

# Potential conflicts of interest

**Speaker's name: Faustino Miranda**

**I have the following** potential conflicts of interest to report:

- Research contracts
- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

**I do not have any potential conflict of interest**

# 6-Month Outcomes of the Placlitaxel Eluting Balloon for the Treatment of in-Stent Restenosis : Insights from the Spanish Multicenter Registry

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## Limitations of DES

- Still some incidence of restenosis in complex subset lesions
- Delayed healing, local inflammation and impaired endothelial function
- Safety Concerns: late and very late ST
- Dependency on prolonged dual antiplatelet therapy
- Permanent implant, might limit further revascularizations

## Potential advantages of DEB

- Delivery of high drug concentrations at the vessel wall at the moment of injury
- Immediate and homogeneous drug uptake with up to 6 days retention
- No impact on long-term healing, less need for DAT
- Respects the original anatomy of the vessel (small vessel, bifurcation)
- No permanent polymer (less inflammation) nor implant
- Does not limit the chance of repeated treatments



- **In-vitro:** Brief contact with paclitaxel inhibits the proliferation of vascular smooth-muscle cells
- **Animal Model:** Dior balloon better than non-coated balloon in inhibiting of neointimal hyperplasia
- **Novel coating method: “Shellac” 2on G of DIOR:**
  - Resulted in up to 20-fold higher tissue concentration of paclitaxel
  - Reaching a max. tissue concentration with a balloon inflation time 30-45sec (+ tolerated)
- **Homogeneous (Lg and vertical) distribution of paclitaxel in the vessel by simple diffusion, in contrast with DES**

✓ **Prospective real-world multicenter registry : 10 Spanish centers**

✓ **Inclusion criteria:**

- ✓ **Stent restenosis (BMS/DES)**
- ✓ **Small vessel disease (<2.5mm)**
- ✓ **Bifurcated lesions (Dior to treat SB)**
- ✓ **Ostial bifurcated lesions (001)**
- ✓ **Contraindication to prolonged DAT**

✓ **Exclusion criteria:**

- ✓ **Clinical:**
  - ✓ **STEMI <24h**
  - ✓ **Cardiogenic shock**
- ✓ **Angiographic: severe lesion calcification**

## METHODS

Clinically and/or angiographically eligible patient

**Target lesion** pre-dilatation (Shorter balloon than the Dior)

**Dior dilatation:** above nominal pressure + at least during 60sec

**Angiographic success:** a final residual lesion stenosis  $< 50\%$  in the TL and absence of  $>$  type B coronary dissection

**No angio success:** BMS

## Follow-up

DAT for at least 1 month

Clinical FU at 1 and 6 months and 1 year after the index procedure

Angiographic FU at 6 months at 3 centers (40% of population)

**DIOR Population (222 pts)**

**In-stent restenosis (115 pts)**

**De novo lesions in Small vessel (<2.5mm) (89 pts)**

**Other (18 pts)**

- ISR alone (72 pts)
- + Small vessel (< 2.5mm) (21 pts)
- + Bifurcated lesions (26pts)
- + Ostial lesions (9pts)
- + Contraindication to DAT (8 pts)

DES- ISR (54pts)  
BMS-ISR (60pts)

- (No In- stent restenosis)  
(No Small vessels)
- Bif. lesions (111/101/011) (6pts)
  - Bif. lesions (001) (4pts)
  - Contraindication to DAT (11pts)

- De novo lesion in SV alone (45 pts)
- + Bif. lesions (111/101/011) (19pts)
- + Bif. lesions (001) (13pts)
- + Contraindication to DAT (12pts)

Contraindication to prolonged dual antiplatelet therapy\*

- **Age (years) (mean±SD)** **65.3±10.0**
- **Male gender** **80.9 (93)**

## Risc Factors

- ✓ **Diabetes** **34.8 (40)**
- ✓ **Hypertension** **74.8 (86)**
- ✓ **Dyslipidemia** **67.0 (77)**
- ✓ **Current Smoker** **32.2 (37)**
- ✓ **Renal impairment** (creat >1.3mg/dl) **10.4 (12)**

