

# PRECISE STUDY

Occurrence of significant long PR intervals in patients implanted for sinus node dysfunction and monitored with SafeR

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## Liens d'interet

Etude menée avec le soutien logistique de SORIN group devenu Microport CRM

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# Occurrence of significant long PR intervals in patients implanted for sinus node dysfunction and monitored with SafeR: the PRECISE study

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# Rappel

- Allongement du PR le plus souvent benin et asymptomatique
- Certaines études suggèrent toutefois une augmentation du risque de
  - FA
  - implantation de PM
  - mortalité
- Définition clinique du BAV 1: PR > 200 ms
- La prévalence et incidence sont mal connus
- Le mode Safe R de MicroPort CRM préserve la conduction spontanée et gère le délai AV

# But

Etudier à 12 mois chez des patients implantés pour dysfonction sinusale sans BAV d'un stimulateur cardiaque double chambre REPLY dual chamber pacemaker (Sorin CRM, Clamart, France)

1. l'incidence de l'allongement du PR
2. les facteurs predictifs de cet allongement
3. L'association de l'allongement du PR et de l'incidence de FA

# Methode

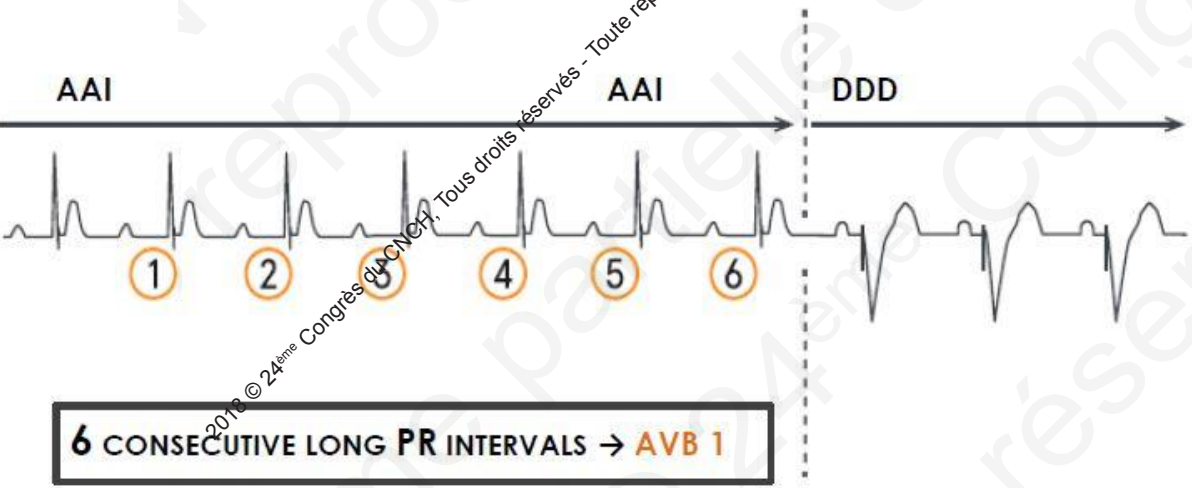
- Etude française multicentrique, prospective de cohorte
- Inclusion Avril 2012 à septembre 2013
- Cloture janvier 2015
- Pt  $\geq 18$  ans implanté avec un PM DC safe R
- Exclusion: BAV haut grade, FA permanente
- Safe R activé à l'implantation

# Methode

- Critere primaire : switchs sur BAV1 (statistique Safe R)
  - Critere secondaire: Repli  $> 1$  mn/ 24h
-



# SafeR BAV 1



## SafeR pacing mode

In the presence of an AVB1, the algorithm does not allow more than 6 consecutive PR or AR intervals longer than a programmable value (nominally 350 and 450 ms, respectively).

