

Does Late Catch-up Exist in DES?

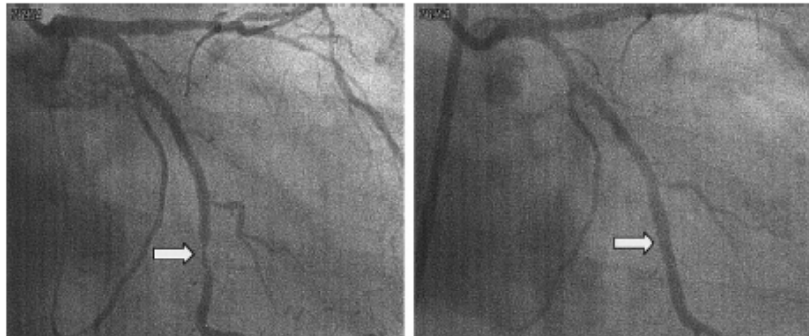
: *Quantitative Coronary Angiography Analysis*

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Seoul National University Hospital

Clinical Investigation and Reports

Sustained Suppression of Neointimal Proliferation by Sirolimus-Eluting Stents

One-Year Angiographic and Intravascular Ultrasound Follow-Up

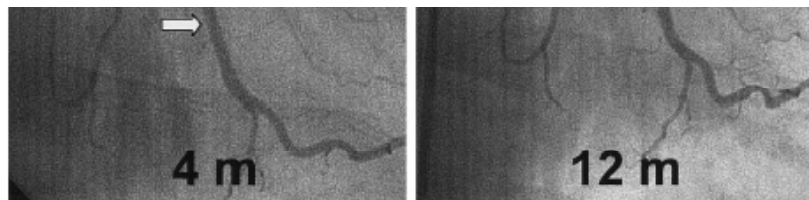


Patrick Serruys – “If I am in a dream, please don’t wake me”

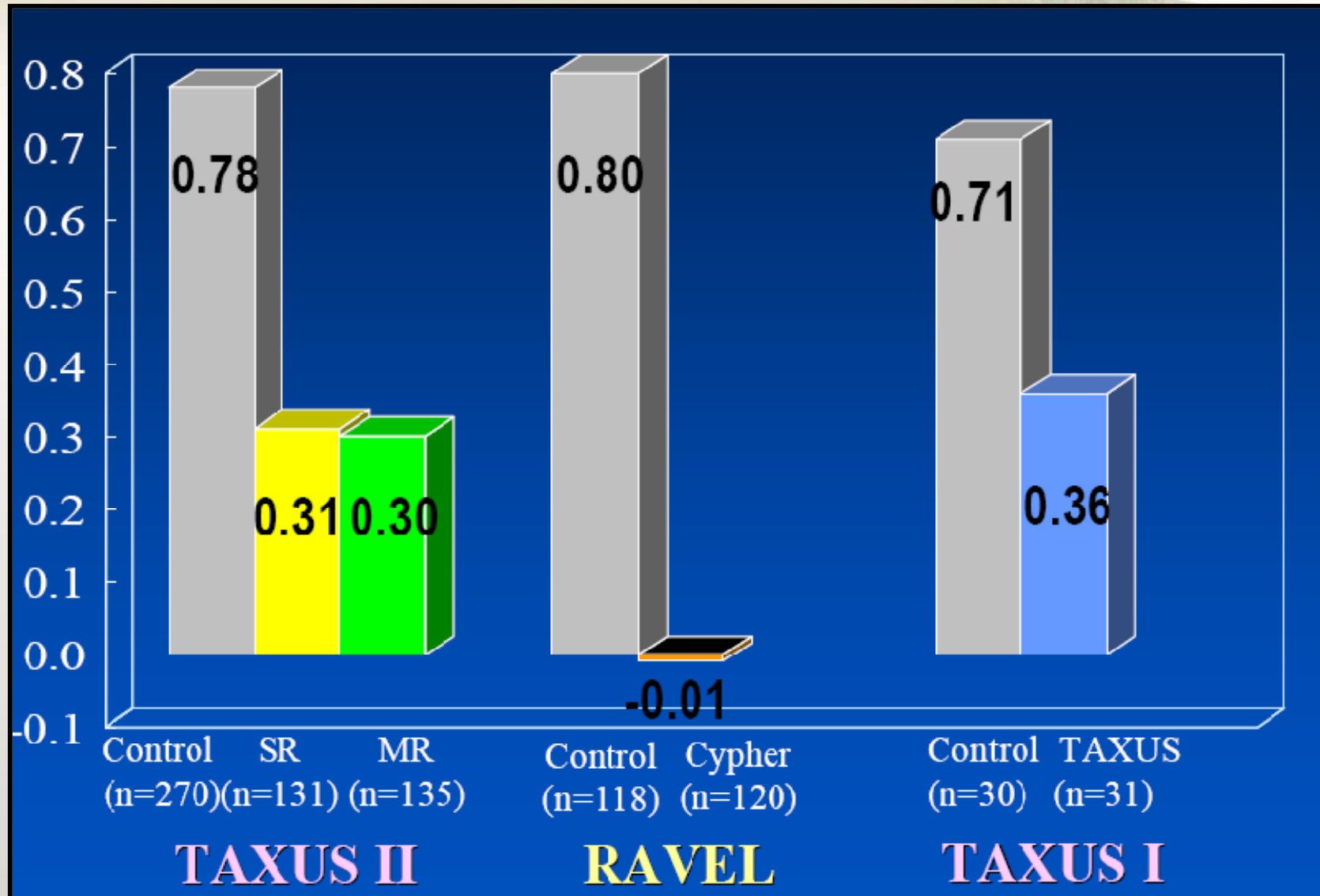
Editorial

Living the Dream of No Restenosis

Paul S. Teirstein, MD

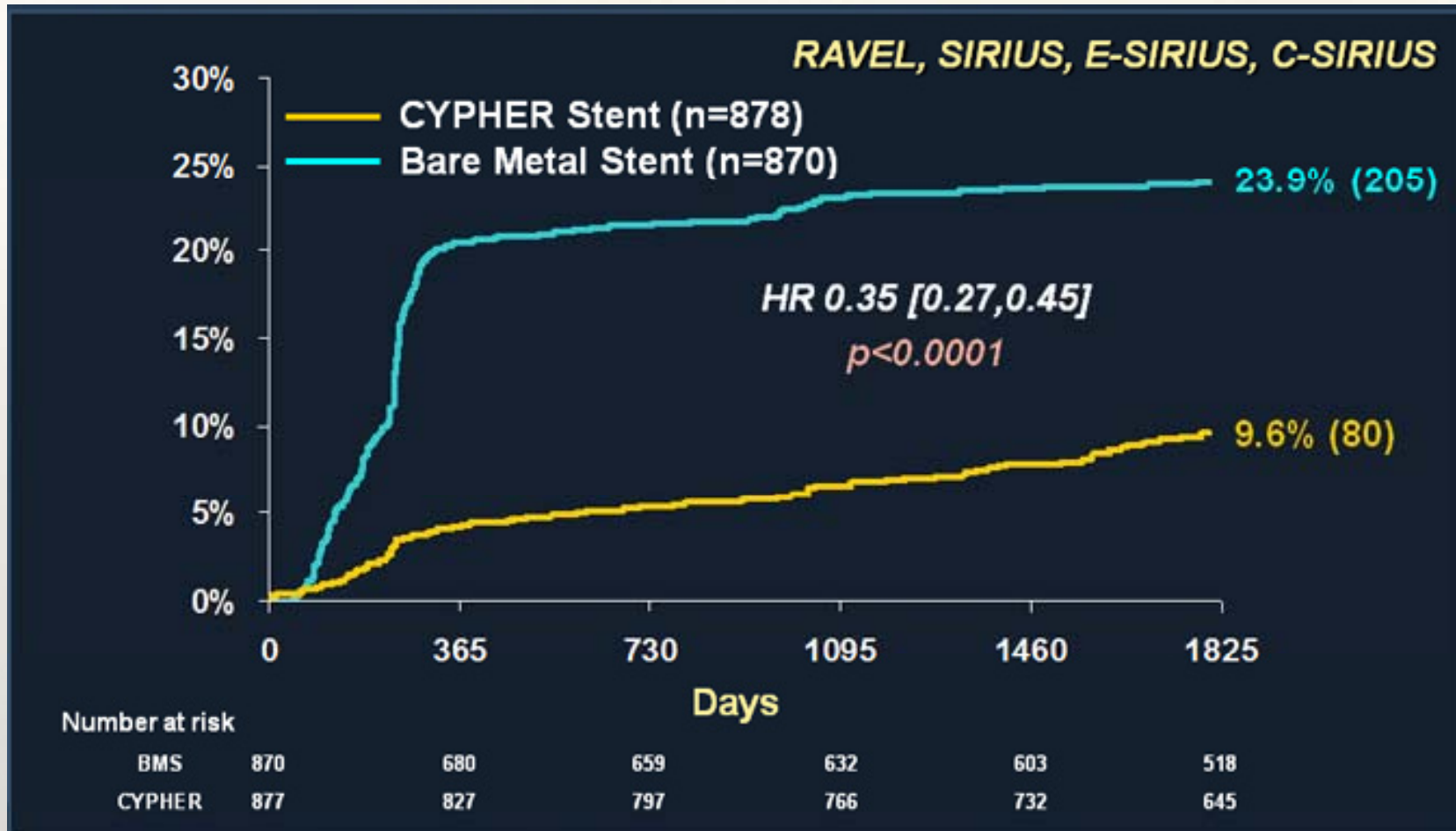


Hey Ma? “Cypher[®] No Late Loss!!”



