

# Disclosures

- No conflict of interest
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Non-Steroidal Anti-Inflammatory (NSAIDs)  
Treatment for Post-Operative Pericardial Effusion:  
The POPE Study  
**A Multicenter, Double-Blind,  
Randomized Trial**

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on behalf of the French Society of Cardiology

Les Grands Prés, Villeneuve Saint Denis; Hôpital Broussais, Paris; Hôpital Bichat,  
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# Post Operative Pericardial Effusions

- Frequent:
  - ✓ 50-80% of cardiac operated patients
- Asymptomatic; spontaneously decrease within 2-4 weeks
- Can convert into cardiac tamponade (CT):
  - 1 % of operated patients:
    - 1/3: early CTs: day 1- day 7: due to intra-pericardial bleeding
    - 2/3: late CTs: day 8 – day 30: mechanism: inflammation and bleeding

# NSAIDs as a Treatment of Post Operative Pericardial Effusions: an Old Habit

- Prescribed in 40-77% of the patients<sup>1</sup> having an effusion

## Although:

- Is it effective ?:
  - ✓ no study has ever shown their efficacy for this condition
- Is it dangerous ?:
  - ✓ multiplies by 1.5 to 2 the risk of myocardial infarction and acute heart failure
  - ✓ by 3 renal failure (x 6 If ACE-I co-administration)
  - ✓ by 4 gastrointestinal tract bleeding (x 8 if co-administration of a VKA or low dose aspirin).

# POPE Study

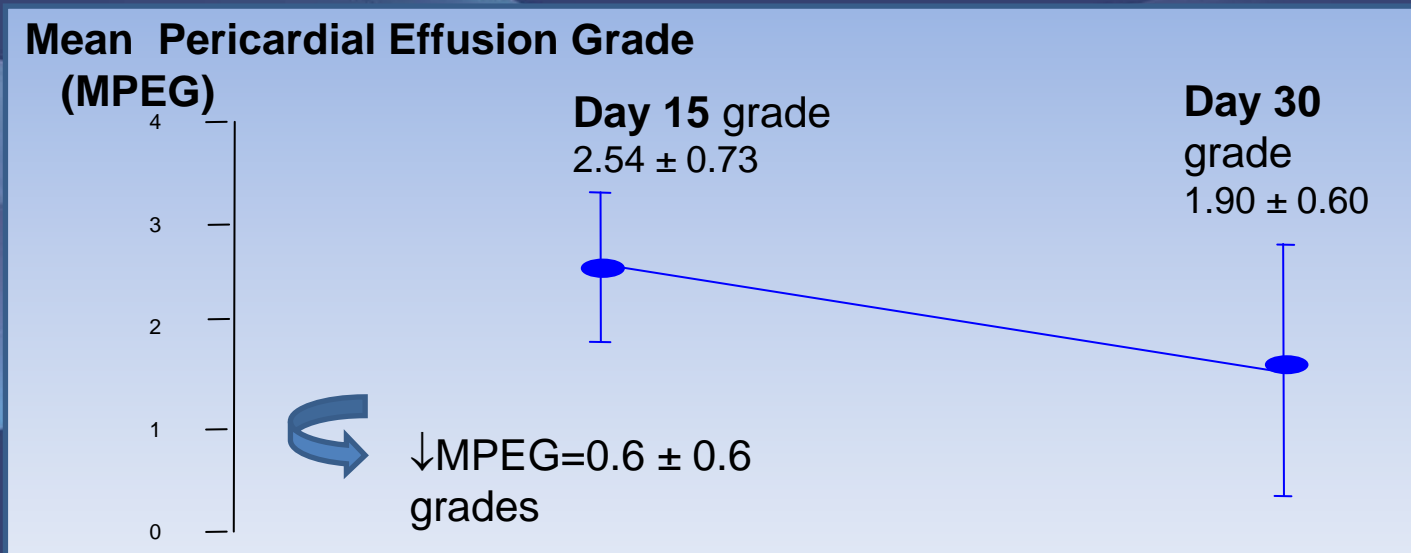
- **Objective**: to assess whether the NSAID diclofenac was effective in reducing post operative pericardial effusion volume.
- **Design**: multicenter, randomized, double-blind, placebo-controlled study
- **Setting**: five post operative cardiac rehabilitation centers (POCRC).
- **Patients**: 196 patients at high risk of tamponade
- **Treatment administration**: 14 days

