5 6 7 JUIN 2019

APPAC

Le ballon actif en première intention: une approche confortée par la littérature

N. Delarche

CH F. Mitterrand

PAU

APPAC 2019: Symposium BBRAUN, le 06 juin 2019

Conflits d'intêret:

consultant - recherche clinique:

Abbott, Boston, BBraun, Biotronik, Hexacath,

Astra-Zeneca, Amgen, Sanofi, MSD, Bayer, Boehringer,

Un regain d'intêret pour le ballon actif (DCB)?

- **Ne laisser aucun implant tout en délivrant une drogue antiproliférative locale**
  - Retour à une vasomotricité originelle
  - Retour à un remodelage positif
  - Éviter les complications induites par les stents: sous expansion, malapposition, néo-athérome, fracture de stents, réactions polymère-métal, et thromboses tardives à très tardives
- **Réduction de la durée de la DAPT à 1 mois**

Les DCB

- Ballons semi-compliants
- Coating / Agent cytotoxique
  - **Paclitaxel**++ (3 ùg/mm2): délivrance homogène pendant l'inflation++, et ½ vie de 2 mois
  - Sirolimus
- L'excipient retient la drogue sur le ballon, et lors de l'inflation autorise une délivérabilité rapide dans la paroi du vaisseau par sa **lipophilie**

Les DCB

DCB type	Excipient / coating technique
Sequent Please **B.Braun**	Iopromide matrix coating
Pantera Lux **BIOTRONIK**	BTHC matrix coating
IN.PACT Falcon **Medtronic**	FreePac matrix coating
Dior second generation **Eurocor**	Shellac matrix coating
Elutax SV Aachen Resonance	No excipient
Lutonix Bard	Polysorbate
Danubio APR Medtech	BHTC excipient

Le ballon actif
en première intention:
une approche confortée par la **littérature**

Les Lésions de Novo

- Petits Diamètres

DCB et lésions de novo: les évidences: les études Pilotes

Petits vaisseaux <= 2,75 mm

études	N pts	décès	MI	TLR-TVR >=6 m
Zeymer	479			3,6%
SeQuent Please registry	390			1%-1%
Elutax small registry	251	0%	0,7%	2%
Ho et al	320	0,8%	0%	4%
Valentines-II Trial	103			2,9%-4%
Leipzig Prospective Reg	76	0%	1%	0%
PICCOLETO study Dior	60	8%	3,9%	32% vs 10%DES
BELLO study IN.Pact	180			Late loss++
PEPCAD-BIF (vs poba)	64			6% vs 26%
Wohrle 2012	572/2095			1%

DCB et lésions de novo: les évidences: les études Pilotes

études	N pts	TLR – late loss	MACE
		Lésions de novo	
Rosenberg 2018	1025	2,3% (731 de novo lesions)	5,6%
Nishiyama 2016 (IVUS)	30	0% (vs 6,1% DES)	
Kleber 2014	58	Late lumen increases 4 mth	
Rosenberg 2019	234	3,8% (small vl)-1% (large vl)	

DCB et lesions de novo: les évidences: les études Pilotes

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Wo	572/2095			

TAXUS Lib. (1ère gén.)

Non infériorité à 6 et 36 mois +

DEB et lésions de novo: les évidences

Drug-Coated Balloons for Small Coronary Artery Disease: BASKET-SMALL 2

Rabah V. Jeger, Ahmed Farah, Marc-Alexander Ohlow, Norman Mangner, Sven Möbius-Winkler, Gregor Leibundgut, Daniel Weilenmann, Jochen Wöhrle, Stefan Richter, Matthias Schreiber, Felix Mahfoud, Axel Linke, Frank-Peter Stephan, Christian Mueller, Peter Rickenbacher, Michael Coslovsky, Nicole Gilgen, Stefan Osswald, Christoph Kaiser, and Bruno Scheller, for the BASKET-SMALL 2 Investigators

Lancet 2018; 392: 849-56

DEB et lésions de novo: les évidences

BASKET-SMALL 2

Rationale

- 2nd-generation drug-eluting stents (DES) are the preferred treatment for de-novo coronary lesions
- Efficacy of DES is limited in small vessels due to high rates of instent-restenosis
- Drug-coated balloons (DCB) are an established treatment strategy for in-stent restenoses of bare metal stents and DES
- The efficacy and safety of DCB in de-novo stenoses is unknown

2 essais randomisés antérieurs
Petits échantillons
Comparatif: stent 1ère génération
Endpoints angiographiques

