

#AHA21



DABIGATRAN VERSUS WARFARIN ON COGNITIVE OUTCOMES IN NONVALVULAR ATRIAL FIBRILLATION: RESULTS OF THE GIRAF TRIAL

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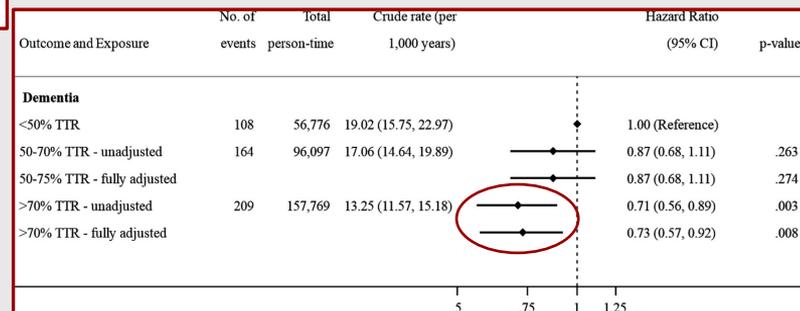
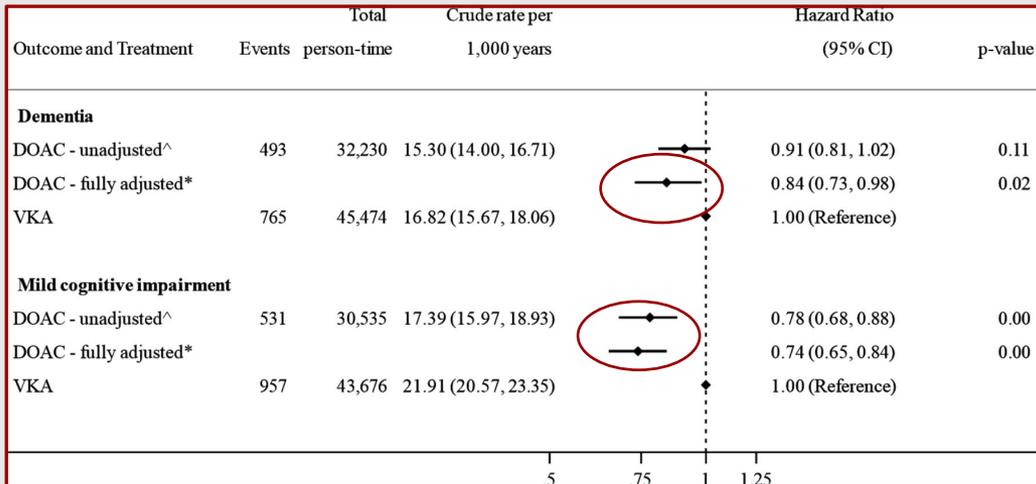


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DISCLOSURES

- ✓ **GIRAF PREVENTION TRIAL** IS AN INVESTIGATOR-INITIATED STUDY (IIS) THAT WAS PARTIALLY SUPPORTED BY BOEHRINGER INGELHEIM DO BRASIL QUÍMICA E FARMACÊUTICA
- ✓ THE SPONSOR HAD NO ROLE IN STUDY DESIGN, TRIAL EXECUTION, DATA ANALYSIS, WRITING/REVIEWING THE MANUSCRIPT OR IN THE DECISION TO SUBMIT FOR PUBLICATION.

ANTICOAGULATION IN AF PATIENTS AND THE RISK OF INCIDENT DEMENTIA HISTORICAL COHORT STUDY



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THE GIRAF PREVENTION TRIAL

IIS TRIAL ADDRESSING COGNITIVE OUTCOMES IN AF PATIENTS

OBJECTIVE

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

ATRIAL FIBRILLATION/ ATRIAL FLUTTER

**AGE \geq 70 YEARS
CHAD2DS2-VASC SCORE $>$ 1**

MAJOR EXCLUSIONS

- | | |
|--|--|
| <ul style="list-style-type: none">• valvular heart disease• dementia, neurological or psychiatric disorder• recent bleeding• contraindication to Warfarin | <ul style="list-style-type: none">• previous stroke• recent major surgery• active cancer• creatinine clearance $<$ 30 mL/min• active liver disease or LVEF $<$ 35% |
|--|--|

