MEET 2015, Nice

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Drug Coated Balloons in BTK disease

Koen Deloose, MD

Below the knee arterial disease

- A heterogeneous, highly diseased vascular bed, small diameters, most of the time severe Ca++ load
- The association between vessel patency and clinical success (wound healing, improved mobility, pain relief) is not well defined
- Level-1 evidence for endovascular therapies limited

The path to the real world…

Feasibility
Assessing safety and efficacy signals

Level I Gold Standard
Ideal conditions
Head to head unbiased assessment

Switching to all comers
Allow for extensive subanalysis
Ability to detect low rate events

Technical
Clinical endpoints
Economical

Proof of Concept

DCB-BTK Evidence: The LEIPZIG Registry

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CLINICAL RESEARCH — Interventional Cardiology

First Experience With Drug-Eluting Balloons in Infrapopliteal Arteries

Restenosis Rate and Clinical Outcome

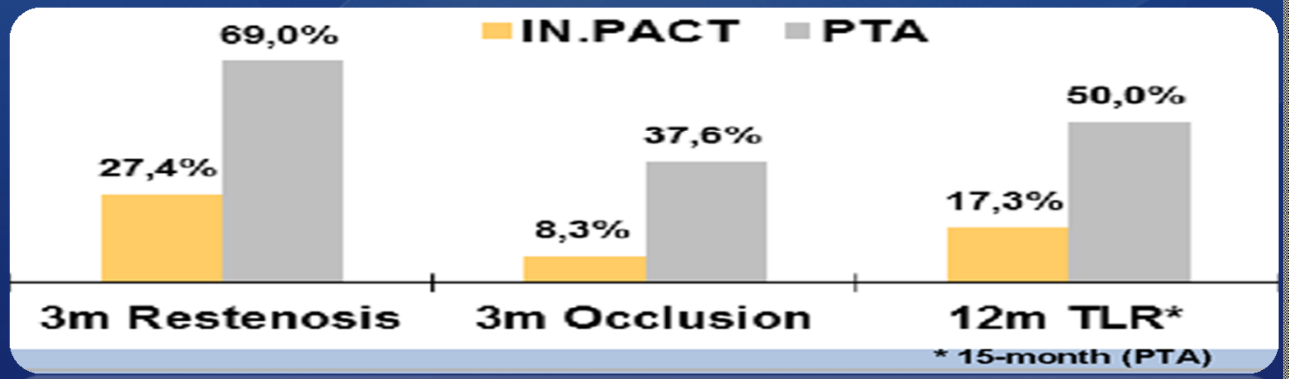
Andrej Schmidt, MD,* Michael Piorkowski, MD,* Martin Werner, MD,* Matthias Ulrich, MD,* Yvonne Bausback, MD,* Sven Bräunlich, MD,* Henrik Ick, MD,* Johannes Schuster, MD,* Spiridon Botsios, MD,* Hans-Joachim Kruse, MD,† Ramon L. Varcoe, MD,‡ Dierk Scheinert, MD*

Leipzig and Zschopau, Germany; and Sydney, Australia

Single Center Registry

- 104 Patients (CLI 82.6%)
- Diabetes 73%
- Mean lesion length 17 cm
- CTO's 62%

IN.PACT Amphirion* vs. matched PTA historical cohort**



* Schmidt A et al. J Am Coll Cardiol. 2011 Sep 6;58(11):1105-9
** Schmidt A et al. Catheter Cardiovasc Interv. 2010 Dec 1;76(7):1047-54

Proof of Concept

DCB-BTK Evidence: The LEIPZIG Registry

Circulation

American Heart Association

Drug-Eluting Balloon in peripherAl inTErvention for Below-the-K
(DEBATE-BTK): A R
Francesco Liistro, Italo Po
Falsini, Giorgio Ver

Circulation is published b
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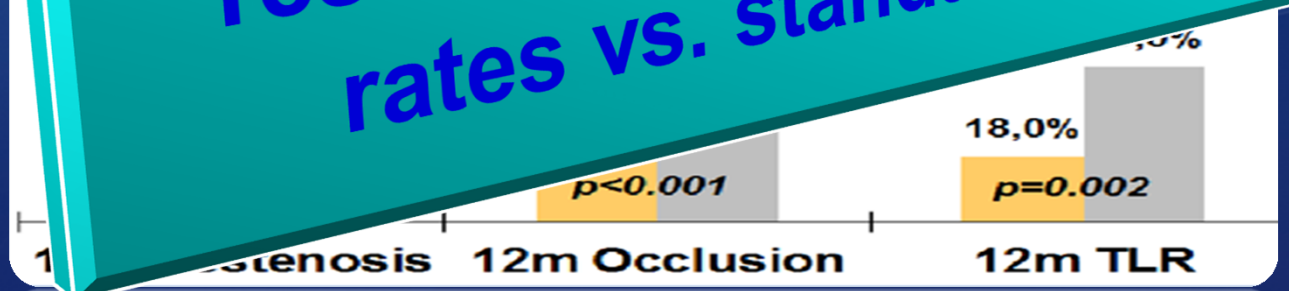
Single Center Registry