## Hystory of

- ✓ **MI** **49.6 (57)**

## Clinical presentation

- ✓ **ACS (%)** **51.3 (59)**
- **LVEF (< 50%)** **35.0 (28)**
- **3 vessel disease** **15.7 (18)**

## Type of ISR

- ISR alone	62.6 (72)
- Small vessel	18.3 (21)
- Bifurcated lesion (001,111,011,101)	22.6 (26)
- Ostial lesion	7.2 (9)
- Contraindication to prolonged DAT	6.9 (8)

## ISR of

- BMS	52.6 (60)
- DES	47.4 (54)

## Angiographic ISR pattern

- Focal	58.9 (43)
- Diffuse (>10mm)	41.1 (30)

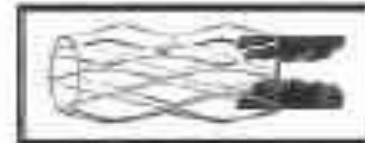
**Vessel: Prox/Mid LAD** 34.8 (40)

ISR pattern: Focal (<10mm) : 59%

*ISR Pattern I: Focal*



*Type IA: Articulation or Gap*



*Type IB: Margin*

21.9%



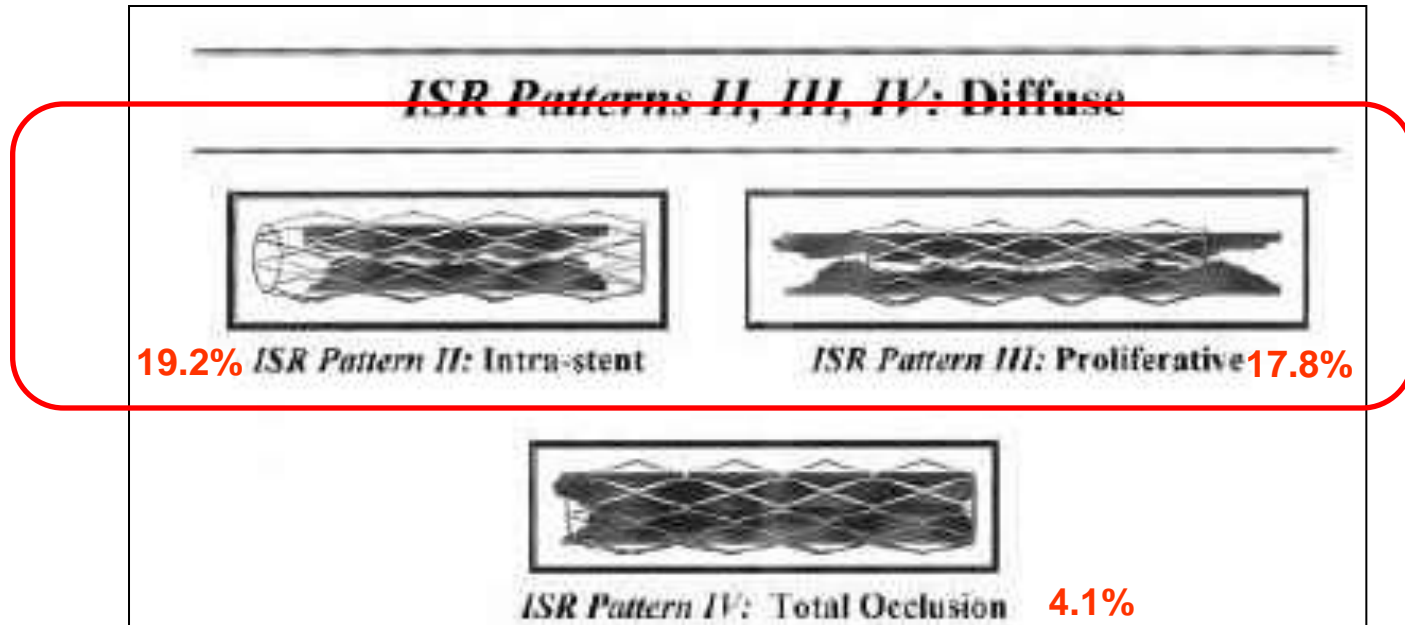
*Type IC: Focal Body*

35.6%



*Type ID: Multifocal*

ISR pattern: Diffuse (>10mm) : 41%



• Radial approach	60.9 (70)
• 6F- guide catheter	93.9 (108)
• Number of stents implanted off the target lesion	22.6 (26)
✓ DES off the target lesion	15.7 (18)
• <b>Pre-dilation (plain balloon)</b>	<b>100 (115)</b>
✓ Diameter, mm (mean±SD)	2.6±0.5
✓ Length, mm (mean±SD)	<b>14.5 ±4.3</b>
• Dior Balloon	
✓ Diameter, mm (mean±SD)	2.9±0.4
✓ Length, mm (mean±SD)	<b>19.2±5.4</b>
✓ Main balloon pressure, mmHg, (mean±SD)	14.7±3.5
✓ <b>Inflation time (sec).</b> (mean±SD)	<b>92.2±31.7</b>
• Post-dilatation	8.8 (10)
• IIb-IIIa inhibitor	1.7 (2)

*Unless otherwise specified, values are % and (n) of patients*

# RESULTS (n=115)

Cumulative Events	1-month	6-month
Angiographic success	95.6% (109)	
<i>(N) FU completed</i>	<i>105</i>	<i>66</i>
Death % (n)	1.9 (2)	6.1 (4)
