Speaker's name: Thomas Cuisset, MD, PhD

X **I have the following potential conflicts of interest to report:**

x Consulting: Astra Zeneca, Daiichi Sankyo, Eli Lilly, Medicines Company

❒ Employment in industry

❒ Stockholder of a healthcare company

❒ Owner of a healthcare company

x Others: Lecture Fee

Abbott Vascular, Astra Zeneca, Biotronik, Boston Scientific, Cordis, Daichi Sankyo, Edwards, Eli Lilly, Hexacath, Iroko Cardio, Medtronic, Servier , Terumo

❒ **I do not have any potential conflict of interest**

Apport d'un polymère biorésorbable?

Thomas Cuisset, Marseille

Congrès de l'APPAC, Juin 2015

Concept

Why Biodegradable (BP)-DES ?

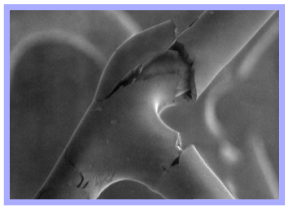
DES polymer considerations

Polymer:

Matrix to modulate drug release into vessel wall

No function after drug release is complete

Have potential to be damaged



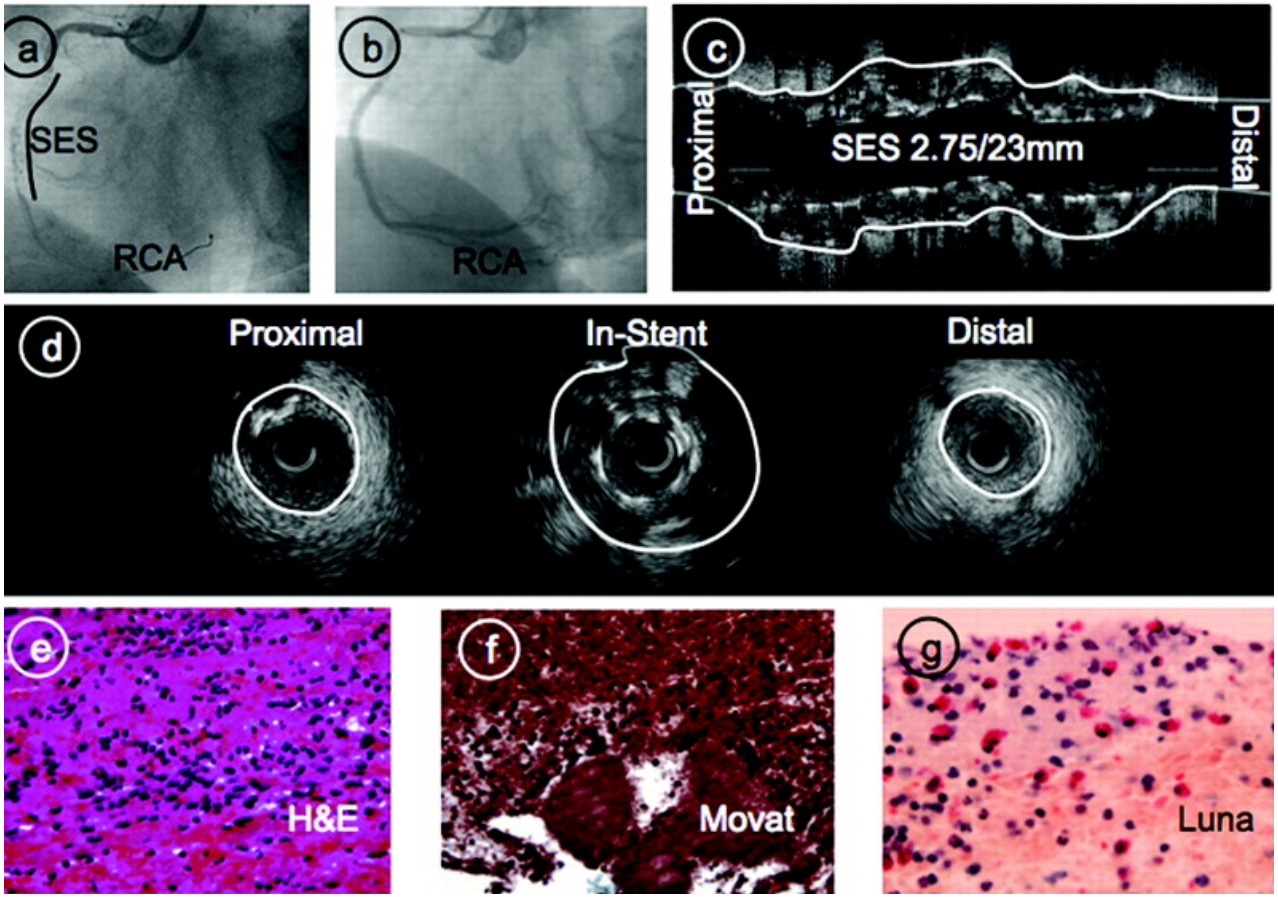
Safety issues

- Late / very late **stent thrombosis**
- Potentially require **long-term DAPT**

Efficacy

- Chronic inflammation with **neoatherosclerosis**
- Constant irritant may lead to late **restenosis**

Polymer as a factor of late stent failure ?



Very late SES-thrombosis

Late malapposition

Inflammatory reaction

Benefit of BP-DES ?

Cook S et al. Circulation 2009

Concept

Why BP-DES ?

Absence of polymer could improve long term efficacy and safety of DES

Biodegradable Polymer DES

Better than other DES ?

Shorter DAPT possible ?

Stent thrombosis and BP-DES ?
« Direct evidence » ?

RCT between two DES
Stent thrombosis as Primary endpoint
Same strut thickness and drug
Permanent vs Biodegradable polymer
Lower rate of stent thrombosis if BP-DES

NO

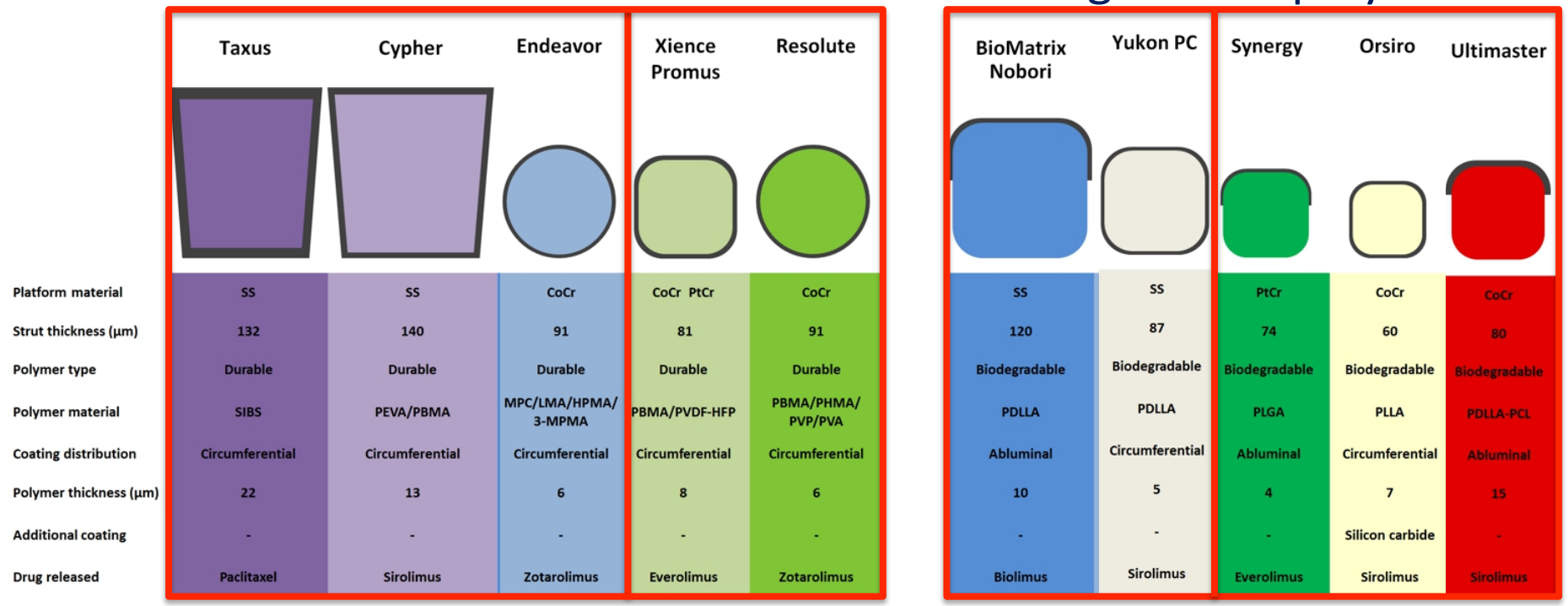
Any indirect arguments ?

