



Drug-Coated Balloons (DCBs): Mechanism of Action and Current Results

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Disclosures



- None



Background



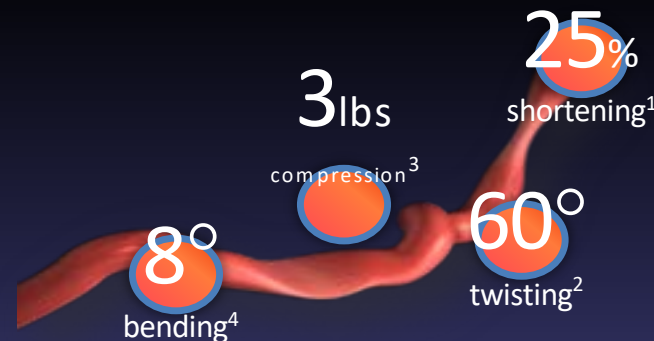
- Drug-coated Balloons
 - Currently three in the US market
 - All paclitaxel based
 - Goal is to avoid stenting and complications
 - In-stent stenosis
 - Fracture
 - Occlusions





Background

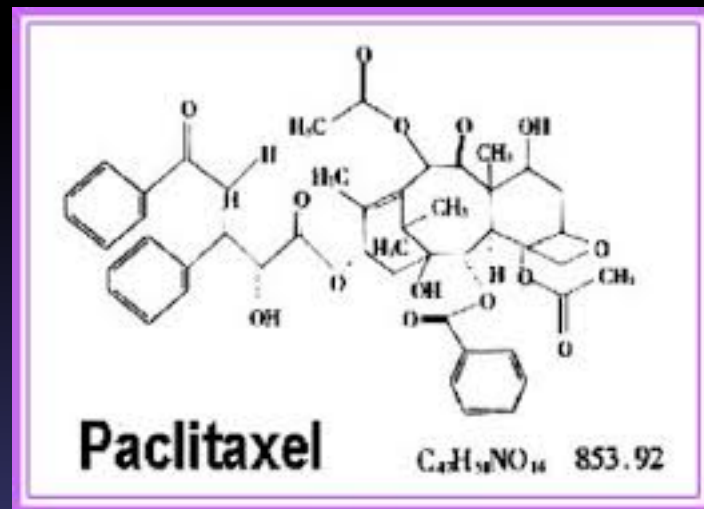
- SFA and popliteal arteries associated with a high rate of restenosis
- Nitinol stents have improved the durability
 - Patency rates now 60-75% at 1 year
 - Goal is to avoid placement of stents that could lead to future problems in this vascular bed

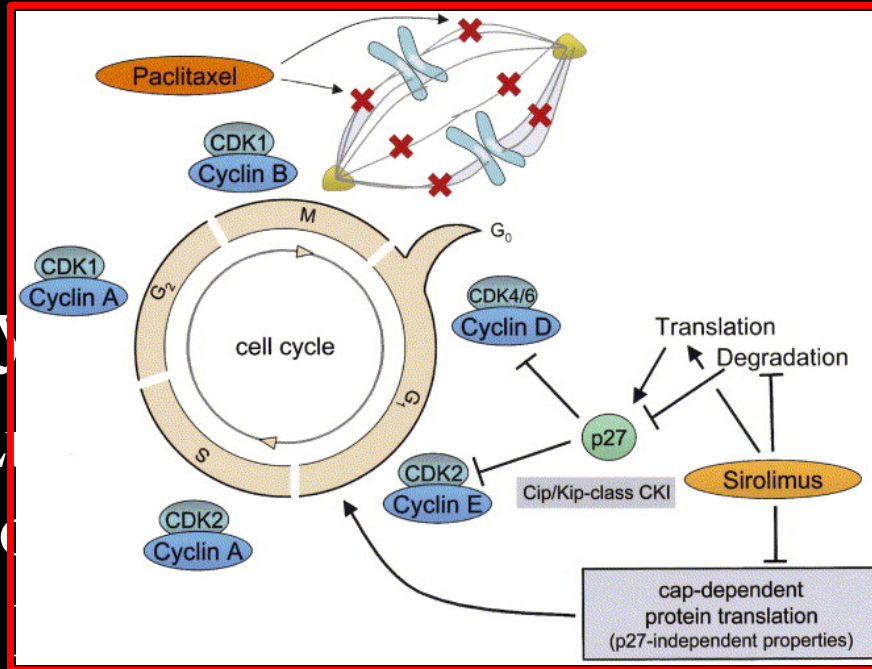




Drug Utilized

- Paclitaxel
 - Proven anti-proliferative agent
 - Lipophilic, hydrophobic
 - Requires an excipient (carrier molecule)
 - Can remain in treatment site for up to 180 days





