CADRENAL THERAPEUTICS™

Cadrenal Therapeutics, Inc.

NASDAQ: CVKD

September 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 and our Quarterly Reports for the quarters ended March 31, 2024 and June 30, 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 Biopharma Developing a New Anticoagulant to Improve Care for Underserved Warfarin-dependent Patients

Our Phase 3-ready drug candidate, tecarfarin, is a new vitamin K antagonist (VKA) anticoagulant expected to be superior and safer than warfarin

Striving to overcome the many challenges of warfarin and result in improved outcomes and fewer major events such as heart attacks, strokes, bleeds and deaths and lower cost of care by avoiding costly hospitalizations

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Three Top Potential Indications of Tecarfarin

Two Orphan Drug and One Fast Track Designations

Focused on patients with implanted cardiac devices or
rare cardiovascular (CV) conditions that require chronic anticoagulation

Left Ventricular Assist Devices (LVAD) for advanced heart failure patients

FDA Orphan Drug Designation (ODD)

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

FDA Orphan Drug Designation + Fast Track

Mechanical Heart Valve (MHV) patients with difficult-to-control TTR* or genetic resistance to warfarin

*Time in therapeutic range (TTR) as measured by the international normalized ratio (INR)

Key Investment Highlights for Cadrenal Opportunity

1 Large Market of Underserved Patients	NO anticoagulation drugs are indicated for those with LVADs or many rare CV conditions requiring chronic anticoagulation
2 Data Shows Safety and Efficacy Superiority to Warfarin	Extensive safety data from 11 clinical trials demonstrates fewer major events such as strokes, heart attacks, bleeding and death
3 Opportunistic Strategy & Bus Dev Potential	Pursuing fastest path to market and partnerships for pivotal clinical trials, including collaboration with LVAD maker Abbott
4 Accelerated Regulatory Path	Tecarfarin was granted ODD by FDA for LVADs and ESKD + AFib; intend to pursue ODD for MHV subset
5 Strong Projected Adoption & Pricing	Costly warfarin complications should drive premium tecarfarin orphan pricing and rapid market adoption

Experienced management team with a late-stage drug candidate

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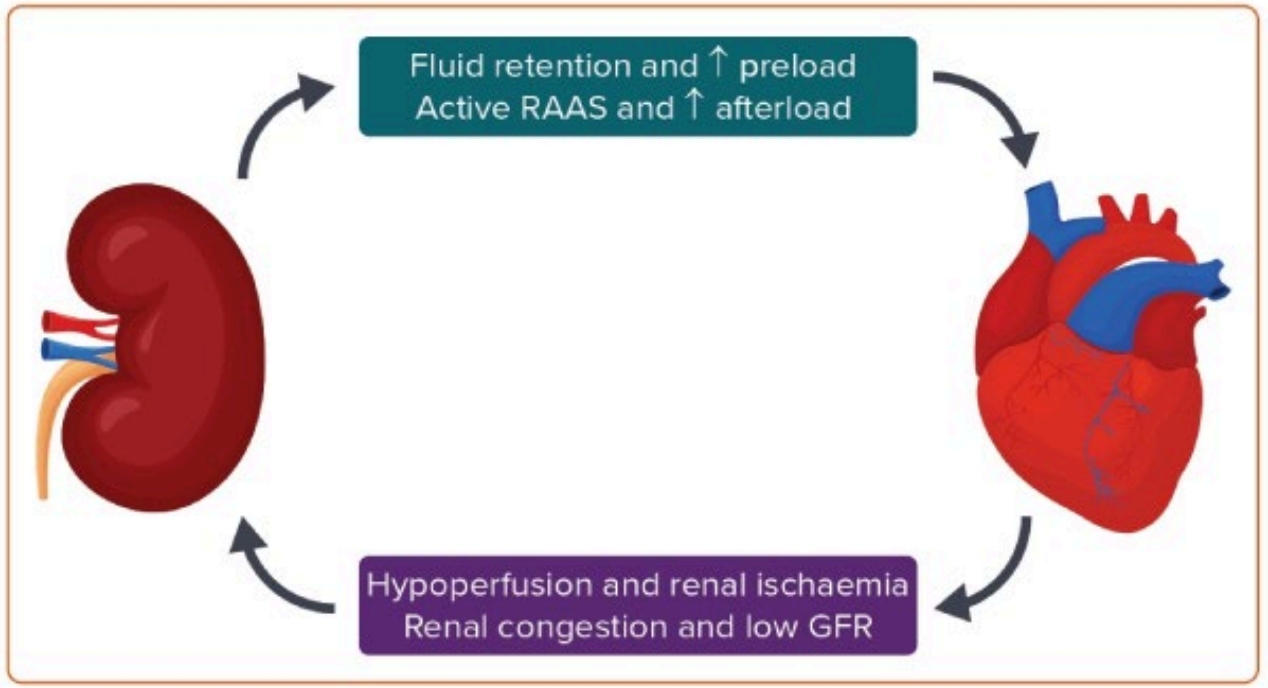
Gaps in Modern Heart Failure and Chronic Kidney Disease Research

Interdependence of the Heart and Kidney in Chronic Kidney Disease (CKD) and Heart Failure (HF)



GFR = glomerular filtration rate; RAAS = renin–angiotensin–aldosterone system.

49% of HF patients also have CKD, and an estimated 17–21% of CKD patients develop de novo HF[1]

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[1]Damman K, Valente MAE, Voors AA, et al. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. *Eur Heart J* 2014;35:455–69.

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 • Finalizing Trial Protocol • Developing EMA Orphan Drug Application
	End-stage Kidney Disease with AFib	• FDA Orphan Drug Designation Granted • FDA Fast Track Designation Granted • Developing EMA Orphan Drug Application
	Mechanical Heart Valve (MHV) patients with difficult-to-control TTR or genetic resistance to warfarin	• Developing FDA and EMA Orphan Drug Applications

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

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A Review of Tecarfarin

Tecarfarin is the ONLY anticoagulant in development for patients with LVADs

HOW TECARFARIN COMPARES

- Tecarfarin is metabolized via a different pathway than warfarin, thus its efficacy is not affected by drug-drug interactions or kidney impairment, which are common in these patients
- Based on data from Phase 2/3 trials, tecarfarin performed better than warfarin and provided more stable anticoagulation with a higher TTR, fewer major events
- Extensive safety data (n=1000)
- Potential solution for patients with genetic variants, estimated at 18 percent of all CV patients*
- Direct Oral Anticoagulants (DOACs) such as Eliquis not indicated for LVADs and many rare CV conditions, provide little or negative data with these patients
- Being championed by LVAD and ESKD KOLs and clinicians

*Source: https://www.nature.com/articles/jhg201073

The Problem: Patients with Implanted Cardiac Devices and Rare CV Conditions Lack Effective Anticoagulation

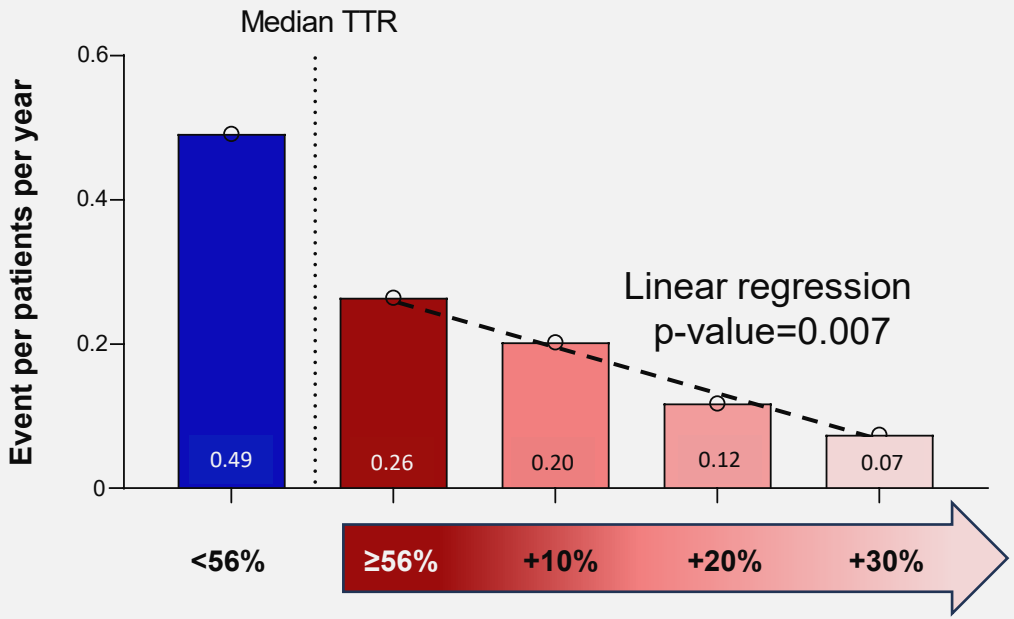
Both warfarin and DOACs are not FDA-approved for patients with LVADs or many rare CV conditions