BP-DES: Less Stent thrombosis ?

All BP-DES are not the Same !

Permanent polymer DES

Biodegradable polymer DES



1st GEN. 2nd GEN. 1st GEN. 2nd GEN.

Stefanini, Taniwaki, Windecker. Heart 2013, ahead of print

« First generation » Head-to-Head BP-DES

LEADERS (n = 1707)
BP-BES (Biomatrix) vs SES :Non inferiority

Windecker et al, Lancet 2008

ISAR TEST 4 (n=2609)
BP-DES vs EES or SES: Non inferiority

Byrne et al, EHJ 2009

SORT OUT V (n=1229)
BP-BES (Nobori) vs SES (Cypher): Non inferiority

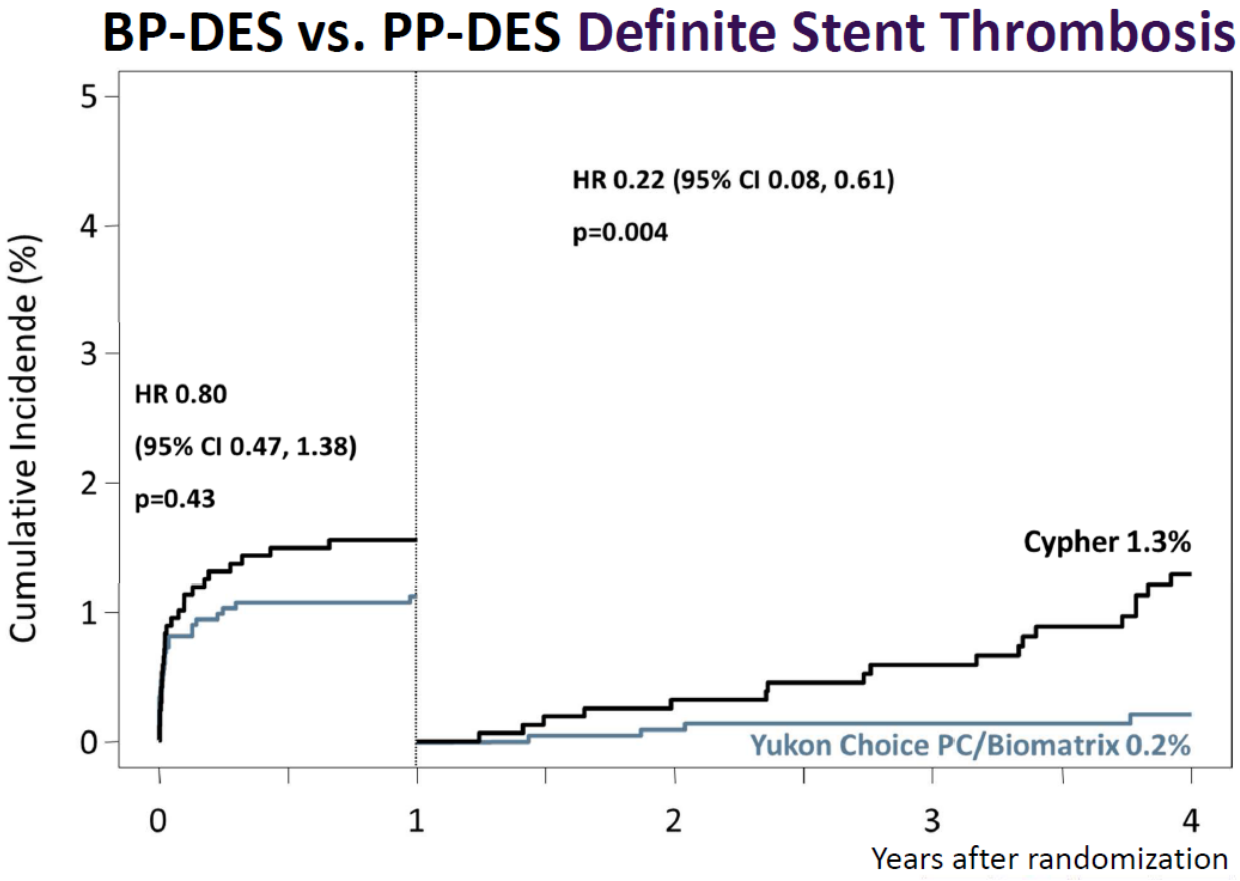
Christiansen et al, Lancet 2013

SORT OUT VI (n=2999)
BP-DES (Biomatrix) vs ZES (Resolute): Non inferiority

Raungaard et al, TCT 2013

BP-DES and stent thrombosis

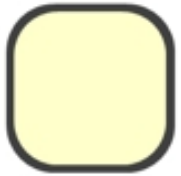
Definitive stent thrombosis / Pooled analysis ISAR TEST and LEADERS



Stefanini G et al. Eur Heart J 2012

« New generation » BP-DES

STENT	Synergy	Ultimaster	Orsiro
Company	Boston Scientific	Terumo	Biotronik
Strut	**74 µm**	**80 µm**	**60 µm**
Drug	Everolimus	Sirolimus	Sirolimus
Drug release	3 months	3 months	3 months
Polymer Release	**3-4 months**	**3-4 months**	**12-18 months**
Polymer	Abluminal	Abluminal	Circumferencial
Study	EVOLVE II	CENTURY II	BIOSCIENCE



« New generation » Head-to-Head BP-DES

Evidence versus permanent polymer DES

EVOLVE II (n=1684)
Synergy BP-EES vs EES: Non inferiority

Kereiakes et al, JACC 2014

CENTURY II (n = 1123)
Ultimaster BP-SES vs EES :Non inferiority

Saito et al, EHJ 2014

BIOSCIENCE (n=2119)
Orsiro BP-SES vs EES: Non inferiority

Pilgrim et al, Lancet 2014

BP-DES: Specific interest in STEMI ?

LEADERS STEMI (n=275)

BP-DES (BES) vs SES : Potential benefit of BP-DES