**DABIGATRAN
110/150 mg
BID**

**PARALLEL, RANDOMIZED, OPEN LABEL
200 PATIENTS**

**WARFARIN
INR 2-3
ONCE DAILY**

**ENDPOINT: COGNITIVE IMPAIRMENT AT
TWO YEARS**

GIRAF TRIAL STUDY DESIGN

METHODS

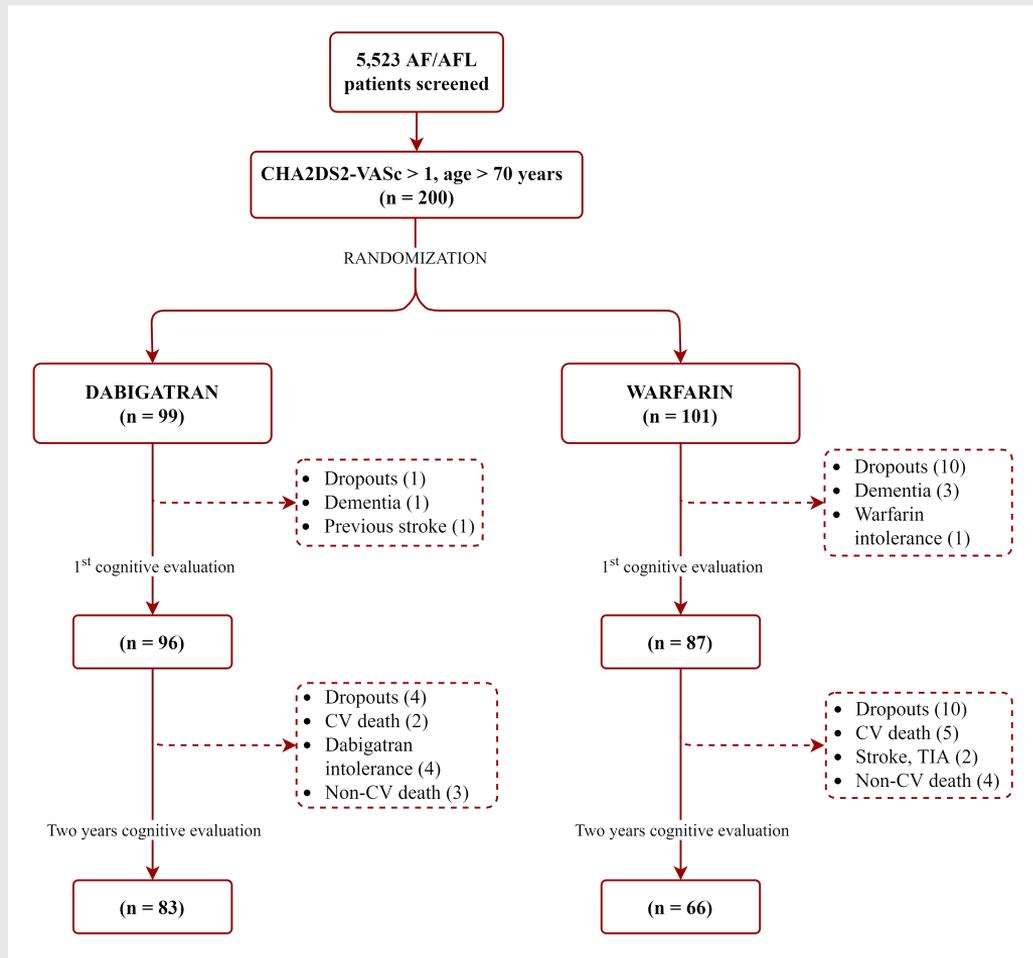
EXTENSIVE COGNITIVE EVALUATION AT BASELINE AND AFTER TWO-YEARS

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 - BLEED, 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.

