Garfield
global anticoagulant registry in the field

Comparative Effectiveness of Oral Anticoagulants in Everyday Practice

Results from the GARFIELD-AF Prospective Registry

A. John Camm, Keith A.A. Fox, Saverio Virdone, Jean-Pierre Bassand, David A. Fitzmaurice, Bernard J. Gersh, Samuel Z. Goldhaber, Shinya Goto, Sylvia Haas, Frank Misselwitz, Karen Pieper, Alexander G.G. Turpie, Freek W.A. Verheugt, Ajay K. Kakkar

for the GARFIELD-AF Investigators

Disclosures

AJC has served as an advisor to Bayer, Boehringer Ingelheim, Pfizer/BMS, and Daiichi Sankyo.

Declaration of interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company (see declaration on ESC website)
- Research contracts (see declaration on ESC website)

Introduction

- Comparative effectiveness provides a measure of the benefits and harms of treatments delivered to the diversity of patients in everyday practice; however, we need to account for differences in the distribution of characteristics between treatment groups[1]
- **Aim of this study**: Compare baseline characteristics and comparative safety and effectiveness of: **OACs vs no anticoagulant and NOACs vs VKAs** in patients with newly diagnosed AF and a CHA_2DS_2-VASc score ≥2 (including gender)
- **Methods**: All-cause mortality, stroke/SE, major bleeding manifest over 2 year follow-up were analysed
- Cox proportional hazards models with propensity score weighting for treatment, defined as the first treatment received at enrolment[2]

1. Rosenbaum PR, Rubin DB. *Biometrika* 1983;70:41-55. 2. Li F et al. *J Am Stat Assoc* 2018;113:390–400.
OAC: Oral anticoagulants; NOACs: non-vitamin K antagonist oral anticoagulants; SE: Systemic embolism; VKAs: Vitamin K antagonists