Windecker et al, Lancet 2008

BIOSCIENCE STEMI(n=407)

Orsiro (SES) vs EES : Potential benefit of BP-DES

Pilgrim et al, Lancet 2014

Subgroup, Secondary endpoint, non-inferiority study

Shorter DAPT with BP-DES: Evidence ?

	n	% SCA	Ischemic	Bleeding
DES LATE, *NEJM 2010*	2117	60%	12 Mo = >12Mo	No difference
EXCELLENT, *JACC 2012*	1443	50%	6 Mo = 12Mo	No Difference
PRODIGY, *Circulation 2012*	2013	75%	6 Mo = 24 Mo	More bleeding
RESET, *JACC 2012*	2117	55%	3 Mo = 12 Mo	No difference
OPTIMIZE, *JAMA 2013*	3119	30%	3 Mo = 12 Mo	More bleeding
ARCTIC, *TCT 2013*	1259	25%	12 Mo = >12Mo	More Bleeding
SECURITY, *JACC 2014*	1399	40%	6Mo = 12Mo	No difference
ISAR SAFE, *AHA 2014*	4005	40%	6Mo = 12 Mo	More Bleeding
ITALIC, *JACC 2014*	2031	25%	6 Mo = 24 Mo	No difference

Few BP-DES, No specific data

EVOLVE II study

SYNERGY stent

Thin strut
Biodegradable polymer
Abluminal polymer
3 Mo release for drug-polymer

Concept

3 Mo release → Short DAPT

Marketing

« PCI with short DAPT »

SYNERGY stent study: EVOLVE II

Short DAPT: really ?
98% DAPT at 6 months
90% at 12 months

0.4% stent thrombosis with new DES …but with long term DAPT

Ongoing studies with BP-DES and 1 month DAPT !

Kereiakes et al, AHA 2014

What to expect from BP-DES ?

Permanent polymer associated with late stent failure?

BP-DES could improve long-term stent results

No head-to-head evidence against other DES

Demonstration of possible shorter DAPT could be key

Conclusion

« Qu'attendre des DES à polymère biorésorbable ? »

Superiority will probably never been demonstrated

Non inferiority + Studies with short DAPT + Concept

→ BP-DES becoming the new 'gold standard' ?

