



A Randomized Comparison of Drug-Eluting Balloon Versus Everolimus-Eluting Stent in Patients With Bare-Metal In-Stent Restenosis: The RIBS V Clinical Trial

**Fernando Alfonso MD, PhD, FESC
Hospital Universitario “La Princesa” Madrid.**

**On Behalf of the RIBS V Investigators
(Coordinator Center: Hospital Universitario Clínico San Carlos. Madrid)**



DISCLOSURE

Nothing to disclose



Background:

- Treatment of patients with BMS-ISR remains a challenge
- In this setting, DES provide better results than classical coronary interventions (BA, BMS, Brachytherapy).
- Drug-eluting balloons (DEB) are also very effective in patients with BMS-ISR, with results superior to those obtained by conventional BA and equivalent to those seen with 1st Generation DES
- However, the value of DEB compared with 2nd Generation DES in patients with BMS-ISR remains unknown



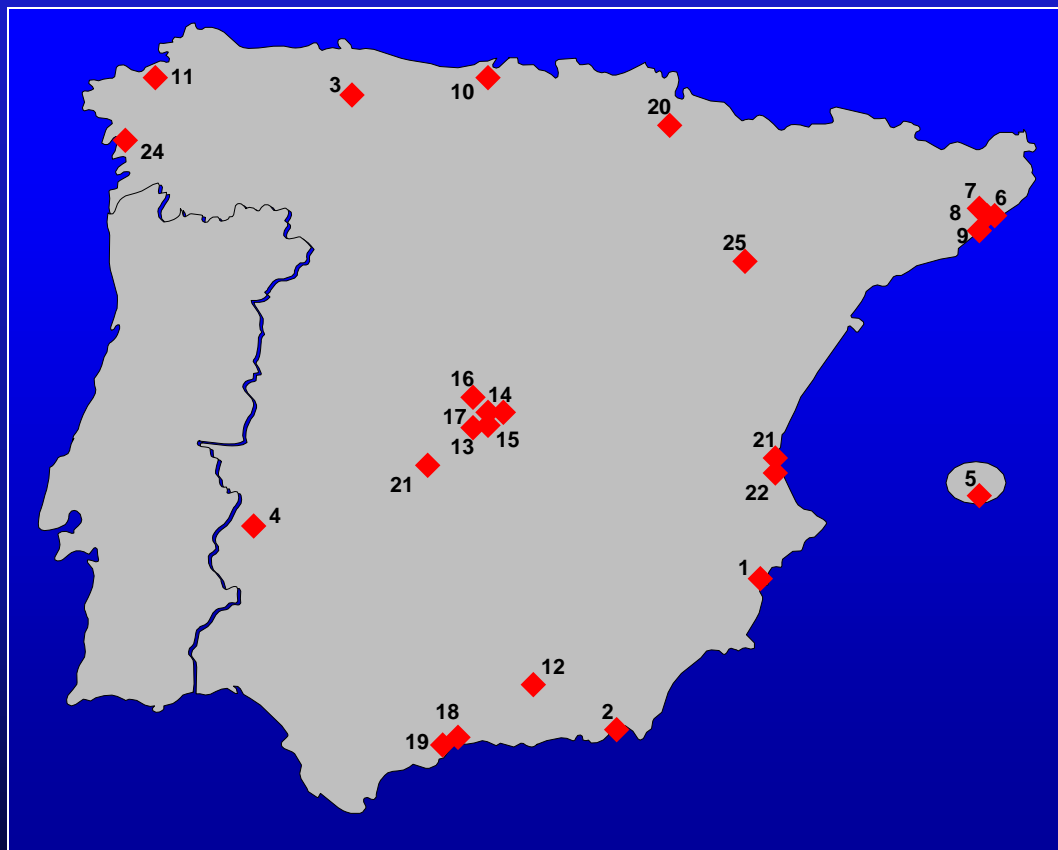
Objective:

- We sought to compare the efficacy of EES vs DEB in patients with BMS-ISR



RIBS V: (*Restenosis Intra-stent: DEB vs EES*)

Multicenter, Prospective, Randomized



- 1.- ALICANTE H General U.
- 2.- ALMERIA H U Torrecardenas.
- 3.- ASTURIAS H U Central Asturias.
- 4.- BADAJOZ H U Infanta Cristina.
- 5.- BALEARES. H U Son Espases.
- 6.- BARCELONA H U Bellvitge.
- 7.- BARCELONA H U Clinico.
- 8.- BARCELONA H U Santa Cruz y San Pablo.
- 9.- BARCELONA H U Valle de Hebrón.
- 10.- CANTABRIA H U Marques de Valdecilla.
- 11.- CORUÑA H U Juan Canalejo.
- 12.- GRANADA H U Virgen de las Nieves.
- 13.- MADRID H U Doce de Octubre.
- 14.- MADRID H U (Ia) Paz.
- 15.- MADRID H U (Ia) Princesa
- 16.- MADRID H U Puerta de Hierro.
- 17.- **MADRID H U Clínico San Carlos.**
- 18.- MALAGA H U Carlos Haya
- 19.- MALAGA H U Virgen de la Victoria.
- 20.- NAVARRA H U Provincial Navarra.
- 21.- TOLEDO. H U Virgen de la Salud Toledo
- 22.- VALENCIA H Clinico U.
- 23.- VALENCIA H General U.
- 24.- VIGO H U Meixoeiro. Pontevedra
- 25.- ZARAGOZA H U. Miguel Servet.

Steering Committee. QCA & Clinical Events Committee
Under the Auspices PCI WG Sociedad Española Cardiología
Coordinator Center : HU Clínico San Carlos. Madrid.

Investigators´ Driven Initiative
Unrestricted Grants:
B. Braun Surgical & Abbott Vascular



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Multicenter, Prospective, Randomized

Coordinating Center: Hospital Universitario Clínico San Carlos. Madrid.

Steering Committee: F. Alfonso (Chairman and Principal Investigator), J. Zueco, A. Cequier, C. Morís, C. Macaya.

Clinical Events Committee: R. Hernández, M. Sabaté, C. Saenz de la Calzada.

Coronary Angiography Core Laboratory: (Hospital Universitario Clinico San Carlos, Madrid) A. Cárdenas, M.J. Pérez-Vizcayno.

Data Coordination, Safety Monitoring and Statistical Committee: M.J. Pérez-Vizcayno, C. Fernández.

Intravascular Ultrasound and Optical Coherence Tomography Committee: N. Gonzalo, F. Alfonso.

