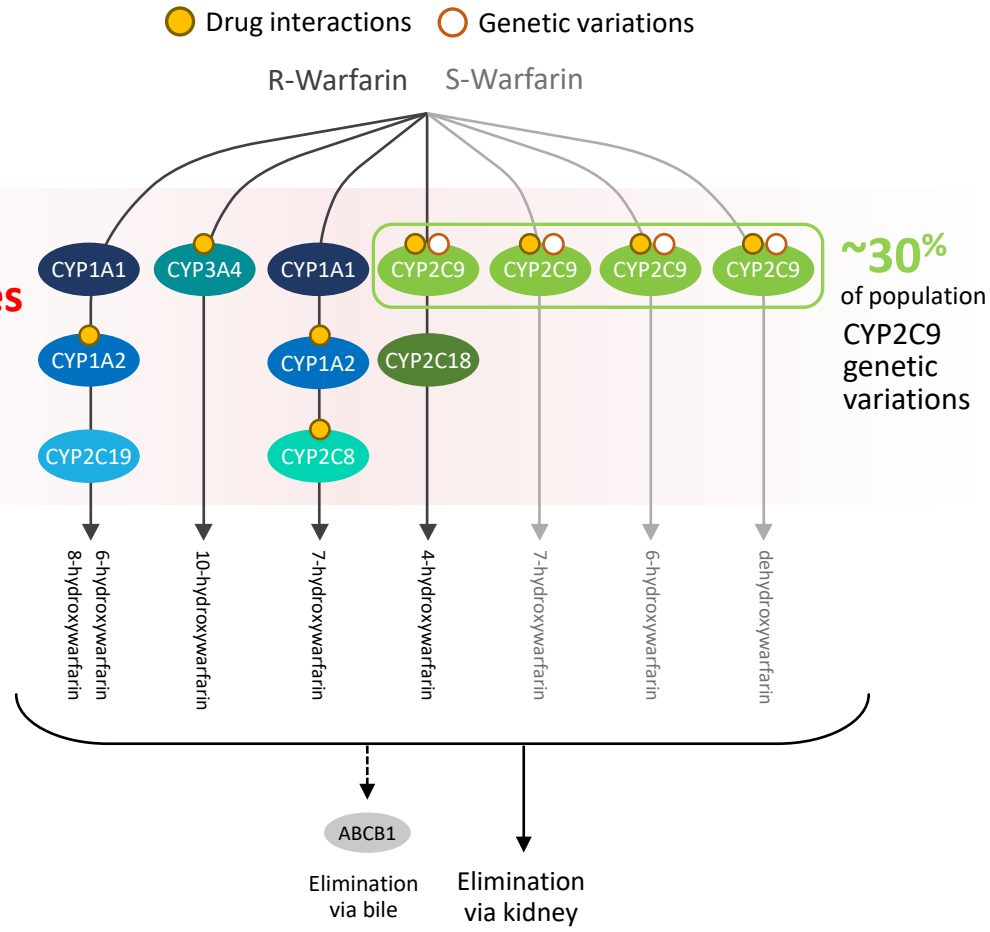
Tecarfarin's Metabolic Advantage

Tecarfarin is metabolized via an alternate pathway that is abundant and essentially insaturable, thereby avoiding the bottleneck in the CYP450 pathway where warfarin in metabolized.

Warfarin

CYP450

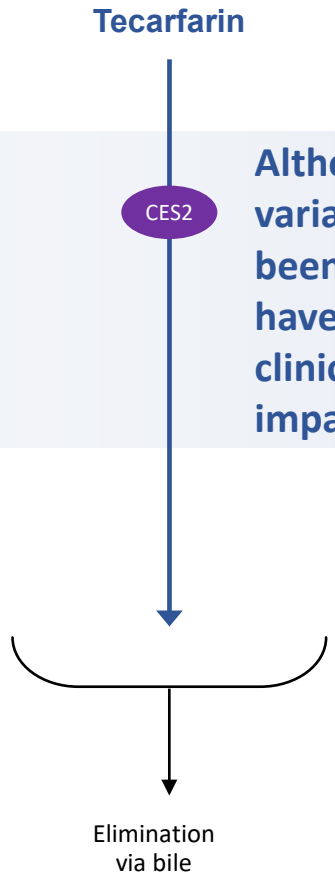


7 Different CYP450 Isoenzymes involved in Warfarin Metabolism!

~30% of population CYP2C9 genetic variations

Tecarfarin

Human CarboxylEsterase 2 (CES2)



Although genetic variation in CES2 has been identified there have been no reports of clinically significant impact

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Warfarin Metabolism via CYP450 is Complicated by Known Competitors, Inhibitors and Inducers and the Established Impact of Genetic Variants

Enzymes	Substrates	Inhibitors	Inducers
CYP 3A4	amlodipine, simvastatin, **warfarin**, amiodarone, sildenafil, midazolam, fluoxetine, haloperidol, codeine, oxycodone, methadone, fentanyl	ciprofloxacin, ketoconazole, ritonavir, methylprednisone, imatinib, tamoxifen, cimetidine, grapefruit juice	simvastatin, efavirenz, pentobarbital, carbamazepine, phenobarbital, phenytoin, valproic acid, caffeine
CYP IA2	alosetron, caffeine, duloxetine, melatonin, ramelteon, tacrine, tizanidine	ciprofloxacin, enoxacin, fluvoxamine, oral contraceptives, phenylpropanolamine	montelukast, phenytoin, smoking components of cigarettes
CYP 2C8	repaglinide, paclitaxel, methadone	gemfibrozil, fluvoxamine, ketoconazole, trimethoprim	rifampin
CYP 2C9	celecoxib, **warfarin**, phenytoin	amiodarone, fluconazole, miconazole, oxandrolone, capecitabine, etravirine, fluvastatin, metronidazole, Sulfinpyrazone, tigecycline	carbamazepine, rifampin, aprepitant, bosentan, phenobarbital, St. John's wort
CYP 2D6	lidocaine, metoprolol, haloperidol, fluoxetine, amitriptyline, metoclopramide, codeine, oxycosone, tramadol	amiodarone, chlorpromazine, citalopram, bupropion	rifampin, dexamethasone