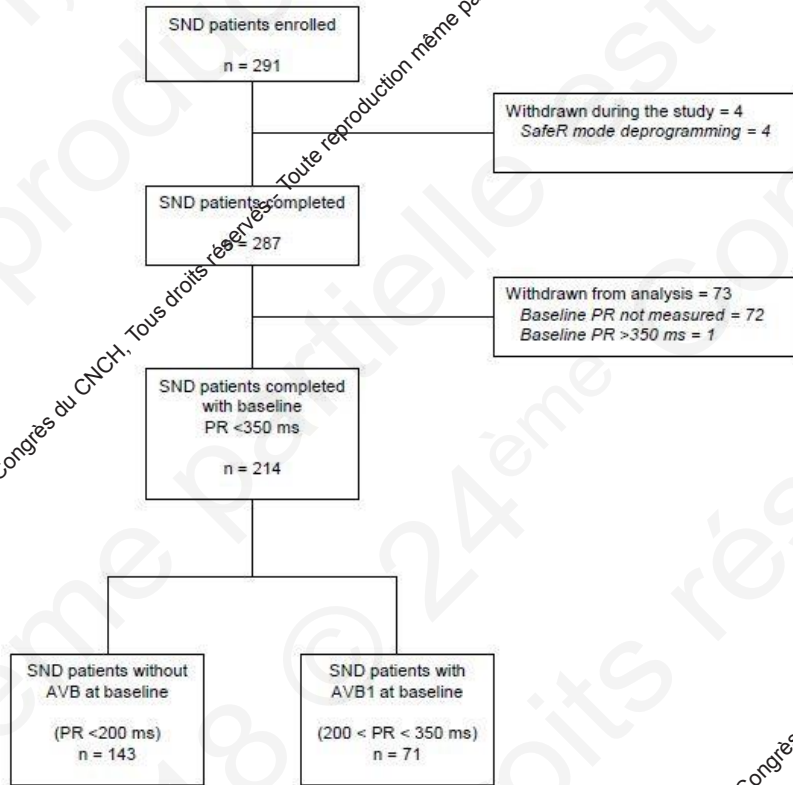
If a 7th long PR interval is detected, the algorithm switches to DDD pacing mode.

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# Resultats

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# PRECISE: results - population



291 patients DS

- 4 pts Safe R off
- 72 patients, PR basal non mesuré
- 1 pt PR > 350 ms.

Analyse sur **214 patients**

143 patients PR basal < 200 ms

71 patients PR basal 200-350 ms.

**Baseline characteristics of sinus node dysfunction patients with baseline PR <350 ms (n=214)**

**Clinical characteristics**

Male	95 (44.4%)
Age at enrollment (years)	78.9±8.4
Atrial rhythm disorder*	113 (55.4%)
Flutter	8 (3.9%)
Fibrillation	99 (48.5%)
Other	6 (2.9%)
Medication#	
Sotalol	14 (6.9%)
Digoxin	3 (1.5%)
Non-dihydropyridine CCB**	3 (1.5%)
Flecainide	13 (6.4%)
Beta-blocker	65 (32.2%)
Amiodarone	43 (21.3%)
Other	81 (40.1%)
None	44 (21.8%)

**Electrical characteristics**

PR, mean (ms)	192±49
PR, median (ms)	188 (160; 220)
AP, mean (ms)	244±56
AR, median (ms)	240 (200; 266)

**Intervention**

First implant	193 (90.2%)
Replacement	20 (9.3%)
Upgrade	1 (0.5%)