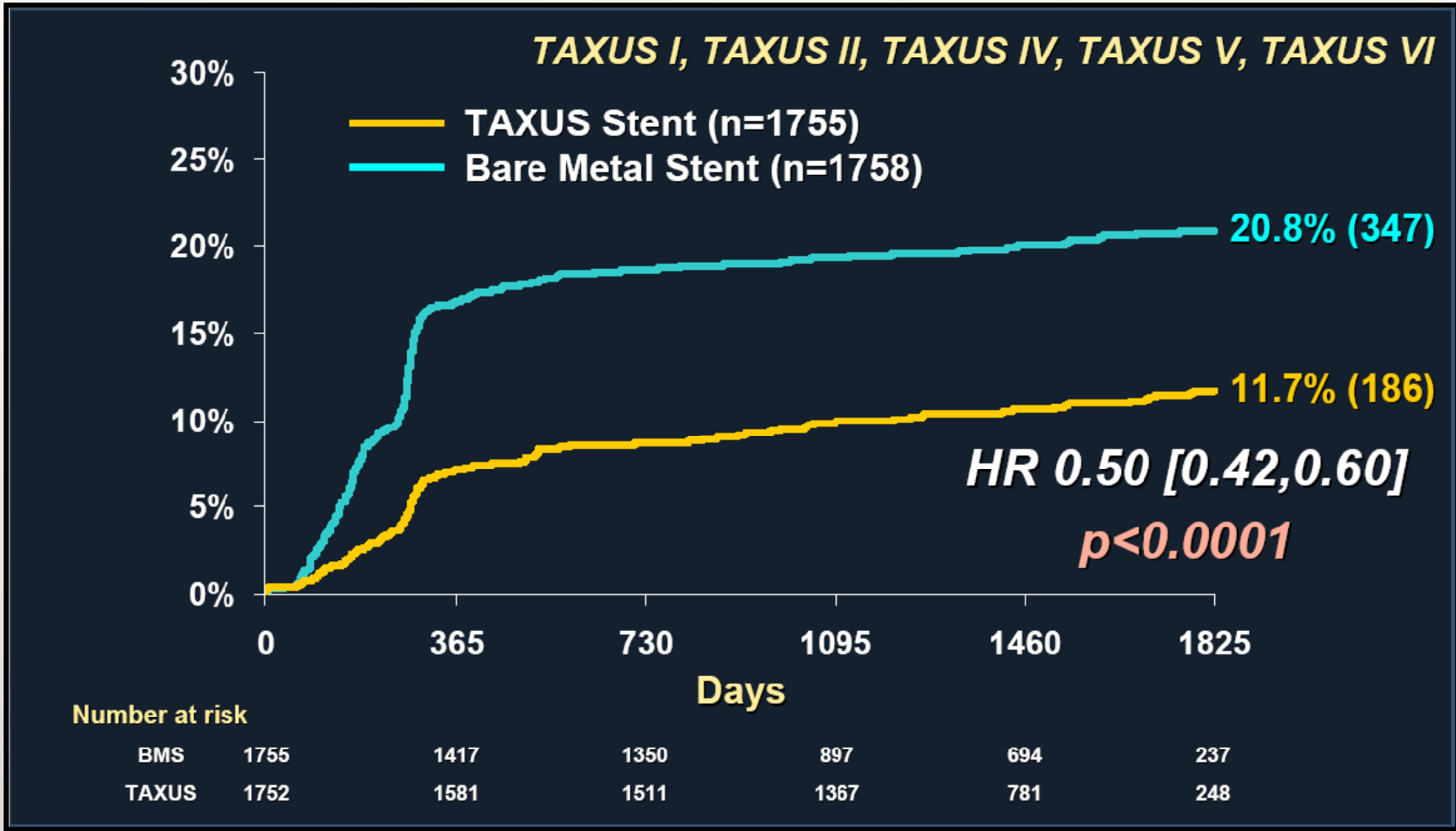
CYPHER vs. BMS : Pooled Analysis

TLR rate from 4 RCTs

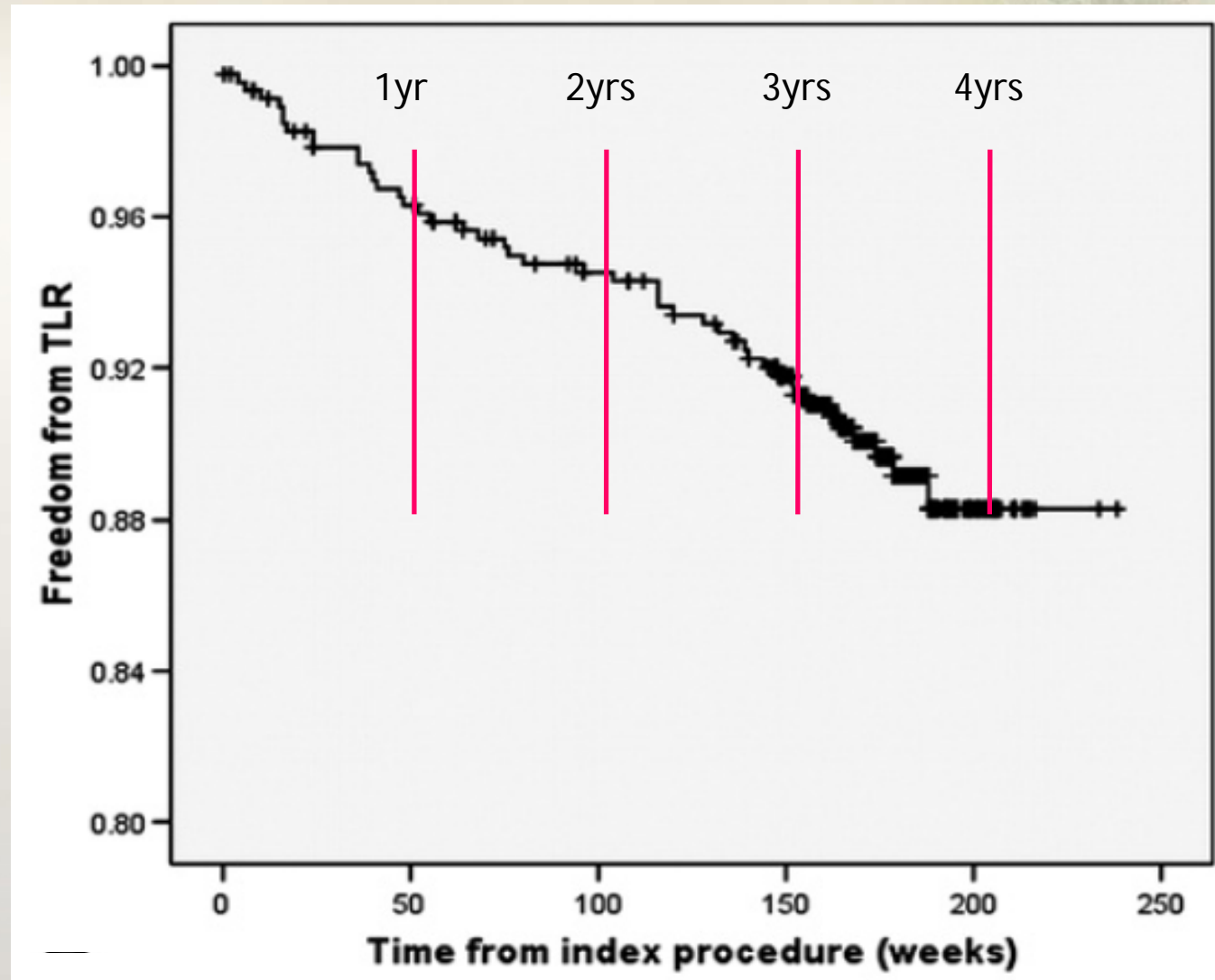


TAXUS vs. BMS : Pooled Analysis

TLR rate from 5 RCTs



TLR in Cypher : continuous occurrence of events?



Long-term (<3 years) outcome and predictors of clinical events after insertion of sirolimus-eluting stent in one or more native coronary arteries (from the Israeli arm of the e-Cypher registry), David Planer, et al., Am J Cardiol 2008;101:953-959



CYPHER wins the Late Loss Competition

| | TAXUS | Cypher | p-value | mean follow-up interval |
|----------------------------|-------------|-------------|---------|-------------------------|
| SIRTAX ^a | n = 273 | n = 267 | | 8 months |
| in segment | 0.32 ± 0.55 | 0.19 ± 0.45 | 0.001 | |
| in stent | 0.25 ± 0.49 | 0.12 ± 0.36 | <0.001 | |
| REALITY ^b | n = 941 | n = 970 | | 8 months |
| in segment | 0.16 ± 0.40 | 0.04 ± 0.38 | <0.001 | |
| in stent | 0.31 ± 0.44 | 0.09 ± 0.43 | <0.001 | |
| LONG DES II ^c | n = 250 | n = 250 | | 9 months |
| in segment | 0.61 ± 0.54 | 0.24 ± 0.38 | <0.001 | |
| in stent | 0.45 ± 0.55 | 0.09 ± 0.37 | <0.001 | |
| ISAR-SMART 3 ^d | n = 174 | n = 176 | | 6-8 months |
| in segment | 0.34 ± 0.57 | 0.13 ± 0.56 | <0.001 | |
| in stent | 0.56 ± 0.59 | 0.25 ± 0.55 | <0.001 | |
| ISAR-DIABETES ^e | n = 103 | n = 102 | | 6.5 months |
| in segment | 0.67 ± 0.62 | 0.43 ± 0.45 | 0.001 | |
| in stent | 0.46 ± 0.44 | 0.19 ± 0.44 | <0.001 | |
| ISAR-DESIRE ^f | n = 92 | n = 91 | | 6.5 months |
| in segment | 0.55 ± 0.57 | 0.32 ± 0.39 | 0.02 | |
| in stent | 0.26 ± 0.39 | 0.10 ± 0.13 | 0.004 | |

A ; Sirolimus-eluting and paclitaxel-eluting stents for coronary revascularization. Windecker S, et al., N Engl J Med 2005;353:653-662

B ; Sirolimus- vs paclitaxel-eluting stents in de novo coronary artery lesions: the REALITY trial: a randomized controlled trial. Morice MC, et al., JAMA 2006;295:895-904

C ; Sirolimus-eluting stent versus paclitaxel-eluting stent for patients with long coronary artery disease. Kim YH et al., Circulation 2006;114:2148-2153

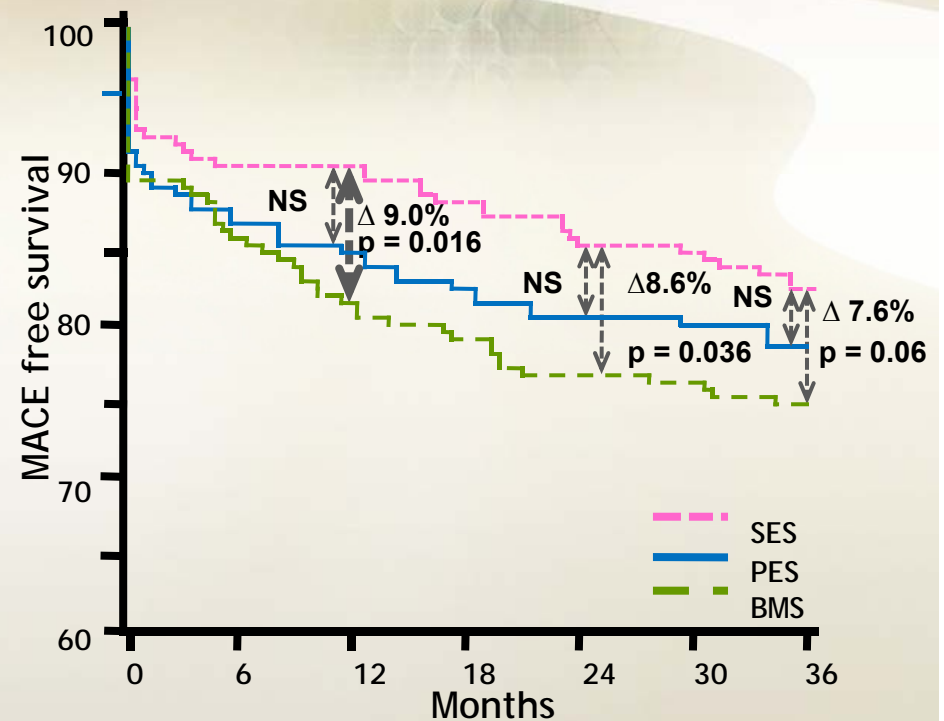
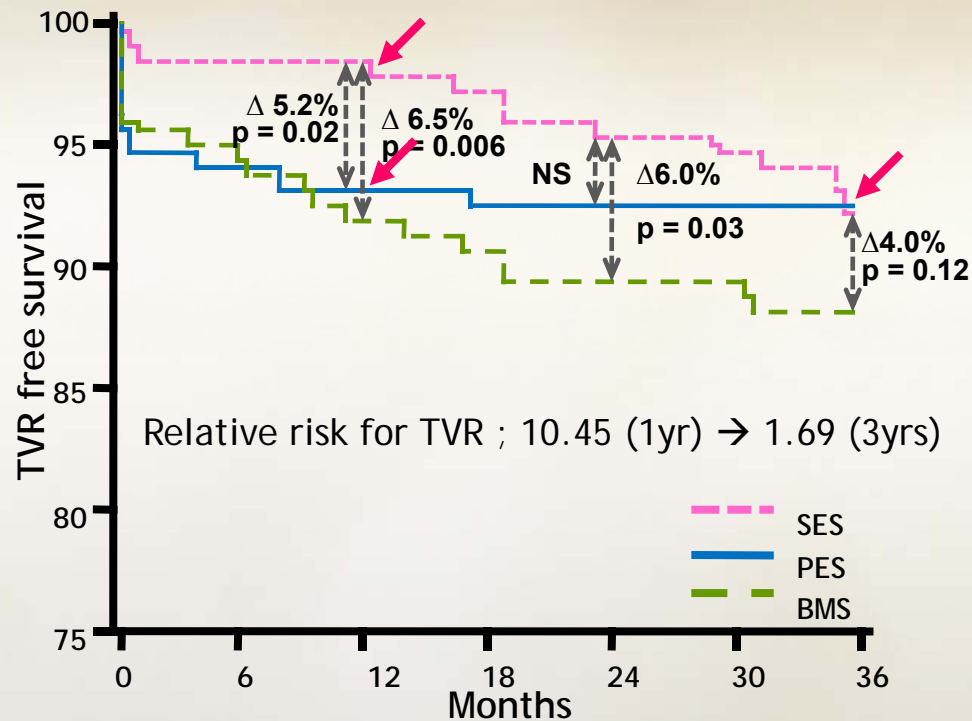
D ; Randomized trial of paclitaxel- and sirolimus-eluting stents in small coronary vessels. Mehilli J, et al., Eur Heart J 2006;27:260-266

