ATRIAL FIBRILLATION
NETWORK

NOAH - AFNET 6

Hauptergebnis

Universitäres
Herz- und Gefäßzentrum
Hamburg

Anticoagulation with Edoxaban in Patients with Atrial High-Rate Episodes (AHRE)
Results of the NOAH – AFNET 6 Trial

Paulus Kirchhof, Tobias Toennis, Andreas Goette, A John Camm, Hans Christoph Diener, Nina Becher, Emanuele Bertaglia, Carina Blomstrom Lundqvist, Martin Borlich, Axel Brandes, Nuno Cabanelas, Melanie Calvert, Gregory Chlouverakis, Gh.-Andrei Dan, Joris R. de Groot, Wolfgang Dichtl, Borys Kravchuk, Andrzej Lubiński, Eloi Marijon, Béla Merkely, Lluís Mont, Ann-Kathrin Ozga, Kim Rajappan, Andrea Sarkozy, Daniel Scherr, Rafał Sznajder, Vasil Velchev, Dan Wichterle, Susanne Sehner, Emmanuel Simantirakis, Gregory Y. H. Lip, Panos Vardas, Ulrich Schotten, Antonia Zapf

p.kirchhof@uke.de

NOAH – AFNET 6 Hypothesis

The **N**on vitamin K antagonist **O**ral anticoagulants in patients with **A**trial **H**igh-rate episodes trial (NOAH-AFNET 6)

Oral anticoagulation with edoxaban prevents stroke and systemic embolism in patients with atrial high-rate episodes and stroke risk factors compared to no anticoagulation.

NOAH – AFNET 6 Clinical Characteristics

Characteristics	Edoxaban (N=1270)	Placebo (N=1266)
Age, mean ± SD	77.4 ± 6.5	77.5 ± 6.8
Age ≥ 75 years, N	845/1270 (66.5%)	855/1266 (67.5%)
Female Sex, N (%)	469/1270 (36.9%)	480/1266 (37.9%)
Acetylsalicylic acid indication at randomization, N (%)	684/1270 (53.9%)	683/1266 (53.9%)
CHA_2DS_2-VASc score, median (IQR)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)
AHRE with atrial rates >200 beats per minute, N (%)	918/944 (97%)	896/925 (97%)
AHRE episode duration [hours:minutes], median (IQR)	2:50 (0:50, 9:14)	2:47 (0:43, 9:28)
Device recording AHRE, N (%)		
Pacemaker	1017/1270 (80.1%)	1055/1266 (83.3%)
Defibrillator	100/1270 (7.9%)	88/1266 (7.0%)
Cardiac Resynchronization device	138/1270 (10.9%)	113/1266 (8.9%)
Implanted loop recorder	15/1270 (1.2%)	10/1266 (0.8%)

NOAH – AFNET 6 Early Termination

The unanimous decision to terminate NOAH – AFNET 6 was taken in Sep 2022 after enrolment of all planned patients at a median follow-up of 21 months.

Final visits were conducted until 31 December 2022,
capturing 184/220 (84%) of the planned primary outcome events.