Multiple factors were considered as potential confounders

Demographics

- Age
- Gender
- Race
- Country

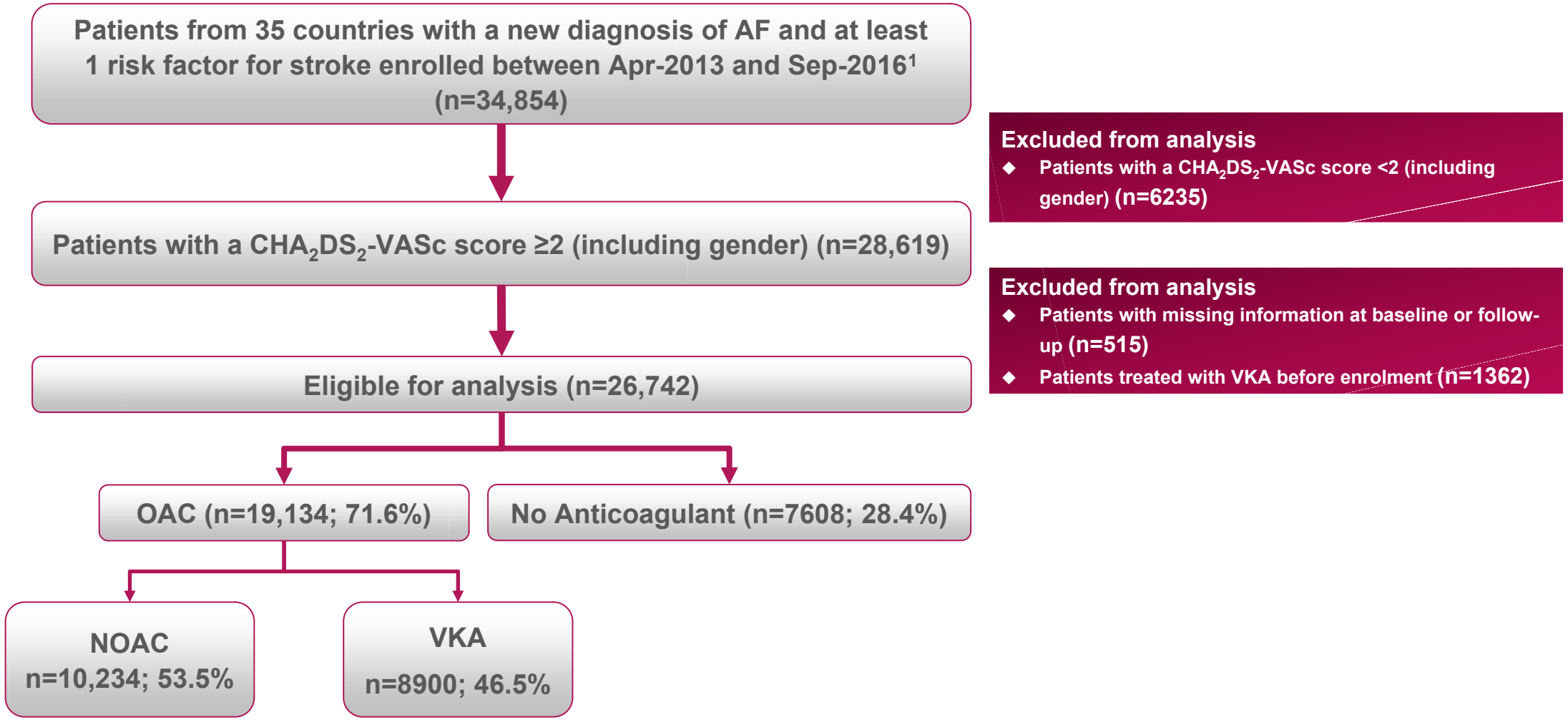
Other baseline features

- Year (cohort of enrolment)
- Care setting location
- Care setting specialty

Medical history

- Type of AF
- Heart failure
- Diabetes
- History of hypertension
- Stroke
- Transient ischaemic attack
- Systemic embolism
- Carotid occlusive disease
- ACS
- Coronary artery bypass
- Vascular disease
- Heart rate
- Chronic kidney disease
- Bleeding
- Antiplatelet use
- Dementia
- Smoking
- Alcohol consumption
- BMI
- Hypo- or Hyper-thyroidism
- Cirrhosis
- Systolic blood pressure
- Diastolic blood pressure

