

# Anticoagulation for NVAf: NAOs or AVKs?

**Giancarlo Agnelli**

Medicina Interna & Cardiovascolare - Stroke Unit  
Scuola di Specializzazione in Medicina di Emergenza - Urgenza  
Università di Perugia



# My talk today

- Achievements with traditional anticoagulants
- Clinical evidence about NOAs
- What's about my patients?

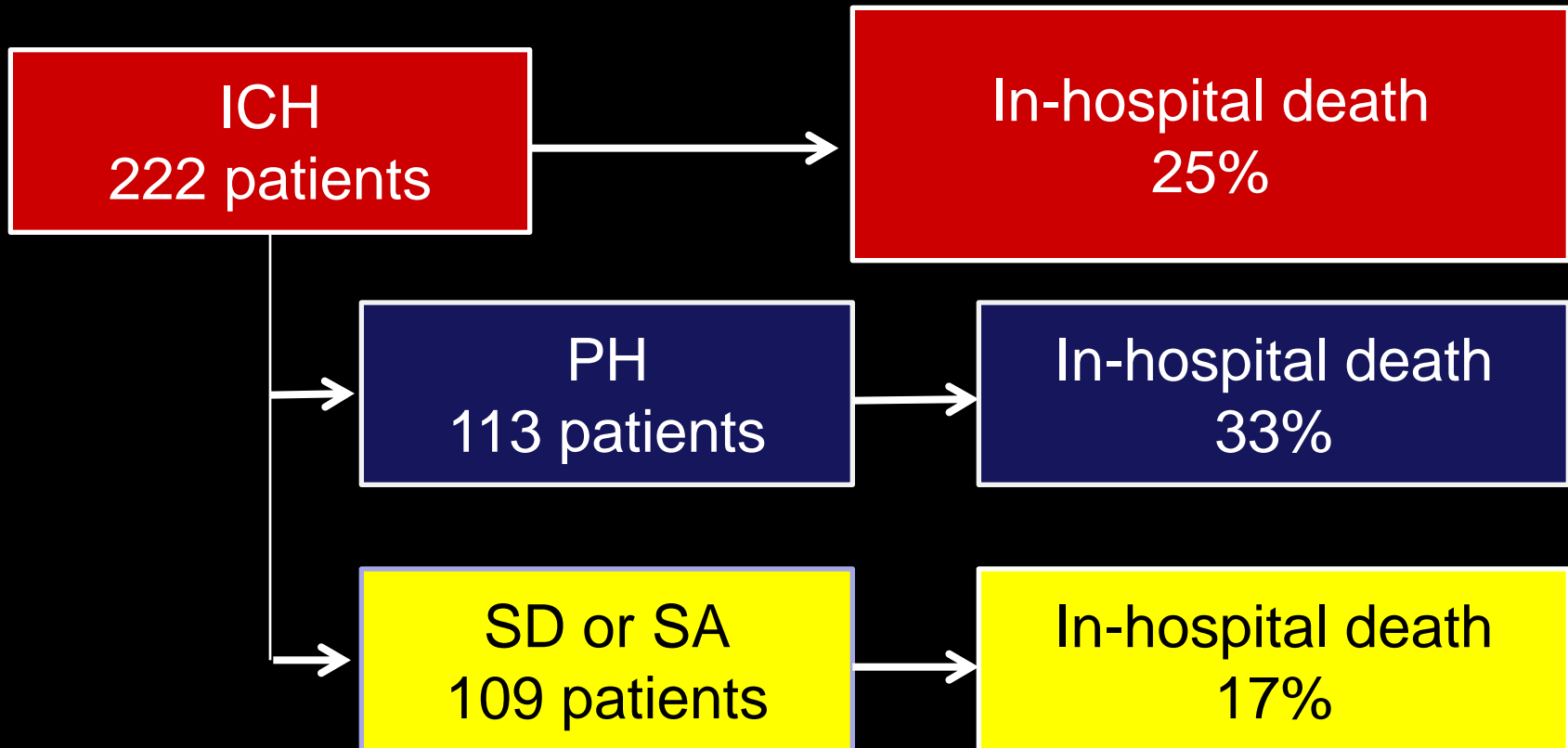
# Achievements with available antitrombotic agents

- Heparin and LMWH reduce by about 60% the incidence of VTE after high risk surgery
- Vitamin K inhibitors reduce by more than 90% the risk of VTE recurrence
- Vitamin K inhibitors reduce by about 60% the rate of stroke in patients with atrial fibrillation



# Anticoagulation-related bleeding: the burden

The CLIMBING study: VKAs-associated bleeding



# AVK treatment: room for improvement

- Eliminate the inconvenience of INR monitoring
- Improve safety
- Confirm (improve?) efficacy

# My talk today

- Achievements with traditional anticoagulants
- **Clinical evidence about NOAs**
- What's about my patients?