# Quantification and Spontaneous Evolution of Post Operative Pericardial Effusions

## Echocardiographic classification<sup>1</sup>

Grade at day 15	Loculated	Circumferential	Estimated Late CT risk at day 30 <sup>1</sup>
0	0	0	0%
1 Small	< 10 mm	0	0%
2 Moderate	10-14 mm	< 10 mm	<b>7%</b>
3 Medium	15-19 mm	10 -14 mm	<b>15%</b>
4 large	≥ 20 mm	≥ 15 mm	<b>43%</b>

## Spontaneous evolution<sup>1</sup>



(1) Meurin P, Weber H, Renaud N et al. Chest 2004;125:2182-87.

# POPE Study: Methods (1)

- Inclusion criteria:
  - ✓ Persistent pericardial effusion  $\geq$  grade 2 on the echocardiography performed at admission in POCRC (8 to 30 days after surgery)
- Exclusion criteria:
  - ✓ NSAID contra-indication (allergy, pregnancy, renal failure, evolutive gastro duodenal ulcer...)
  - ✓ Cardiac transplantation or correction of congenital heart anomalies

# Methods (2): Primary Efficacy (Echographic) Endpoint and Statistical Power

- Mean pericardial effusion grade (MPEG) decrease
  - ✓ Between the inclusion and the final echocardiographies
  - ✓ Expected to be of 0.6 grade in the placebo group
- Sample size assessment: 86 patients by group
  - ✓ 80% power to detect a supplementary reduction of 50% of the MPEG with diclofenac (versus placebo)
  - ✓ two-sided type 1 error of 5 %

# Results

The background of the slide is a deep blue color with a complex, abstract pattern of overlapping, flowing, and wavy lines. These lines create a sense of movement and depth, with some areas appearing lighter and more translucent than others, giving the overall effect a dynamic and modern feel.

# From January 2006 to January 2009

Echocardiography at

5455

admission ( $15.9 \pm 6$  days after surgery)

262 Grade  $\geq 2$

5193 Grade 0 or 1 :  
STOP

196 pts randomized

66 excluded :

- 47 refused consent
- 13 NSAID contra indication
- 6 immediate drainages

**Diclofenac**  
50mg b.i.d  
N = 98

**Placebo**  
N = 98

ITT: n = 196  
(Per Protocol: n = 185)