Tecarfarin was specifically designed to avoid metabolism via the CYP450 Pathway, thus improving safety and efficacy over warfarin

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Tecarfarin is Metabolized via the Human Carboxyl Esterase 2 Pathway (CES2) Provides More Effective, Safe, and More Consistent Anti-coagulation

Enzymes	Substrates	Inhibitors	Inducers
CYP 3A4	amlodipine, simvastatin, warfarin, amiodarone, sildenafil, midazolam, fluoxetine, haloperidol, codeine, oxycodone, methadone, fentanyl	ciprofloxacin, ketoconazole, ritonavir, methylprednisone, imatinib, tamoxifen, cimetidine, grapefruit juice	simvastatin, efavirenz, pentobarbital, carbamazepine, phenobarbital, phenytoin, valproic acid, caffeine
CYP IA2	alosetron, caffeine, duloxetine, melatonin, ramelteon, tacrine, tizanidine	ciprofloxacin, enoxacin, fluvoxamine, oral contraceptives, phenylpropanolamine	montelukast, phenytoin, smoking components of cigarettes
CYP 2C8	repaglinide, paclitaxel, methadone	gemfibrozil, fluvoxamine, ketoconazole, trimethoprim	rifampin
CYP 2C9	celecoxib, warfarin, phenytoin	amiodarone, fluconazole, miconazole, oxandrolone, capecitabine, etravirine, fluvastatin, metronidazole, Sulfinpyrazone, tigecycline	carbamazepine, rifampin, aprepitant, bosentan, phenobarbital, St. John's wort
CYP 2D6	lidocaine, metoprolol, haloperidol, fluoxetine, amitriptyline, metoclopramide, codeine, oxycosone, tramadol	amiodarone, chlorpromazine, citalopram, bupropion	rifampin, dexamethasone

CES2 Substrate Drugs

Antiplateletes/Anticoagulants
- Acetylsalicylic acid
- Prasugrel
- Dabigatran etexilate

Angiotensin receptor blockers
- Candesartan cilexetil
- Olmesartan medoxomil
- Azilsartan medoxomil

Antivitral agents
- Tenfovir disoproxil
- Adefovir dipivoxil
- Valacyclovir

CNS agents
- Cocaine
- Heroin
- 6-monoacetylmorphine

Immunosuppressive agents
- Methylprednisolone sodium succinate
- Deflazacort

Oncology agents
- Irinotecan
- Capecitabine

Anesthetic drug
- Procaine

Limited Substrates Identified

Genetic variation exists, but limited evidence of clinical impact

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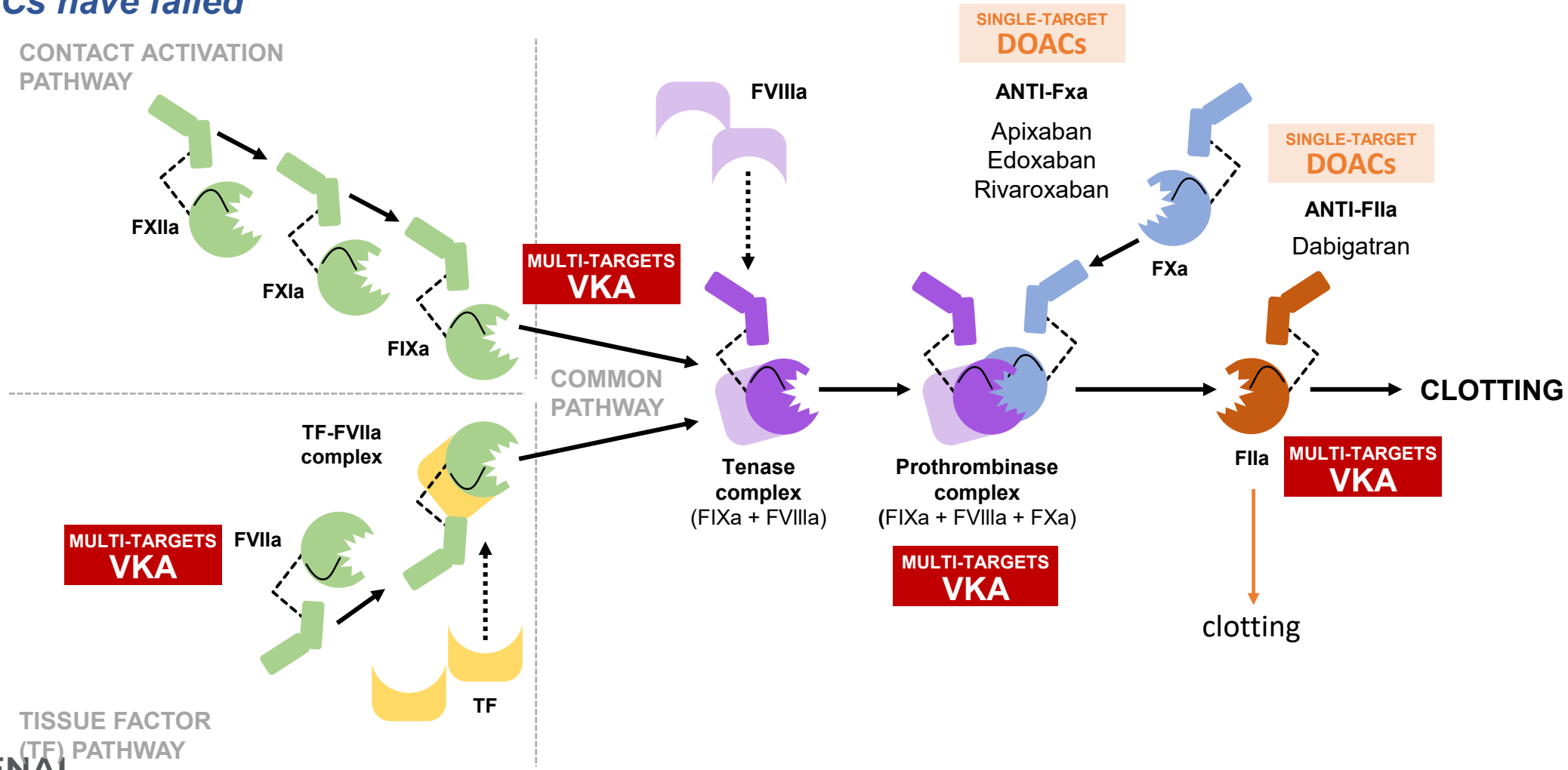
Vitamin K Antagonism Inhibits Multiple Factors (II, VII, IX, X, Proteins C & S) in the Clotting Cascade vs. Single Targets of Newer Agents