# New anticoagulants (year 2015)

## Oral

TTP889

Rivaroxaban

Apixaban

Edoxaban

Betrixaban

Darexaban

LY517717

TAK 42

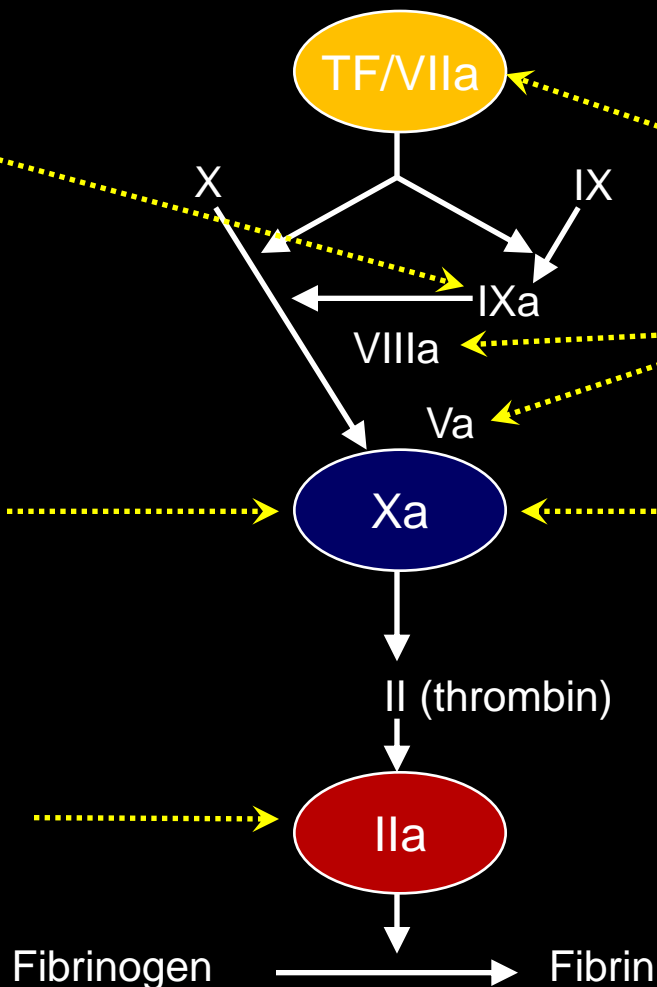
Dabigatran

## Parenteral

TFPI (tifacogin)

APC (drotrecogin alfa)  
sTM (ART-123)

Semuloparin  
DX-9065a  
Otamixaban



# NOAs: prevention of stroke in AFib

- Rely
- Rocket-AF
- Aristotle
- Engage AF
- Averroee (vs. aspirin)



## NOAs for AFib: common achievements

All four NOAs are non-inferior to warfarin in reducing the risk of stroke and SSE

All four NOAs reduce the risk of bleeding (fatal for rivaroxaban, major for apixaban and dabigatran at 110 mg ) and intracranial hemorrhage

The directionality and magnitude of the mortality reduction is consistent and approximates a RRR of 10% per year

# Good reasons for a non-inferiority study

New agent as effective as but safer  
(less ICH)

