Future Clinical Study for NOBORI stent

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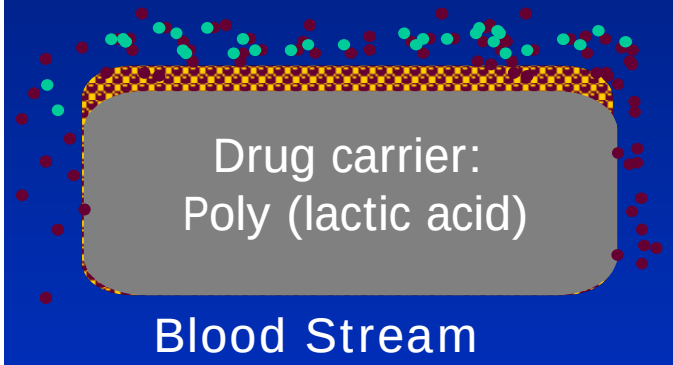
Nobori DES Components

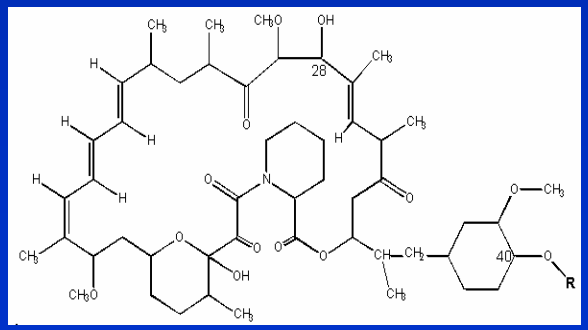
S-Stent™ (stainless steel)

- Quadrature-link design
- Excellent flexibility and scaffolding



PLA Biodegradable Polymer

- Abluminal coating; Controlled biodegradability
- Simultaneous release of drug & polymer into tissue
- Minimal polymer weight

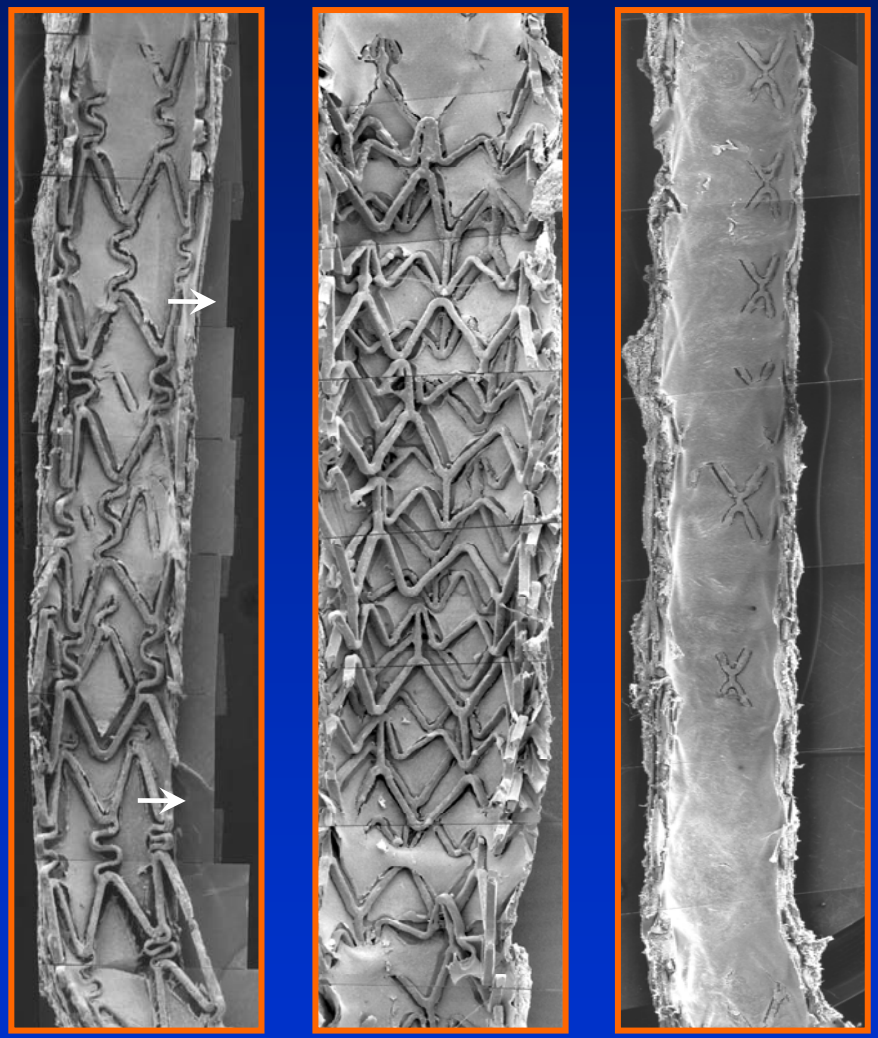


Biolimus A9™ (rapamycin derivative)