E ; Paclitaxel-eluting or sirolimus-eluting stents to prevent restenosis in diabetic patients. Dibra A, et al., N Engl J Med 2005;353:663-670

F ; Sirolimus-eluting stent or paclitaxel-eluting stent vs balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. Kastrati A, et al., JAMA 2005;293:165-171



But why do event curves meet at 3 yrs?



| Major adverse cardiac events up to three years | | | |
|------------------------------------------------|---------------------|---------------------|---------------------|
| Variable at 1yr / at 3yrs | BMS group (n = 183) | SES group (n = 186) | PES group (n = 136) |
| Mortality | 9.4% / 13.3% | 9.1% / 11.5% | 8.1% / 12.4% |
| Nonfatal MI | 3.5% / 3.5% | 1.2% / 4.0% | 4.7% / 4.7% |
| TVR | 8.2% / 12.0% | 1.7% / 8.0% | 6.9% / 7.7% |
| MACEs (death, MI, and TVR) | 18.7% / 25.5% | 9.7% / 17.9% | 15.5% / 20.6% |

Comparison of three-year clinical outcome of Sirolimus- and Paclitaxel-eluting stents versus Bare metal stents in patients with ST-segment elevation myocardial infarction (from the RESEARCH and T-SEARCH Registries), Joost Daemen, et al., AM J Cardiol 2007;99:1027-1032



I am CONFUSED!!

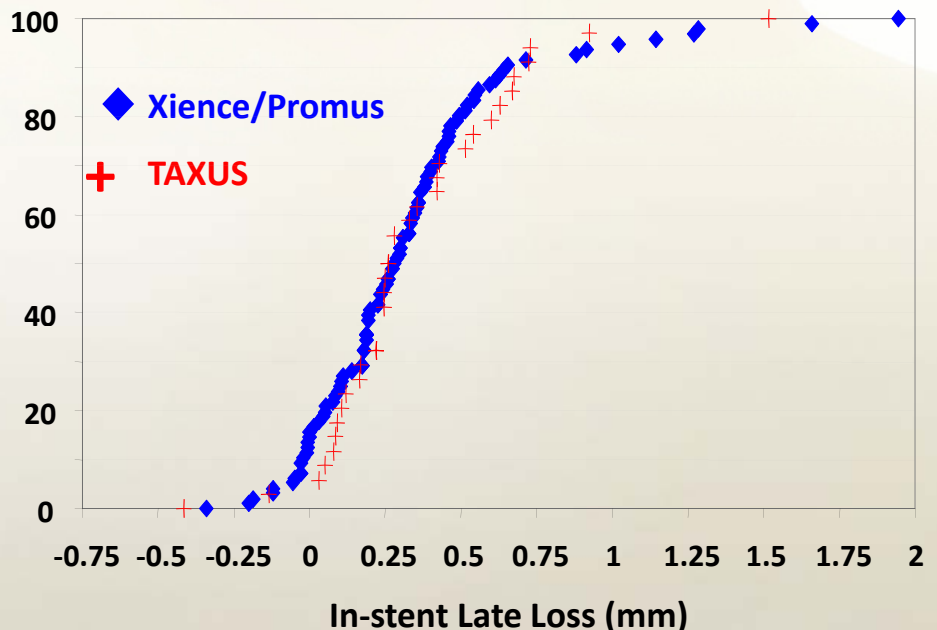
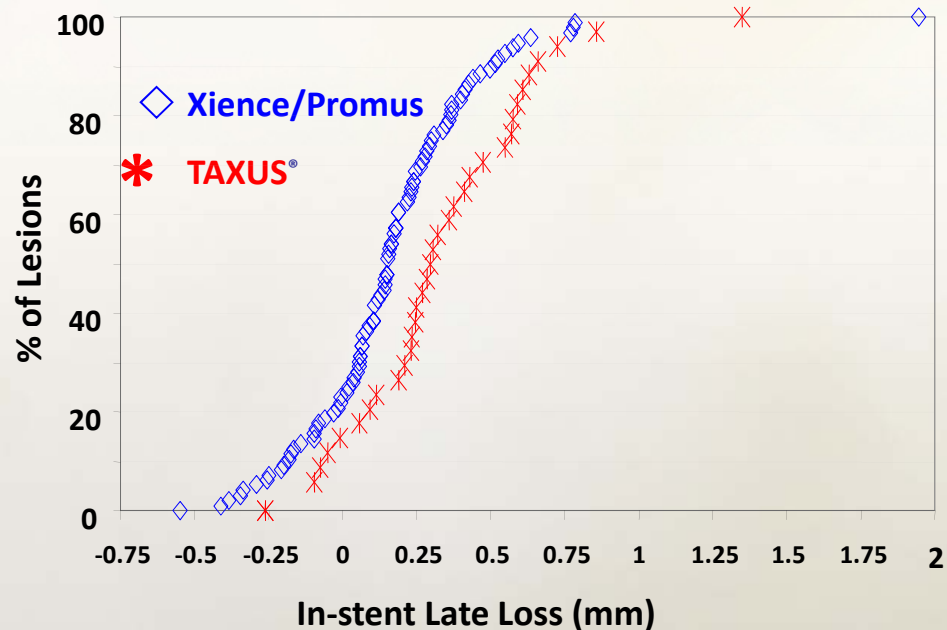
What's happening after one year?

Especially in Sirolimus-eluting stents?

SPIRIT II : Long term angiographic FU

6 Months

2 Years



Xience/Promus: 0.17 ± 0.32 (nL=97)

Xience/Promus: 0.33 ± 0.37 (nL=97)

TAXUS: 0.33 ± 0.32 (nL=35)

TAXUS: 0.34 ± 0.34 (nL=35)

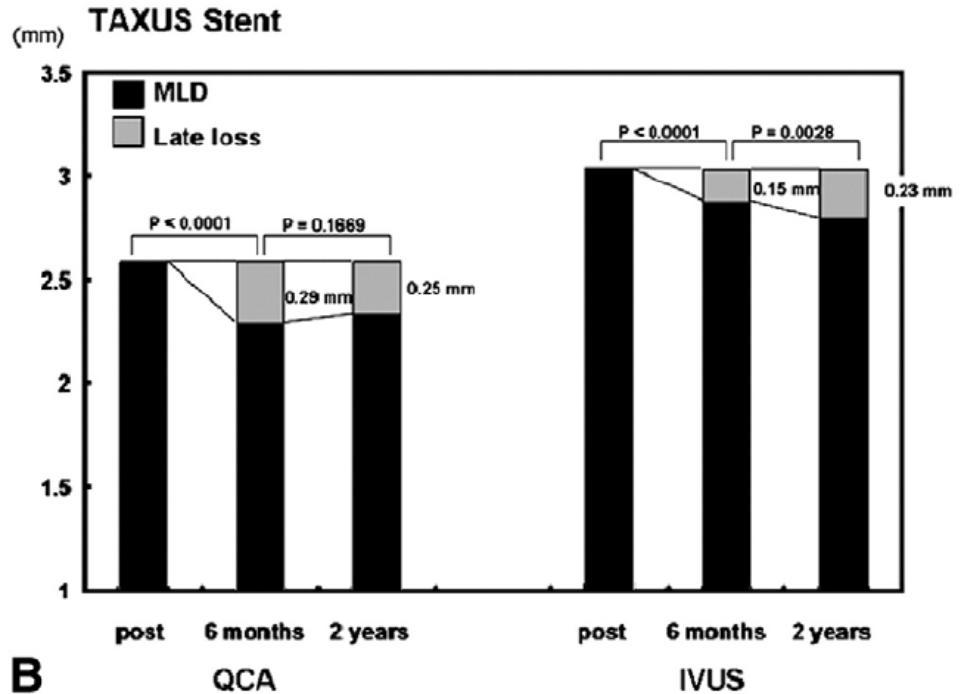
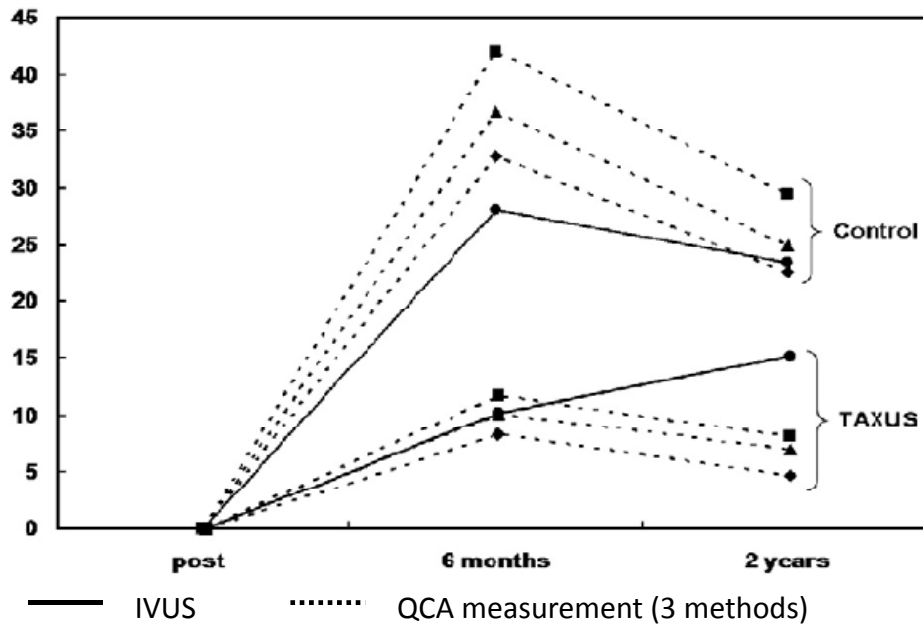
P=0.0037

P=0.6026



Late loss in TAXUS : 2 year f/u

Long term f/u of neointimal volume ;



