

Endeavor Performance in Diabetes

Overview of Safety and Efficacy Outcomes in Diabetic Patients from the Endeavor IV and V Trials

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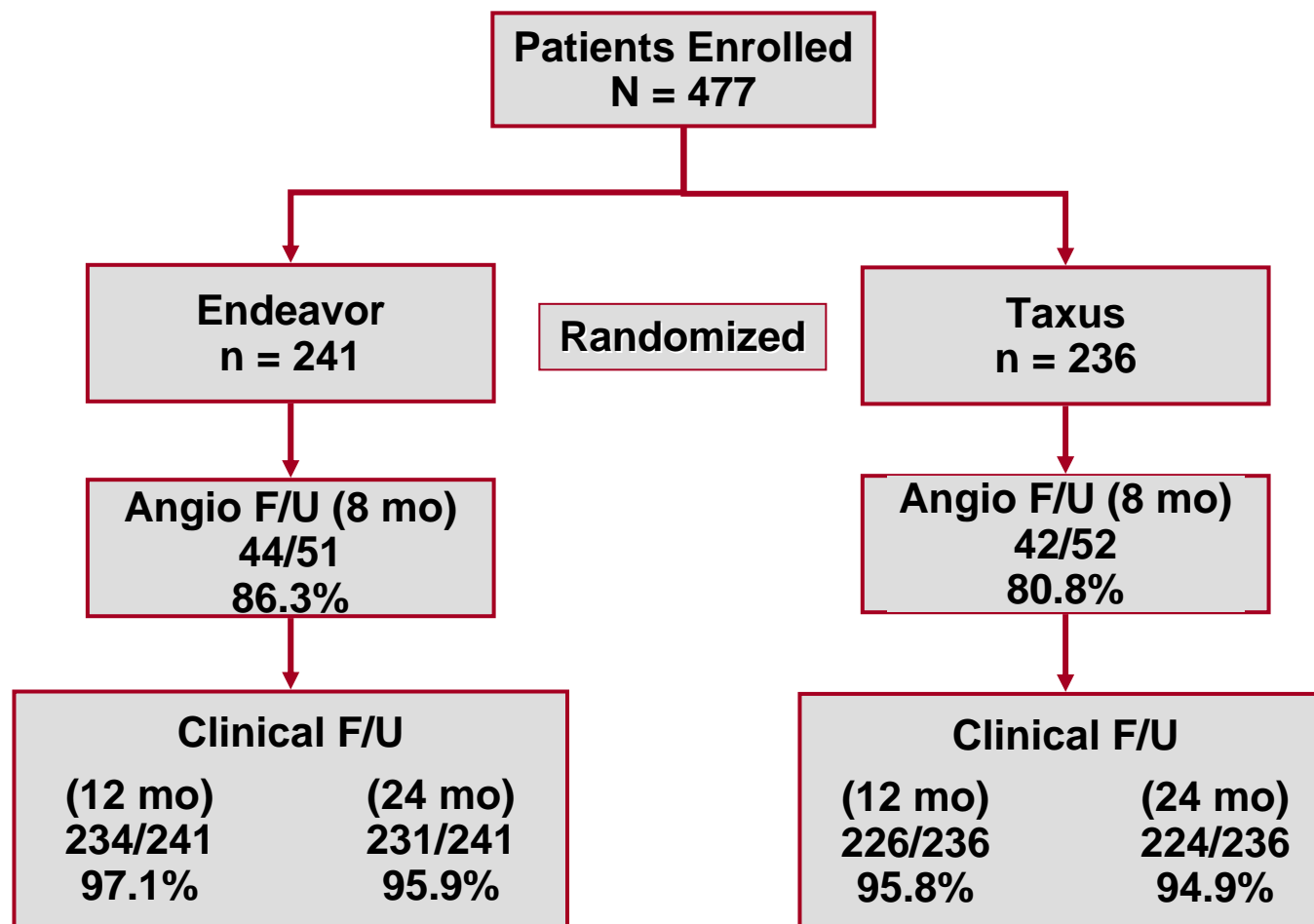
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Endeavor IV