Sites and Investigators: In order of enrollment:

¹Hospital Universitario Clínico San Carlos, Madrid, (F. Alfonso, P. Jiménez-Quevedo, N. Gonzalo, J. Escaned, A. Fernández-Ortiz, C. Macaya); ²Hospital Universitario Vall d'Hebron, Barcelona, (B. García del Blanco); ³Hospital Universitario de la Princesa, Madrid, (B. Seidelberger); ⁴Complejo Hospitalario Universitario de Vigo, Vigo, (A. Iñiguez); ⁵Hospital Universitario de Torrecárdenas, Almería, (M. Gómez-Recio); ⁶Hospital Universitario Clinic de Barcelona, Barcelona, (M. Masotti); ⁷Hospital Universitario 12 de Octubre, Madrid, (T. Velazquez); ⁸Hospital Universitario Clínico de Valencia, Valencia, (J. Sanchís); ⁹Hospital Universitario Puerta de Hierro, Majadahonda, (A. García-Touchard); ¹⁰Hospital Universitario Marqués de Valdecilla, Santander, (J. Zueco); ¹¹Hospital Universitario Son Espases, Palma de Mallorca, (A. Bethecourt); ¹²Hospital Universitario Virgen de las Nieves, Granada, (R. Melgares); ¹³Hospital Universitario de Bellvitge, Barcelona, (A. Cequier); ¹⁴Hospital Universitario Virgen de la Victoria, Málaga, (J.M. Hernández); ¹⁵Hospital Universitario de Alicante, Alicante, (V. Mainar); ¹⁶Hospital Universitario Infanta Cristina. Badajoz, Badajoz, (J.R. López-Míguez); ¹⁷Hospital Universitario Virgen de la Salud Toledo, Toledo, (J. Moreu); ¹⁸Hospital Universitario Sant Pau, Barcelona, (V. Martí); ¹⁹Hospital Universitario La Paz, Madrid, (R. Moreno); ²⁰Hospital Universitario General de Valencia, Valencia, (F. Pomar); ²¹Complejo Hospitalario Universitario de Navarra, Pamplona, (R. Lezaun); ²²Hospital Universitario Carlos Haya, Malaga, (C.A. Urbano-Carrillo); ²³Hospital Universitario Miguel Servet, Zaragoza, (M.C. Ferrer-García); ²⁴Complejo Hospitalario Universitario de A Coruña, La Coruña, (N. Vázquez); ²⁵Hospitalario Universitario Central de Asturias, Oviedo, (C. Morís).



Inclusion / Exclusion Criteria

Inclusion:

- Informed consent
- Age 20 - 85 y
- *BMS ISR (> 50% stenosis)*
- *Angina or silent ischemia*
- ISR amenable for BA & Stent

Exclusion:

Stent Related:

- Stent location undefined
- ISR <1 Month
- Thrombus or TIMI 0.
- *Vessel diameter < 2 mm*
- *ISR length > 30 mm*
- ISR outside the Stent

General:

- Life expectancy < 1 y
- Female in childbearing age
- Problems FU angiography
- Intolerance ASA/Clopidogrel
- LVEF < 25%



Sample Size Calculation

EES

- After EES implantation: MLD: 2.6 mm
RIBS I and RIBS II (1,2)
- Late loss: 0.3 mm (2)
- MLD at FU: 2.3 ± 0.7 mm

DEB

- After DEB dilation: MLD: 2.2 mm
RIBS I and RIBS II (1,2)
- Late loss: 0.2 mm (3)
- MLD at FU: 2.0 ± 0.7

- 172 Pts (86 per arm) (power 80%, alpha error 5%)
- 190 Pts (95 per arm) assuming a drop-out rate ~10%



(January 2010 to January 2012)

Inclusion Criteria
Informed Consent

189 Pts BMS ISR
Randomization

Rx Centralized
Stratification:
ISR Length & Edge

Xience Prime
(Abbott Vascular)

94 Pts
EES

95 Pts
DEB

SeQuent Please
(B. Braun Surgical)

100% Angiographic Success

8 Refused

3 Died
1 Thrombosis
7 Refused

Mean: 270 days

86 Pts
Angio FU

QCA
Primary
End-point

84 Pts
Angio FU

Mean: 271 days

(170 Patients: 92% of Eligible)



Clinical Data (I)

| | All (N 189) | EES (N 94) | DEB (N 95) |
|----------------------------|-------------|-------------|---------------|
| Age (years) | 66 \pm 12 | 64 \pm 12 | 67 \pm 11 * |
| Female | 25 (13) | 12 (13) | 13 (14) |
| <i>Risk Factors</i> | | | |
| Diabetes | 49 (26) | 19 (20) | 30 (32) |
| Hyperlipidemia | 131 (69) | 62 (66) | 69 (73) |
| Hypertension | 136 (72) | 68 (72) | 68 (72) |
| Ever smoked | 126 (68) | 70 (75) | 56 (59) ** |
| Family history | 12 (6) | 8 (9) | 4 (4) |

* $p=0.04$; ** $p=0.02$



Clinical Data (II)

| | All (N 189) | EES (N 94) | DEB (N 95) |
|----------------------------------|-------------------|-------------------|-------------------|
| <i>Previous History</i> | | | |
| Myocardial infarction | 113 (60) | 56 (60) | 57 (60) |
| Bypass surgery | 11 (6) | 7 (7) | 4 (4) |
| <i>Clinical Features</i> | | | |
| Unstable angina | 80 (42) | 42 (45) | 38 (40) |
| Stable angina | 84 (44) | 41 (44) | 43 (45) |
| Silent ischemia | 25 (13) | 11 (12) | 14 (15) |
| <i>Time to ISR (days)</i> | 363 (148-2730) | 350 (151-2679) | 390 (142-2815) |



Angiographic Data (I)

| | All (N 189) | EES (N 94) | DEB (N 95) |
|------------------------|--------------------|--------------------|--------------------|
| Target Vessel : | | | |
| LAD | 72 (38) | 37 (39) | 35 (37) |
| LCX | 43 (23) | 22 (23) | 21 (22) |
| RCA | 69 (37) | 32 (34) | 37 (39) |
| SVG | 5 (3) | 3 (3) | 2 (2) |
| LVEF (%) | 58 _± 12 | 59 _± 12 | 58 _± 13 |



Angiographic Data (II)

| | All (N 189) | EES (N 94) | DEB (N 95) |
|--------------------|-------------|------------|------------|
| <i>Mehran:</i> | | | |
| Ib | 20 (11) | 14 (15) | 6 (6) |
| Ic | 46 (24) | 17 (18) | 29 (31) |
| Id | 6 (3) | 3 (3) | 3 (3) |
| II | 87 (46) | 42 (45) | 45 (47) |
| III | 29 (15) | 17 (18) | 12 (13) |
| IV | 1 (0.5) | 1 (1) | 0 (0) |
| ACC/AHA B2C | 99 (52) | 51 (54) | 48 (51) |