Δ MLD at 1st f/u > Δ MLD at 2nd f/u

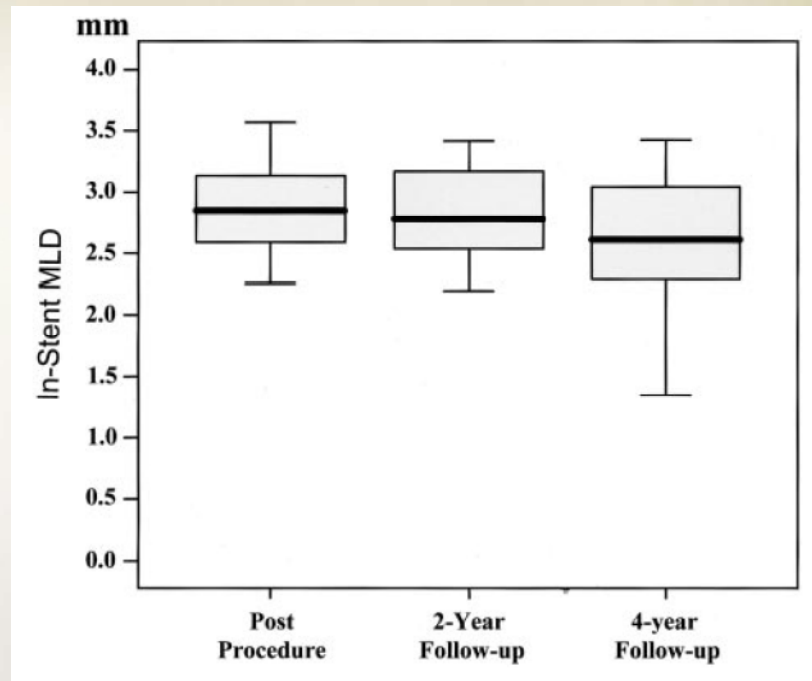
Two-year serial coronary angiographic and intravascular ultrasound analysis of in-stent angiographic late lumen loss and ultrasonic neointimal volume from the TAXUS II trial.
Keiichi Tsuchida, et al., Am J Cardiol 2007;99:607-615



Seoul National University Hospital Cardiovascular Center



Late loss in SES : 4 year f/u



Temporal evolution of In-stent Late Loss over 4-year follow-up (n = 26)

| up to 1 year | 1~2 year | 2~4 year | Overall up to 4 year |
|--------------|--------------|-------------|----------------------|
| 0.08 ± 0.26 | -0.03 ± 0.26 | 0.20 ± 0.31 | 0.25 ± 0.41 |

Δ MLD at 1st f/u < Δ MLD at 2nd f/u

Four-year angiographic and intravascular ultrasound follow-up of patients treated with sirolimus-eluting stents. J. Eduardo Sousa, et al., Circulation 2005;111;2326-2329



Purpose of the study

- ✓ *To see whether the late catch-up phenomenon exists in DES*
- ✓ *Analyze the late loss at two different follow up time points (early and late angiographic fu)*
- ✓ *To compare the natural course of neointimal formation in two different 1st generation DES*
- ✓ *To test whether the late loss that occurs until the first f/u [early late loss] or the added late loss after first f/u till second f/u [delayed late loss] can adequately explain or predict the total late loss observed at long term angiographic f/u.*

Method

Two different patient cohorts analyzed (From January 2003 to December 2006)

1. Primary analysis cohort: *Patients that received only SES implantation or PES implantation. Consecutive patients were recommended two angiographic follow-ups*

2. Proof-of-concept 'Hybrid' cohort: *Patients that received both SES and PES implantation in the same index procedure. Consecutive patients were recommended two angiographic follow-ups*

1st angiographic follow up : recommended at 6-9 months post index PCI

2nd angiographic follow up : recommended at 18-24 months post index PCI

Primary analysis cohort ; PES (Taxus)

Patients that underwent both early and late angiographic f/u: n = 114

Excluded d/t Revascularization at 1st f/u : n = 28

Study population n = 86 (128 lesions)

Primary analysis cohort ; SES (Cypher)

Patients that underwent both early and late angiographic f/u: n = 233

Excluded d/t Revascularization at 1st f/u : n = 12

Study population n = 221 (284 lesions)

Proof-of-concept Hybrid cohort ; PES + SES at index PCI

Patients that underwent both early and late angiographic f/u without repeat revascularization

SES 24 lesions

Study population n = 18

PES 23 lesions

Methods

Definitions:

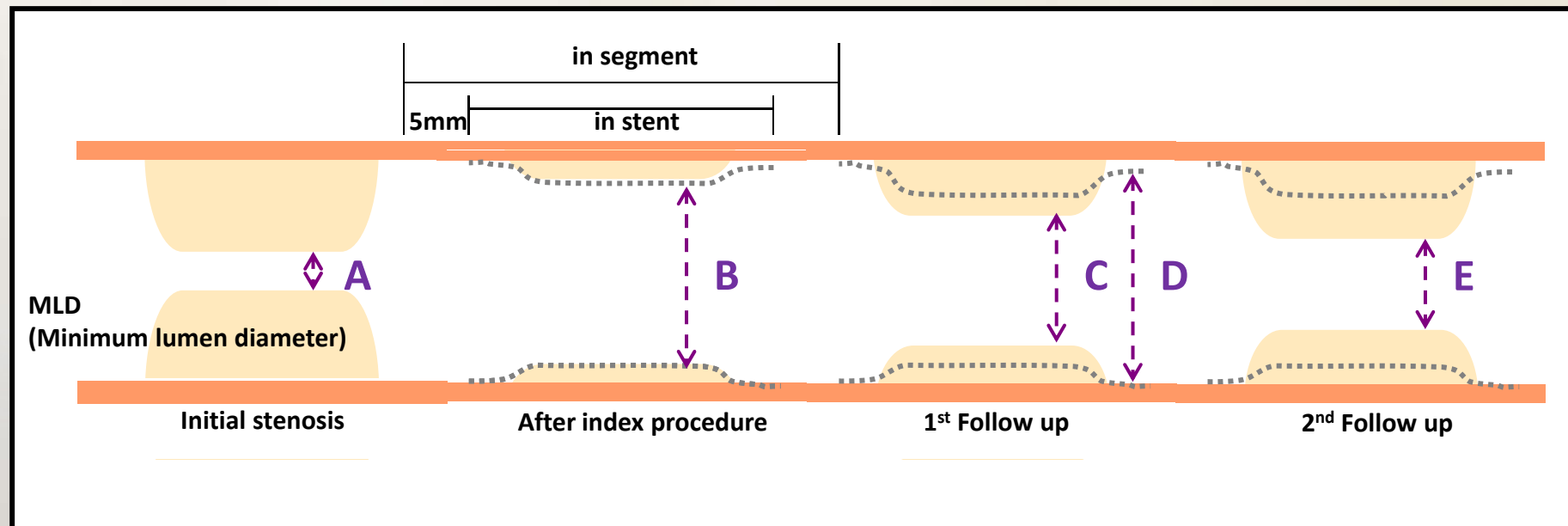
Acute gain : increment of MLD after index procedure from initial MLD (=B-A)

Early late loss : MLD after index procedure – MLD at 1st angiographic fu (=B-C)

Delayed late loss : MLD at 1st angiographic fu – MLD at 2nd angiographic fu (=C-E)

Total late loss ; MLD after index procedure – MLD at 2nd angiographic f/u (=B-E)

Quantitative Coronary Angiography : performed at SNUH Angiographic Core Lab



Study population

| | TAXUS | CYPHER | Sig. |
|------------------------------------------------|--------------------|--------------------|-------|
| Patients' characteristics | | | |
| No. patient / lesion (mean lesion per patient) | 86 / 128 (1.49) | 221 / 284 (1.29) | |
| Mean age (years, SD) | 62.8 (\pm 8.59) | 61.0 (\pm 10.3) | 0.125 |
| BMI (kg/m ² , SD) | 25.6 (\pm 3.74) | 24.6 (\pm 2.77) | 0.030 |
| Male | 53 (61.6%) | 157 (71.0%) | 0.125 |
| Diabetes | 29 (33.7%) | 92 (41.6%) | 0.197 |
| Hypertension | 51 (62.2%) | 150 (67.9%) | 0.407 |
| Dyslipidemia | 56 (65.1%) | 122 (55.2%) | 0.110 |
| Current smoker | 17 (19.8%) | 29 (13.1%) | 0.176 |
| Previous myocardial infarction | 3 (3.5%) | 36 (16.3%) | 0.000 |
| Previous revascularization | 5 (5.8%) | 37 (16.7%) | 0.002 |
| Diagnosis | | | |
| Stable angina (including silent ischemia) | 56 (65.1%) | 85 (38.5%) | 0.000 |
| Unstable angina / myocardial infarction | 30 (34.9%) | 136 (61.5%) | |

Study population

| | TAXUS | CYPHER | Sig. |
|---------------------------------------|-------------|-------------|-------|
| Lesion and procedural characteristics | | | |
| Lesion location | | | |
| LAD | 57 (44.5%) | 131 (46.1%) | 0.190 |
| LCx | 41 (32.0%) | 74 (26.1%) | |
| RCA | 30 (23.4%) | 79 (27.8%) | |
| Type B2/C lesions | 109 (85.2%) | 149 (52.5%) | 0.000 |
| Total occlusion | 9 (7.4%) | 32 (11.3%) | 0.152 |
| Mean number of stents per lesion (SD) | 1.15 (0.36) | 1.15 (0.43) | 0.872 |
| Mean stent length per lesion (mm, SD) | 28.3 (11.8) | 29.4 (12.8) | 0.369 |
| Mean stent diameter (mm, SD) | 3.14(0.34) | 3.01 (0.34) | 0.000 |

Clinical characteristics

| | TAXUS (n 86) | CYPHER (n 221) | Sig. |
|---------------------------|---------------------|---------------------|-------|
| Baseline | | | |
| Systolic BP (mmHg) | 130.0 (\pm 22.2) | 127.8 (\pm 22.1) | 0.422 |
| Diastolic BP (mmHg) | 79.8 (\pm 9.9) | 79.2 (\pm 10.2) | 0.641 |
| Total cholesterol (mg/dL) | 177.8 (\pm 51.2) | 180.3 (\pm 39.1) | 0.689 |
| HDL cholesterol (mg/dL) | 43.0 (\pm 12.0) | 40.6 (\pm 9.1) | 0.099 |
| LDL cholesterol (mg/dL) | 103.0 (\pm 36.1) | 112.3 (\pm 33.0) | 0.041 |
| Hemoglobin (g/dL) | 13.4 (\pm 1.9) | 13.4 (\pm 1.7) | 0.938 |
| Serum creatinine (mg/dL) | 1.0 (\pm 0.2) | 1.1 (\pm 0.8) | 0.033 |
| hs-CRP (mg/dL) | 0.32 (\pm 0.72) | 0.83 (\pm 1.65) | 0.001 |