Prespecified Diabetic Subgroup



Endeavor IV

8 Month Angiographic Outcomes

| | DM | | | No DM | | |
|---------------------------------|--------------------|-----------------|-------------------|---------------------|-----------------|----------------|
| | Endeavor N = 44 | Taxus N = 42 | <i>P</i> value | Endeavor N = 100 | Taxus N = 93 | <i>P</i> value |
| Binary Restenosis (%) | | | | | | |
| In-segment | 27.3 | 23.8 | 0.81 | 10.0 | 4.3 | 0.17 |
| In-stent | 25.0 | 16.7 | 0.43 | 8.1 | 2.2 | 0.10 |
| In-segment Late Loss Mean±SD | 0.46±0.5 5 | 0.38±0.5 8 | 0.45 | 0.31±0.42 | 0.16±0.35 | 0.009 |
| In-stent Late Loss Mean±SD | 0.81±0.5 8 | 0.56±0.6 6 | 0.07 | 0.61±0.44 | 0.35±0.39 | <.001 |

Endeavor IV

Clinical Outcomes at 2 Years

| | DM | | | No DM | | |
|------------------|---------------------|------------------|----------------|---------------------|------------------|----------------|
| | Endeavor N = 231 | Taxus N = 224 | <i>P</i> value | Endeavor N = 511 | Taxus N = 515 | <i>P</i> value |
| Death (all) (%) | 1.3 (3) | 2.7 (6) | 0.33 | 3.9 (20) | 2.5 (13) | 0.22 |
| Cardiac Death | 0.9 (2) | 1.8 (4) | 0.44 | 1.8 (9) | 1.0 (5) | 0.30 |
| MI (all) % | 0.9 (2) | 2.7 (6) | 0.17 | 2.5 (13) | 4.7 (24) | 0.09 |
| Q Wave | 0 | 0.4 (1) | 0.49 | 0.6 (3) | 0.6 (3) | 1.00 |
| Non-Q Wave | 0.9 (2) | 2.2 (5) | 0.28 | 2.0 (10) | 4.1 (21) | 0.07 |
| Definite ST | 0.9 (2) | 0.9 (2) | 1.00 | 0.8 (4) | 0.8 (4) | 1.00 |
| TLR (%) | 8.7 (20) | 6.7 (15) | 0.48 | 4.7 (24) | 3.7 (19) | 0.44 |
| TVR (non-TL) (%) | 4.8 (11) | 6.7 (15) | 0.42 | 3.9 (20) | 5.4 (28) | 0.30 |
| MACE (%) | 9.5 (22) | 10.7 (24) | 0.76 | 10.0 (51) | 9.7 (50) | 0.92 |
| TVF (%) | 12.6 (29) | 15.2 (34) | 0.54 | 10.4 (53) | 12.2 (63) | 0.38 |