Proven mechanism of action resulting in clinically meaningful anticoagulation in certain conditions where DOACs have failed



Tecarfarin Demonstrates TTR Above Anticoagulation Control Threshold

Phase 2/3 trial shows Tecarfarin provides stable anticoagulation with >72% TTR overall and across key subgroups

Phase 2/3 Trial completed (N=607)

- Tecarfarin vs. well-controlled warfarin trial
- Randomized, double-blind trial designed to compare the quality of anticoagulation
- Average Time in Therapeutic Range (TTR) as measured by the International Normalized Ratio (INR)
- Dosing managed by a centralized dose control center

Key Tecarfarin Findings

Tecarfarin Demonstrated

TTR >72%

overall and across key subgroups

Demonstrated trends suggesting **improved TTR control** in key subgroups expected to do poorly with warfarin

Demonstrated **similar major bleeding** as warfarin and **no thrombotic events**

TTR of 70% or greater is generally accepted as the goal for stable anticoagulation with a VKA

In real world use of warfarin, TTR averages approximately 40-59%

Source: EmbraceAC Review by Whitlock et al., 2016

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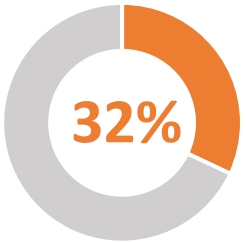
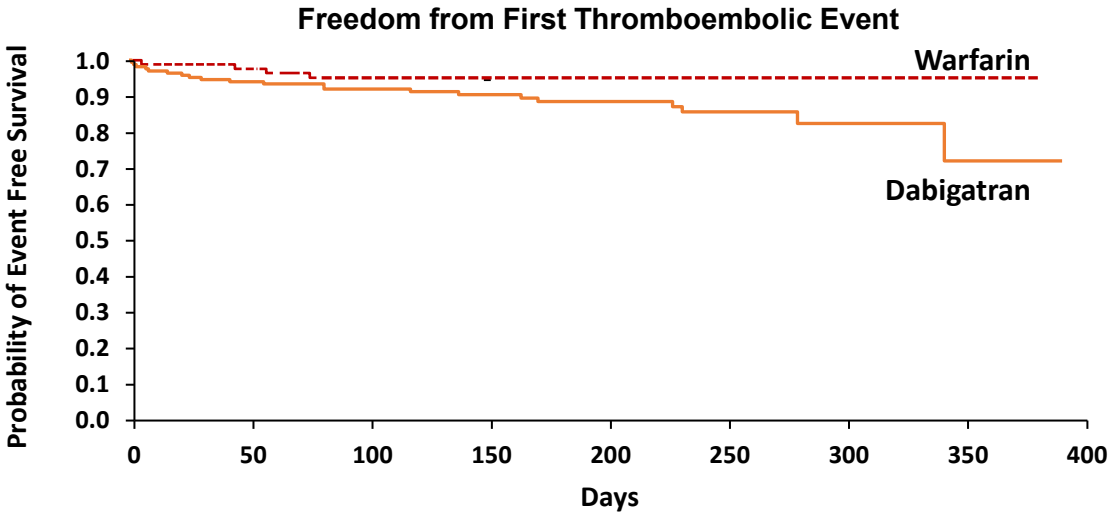
Dabigatran Versus Warfarin in Patients with Mechanical Heart Valves
EXCESS RISK AND NO BENEFIT

