



17-20  
Dicembre  
2025  
Napoli

70<sup>o</sup> CONGRESSO  
NAZIONALE  
**SIGG**  
LIBERI E LONGEVI

Università degli  
Studi di Napoli  
Federico II  
Polo Didattico  
di **SCAMPIA**



SOCIETÀ ITALIANA  
DI GERONTOLOGIA  
E GERIATRIA



**Auxologico**  
Ricerca e cura per la tua salute IRCCS

# Terapia del fenotipo bradicardico

**Michele Brignole**

*IRCCS Istituto Auxologico Italiano*

*Milan, Italy*

# Reflex syncope and bradycardiac phenotype

<b>DIAGNOSIS</b>	<b>TEST</b>	<b>BRADYCARDIAC PHENOTYPE LIKELY</b>
CI reflex syncope	Supine and standing 10 s CSM	Reproduction of spontaneous (pre)syncope, with asystolic pause/s >3 s.
CI reflex syncope	Tilt table test	Typical ECG pattern of of hypotension and bradycardia with asystolic pauses >3 s
CI reflex syncope	Prolonged ECG monitoring (wearable and ILR)	Typical ECG pattern of asystolic (>3 s) vasovagal syncope or documentation of asymptomatic asystolic pause >6 s of likely reflex origin
Idiopathic AV block (low adenosine syncope)	Prolonged ECG monitoring (wearable and ILR)	Typical ECG pattern of idiopathic AV block

# Practical guide for personalised mechanism-based therapy of non-cardiac syncope

Phenotypes

**Hypotensive**

**Mixed (hypo and brady)**

**Bradycardic (asystolic)**

Hypertension?

Yes

No

Deprescription/optimization  
of antihypertensive drugs

Psychoactive drugs?

Yes

No

Deprescription/optimization  
of psychoactive drugs

Any other form of  
hypotension?

Elastic garments  
Fludrocortisone  
Midodrine

Age?

<60 yrs

<60 yrs

≥60 yrs

**Theophylline**  
(idiopathic AV block)

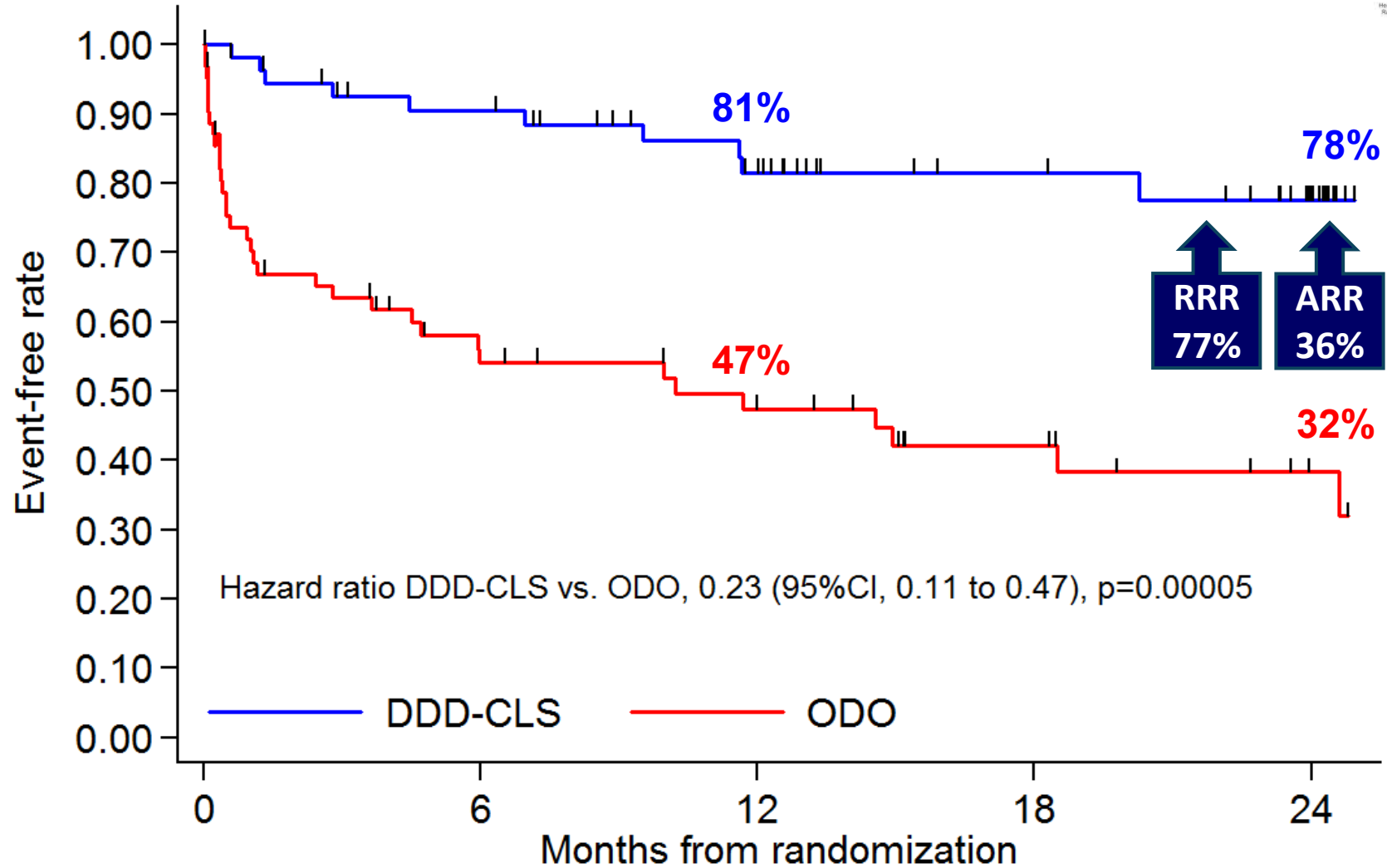
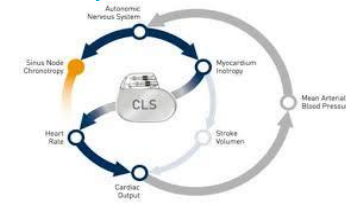
**Cardio-neuro  
ablation**