Changing practice: Evidence vs Concept

Medical community adopts new technology when:

Superiority compared to gold standard (EBM)

OR

Non inferiority and …

- Answer to a clinical need
- Modifications with underlying meaningful concept
- Solution for prior technology limitations

Changing practice: Evidence vs Concept

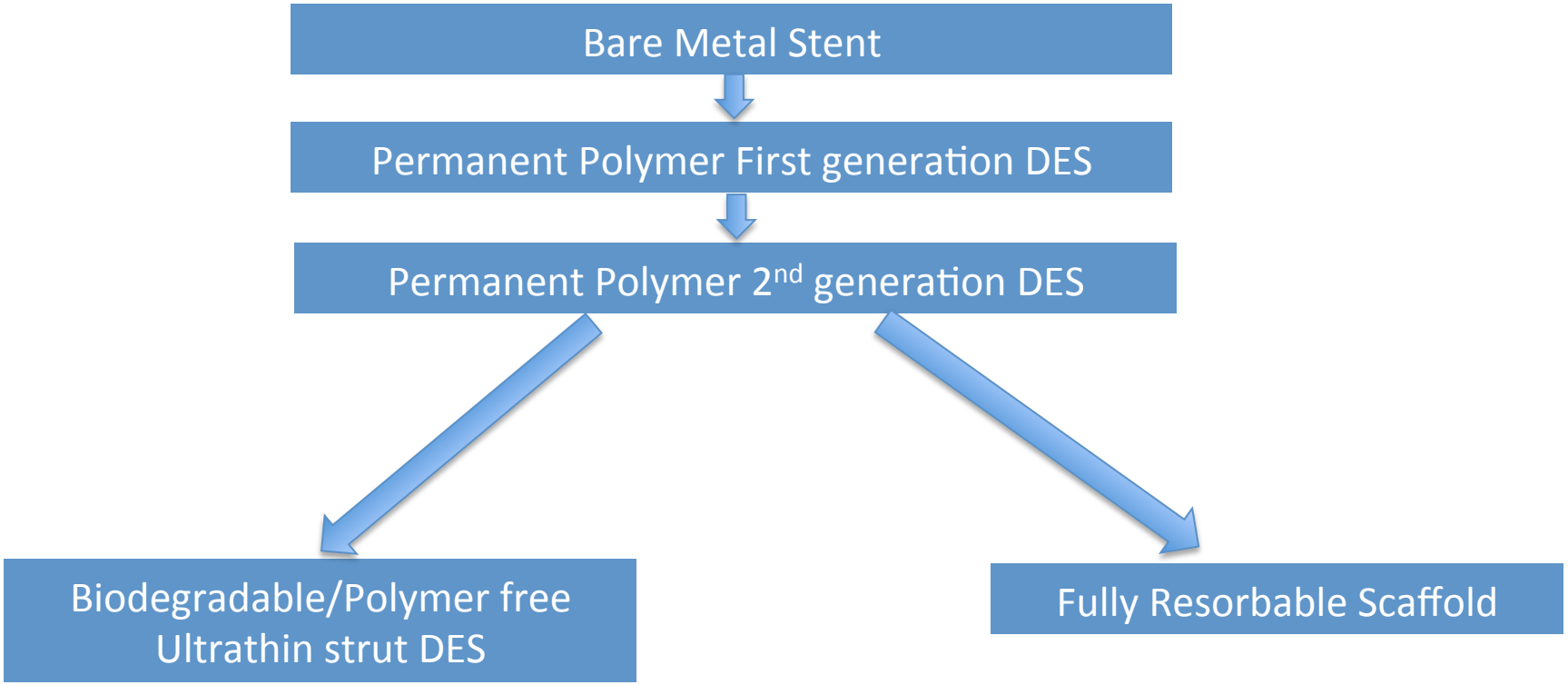
Metalic stent — Late Stent failure? — BVS

RCT showing lower rate of late ST with BVS ?

Permanent polymer DES — Late Stent failure? — **BP-DES**

RCT showing lower rate of late ST with PF/BP DES ?

Evolution of 'Stent' Technology



'BMS after 3 months vs No more stent after 3 years' ??

Thank You