<b>Cardiac</b>	1.0 (1)	<b>4.5 (3)</b>
Non-cardiac	1.0 (1)	0.9 (1)
<b>MI % (n)</b>	1.0 (1)	<b>3.0 (2)</b>
<b>TLR (%)</b>	1.0 (1)	<b>7.6 (5)</b>
<b>MACE<sup>†</sup> (%)</b>	1.9 (2)	<b>10.6 (7)</b>
Stent Thrombosis (%)*	0	0

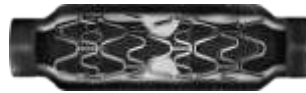
\*Definite stent thrombosis (ARC)

†Cumulative Non hierarchical MACE

# Low rate of adverse events to find independent predictors of TLR....HOWEVER

## ISR Pattern IC: Focal Body (<10mm)

The most frequent ISR pattern 35.6% (26 lesions)



**0% TLR, 0% ST, 0% MACE, at 6 months**

	Focal Body IC	Focal Margin IB and Diffuse	P value
TLR (%)	0.0	15.2	NS
MACE (%)	0.0	21.2	0.039

# Other ISR patterns: we need to wait a complete follow-up...

**Patients who underwent TLR after Dior because of Restenosis 5 (7.6%)**

Angiographic ISR pattern	n	Bifurcation /	DES /	RD $\leq$ 2.75mm
- <b>Focal (&lt;10mm)</b>				
- IB (Margin)	1	<u>1</u>	1 DES	0
- <b>Diffuse (&gt;10mm)</b>				
- II (Intra-stent)	2	<u>1</u>	2 BMS	0
- III (Proliferative)	2	<u>2</u>	1DES/1BMS	2

ISR	Bifurcation	No Bifurcation	P value
TLR (%)	18.2	2.3	0.039
MACE (%)	22.7	4.5	0.036

The treatment of coronary **in-stent restenosis** with this **paclitaxel-eluting balloon (Dior<sup>MT</sup> balloon)**, according to the strategy described, provides excellent immediate and mid-term outcomes with **single digit TLR at 6 months**

- Consistent with previous results using DEB in randomized trials
  - Moreover, this **is a real world registry**, providing additional information about ISR in small vessels (18%), ISR including Bifurcated lesions (23%), DES-ISR (49%)...