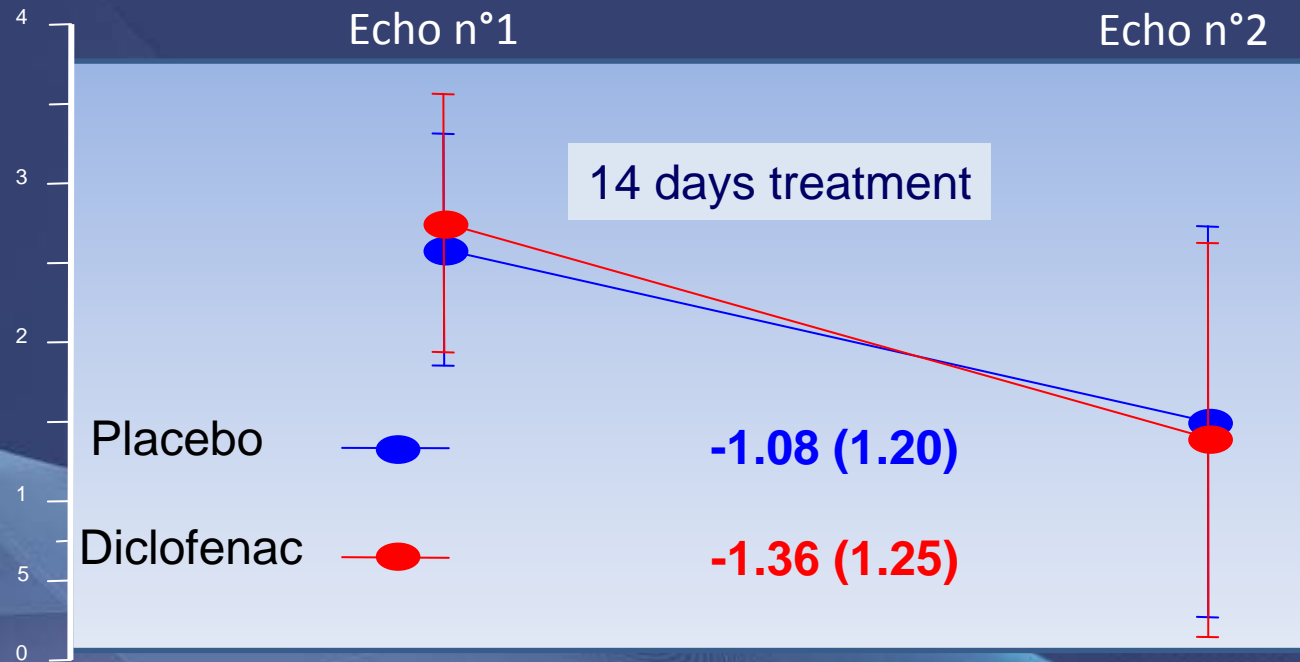
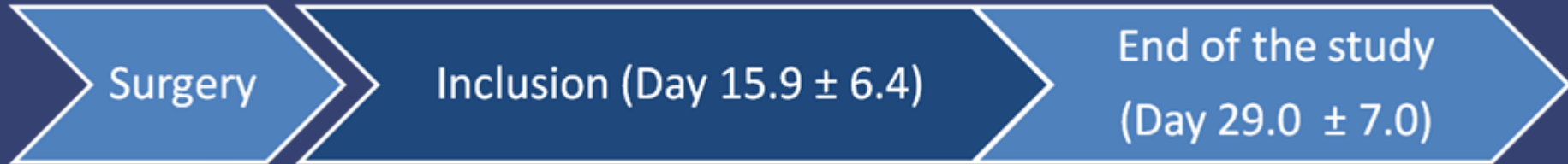
Treatment duration: 14 days

# Baseline Characteristics

	Placebo Group (n = 98)	Diclofenac Group (n = 98)
Mean Age (SD ), years	62.5 (12)	64.1 (11)
Male (%)	78%	82%
Surgery performed		
- CABG	57%	60%
- Ao Valve Replacement	32%	35%
- Mitral Valve Surgery	20%	11%
- Root Aorta Surgery	8%	10%
Delay surgery-inclusion	15.9 (5.1)	15.9 (4.3)
Oral anticoagulants	43%	44%
- INR at inclusion (SD)	2.77 (1.12)	2.51 (0.91)
Aspirin	75%	72%