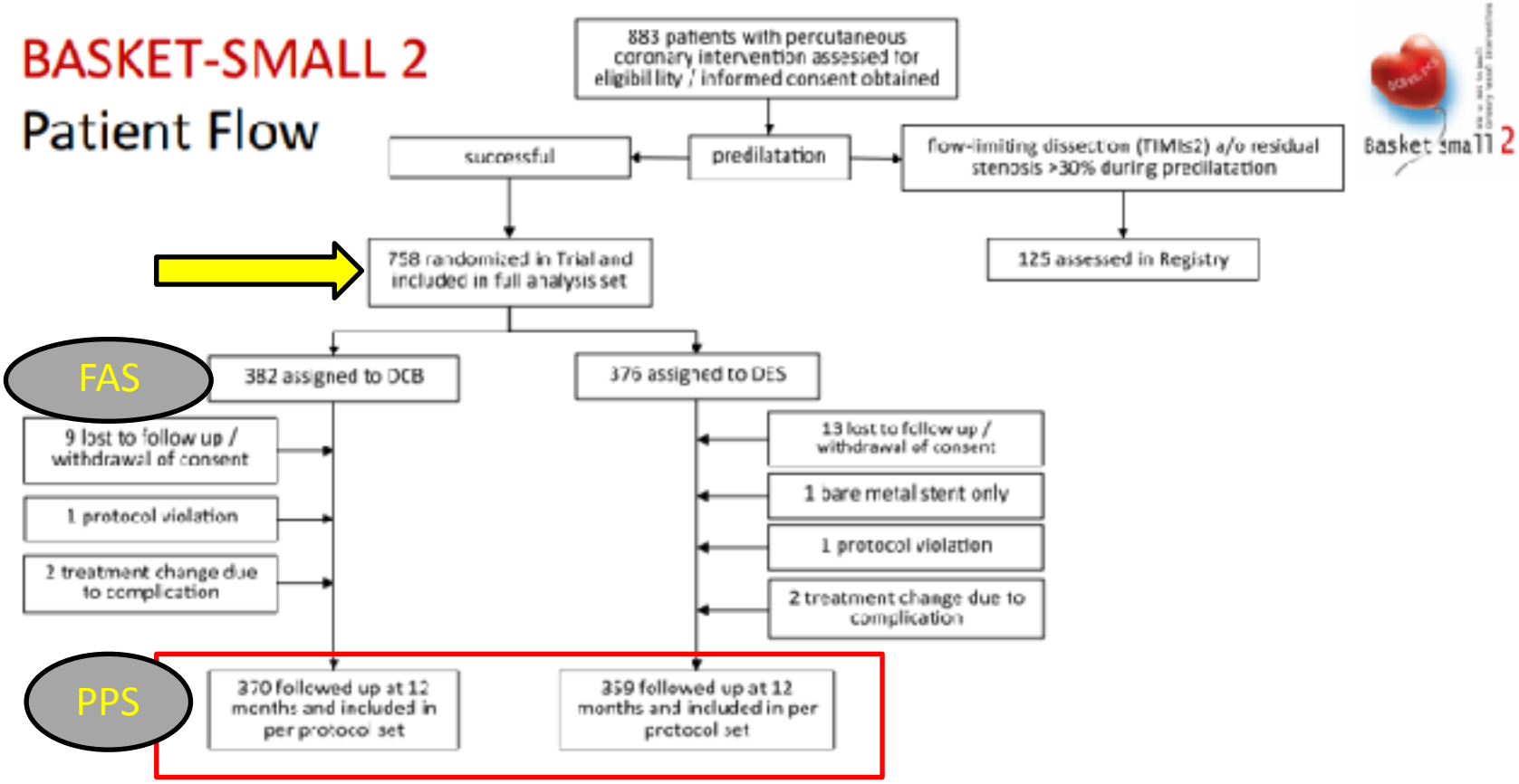
DEB et lésions de novo: les évidences

BASKET-SMALL 2

Design

- Multicenter, randomized controlled non-inferiority trial (14 centers in Germany, Switzerland, and Austria)
- Patients undergoing PCI in native coronary arteries <3 mm
- Initial comparison Sequent Please® DCB (B.Braun Melsungen) vs. Taxus Element® DES (Boston Scientific), then changed to Xience® DES (Abbott Vascular) after appr. 25% of patients
- Primary endpoint: Non-inferiority for major adverse cardiac events (MACE; cardiac death, non-fatal myocardial infarction, and target vessel revascularization) @ 12 months
- Expected MACE rates of 7% for DCB and 10% for DES with non-inferiority margin <4% (upper limit of the two-sided 95% confidence interval of the absolute risk difference)
- Sample size calculation (based on Xience®): 758 patients

DEB et lésions de novo: les évidences



DEB et lésions de novo: les évidences

BASKET-SMALL 2

Clinical Baseline Characteristics

	DCB (n=382)		DES (n=376)		
Age (mean, SD)	67.2	(10.3)	68.4	(10.3)	
Sex Male (%)	295	(77.2)	262	(69.7)	p=0.0232
Current/former smoker (%)	226	(60.4)	195	(53.1)	
Hypercholesterolemia (%)	262	(68.8)	259	(70.0)	
Arterial hypertension (%)	324	(84.8)	332	(88.8)	
Family history of CAD (%)	150	(42.6)	128	(38.0)	
Diabetes mellitus (%)	122	(32.0)	130	(34.9)	
Previous MI (%)	160	(41.9)	133	(35.4)	
Cerebrovascular insult (%)	29	(7.6)	37	(9.8)	
PAOD (%)	27	(7.1)	26	(6.9)	
COPD (%)	28	(7.3)	36	(9.6)	
Renal failure (%)	54	(14.1)	59	(15.7)	

