





Future Studies and Challenges for Drug Coated Balloons



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Endovascular Areas of Challenge

- Small vessels
 - Stent restenosis
 - Venous stenosis
 - Dialysis Fistulae
 - Aortic Stenosis
 - Cerebral vasculature
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Planned Cotavance Studies

- RIVER trial - POBA versus Paclitaxel coated balloon angioplasty (Cotavance) for prevention of restenosis in atherosclerotic lesions of the femoral-popliteal arteries.
 - National Co-Primary Investigators:
 - **Dr Bill Gray** – Columbia Presbyterian Hospital, New York, NY
 - **Dr Gary Ansel** – Riverside Methodist Hospital, Columbus, OH
 - The RIVER study is a prospective, multi-center, randomized trial for safety and efficacy
 - In FDA review process
 - The primary efficacy endpoint will be Duplex-determined Binary Restenosis Rate: 12 month treatment segment patency as defined by 12 month Doppler Ultrasound (DUS)

Planned Cotavance Studies

- COPA COBANA Trial - Cotavance Paccocath versus uncoated balloon angioplasty for treatment of in-stent restenosis in peripheral arteries
 - Primary Investigator;
 - **Professor Gunnar Tepe**
 - The COPA COBANA study is an investigator sponsored prospective, multi-center, randomized trial for safety and efficacy in Europe
 - The primary efficacy endpoint will be LLL (late lumen loss) at 12 months with important secondary endpoint of freedom from restenosis at 6, 12, 24 months

Planned Cotavance Studies

- Euro-CANAL – European study of POBA versus Cotavance - Paclitaxel Coated Balloon for Infrapopliteal Lesions in Critical Limb Ischemia
 - Primary Investigator:
 - Dr med Nicolas Diehm – University Hospital Bernd, Switzerland
 - The EURO-CANAL study is a prospective, multi-center, randomized trial being conducted in Europe
 - Co-Primary Efficacy endpoints:
 - Angiographically-defined late lumen loss (LLL) of all randomized subjects at 6 months (as adjudicated by an independent angiographic core laboratory)
 - Major amputation free survival rate in both arms at 12 months. A major amputation is defined as above the ankle and specified as below-the-knee or above-the-knee
 - “Clinically-driven” target lesion revascularization (TLR) rate through 12 months
- CANAL – IDE Study of POBA versus Cotavance - Paclitaxel Coated Balloon for Infrapopliteal Lesions in Critical Limb Ischemia
 - Co-Primary Investigators:
 - Dr Gary Ansel – Riverside Methodist, Ohio
 - Dr Bill Gray – Columbia University Hospital, NY

Additional DEB Studies

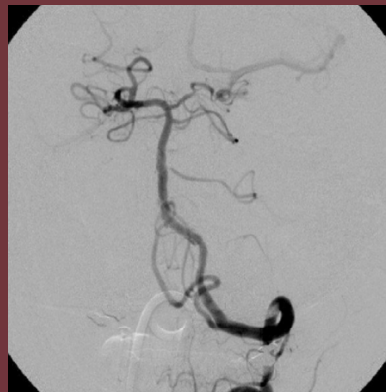
- B Bruan (Sequent Please DEB) – Paccocath Technology Coronary
 - PEPCAD III (DEB + BMS vs Cypher), PEPCAD IV (DEB + BMS vs Taxus in Diabetics), PEPCAD V (DEB + BMS in Bifurcations)
- Paccocath Technology (Speck, Tepe, Zeller et al.)
 - PICCOLO study (BTK) enrollment closed
- In-pact (Invatec)
 - Femoro-popliteal study planned for IV/2009
- In-pact (Invatec)
 - BTK study currently recruiting in Europe (Inpact deep)
- Lutonix Drug Coated Balloon Catheter (Lutonix)
 - SFA study started recruitment 6-2009 in Europe (Levant I study)
- Advance 18 PTX (Cook)
 - SFA study ongoing (Advance 18 PTX)

Possible Future Investigations

- Post Atherectomy
- Aortic Valve
 - EuroCor - A Paclitaxel-Eluting Valvuloplasty Balloon to Prevent Aortic valve Restenosis – Preliminary animal work done
- Renal – Denovo and In-Stent Restenosis
- Dialysis Fistula
- Venous – Subclavian vein/SVC Aachen has done first in man
- Intracranial – Aachen has done first in man for intracranial basilar artery DEB