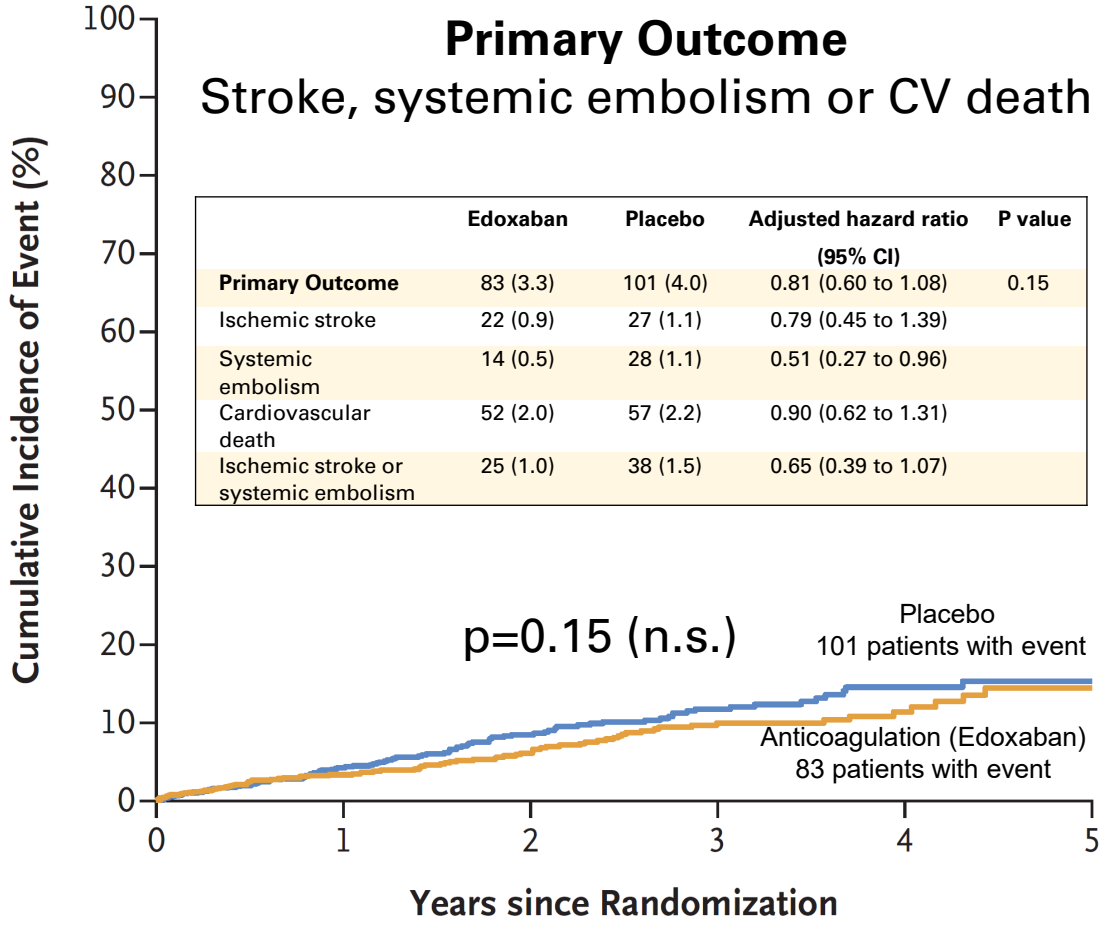
Anticoagulation (Edoxaban):
232/1,270 patients developed atrial fibrillation (8.7%/year), 134 withdrew consent

No anticoagulation:
230/1,266 patients developed atrial fibrillation (8.8%/year), 134 withdrew consent