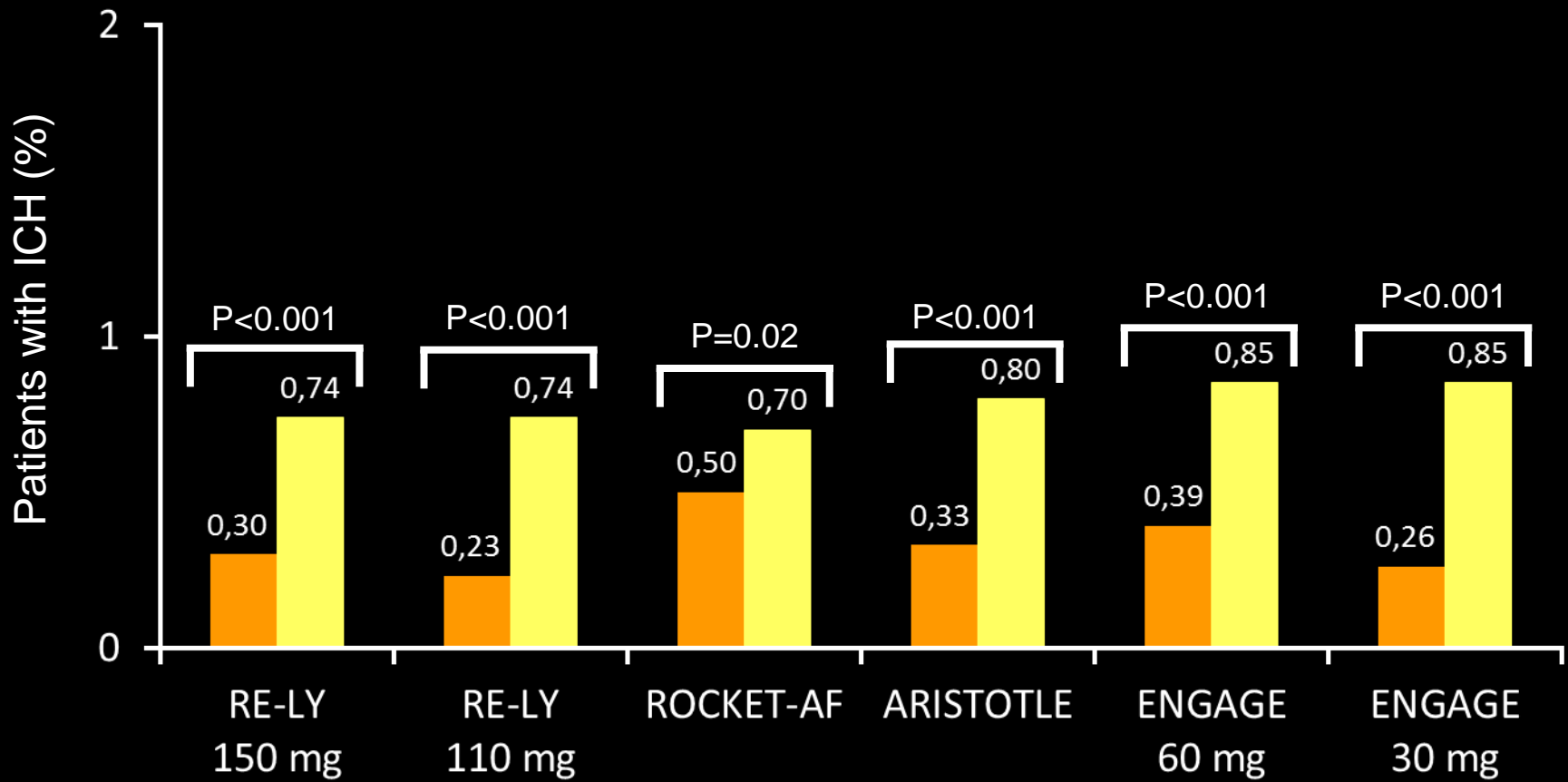
New agent as effective as but cheaper

New agent as effective as but more practical  
(route of administration, no lab monitoring, in/off procedures)

New agent as effective as but more properly used  
(more extended use in high risk population)

# Phase III AF trials: intracranial bleeding

■ NOAC ■ Warfarin



## NOACs for AFib: some differences

Dabigatran at a dose of 150 mg was associated with a reduction in ischemic stroke

Rivaroxaban given once a day was associated with a lower rate of fatal bleeding

Apixaban was associated with a reduction in all cause mortality

Both doses of edoxaban were associated with a reduced bleeding risk

# My talk today

- Achievements with traditional anticoagulants
- Clinical evidence about NOAs
- What's about my patients

# What's about my patients?

- Patients > 80 years
- CrCl 30-50 l/min
- Prior GI bleeding
- Prior intracerebral bleeding
- Gait apraxia and falls
- Cognitive impairment
- Secondary prevention after TIA or stroke
- Afib and carotid stenosis

# What's about my patients?

- **Patients > 80 years**
- CrCl 30-50 l/min
- Prior GI bleeding
- Prior intracerebral bleeding
- Gait apraxia and falls
- Cognitive impairment
- Secondary prevention after TIA or stroke
- Afib and carotid stenosis

# Age and VKA treatment for Afib

## Perugia University Anticoagulation Clinic II

**Patients:** 1675

### Gender

Males 868 (51.8%)

Females 808 (48.2%)