SIGNIFICANT **ISSUES** WITH ONLY CHOICES FOR THESE PATIENTS

	Warfarin	DOACs (Pradaxa, Xarelto, Eliquis & Savaysa)
LVAD 	⛔ High frequency of bleeding events, with LVAD patients being hospitalized more than twice on average within six months of implant* ⛔ Unstable metabolism due to drug-drug interactions, genetic variability of pathway ⛔ Late-stage heart failure and kidney dysfunction are often seen in conjunction. Chronic kidney disease (CKD) inhibits the metabolism of warfarin.	⛔ Cost and time of reversal compared to VKA is not acceptable for patients at high risk of bleeding or intervention ⛔ LVAD patients were excluded from all approval studies, leaving void or negative data from earlier clinical trials ⛔ DOACs not approved for or in guidelines for LVAD patients *Source: Annals of Trans Medicine Antiplatelet and anticoagulation strategies for left ventricular assist devices - PubMed (nih.gov)
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 approved or included in ESKD treatment guidelines ⛔ Ambiguity in dosing recommendations

ARIES-HM3 Study (Sponsored by Abbott) Documents the Impact of Poor Anticoagulation Quality of Adverse Events in LVAD patients

- **Rate of severe bleeding significantly increased when TTR falls below 56%**
- **Mean TTR in LVAD patients treated with warfarin is <50% (Martinez et al 2018)**



Events are Hemocompatibility Related Adverse Events (HRAE) = Any Stroke, Pump Thrombosis, Major Bleeding, and Arterial Peripheral Thromboembolism

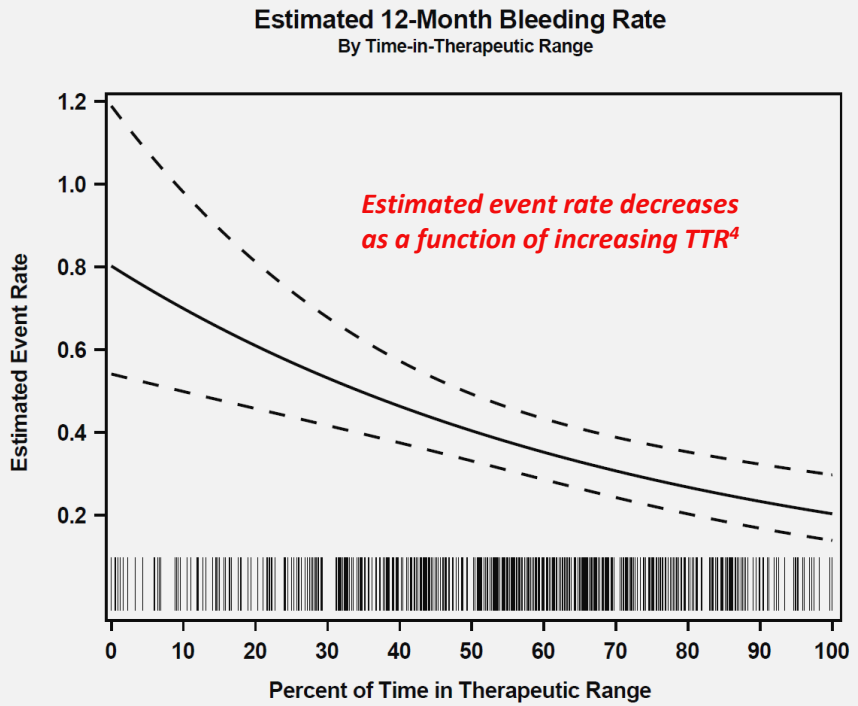
Source: Mehra et al; Impact Of Vitamin K Antagonist Therapy On Outcomes In a Randomized Controlled Trial of Aspirin Removal In Left Ventricular Assist Device Patients - A Pre-specified Analysis From the ARIES-HM3 Trial; Presented April 2024 at the ISHLT Annual Meeting

Bleeding Rate in LVAD Patients is a Major Problem

Poor quality anticoagulation, manifest as sub-target TTR, is the cause

Recent clinical evidence from the ARIES-HM3 (Abbott) study documents the consequences of suboptimal anticoagulation with warfarin in LVAD patients

- **Time in Therapeutic Range (TTR)[1,2]**
  - Well-established marker used to evaluate anticoagulation quality (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**
  - Quality of VKA management as measured by TTR correlates strongly with the occurrence of non-surgical bleeding risk in patients with the HM3 LVAD3
  - TTR measurements correlate linearly with bleeding risk (Linear regression p-value=0.007)[3]



1) White et al. 2007; 2) Currie et al. 2006; 3) Jones et al. 2005
2) TTR quantifies the percentage of time a patient is at the desired level of anticoagulation

3) Mehra et al; Impact Of Vitamin K Antagonist Therapy On Outcomes In a Randomized Controlled Trial of Aspirin Removal In Left Ventricular Assist Device Patients - A Pre-specified Analysis From the ARIES-HM3 Trial; Presented April 2024 at the ISHLT Annual Meeting

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Phase 2/3 Trial Shows Tecarfarin results in improved TTR, with Fewer Thrombotic and Hemorrhagic Events[1]

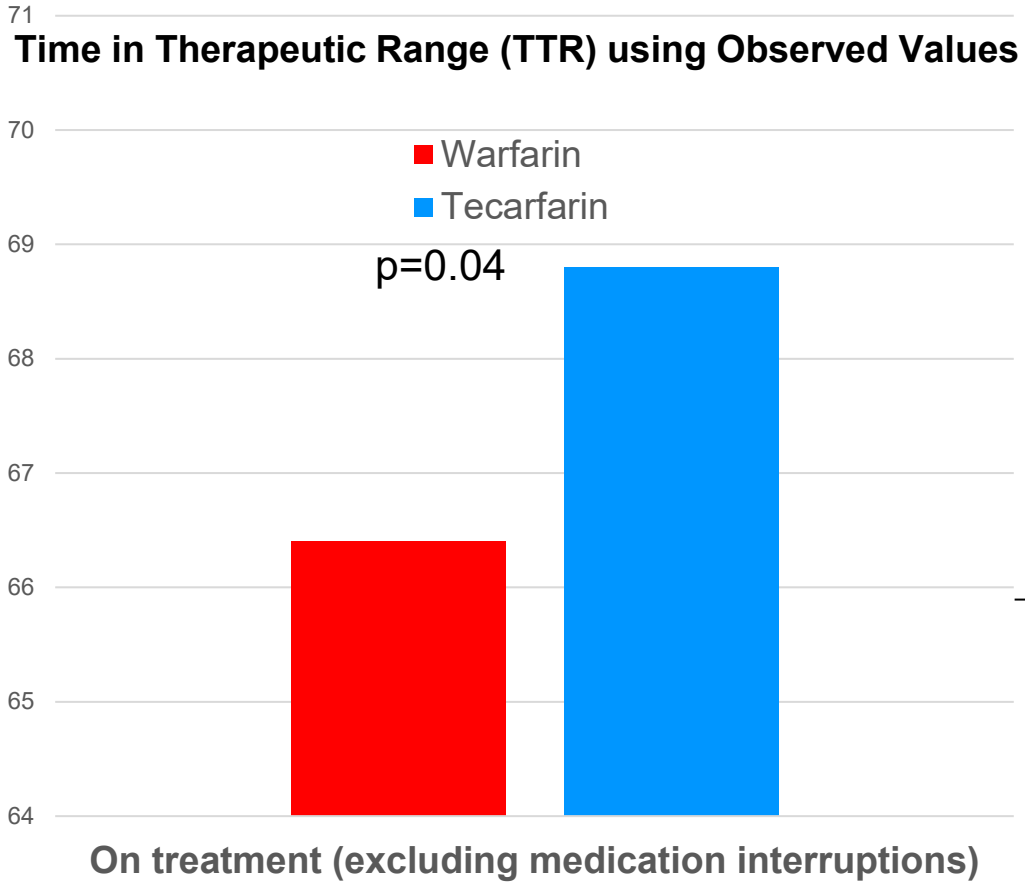
Tecarfarin had fewer thrombotic events compared to warfarin