Clinical characteristics

| | TAXUS (n 86) | CYPHER (n 221) | Sig. |
|------------------------------------------------|--------------------|--------------------|-------|
| 1st follow-up | | | |
| Mean interval of follow up (day) | 194.3 ±29.0 | 220.7 ±142.1 | 0.009 |
| Systolic BP (mmHg) | 129.8 (±23.6) | 127.3 (±22.5) | 0.400 |
| Diastolic BP (mmHg) | 79.8 (±10.4) | 78.5 (±10.1) | 0.324 |
| Total cholesterol (mg/dL) | 149.7 (±35.0) | 150.7 (±34.5) | 0.827 |
| HDL cholesterol (mg/dL) | 42.7 (±12.3) | 41.0 (±9.6) | 0.287 |
| LDL cholesterol (mg/dL) | 79.6 (±29.5) | 81.7 (±27.1) | 0.596 |
| Hemoglobin (g/dL) | 13.1 (±1.6) | 13.3 (±1.7) | 0.527 |
| Serum creatinine (mg/dL) | 1.1 (±0.2) | 1.2 (±0.9) | 0.070 |
| hs-CRP (mg/dL) | 0.35 (±0.63) | 0.33 (±0.57) | 0.806 |
| 2nd follow-up | | | |
| Mean interval of follow up (day) | 668.1 ±199.5 | 690.8 ±258.8 | 0.411 |
| Systolic BP (mmHg) | 131.2 (±22.2) | 128.0 (±20.0) | 0.257 |
| Diastolic BP (mmHg) | 79.4 (±9.6) | 78.3 (±10.4) | 0.373 |
| Total cholesterol (mg/dL) | 140.0 (±35.4) | 144.2 (±30.9) | 0.338 |
| HDL cholesterol (mg/dL) | 42.2 (±10.0) | 41.0 (±9.1) | 0.395 |
| LDL cholesterol (mg/dL) | 73.1 (±28.8) | 78.3 (±29.7) | 0.207 |
| Reduction of LDL up to 2 nd f/u (%) | 29.9 ±55.4, -29.0% | 34.0 ±44.9, -30.3% | 0.498 |
| Hemoglobin (g/dL) | 13.1 (±1.6) | 13.3 (±1.7) | 0.268 |
| Serum creatinine (mg/dL) | 1.2 (±0.3) | 1.3 (±0.9) | 0.081 |
| hs-CRP (mg/dL) | 0.29 (±0.31) | 0.35 (±0.62) | 0.371 |

Question

***Is there late catch-up
in Drug-Eluting Stents?***

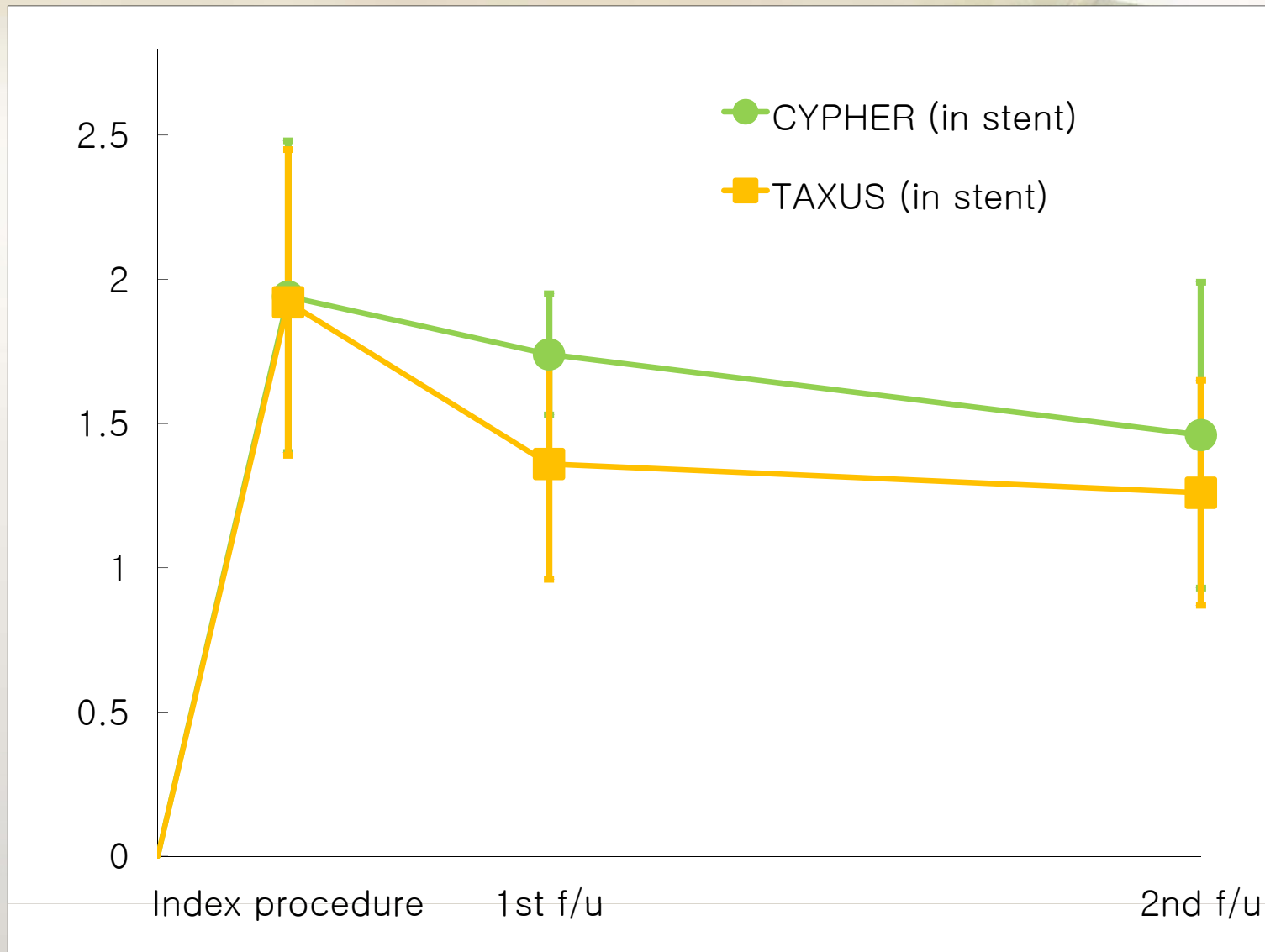
Angiographic results : QCA

| | TAXUS (86/128) | CYPHER (221/284) | Sig. |
|------------------------------------------------|----------------|------------------|-------|
| Reference vessel diameter (mm) | 2.62 (0.52) | 2.69 (0.63) | 0.246 |
| Lesion length (mm) | 35.18 (12.44) | 29.00 (13.82) | 0.000 |
| Minimum lumen diameter in segment (mm) | | | |
| Before procedure | 0.65 (0.41) | 0.65 (0.48) | 0.956 |
| After procedure | 2.18 (0.52) | 2.25 (0.48) | 0.237 |
| At 1 st follow-up | 1.85 (0.47) | 2.11 (0.50) | 0.000 |
| At 2 nd follow-up | 1.76 (0.46) | 1.87 (0.63) | 0.044 |
| Minimum lumen diameter in stent (mm) | | | |
| After procedure | 2.54 (0.41) | 2.59 (0.40) | 0.205 |
| At 1 st follow-up | 1.99 (0.49) | 2.39 (0.45) | 0.000 |
| At 2 nd follow-up | 1.88 (0.49) | 2.11 (0.65) | 0.000 |
| Diameter of stenosis in segment (%) | | | |
| Before procedure | 75.33 (15.05) | 76.38 (16.76) | 0.529 |
| After procedure | 23.12 (11.23) | 22.08 (10.07) | 0.370 |
| At 1 st follow-up | 29.21 (12.59) | 23.65 (10.92) | 0.000 |
| At 2 nd follow-up | 30.00 (12.43) | 29.85 (18.80) | 0.920 |
| Diameter of stenosis in stent (%) | | | |
| After procedure | 15.78 (6.90) | 15.00 (6.23) | 0.271 |
| At 1 st follow-up | 23.71 (10.24) | 18.22 (8.04) | 0.000 |
| At 2 nd follow-up | 25.91 (11.01) | 25.43 (17.80) | 0.739 |
| Binary restenosis at 1 st follow-up | | | |
| In segment | 7 (5.5%) | 9 (3.2%) | 0.312 |
| In stent | 1 (0.8%) | 1 (0.4%) | 0.617 |
| Binary restenosis at 2 nd follow-up | | | |
| In segment | 10 (7.8%) | 25 (8.8%) | 0.734 |
| In stent | 2 (1.6%) | 21 (7.4%) | 0.002 |

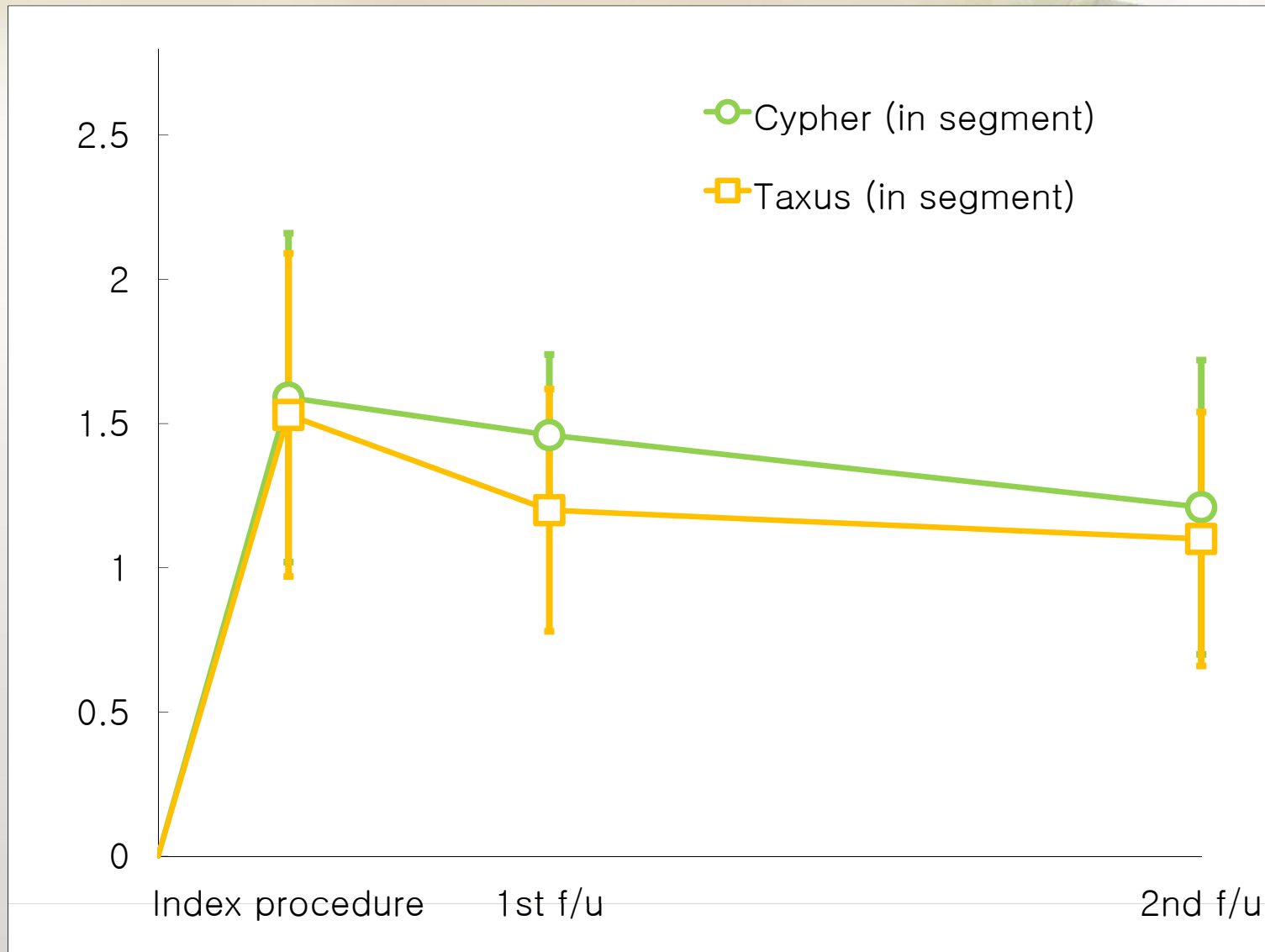
QCA results: Late loss

| | TAXUS (n 128) | CYPHER (n 284) | Sig. |
|----------------------------------|---------------|----------------|-------|
| Acute gain after index procedure | | | |
| In segment | 1.53 (0.56) | 1.59 (0.57) | 0.308 |
| In stent | 1.92 (0.53) | 1.94 (0.54) | 0.329 |
| Early late loss | | | |
| In segment | 0.33 (0.42) | 0.13 (0.28) | 0.000 |
| In stent | 0.56 (0.40) | 0.20 (0.21) | 0.000 |
| Delayed late loss | | | |
| In segment | 0.10 (0.25) | 0.25 (0.47) | 0.000 |
| In stent | 0.10 (0.24) | 0.28 (0.48) | 0.000 |
| Total late loss | | | |
| In segment | 0.43 (0.44) | 0.38 (0.51) | 0.337 |
| In stent | 0.66 (0.39) | 0.48 (0.53) | 0.000 |

Cypher vs. Taxus (in stent)



Cypher vs. Taxus (in-segment)



Question

Early vs Delayed late loss

: Which best predicts total late loss?