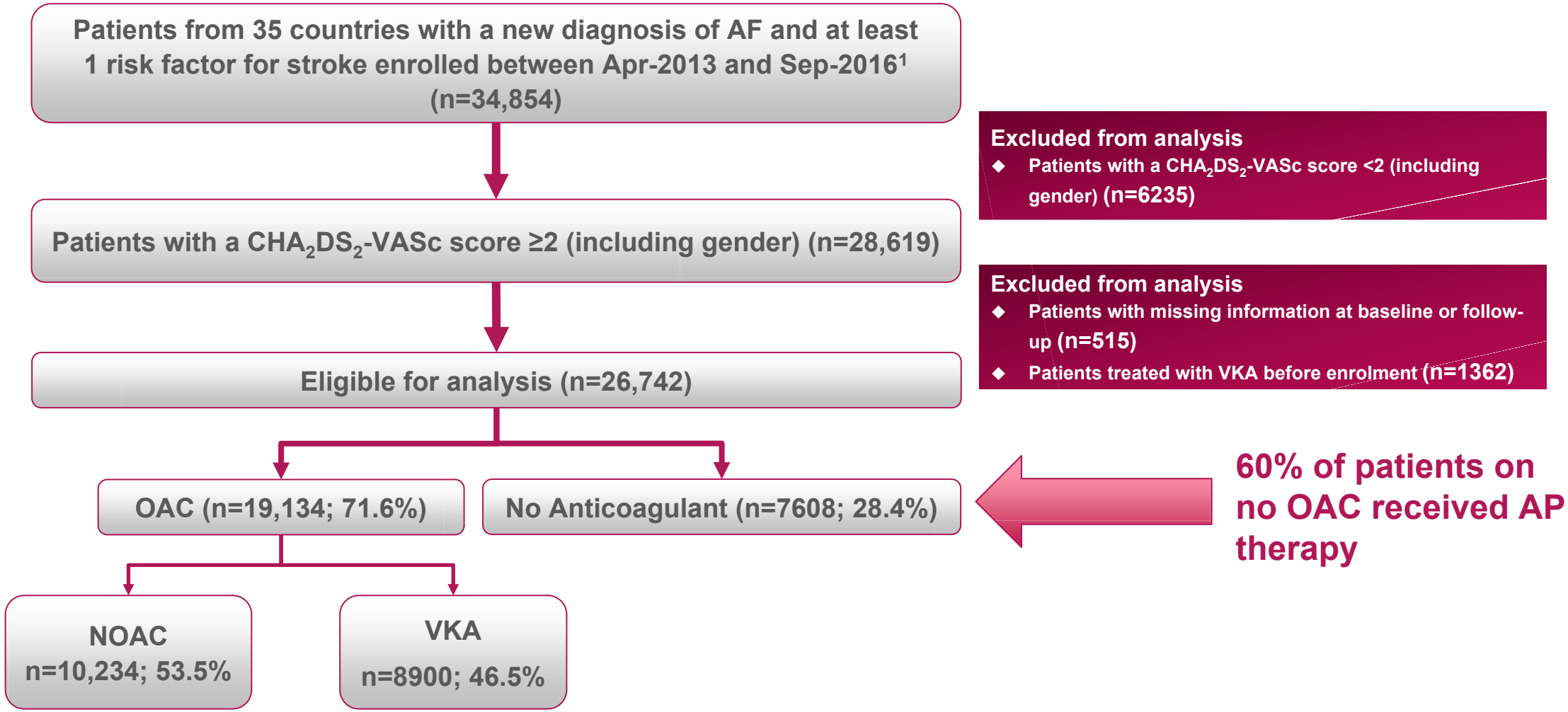
GARFIELD-AF patient population



GARFIELD-AF Global Anticoagulant Registry in the FIELD–Atrial Fibrillation; OAC: Oral anticoagulants; NOACs: non-vitamin K antagonist oral anticoagulants; VKAs: Vitamin K antagonists

[1] Kakkar AK et al. *Am Heart J* 2012;163:13–19.e1.

GARFIELD-AF patient population



GARFIELD-AF Global Anticoagulant Registry in the FIELD–Atrial Fibrillation; OAC: Oral anticoagulants; NOACs: non-vitamin K antagonist oral anticoagulants; VKAs: Vitamin K antagonists

[1] Kakkar AK et al. *Am Heart J* 2012;163:13–19.e1.

Baseline characteristics

	OAC			No Anticoagulant (N= 7608)
	NOAC (N = 10,234)	VKA (N = 8900)	All OAC (N = 19,134)	
Age, median [IQR] (years)	74.0 (67.0; 80.0)	73.0 (66.0; 79.0)	73.0 (67.0; 79.0)	72.0 (65.0; 79.0)
Gender, female, %	49.8	51.0	50.4	51.9
Race, %				
Caucasian	65.9	69.5	**67.6**	**53.0**
Asian	27.2	19.7	**23.8**	**38.4**
Hispanic/Latino	4.6	8.7	6.5	6.7
Medical history, %				
Heart failure	20.9	21.5	**21.2**	**24.7**
Coronary artery disease	20.2	23.9	**21.9**	**31.7**
Acute coronary syndromes	9.7	11.5	10.5	12.5
Stroke	8.3	8.3	8.3	7.7
Systemic embolism (history)	0.6	0.9	0.8	4.6
Hypertension (history)	82.0	85.3	83.5	80.5
Diabetes, Type 1 or Type 2	24.8	28.8	26.6	24.8
Moderate to severe renal disease	11.5	14.4	12.8	12.2
CHA_2DS_2-VASc score, mean (SD)	3.6 (1.3)	3.6 (1.3)	3.6 (1.3)	3.5 (1.3)

OAC: Oral anticoagulants; NOACs: Non-vitamin K antagonist OAC; VKAs: Vitamin K antagonists