Procedural Data

| | All (N 189) | EES (N 94) | DEB (N 95) |
|--------------------------------|---------------|---------------|----------------|
| <i>Initial Stent:</i> | | | |
| Length of initial stent (mm) | 18 \pm 6 | 18 \pm 6 | 19 \pm 6 |
| Maximal pressure (atm) | 15 \pm 3 | 15 \pm 3 | 15 \pm 3 |
| <i>Index Procedure:</i> | | | |
| Maximal pressure (atm) | 19 \pm 4 | 19 \pm 3 | 18 \pm 4 |
| Maximal Balloon Diam (mm) | 3.2 \pm 0.4 | 3.2 \pm 0.4 | 3.2 \pm 0.5 |
| EES / DEB Length (mm) | 22 \pm 8 | 23 \pm 9 | 20 \pm 7 * |
| Total inflation time (sec) | 71 (45-112) | 60 (30-92) | 90 (60-120) ** |
| Cross-over | 8 (4) | 0 (0) | 8 (8) * |

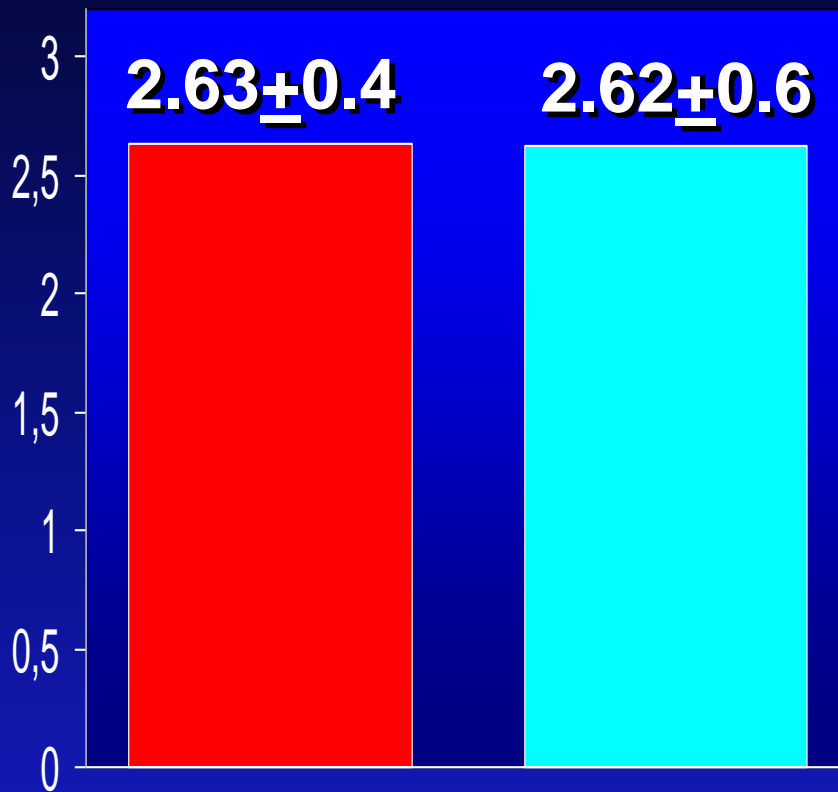
* $p < 0.05$ ** $p = 0.0001$



QCA: In-Segment Analysis

Reference Diameter

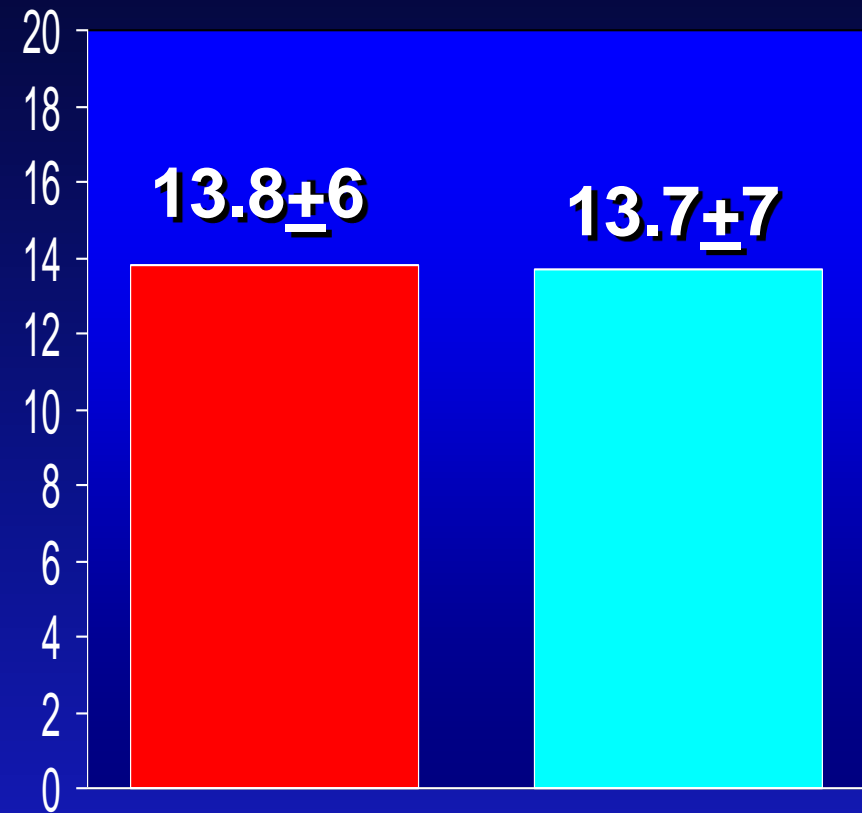
(mm)



$p = 0.91$

Lesion Length

(mm)