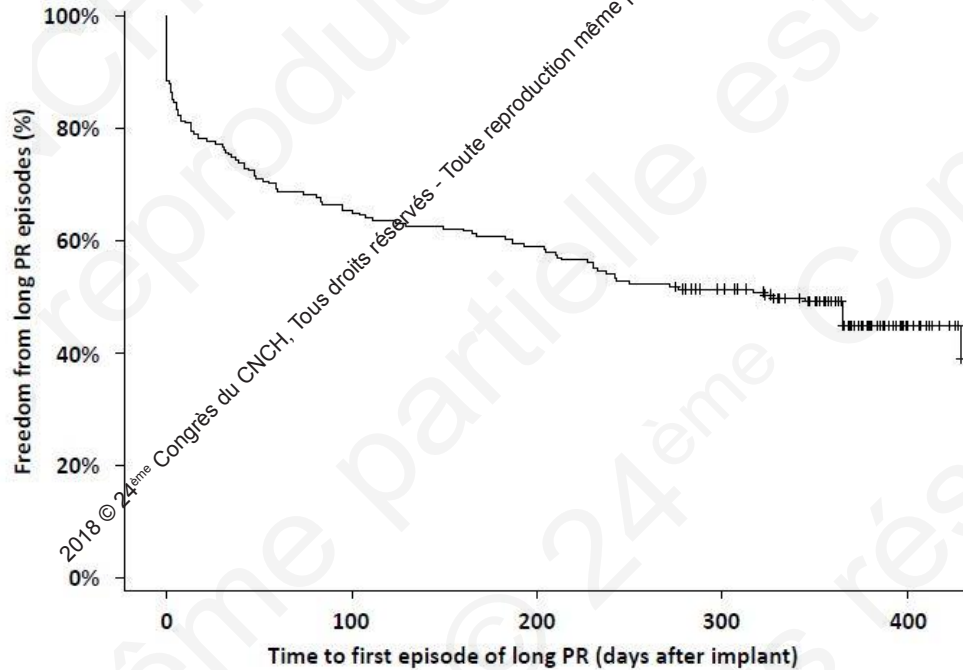
**Pacemaker model**

REPLY DR™	213 (99.5%)
REPLY D™	1 (0.5%)

\*Values missing for 10 patients. #Values missing for 12 patients. \*\*Diltiazem or verapamil.

Suivi moyen 370±78 days.

# Incidence des Switch sur PR long



54.2% des 214 patients ont eu 1 épisode ou plus de switch sur PR long

62% de switch si  $200 < \text{PR basal} < 350$  ms

50,4% de switch si  $\text{PR basal} < 200$  ms

79.3% jour et nuit

17.2% seulement le jour

3.5% seulement la nuit

# PRECISE: results – Primary endpoint

UNIVARIATE ANALYSIS OF THE INCIDENCE OF LONG PR IN PATIENTS WITH SINUS NODE DISEASE AND BASELINE PR <350 MS

Variable	n	Incidence of long PR episodes		Comparison	OR (95% CI)	P-value
		Yes (N=116)	No (N=98)			
Age	214			>75 vs <75 years	1.06 (0.59 to 1.91)	0.854
<75 years	62 (29.0%)	33 (53.2%)	29 (46.8%)			
>75 years	152 (71.0%)	83 (54.6%)	69 (45.4%)			
Gender	214			Male vs Female	1.31 (0.76 to 2.25)	0.334
Female	119 (55.6%)	61 (51.3%)	58 (48.7%)			
Male	95 (44.4%)	55 (57.9%)	40 (42.1%)			
<b>Atrial rhythm disorder*</b>	204			Yes vs No	1.78 (1.02 to 3.10)	<b>0.044</b>
No	91 (44.6%)	41 (45.1%)	50 (55.0%)			
Yes	113 (55.4%)	67 (59.3%)	46 (40.7%)			
<b>PR</b>						<b>0.094</b>
Patients	199	105 (52.8%)	94 (47.2%)		1.01 (1.00 to 1.01)	
Duration (ms)		198±50	186±46			
AR						0.599
Medic						0.107
Sotalc						0.564
Digoxi						0.734
Non-dihydropyridine CCB‡	214			Yes vs No	NA	NA
No	211 (98.6%)	116 (55.0%)	95 (45.0%)			
Yes	3 (1.4%)	0 (0.00%)	3 (100.00%)			
<b>Flecainide</b>	214			Yes vs No	0.31 (0.09 to 1.04)	<b>0.057</b>
No	201 (93.9%)	112 (55.7%)	89 (44.3%)			
Yes	13 (6.1%)	4 (30.8%)	9 (69.2%)			
Beta-blockers	214			Yes vs No	1.24 (0.65 to 2.35)	0.519
No	149 (69.6%)	77 (51.7%)	72 (48.3%)			
Yes	65 (30.4%)	39 (60.0%)	26 (40.0%)			
<b>Amiodarone</b>	214			Yes vs No	2.12 (1.00 to 4.46)	<b>0.049</b>
No	171 (79.9%)	86 (50.3%)	85 (49.7%)			
Yes	43 (20.1%)	30 (69.8%)	13 (30.2%)			