- Currently
– 2014 L
(Medtronic)
– Utilize

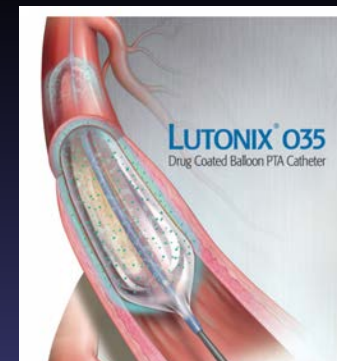
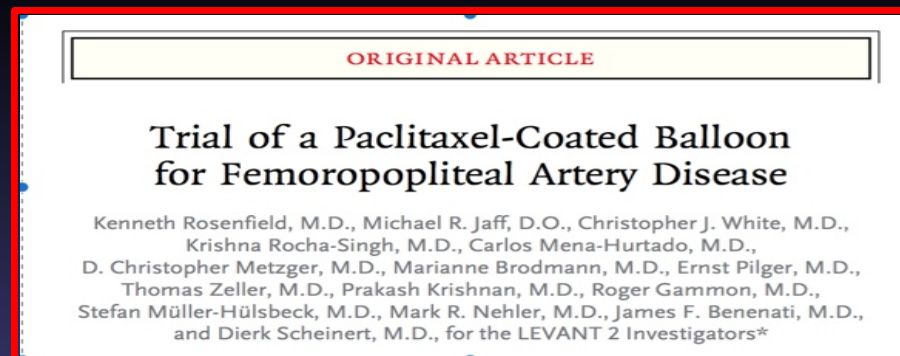
et
Admiral
netics)

- Binds to the beta subunit of tubulin leading to inhibition of microtubule disassembly which prevents cell progression from G2 to M and ultimately inhibits smooth muscle cell migration and signal transduction



Bard Lutonix

- LEVANT 2 Trial
 - Single-blind randomized trial of 476 patients with IC or rest pain
 - Treated with PTA vs DCB-PTA
 - 12 -month primary patency was 65.2% for DCB vs 52.6% for PTA p=0.02
 - Led to the unanimous FDA approval





LEVANT 2 Trial

Table 2. Primary and Secondary End Points.*

End Point	Drug-Coated Balloon	Standard Angioplasty Balloon	Difference	P Value
	<i>no./total no. (%)</i>		<i>percentage points (95% CI)</i>	
Primary end points				
Primary patency at 12 mo†	172/264 (65.2)	71/135 (52.6)	12.6 (2.4 to 22.8)	0.02‡
Restenosis without target-lesion revascularization§	57/92 (62.0)	40/64 (62.5)	-0.5 (-16.0 to 14.9)	—
Target-lesion revascularization§	35/92 (38.0)	24/64 (37.5)	0.5 (-14.9 to 16.0)	—
Safety composite¶	240/286 (83.9)	113/143 (79.0)	4.9 (-2.6 to 12.3)	0.005
Perioperative death	0/308	0/155	0**	—
Index-limb amputation	1/286 (0.3)	0/140	0.3 (-0.3 to 1.0)	—
Index-limb reintervention	44/285 (15.4)	30/143 (21.0)	-5.5 (-13.4 to 2.3)	—
Index-limb-related death	0/285	0/140	0	—
Secondary end points				
Total target-lesion revascularization	35/285 (12.3)	24/143 (16.8)	-4.5 (-11.7 to 2.7)	0.21‡
Total target-vessel revascularization	38/285 (13.3)	26/143 (18.2)	-4.8 (-12.3 to 2.6)	0.19
Death	7/290 (2.4)	4/144 (2.8)	-0.4 (-3.6 to 2.8)	0.82
Major amputation	1/286 (0.3)	0/140	0.3 (-0.3 to 1.0)	0.37
Reintervention for thrombosis	1/285 (0.4)	1/140 (0.7)	-0.4 (-1.9 to 1.2)	0.62