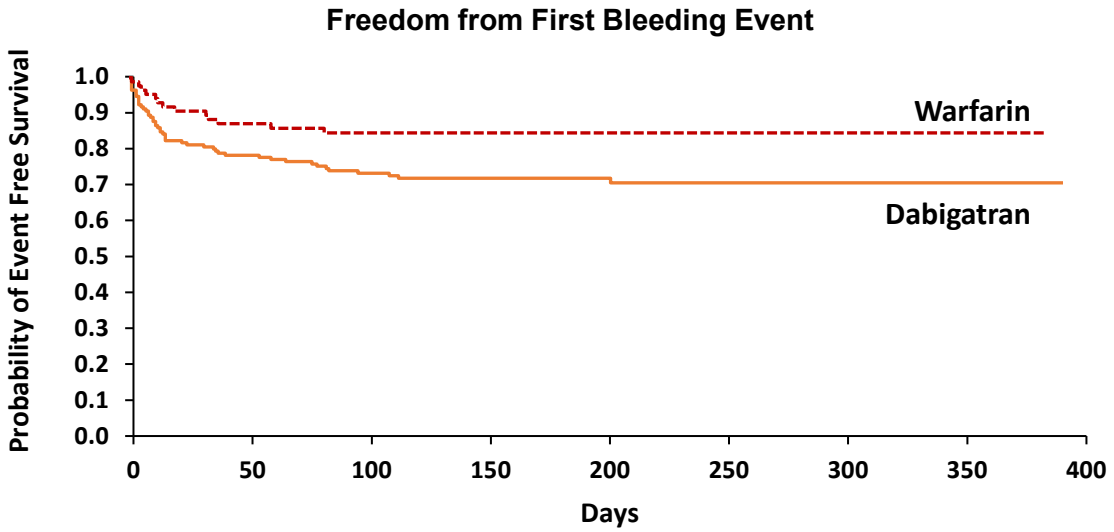
Trial terminated prematurely
due to an excess of thromboembolic and bleeding events among patients in the **dabigatran group**

	Dabigatran N=168 N (%)	Warfarin N=84 n (%)
Ischemic or unspecified stroke	9 (5.4)	0
Major bleeding	7 (4.2)	2 (2%)



Dose adjustment or discontinuation of dabigatran
(as-treated analysis)





CADRENAL THERAPEUTICS

Eikelboom, JW. et al. *New England Journal of Medicine.* 2013. DOI: 10.1056/NEJMoa1300615

TTR Decreases with CKD Severity for AFib Patients on Warfarin

AFib Patients with ESKD on Warfarin are Poorly Controlled with TTR of 42-51%, compared to the TTR goal of 70% or greater

- Time in Therapeutic Range (TTR)[1,2,5]
  - Well-established FDA metric used to evaluate anticoagulation control (safety and efficacy)
  - Higher TTR levels correlate directly with improved clinical outcomes including rates of death, bleeding, myocardial infarction, stroke, and systemic embolism
- TTR predictive of clinical outcomes
  - Stage 4 and 5 CKD with AFib: Similar TTR cutoffs predictive of mortality and cardiovascular outcomes[3,4]
- Overall TTR for AFib Patients with ESKD on warfarin is 42-51%[6]
- Only 21% of ESKD patients on dialysis using warfarin achieve TTR ≥60%[6]

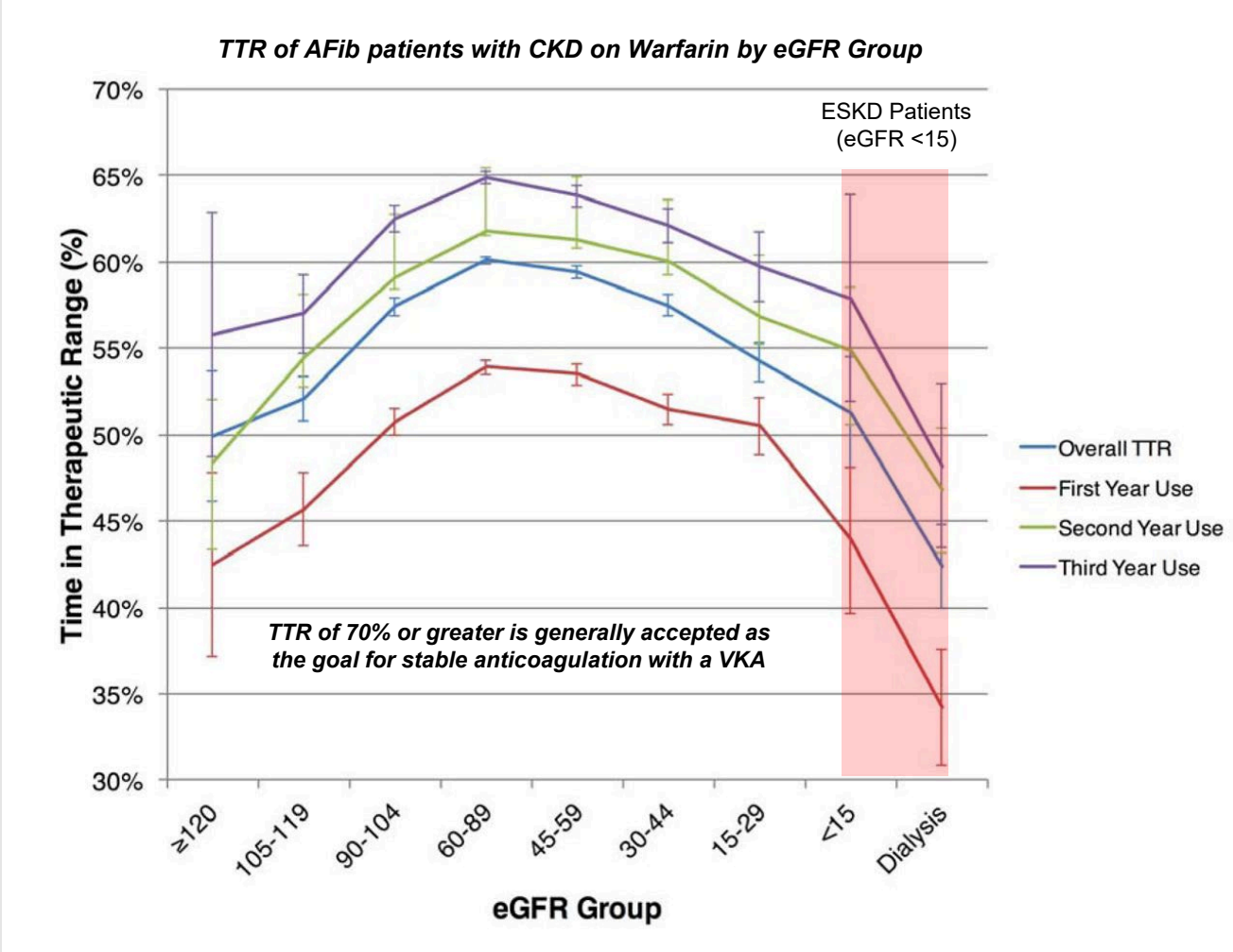


Figure 2. Warfarin Utilization and Anticoagulation Control in Patients with Atrial Fibrillation and Chronic Kidney Disease[6]