**Cardiac pacing**  
(DDD-CLS better)

## Randomised controlled trials of cardiac pacing in patients with cardioinhibitory reflex syncope

	Test	Pacing mode	Age, yrs	Syncope recurrence at 1 year		P value
				Active	Control	
ISSUE 3	ILR	DDD-RDR vs Pm Off	63	<b>25%</b>	<b>37%</b>	0.039
Claesson	CSS	DDD vs no Pm	75	<b>10%</b>	<b>40%</b>	0.008
Brignole	CSS	DDD vs no Pm	70	<b>0%</b>	<b>36%</b>	0.001
VASIS PM	HUT	DDI hysteresis vs no Pm	63	<b>0%</b>	<b>39%</b>	0.0006
SYDIT	HUT	DDD-RDR vs no Pm	58	<b>3%</b>	<b>24%</b>	0.004
SPAIN	HUT	DDD-CLS vs DDI 40	56	<b>9%</b>	<b>46%</b>	0.0001
BIOSync CLS	HUT	DDD-CLS vs Pm Off	62	<b>19%</b>	<b>53%</b>	0.00005

# Primary endpoint: Syncope recurrence



**RRR 77%**  
**ARR 36%**  
**NNT=2.2**

Number at risk		0	6	12	18	24
DDD-CLS	63	45	34	22	12	6
ODO	64	28	20	13	6	3

# Recommendations for pacing for reflex syncope (2021 ESC guidelines on cardiac pacing)

Recommendations	Class	Level
<p>Dual-chamber cardiac pacing is indicated to reduce recurrent syncope in patients aged &gt;40 years, with <b>severe, unpredictable, recurrent</b> syncopes who have <b>asystolic pauses</b> documented by:</p> <ul style="list-style-type: none"><li>• spontaneous documented symptomatic asystolic pause/s &gt;3 s or asymptomatic pause/s &gt;6 s due to sinus arrest or AVB; or</li><li>• cardioinhibitory asystolic carotid sinus syndrome; or</li><li>• asystolic syncope during tilt testing</li></ul>	I	A

# Idiopathic paroxysmal AV block

## Case study

- 26 yrs, female, 2 syncopes **w/t prodrome**
- **normal heart, normal ECG**, negative EPS
- Holter monitoring

A)

1:54:25 Bradys; Nb QRS=10; Durée=27,73s; FC moy=19min<sup>-1</sup>



B)

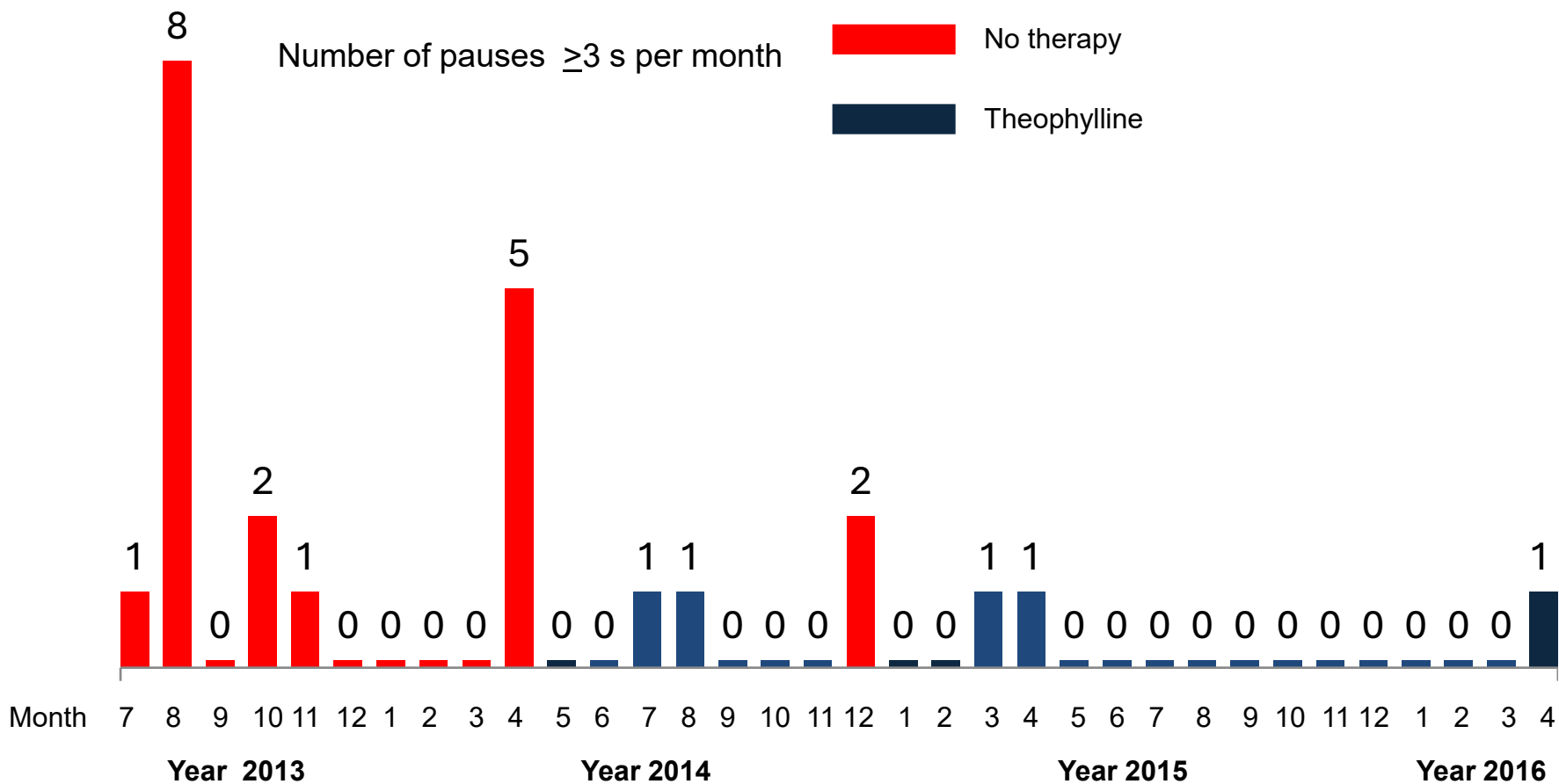
2:06:00 Bradys; Nb QRS=6; Durée=20,55s; FC moy=15min<sup>-1</sup>