Correlation of 1st & 2nd late loss with final late loss

TAXUS (n 128)

| In segment | | | In stent | | | | |
|------------|-----------------------------------------------------|---------------------------------------------|---------------------------------------------|---|-----------------------------------------------------|---------------------------------------------|---------------------------------------------|
| | Δ 1 st & Δ 2 nd | Δ 1 st & Δ overall | Δ 2 nd & Δ overall | | Δ 1 st & Δ 2 nd | Δ 1 st & Δ overall | Δ 2 nd & Δ overall |
| r | -0.233 | 0.827 | 0.354 | r | -0.306 | 0.816 | 0.300 |
| p | 0.008 | 0.000 | 0.000 | p | 0.000 | 0.000 | 0.001 |

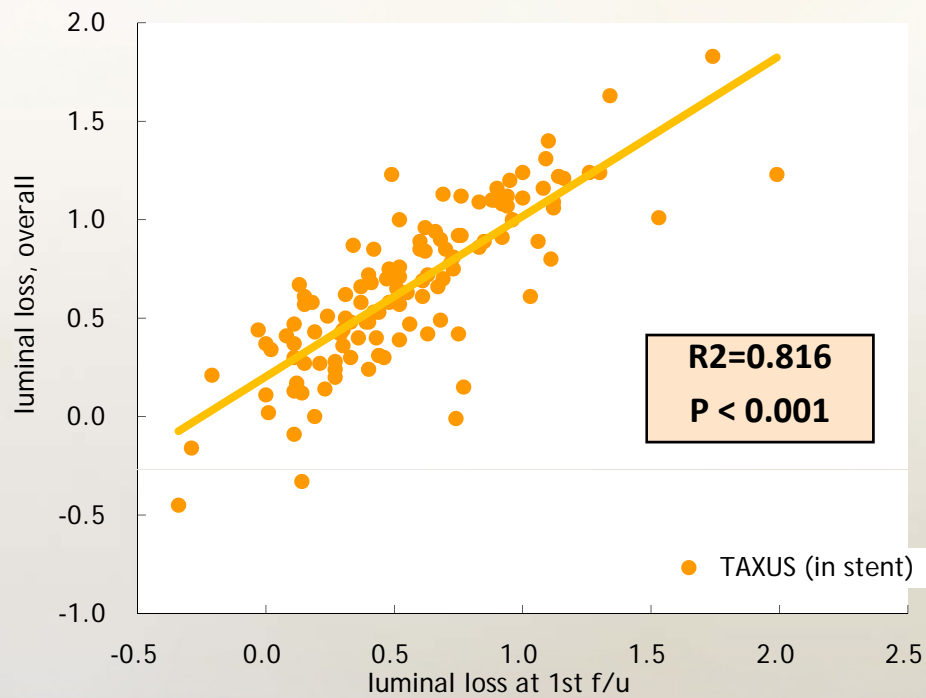
CYPHER (n 284)

| In segment | | | In stent | | | | |
|------------|-----------------------------------------------------|---------------------------------------------|---------------------------------------------|---|-----------------------------------------------------|---------------------------------------------|---------------------------------------------|
| | Δ 1 st & Δ 2 nd | Δ 1 st & Δ overall | Δ 2 nd & Δ overall | | Δ 1 st & Δ 2 nd | Δ 1 st & Δ overall | Δ 2 nd & Δ overall |
| r | -0.138 | 0.420 | 0.841 | r | 0.017 | 0.421 | 0.914 |
| p | 0.020 | 0.000 | 0.000 | p | 0.001 | 0.000 | 0.000 |

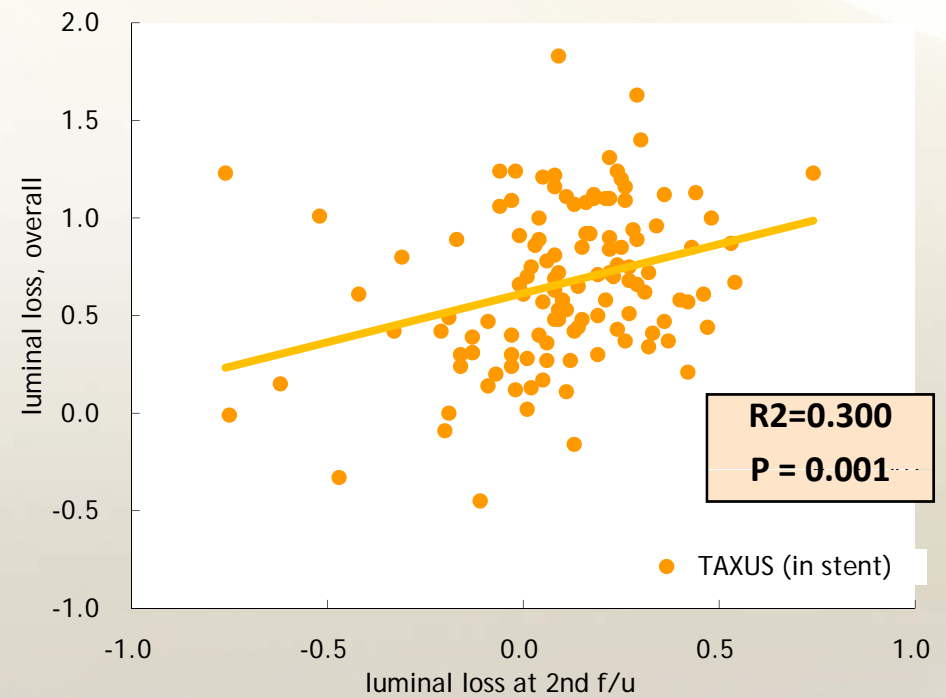
cf. r = Pearson's correlation coefficient, p = significance (2-tailed)

Correlation with overall late loss (in stent)

Taxus Stent



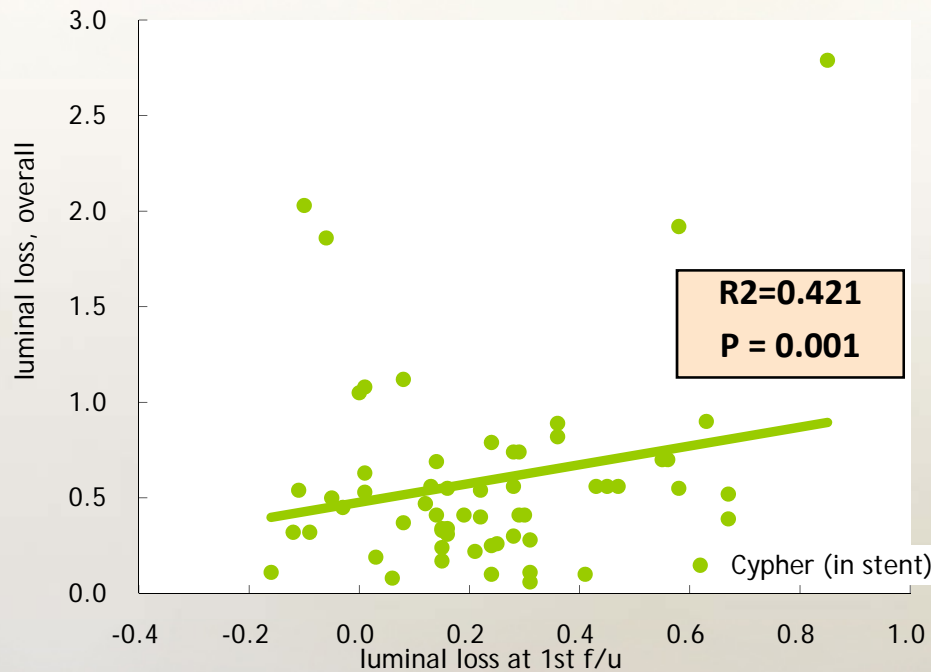
Early Late Loss



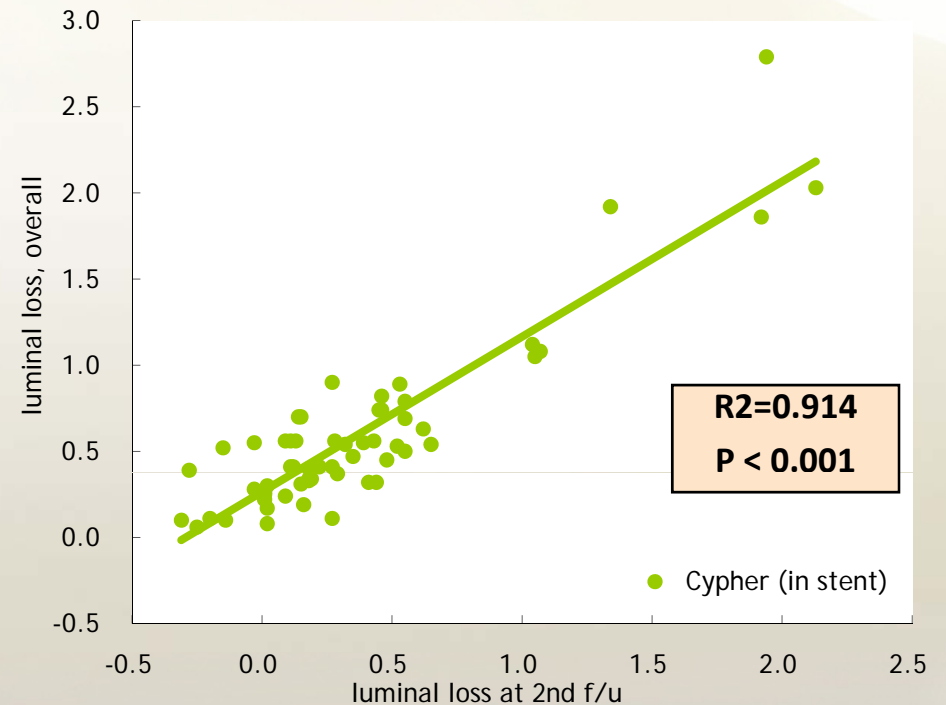
Delayed Late Loss

Correlation with overall late loss (in stent)