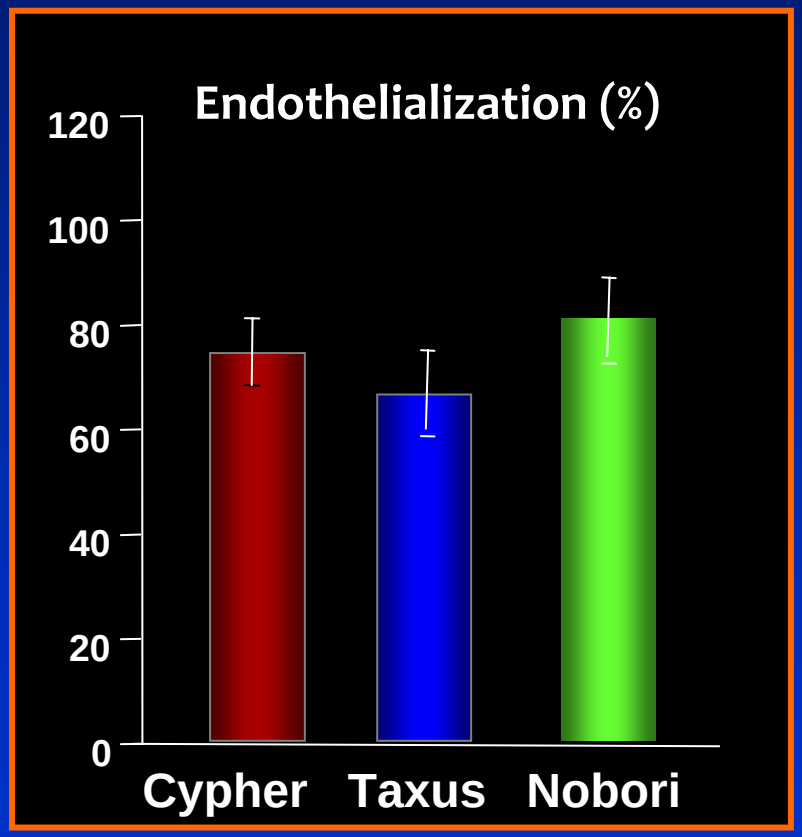
- A potent new "Limus" designed for stent applications
- Powerful immunosuppressant, anti-inflammatory
- More lipophylic; elutes fast from stent

