Session: DEB – their Utility

Innovation in Drug Coated Balloons

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Disclosure

I, Upendra Kaul, do not have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
EVOLUTION OF PCI TREATMENT

1980s
POBA Treatment
"Get Artery Open"

Late 1980s
BMS Stents
"Keep Artery Open"

Post 2003
DES Stents
"Decrease Restenosis"

Beyond 2013
Next Gen Device
"Optimize Healing & Long term results"

Continuous improvement in Device Design and Acute Performance

DRUG COATED BALLOON
"In-Device Restenosis & Leave nothing behind"
Modes of Local Drug Delivery

Target Site

Administration

Clearance

Uptake

Treatment Devices

Drug Eluting Stent

Drug Coated Balloon
Differences in Drug Distribution

**Drug Eluting Stent**
- Release from the Stent Surface
- Slow Release with Persistent Exposure
- Dose: 100 ~ 250 mcg
- Polymeric matrix
- Stent implanted permanently

**Drug Coated Balloon**
- Immediate release in ~ 60 seconds
- Short lasting exposure
- Drug retention is difficult
- Dose: 300 ~ 600 mcg
- No polymers or permanent implant
Innovations in DCB – Limus DCBs

All the DCBs are with Taxanes due to lipophilic property
Issues with other Drugs – specifically Limus:

Biological and Technological Challenges in DCB

• **Biological:** Tissue binding capacity had direct impact on drug uptake and retention (Limus behaves different than Taxanes)

• **Technological:** Drug formulation and carrier impact uptake, but retention is key factor of difference in Taxanes and Limus
Innovations in DCB – Limus DCBs

Sirolimus DCB and DEB Concepts

- Microcrystalline Coating
- Nano-Encapsulated Delivery
- Nano-Carrier Coating
- Vitamin-Fatty Acid Coating
Biological Challenge – Tissue Binding

Specific binding to intracellular proteins determines arterial transport properties for rapamycin and paclitaxel. Andrew D. Levin*, Neda Vukmirovic*, Chao-Wei Hwang*, and Elazer R. Edelman**‡

*Harvard–MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA 02139; and **Cardiovascular Division, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA 02115

Tissue Binding Capacity or Tissue residence time determines drug effect and toxicity.

Drug residence in arterial tissue is dependent on the Binding Proteins and their distribution. Coronary is different than Peripheral.

Paclitaxel distribution is more heterogeneous compared to Rapamycin which is more uniform in media and adventitia layer.

Fig. 2. Pharmacokinetic tissue-elution profile of labeled dextran (♦), paclitaxel (□), and rapamycin (◇) in bovine internal carotid tissue segments normalized to initial load values.
Innovations in DCB – Limus DCBs

Late Loss Predicts Restenosis Rate for Coronary DES but the setpoints for BTK DES are different!

Mean Late Loss vs. Predicted Restenosis Rate

Peripheral ≠ Coronaries

Destiny, Bosiers, et al. JVS 2012
Innovations in DCBs

Applications (Each requires specific properties of device)

• Coronary Arteries – different uptake & retention
  • In-stent Restenosis
  • Small diameter vessels
  • Bifurcation lesions
  • High flexion sites

• Peripheral Arteries – vessel architecture is muscular
  • SFA Artery
  • BTK Vessels
Innovations in DCBs

New Drug Coated Balloons with Limus Drugs:

- **Concept Medical – Magic Touch® Sirolimus DCB**
- **Nanolute®** - Nano carrier drug delivery technology
- Lipid based Excipient drug carrier
- Available in India

- **DSM /Caliber Technologies – Limus DCB**
  - **Transcerta™** – Bioresorbable material platform
  - **TADD Balloon** from Caliber Technologies (TADD - Targeted Angioplasty Drug Delivery)

- **Micell Technologies** – Limus Drug Coated Balloon
Innovations in DCBs
Concept Medical – Magic Touch® Sirolimus DCB

Sirolimus Coated Balloon

[Images of SEM micrographs showing Sirolimus coated balloon at 500X and 1000X magnification]
Innovations in DCBs
Concept Medical – Magic Touch® Sirolimus DCB
SAFETY: DRUG LEVELS IN BLOOD

Summary of SRL in Blood

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<th>Hours</th>
<th>0.5</th>
<th>1</th>
<th>3</th>
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<td>Conc. ng/ml of Blood</td>
<td>9.32</td>
<td>7.08</td>
<td>4.09</td>
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Sirolimus Concentration [Blood]

Study done at CV Path Institute, Washington USA
EFFECTIVE: SUSTAINED DRUG LEVELS

Summary of SRL in Tissue

<table>
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<tr>
<th>Days</th>
<th>Conc. ng/mg of Tissue</th>
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<tr>
<td>1</td>
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<td>8</td>
<td>15.50</td>
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<td>14</td>
<td>5.50</td>
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Study done at CV Path Institute, Washington USA
ONGOING CLINICAL STUDY - INDIA

COHORT A: Magic touch ISRe
BMS ISR to be treated with Magic Touch DCB

COHORT B: Magic touch DeNovo TRe
De Novo lesions to be treated with Magic Touch DCB

COHORT C: Magic touch TRe
All comers protocol for evaluation of Magic Touch DCB
ONGOING CLINICAL STUDY - INDIA

SITES: 5

- Multicenter, Randomized (1:1), (n=40)
  - Amazonia CroCo BMS + conventional semi-compliant balloon
  - Amazonia CroCo BMS + MAGIC TOUCH-Nano Carrier Eluting PTCA Balloon Catheter
  - Amazonia CroCo BMS + MAGIC TOUCH-Nano Carrier Eluting PTCA Balloon Catheter post dilatation
  - Patients will be analysed Post Procedure and at 6 months follow up with QCA
  - Patients will be clinically followed up at 30 days, 6 months, 1, 2 and 3 years

- Prospective, Multicenter, ISR (n=20)
  - MAGIC TOUCH-Nano Carrier Eluting PTCA Balloon Catheter
  - Patients will be analysed Post Procedure and at 6 months follow up with QCA
  - Patients will be clinically followed up at 30 days, 6 months, 1, 2 and 3 years

- Prospective, Multicenter, Registry, (n=60)
  - Amazonia CroCo BMS + MAGIC TOUCH-Nano Carrier Eluting PTCA Balloon Catheter post dilatation
  - Patients will be analysed Post Procedure and at 6 months follow up with QCA
  - Patients will be clinically followed up at 30 days, 6 months, 1, 2 and 3 years
ONGOING CLINICAL STUDY - INDIA

ISR Patient

PRE PROCEDURE

TREATMENT

POST PROCEDURE
Innovations in DCBs

Most common application of DCB:

- **In-stent Restenosis in Coronary Arteries**
  - PTx Balloons used commonly
  - Sirolimus DCB can be better with safety profile and good efficiency in NIH inhibition
  - Better distribution in Coronary due to Binding proteins
  - Limus has shown good results with stents

- **Small Vessels**

- **Bifurcation – Side branch lesions**

- **Peripheral Arteries**
  - Limus needs more evaluation as to binding and uptake properties due to muscular vasculature of arteries
Conclusions

DCB application in coming in the years should be seen to satisfy the unmet challenges in the treatment.

Sirolimus or its analogues would be explored and studied in RCTs as a potential treatment option.

Peripheral applications have a vast scope due to location and performance of DCB devices in such cases should give better treatment option.
THANK YOU