Cypher Stent



Early Late Loss



Delayed Late Loss

Question

***Was the difference due differences
in baseline characteristics
(in particular more AMI pt in Cypher)?***

Grouping according to initial Dx at Index PCI

| | Total | SA | ACS | Sig. |
|---------------------------------------|---------------------|--------------------|---------------------|-------|
| Patient characteristics | | | | |
| No. patient / lesion (mean lesion/pt) | 307 / 412 (1.34) | 141 / 200 (1.42) | 166 / 212 (1.28) | |
| Mean age (years, SD) | 61.5 (\pm 9.986) | 61.8 (\pm 8.12) | 61.3 (\pm 11.14) | 0.650 |
| BMI (kg/m ² , SD) | 24.9 (\pm 3.10) | 25.1 (\pm 2.92) | 24.8 (\pm 3.25) | 0.474 |
| Male | 210 (68.4%) | 102 (72.3%) | 108 (65.1%) | 0.170 |
| Diabetes | 121 (39.4%) | 56 (39.7%) | 65 (39.2%) | 0.921 |
| Hypertension | 204 (66.4%) | 97 (68.8%) | 107 (64.5%) | 0.423 |
| Dyslipidemia | 178 (58.0%) | 86 (61.0%) | 92 (55.4%) | 0.325 |
| Current smoker | 46 (15.0%) | 14 (9.9%) | 32 (19.3%) | 0.019 |
| Previous myocardial infarction | 39 (12.7%) | 23 (16.3%) | 16 (9.6%) | 0.086 |
| Previous revascularization | 42 (13.7%) | 23 (16.3%) | 19 (11.4%) | 0.223 |

Grouping according to initial Dx at Index PCI

| | Total | SA | ACS | Sig. |
|----------------------------------------------|-------------|-------------|-------------|-------|
| Lesion and procedural characteristics | | | | |
| Lesion location | | | | |
| LAD | 188 (45.6%) | 82 (41.0%) | 106 (50.0%) | 0.023 |
| LCx | 115 (27.9%) | 69 (34.5%) | 46 (21.7%) | |
| RCA | 109 (26.5%) | 49 (24.5%) | 60 (28.3%) | |
| Type B2/C lesions | 258 (62.6%) | 125 (62.5%) | 133 (62.7%) | 0.961 |
| Total occlusion | 41 (10.0%) | 17 (8.5%) | 24 (11.3%) | 0.339 |
| Stent | | | | |
| TAXUS | 128 (31.1%) | 85 (42.5%) | 43 (20.3%) | 0.000 |
| CYPHER | 284 (68.9%) | 115 (57.5%) | 169 (79.7%) | |
| Mean number of stents per lesion (SD) | 1.15 (0.41) | 1.18 (0.45) | 1.13 (0.36) | 0.190 |
| Mean stent length per lesion (mm, SD) | 29.1 (12.5) | 29.2 (13.9) | 29.0 (11.0) | 0.867 |
| Mean stent diameter (mm, SD) | 3.05 (0.35) | 3.03 (0.35) | 3.08 (0.34) | 0.189 |
| Revascularization at 2 nd f/u CAG | 38 (9.2%) | 16 (8.0%) | 22 (10.4%) | 0.404 |

Grouping according to initial Dx at Index PCI

| | Total | SA | ACS | Sig. |
|---------------------------|---------------------|---------------------|---------------------|-------|
| Baseline | | | | |
| Systolic BP (mmHg) | 128.4 (\pm 22.1) | 131.7 (\pm 23.8) | 125.6 (\pm 20.2) | 0.017 |
| Diastolic BP (mmHg) | 79.3 (\pm 10.1) | 80.1 (\pm 9.9) | 78.7 (\pm 10.3) | 0.239 |
| Total cholesterol (mg/dL) | 179.6 (\pm 42.7) | 175.2 (\pm 42.2) | 183.3 (\pm 42.9) | 0.098 |
| HDL cholesterol (mg/dL) | 41.3 (\pm 10.1) | 41.5 (\pm 8.8) | 41.1 (\pm 11.1) | 0.782 |
| LDL cholesterol (mg/dL) | 109.5 (\pm 34.1) | 103.0 (\pm 36.1) | 113.2 (\pm 34.6) | 0.050 |
| Hemoglobin (g/dL) | 13.4 (\pm 1.8) | 13.6 (\pm 1.8) | 13.3 (\pm 1.7) | 0.207 |
| Serum creatinine (mg/dL) | 1.1 (\pm 0.7) | 1.1 (\pm 0.5) | 1.1 (\pm 0.8) | 0.936 |
| hs-CRP (mg/dL) | 0.67 (\pm 1.44) | 0.47 (\pm 0.74) | 0.82 (\pm 1.80) | 0.029 |

Grouping according to initial Dx at baseline PCI

| | Total | Stable angina | Acute coronary syndrome | Sig. |
|------------------------------------------------|---------------|---------------|-------------------------|-------|
| Reference vessel diameter (mm) | 2.67 (0.60) | 2.66 (0.61) | 2.67 (0.59) | 0.834 |
| Lesion length (mm) | 30.98 (13.69) | 31.62 (14.51) | 30.34 (12.83) | 0.367 |
| Minimum lumen diameter in stent (mm) | | | | |
| After procedure | 2.57 (0.41) | 2.58 (0.42) | 2.57 (0.39) | 0.773 |
| At 1 st follow-up | 2.26 (0.50) | 2.24 (0.51) | 2.29 (0.49) | 0.398 |
| At 2 nd follow-up | 2.04 (0.62) | 2.02 (0.62) | 2.06 (0.62) | 0.444 |
| Diameter of stenosis in stent (%) | | | | |
| After procedure | 15.24 (6.45) | 14.99 (6.37) | 15.48 (6.53) | 0.441 |
| At 1 st follow-up | 19.92 (9.13) | 19.66 (8.90) | 20.17 (9.37) | 0.573 |
| At 2 nd follow-up | 25.68 (15.99) | 25.62 (15.55) | 25.54 (16.42) | 0.963 |
| Binary restenosis at 1 st follow-up | | | | |
| In segment | 16 (3.9%) | 7 (3.5%) | 9 (4.2%) | 0.696 |
| In stent | 2 (0.5%) | 1 (0.5%) | 1 (0.5%) | 0.967 |
| Binary restenosis at 2 nd follow-up | | | | |
| In segment | 35 (8.5%) | 15 (7.5%) | 20 (9.4%) | 0.482 |
| In stent | 23 (5.6%) | 10 (5.0%) | 13 (6.1%) | 0.617 |

Late loss according to initial Dx at Index PCI

| | Total | SA | ACS | Sig. |
|----------------------------------|-------------|-------------|-------------|-------|
| Acute gain after index procedure | | | | |
| In segment | 1.55 (0.59) | 1.57 (0.58) | 1.58 (0.56) | 0.842 |
| In stent | 1.92 (0.53) | 1.93 (0.51) | 1.91 (0.55) | 0.792 |
| Early late loss | | | | |
| In segment | 0.20 (0.34) | 0.19 (0.34) | 0.20 (0.34) | 0.190 |
| In stent | 0.31 (0.33) | 0.34 (0.30) | 0.28 (0.35) | 0.852 |
| Delayed late loss | | | | |
| In segment | 0.20 (0.42) | 0.20 (0.41) | 0.20 (0.43) | 0.142 |
| In stent | 0.23 (0.43) | 0.23 (0.43) | 0.23 (0.43) | 0.982 |
| Total late loss | | | | |
| In segment | 0.39 (0.49) | 0.39 (0.49) | 0.40 (0.49) | 0.692 |
| In stent | 0.54 (0.50) | 0.56 (0.48) | 0.51 (0.51) | 0.881 |

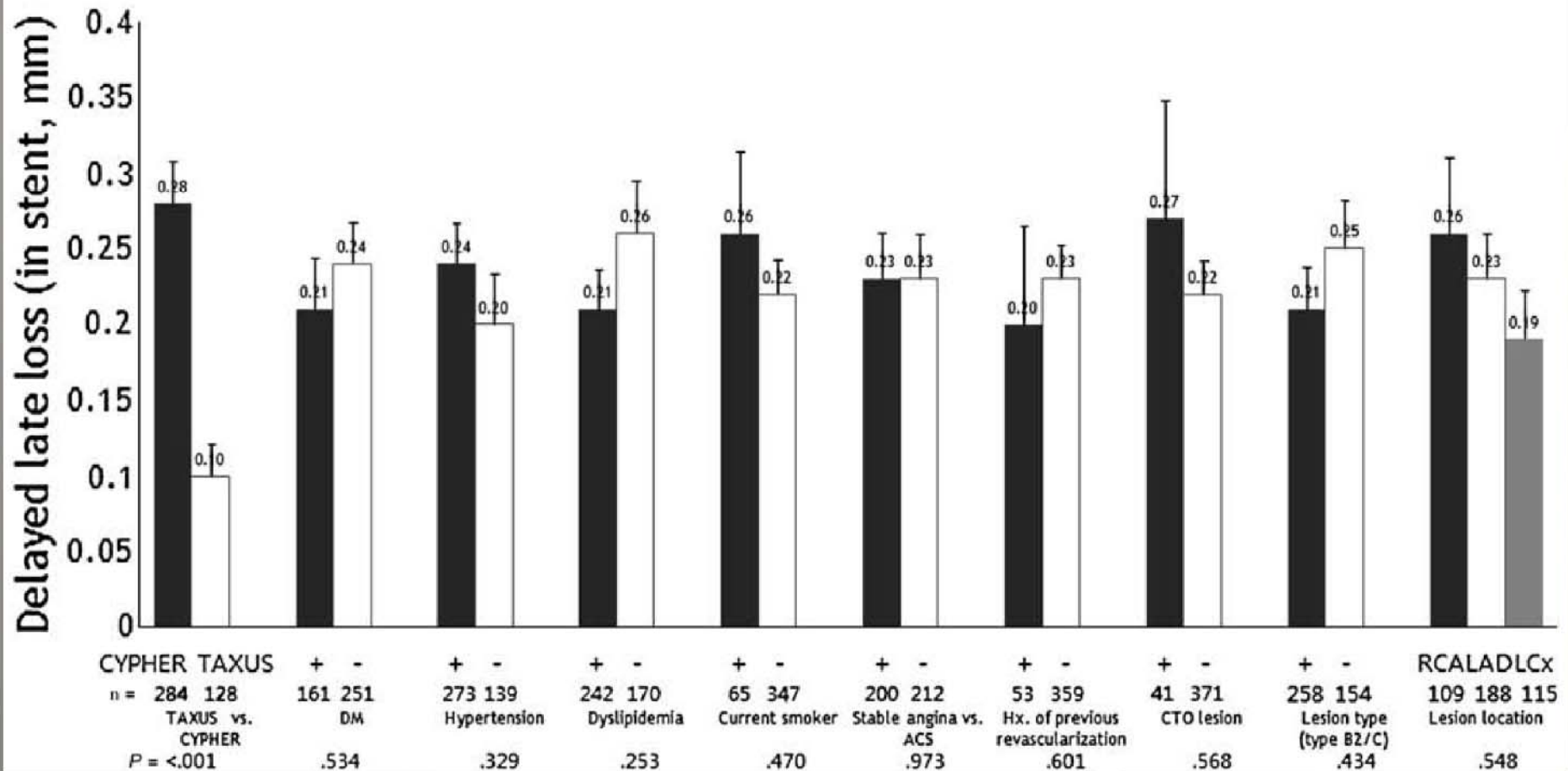
LL in SES vs PES according to initial Dx at Index PCI