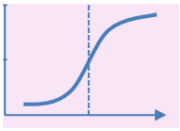
**APL=0.11  $\mu$ M (nv 0.40 – 0.80)**

### Case LAV08/13:

- 72 yrs, male, 2 syncopes w/t prodrome
- normal heart, normal ECG, negative EPS
- negative tilt testing; negative ADO test
- July 2013: ILR implantation
- August 26, 2013:

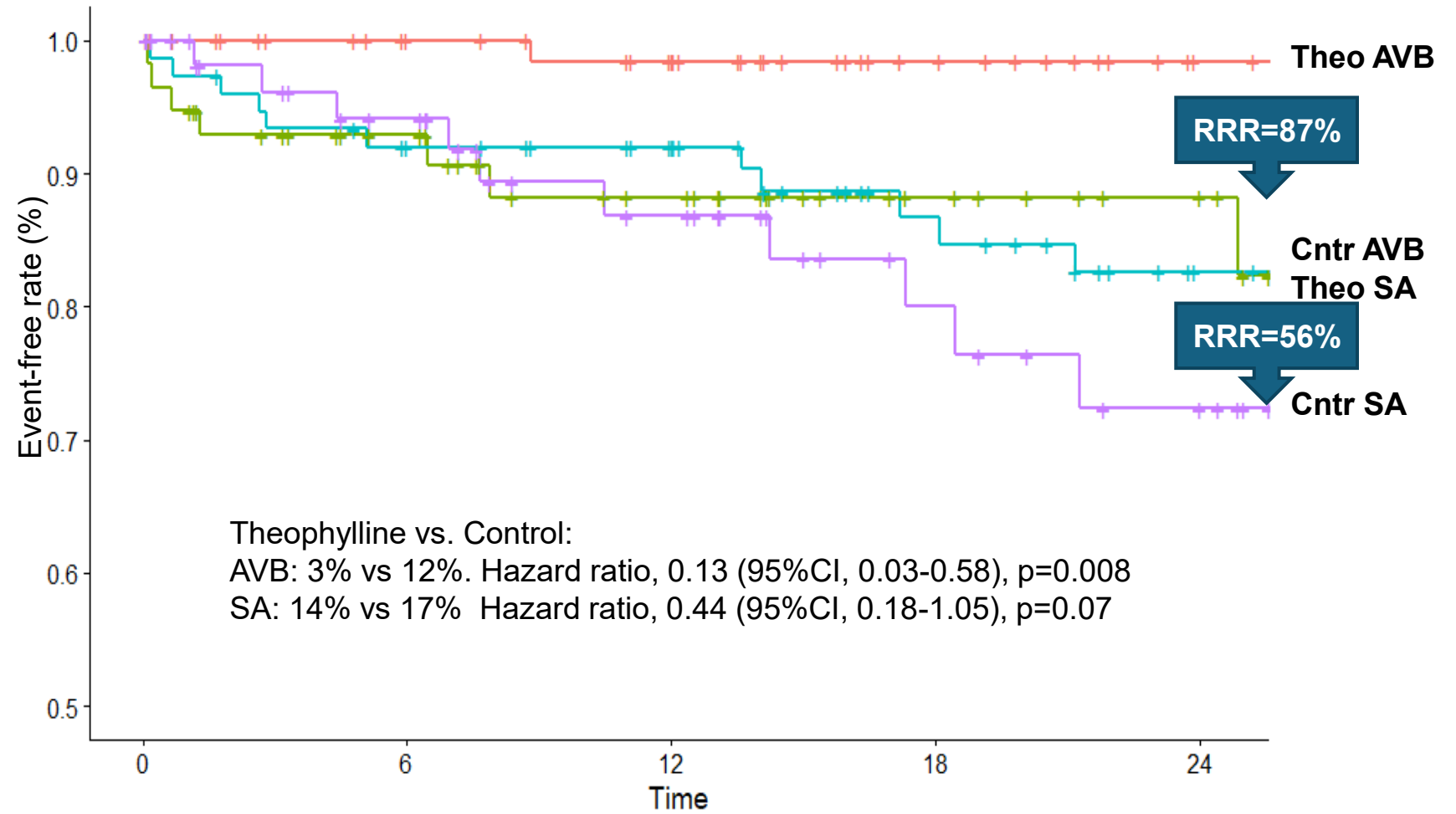


Case #2, M, 72 yrs