IN.PACT SFA trial

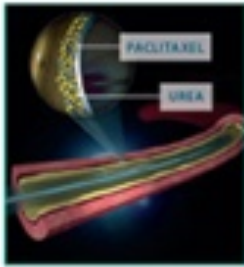
**Drug-Coated Balloon versus Standard Percutaneous Transluminal
Angioplasty for the Treatment of Superficial Femoral and/or Popliteal
Peripheral Artery Disease: 12-Month Results from the IN.PACT SFA
Randomized Trial**

Running title: *Tepe et al.; Drug-coated Balloons and SFA Lesions*

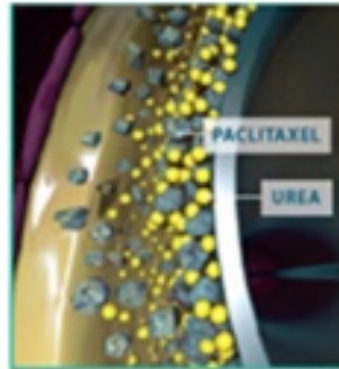
Gunnar Tepe, MD¹; John Laird, MD²; Peter Schneider, MD³; Marianne Brodmann, MD⁴;
Prakash Krishnan, MD⁵; Antonio Micari, MD⁶; Christopher Metzger, MD⁷;
Dierk Scheinert, MD⁸; Thomas Zeller, MD⁹; David J. Cohen, MD, MSc¹⁰;
David B. Snead, PhD¹¹; Beaux Alexander, MBA¹¹; Mario Landini, MS¹¹; Michael R. Jaff, DO¹²
for the IN.PACT SFA Trial Investigators*



Mechanism of Action



1. IN.PACT Admiral is coated with a matrix of paclitaxel and an excipient urea.



2. The coating comes into contact with water in the bloodstream upon inflation, hydrating the urea, which facilitates the release of paclitaxel at the target lesion.



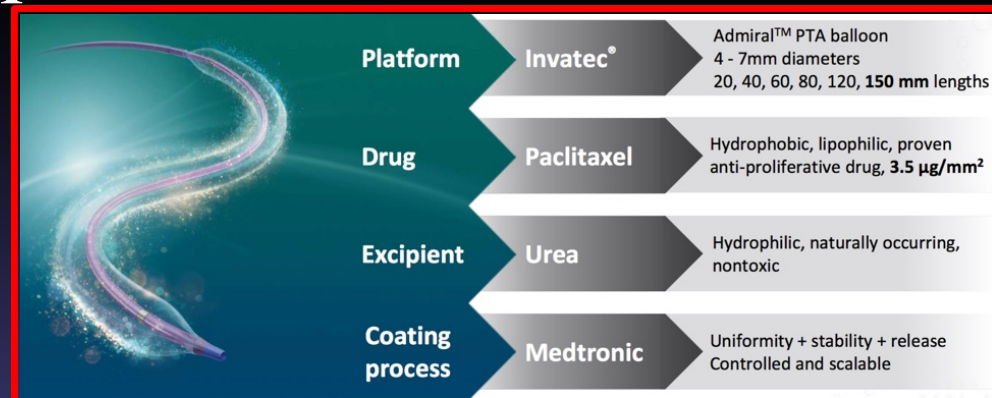
3. Paclitaxel penetrates the vessel wall, where it remains at a therapeutic dose for over 180 days, addressing the causes of restenosis.



Medtronic IN.PACT SFA Trial



- Randomized trial with 331 patients
- Claudication or rest pain
- DCB 12-month primary patency was 82.2% vs PTA 52.4% $P < 0.001$
- TLR was 2.4% vs 20.6%
- Led to FDA approval





ILLUMENATE Trial

- Randomized 300 patients
- 200 to DCB PTA and 100 to POBA
- Safety endpoints met
- 12-month primary patency- 76.3% vs 57.6% POBA
- TLR- DCB- 7.9% vs 16.8% in POBA

stellarex™

Drug-coated
Angioplasty Balloon



Similarities and Differences

- Similarities
 - Drug- Paclitaxel
 - Balloon
- Differences
 - Drug dose
 - IN.PACT- 3.5 ug/mm² vs. Stellarex and Lutonix-2 ug/mm²
 - Excipient
 - IN.PACT Admiral –urea
 - Lutonix-polysorbate, sorbitol and methanol
 - Stellarex- Polyethylene glycol