- 132 Patients (CLI 100%)

Early DCB-BTK evidence showed high promise for IN.PACT Amphirion to reduce restenosis & reintervention rates vs. standard PTA



Liistro F et al. Ciculation. 2013 Aug 6;128(6):615-21

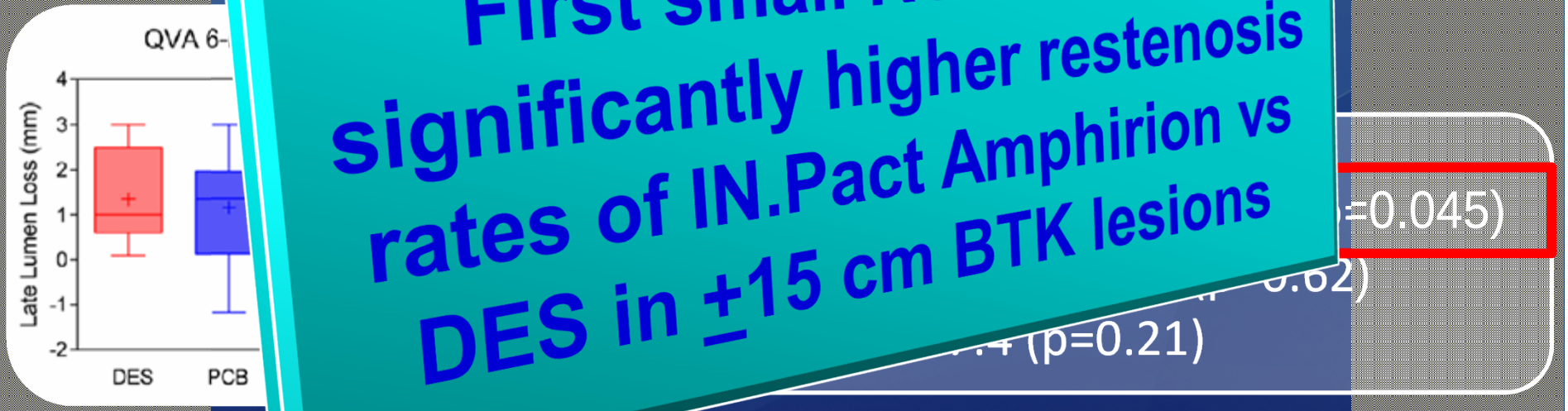
RCT

DCB-BTK Evidence: small RCT DCB-DES

Single Center RCT

- 50 Patients (CLI + CI)
- Mean lesion length : 14,8 cm (DCB) vs 12,7 cm (DES) ; p=0,33)

First small RCT showed significantly higher restenosis rates of IN.Pact Amphirion vs DES in ±15 cm BTK lesions