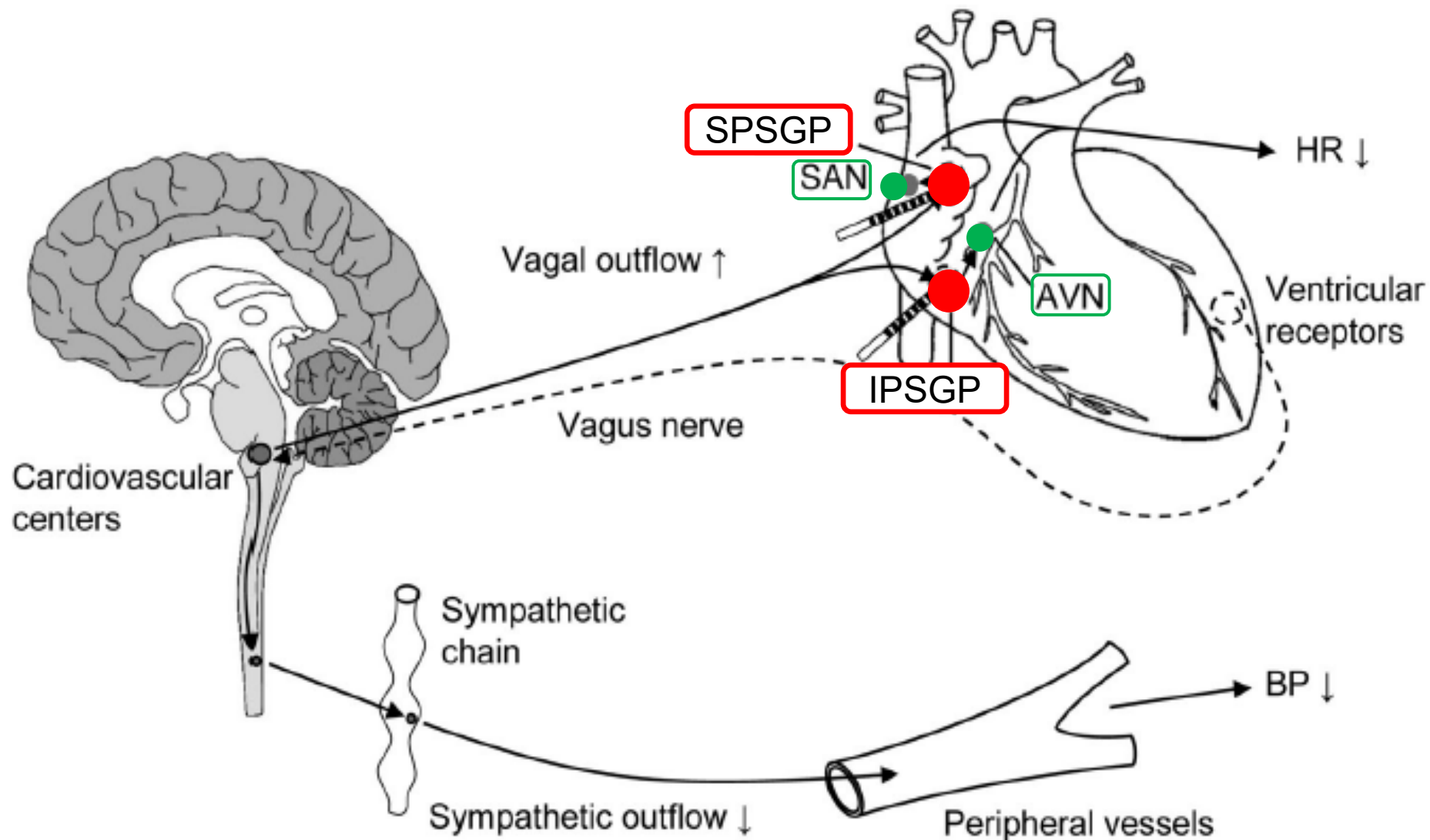


# TheoUSA trial

## Recurrence of syncope due to AVB and SA



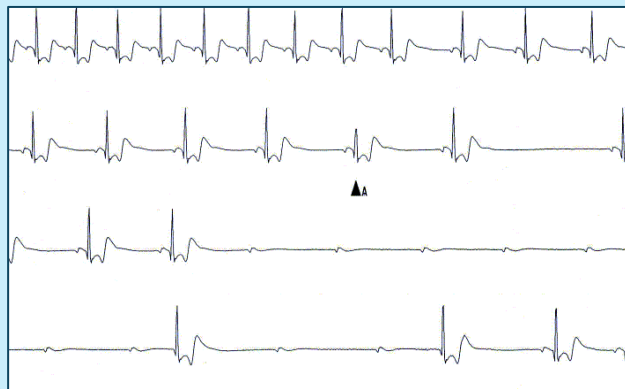
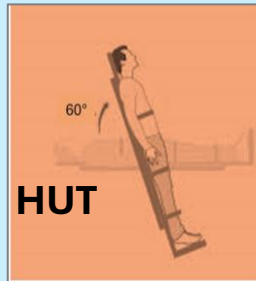
# The rationale for GP ablation: vagal denervation of SAN and AVN



# IDENTIFY the proper candidate for CNA

What  
is  
known

Asystolic reflex syncope  
documented by:



What  
is not  
known

*Less suitable in:*

- Mixed forms
- Non-syncopal extrinsic SND/AVB

*Do not perform in:*

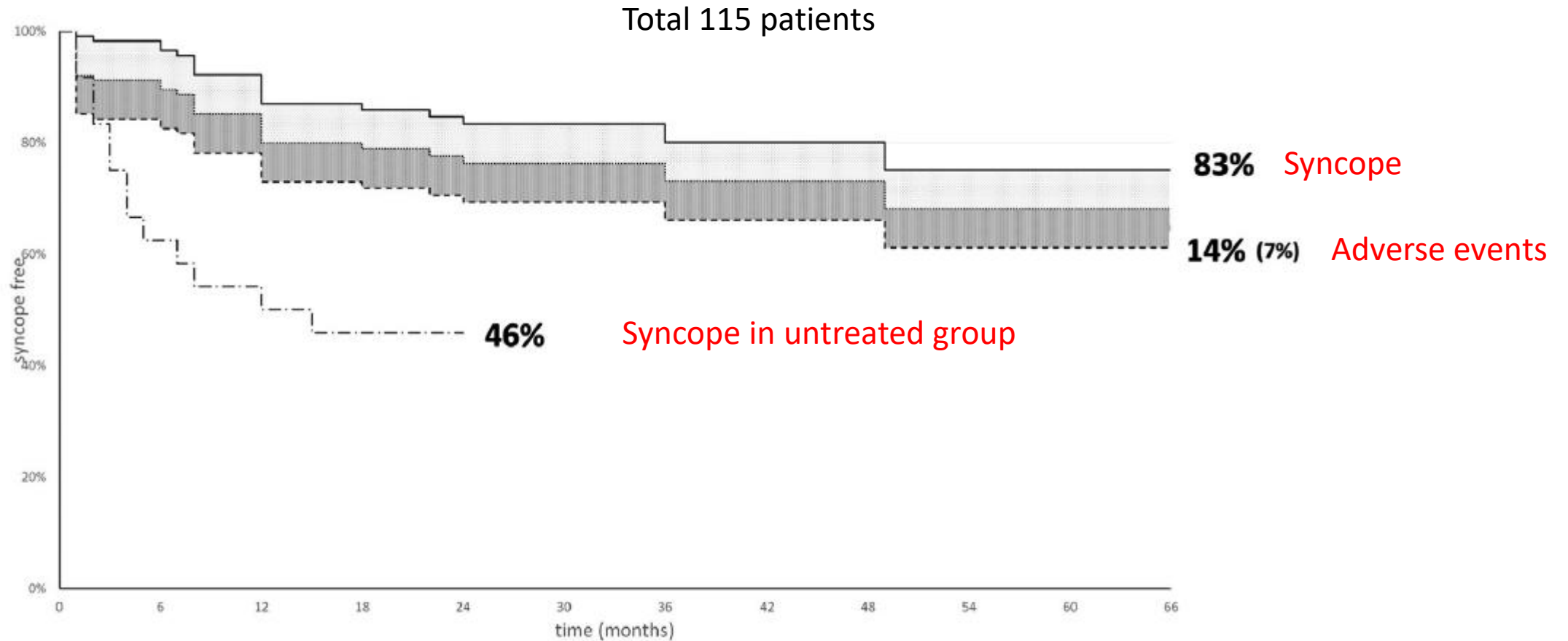
- VD forms
- Intrinsic SND/AVB

# Cardioneuroablation for reflex asystolic syncope: Mid-term safety, efficacy, and patient's acceptance <sup>e</sup>

Piotr Kulakowski, MD, PhD, Jakub Baran, MD, PhD, Agnieszka Sikorska, MD, PhD, Tomasz Krynski, MD, Michal Niedzwiedz, MD, Malgorzata Soszynska, BSN, Roman Piotrowski, MD, PhD

Heart Rhythm 2024; 21: 282-291

**Bi-atrial ablation**



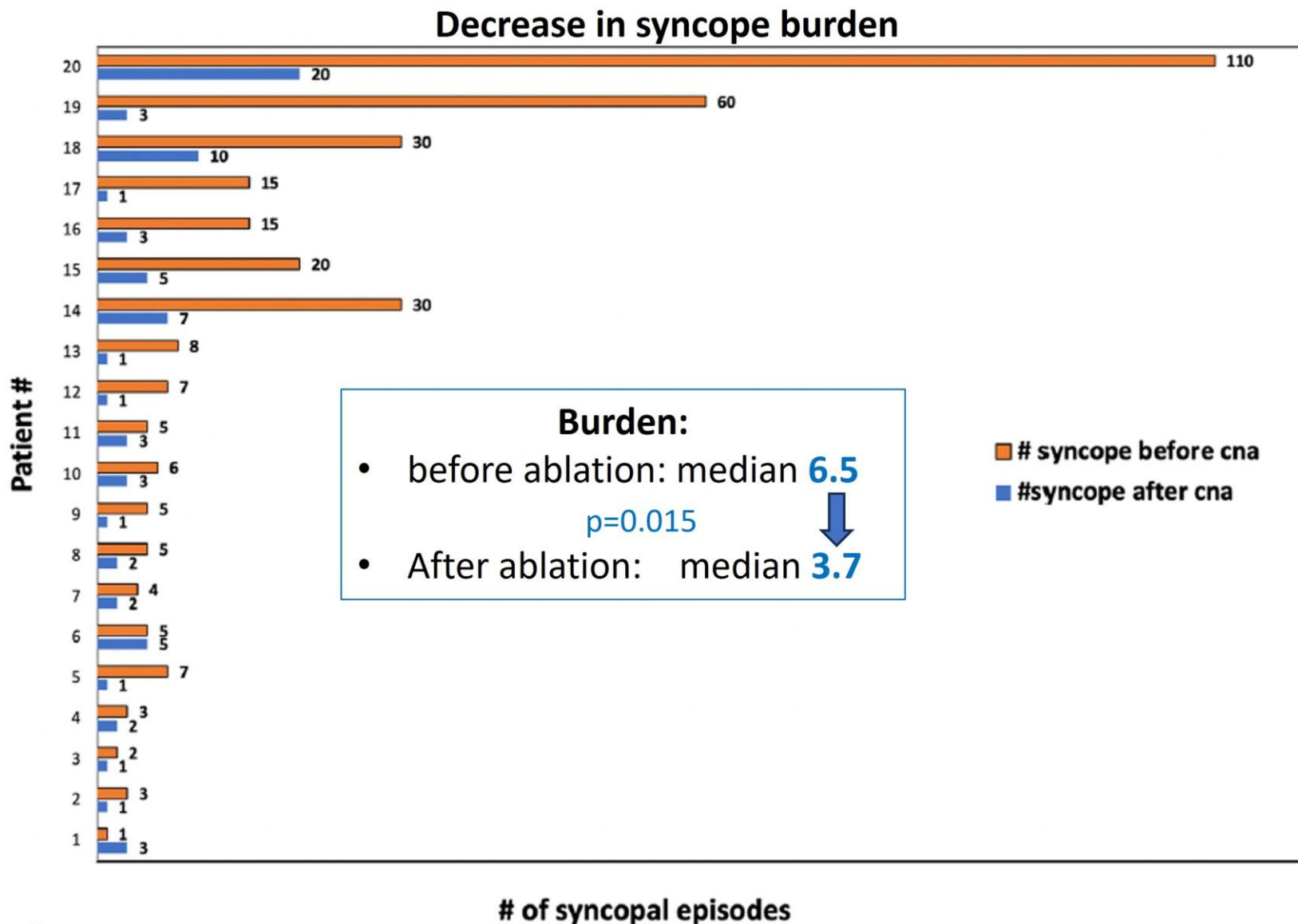
Time (months)	12	18	24	30	36	42	48	54	60
Number at risk	106	81	64	44	26	22	16	8	2