### Age

Range: 20-97

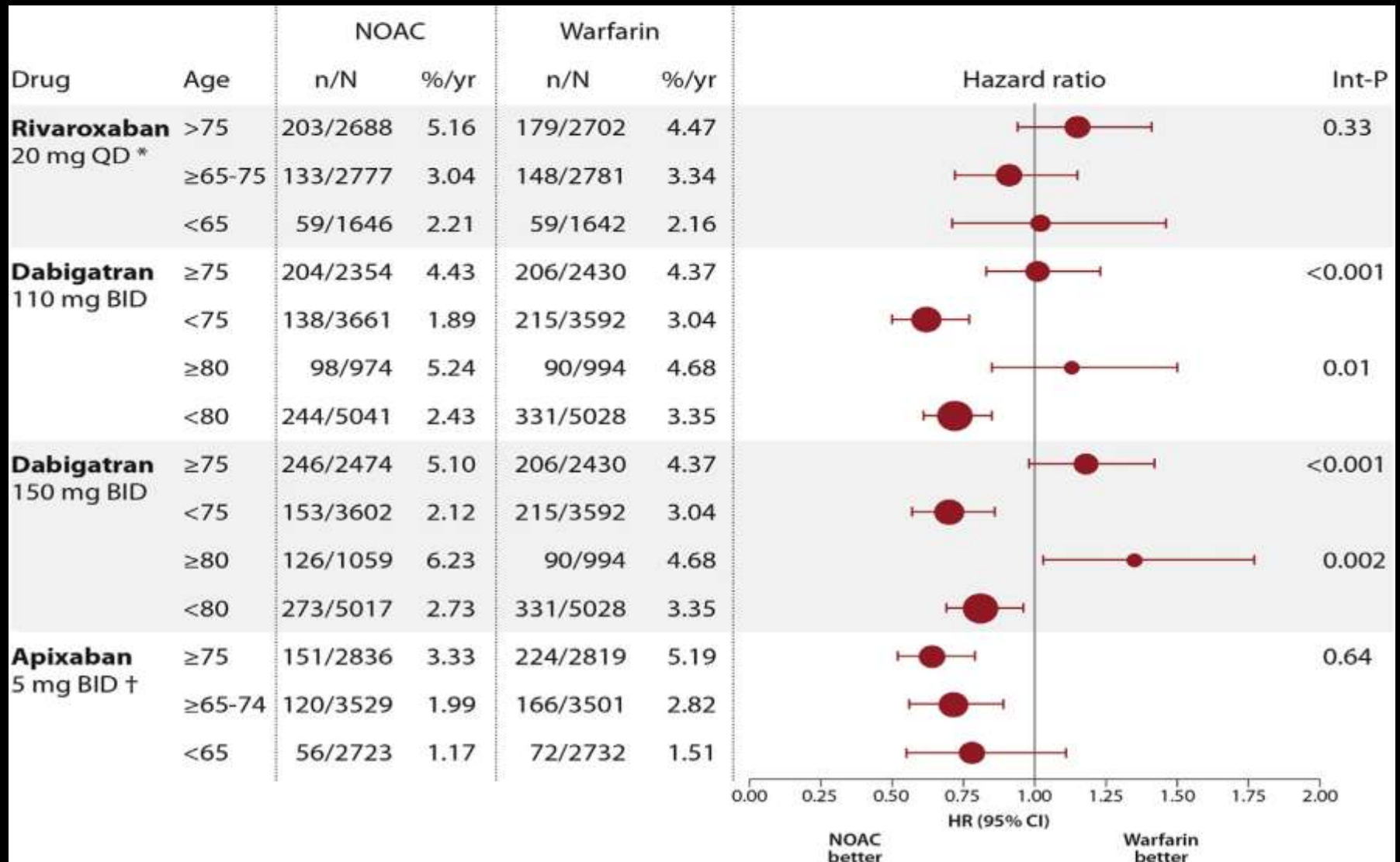
**Classe età**                      **N**                      **%**

< 65 years	142/1675	8.5
65-75 years	434/1675	25.9
76-79 years	307/1675	18.3
> 80 years	674/1675	40.2
> 90 years	118/1675	7.0

} 981  
patients  
(58.5%)



# Age and bleeding: NOAS vs. AVK in AFib



# NOAs-treated patients with NVAF: the Umbria Registry

NOAs patients: clinical trials vs. “regulatory therapeutic plan”

	NOAC Reg AF*(%)	Aristotle (%)	Rocket (%)	RE-LY (%)
CHADS2: 0-1	18	34	-	32
2	34	36	13	35
≥3	48	30	87	33
HASBLED: ≤ 3	55	77	79	
> 3	45	33	31	
Mean age, years	78	70 (median)	73 (median)	71

640 patients with NVAF

\*Study centers: Perugia, Assisi, Foligno, Spoleto

# NOAs-treated patients with VTE: the Umbria Registry

	Perugia VTE		Einstein DVT	Einstein PE
	DVT	PE		
Unprovoked, %	68.2	65.1	62.0	64.5
Cancer-related, %	10.8	11.6	6.0	4.6
Mean age, y	65.2	65.7	56.1	57.7

# The new scenario of oral anticoagulation

- New oral anticoagulants (NOAs) have been shown to be a valid alternative to AVK (and candidate to replace them in the near future)
- The proper use of NOAs will require new approaches in some specific clinical situations
- Simple and practical solutions are required to handle these situations to preserve the improved practicality associated with the use of NOAS

# Responsible use of NOAs

- Although safer than VKA, NOAs hold the risk of bleeding
- NOAs should be given for approved indications at validated doses (assessing the potential benefit in the individual patient)
- Patients should receive a complete information about the NOAs treatment at the start-up visit
- An adherence to treatment plan as well as a follow-up plan with regular visits should be set-up
- A hospital policy to deal with bleeding complications and emergency surgery should be set-up and spread-out