DEB et lésions de novo: les évidences

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STEMI	11 (3%)	4 (1%)
NSTEMI	53 (14%)	56 (15%)
UA	48 (13%)	42 (11%)
STABLE ANGINA	270(70%)	274 (73%)

DEB et lésions de novo: les évidences

BASKET-SMALL 2

Angiographic Baseline Characteristics

	DCB (n=382)		DES (n=376)	
Target vessel				
Left anterior descending artery (%)	128	(33.5)	116	(30.9)
Left circumflex artery (%)	179	(46.9)	183	(48.7)
Right coronary artery (%)	75	(19.6)	77	(20.5)
Bifurcation lesion (%)	22	(5.8)	29	(8.0)
Procedural success (%, mean, SD)	96	(19)	98	(13)
Number of DCB or DES (mean, SD)	1.68	(0.82)	1.26	(0.55)
Length of DCB or DES (mm; mean, SD)	23.93	(11.74)	23.18	(12.85)
Effective size of DCB or DES (mm; mean, SD)	2.75	(2.14)	2.57	(0.25)
Inflation pressure (atm; mean, SD)	11.06	(3.54)	13.58	(3.90)
Duration of inflation (sec; mean, SD)	48.45	(28.24)	23.36	(18.92)

DEB et lésions de novo: les évidences

BASKET-SMALL 2

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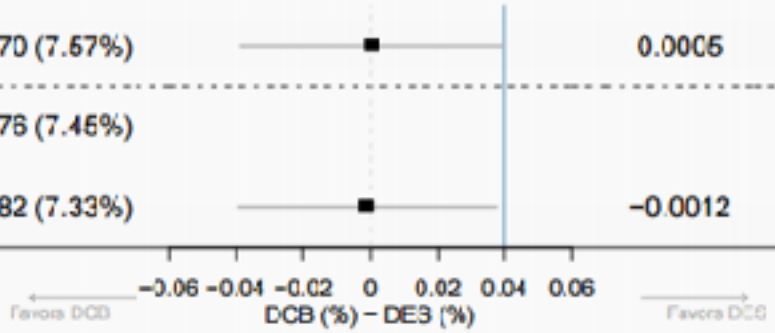
DEB + stent: 19 pts (5,1%)
DES Taxus: 94 pts (28%)

DEB et lésions de novo: les évidences

BASKET-SMALL 2

Primary Endpoint (Non-Inferiority)

Set	Level	Events	Difference	CI	p
PPS	DES	27 / 359 (7.52%)			
	DCB	28 / 370 (7.57%)	0.0005	[−0.038, 0.039]	0.0217
FAS	DES	28 / 376 (7.46%)			
	DCB	28 / 382 (7.33%)	−0.0012	[−0.040, 0.037]	0.0152

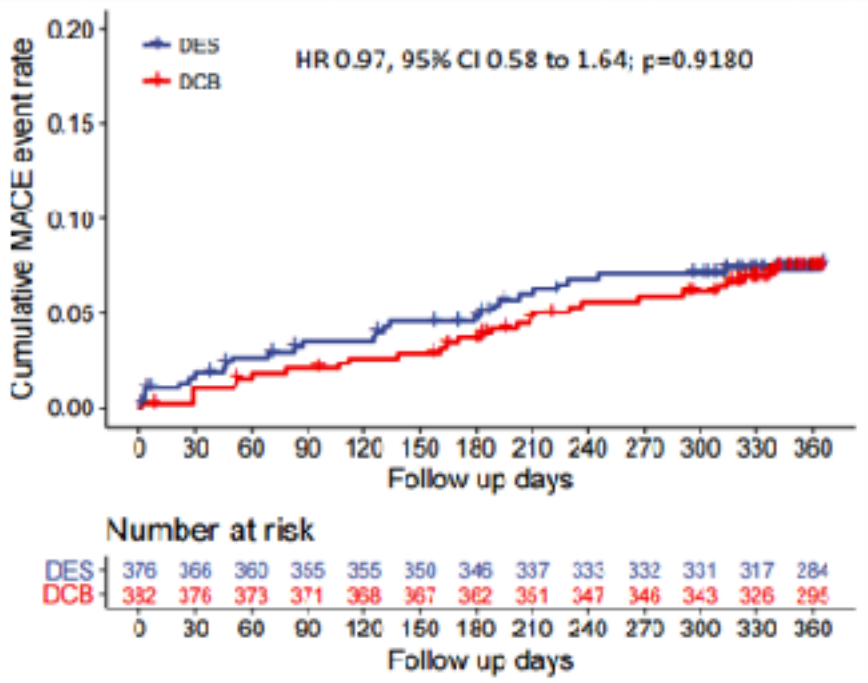


PPS: per protocol set; FAS: full analysis set.

