

Impatto di Dabigatran e Warfarin sulla funzione cognitiva in pazienti con fibrillazione atriale

Risultati del trial GIRAF

Background

Outcome and Treatment	Events	Total person-time	Crude rate per 1,000 years		Hazard Ratio (95% CI)	p-value
Dementia						
DOAC - unadjusted^	493	32,230	15.30 (14.00, 16.71)		0.91 (0.81, 1.02)	0.11
DOAC - fully adjusted*					0.84 (0.73, 0.98)	0.02
VKA	765	45,474	16.82 (15.67, 18.06)		1.00 (Reference)	
Mild cognitive impairment						
DOAC - unadjusted^	531	30,535	17.39 (15.97, 18.93)		0.78 (0.68, 0.88)	0.00
DOAC - fully adjusted*					0.74 (0.65, 0.84)	0.00
VKA	957	43,676	21.91 (20.57, 23.35)		1.00 (Reference)	

Outcome and Exposure	No. of events	Total person-time	Crude rate (per 1,000 years)		Hazard Ratio (95% CI)	p-value
Dementia						
<50% TTR	108	56,776	19.02 (15.75, 22.97)		1.00 (Reference)	
50-70% TTR - unadjusted	164	96,097	17.06 (14.64, 19.89)		0.87 (0.68, 1.11)	.263
50-75% TTR - fully adjusted					0.87 (0.68, 1.11)	.274
>70% TTR - unadjusted	209	157,769	13.25 (11.57, 15.18)		0.71 (0.56, 0.89)	.003
>70% TTR - fully adjusted					0.73 (0.57, 0.92)	.008

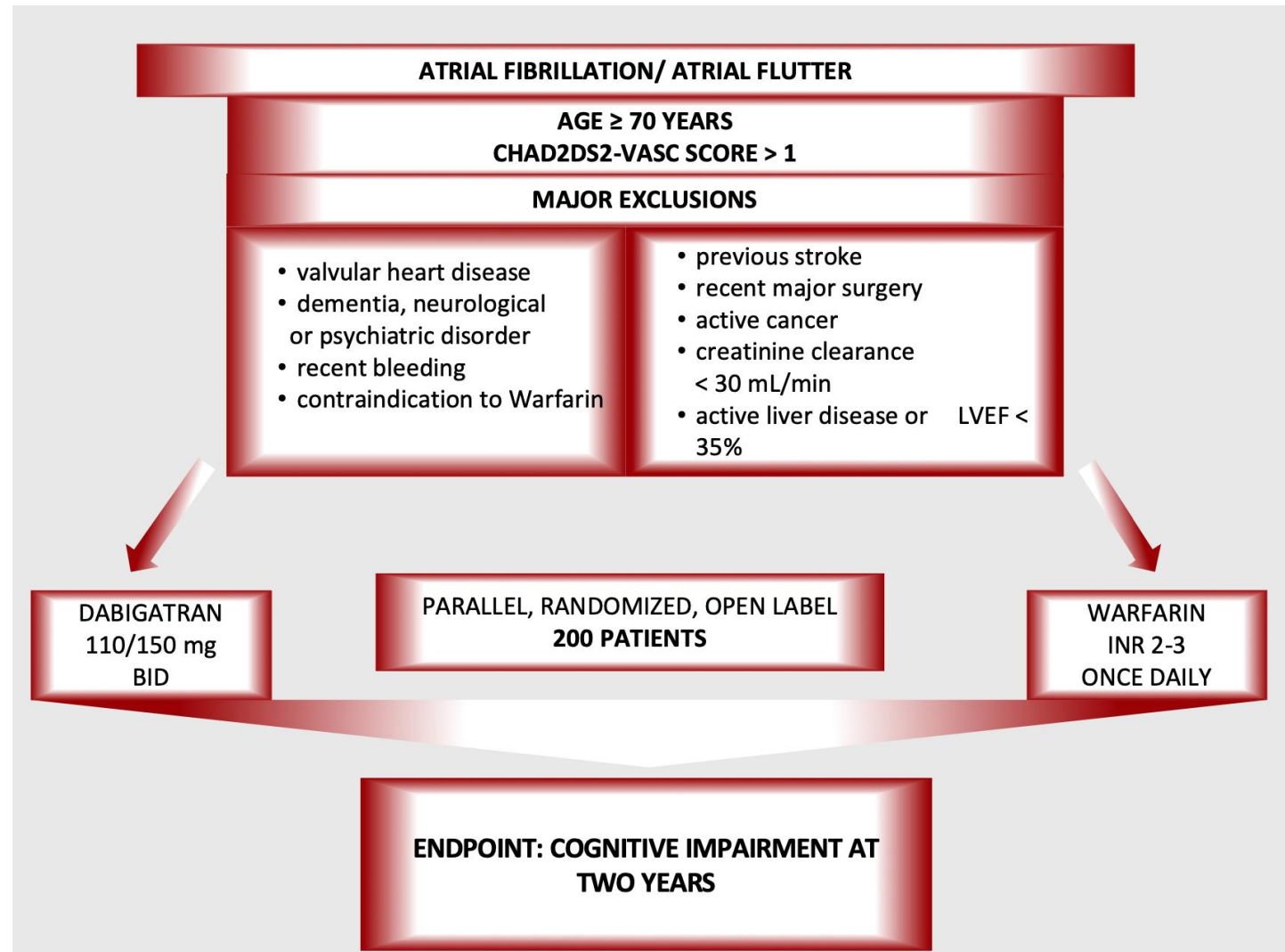
Sharon Louise Cadogan et al. Heart doi:10.1136/heartjnl-2021-319672