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1) White et al. 2007; 2) Currie et al. 2006; 3) Szumer et al., 2017; 4) Inoue et al., 2018; 5) Jones et al. 2005 6) Yang et al. Heart (2017 June)

Phase 2/3 Trial Shows Tecarfarin is Well-Tolerated for Stroke and Thrombus Prevention, with Fewer Hemorrhagic Events

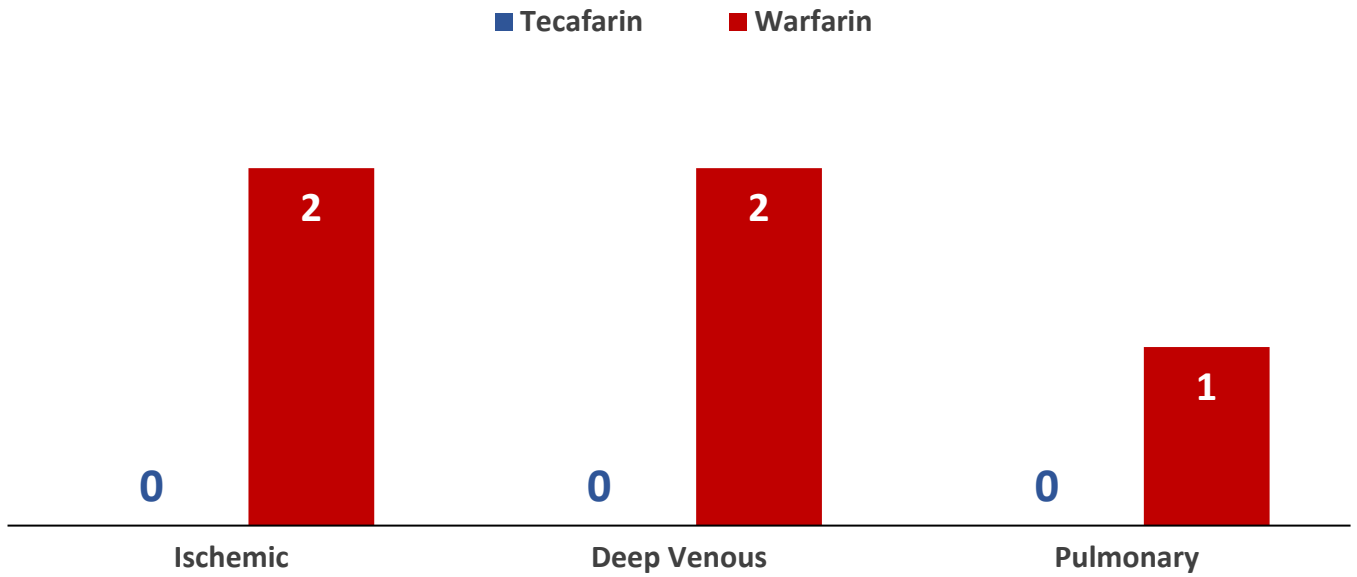
Tecarfarin had fewer thrombotic events compared to warfarin

Randomized, double-blind clinical trial

N=607
Patients with indications for chronic anticoagulation

Tecarfarin (n = 304)

Warfarin (n = 303)

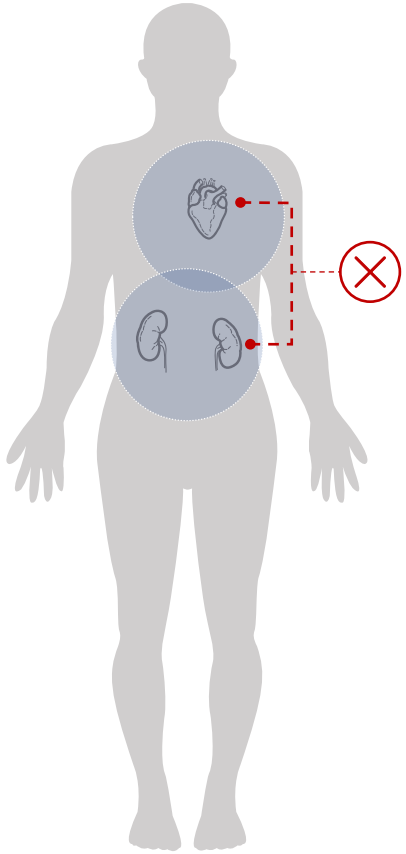


Tecarfarin-treated subjects experienced numerically fewer major hemorrhages than the warfarin-treated patients and had numerically fewer thrombotic events