Comparison of Various overlapped DES in Rabbit Iliac Arteries at 28-days

overlapped



CYPHER TAXUS NOBORI



Finn A, et al. Circulation 2005

Nobori Study in Asan Medical Center

Planning the RCT using the NOBORI stent in complex subsets

: Long-Lesion, Diabetes

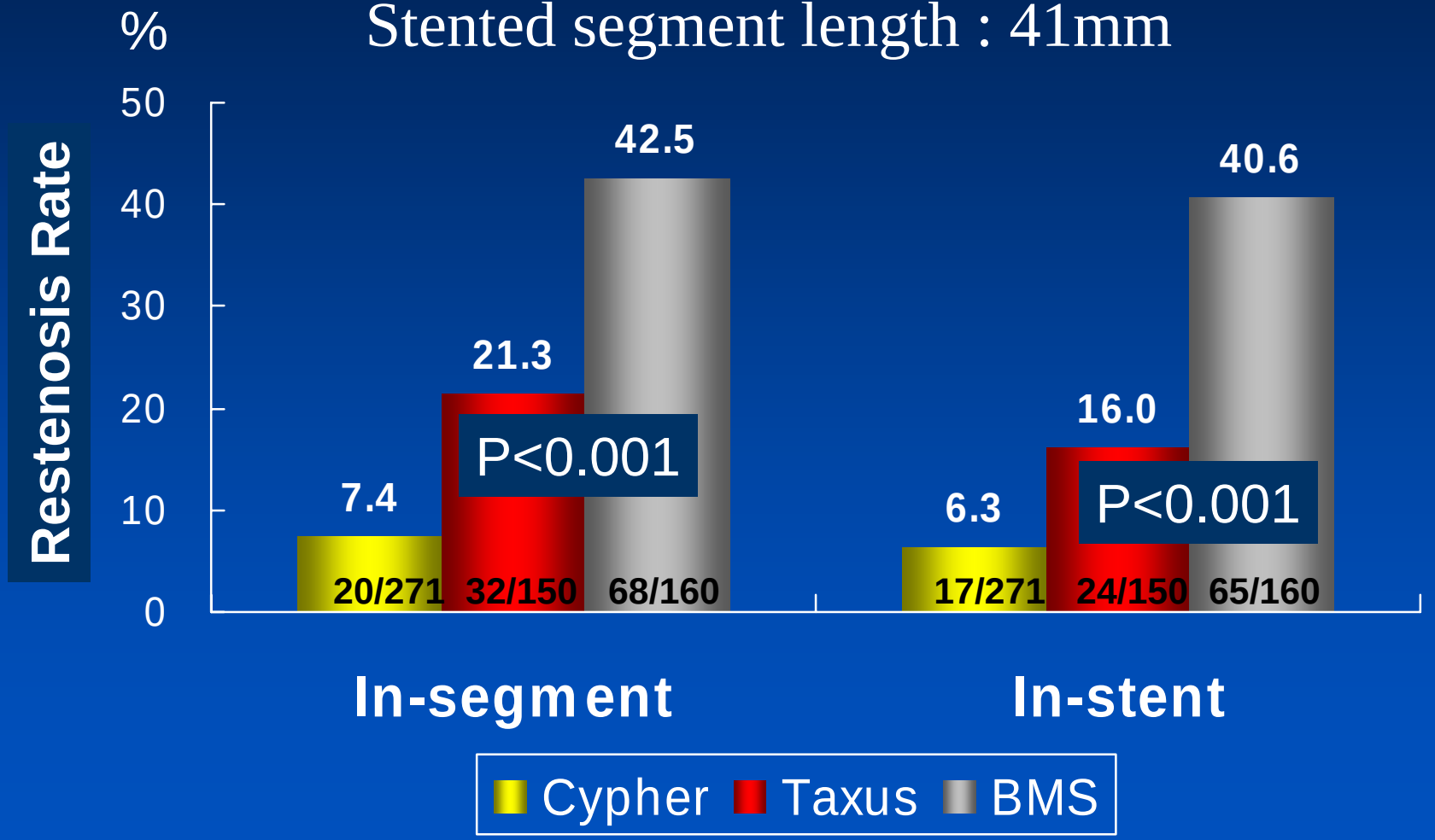
“Best stent” showed good performance at worst patient and lesion subsets

DM and LONG-DES Series

Long DES-I Study

Multicenter Registry Study

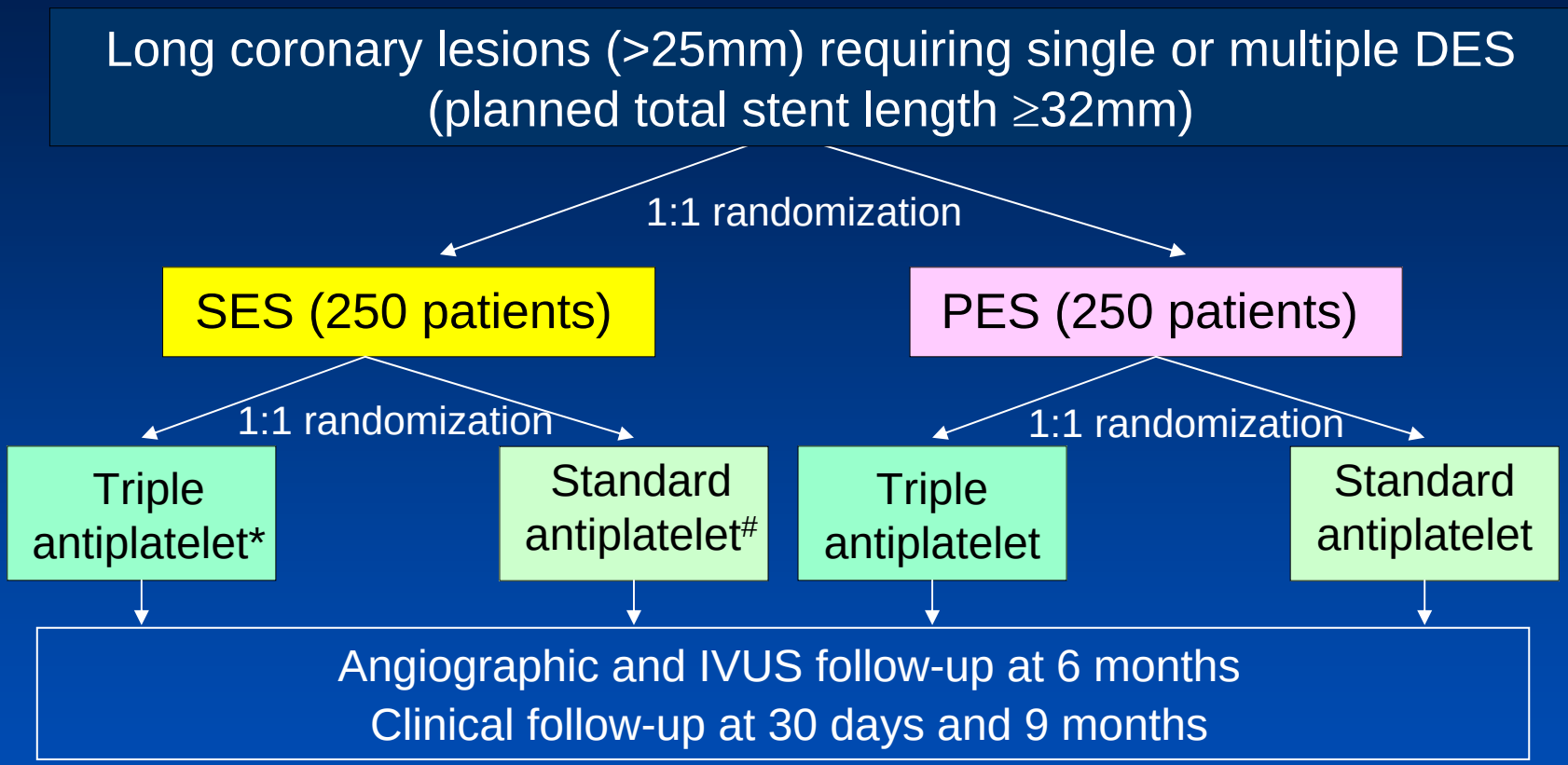
Lesion length :36 mm
Stented segment length : 41mm