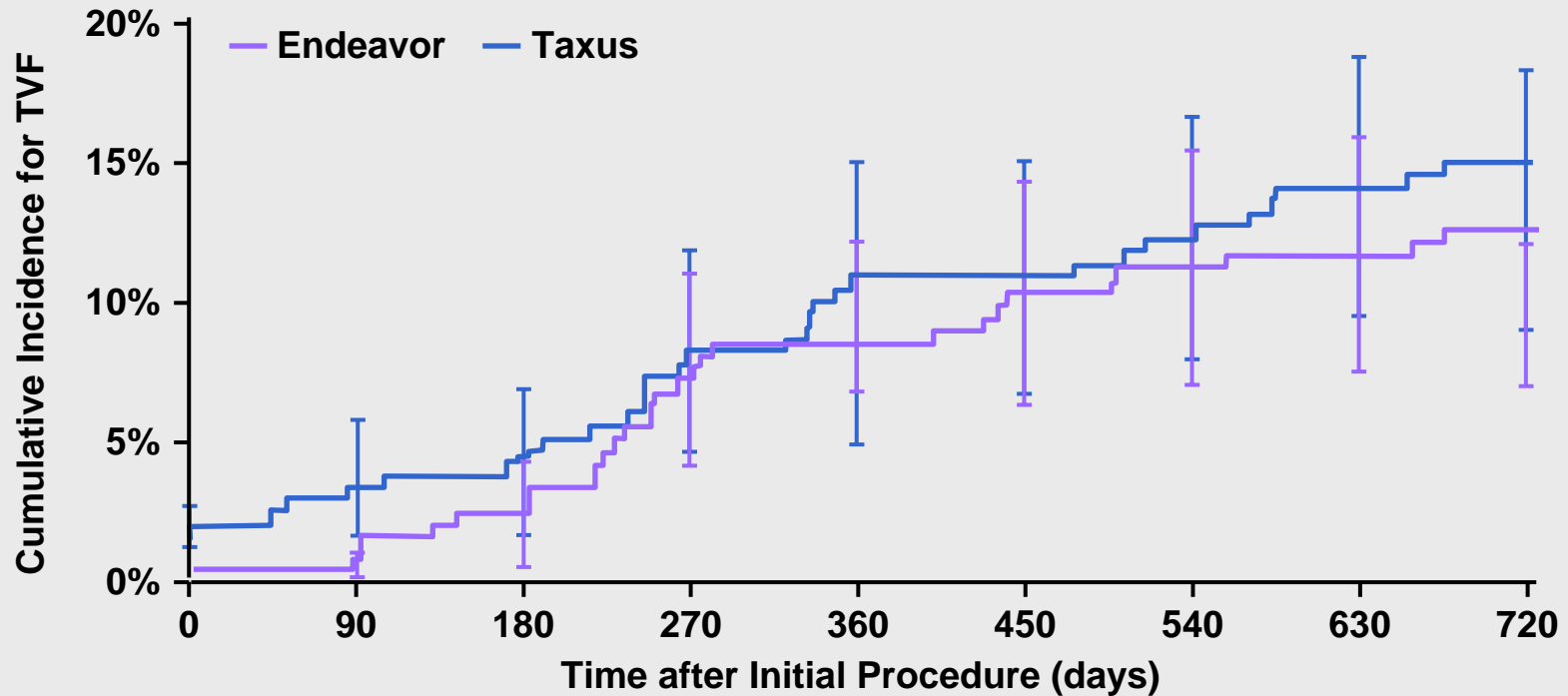
Endeavor IV

Clinical Outcomes at 2 Years: IDDM vs non-IDDM

| | IDDM | | | Non IDDM | | |
|------------------|--------------------|-----------------|----------------|---------------------|------------------|----------------|
| | Endeavor N = 76 | Taxus N = 58 | <i>P</i> value | Endeavor N = 155 | Taxus N = 166 | <i>P</i> value |
| Death (all) (%) | 1.3 (1) | 1.7 (1) | 1.00 | 1.3 (2) | 3.0 (5) | 0.45 |
| Cardiac Death | 1.3 (1) | 0 | 1.00 | 0.6 (1) | 2.4 (4) | 0.37 |
| MI (all) % | 1.3 (1) | 1.7 (1) | 1.00 | 0.6 (1) | 3.0 (5) | 0.22 |
| Q Wave | 0 | 0 | | 0 | .06 (1) | 1.00 |
| Non-Q Wave | 1.3 (1) | 1.7 (1) | 1.00 | 0.6 (1) | 2.4 (4) | 0.37 |
| TLR (%) | 7.9 (6) | 5.2 (3) | 0.73 | 5.8 (9) | 7.2 (12) | 0.68 |
| TVR (non-TL) (%) | 2.6 (2) | 5.2 (3) | 0.65 | 5.8 (9) | 7.2 (12) | 0.66 |
| MACE (%) | 7.9 (6) | 8.6 (5) | 1.00 | 10.3 (16) | 11.4 (19) | 0.86 |
| TVF (%) | 9.2 (7) | 12.1 (7) | 0.78 | 14.2 (22) | 16.3 (27) | 0.64 |