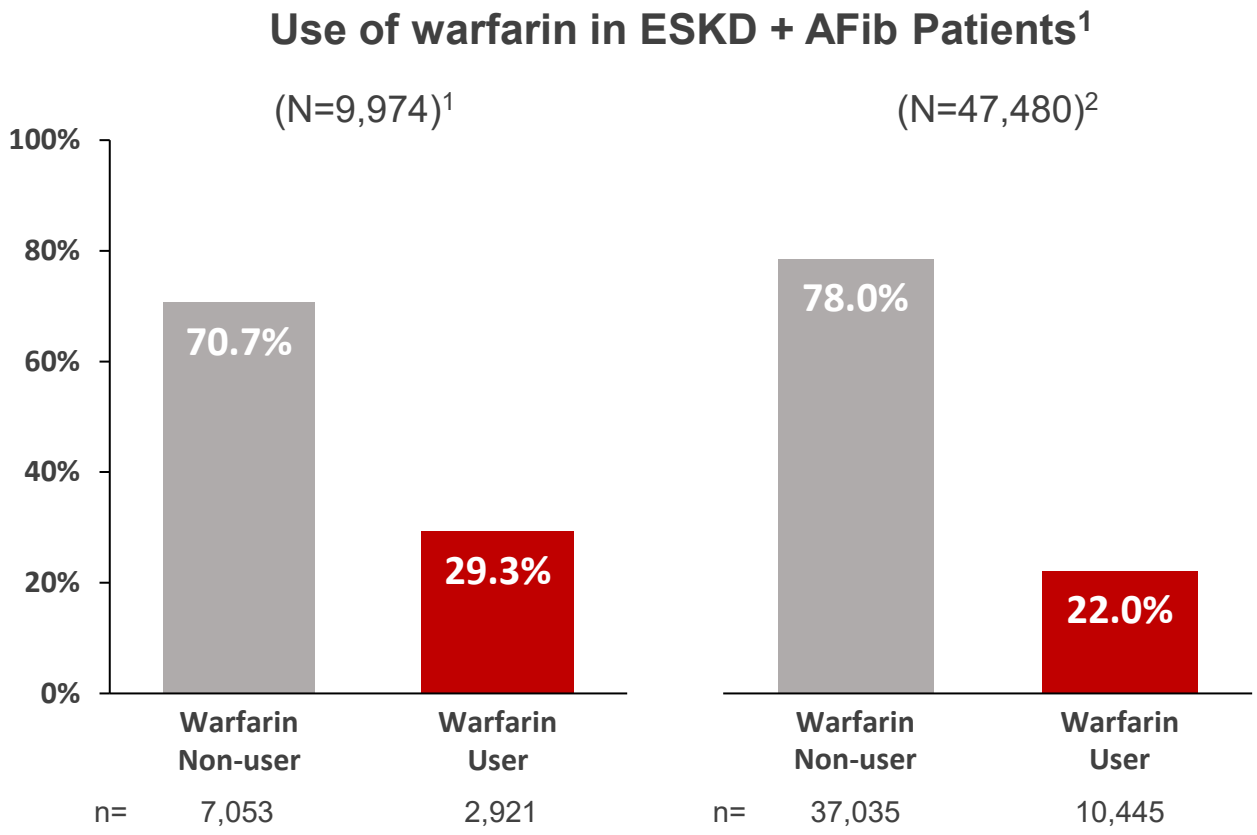
Whitlock RP, Fordyce CB, Midei MG, et al. A randomised, double blind comparison of tecarfarin, a novel vitamin K antagonist, with warfarin. The EmbraceAC Trial. *Thromb Haemost.* 2016;116(2):241-250. doi:10.1160/TH15-11-0910

Significant Underserved Patient Populations

Despite the significantly increased risk of stroke in ESKD patients with AFib, most patients are not anticoagulated due to the lack of evidence of benefit



Most patients with ESKD + AFib <u>are not prescribed</u> ANY anticoagulation to reduce their risk of stroke



1. Yoon CY, Noh J, Jhee JH, et al. Warfarin Use in Patients With Atrial Fibrillation Undergoing Hemodialysis: A Nationwide Population-Based Study. *Stroke*. 2017;48(9):2472-2479. doi:10.1161/STROKEAHA.117.017114
2. Randhawa MS, Vishwanath R, Rai MP, et al. Association Between Use of Warfarin for Atrial Fibrillation and Outcomes Among Patients With End-Stage Renal Disease: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2020;3(4):e202175. doi:10.1001/jamanetworkopen.2020.2175

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Tecarfarin Phase 1 PK Trial in Stage 4 CKD Patients Provides Evidence that CKD Does Not Alter Tecarfarin Exposure While Warfarin Exposure is Increased

Summary Table

% change between Stage 4 CKD patients vs healthy subjects matched for each drug using a randomized crossover design (n=23)

	Tecarfarin (% change)	(S)-Warfarin (% change)
AUC	+15%	+44%
C_{max}	+6%	+7%
$t_{1/2}$	-8%	+19%

Result Highlights

Tecarfarin	Warfarin
Elimination from the body was not affected by severe kidney dysfunction	**Exposure increased 44% in Stage 4 CKD patients**
Half-life and the amount of drug in the body were similar in Stage 4 CKD patients and healthy subjects	**Plasma concentration and half-life increased in Stage 4 CKD patients**

Tecarfarin may lead to dosing that is more predictable than warfarin in CKD patients who require anticoagulation therapy