DEB et lésions de novo: les évidences

BASKET-SMALL 2

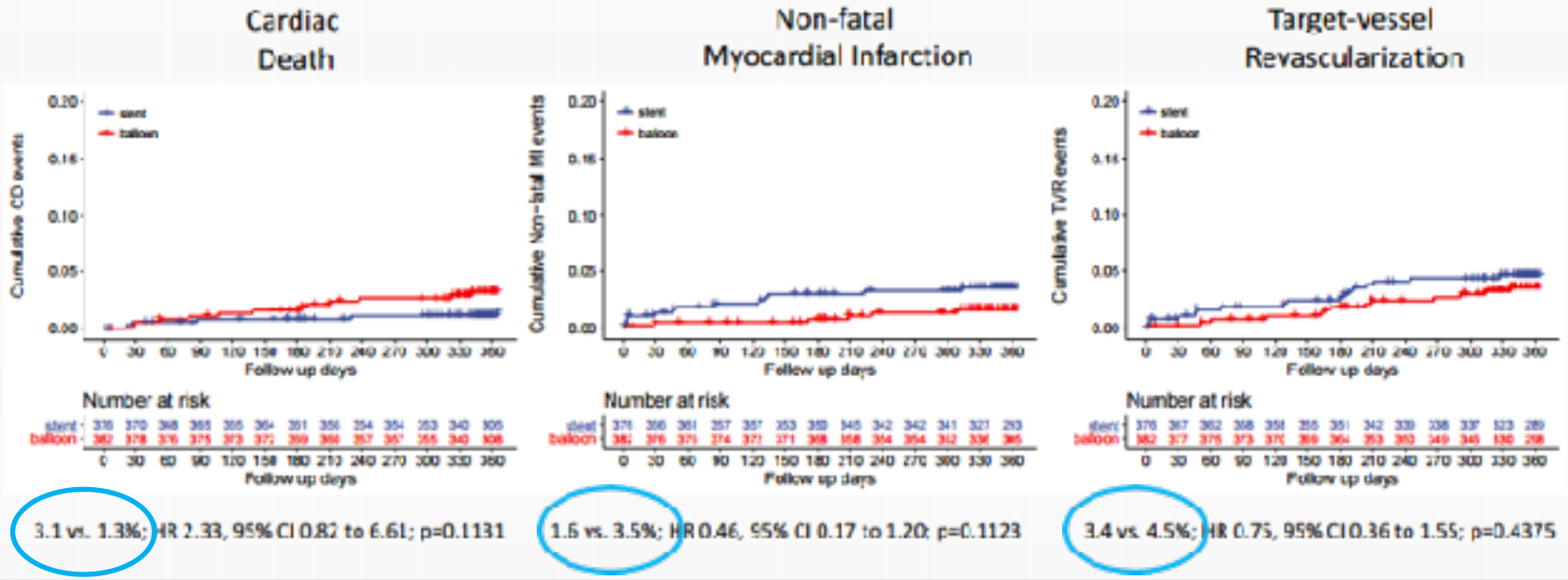
MACE (12 Months)



DEB et lésions de novo: les évidences

BASKET-SMALL 2

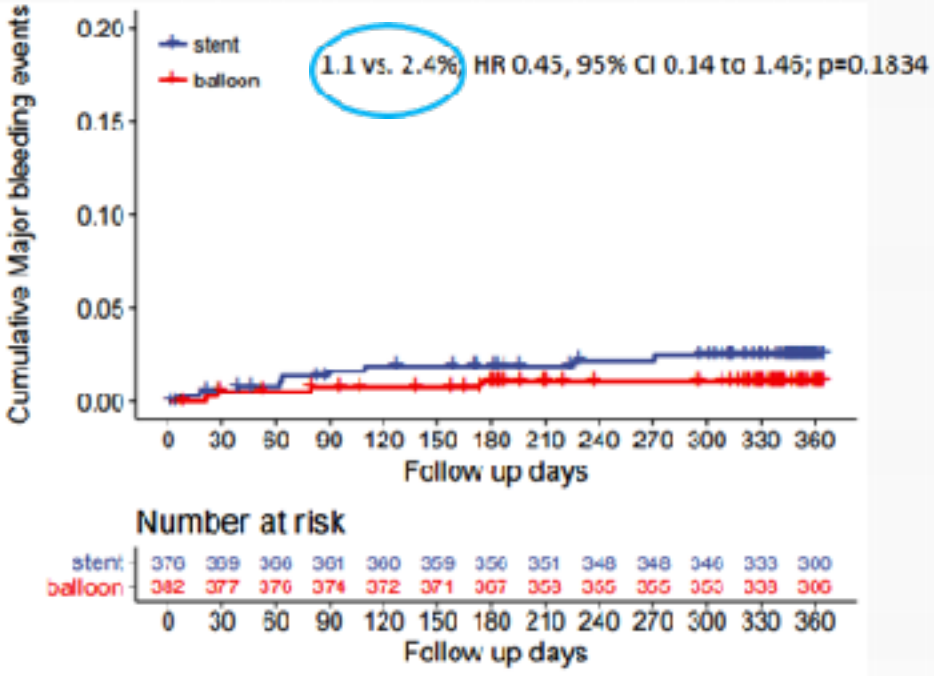
Single Components of MACE (12 Months)