Kim et al, Catheter Cardiovasc Interv 2006;67:181-7

Long-DES II

Prospective, Randomized Multicenter trials



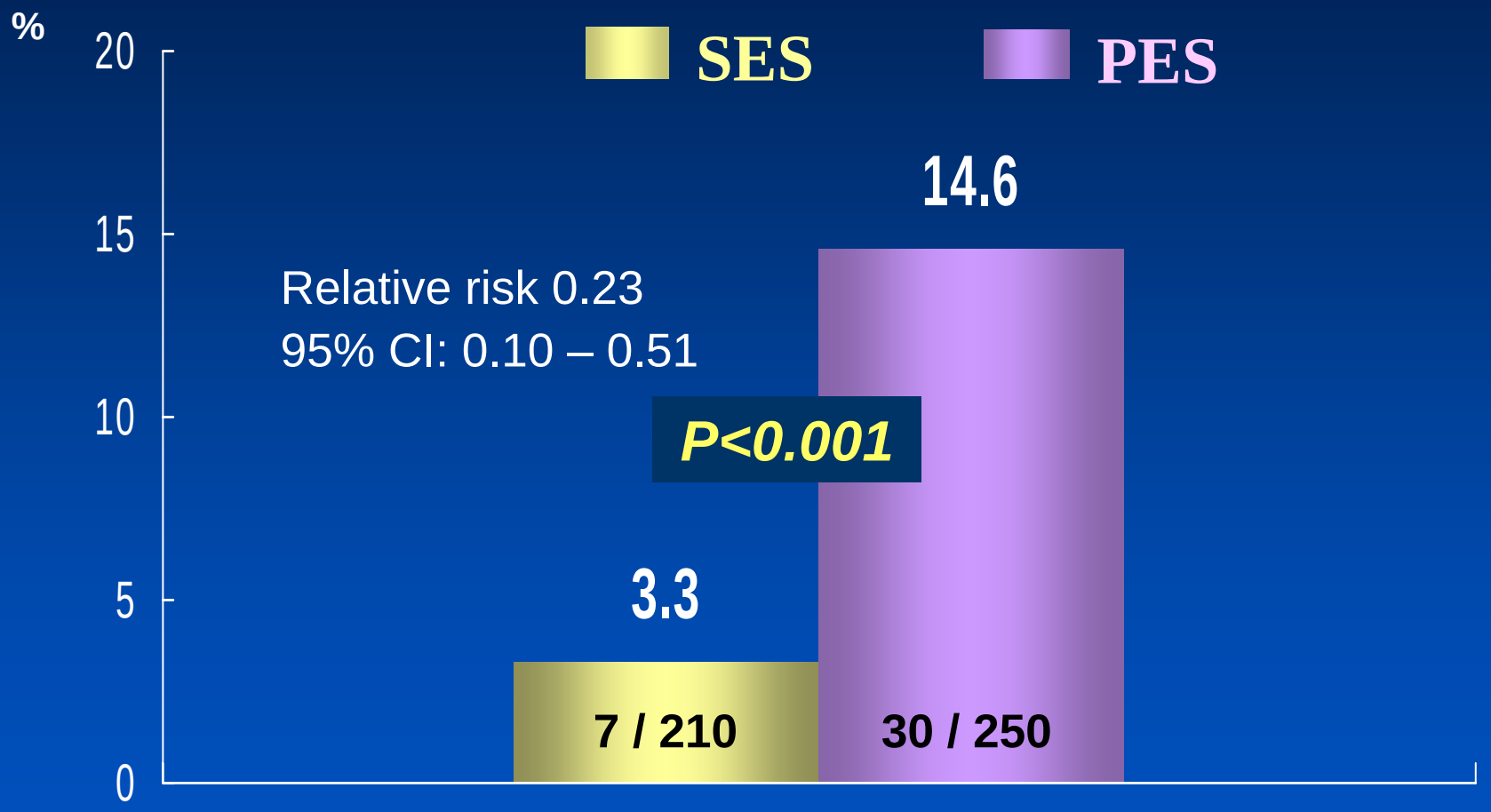
* Triple antiplatelet : aspirin plus clopidogrel plus cilostazol for 6 months

