

# NOACs vs VKA trials in AF: Noninferiority

A New Era:

Understanding Trials of Anticoagulation for Afib



*ARISTOTLE*

- 5 Trials
- 4 Drugs
  - Dabigatran
  - Apixaban
  - Rivaroxaban
  - Edoxaban
- > 75,000 patients
- Global experience
- Strong foundation for evidence-based clinical decisions

AVERROES

- **Background / Introduction:**
- **Subgroup analyses are commonly performed in RCTs showing no overall or significant difference between treatments.**
- **The rationale for these analyses is to identify subgroups that might be benefited from treatment when the overall results show no benefit.**

# **Aim of the study**

- **to analyze the characteristics of subgroup analysis from the RCTs regarding the use of NOACs in AF**

# How to Use a Subgroup Analysis

## Users' Guides to the Medical Literature

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### Issues for Individual Studies and Systematic Reviews

Can Chance Explain the Subgroup Difference?

Is the subgroup difference consistent across studies?

Was the subgroup difference one of a small number of a priori hypotheses in which the direction was accurately prespecified?

Is there a strong preexisting biological rationale supporting the apparent subgroup effect?

***JAMA. 2014;311:405-411***

# Results

RE LY ROCKET AF ARISTOTLE ENGAGE

- Primary(n)

18

18

12

16

- Full publications(n)

33

29

30

13

# Results

- **Test( $p < 0.05$  or  $0.001$ ) for interaction almost in all**
- **Most post hoc**
- **No replication done or hypothesis raised**
- **No biological support**

	RE-LY	ROCKET AF	ARISTOTLE	ENGAGE
Age	1	1	1	1
Sex			1	
Race	2	2	2	1
Hypertension	1		1	
Diabetes mellitus	1	1		
CHADs score	1		1	
TTR	2	2	1	
Warfarin naive	1	1	1	1
Prior Stroke	1	1	1	1
CKD	2	2	2	1
Heart failure	1	1	1	
Types AF	1	1	1	
Cardioversion	1	1	1	1
Bleeding Risk factors Outcome GI ICH	1 1 1	1 1 2 1	1 1	
Discontinuation At the end Temporary-period	2	1 2	1 1	1
PAD		1		
CHD	1	2(		
Valve disease	1	1	1	
Biomarkers	4		6	
Plus antiPLTs	1	1	1	1
Amiodarone			1	1
digoxin		1		
Anaemia	1			
Poly pharmacy		1	1	
Dose adjustment	1		1	1
Ειδη εγκεφαλικού				1
Death causes	1	1	1	
Genetics	1			1
Pharmacokinetics	2			

# Conclusions

- **Subgroup analyses are commonly performed in the RCTs of NOACs in AF. The vast majority of them simply confirmed the result of the overall trial in the specific subgroups. The criteria that have been recommended to differentiate credible from less credible subgroup claims are not often used**
- **? Do they impact clinical practice**



**Are the results of the subgroup analysis and the overall analysis different enough that they would lead to different decisions?”**