Late Lumen Loss (mm)
Group DES: 1.35 ± 0.2
Group PCB: 1.15 ± 0.3
P=0.62

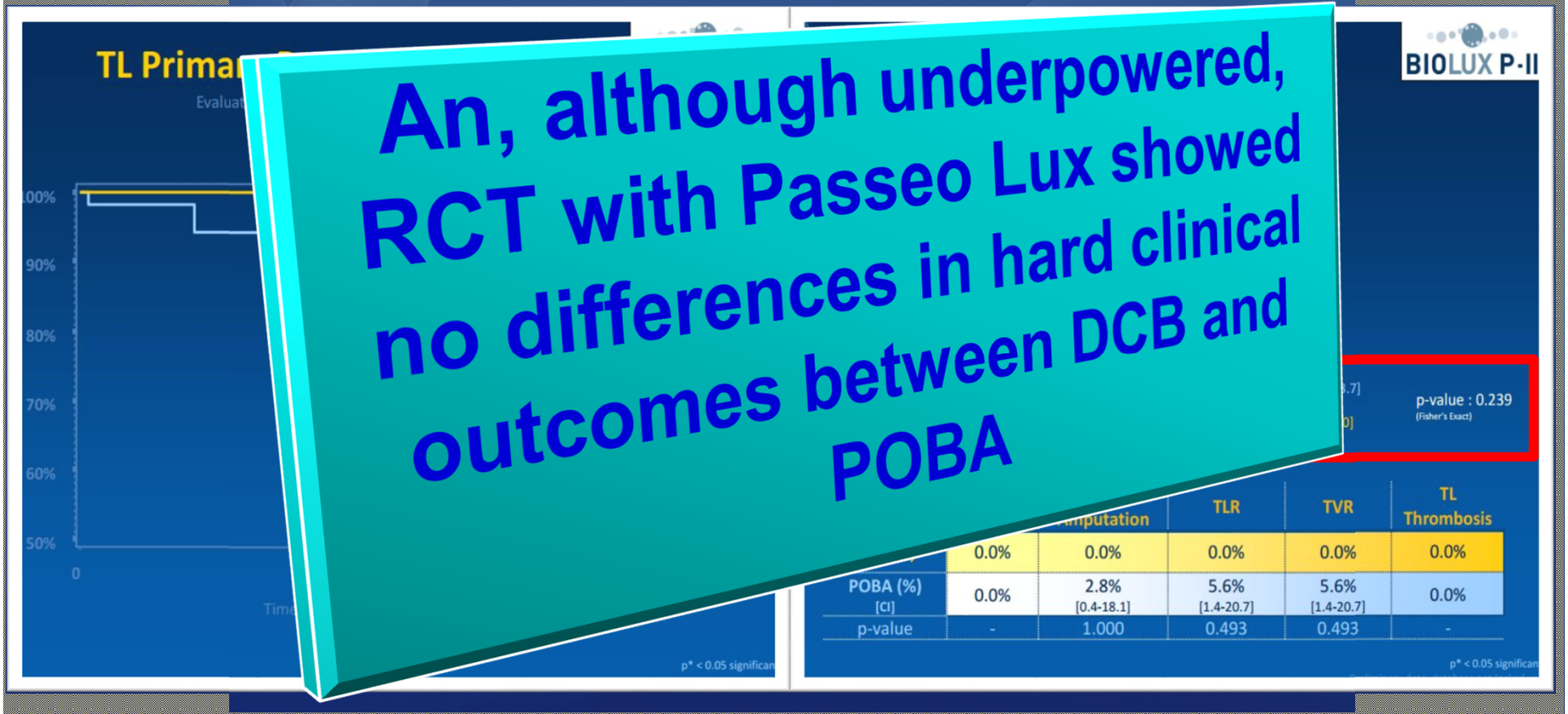
ES: 3.6 ± 1.5
Group PCB: 4.3 ± 1.6
p=0.16

P.M. Kitrou, MD, PhD – LINC 2014

RCT

DCB-BTK Evidence : BIOLUX P-II

- prospective, multi-center 1:1 RCT: DEB vs. POBA



An, although underpowered, RCT with Passeo Lux showed no differences in hard clinical outcomes between DCB and POBA

RCT

DCB vs. PTA in C IN.PACT DEEP

- IN. CT: DEB

IN.PACT Deep showed no "corelab" difference in efficacy between DCB & POBA.

There is a trend towards higher major amputation rates with DCB, although no statistical significant.

There is no evidence of beneficial subgroups.

There are no predictors of failure identified

Zeller et al. JACC , 15

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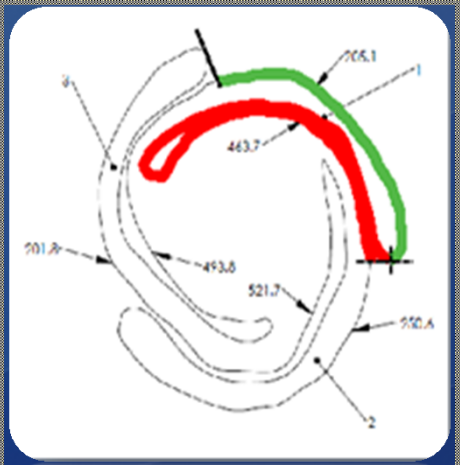
- DEVICE RELATED?
- STUDY DESIGN RELATED?
- BTK/CLI RELATED?

DEVICE RELATED?

	DCB	PTA	*p*
12-month LLL (mm)	0.61±0.78	0.62±0.78	*0.950*

Lack of drug effect?