| | SA | TAXUS | CYPHER | Sig. |
|----------------------------------|--------------------|--------------|---------------|-------------|
| Acute gain after index procedure | | | | |
| In segment | 1.54 (0.57) | 1.54 (0.59) | 1.59 (0.58) | 0.626 |
| In stent | 1.92 (0.50) | 1.87 (0.50) | 1.97 (0.51) | 0.189 |
| Early late loss | | | | |
| In segment | 0.21 (0.37) | 0.31 (0.38) | 0.10 (0.29) | 0.000 |
| In stent | 0.38 (0.35) | 0.52 (0.33) | 0.21 (0.19) | 0.000 |
| Delayed late loss | | | | |
| In segment | 0.17 (0.40) | 0.12 (0.21) | 0.26 (0.50) | 0.010 |
| In stent | 0.21 (0.41) | 0.11 (0.20) | 0.31 (0.52) | 0.000 |
| Total late loss | | | | |
| In segment | 0.39 (0.48) | 0.44 (0.42) | 0.36 (0.53) | 0.254 |
| In stent | 0.58 (0.48) | 0.63 (0.37) | 0.52 (0.55) | 0.087 |
| | ACS | TAXUS | CYPHER | Sig. |
| Acute gain after index procedure | | | | |
| In segment | 1.58 (0.56) | 1.51 (0.52) | 1.60 (0.57) | 0.307 |
| In stent | 1.91 (0.55) | 1.91 (0.45) | 1.92 (0.57) | 0.917 |
| Early late loss | | | | |
| In segment | 0.20 (0.34) | 0.37 (0.50) | 0.16 (0.27) | 0.010 |
| In stent | 0.28 (0.35) | 0.63 (0.49) | 0.19 (0.23) | 0.000 |
| Delayed late loss | | | | |
| In segment | 0.20 (0.43) | 0.04 (0.32) | 0.24 (0.45) | 0.001 |
| In stent | 0.23 (0.43) | 0.08 (0.31) | 0.27 (0.45) | 0.002 |
| Total late loss | | | | |
| In segment | 0.40 (0.49) | 0.41 (0.47) | 0.40 (0.50) | 0.843 |
| In stent | 0.51 (0.51) | 0.71 (0.45) | 0.50 (0.51) | 0.002 |

Differences d/t initial diagnosis & stent type

| | CYPHER | Stable angina | ACS | Sig. |
|----------------------------------------------------------|-------------|---------------|-------------|-------|
| Acute gain after index procedure | | | | |
| In segment | 1.59 (0.57) | 1.59 (0.58) | 1.60 (0.57) | 0.854 |
| In stent | 1.94 (0.54) | 1.97 (0.51) | 1.92 (0.57) | 0.416 |
| Late luminal loss at 1 st follow-up | | | | |
| In segment | 0.13 (0.28) | 0.10 (0.29) | 0.16 (0.27) | 0.120 |
| In stent | 0.20 (0.21) | 0.21 (0.19) | 0.19 (0.23) | 0.600 |
| (Further) Late luminal loss at 2 nd follow-up | | | | |
| In segment | 0.25 (0.47) | 0.26 (0.50) | 0.24 (0.45) | 0.779 |
| In stent | 0.28 (0.48) | 0.27 (0.45) | 0.27 (0.45) | 0.448 |
| Late luminal loss, overall | | | | |
| In segment | 0.38 (0.51) | 0.36 (0.53) | 0.40 (0.53) | 0.558 |
| In stent | 0.48 (0.53) | 0.52 (0.55) | 0.46 (0.51) | 0.368 |
| | TAXUS | Stable angina | ACS | Sig. |
| Acute gain after index procedure | | | | |
| In segment | 1.53 (0.56) | 1.54 (0.59) | 1.52 (0.52) | 0.847 |
| In stent | 1.92 (0.53) | 1.87 (0.50) | 1.91 (0.46) | 0.627 |
| Late luminal loss at 1 st follow-up | | | | |
| In segment | 0.33 (0.42) | 0.32 (0.37) | 0.37 (0.51) | 0.546 |
| In stent | 0.56 (0.40) | 0.51 (0.33) | 0.64 (0.50) | 0.139 |
| (Further) Late luminal loss at 2 nd follow-up | | | | |
| In segment | 0.10 (0.25) | 0.12 (0.21) | 0.05 (0.32) | 0.209 |
| In stent | 0.10 (0.24) | 0.12 (0.20) | 0.07 (0.30) | 0.358 |
| Late luminal loss, overall | | | | |
| In segment | 0.43 (0.44) | 0.43 (0.42) | 0.42 (0.48) | 0.853 |
| In stent | 0.66 (0.39) | 0.63 (0.36) | 0.71 (0.45) | 0.327 |

Various clinical factors and delayed LL



Question?

There is a wide person to person variation in the tendency to form neointima. Some people are just more susceptible to restenosis. There may be an unknown factor (ex: genetic factor) that goes into play.

How can we exclude that such inter-patient variability or susceptibility to formation of neointima was reason for the differences seen?

Proof-of-concept: a hybrid cohort

If we can compare the late loss between these stents in the same patient who had the stents implanted at the same index PCI, we would be able to at least exclude the interpersonal susceptibility factor.

Thus a hybrid cohort (patients that received both SES and PES in the same index PCI) would be a great cohort to provide proof-of-concept!

Early and delayed LL : Hybrid Cohort

| | PES (N=23) | SES (N=24) | P value |
|-----------------------------------------|-----------------------|-----------------------|-----------------|
| Acute gain after index procedure | | | |
| In segment | 1.61 (0.70) | 1.57 (0.67) | 0.87 |
| In stent | 1.95 (0.55) | 1.94 (0.62) | 0.97 |
| Early late loss | | | |
| In-segment | 0.24 (0.37) | 0.11 (0.29) | 0.09 |
| In-stent | 0.55 (0.36) | 0.24 (0.24) | <0.01 |
| Delayed late loss | | | |
| In-segment | 0.14 (0.26) | 0.29 (0.44) | 0.15 |
| In-stent | 0.10 (0.22) | 0.26 (0.39) | 0.10 |
| Overall late loss | | | |
| In-segment | 0.41 (0.42) | 0.40 (0.51) | 0.91 |
| In-stent | 0.65 (0.34) | 0.50 (0.54) | 0.24 |

Summary

1. Both Taxus & Cypher showed statistically significant delayed late loss after 1st angiographic follow up.

2. In Cypher stents

A considerable amount of delayed late loss after 1st angiographic fu was observed. [suggests possibility of late catch up]

Better correlation of delayed late loss rather than early late loss with total late loss

3. In Taxus stents,

the delayed late loss after 1st angiographic fu was relatively minimal.

Better correlation between early late loss and total late loss

Summary

4. Both stents show excellent late loss profile at 18 to 24 months
[0.5-0.6mm in very tough lesions]
5. The difference in delayed late loss was not due to the baseline difference in the proportion of patients with ACS and SA.
6. A hybrid cohort analysis supports the findings that the difference in delayed late loss was due to differences between stents rather than innate susceptibility of patients to neointima formation.

Limitations

Relatively small study population [difficulty in obtaining long term angiographic follow up in all patients]

Thus there is a possibility of selection bias.

Therefore, the results need to be interpreted with caution and can be considered hypothesis generating at best.

Conclusion

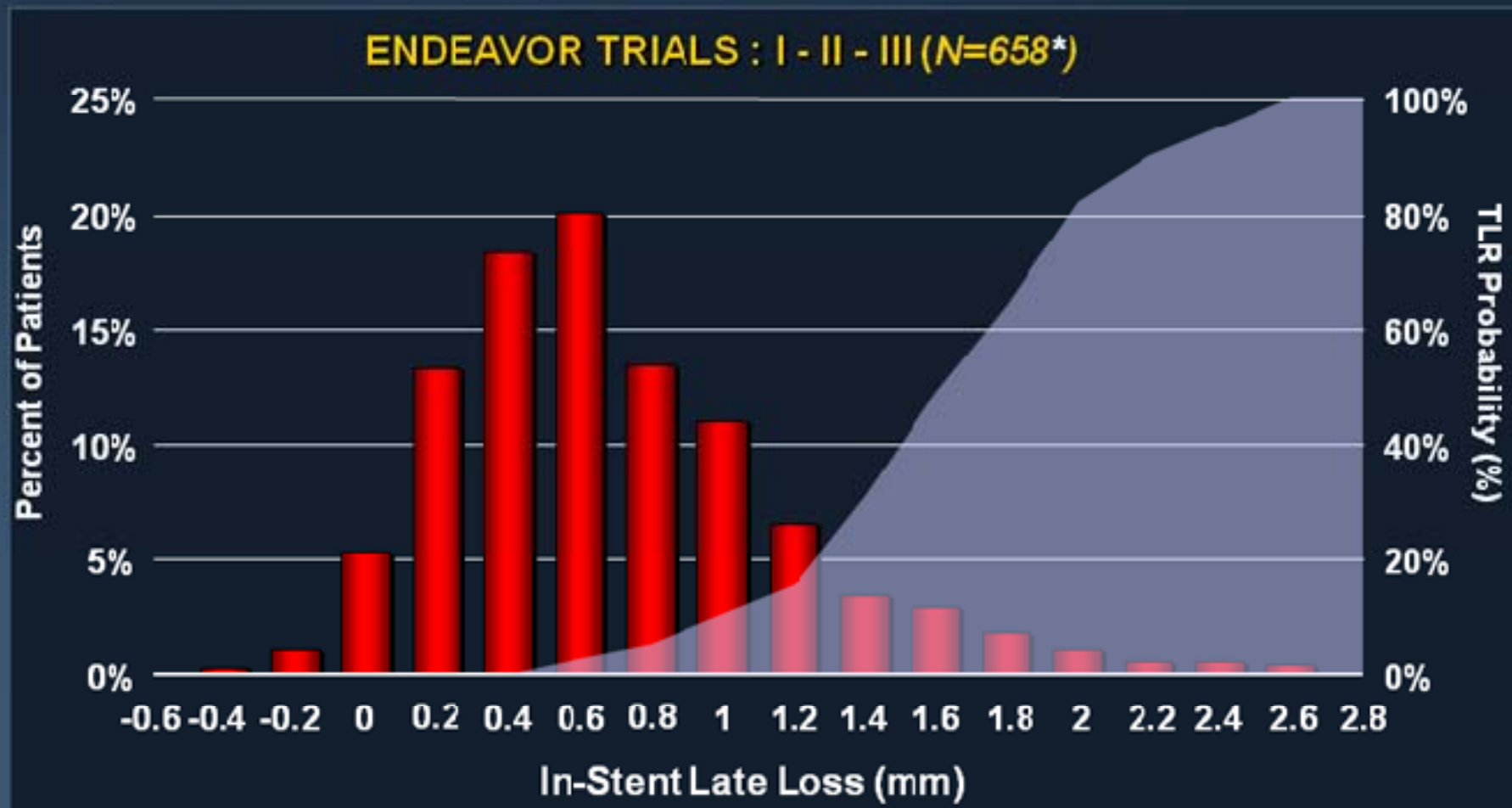
- 1. Both Taxus and Cypher showed delayed catchup.**
- 2. Cypher showed slightly more delayed catchup than Taxus.**
- 3. Our data suggest that the process of neointima formation after SES and PES implantation may follow a slightly different timeline.**
- 4. Whether the late catchup phenomenon has clinical impact [results in increased or sustained occurrence of TLR] needs to be studied in a larger population.**



Thank you for your attention !!



In-Stent Late Loss / TLR Relationship



* Patients undergoing angiographic follow-up.