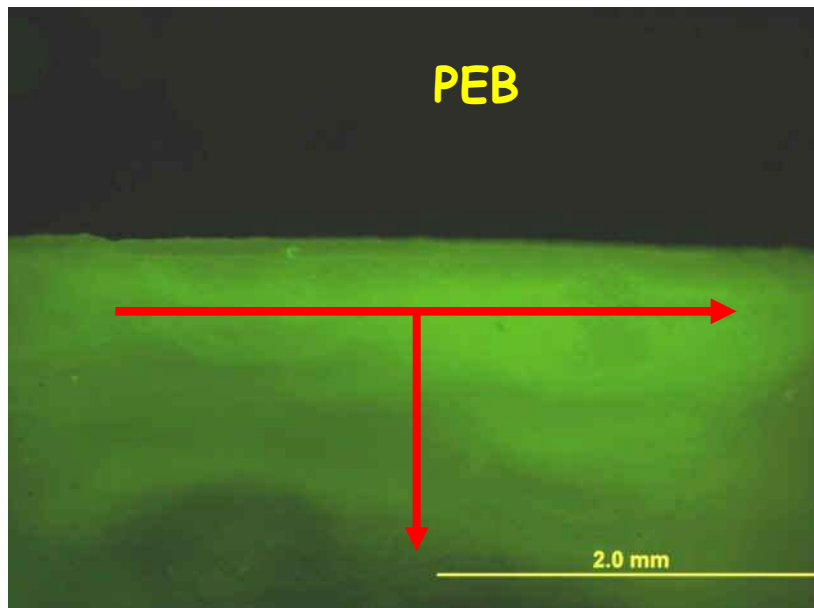
- The angiographic ISR pattern could predict the mid-term outcome...
- With current follow-up, excellent results in focal body (IC) ISR.
- The characteristics of the original lesion might also influence outcome:
  - ISR involving bifurcation lesions might be related to a higher risk of TLR and MACE at 6 mo

# BACK-UP SLIDES

# Tissue distribution of the drug on the vessel

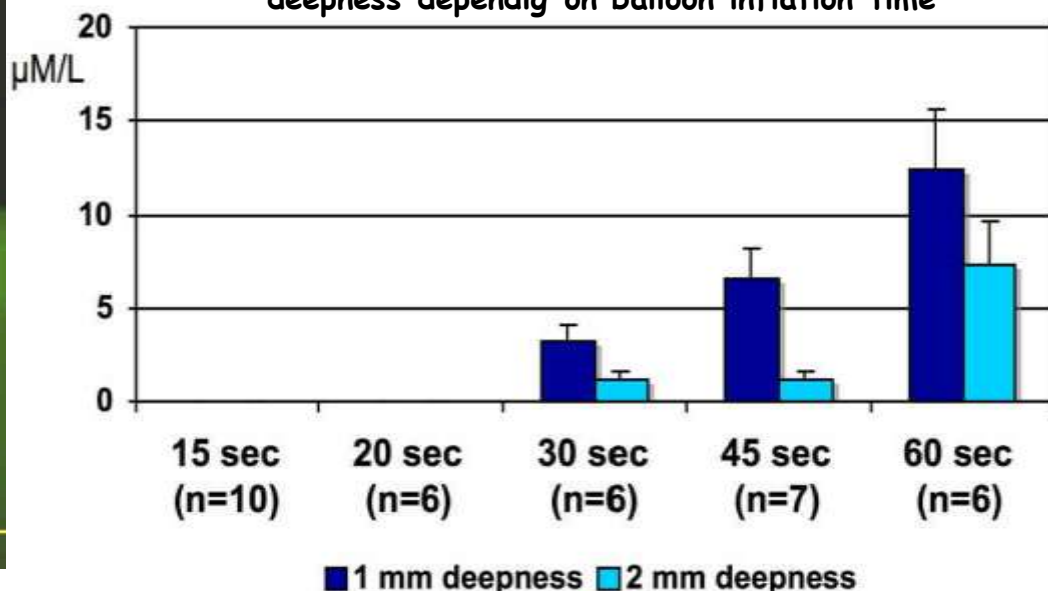
Fluorescence images of DIOR showed: ("Oregon green 488 Fluorescent paclitaxel conjugate")