DEB et lésions de novo: les évidences

BASKET-SMALL 2

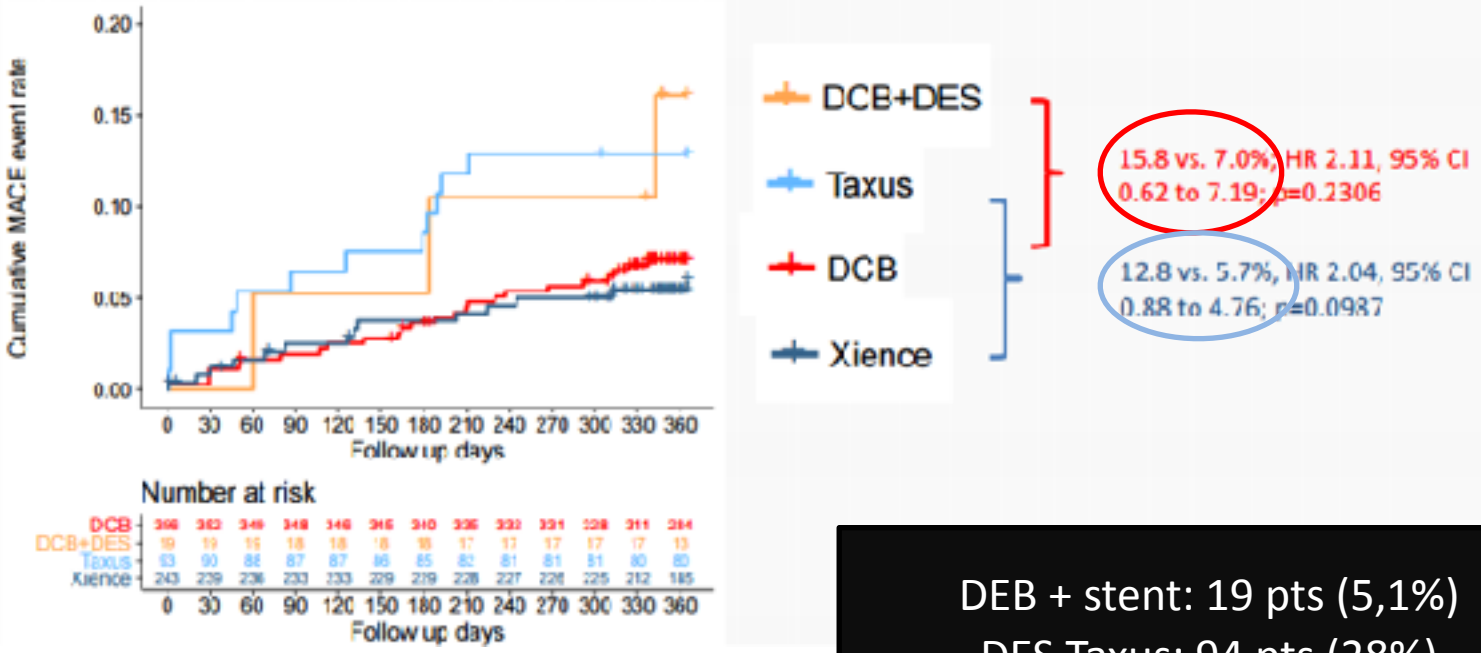
Major Bleeding (BARC ≥3, 12 Months)



DEB et lésions de novo: les évidences

BASKET-SMALL 2

MACE (12 Months) for Device Subgroups



DEB + stent: 19 pts (5,1%)
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DEB et lésions de novo: les évidences