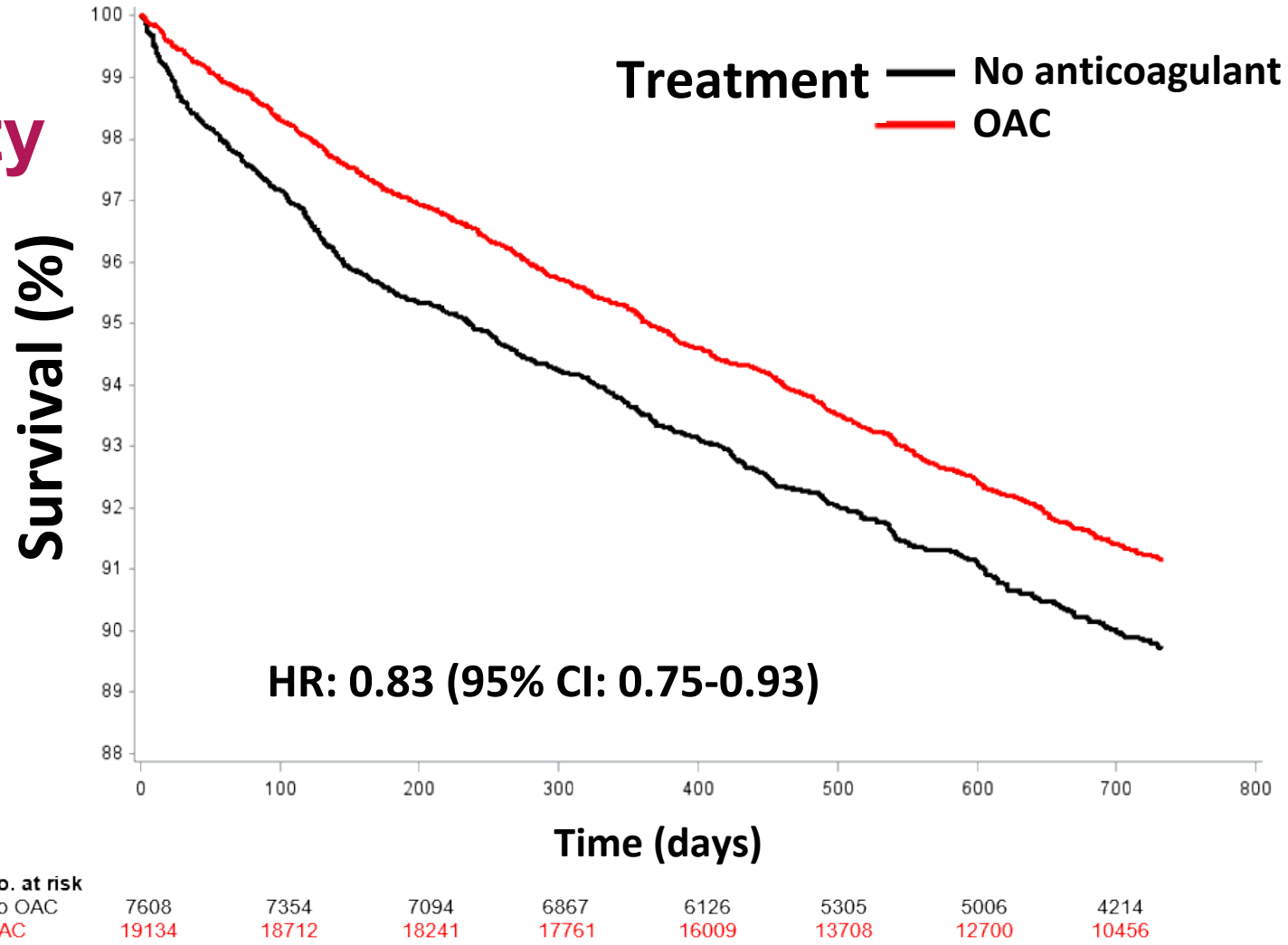
Baseline characteristics

	OAC			No Anticoagulant (N= 7608)
	NOAC (N = 10,234)	VKA (N = 8900)	All OAC (N = 19,134)	
Age, median [IQR] (years)	74.0 (67.0; 80.0)	73.0 (66.0; 79.0)	73.0 (67.0; 79.0)	72.0 (65.0; 79.0)
Gender, female, %	49.8	51.0	50.4	51.9
Race, %				
Caucasian	65.9	69.5	67.6	53.0
Asian	**27.2**	**19.7**	23.8	38.4
Hispanic/Latino	**4.6**	**8.7**	6.5	6.7
Medical history, %				
Heart failure	20.9	21.5	21.2	24.7
Coronary artery disease	**20.2**	**23.9**	21.9	31.7
Acute coronary syndromes	**9.7**	**11.5**	10.5	12.5
Stroke	8.3	8.3	8.3	7.7
Systemic embolism (history)	0.6	0.9	0.8	4.6
Hypertension (history)	82.0	85.3	83.5	80.5
Diabetes, Type 1 or Type 2	24.8	28.8	26.6	24.8
Moderate to severe renal disease	**11.5**	**14.4**	12.8	12.2
CHA_2DS_2-VASc score, mean (SD)	3.6 (1.3)	3.6 (1.3)	3.6 (1.3)	3.5 (1.3)

OAC: Oral anticoagulants; NOACs: Non-vitamin K antagonist OAC; VKAs: Vitamin K antagonists

OAC vs no anticoagulant Adjusted survival and HR for all-cause mortality over 2 year follow-up

Patients with a CHA_2DS_2-VASc score ≥2 (including gender)