\# Standard antiplatelet : aspirin plus clopidogrel for 6 months

Primary endpoint:

1. Comparison of SES or PES: binary in-segment restenosis at 6 months
2. Comparison of triple and standard antiplatelet: in-stent late loss at 6 months

Primary Study End Point
In-Segment Restenosis Rate



Kim YH, Long DES-II investigator, ***Circulation, 2006;114:2148-2153***

Percutaneous Treatment of *LONG* Native Coronary Lesions with *D*rug-*E*luting *S*tent-III: Sirolimus vs. Biolimus-eluting Stent

The LONG-DES V Trial

Seung-Jung Park, MD, PhD, FACC
for the LONG-DES III Trial investigators

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AMC data

Percutaneous treatment of *LONG* native coronary lesions with *D*rug-*E*luting *S*tent-V: Cypher vs. Nobori

Long-DES-V Trial

Patients requiring PCI with DES for long coronary lesions:
***Lesion length* ≥ *25mm* receiving single or multiple stents (*total stent length* ≥ *28mm*)**

Stratified randomization by
• Enrolling sites

Sirolimus-eluting stent:
CYPHER
(n=250)

Biolimus A9-eluting stent:
NOBORI
(n=250)

9 months Angiographic follow-up
12 months Clinical follow-up

**Primary endpoint: In-segment late loss at 9 months angiographic follow-up

PI: Seung-Jung Park, MD, PhD

Study endpoints

Primary

In-segment late luminal loss at 9 Mo angio-FU

Secondary

- Death
- MI
- TLR and TVR
- Stent thrombosis
- Angiographic parameters at FU
- IVUS parameters at FU
- Procedural success

Major inclusion criteria

- Clinical indication for PCI (SA,US,NSTEMI)
- Angiographic criteria of long lesion
  - Native coronary lesion (>50% reduction in lumen diameter)
  - Lesion length ≥25 mm segment requiring single or multiple stent
- Men or women aged ≥18 years

Major exclusion criteria

- STEMI or cardiogenic shock
- LVEF <30%
- In-stent restenosis at target vessel
- Serum creatinine >2.0 mg/dl or dialysis
- Left main stenosis
- Limited life expectancy < 1 year
- No limitation for other lesion types (bifurcation, ostial, small vessel, etc)