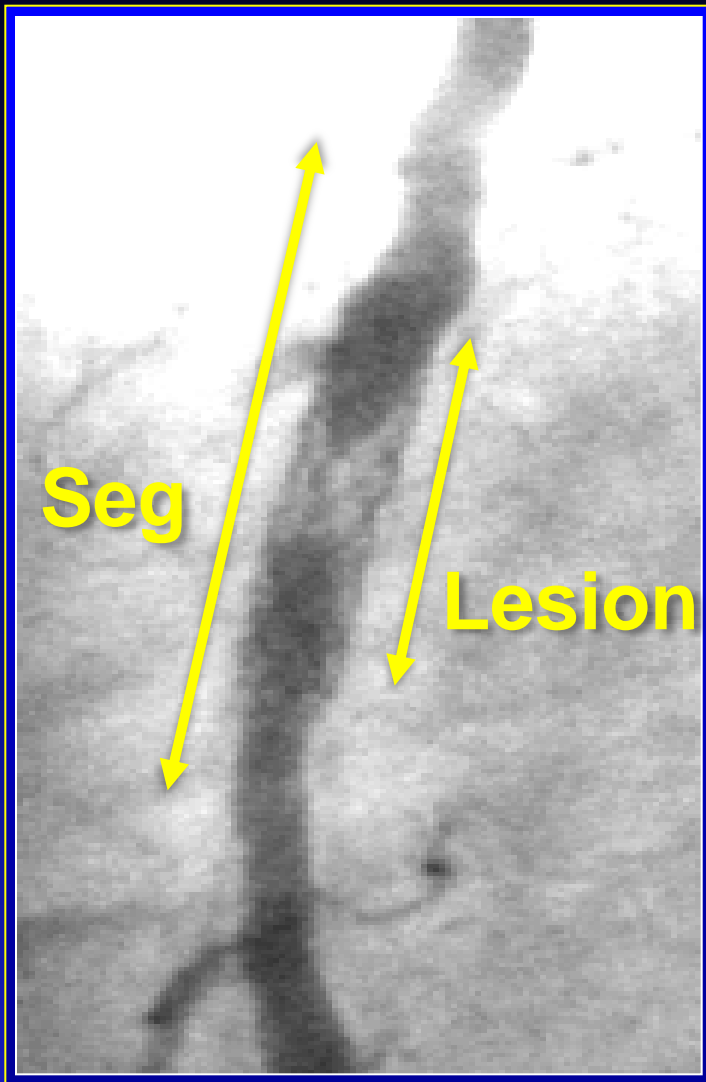


$p = 0.96$

EES DEB



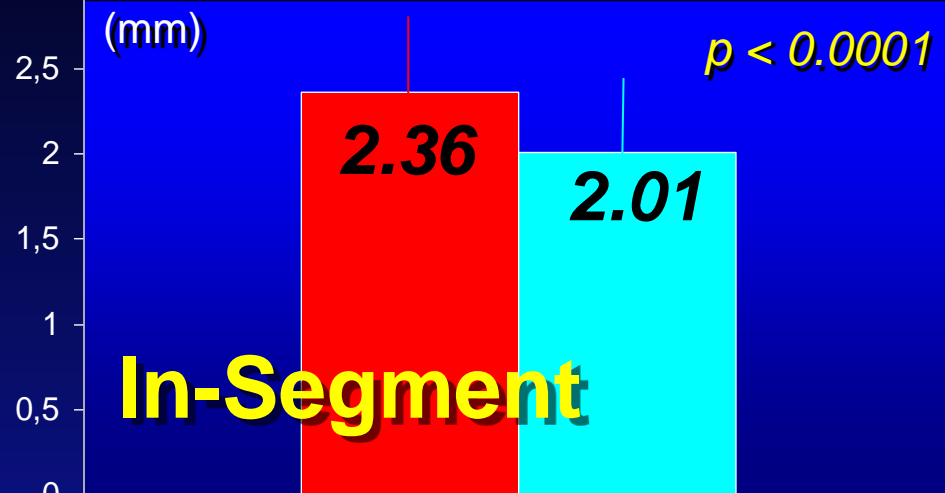
1ry Endpoint: MLD at FU



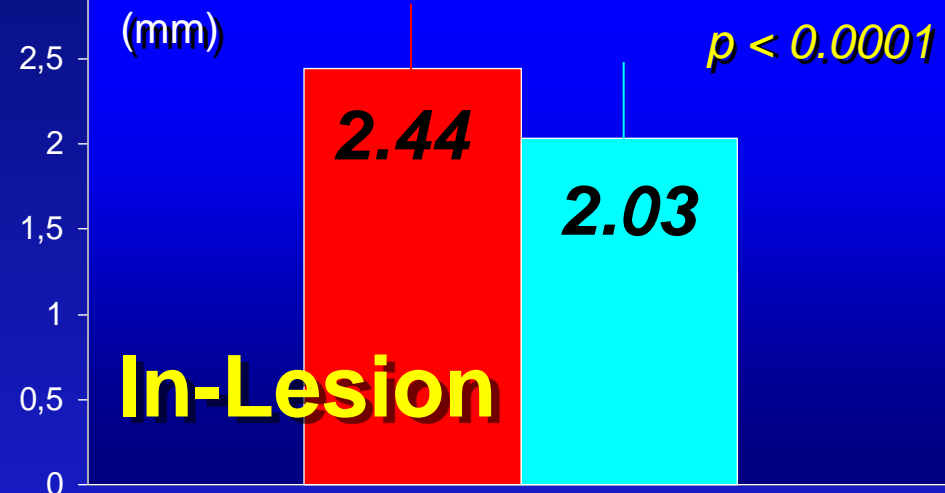
Adjusted (age, smoker, stenosis, diabetes) $p = 0.001$