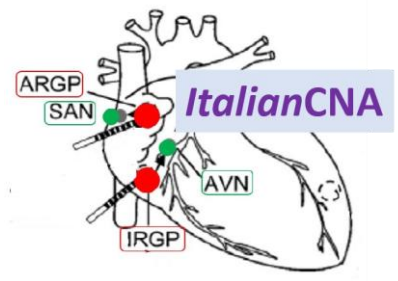
# Cardioneuroablation for reflex asystolic syncope: Mid-term safety, efficacy, and patient's acceptance <sup>e</sup>

Piotr Kulakowski, MD, PhD, Jakub Baran, MD, PhD, Agnieszka Sikorska, MD, PhD, Tomasz Krynski, MD, Michal Niedzwiedz, MD, Malgorzata Soszynska, BSN, Roman Piotrowski, MD, PhD

Heart Rhythm 2024; 21: 282-291

**Bi-atrial ablation**

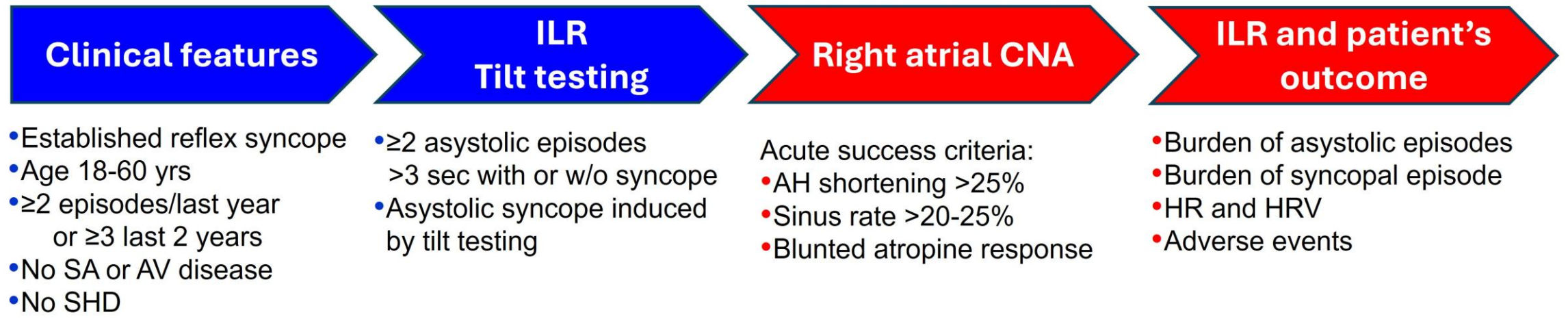




# Right atrial cardioneuroablation of asystolic reflex syncope

## Eligibility

## Study



### Clinical features

- Established reflex syncope
- Age 18-60 yrs
- ≥2 episodes/last year or ≥3 last 2 years
- No SA or AV disease
- No SHD

### ILR Tilt testing

- ≥2 asystolic episodes >3 sec with or w/o syncope
- Asystolic syncope induced by tilt testing

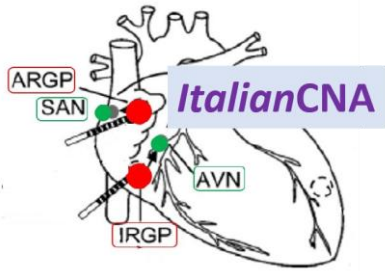
### Right atrial CNA

- Acute success criteria:
- AH shortening >25%
  - Sinus rate >20-25%
  - Blunted atropine response