OAC: Oral anticoagulants; HR: Hazard ratio; CI: Confidence intervals

OAC (compared to no anticoagulant) was associated with decreased risks of all-cause mortality and stroke/SE but a higher risk of major bleeding

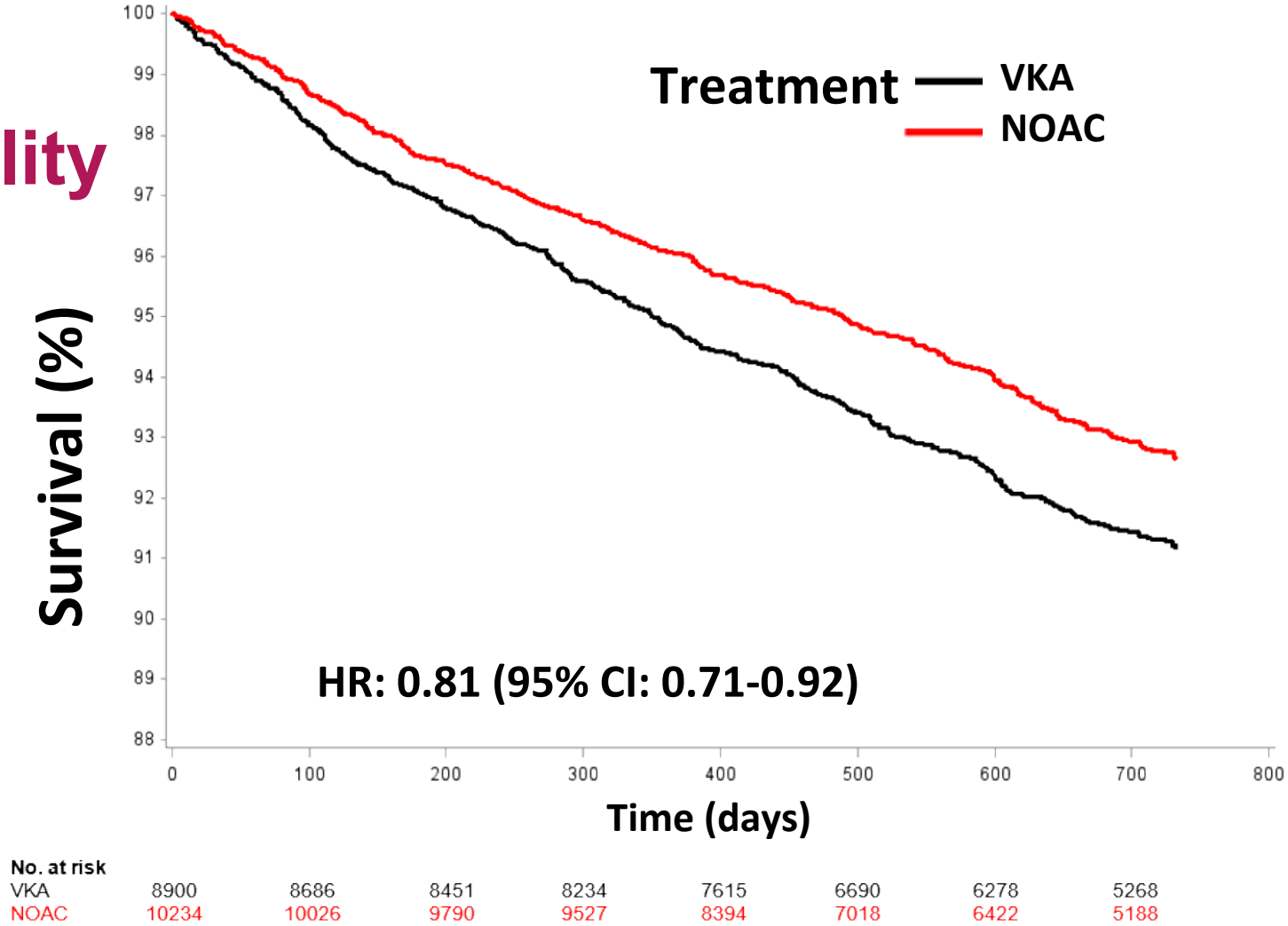
Events over 2-year follow-up of patients with a CHA_2DS_2-VASc score ≥2 (including gender)

	OAC (N = 19,134)		No Anticoagulant (N= 7608)		HR (95% CI) ref. No OAC	P-value
	Events	Rate (per 100 person years)	Events	Rate (per 100 person years)		
All-cause mortality	1297	4.1	676	5.5	0.83 (0.75, 0.93)	<0.001
Stroke/SE	313	1.0	173	1.4	0.73 (0.59, 0.90)	0.003
Major bleeding	247	0.8	63	0.5	1.36 (1.00, 1.85)	0.053