MLD-FU

■ EES ■ DEB

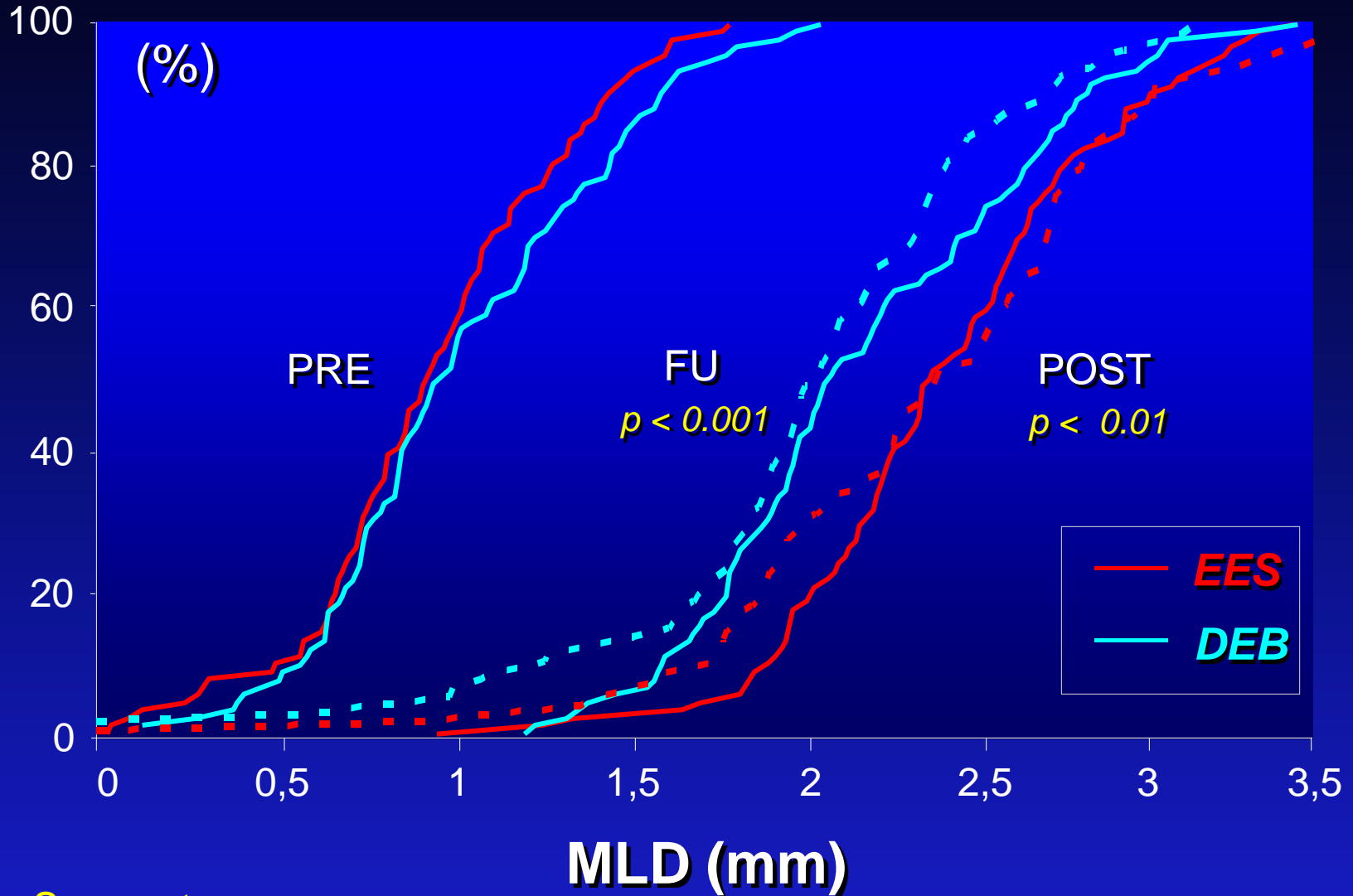


MLD-FU





Cumulative Frequency Distribution Curves



In-Segment

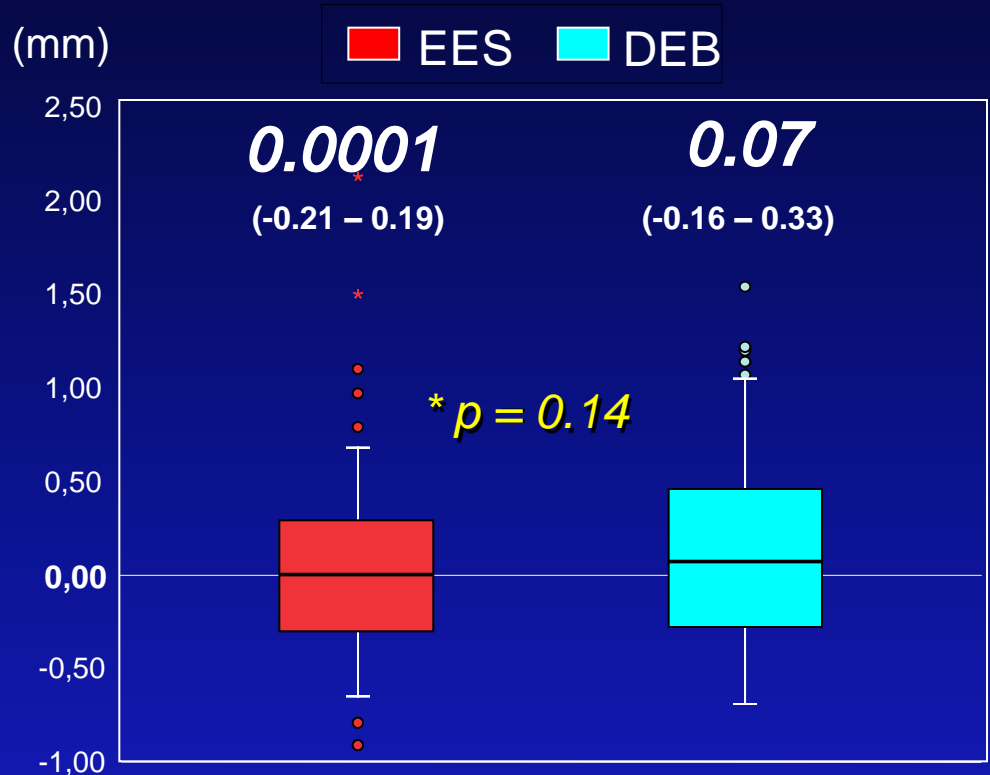
Intention to Treat



In-Segment Analysis (QCA)

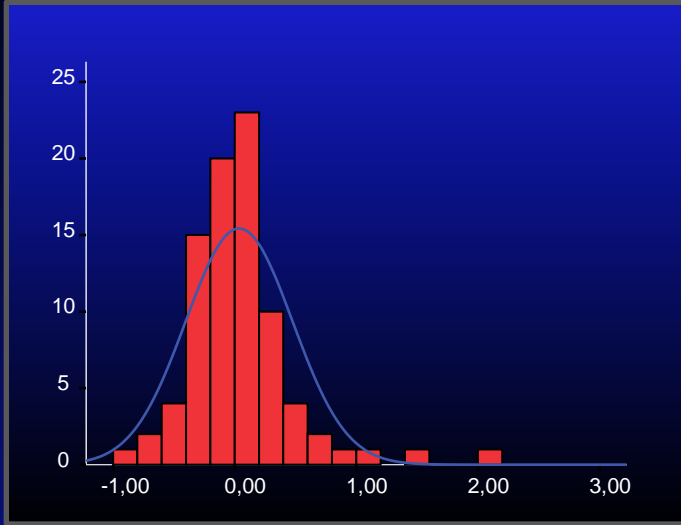
Late Loss

0.04±0.5 vs 0.14±0.5 mm

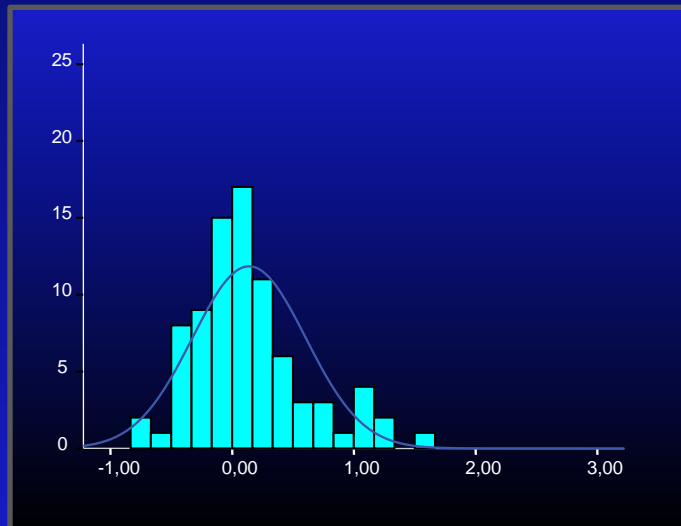


* median (IQR); Mann-Whitney "U"