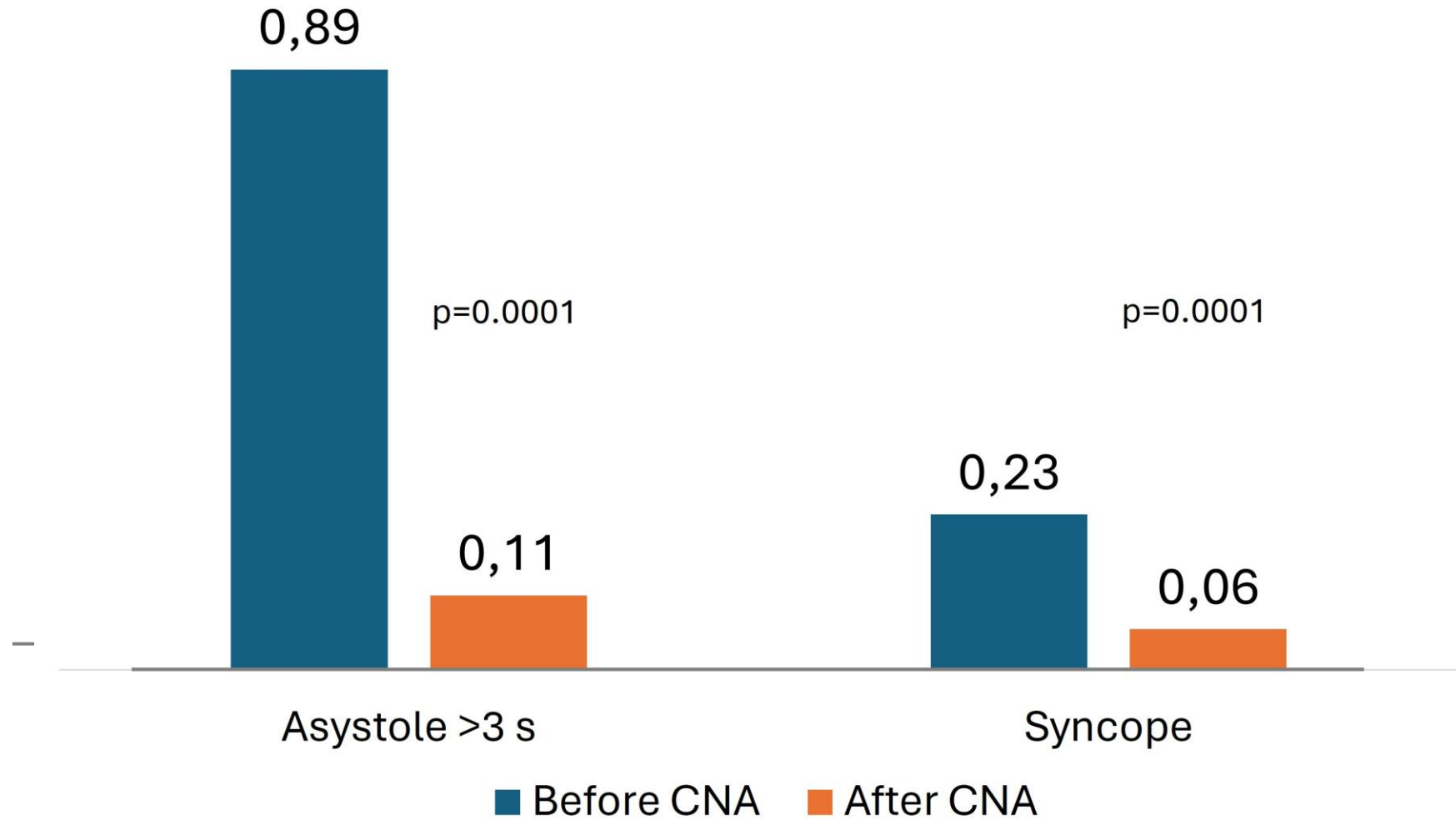
### ILR and patient's outcome

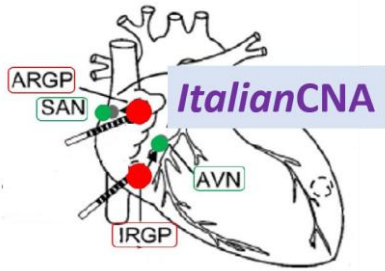
- Burden of asystolic episodes
- Burden of syncopal episode
- HR and HRV
- Adverse events