Pre



Post

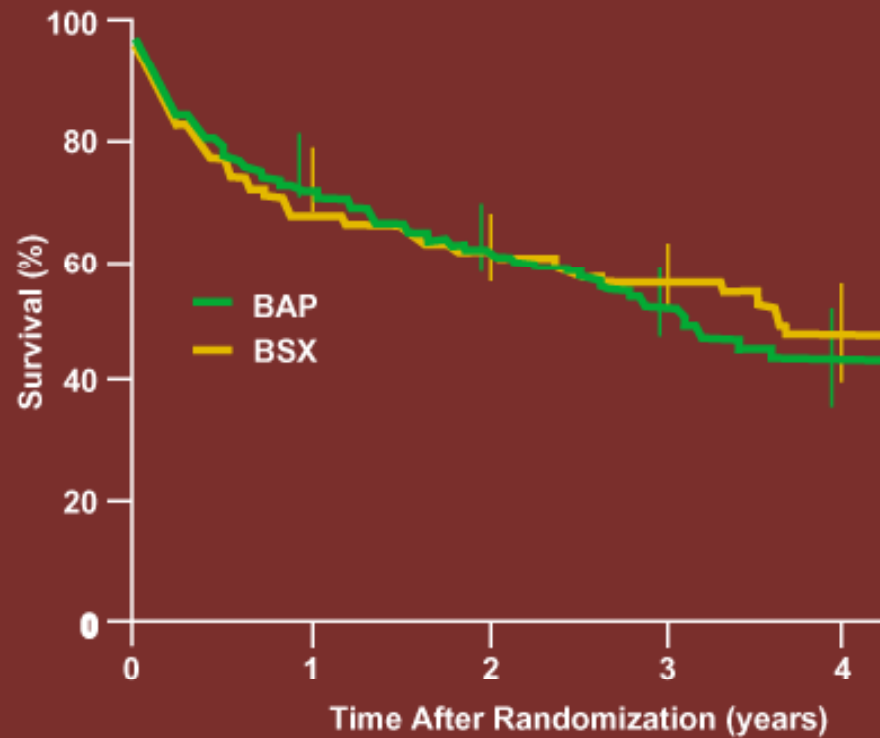


5 Month F/U

Study Endpoints

- SFA/popliteal
 - Patency is acceptable surrogate endpoint
 - Claudicants, Rutherford 2-4 or 5
 - Secondary therapeutic endpoints include pain-free mobility / resolve rest pain
- Infrapopliteal
 - Critical Limb Ischemia, Rutherford 5-6
 - Therapeutic endpoints: wound healing, amputation, restoration of mobility
 - No proven surrogate endpoints
 - Return to mobility secondary metric

BASIL Trial: Amputation-Free Survival



Number at risk

Angioplasty	224	149	100	51	19
Surgery	228	148	108	64	23

Recently Published PTA in CLI Meta-analysis

- 30 articles (1990-2006):
 - At least 15 infrapopliteal PTAs reported with 12 mo follow-up; RC 4-6
 - Reported 12 mo cumulative patency or limb salvage
 - Assessed: Immediate technical success, 1^o/2^o patency, limb salvage, patient survival
- Comparison to distal fem-tibial bypass surgery

Romiti M, Albers M, Brochado-Neto FC, Durazzo AE, et al. Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia. *J Vasc Surg.* 2008;47:975-981

Meta-analysis results of crural percutaneous transluminal angioplasty and popliteal-to-distal bypass

Result	1 month	6 months	1 year	2 years	3 years
Primary patency					
PTA	77.4 ± 4.1	65.0 ± 7.0	58.1 ± 4.6	51.3 ± 6.6	48.6 ± 8.0
Bypass	93.3 ± 1.1	85.8 ± 2.1	81.5 ± 2.0	76.8 ± 2.3	72.3 ± 2.7
P	< .05	< .05	<.05	< .05	< .05
Secondary patency					
PTA	83.3 ± 1.4	73.8 ± 7.1	68.2 ± 5.9	63.5 ± 8.1	62.9 ± 11.0
Bypass	94.9 ± 1.0	89.3 ± 1.6	85.9 ± 1.9	81.6 ± 2.3	76.7 ± 2.9
P	< .05	< .05	< .05		
Limb salvage					
PTA	93.4 ± 2.3	88.2 ± 4.4	86.0 ± 2.7	83.8 ± 3.3	82.4 ± 3.4
Bypass	95.1 ± 1.2	90.9 ± 1.9	88.5 ± 2.2	85.2 ± 2.5	82.3 ± 3.0
Patient survival					
PTA	98.3 ± 0.7	92.3 ± 5.5	87.0 ± 2.1	74.3 ± 3.7	68.4 ± 5.5
Bypass	NA	NA	NA	NA	NA

NA, Estimates not available; PTA, percutaneous transluminal angioplasty.

^aValues are pooled estimate and standard error.