QCA = CASS II System

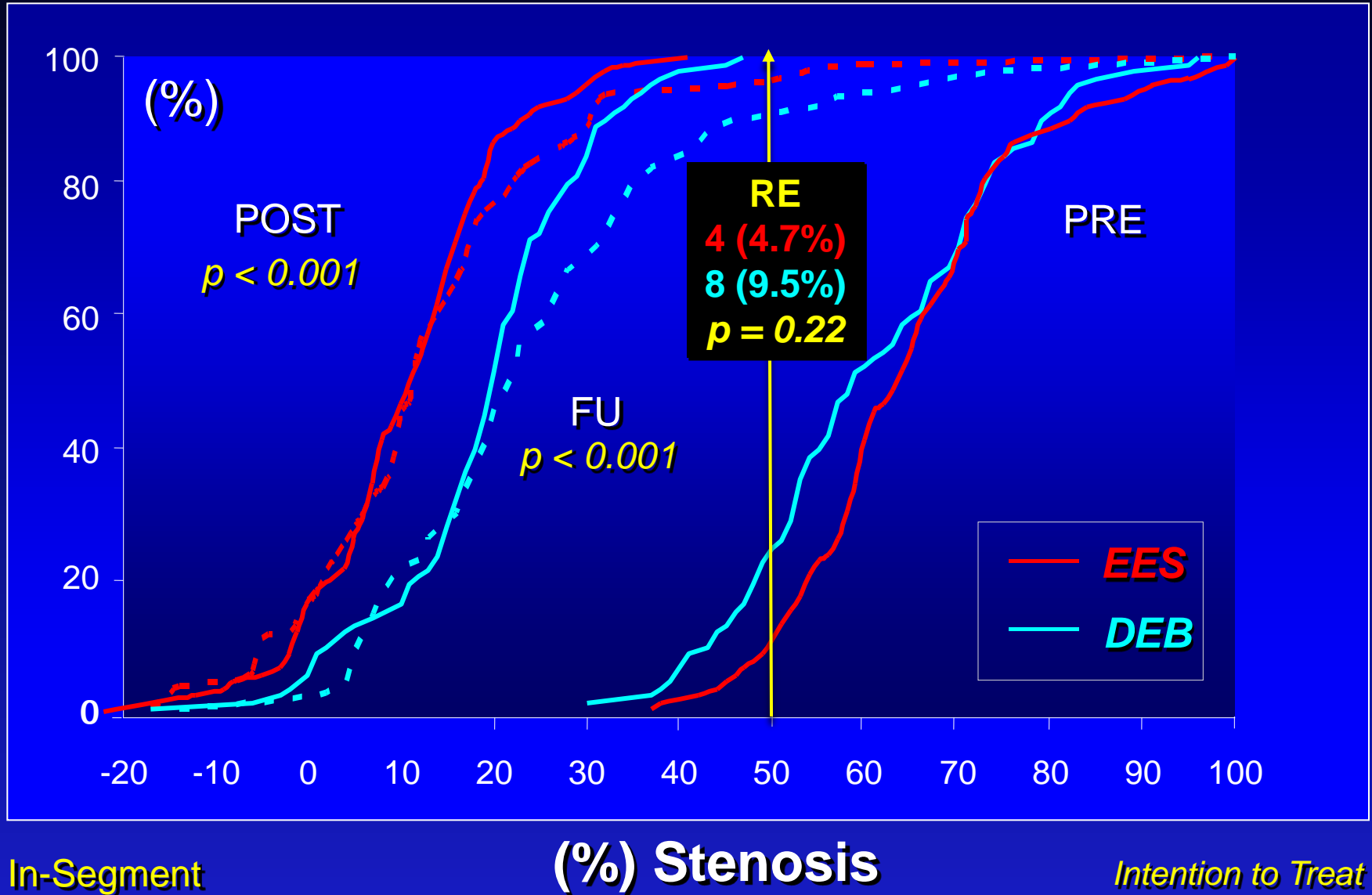


Kolmogorov-Smirnov <0.05





Cumulative Frequency Distribution Curves

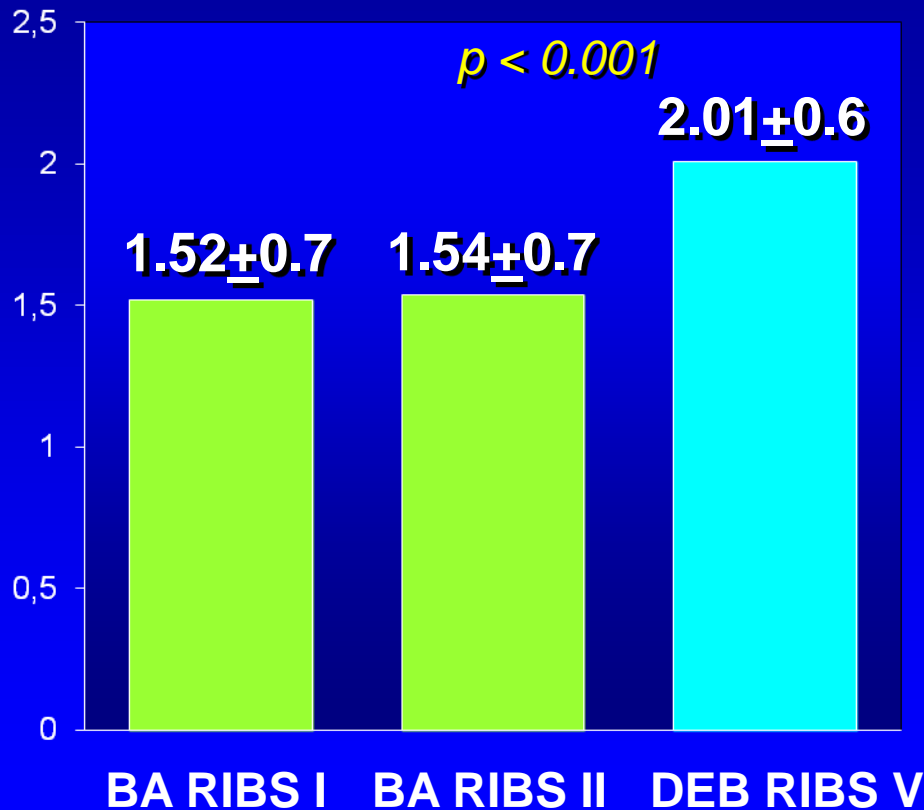