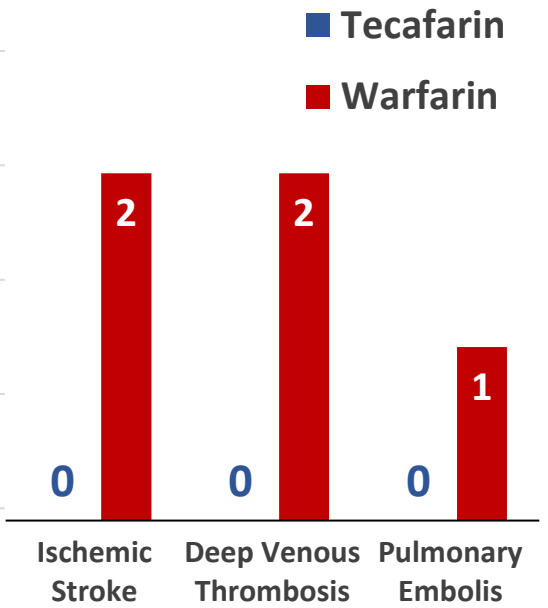
Randomized, double-blind clinical trial

N=607
Patients with indications for chronic anticoagulation

Tecarfarin (n = 304)

Warfarin (n = 303)



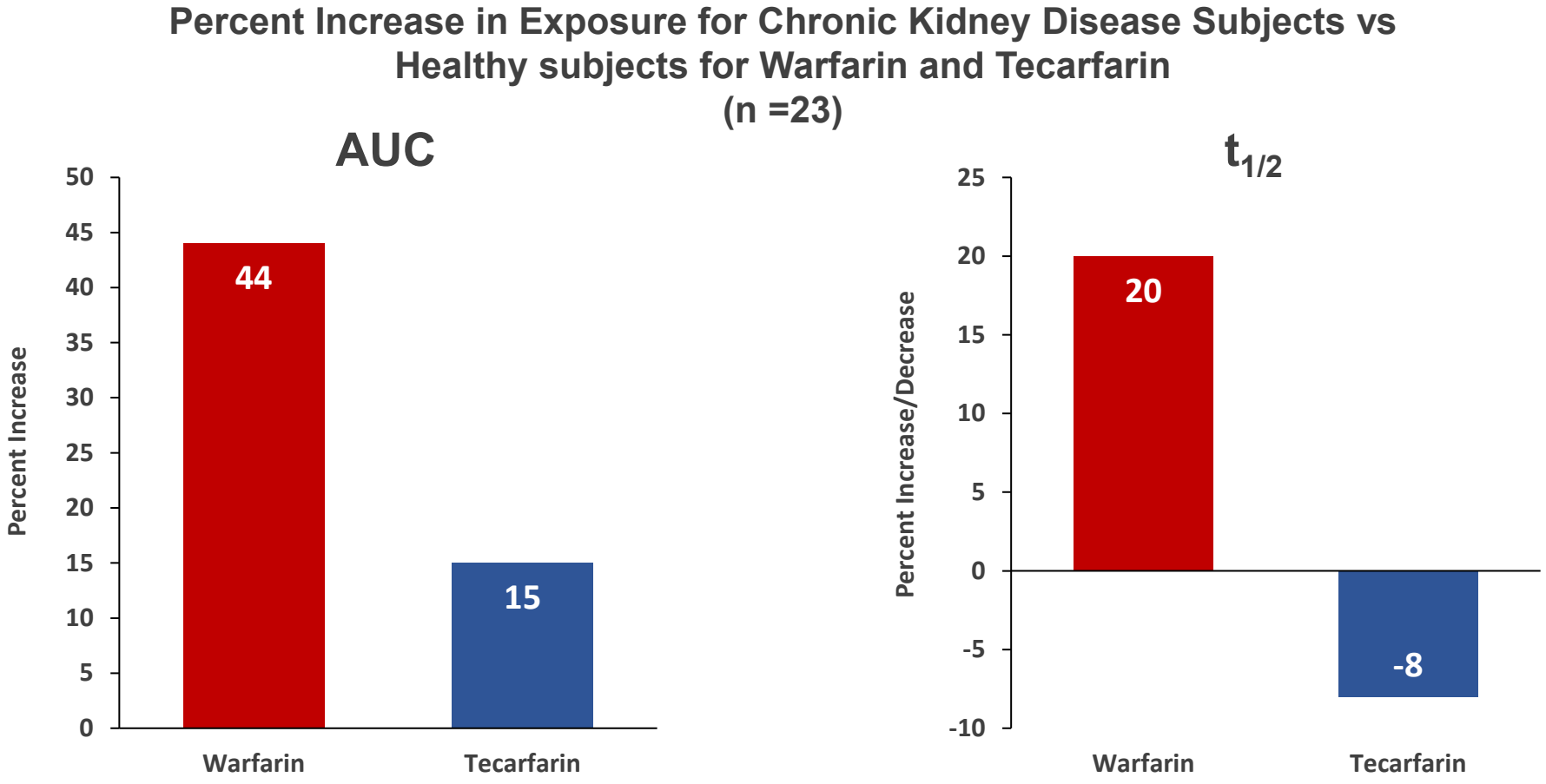


Tecarfarin-treated subjects experienced numerically <u>fewer</u> major hemorrhages than the warfarin-treated patients and had numerically fewer thrombotic events

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

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

Tecarfarin metabolism not as impacted by kidney failure



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

The Solution: Tecarfarin Aims to Solve Warfarin's Major Problems and Be the Superior, Safer Choice

Warfarin: High risk for bleeding and other major events

Significant variability with frequent dosing adjustments

MAJOR PROBLEM
for implanted CV devices or rare CV patients

Challenging to control

Drug-drug interactions

Variable PK profile due to genetic variants and interference from other drugs

SOLUTION: Tecarfarin

designed to **solve warfarin challenges**

DECREASING MAJOR EVENTS SUCH AS STROKE & BLEEDING

Metabolized via an alternate pathway to avoid effects of common drug interactions

Reliable, stable PK profile. Tecarfarin is not impacted by kidney impairment.

STABLE ANTICOAGULATION
with longer TTR
and extensive safety data

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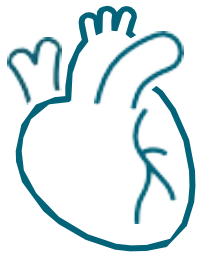
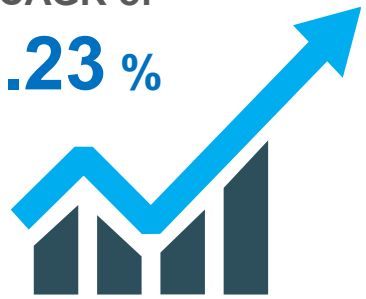
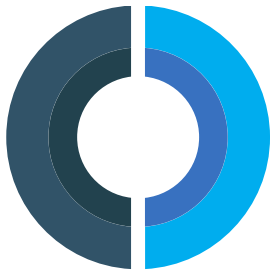
LVADs are a Double-digit Growth Market



LVAD Market by Application and Geography – Forecast and Analysis 2021-2025

Market growth will
ACCELERATE
at a CAGR of
12.23 %





46%
of the growth will originate from
North America

Source: [LVADS Market Size, Share, Growth, Trends Industry Analysis Forecast 2025 Technavio]

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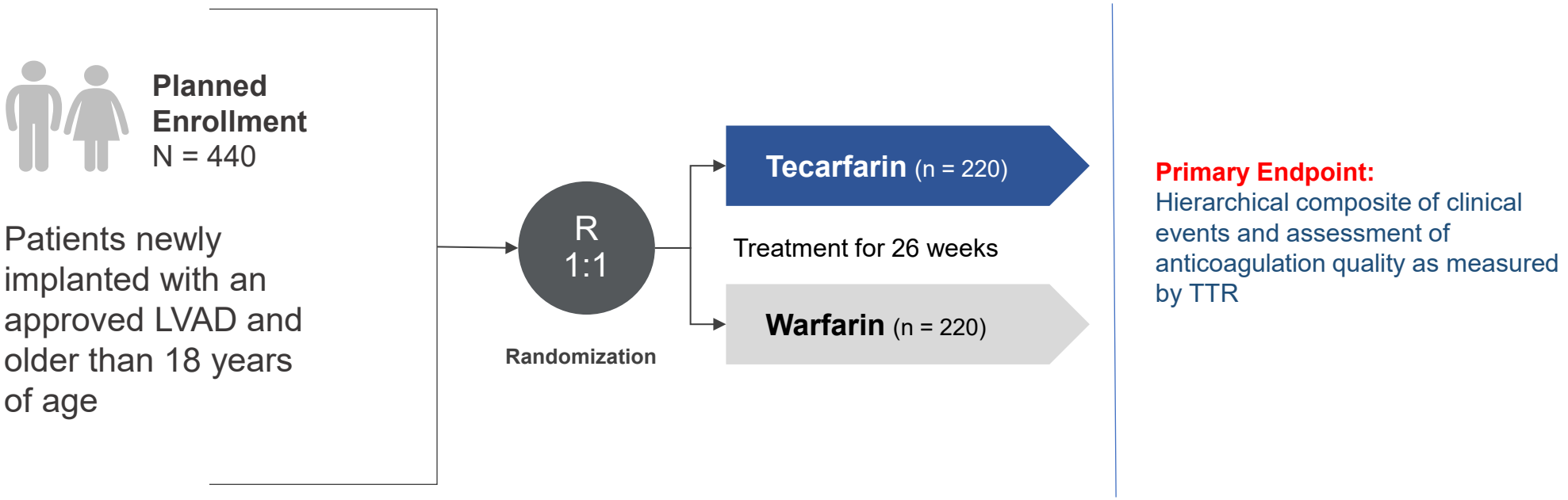
Proposed Tecarfarin Pivotal Trial Design for LVAD Patients