Caramelli B. Presented at: AHA 2021. November 14, 2021

Aim of the study

- To investigate the effects of Dabigatran compared with Warfarin on cognitive outcomes in older adults with Atrial Fibrillation/Atrial Flutter

Study design



Methods

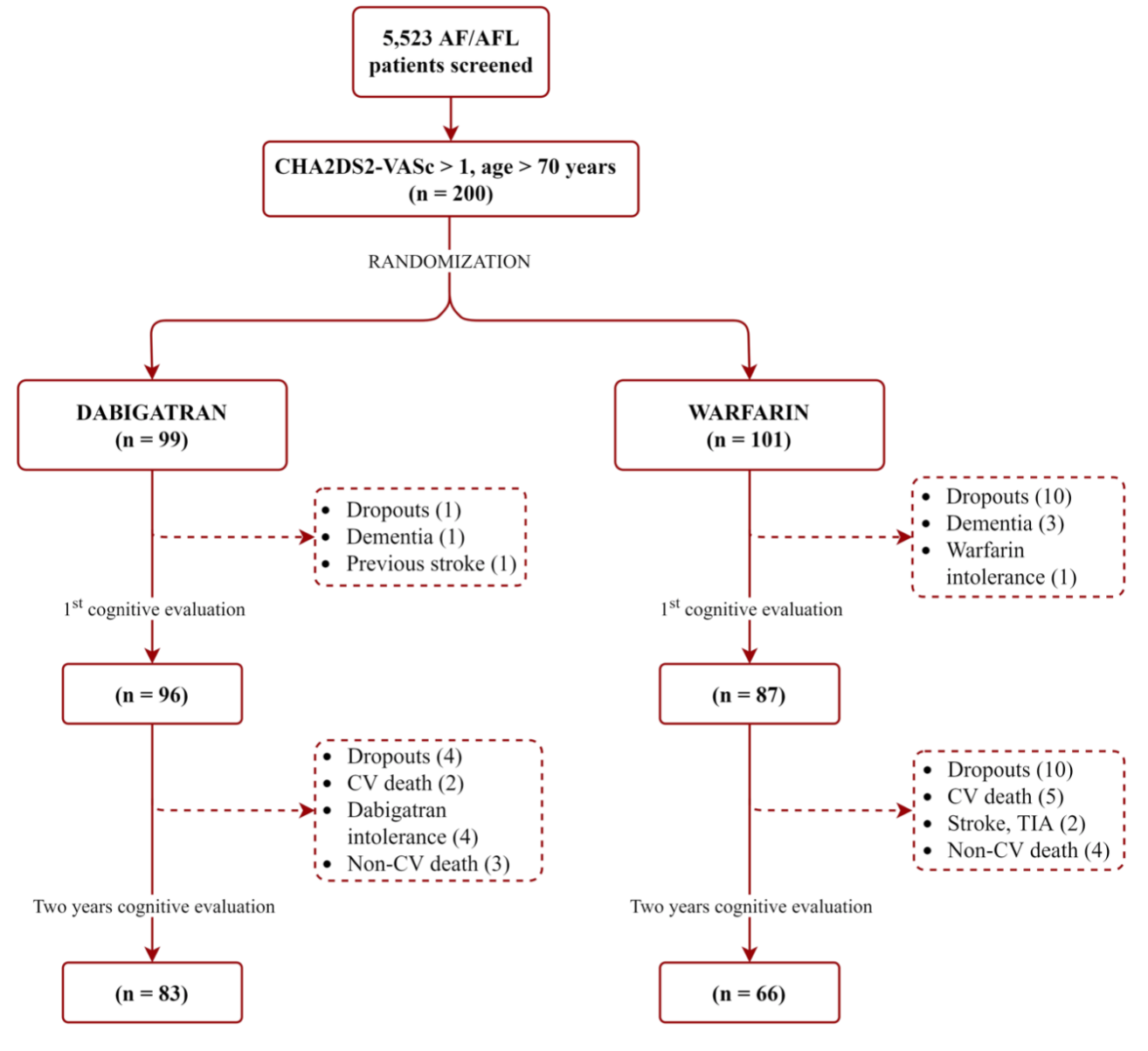
EXTENSIVE COGNITIVE EVALUATION AT BASELINE AND AFTER TWO-YEARS

TEST	ACRONYM	COVERAGE PATTERN
MONTREAL COGNITIVE ASSESSMENT	MOCA	GLOBAL
MINI-MENTAL STATE EXAM	MMSE	GLOBAL
NEUROPSYCHOLOGICAL BATTERY (DIGIT SYMBOL SUBSTITUTION TEST, FIGURE MEMORY TEST, SEMANTIC VERBAL FLUENCY, PHONEMIC VERBAL FLUENCY, BOSTON NAMING , TRAIL MAKING A&B, CLOCK-DRAWING)	NTB	ATTENTION MEMORY, LANGUAGE, EXECUTIVE FUNCTIONS
COMPUTER GENERATED NEUROPSYCHOLOGICAL MEASURING ACCURACY AND REACTION TIME	CGNT	SUSTAINED, SELECTIVE AND DIVIDED ATTENTION