ENDEAVOR IV Diabetes

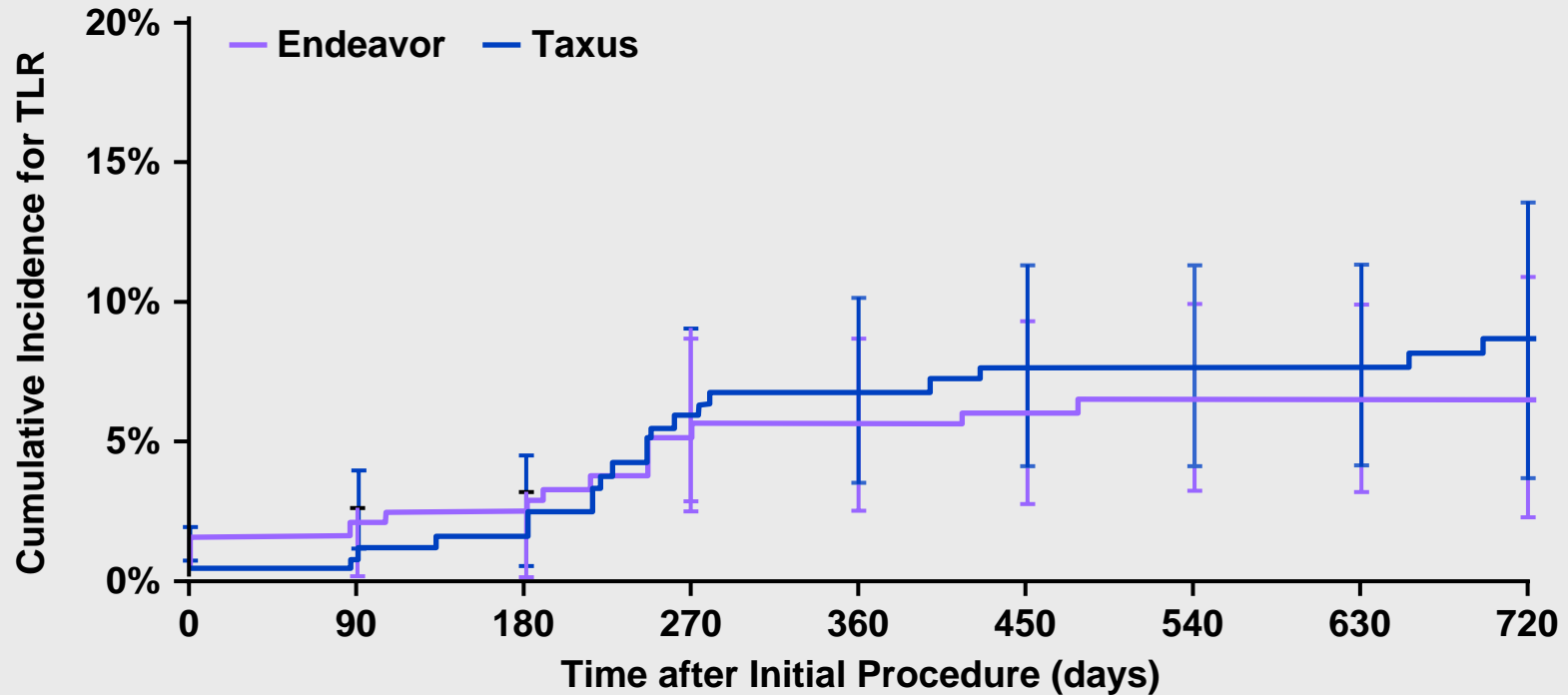
Cumulative Incidence of TVF to 24 months



| TVF | 0 | 180 | 270 | 360 | 720 |
|-----------------|-----|-----|-----|-----|-----|
| Endeavor | | | | | |
| # Entered | 241 | 233 | 229 | 215 | 195 |
| Taxus | | | | | |
| # Entered | 236 | 225 | 219 | 206 | 188 |