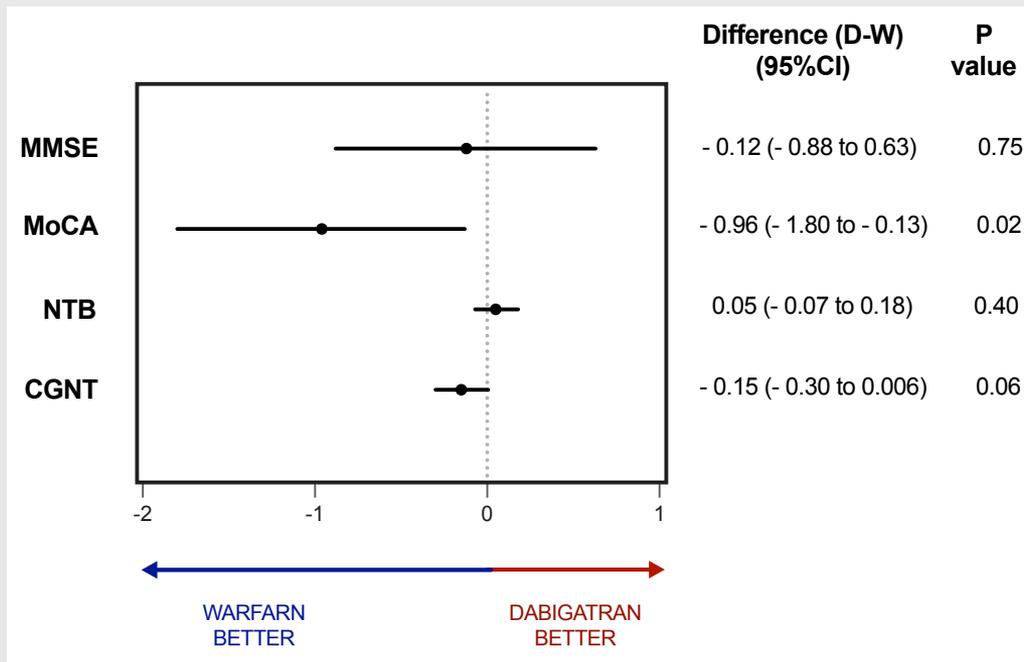
ADJUSTED MEAN CHANGES FROM BASELINE

HIGHER SCORES INDICATE BETTER COGNITIVE PERFORMANCE

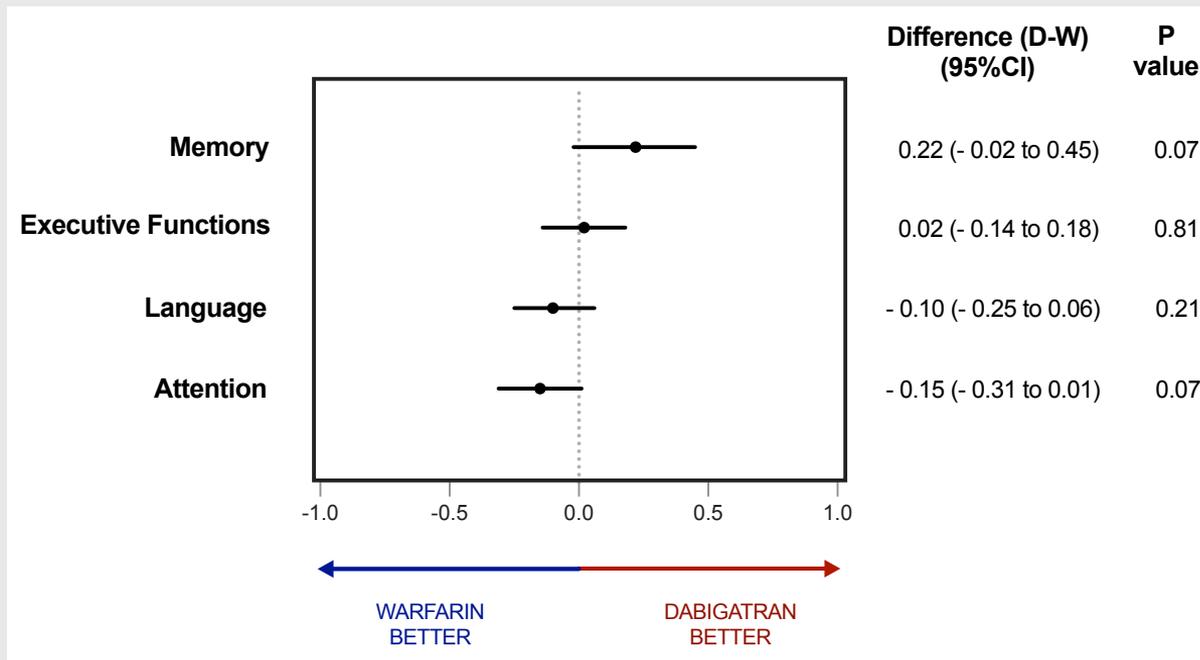
COGNITIVE ASSESSMENT	DABIGATRAN (N=83)	WARFARIN (N=66)	DIFFERENCE (D-W) (95% CI)	P VALUE	EFFECT SIZE COHEN'S D
MMSE SCORE	-0.69 (-1.18 to -0.2)	-0.57 (-1.12 to -0.01)	-0.12 (-0.88 to 0.63)	0.75	-0.06
MoCA SCORE	-0.39 (-0.94 to 0.16)	0.58 (-0.04 to 1.19)	-0.96 (-1.8 to -0.13)	0.02	-0.39
NTB SCORE	0.02 (-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.**

ACKNOWLEDGEMENTS

INVESTIGATORS

- | | |
|--|---|
|  AMADO D |  MAGALHAES I |
|  BORGES JR F |  MATHEUS M |
|  BRUCKI S |  NITRINI R |
|  CALDERARO D |  PASTANA A |
|  CARAMELLI B |  RODRIGUES A |
|  CARAMELLI P |  ROJAS M |
|  CARDOZO F |  SPERA R |
|  FEITOSA R |  TAVARES C |
|  GUALANDRO D |  YU P |



TO THE PATIENT, TO THE BRAZILAN PUBLIC HEALTH SYSTEM AND TO THE BRAZILIAN PEOPLE, WHO RESIST DESPITE EVERYTHING