Sample Size Calculation

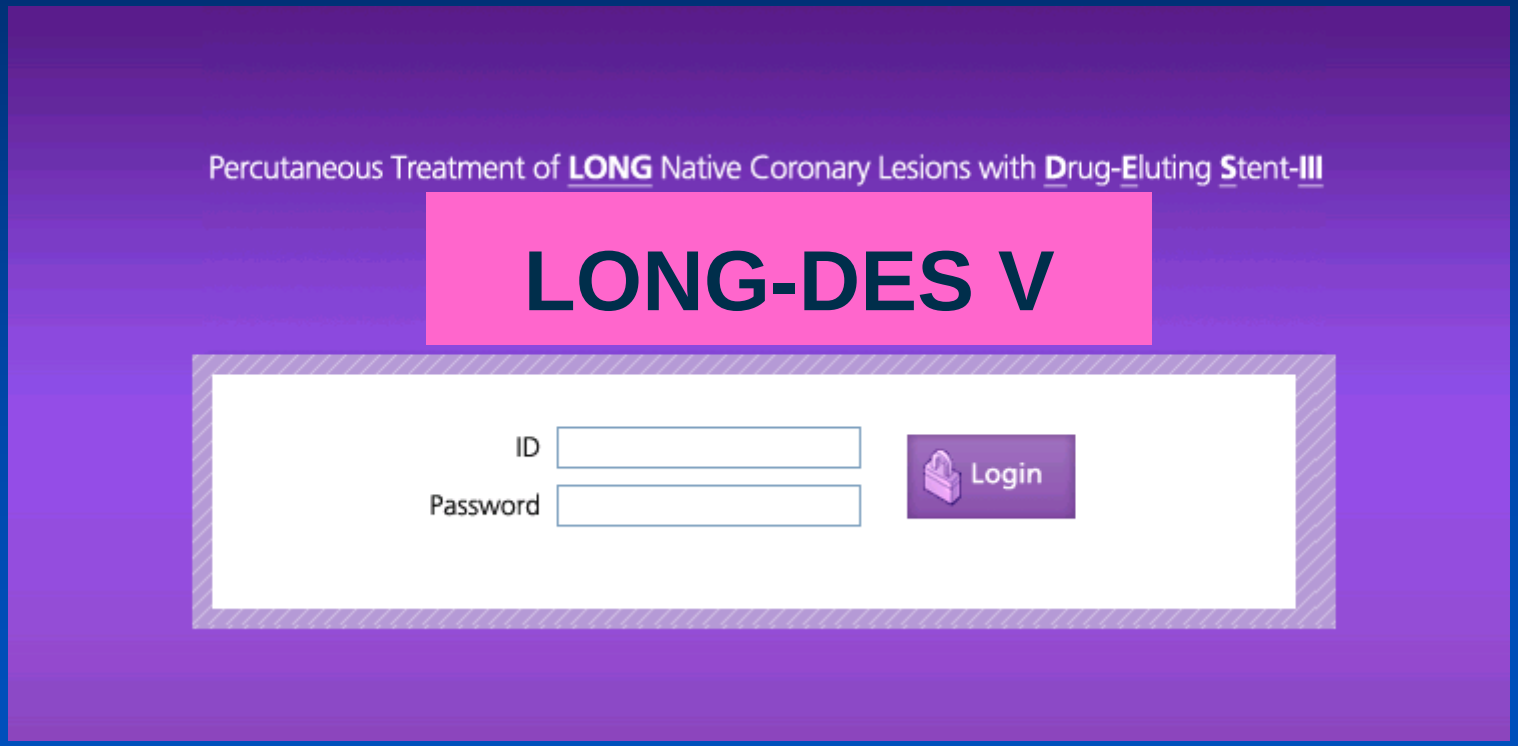
- Assumptions for the primary endpoint
- Long-DES II: cypher late loss 0.24±0.38
- Margin of Non-Inferiority for in-segment late loss 0.10 (equal to 40% of an assumed mean late loss of cypher)
- Non-inferiority trial, 80% power, one-sided a level 0.05, standard deviation=0.38, allocation ratio=1:1 and 15% not return for follow-up CAG
- 250 patients per group ➔ total 500 patients needed

PCI protocol guideline

- Select index (target) lesion for enrolment
- Randomization after guide-wire passage
- Use same stents for all other lesions
- No limitation for stent number or length
- Predilation or direct stenting: O.K.
- DCA or Rota: O.K.
- Antiplatelet therapy:
  - aspirin lifelong
  - clopidogrel > at least 12 months
  - cilostazol use by physician discretion

Randomization and CRF

- Web-based randomization (1:1 ratio)
- Web-based CRF



Randomized Comparison of Biolimus-*E*luting *S*tent versus *S*irolimus-*E*luting Stent Implantation for De *N*ovo *C*oronary Artery Dis*E*ase in Patients with *DIABETES* Mellitus