Calò et al. Heart Rhythm 2025; 22: e951-e958

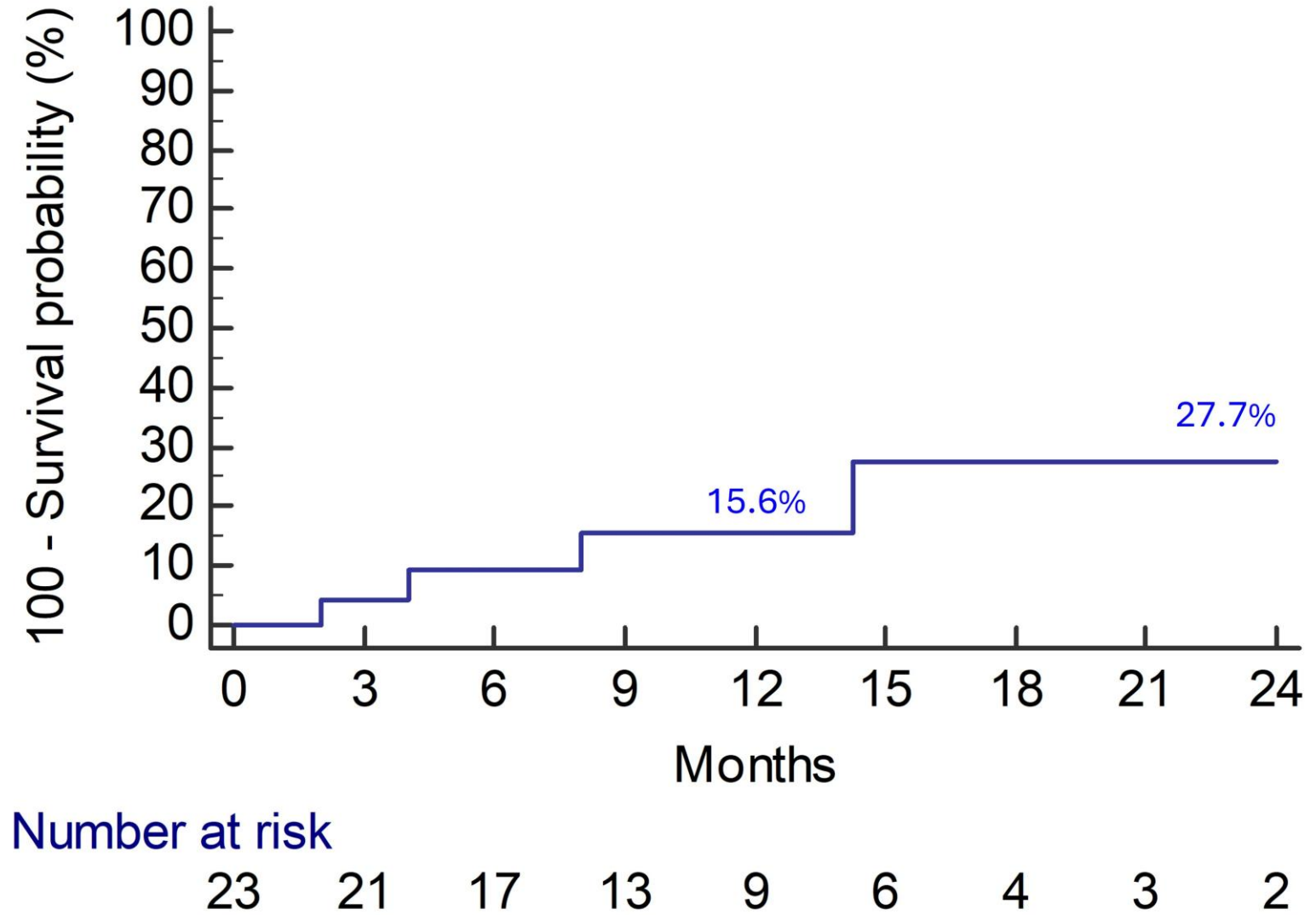


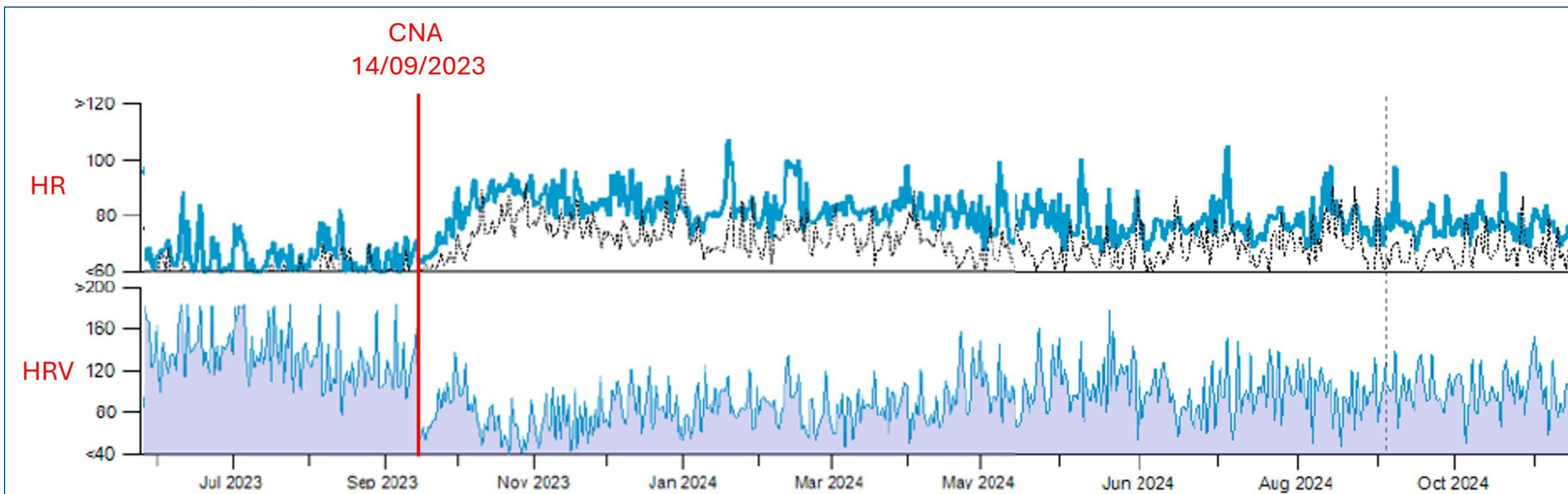
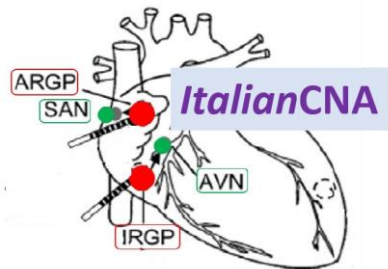
## Episodes per month





## Recurrence of syncope





# Bi-atrial CNA

Kulakowski P. Heart Rhythm 2023

Adverse event	Population (n=115)
Redo CNA	3 (3%)
Pacemaker implantation	5 (4%)
Transient dyspnoea	6 (5%)
Chronic chest pain	4 (3%)
Decreased exercise capacity	14 (12%)
Transient palpitations (<3mos)	31 (27%)
Persistent palpitations	8 (7%)

# Right atrial CNA

Italian CNA. Heart Rhythm 2025

Adverse event	Population (n=28)
Redo CNA	1 (4%)
Pacemaker implantation	2 (7%)
Transient dyspnoea	1 (4%)
Chronic chest pain	0 (0%)
Decreased exercise capacity	0 (0%)
Transient palpitations (<3 mos)	3 (11%)
Persistent palpitations	0 (0%)

## Therapy of mixed (hypotensive and bradycardiac) phenotype

Goal: to increase average 24-hour SBP, to prevent SBP drops on ABPM and to prevent asystolic episodes

Interventions and target: the most appropriate among dual (antihypotensive and antibradycardiac) therapies

*Goal: to prevent asystolic episodes*

**Theophylline**

Idiopathic AV block

Intervention:  
300 mg b.i.d.  
(range 100 mg b.i.d.  
to 300 mg t.i.d.)

**Cardio-neuro-ablation**

Ablation of the superior and  
inferior paraseptal ganglia,  
age < 60 years

Target:  
Increase in heart rate,  
shortening of AH interval  
and of Wenckebach cycle

**Cardiac pacing**

DDD-CLS pacing,  
age ≥ 60 years

CLS programming:  
Basic rate of 50 bpm,  
max CLS rate 120 bpm,  
CLS response “Medium”,  
resting rate control OFF