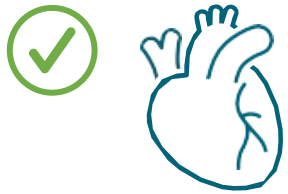
Tecarfarin Anticoagulation and Hemocompatibility in LVAD Patients

A randomized, blinded, phase 3, multicenter study to evaluate the efficacy and safety of tecarfarin compared to warfarin in patients with an approved left-ventricular assist device (LVAD)



Attractive Addressable Market Opportunities

US market potential estimated @ $2 billion+ for three targeted implanted CV device and rare CV conditions



Left Ventricular Assist Devices

+

End-stage Kidney Disease with AFib

+

Mechanical Heart Valves with Difficult-to-control TTR

Approximately

>$2 Billion

Combined Peak Annual Market Potential*

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

Financial Summary

Cap Table (reflects August '24 reverse split)

Cash (at 6/30/2024)	$5.0 million
Debt	NONE
Common Shares Outstanding	1,182,225
Warrants – Investors (avg. $26.25)	285,714
Warrants - Underwriter & Place Agt. Warrants (avg. $40.20)	25,938
Stock Options Outstanding (avg. $13.20)	156,333

2024 Financial Results – 6 Months ended June 30th

Operating Expenses (excluding non-cash items)	$3.9 million
Cash used in operating activities	$3.4 million

Market Capitalization

As of 9/24/24	$14 million

Insider Ownership (Common Stock)

Insider Ownership as Percent of Shares Outstanding	42%

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Leadership Team: Clinical to Commercial Expertise

Quang Pham

CEO & Founder, Chairman

espero BIOPHARMA

D+R LATHIAN HEALTHCARE MULTICHANNEL MARKETING

Genentech

Douglas Losordo, MD

Chief Medical Officer

NYU Langone MEDICAL CENTER

KBP BIOSCIENCES

caladrius BIOSCIENCES

Northwestern University

LONGEVERON

Matthew Szot, CPA

Chief Financial Officer

S&W SEED COMPANY

KPMG

RIPCURL

SENESTECH

INVO bioscience

Jeff Cole

Chief Operating Officer

espero BIOPHARMA

VALEANT Pharmaceuticals International

Solco Healthcare U.S.

MarcasUSA

John R. Murphy

Board Member

O'Reilly AUTO PARTS

SUMMIT Materials

APRIA

Steven Zelenkofske, DO

Board Member

AstraZeneca

sanofi aventis

NOVARTIS

Boston Scientific

ACHILLION

SwanBio THERAPEUTICS

RegadoBiosciences

Glynn Wilson, PhD

Board Member

JUPITER WELLNESS

SB SmithKline Beecham

TAPIMMUNE

Robert Lisicki

Board Member

ARENA PHARMACEUTICALS

InCarda4 THERAPEUTICS

REGENERON

Daiichi-Sankyo

AMGEN

Scientific Advisors with Deep Experience in CV and Beyond

Mandeep, Mehra MD, MSc, FRCP

Medical Director of the
Brigham Heart and Vascular Center,

William Harvey Distinguished Chair in Advanced Cardiovascular Medicine

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,
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Boston University School of Medicine

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

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Professor of Medicine,
Baylor University

Director,
Selzman Institute for Kidney Health

C. Michael Gibson, MD

Professor of Medicine,
Harvard Medical School

Interventional Cardiologist,
Beth Israel Deaconess Medical Center

President & CEO,
Baim Institute for Clinical Research

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

Why Cadrenal Now?

CLEAR FROM RECENT DATA that tecarfarin has attractive, defined opportunity in patients where warfarin CHALLENGES ARE HUGE BURDEN and DOACs, with little or negative relevant data, are not the solution

Phase 3-ready Candidate

Tecarfarin is advancing toward pivotal trials in patients with implanted CV devices or rare CV conditions. KOLs express need and support for a new VKA that is superior, safer and saves the healthcare system hospitalization costs.

Data Shows Superior Efficacy and Safety

Phase 1 and 2/3 clinical data shows that tecarfarin is an effective, stable and safe anticoagulant and expected to be superior to warfarin in these underserved patients.

Bus Dev Progress and Opportunistic Approach

Pursuing business development strategies to help fund pivotal clinical trials; Multiple potential indications provides optionality.

Orphan 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.

Attractive Market with Orphan Drug Pricing

Drugs for rare CV conditions that save money and lives command price premiums that value the tecarfarin addressable market @ $2B+; Experienced team to deliver results.

Contact Us

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CFO
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APPENDIX

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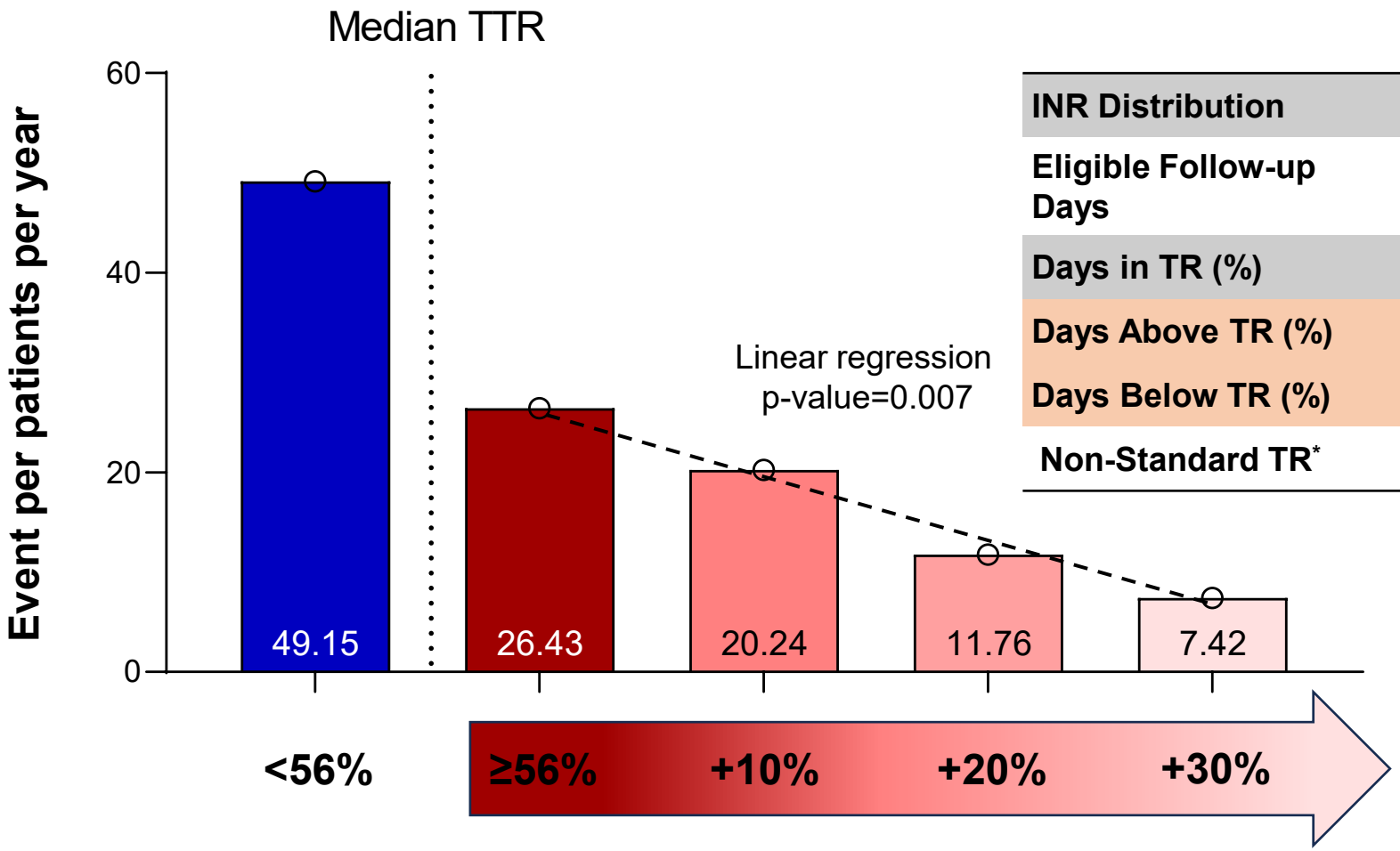
Bleeding Rate by TTR Increments