The ESSENCE-DIABETES II Trial

Seung-Jung Park, MD, PhD, FACC
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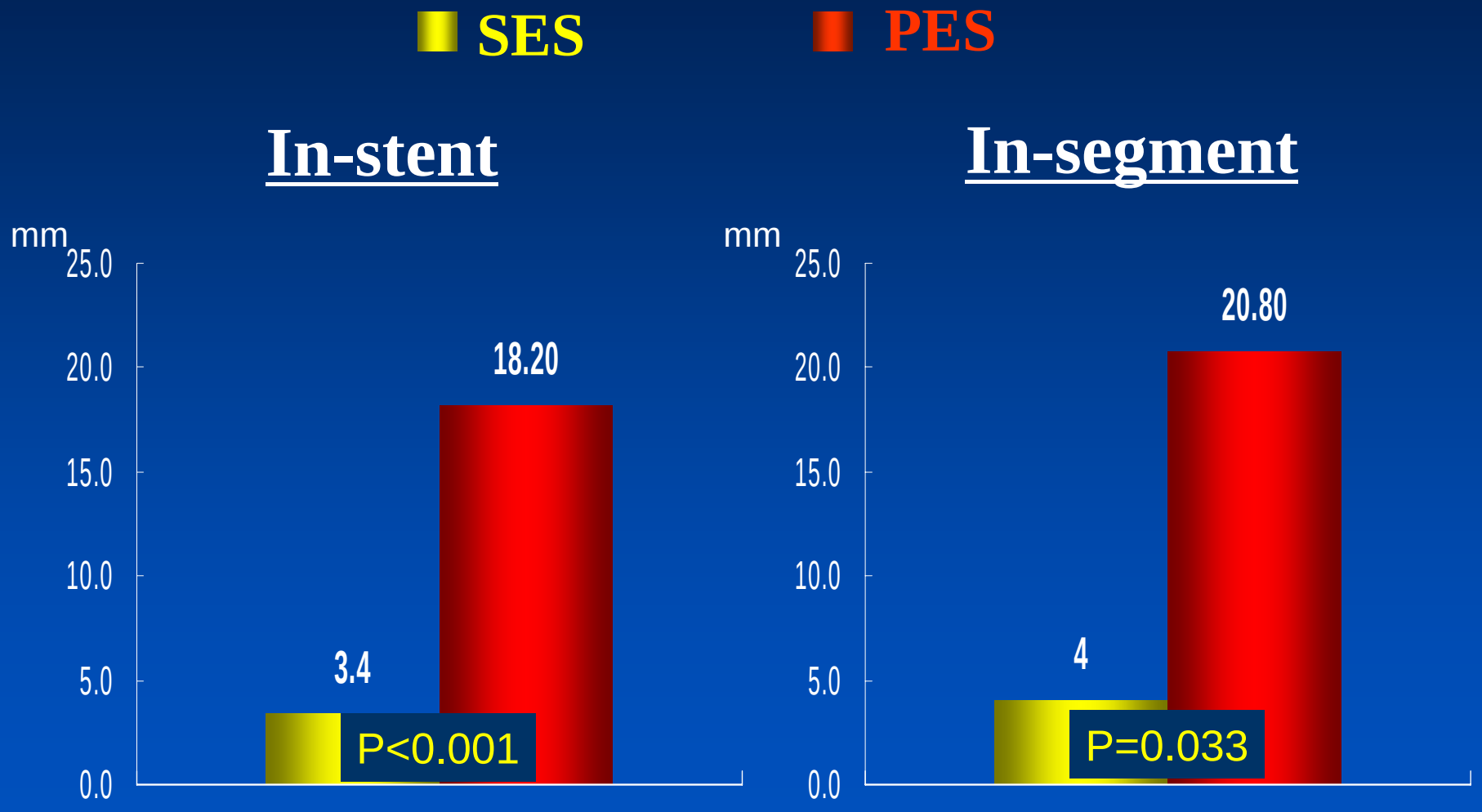
Background