- ✓ Tests performed by neurologists blinded to group assignments
- ✓ Modified Intention to Treat statistical analysis, no imputation
- ✓ Only patients that performed evaluations at baseline and after 2 years were considered.

Patient flow diagram



Baseline characteristics

CHARACTERISTICS	DABIGATRAN (N=83)	WARFARIN (N=66)	P VALUE
AGE, MEAN (SD) IN YEARS	74 (71-77)	76 (72-77)	0.06
SEX (MALE)	51 (61.4%)	39 (59.1%)	0.90
EDUCATION YEARS, MEAN (SD)	7 (4-12)	4 (4-9)	0.21
MMSE SCORE, MEDIAN (IQR)	27 (26-29)	27 (26-29)	0.85
MoCA SCORE, MEDIAN (IQR)	23 (21 to 26)	22 (18-24.8)	0.03
NTB Z-SCORE, MEDIAN (IQR)	0.08 (0.60)	-0.12 (0.58)	0.04
CGNT Z-SCORE, MEDIAN (IQR)	0.24 (0.02-0.47) N=72	-0.04 (-0.27-0.31) N=57	0.004
CHA2DS2-VASC, MEDIAN (IQR)	4 (3-4)	4 (3-5)	0.24
HAS - BLED, MEDIAN (IQR)	1 (1-1.25)	1 (1-1)	0.12