Homogeneous (vertical and longitudinal) distribution of paclitaxel\* on the vessel by simple diffusion



Fluorescence microscopy images

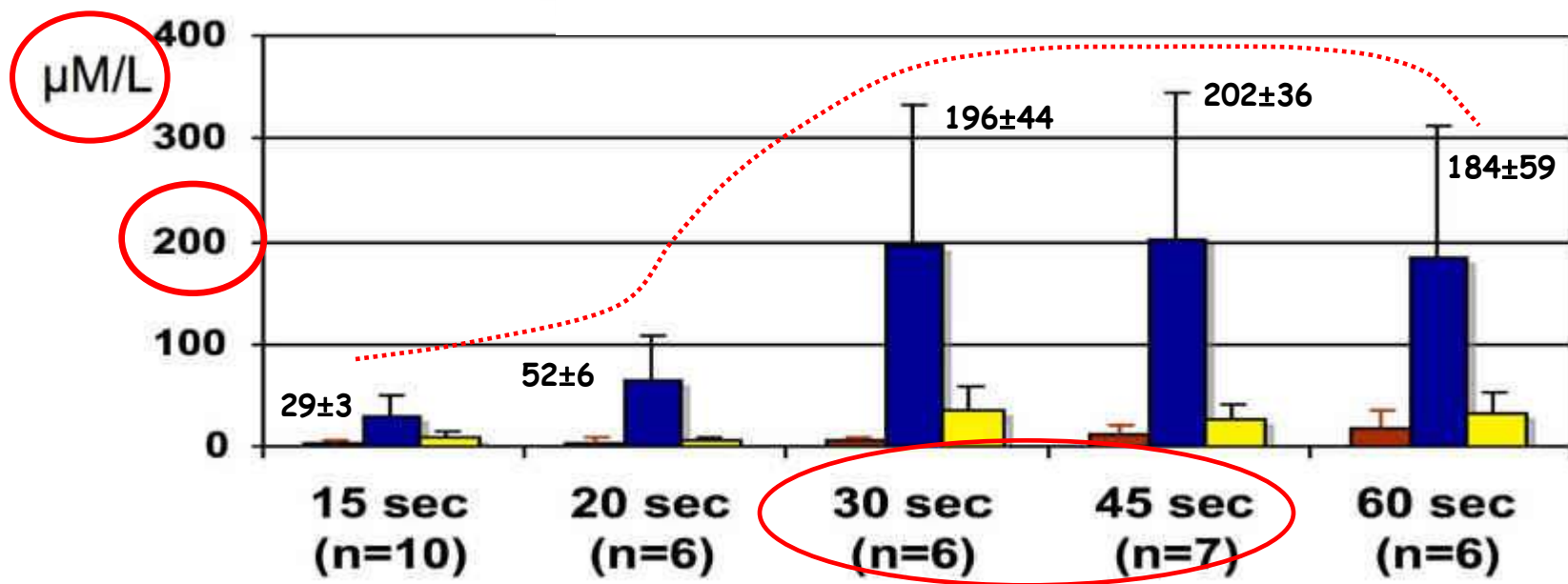
Vertical penetration of paclitaxel at 1 and 2 mm deepness dependig on balloon inflation time



# Inflation time-dependent tissue concentrations

Tissue concentration of paclitaxel dependig on balloon inflation time

Plateau concentration of the drug tissue



## Novel coating technology (Shellac) of DIOR 2G compared with 1st G:

- Maximum tissue concentration of paclitaxel- inflation time of 30-45sec (60 sec Dior 1G) (better tolerated)