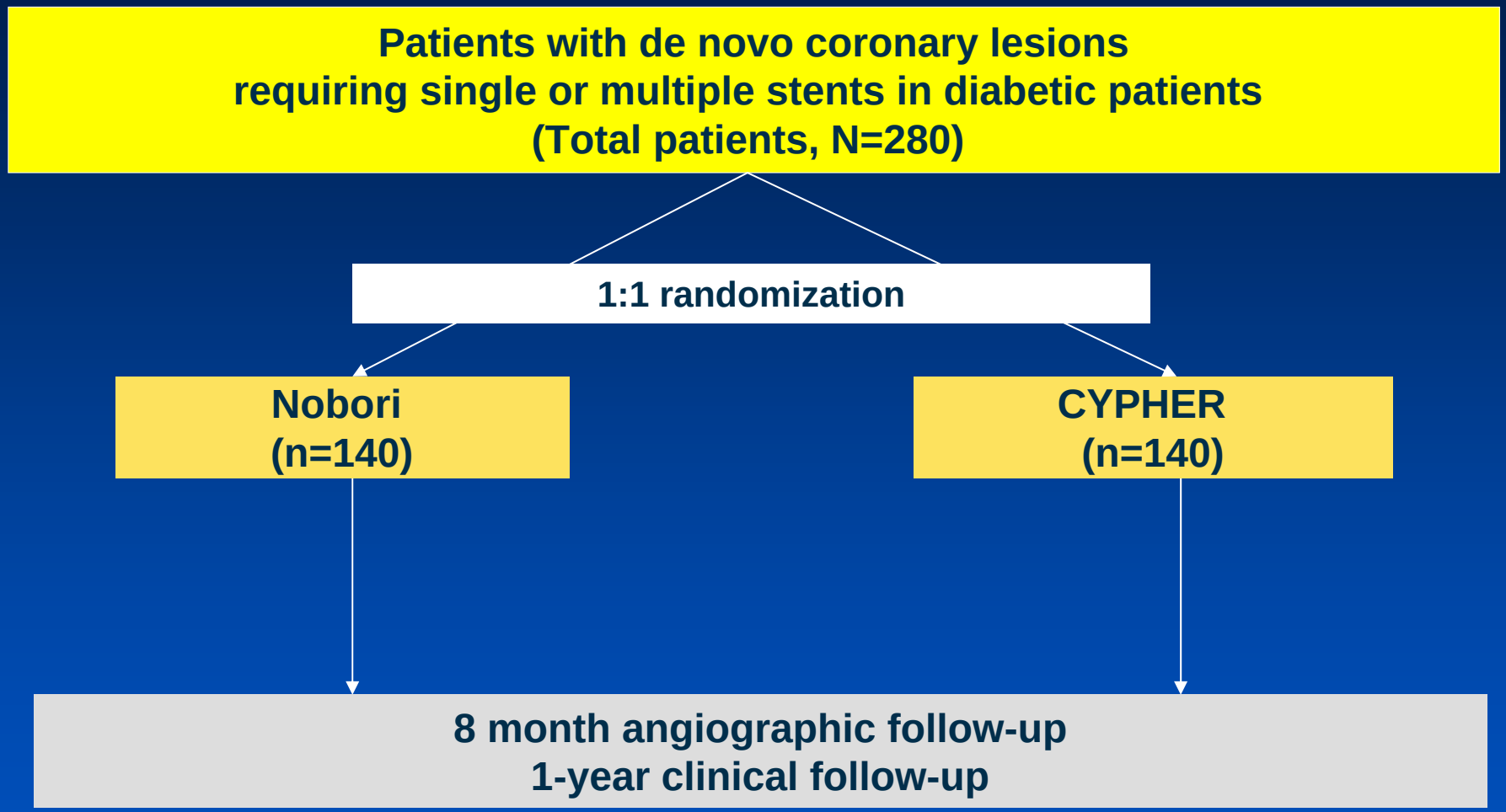
- Diabetic patients often present unfavorable coronary anatomy with small and diffusely diseased vessels and exhibit exaggerated neointimal hyperplasia after BMS implantation as compared with non-diabetics.

- Although DES implantation significantly reduced the neointimal hyperplasia and angiographic restenosis compared to BMS in diabetic patients, presence of DM have been still associated with an increased risk of restenosis and unfavorable clinical outcomes in the era of DES.

Restenosis rate



ESSENCE-DIABETES II Trial



Primary end-point: Angiographic in-segment late loss at 8-month angiography
Secondary end-point: Clinical outcomes at 12 month follow-up
IVUS results at 8 month angiographic follow-up (selected center)

Objective

- To establish the safety and effectiveness of coronary stenting with the Nobori stent compared to the Cypher stent in the treatment of de novo coronary stenosis in patients with diabetic patients

Inclusion Criteria

Clinical

- Diabetic patients treated with **OHA or Insulin**
- Patients with angina and documented ischemia or patients with documented silent ischemia
- Age >18 years, <75 ages
- Written informed consent

Angiographic

- *De novo* coronary lesion suitable for stent implantation
- Target lesion stenosis >50% by visual estimate
- Reference vessel size ≥ 2.5 mm by visual estimation

Exclusion Criteria

- Contraindication to aspirin, clopidogrel
- Left main disease
- Graft vessel stenosis
- LVEF<30%
- ST elevation AMI
- History of bleeding diathesis or coagulopathy
- Renal dysfunction (Cr ≥2.0mg/dL)
- Life expectancy < 1 year
- Inability to follow the protocol
- Bifurcation lesion requiring a planned stenting in the side branch

Primary Endpoint

- Comparison of Nobori and Cypher stent: In-segment late loss at 8- month angiographic follow-up study

- Target lesion: 1st treated lesion meeting inclusion criteria (all lesion should be treated with allocated stent)

Secondary Endpoint

In-stent late loss

- In-stent and In-segment restenosis
- MACE: death, MI, and TLR at 12 months
- TVR
- Stent thrombosis during 12 months (ARC criteria)

Sample Size Calculation

- Assumptions for the primary endpoint
  - Cypher in-segment late loss: 0.43 mm
  - Non-inferiority margin: 0.15 (35% of an assumed mean late loss after the implantation of Cypher)
  - Standard deviation: 0.45 mm
  - Significant level α (one-sided): 0.05
  - Power: 80% to reject null hypothesis
  - Assumption; 20% follow-up loss of angiographic re-study
  - Sample size: total 280 patients (140 patients per group)

PCI protocol guideline

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- Randomization after guide-wire passage
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- No limitation for stent number or length
- Predilation or direct stenting: O.K.
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Thank You !!
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