Incremental improvement of 10% above the median of 56% trends in a significant reduction in bleeding rate



	Placebo Median (Q1, Q3)	Aspirin Median (Q1, Q3)	P-value
INR Distribution	2.3 (2.1, 2.4)	2.3 (2.0, 2.5)	0.8227
Eligible Follow-up Days	344.0 (247.0, 364.0)	336.0 (213.0, 365.0)	0.4620
Days in TR (%)	55.8 (41.2, 73.9)	57.3 (38.3, 68.0)	0.4127
Days Above TR (%)	8.4 (0.8, 17.4)	9.5 (2.2, 19.3)	0.2206
Days Below TR (%)	26.2 (13.2, 44.5)	27.4 (14.4, 47.6)	0.3653
Non-Standard TR*	14.4% (40/277)	16.6% (46/277)	0.5576

*TR=Therapeutic Range (INR from 2 to 3)

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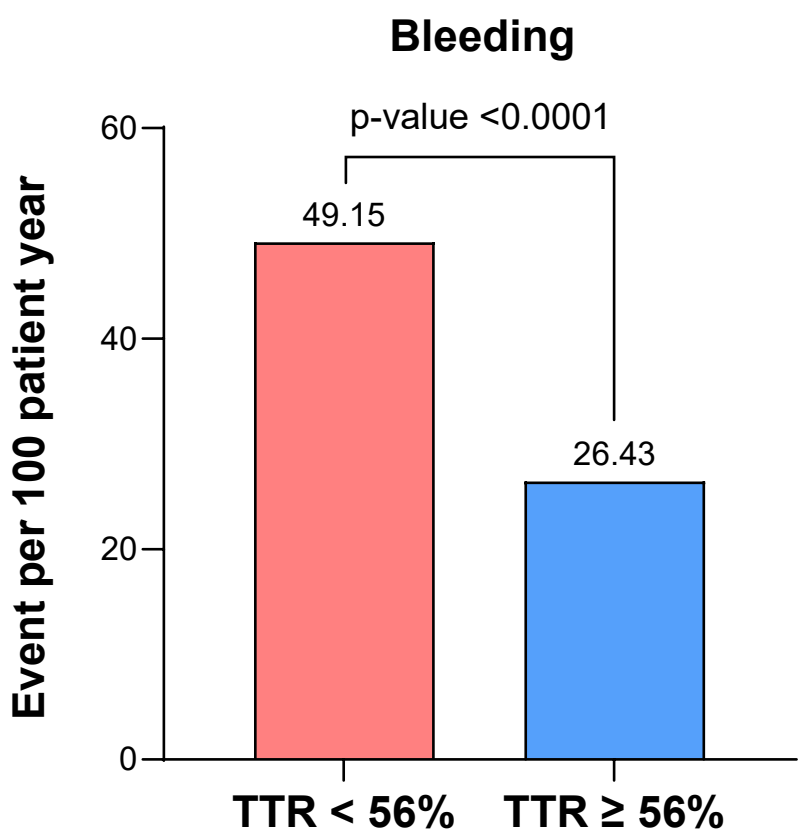
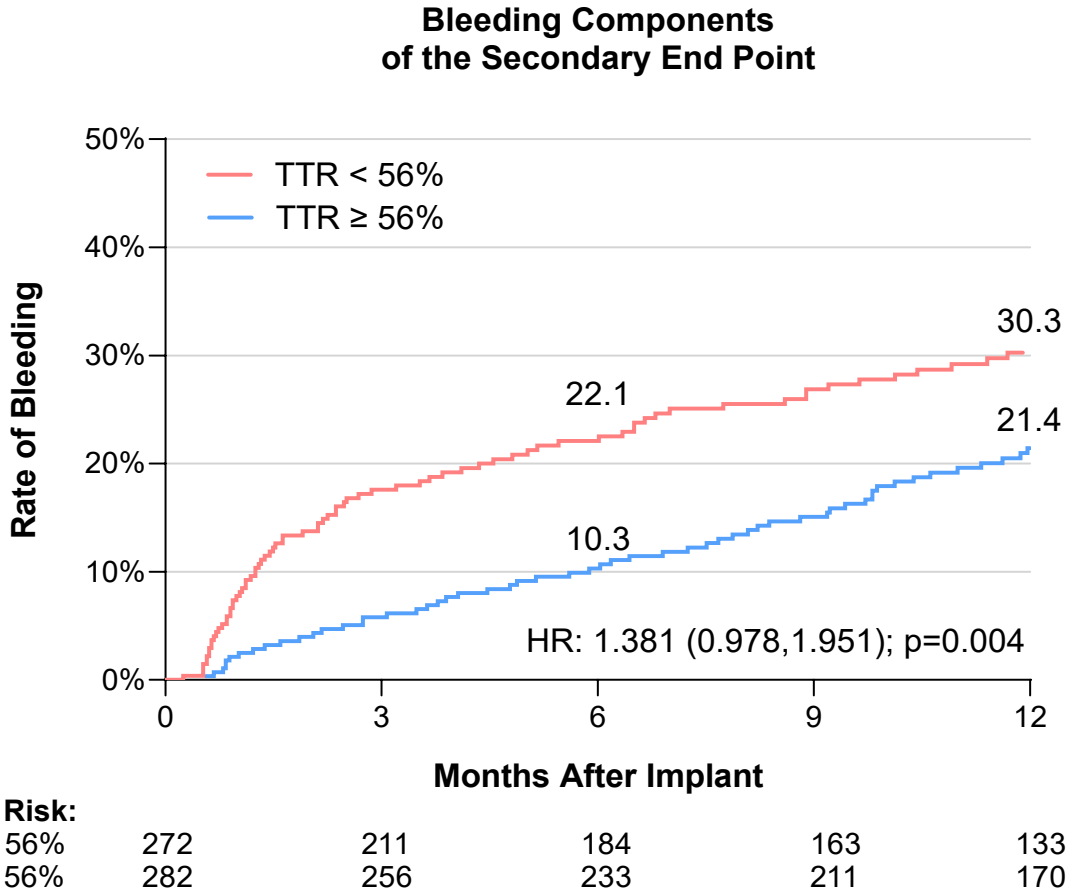
Connors/Netuka/Mehra. ARIES VKA Analysis *(ISHLT Thursday April 11, 2024)*

The Impact of TTR on Bleeding in ARIES-HM3





No. at Risk:

TTR < 56%	272	211	184	163	133
TTR ≥ 56%	282	256	233	211	170

Analysis from ARIES-HM3 presented at ISHLT 2024 (Mehra et al)

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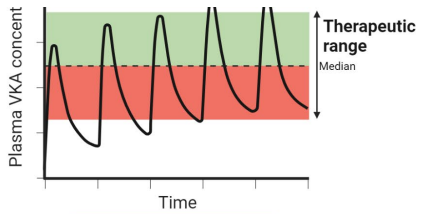
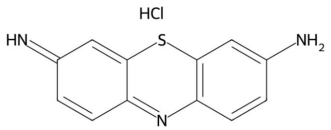
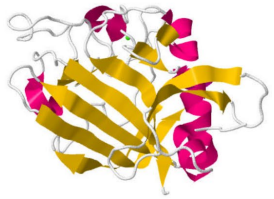
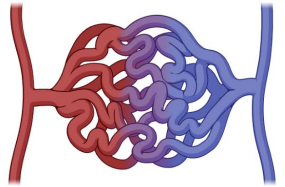
Strategies to Mitigate Bleeding Complications with HM3 LVAD

A Bleeding Paradox?