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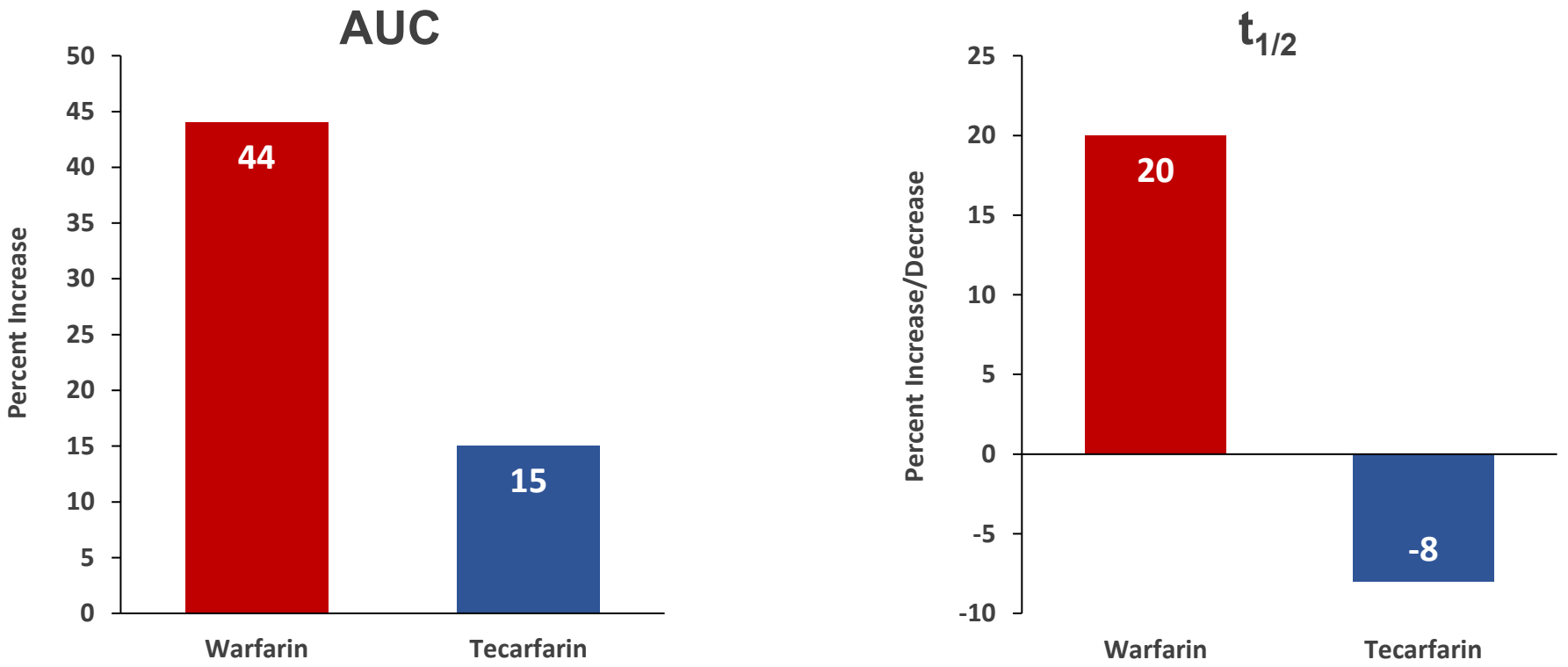
Kidney Failure Has a Significant Impact on Warfarin PK vs Tecarfarin

Tecarfarin metabolism not as impacted by kidney failure

Percent Increase in Exposure for Chronic Kidney Disease Subjects vs Healthy subjects for Warfarin and Tecarfarin (n =23)



Albrecht D, Turakhia MP, Ries D, et al. Pharmacokinetics of Tecarfarin and Warfarin in Patients with Severe Chronic Kidney Disease. *Thromb Haemost.* 2017;117(11):2026-2033. doi:10.1160/TH16-10-0815

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APS Patients Randomized to DOACs Have Increased Arterial Thrombosis Risk

TRIAL SITES

RAPS	UK	(N = 116)
TRAPS	Italy	(N = 120)
Ordi-Ros, et al.	Spain	(N = 190)
ASTRO-APS	US	(N = 48)

Patients with Thrombotic APS
N = 474

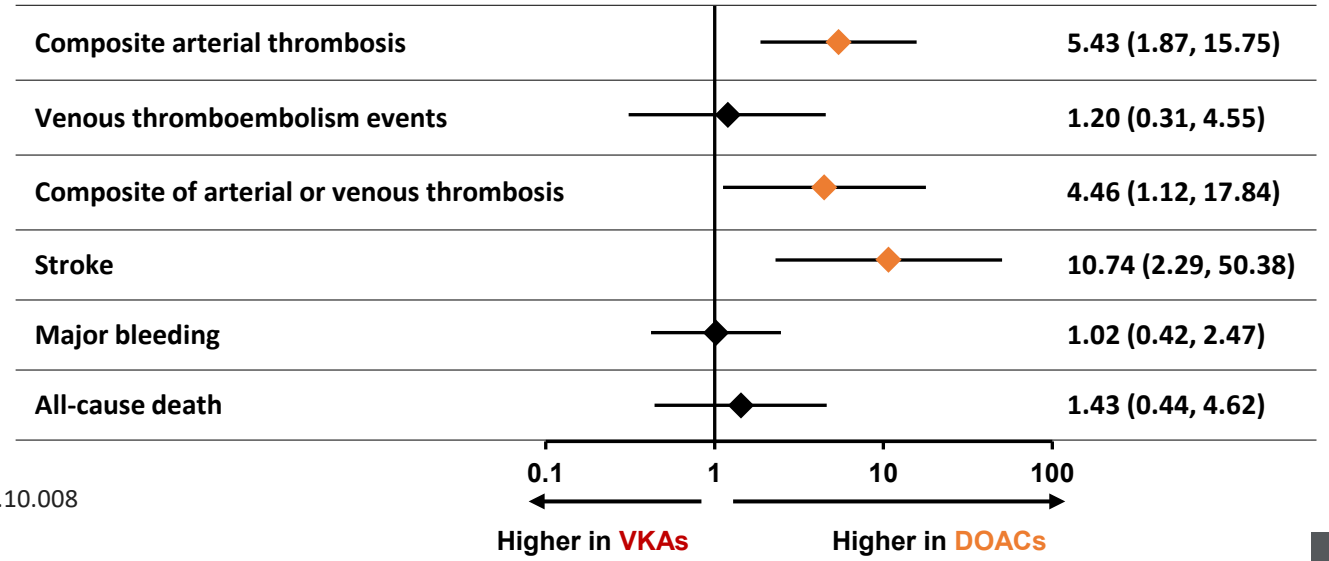
R

- Vitamin K Antagonists (VKAs)
- Direct Oral Anticoagulants (DOACs)