IN.PACT SFA

24- Months Results

- 331 patients
- Rutherford 2-4
- Lesion length-DCB- 8.94 ± 4.89 cm vs PTA only- 8.81 ± 5.12 cm
- Primary patency- DCB-78.9% vs PTA-50.1%
 $p < 0.001$
- CD-TLR- 9.1% vs 28.3%

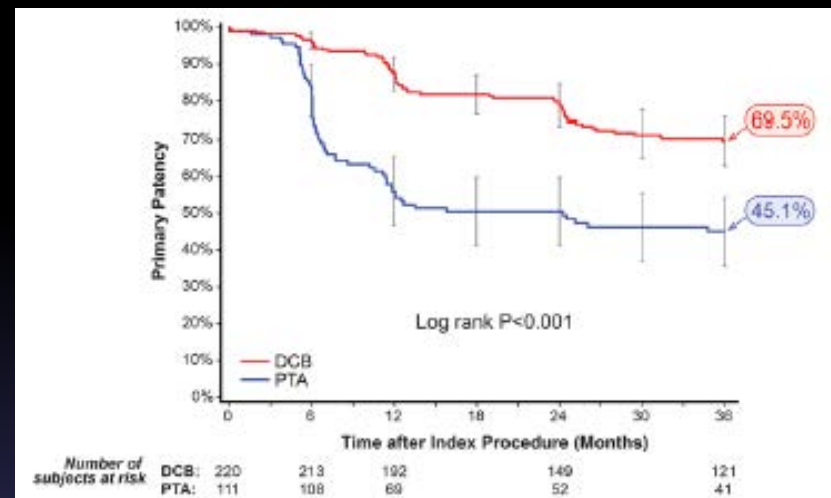
TABLE 2 Effectiveness Outcomes at 24 Months

	IN.PACT (n = 220)	PTA (n = 111)	p Value*
Primary patency†	78.9 (42)	50.1 (54)	<0.001‡
CD-TLR§	9.1 (18/198)	28.3 (30/106)	<0.001
Time to first CD-TLR, days	351.9 ± 165.9	261.7 ± 139.0	0.049
All TLR	10.1 (20/198)	29.2 (31/106)	<0.001
Primary sustained clinical improvement¶	76.9 (133/173)	59.2 (61/103)	0.003
ABI/TBI#	0.924 ± 0.261	0.938 ± 0.184	0.611



IN.PACT SFA 36- Months Results

- 331 patients
- Primary patency- DCB-69.5% vs PTA-45.1%
 $p < 0.001$
- CD-TLR- 15.2% vs 31.1%





Tips on Using

- The length of the DCB should exceed the lesion by 1 cm on either side
- Vessel preparation with standard PTA is required
- Expeditious passage of the balloon to target (some report 30 seconds; Lutonix IFU states less than 3 minutes)
- Prolonged inflation not specified for Lutonix but 180 seconds for Admiral IN.PACT and 60 seconds for Stellarex



DCB Role




- It will affect your practice
- Known success for short and intermediate length lesions
- Longer lesions still in question- await results of the registries and studies that are ongoing
- Cost will always be an issue

U.S. Drug-Coated Balloons Market Threatened by Reimbursement Cuts and Competitive Pressure

With reimbursement changes, new product launches, and broadening indications for established platforms, what will the future hold?

As of January 1, 2018, the cost of DCBs has been packaged into payments for associated procedures. As a result, plain-old balloon angioplasty (POBA), a procedure often performed using standard PTA balloons, and DCB procedures are now reimbursed at the same rate. The price differential between the standard PTA balloons (~\$110) and DCBs (~\$1500) threatens to price some cost-sensitive facilities out of the DCB market, limiting access to DCB technology and causing DCB unit sales to decline in 2018.³ The reimbursement cut is also expected to accelerate ASP erosion in the DCB market. However, annual declines are anticipated to remain in the low-single digits over the near term.



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