OAC: Oral anticoagulants; SE: Systemic embolism; HR: Hazard ratio; CI: Confidence intervals

NOAC vs VKA: Adjusted survival and HR for all-cause mortality over 2 years follow-up

Patients with a CHA_2DS_2-VASc score ≥2 (including gender)



OAC: Oral anticoagulants; NOACs: Non-vitamin K antagonist OAC VKAs: Vitamin K antagonists; HR: Hazard ratio; CI: Confidence interval

NOAC (compared to VKA) was associated with a decreased risk of all-cause mortality with no significant differences in stroke/SE or major bleeding

Events over 2-year follow-up of patients with a CHA_2DS_2-VASc score ≥2 (including gender)

	NOAC (N = 10,234)		VKA (N = 8900)		HR (95% CI) ref. VKA	P-value
	Events	Rate (per 100 person years)	Events	Rate (per 100 person years)		
All-cause mortality	585	3.5	712	4.8	0.81 (0.71, 0.92)	0.001
Stroke/SE	142	0.9	171	1.2	0.85 (0.65, 1.11)	0.237
Major bleeding	102	0.6	145	1.0	0.81 (0.59, 1.11)	0.192

OAC: Oral anticoagulants; NOACs: Non-vitamin K antagonist OAC VKAs: Vitamin K antagonists; SE: Systemic embolism; HR: Hazard ration; CI: Confidence intervals

A similar proportion of cardiovascular and non-cardiovascular deaths were reported in this population

2-year follow-up of patients with a CHA_2DS_2-VASc score ≥2 (including gender)

Cause of death	% Patients who died
Cardiovascular	**32.8**
Heart failure	12.2
Myocardial infarction	3.7
Ischaemic stroke	3.6
Non-cardiovascular	**38.1**
Cancer	12.2
Respiratory failure	6.5
Infection	4.6
Sepsis	4.1
Unknown	**29.1**

Relative effectiveness of oral anticoagulants in reducing all-cause mortality over time since start of treatment

Patients with a CHA_2DS_2-VASc score ≥2 (including gender)

Patients stratified according to the first OAC after diagnosis of AF

Follow-up	OAC vs no Anticoagulant		NOAC vs VKA	
	HR (95% CI)	P-value	HR (95% CI)	P-value
3 months	0.54 (0.43, 0.68)	<0.001	0.68 (0.50, 0.92)	0.014
12 months	0.76 (0.66, 0.86)	<0.001	0.76 (0.64, 0.89)	0.001
24 months	0.83 (0.75, 0.93)	<0.001	0.81 (0.71, 0.92)	0.001

OAC: Oral anticoagulants; SE: Systemic embolism; HR: Hazard ratio; CI: Confidence intervals

Strengths and limitations

Strengths

- GARFIELD-AF is the largest multinational prospective registry in patients with AF
- The registry captures the diversity of treatment and outcomes in populations beyond the constraints of randomised clinical trials
- The registry employs regular audits including a combination of remote and onsite monitoring to ascertain completeness and accuracy of all records
    - Source data verification was conducted on the data for 20% of patients in the study

Limitations

- Treatments were not randomised and although the reflects the results seen in RCTs, we cannot account for potential unmeasured confounders
- This analysis reflects the “Intention to Treat” over the duration of follow-up. Treatments may change over time and these changes are not reflected in these analyses

Further analyses are now ongoing to assess the impact of changes in treatments on outcomes

RCT: Randomised controlled studies

Conclusions

- There were significant mortality differences in favour of OACs (vs no anticoagulant) and NOACs (vs VKAS) even after adjustment for baseline variables
- Patients on OACs (vs no anticoagulants) also had significantly lower risk of stroke/systemic embolism but a higher risk of major bleeding over the 2 years of follow-up
- Differences between NOACS and VKAs were not significant for risks of stroke/systemic embolism and major bleeding

Clinical implications

- These observations suggest that the effectiveness of OACs in randomised clinical trials can be translated to the broad cross-section of patients treated everyday practice
- The study also raises questions about the impact of anticoagulation, beyond stroke prevention

Acknowledgements

We thank the physicians, nurses, and patients involved in the GARFIELD-AF registry

TRI Thrombosis Research Institute

www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field