NOAH – AFNET 6 Outcomes

Primary Outcome
Stroke, systemic embolism or CV death

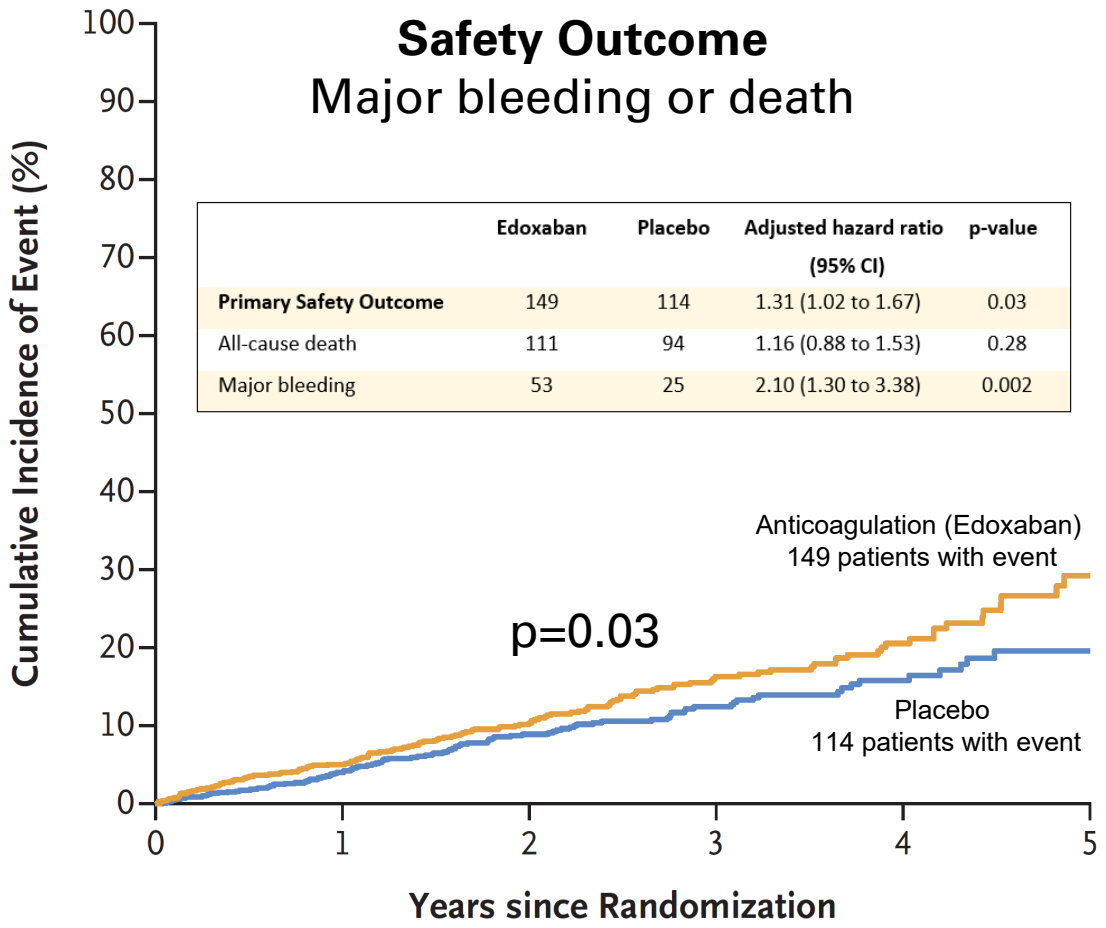
	Edoxaban	Placebo	Adjusted hazard ratio (95% CI)	P value
Primary Outcome	83 (3.3)	101 (4.0)	0.81 (0.60 to 1.08)	0.15
Ischemic stroke	22 (0.9)	27 (1.1)	0.79 (0.45 to 1.39)	
Systemic embolism	14 (0.5)	28 (1.1)	0.51 (0.27 to 0.96)	
Cardiovascular death	52 (2.0)	57 (2.2)	0.90 (0.62 to 1.31)	
Ischemic stroke or systemic embolism	25 (1.0)	38 (1.5)	0.65 (0.39 to 1.07)	



No. at Risk (no. of events)						
Edoxaban	1270 (37)	873 (20)	559 (19)	327 (3)	148 (4)	42
Placebo	1266 (44)	822 (30)	534 (16)	329 (7)	137 (1)	50

Safety Outcome
Major bleeding or death

	Edoxaban	Placebo	Adjusted hazard ratio (95% CI)	p-value
Primary Safety Outcome	149	114	1.31 (1.02 to 1.67)	0.03
All-cause death	111	94	1.16 (0.88 to 1.53)	0.28
Major bleeding	53	25	2.10 (1.30 to 3.38)	0.002



No. at Risk (no. of events)						
Edoxaban	1270 (57)	866 (41)	551 (30)	324 (11)	145 (10)	44
Placebo	1266 (42)	829 (36)	538 (17)	332 (9)	138 (5)	49

The findings were robust in sensitivity analyses with and without censoring at the time of study drug discontinuation, Covid-19 infections, Ukrainian patients after 24 Feb 2022, or ECG-diagnosed AF.

NOAH – AFNET 6 Strengths and Limitations

Double-blind, double-dummy design (aspirin in 54% of patients without anticoagulation).
Complete follow-up of entire primary analysis population for primary outcome and safety outcome.
Expected increase in bleeding with anticoagulation compared to no anticoagulation.

Not sufficient power to rule out a small effect of oral anticoagulation on cardiovascular events.
Only one NOAC tested (edoxaban).
Trial conducted in 18 European countries. Effects in other ethnicities unknown.

Universitäres Herz- und Gefäßzentrum Hamburg

NOAH – AFNET 6 Conclusions

AFNET 6 N O A H

In patients with atrial high-rate episodes (AHRE) and clinical stroke risk factors, anticoagulation with edoxaban in the dose approved for atrial fibrillation does not reduce a composite outcome of stroke, systemic embolism, or cardiovascular death.

As expected, anticoagulation increases major bleeding.

Stroke rate was low with and without anticoagulation.

Based on these results, patients with AHRE should be managed without anticoagulation until atrial fibrillation is diagnosed by ECG.

Additional methods are needed to estimate stroke risk in patients with rare atrial arrhythmias such as AHRE.

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Daiichi-Sankyo

DZHK DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.

AFNET 6

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