BASKET-SMALL 2
Les sous groupes

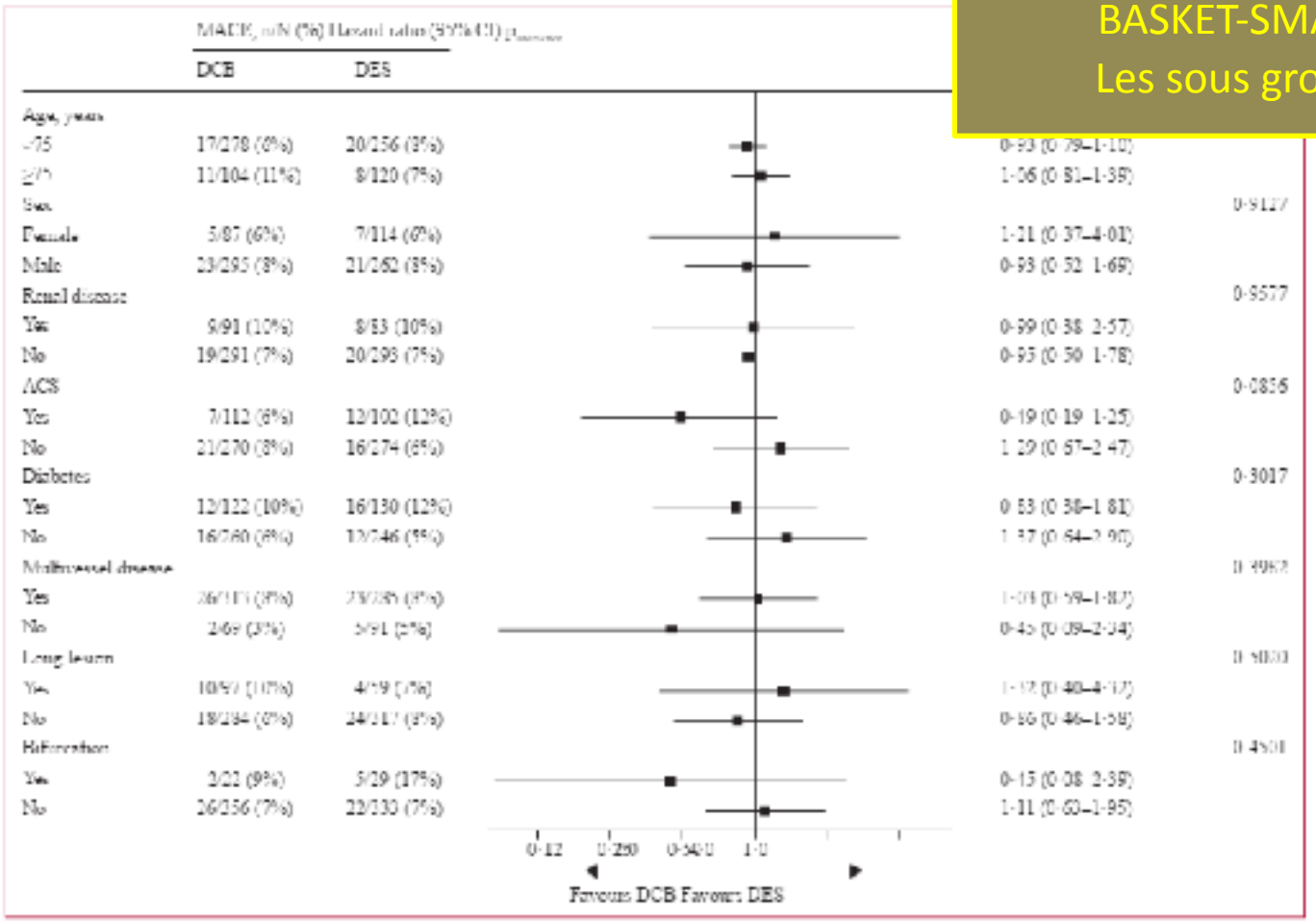


Figure 4: Subgroup analyses of MACE and hazard ratios

Cox proportional hazards models were fitted with time-to-MACE as outcome and with patients censored at last observation if experiencing no event. All analyses were done on the full analysis population with the treatment group as assigned to patients at randomisation. MACE=major adverse cardiac events. DCB=drug coated balloons. DES=drug-eluting stents. ACS=acute coronary syndrome