	"Old" IN.PACT Amphirion	"New" (Next Gen) IN.PACT Pacific Admiral
Coating method	**Manually-coated on folded balloon**	**Automatically-coated on semi-inflated balloon**



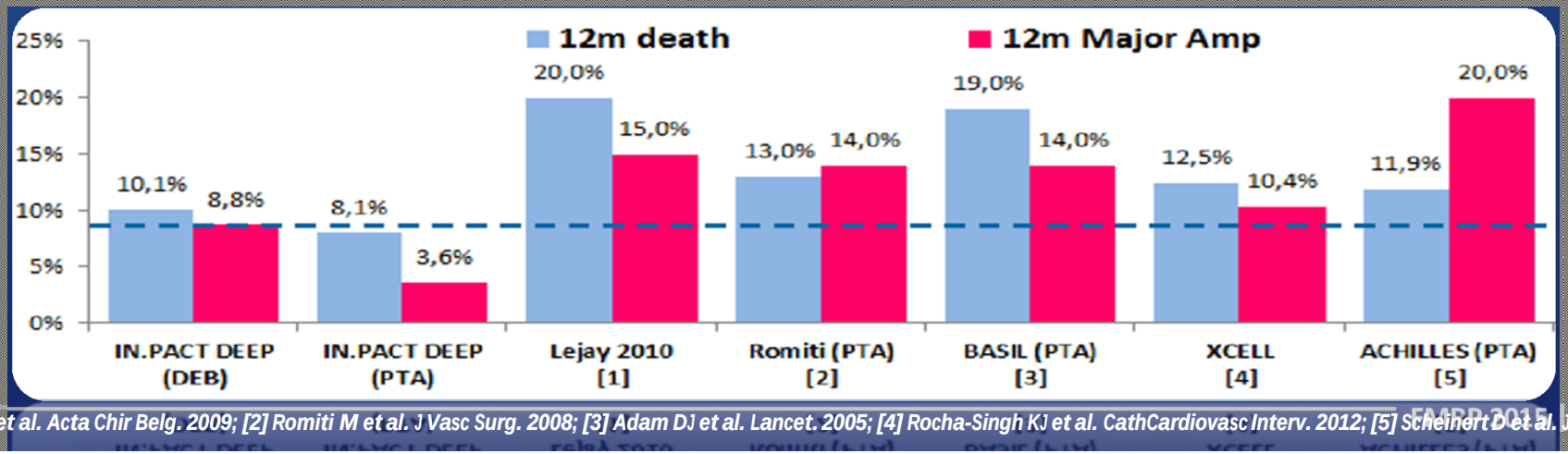
Animal studies confirmed balloon material can impact drug delivery:

- New design delivered more drug to vessel → Folds protect the drug
- New design had less residual drug on balloon → Better drug release

With the courtesy of T. Zeller, presented @ LINC 2015

STUDY DESIGN RELATED?

- Too small control arm (2:1 randomization)?
- Too wide eligibility criteria?
- No standardized wound care protocols?
- No standardized major amputation protocols?
- Low angiographic compliance?
- Very favorable major amputation rates in POBA arm?



[1] Lejay A et al. Acta Chir Belg. 2009; [2] Romiti M et al. J Vasc Surg. 2008; [3] Adam DJ et al. Lancet. 2005; [4] Rocha-Singh KJ et al. CathCardiovasc Interv. 2012; [5] Scheinert D et al. JACC 2012

BTK/CLI RELATED?

- Is there an essential fysiological difference between SFA and BTK? (IN.PACT SFA vs IN.PACT DEEP)
- Is there an essential difference between CLI and CI patients in PTX response/risk?

LUTONIX
BTK Clinical Trial

Trial Summary

PRIMARY ENDPOINTS	Safety at 30 days Limb salvage & primary patency at 12 months
NUMBER OF PATIENTS/ SITES	320 randomized patients at 55 global sites
FOLLOW-UP	**Clinical:** 1, 6, 12, 24, and 36 Months **Duplex Ultrasound (DUS):** 1, 6,12, 24, & 36 months **Angiography :** 12 months **Telephone:** 48 and 60 Months
NATIONAL PRINCIPAL INVESTIGATORS	**Patrick Geraghty:** Washington University, St. Louis, MO **Jihad Mustapha:** Metro Health Hospital, Wyoming, MI **Marianne Brodmann:** Medical University Graz, Austria
SPONSOR	Lutonix Inc., Minneapolis, MN

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BARD | LUTONIX

CONCLUSION

- No major differences in hard clinical outcomes across all studies between **ANY DCB** & control group

- **Further research** is mandatory in this DCB-BTK field :

✓ Is PTX the best and safest drug in tibial arteries?
✓ Is PTX the best and safest drug in CLI patients?
✓ Are there more efficient excipients upcoming?
✓ What is the best study design for CLI-BTK trials?