The family of drug eluting balloons from Eurocor preclinical results

Mariann Gyöngyösi MD PhD FESC

Medical University of Vienna, Austria
Speaker’s name: Mariann Gyöngyösi

☐ 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)

X I do not have any potential conflict of interest
The family of drug-eluting balloons of Eurocor:

Preclinical experiments and results

1. 1st Generation DIOR for coronary PCI
2. 2nd Generation DIOR for coronary PCI
3. DEB-Balloon Aortic Valve Valvuloplasty
4. Coated cutting ballon for in-stent restenosis
5. FREEWAY (DEB) for peripheral angioplasty
Single vessel Dior balloon dilatation

Bifurcation Dior balloon dilatation

PORCINE CORONARY ARTERY PCI
CORONARY ARTERY TISSUE PACLITAXEL CONCENTRATION

1. Generation of Dior

2. Generation of Dior

Distal ref.  Proximal ref.  Dilated

Inflation time: 2x30 sec
CORONARY ARTERY TISSUE PACLITAXEL CONCENTRATION

1st generation DIOR

μM/L

post-dilation

1.5 h  12 h  24 h  48 h

distal reference  distal dilated segment  bifurcation opposite site  proximal dilated segment  proximal reference

μM/L

Bifurcation
INFLATION TIME-DEPENDENT TISSUE PACLITAXEL CONCENTRATION

45 min post-dilation

12 h post-dilation

INFLATION TIME-DEPENDENT VERTICAL PENETRATION OF PACLITAXEL

45 min post-dilation

HISTOLOGICAL RESULTS 14 DAYS POST-BALLOON OVERSTRETCH INJURY

Uncoated balloon

Dior balloon

neointima
media
adventitia

QUANTITATIVE HISTOLOGY 14 DAYS POST-BALLOON OVERSTRETCH INJURY

Replacing the paclitaxel through fluorescent-conjugated paclitaxel (Oregon green 488)

Artery post-paclitaxel-eluting stent: small amount of drug penetrated into the arterial wall, uneven drug distribution

Artery post-paclitaxel-eluting Dior balloon: large amount of drug within the arterial wall, uniform drug distribution

1. Balloon aortic valve valvuloplasty (BAV) is the choice of therapy, if aortic valve replacement (AVR, surgical or percutaneous) cannot be performed due to serious comorbidity, or as a bridge to surgery in hemodynamically unstable patients who are at high risk for AVR.

2. The drawback of the BAV is the moderate acute success and the lost of the valve area gain within the first 6-12 months, due to hyperplastic reaction of the AV post-BAV (active capillary growth, cellular proliferation with granulation tissue and fibrosis).

3. The use of drug-eluting balloon for BAV might prevent the restenosis of the aortic valve due to inhibition of the active inflammatory processes and cell migration by penetration of the paclitaxel into the valve and aortic ring.
8 healthy domestic pigs
BAV with 22/24 mm paclitaxel-eluting balloons (2 µg/mm², DIOR technology)
2 or 4 X 15-second inflations

Spargias K, Athen
Paclitaxel-eluting valvuloplasty balloon

DIOR II™ Technology *(Eurocor GmbH)*

- Paclitaxel loading/balloon surface: 3 µg/mm²
- Coating method: directly on balloon surface, 1:1 mixture of aleuritic & shellolic acid with Paclitaxel
- Complete drug release @ 30 sec
STUDY PROTOCOL OF AS

• Cholesterol-rich diet (0.5% cholesterol) + 50000 IU/day Vit. D2*

3 months

• General anaesthesia, TTE,
• Access: right carotid artery, Aortography
• Pressure measurements of the ascending aorta and left ventricle
• BAV randomly with coated or uncoated balloon (8.0/20 mm, 3x10 sec)

3 weeks

• General anaesthesia, TTE,
• Access: right femoral artery, Aortography
• Pressure measurements of the ascending aorta and left ventricle

• Histology: leaflet thickness, Masson’s trichrom in all, PCNA

*Drolet et al, JACC 2003;41:1211
BAV IN RABBITS

Echocardiography: thickened sclerotic aortic valve

LV - Ao max. pressure gradient: 12 mmHg

Pre-BAV  Positioning of BAV  BAV

Post-DEB-BAV

Gyöngyösi et al. ESC 2009
AORTIC VALVE AREA POST-BAV AND AT FOLLOW-UP

Uncoated

Paclitaxel-coated

p=0.32

p=0.04
HISTOLOGIC CHANGES OF AORTIC VALVE 1-MONTH POST-BAV

Uncoated

Paclitaxel coated

Maisons trichrom

PCNA

N.Narajam.
Chicago
PACLITAXEL-COATED CUTTING BALLOON for treatment of in-stent restenosis

STUDY DESIGN

Induction of in-stent restenosis in pigs by implantation of BMS known to induce high grade restenosis

ISR
Randomization

Coated-Cutting balloon
Cutting balloon

1 months

Control angiography, histology

(Sangiorgi G. Italy, Eurocor, Germany)
PACLITAXEL-COATED CUTTING BALLOON
for treatment of in-stent restenosis

Gyöngyösi et al. ESC Stockholm 2010 accepted abstract
Femoral artery: large elastic artery
Coronary artery: muscular type
Differences:
- size
- relative compositions of elastic and muscle tissue in their tunica media
- composition of internal and external elastic lamina.

Preclinical Safety study:
measurements of tissue paclitaxel concentration after dilation of the femoral and iliac arteries after use of FREEWAY balloon (Paclitaxel-eluting DEB)

Preclinical Efficacy study:
measurements of neointimal hyperplasia post-overstretch injury after use of FREEWAY (Paclitaxel-eluting DEB) or conventional balloon (randomized)

RESULTS IN PROGRESS
CONCLUSIONS

1. DIOR\textsuperscript{2nd generation} coronary DEB:
   1. a maximal balloon inflation time of 30-45 sec is optimal, reducing effectively the neointimal hyperplasia, and causing less arterial injury and is better tolerated by the patients in clinical scenario.
   2. Longer inflation of the balloon might lead to undesirable release of the drug into the systemic circulation.
   3. Short exposure of paclitaxel to the arterial wall results in penetration of the drug in both longitudinal and vertical directions.
   4. In contrast with DES, the drug delivery is rapid and homogenous using DEB, reaching the maximal tissue drug concentration at the time of the highest level of procedure-induced local tissue injury, which in turn triggers the restenotic and thrombotic cascade.

2. DIOR for DEB-BAV: experimental studies are promising, clinical studies just started
3. Coated cutting balloon using DIOR technology: preclinical results are promising
4. FREEWAY: preclinical results on-going