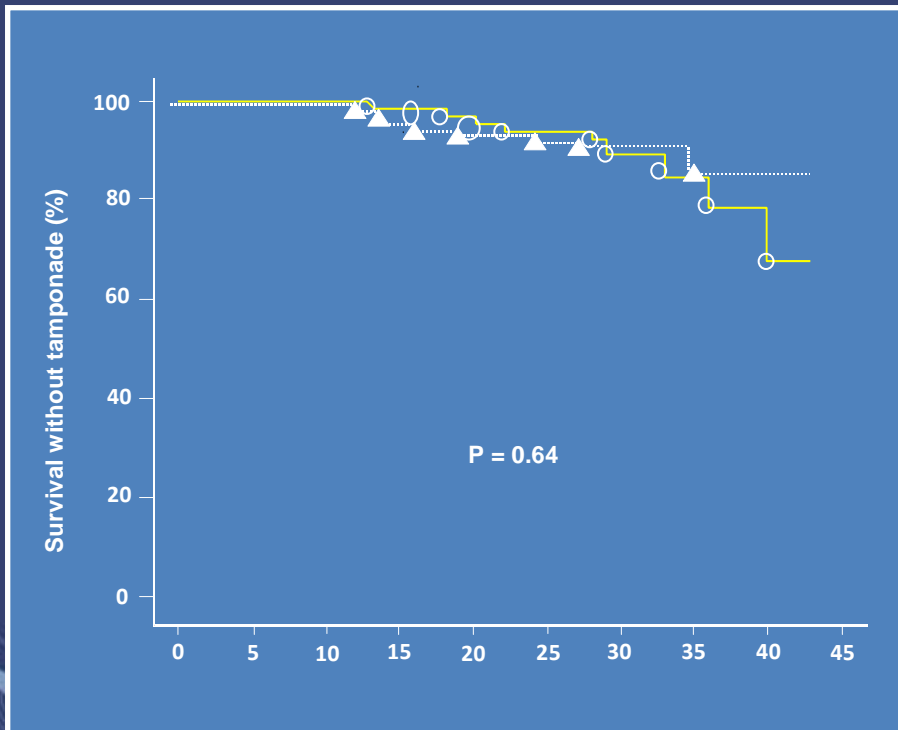
POPE mean grade: MPEG	2.58 (0.73)	2.75 (0.81)
grade 2, n	55	47
grade 3, n	29	28
grade 4, n	14	23

# Primary Endpoint: Mean Pericardial Effusion Grade Decrease



Grade	Placebo	Diclofenac	Mean (95% CI)	p
Initial	2.58 (0.73)	2.75 (0.81)		
Final	1.49 (1.22)	1.39 (1.20)		
Change	-1.08 (1.20)	-1.36 (1.25)	0.28 (-0.63 to 0.06)	0.11

# Secondary Endpoints



Late Tamponades

- placebo group → n = 11 (11.2%)
- ▲ diclofenac group → n = 9 (9.2%)

	Placebo Group (n = 98)	Diclofenac Group (n = 98)	p
Patients with at least 1 grade decrease	<b>73 (74.4%)</b>	<b>71 (72.4%)</b>	0.7
Mean reduction of the pericardial echo free space width (mm)	<b>-4.8 (7.0)</b>	<b>-6.7 (7.4)</b>	0.07

# Prespecified Sub-Groups Analysis

MPEG decrease (grades) in Patients	Placebo Group (n=98)	Diclofenac Group (n=98)	95% CI	p
With CRP level $\geq$ 30mg/l (n=90)	<b>-1.35 (1.26)</b>	<b>-1.64 (1.16)</b>	0.29 (-0.8 to 0.23)	<b>0.26</b>
Receiving an oral anticoagulant (n=85)	<b>-1.17 (1.37)</b>	<b>-1.56 (1.26)</b>	0.38(-0.96 to 0.18)	<b>0.18</b>
Per Protocol Analysis (n=185)	<b>-1.11 (SD 1.21)</b>	<b>-1.35 (SD 1.27)</b>	0.25 (-0.60 to 0.11)	<b>0.25</b>

# Remarks

- High power of the study to assess NSAID effectiveness
  - ✓ Theoretical sample size: 172
    - included: 196
- Study underpowered to test NSAID tolerance

# Conclusion

- Patients with a persistent moderate to large pericardial effusion more than 7 days after cardiac surgery are at high risk:
  - ✓ 10% pericardial drainages in the 2 following weeks
- NSAID administration seems to be useless in this setting

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- ✓ Les Grands Prés (CRCB): P Meurin, H Weber, JY Tabet, A Ben Driss, N Renaud, A Grosdemouge.

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- The Patients