TTR Below Median → ↑ Thrombin Generation → ↑ Angiogenic factors (Angiopoietin-2) → AVM-related mucosal bleeding

Residual Bleeding Risk

- 30% at 2-years even after Aspirin elimination
- Related closely to a lower TTR for VKA

POTENTIAL MITIGATION STRATEGIES

Improve TTR
- Resource-intensive VKA management
- Novel VKA without interactions (Tecarfarin)

Switch VKA to DOAC
- Requires conclusive safety studies
- Concern with bridge to heart transplant

Lower Target INR with VKA
- Requires conclusive studies
- Practically limited
- Uncertain effect on thrombin

VKA, Vitamin K Antagonist; HM 3, HeartMate 3; DOAC, Direct Oral Anticoagulant; INR, International Normalized Ratio; TTR, Time in Therapeutic Range; AVM, Arteriovenous Malformation.

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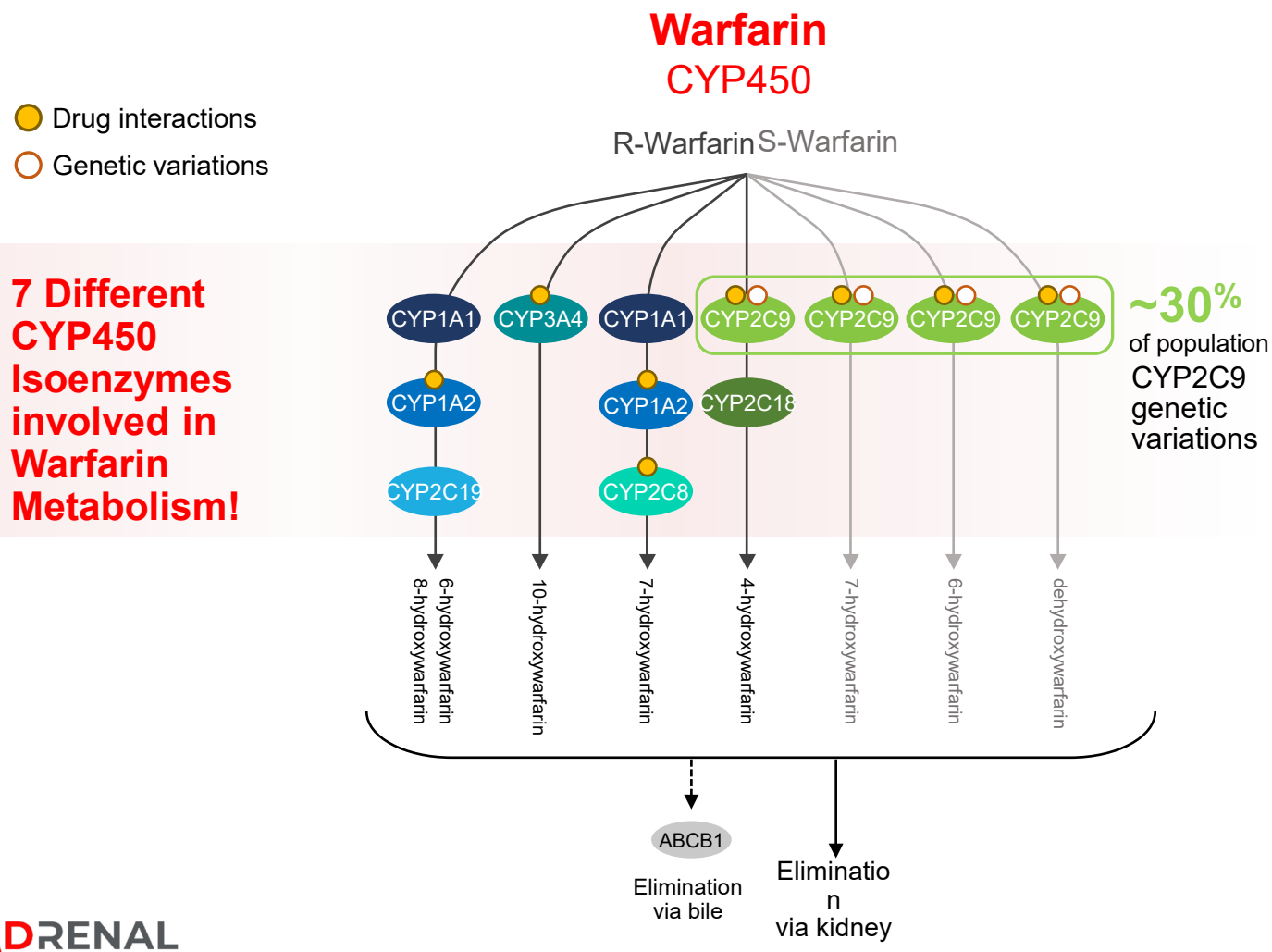
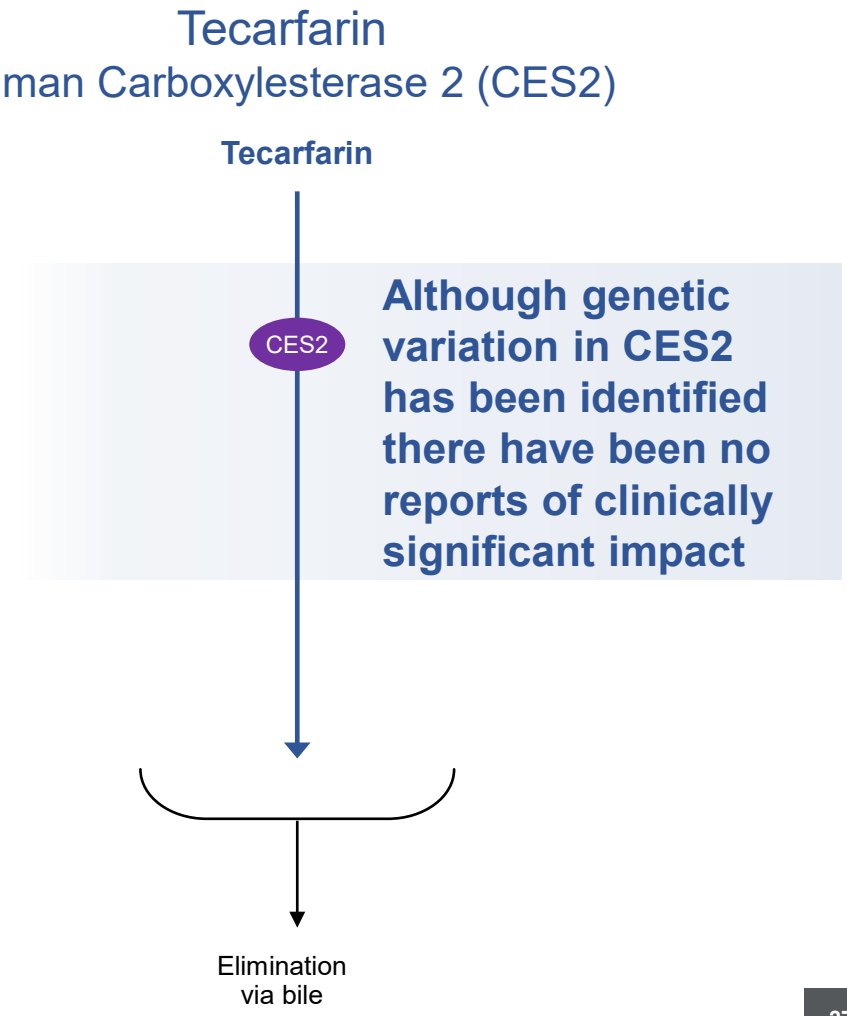
Cikes M, Yuzefpolskaya M, Gustafsson F, Mehra MR. *J Card Fail*. 2024; S1071-9164(24)00318-X.

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.