Le seul facteur predictif de switch sur PR long est l'amiodarone ( multivarié )  
(OR, 2.50; 95 CI, 1.20-5.21; P=0.014)

# Analyse univariée de l'incidence de la FA sur DS

Variable	n (%)	Incidence of atrial fibrillation		Comparison	OR (95% CI)	P
		Yes <sup>a</sup> (n = 64)	No <sup>a</sup> (n = 150)			
Age	214			>75 versus < 75 years	1.90 (0.95–3.83)	0.071
< 75 years	62 (29.0)	13 (21.0)	49 (79.0)			
> 75 years	152 (71.0)	51 (33.6)	101 (66.5)			
Sex	214			Male versus Female	0.96 (0.53–1.74)	0.90
Female	119 (55.6)	36 (30.3)	83 (69.8)			
Male	95 (44.4)	28 (29.5)	67 (70.5)			
Atrial rhythm disorder <sup>b</sup>	202			Yes versus No	5.77 (2.78–11.99)	< 0.001
No	91 (44.6)	11 (12.1)	80 (87.9)			
Yes	111 (55.4)	50 (44.3)	63 (55.8)			
PR interval	199				1.00 (0.99–1.00)	0.32
Patients		60 (30.2)	139 (69.9)			
Duration (ms)		187 ± 48	195 ± 49			
AR interval	102				1.00 (0.99–1.01)	0.68
Patients		30 (29.4)	72 (70.6)			
Duration (ms)		248 ± 55	243 ± 57			
Long PR interval (AVB1 switch)	214			Yes versus No	1.72 (0.92–3.24)	0.091
No	98 (45.8)	23 (23.5)	75 (76.5)			
Yes	116 (54.2)	41 (35.3)	75 (64.7)			
Verapamil	214				1.00 (0.50–2.00)	0.99
No	107 (50.0)	27 (25.2)	80 (74.8)			
Yes	107 (50.0)	37 (34.6)	70 (65.4)			
Metoprolol	214				1.00 (0.50–2.00)	0.99
No	107 (50.0)	27 (25.2)	80 (74.8)			
Yes	107 (50.0)	37 (34.6)	70 (65.4)			
Amiodarone	214			Yes versus No	1.83 (0.90–3.75)	0.097
No	171 (79.9)	44 (25.7)	127 (74.3)			
Yes	43 (20.1)	20 (46.5)	23 (53.5)			

Switch sur PR long prédictif de FA : Tendances univariées

Le seul facteur prédictif de survenue de FA en multivarié est un antécédent de FA (OR, 1.78; 95% CI, 1.02 to 3.10; P=0.044)