DEB et lésions de novo: les évidences

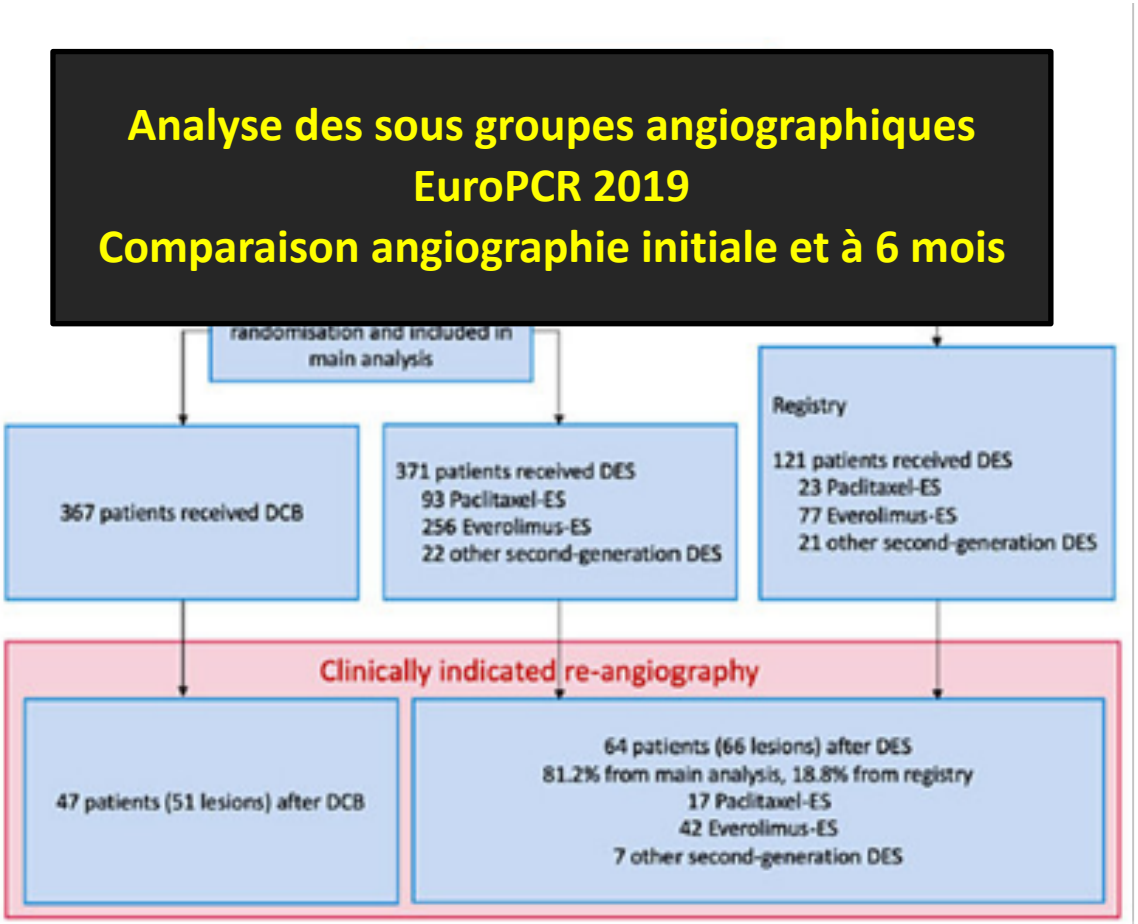
BASKET-SMALL 2

- Limites:
  - Changement de DES 2de génération:
    - nouveau comparateur possible: DES à polymère biodégradable et mailles extra ou ultrafine?
  - Distribution inégale dans le sexe entre les 2 groupes
  - Pas d'extrapolation possible aux autres DCB
  - Pas de suivi angiographique: possible sous estimation des évènements