7 Different CYP450 Isoenzymes involved in Warfarin Metabolism!





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

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

Antiplatelet/Anticoagulants
- Acetylsalicylic acid
- Prasugrel
- Dabigatran etexilate

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

Antivitral agents
- Tenofovir disoproxil
- Adefovir dipivoxil
- Valacyclovir

CNS agents
- Cocaine
- Heroin
- 6-monoacetylmorphine

Immunosuppressive agents
- Methylprednisolone sodium succinate
- Deflazacort

Oncology agents
- Irinotecan
- Capecitabine

Anesthetic drug
- Procaine

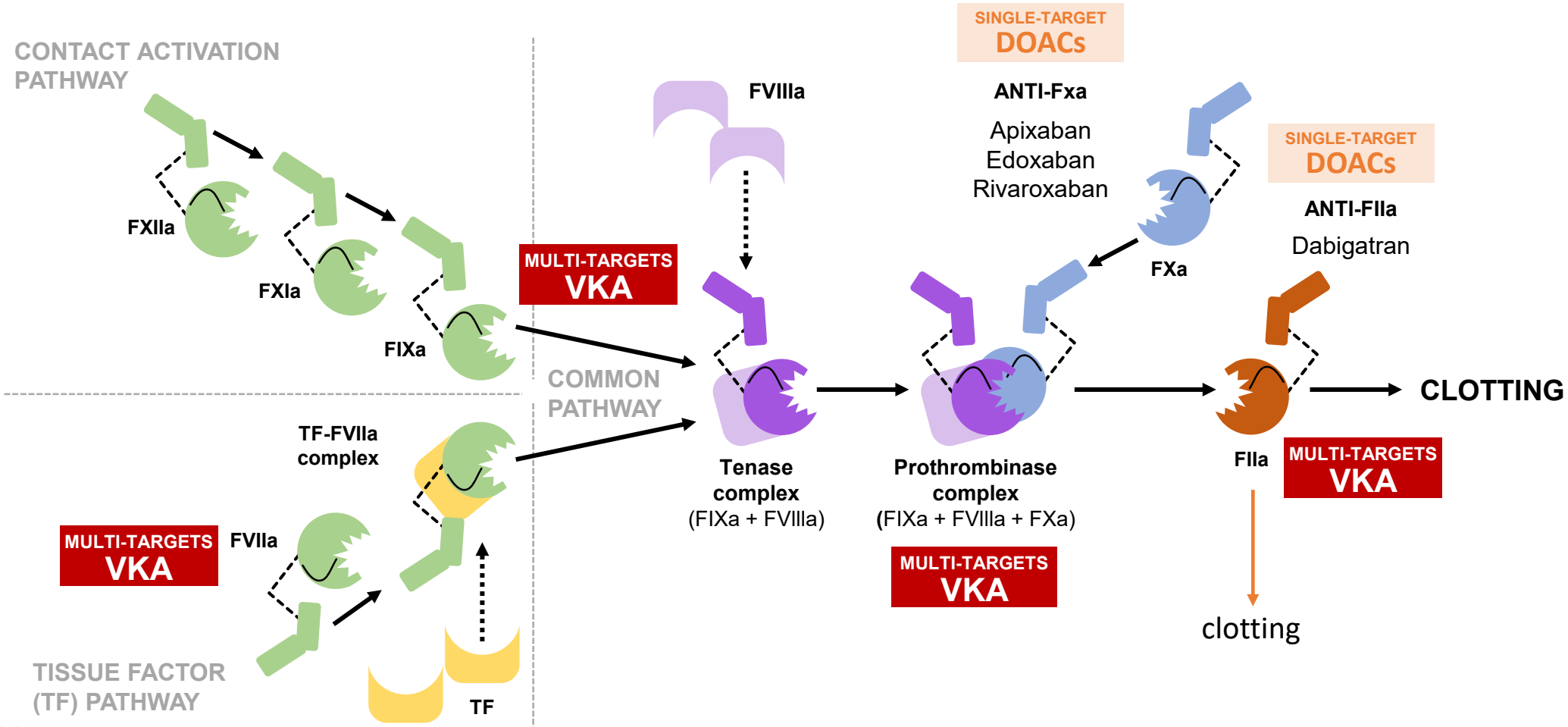
Limited Substrates Identified

Genetic variation exists, but limited evidence of clinical impact

CADRENAL THERAPEUTICS

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

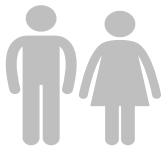
Proven mechanism of action resulting in clinically meaningful anticoagulation in certain conditions where DOACs have failed



CADRENAL THERAPEUTICS

Tecarfarin Phase 3 Trial Design for ESKD and AFib

Tecarfarin vs. Placebo in Patients with ESKD and AFib
Randomized, Double-Blind, Placebo-Controlled



Planned Enrollment
N = 492

ESKD (eGFR < 15 mL/min/1.73 mm^2)
documented chronic paroxysmal, persistent or permanent AFib

Trial Sites:
U.S. and Canada, ROW TBD

R
1:1

Randomization stratified according to VKORC1 status

Tecarfarin (n = 246)

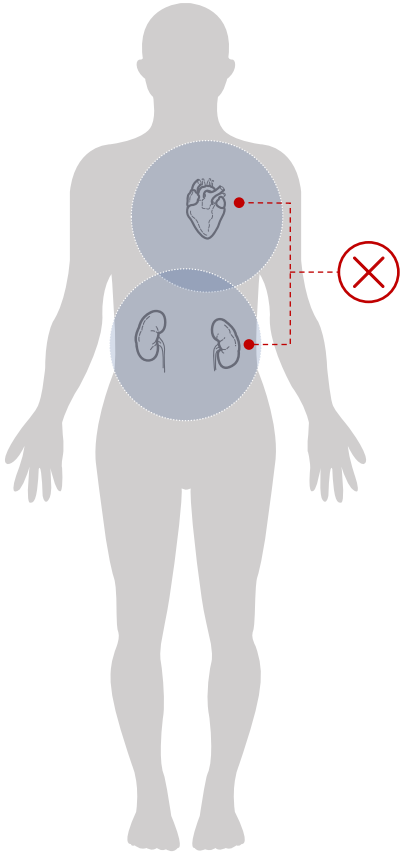
Placebo (n = 246)

12-month follow-up
for Primary Endpoint of time to combined endpoint of ischemic stroke or systemic embolism (80% power to detect a 25% treatment benefit)

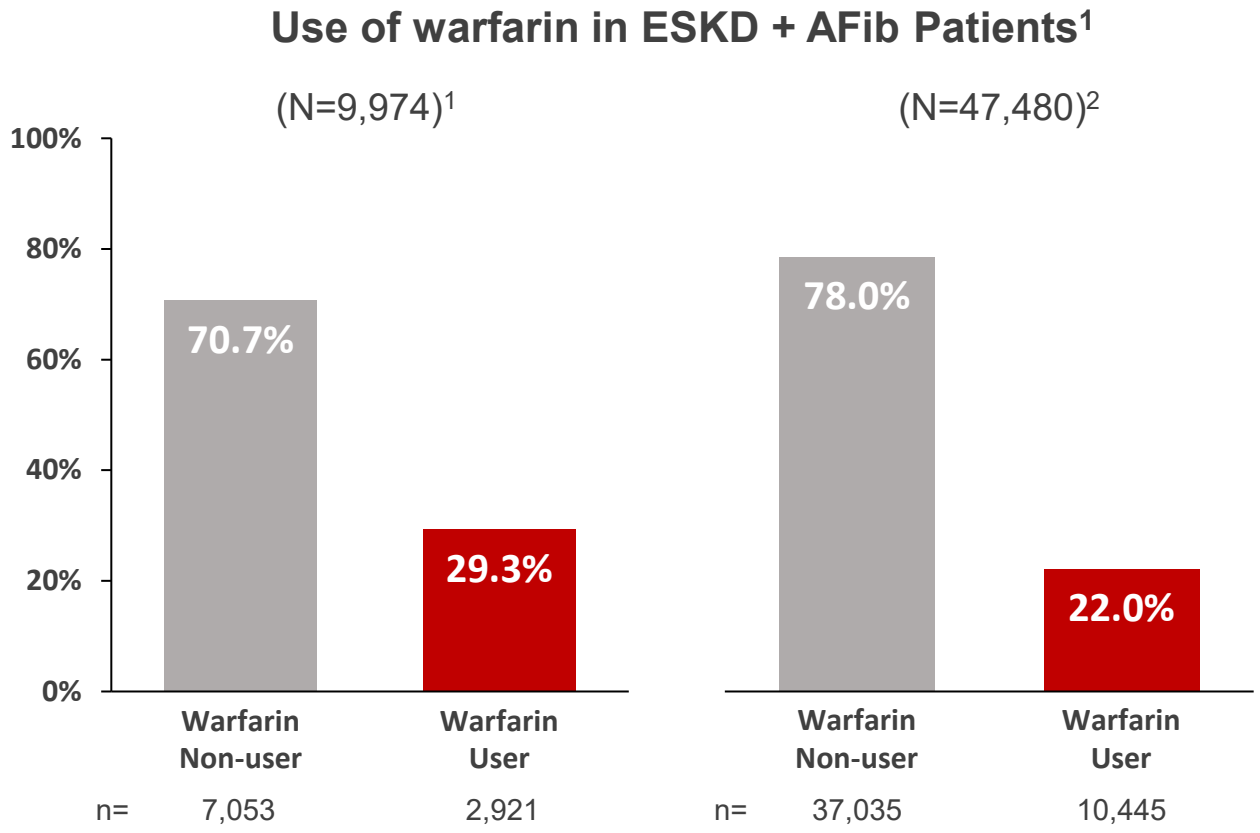
CADRENAL THERAPEUTICS

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

CARDIORENAL THERAPEUTICS

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 quality of 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]