DEB vs BA in the RIBS trials

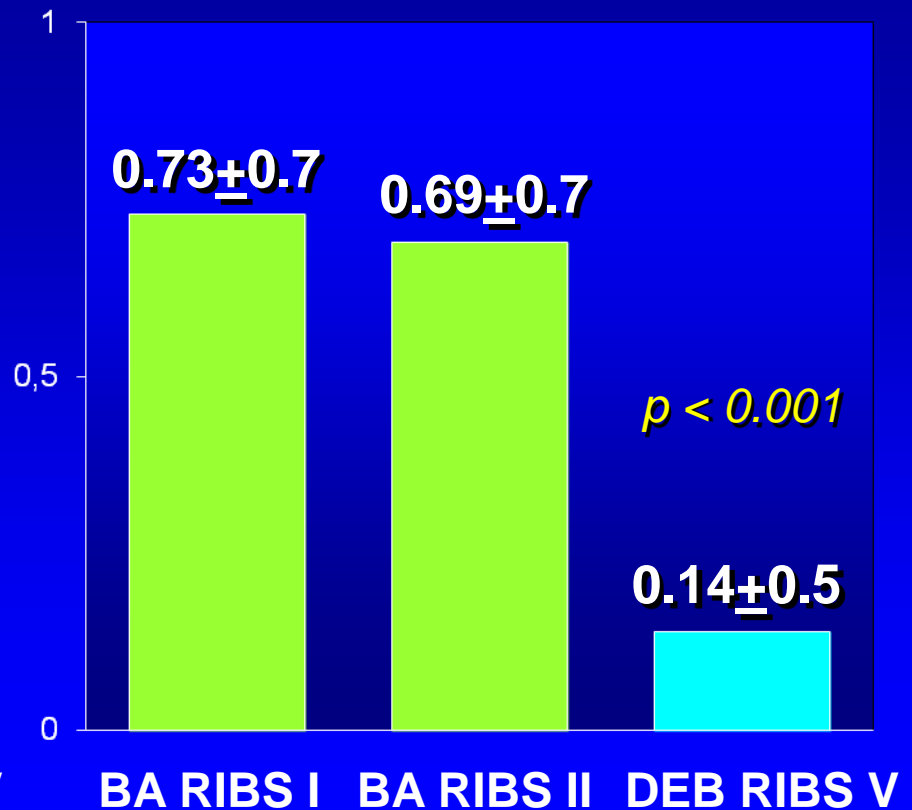
MLD FU

(mm)



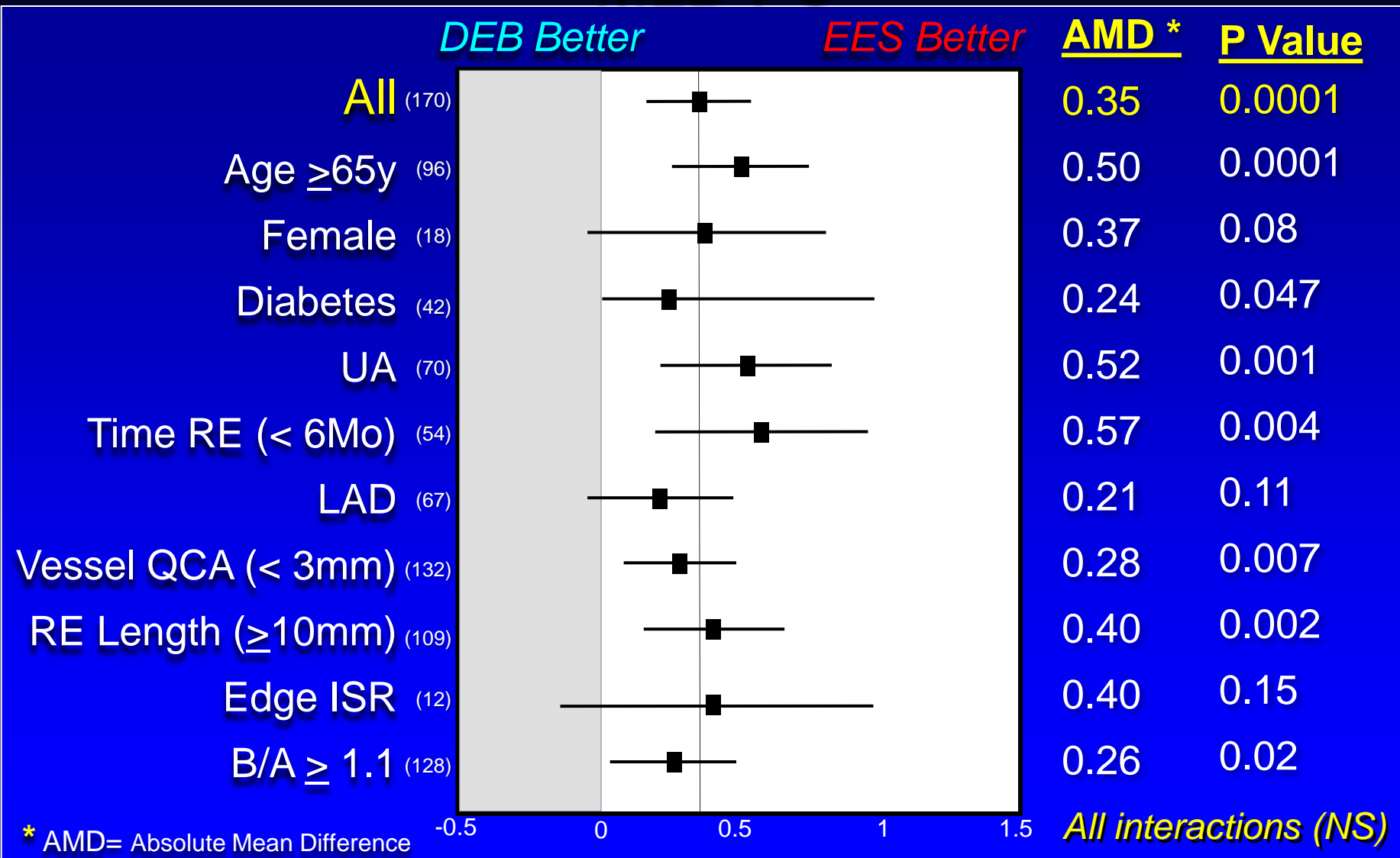
Late Loss

(mm)