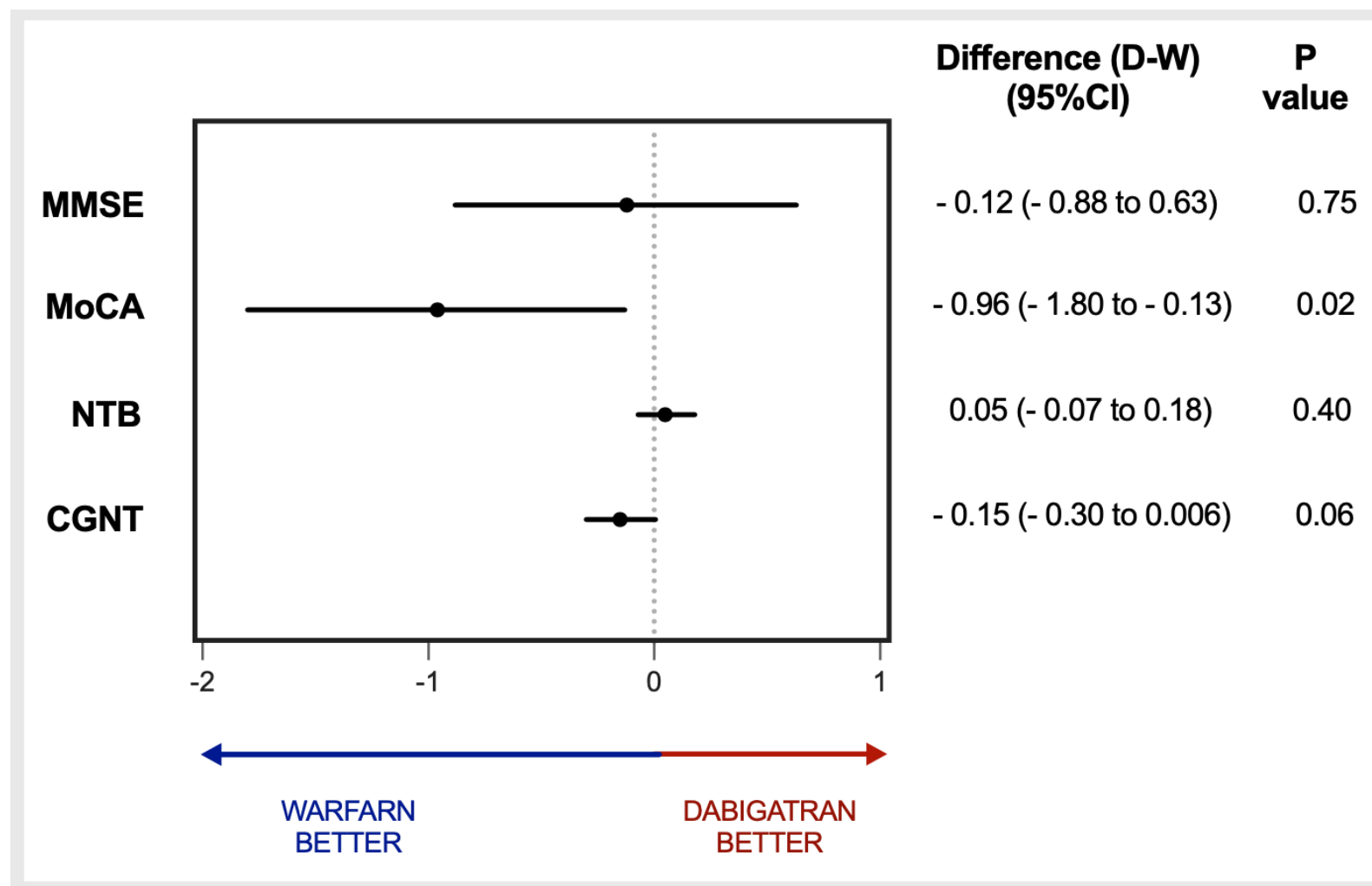
MMSE: Mini-Mental State Exam; **MoCA:** Montreal Cognitive Assessment; **NTB:** composite neuropsychological test battery consisting of the average of the z-scores for Boston naming test, semantics verbal fluency, phonemic verbal fluency, trail making tests, clock-drawing test, and digit symbol test; **CGNT:** a composite score composed of the average of the z-scores of the computer-generated neuropsychological tests.