# conclusions

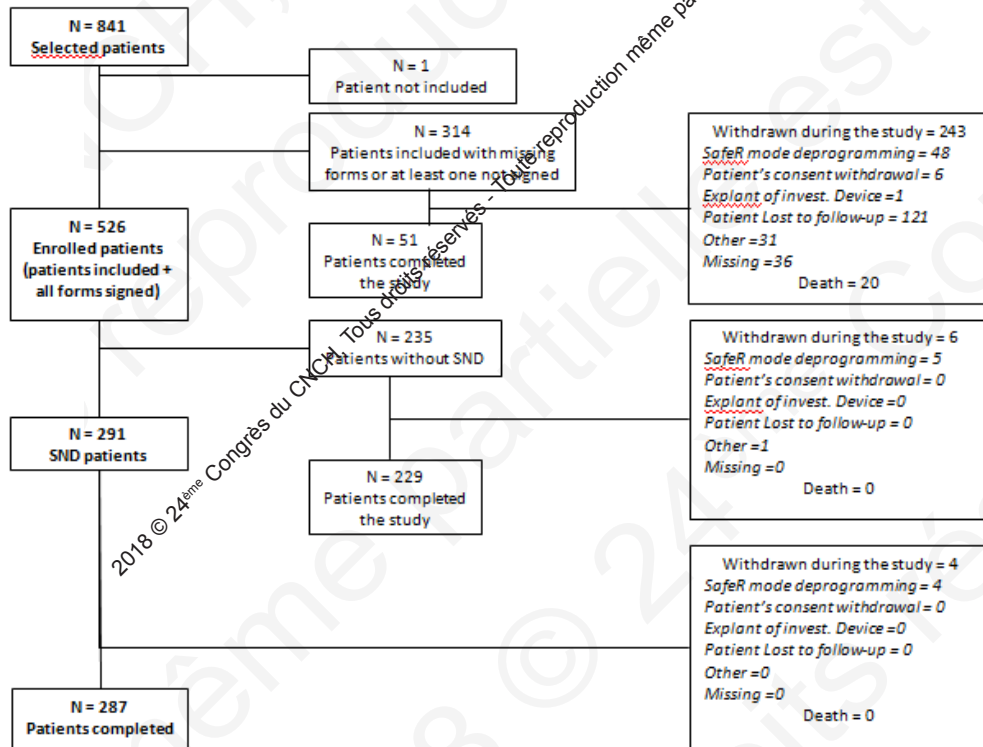
- Plus de 50% de dysfonction sinusale ont présenté au moins un épisode de switch sur 6 PR long consécutifs à 12 mois
- L'amiodarone est le seul facteur prédictif de switch sur BAV. Association forte entre switch sur PR long et survenue de FA. Mécanisme de fibrose binodale ?
- Etude qui plaide pour le double chambre dans la dysfonction sinusale car
  - Switch sur BAV
  - Détection de FA



# PRECISE: results – population

- We wanted to demonstrate that at least 10% of implanted SND patients presented PR lengthening after 1 year
- This calculation was based on additional results of the SAVER study: incidence of patients presenting AVB 1 after 1 year was estimated at 16%
- Original sample size estimated at: 848 patients
- 285 evaluable patients required for primary endpoint

# PRECISE: results - population



## Original patient disposition

848 patients inclus

285 Patients evaluables

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# PRECISE: results – Overview

## Incidence and predictors of long PR

- Over half (n=116 [54.2%]) of the 214 patients experienced one or more episodes of long PR interval during the study
- Amiodarone was the only independent predictor of long PR occurrence (OR 2.50; 95 CI, 1.20-5.21;  $P=0.014$ )

## Incidence and predictors of AF

- Close to a third of patients (29.6% [n=63]) had  $\geq 1$  episode of AF during the study
- History of atrial rhythm disorders, medication, amiodarone (long PR (AVB1 switch)), and age were shown by univariate analysis to be potentially associated with the incidence of AF
- Further analysis (multivariate) confirmed that only a history of atrial rhythm disorders at baseline was associated with AF incidence (OR, 1.78; 95% CI, 1.02 to 3.10;  $P=0.044$ )
- However, almost twice as many patients with long PR occurrence experienced incident AF than patients without long PR occurrence (19.3% versus 10.3%; OR, 1.86; 95 CI, 0.97-3.61;  $P=0.051$ )

# PRECISE: results - safety

## Safety

- There were no deaths in the sinus node dysfunction (SND) population.
- 10 patients (4.7%) developed 12 adverse events, of which nine were serious adverse events: ventricular tachycardia (2), stroke (2), coronary artery procedure (1), pocket infection (1), acute coronary syndrome (1), weakness (1) and renal failure (1).
- There were no events that were related to the study device.
- There was one report of diaphragmatic stimulation related to unipolar stimulation, which was overcome by switching to bipolar stimulation.

# PRECISE: results – Overview

## Incidence and predictors of long PR

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## Incidence and predictors of AF

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