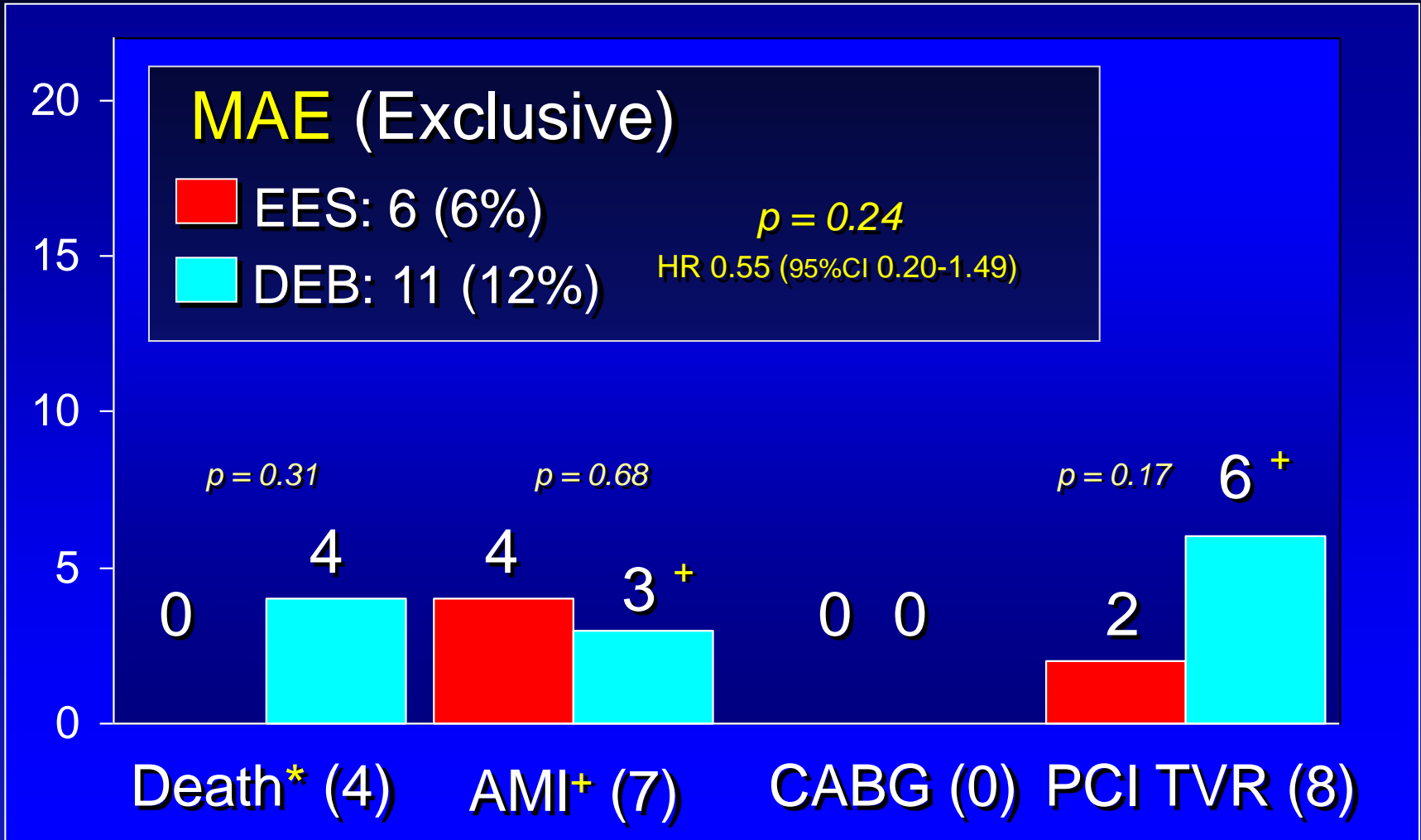
10 Pre-Specified Variables:
MLD FU





Events at Final FU (1 Year)

1 Year FU 189 P (100%); FU Time 361±28 days



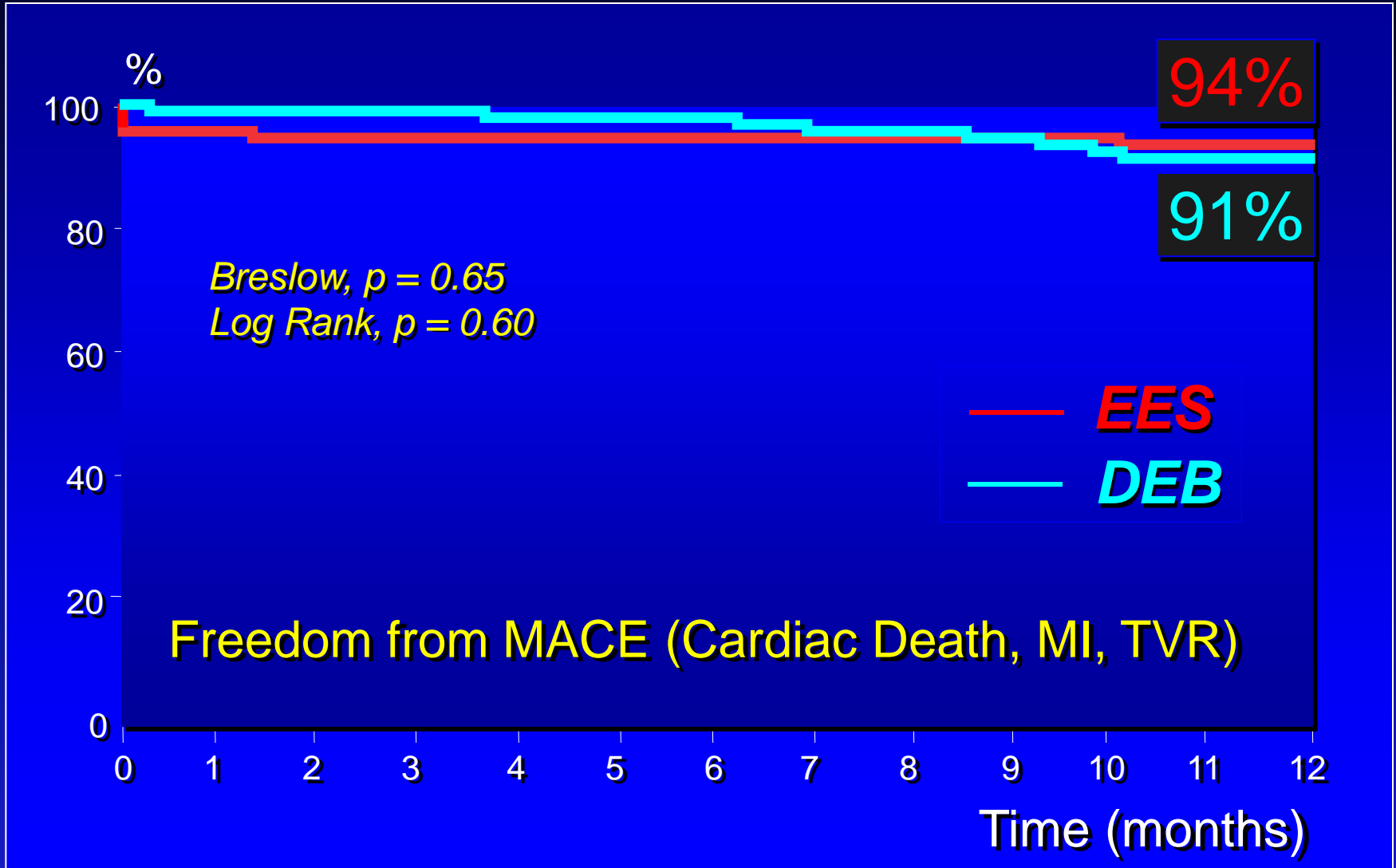
* 3 Non Cardiac Deaths + 1 Definitive ST Thrombosis

Intention to Treat



Clinical Follow-up:

1 Year FU 189 P (100%); FU Time 361±28 days





Conclusions:

- In patients with BMS-ISR both DEB and EES provide excellent long-term clinical outcomes
- In this setting, DEB and EES also offer excellent late angiographic findings with a very low late loss and “single digit” restenosis rates (similar with both techniques)
- However, EES provide superior late angiographic results including MLD (1_{ry} Endpoint) and % diameter stenosis
- Further studies (larger and with longer follow-up) are required to elucidate if these superior late angiographic findings eventually translate into a clinical benefit