DEB et lésions de novo: les évidences

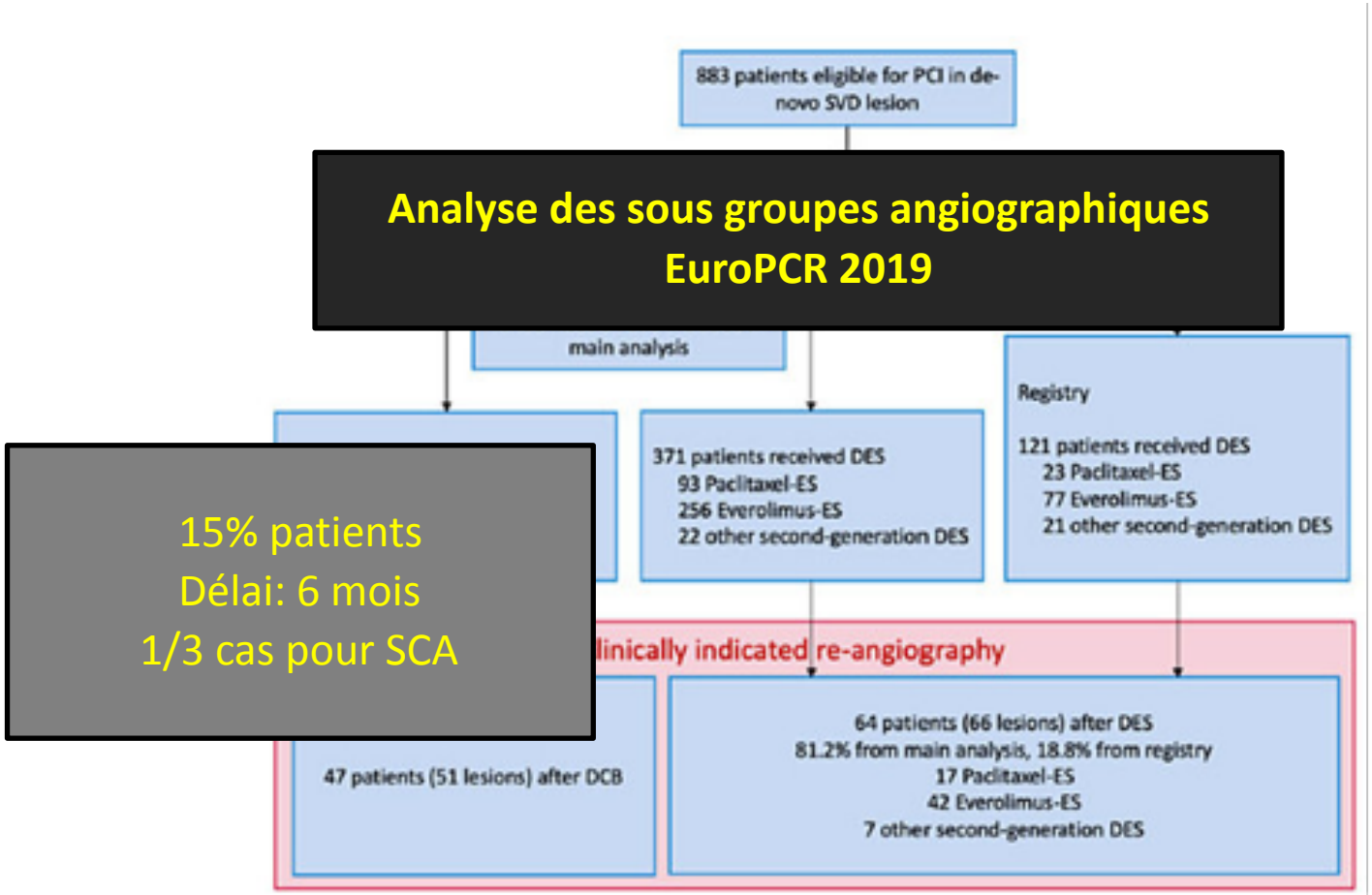
BASKET-SMALL 2

Analyse des sous groupes angiographiques
EuroPCR 2019
Comparaison angiographie initiale et à 6 mois



DEB et lésions de novo: les évidences

BASKET-SMALL 2



DEB et lésions de novo: les évidences

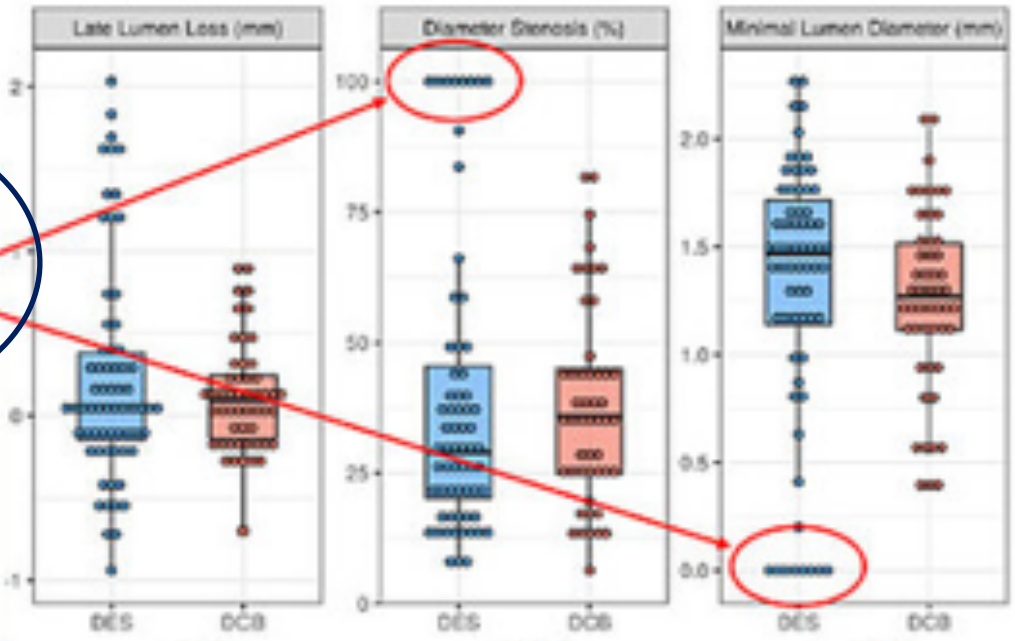
BASKET-SMALL 2

Key Results

Complete thrombotic vessel occlusion in 8 patients with DES (Xience n=5, Taxus n=3) vs. none with DCB (p = 0.009)

Clinical presentation:
- 3 STEMI
- 1 NSTEMI
- 3 unstable angina
- 1 heart failure

All but one on DAPT



Time until follow-up DES vs. DCB 175 (77-224) vs. 170 (82-229) days (p = 0.70)

DEB et lésions de novo: les évidences

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Conclusions

- First large randomized controlled trial testing the efficacy of a paclitaxel-iopromide-coated DCB vs. second-generation DES in a large all-comer population regarding clinical endpoints
- DCB are non-inferior to DES in lesions of small native coronary arteries regarding MACE up to 12 months, with similar event rates for both treatment groups

Small native coronary artery disease may safely be treated with DCB after successful predilatation


Merci pour votre attention