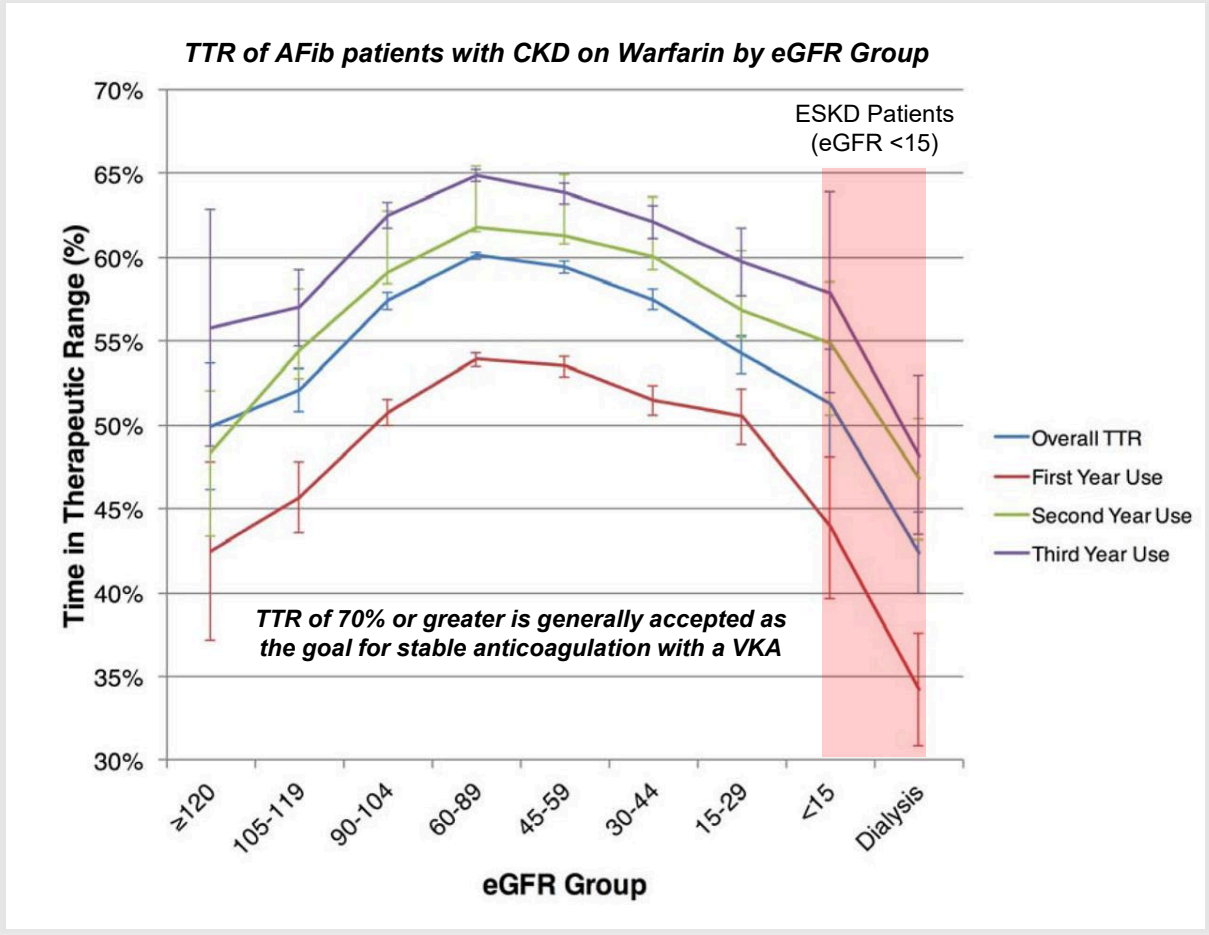


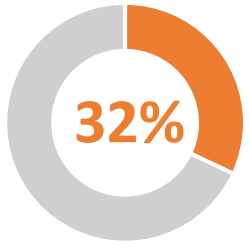
Figure 2. Warfarin Utilization and Anticoagulation Control in Patients with Atrial Fibrillation and Chronic Kidney Disease[6]

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)

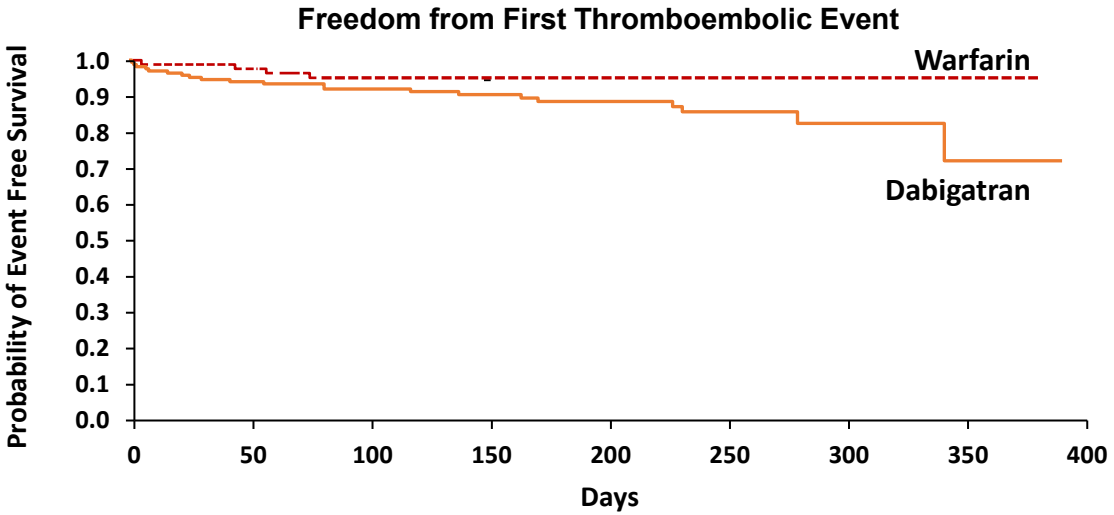
Dabigatran Versus Warfarin in Patients with Mechanical Heart Valves
EXCESS RISK AND NO BENEFIT

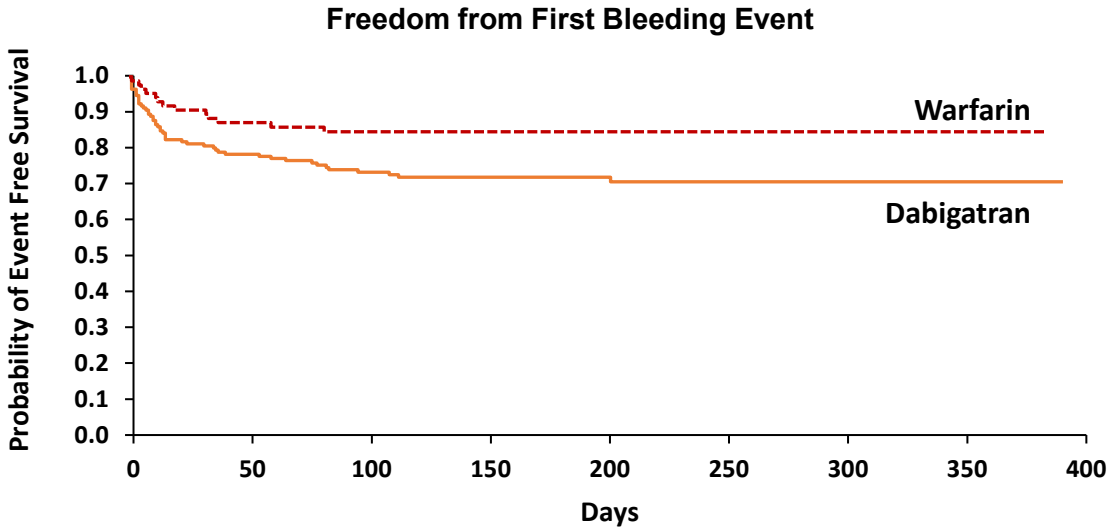
Trial terminated prematurely
due to an excess of thromboembolic and bleeding events among patients in the **dabigatran group**

	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