Adjusted mean changes from baseline

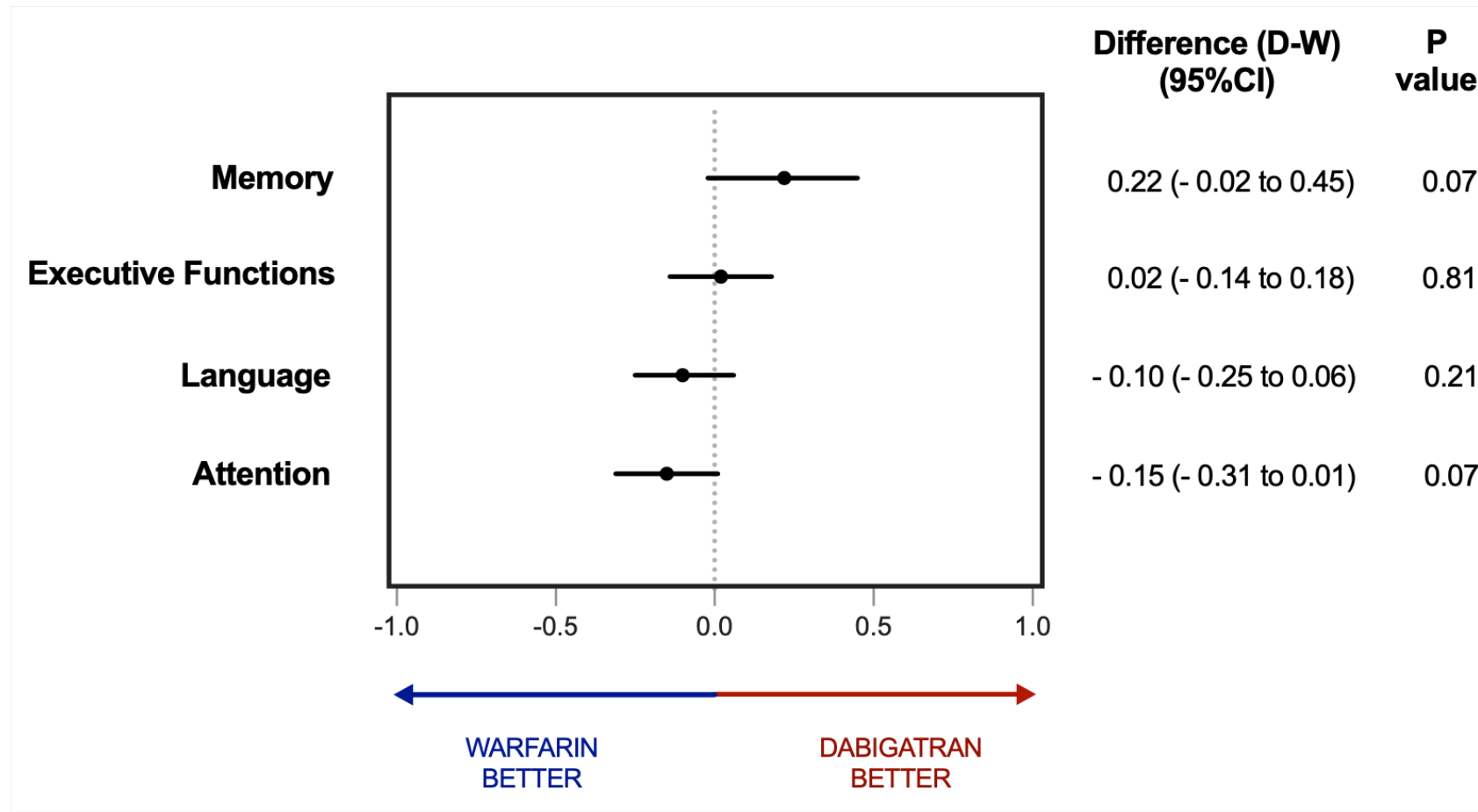
HIGHER SCORES INDICATE BETTER COGNITIVE PERFORMANCE

COGNITIVE ASSESSMENT	DABIGATRAN (N=83)	WARFARIN (N=66)	DIFFERENCE (D-W) (95% CI)	P VALUE	EFFECT SIZE COHEN'S D
MMSE SCORE	-0.69 (-1.18 to -0.2)	-0.57 (-1.12 to -0.01)	-0.12 (-0.88 to 0.63)	0.75	-0.06
MoCA SCORE	-0.39 (-0.94 to 0.16)	0.58 (-0.04 to 1.19)	-0.96 (-1.8 to -0.13)	0.02	-0.39
NTB SCORE	0.02 (-0.06 to 0.1)	-0.03 (-0.12 to 0.06)	0.05 (-0.07 to 0.18)	0.40	0.14
CGNT SCORE	-0.06 (-0.16 to 0.04) N=68	0.09 (-0.02 to 0.2) N=56	-0.15 (-0.3 to 0.006)	0.06	-0.36
ANTICOAGULATION QUALITY			WARFARIN (N=66)		
TTR			69.86% ± 13.94		

Dabigatran and warfarin groups in the 4 co-primary outcome tests



Dabigatran and warfarin groups in cognitive domains' tests



Conclusions

- In older patients with atrial fibrillation or atrial flutter who did not present major cerebrovascular events and were adequately treated with warfarin (TTR 70%) or dabigatran for 2 years, there was no difference in the majority of the cognitive outcomes.