RESULTS

Use of DOACs compared with VKAs was associated with:

- Increased odds of arterial thrombotic events, especially stroke
- No change in the odds of VTE or major bleeding
- Results were consistent within subgroups

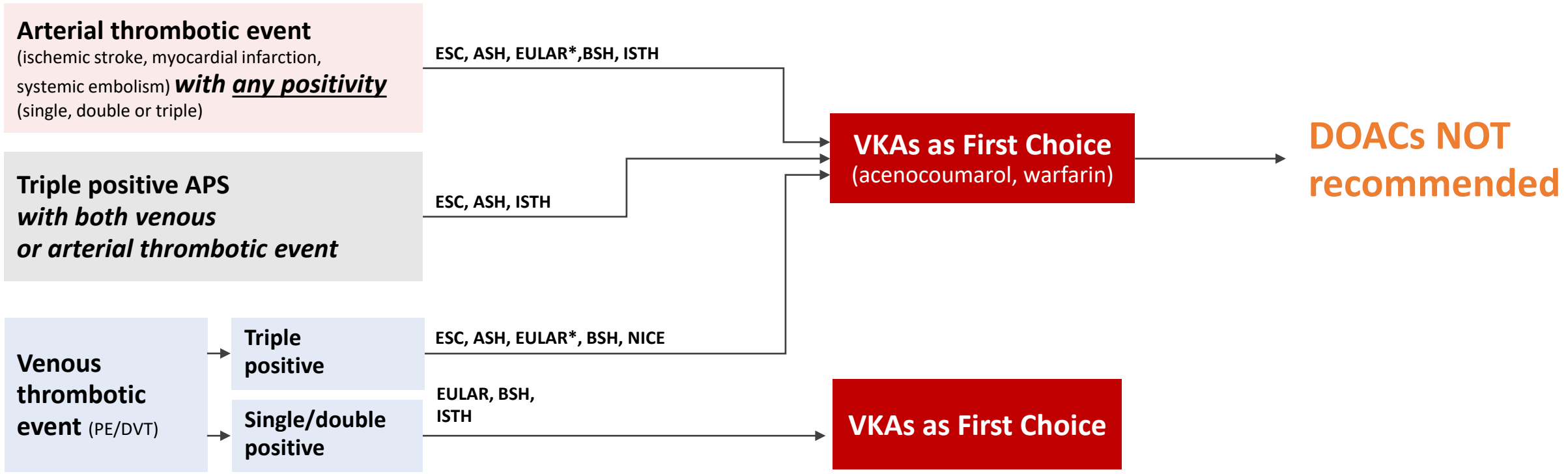


Khairani CD, Bejjani A, Piazza G, et al. *J Am Coll Cardiol*. 2023;81(1):16-30. doi:10.1016/j.jacc.2022.10.008

CARDINAL THERAPEUTICS

Summary of Guidelines Recommendations on Anticoagulant Treatment Prescription in Patients with Antiphospholipid Syndrome

PATIENTS WITH DEFINITE APS



* EULAR recommends to not use Rivaroxaban

ESC = European Society of Cardiology
ASH = American Society of Hematology
EULAR = European Alliance of Associations for Rheumatology
BSH = British Society for Haematology
ISH = International Society of Hematology

Pastori D et al. *Front. Cardiovasc. Med*. 2021. 8:715878. doi: 10.3389/fcvm.2021.715878

CARDIORENAL THERAPEUTICS

Eliquis 2023 Commercial

Eliquis highlights in its own commercial that you should not take for certain conditions.

"Don't take ELIQUIS if you have an artificial heart valve…"

ELIQUIS is not for patients who have antiphospholipid syndrome (APS).

Premium Pay for High Value Cardiovascular Orphan Drugs

Track record of recent transactions for orphan drugs in cardiovascular space

CAMZYOS → Bristol Myers Squibb™

Developed by MyoKardia and the company was subsequently acquired by BMS for $13 billion

FDA DESIGNATIONS	**Orphan Drug, Priority Review**
EXPEDITED APPROVAL	Based on a 251-patient study called EXPLORER, in which patients randomized to take the drug had significantly better peak oxygen consumption and improved on a widely used measurement of heart failure when compared to those who got a placebo.
PRICE	$89,500 a year ($245/day) – *one of the most expensive CV drugs*
NOTABLY	The approval came with a warning for the risk of heart failure and an FDA-mandated plan to manage that risk.

FoldRx → Pfizer

Developed by FoldRx with $88 million in private financing, before FoldRx was subsequently acquired by Pfizer

FDA DESIGNATIONS	**Orphan Drug, Fast Track, Priority Review & Breakthrough Therapy**
EXPEDITED APPROVAL	Based on ATTR-ACT trial (Transthyretin Amyloidosis Cardiomyopathy Clinical Trial) - randomized 441 patients to tafamidis or placebo for 30 months
PRICE	$225,000 a year ($616/day) - *the most expensive CV drug*
YEAR 2 SALES FOLLOWING LAUNCH	$1.3 billion collectively for Vyndaqel® and Vyndamax®