ENDEAVOR IV Diabetes

Cumulative Incidence of TLR to 24 months



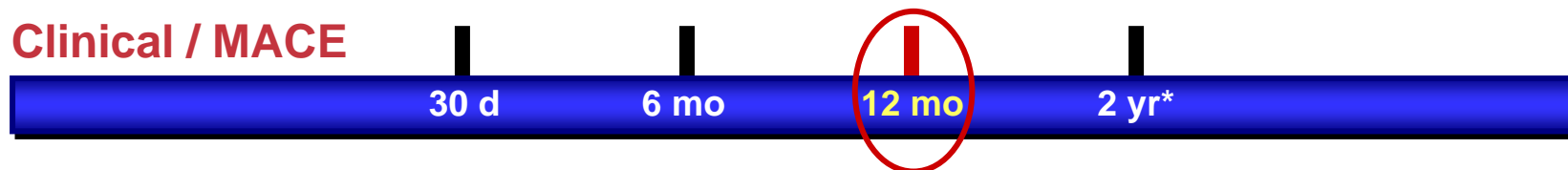
| TLR | 0 | 180 | 270 | 360 | 720 |
|-----------------|-----|-----|-----|-----|-----|
| Endeavor | | | | | |
| # Entered | 241 | 233 | 230 | 213 | 198 |
| Taxus | | | | | |
| # Entered | 236 | 227 | 221 | 203 | 194 |

E-Five Registry

Single and Multiple Coronary Artery Lesions
Stent Diameters: 2.25-4.0 mm
Stent Length: 8/9-30 mm

N = 8,000 patients
200 sites
Europe, Asia Pacific, Israel,
New Zealand, South America

Clinical / MACE



Primary Endpoint: MACE at 12 months

Secondary Endpoints: MACE at 30 days and 6 mo, Stent thrombosis,
procedure success rate; device success rate; lesion success rate

Drug Therapy: ASA and Clopidogrel/Ticlid >3 months

Zotarolimus Dose: 10 µg per mm stent length

E-Five

Baseline Characteristics

| | Non-DM N = 5593 | DM N = 2721 | P value | NIDDM N = 2039 | IDDM N = 682 | P value |
|------------------------------------|----------------------------|------------------------|--------------------|---------------------------|-------------------------|--------------------|
| Age (yrs) | 62.31 | 65.32 | <.001 | 64.90 | 66.57 | <.001 |
| Female – % | 19.8 | 30.7 | <.001 | 28.2 | 37.8 | <.001 |
| Unstable Angina – % | 33.1 | 35.6 | 0.02 | 35.6 | 35.8 | 0.93 |
| Prior MI – % | 31.8 | 33.0 | 0.27 | 32.0 | 35.8 | 0.07 |
| AMI (≤72 hours) – % | 14.8 | 11.9 | <.001 | 12.1 | 11.3 | 0.59 |
| ST AMI (≤72 hours) – % | 9.4 | 6.8 | <.001 | 6.8 | 7.0 | 0.79 |
| Prior PCI – % | 25.5 | 25.0 | 0.63 | 23.5 | 29.3 | 0.003 |
| Prior CABG – % | 7.3 | 8.1 | 0.20 | 7.2 | 10.7 | 0.005 |
| Current Smoker – % | 25.4 | 17.0 | <.001 | 18.0 | 13.9 | 0.01 |
| Hypertension – % | 63.7 | 78.6 | <.001 | 77.5 | 82.1 | 0.01 |
| Hypercholesterolemia – % | 60.8 | 67.7 | <.001 | 67.7 | 67.9 | 0.96 |
| Moderate Renal Impairment* – % | 3.6 | 7.0 | <.001 | 5.5 | 11.5 | <.001 |
| Severe Renal Impairment † – % | 1.0 | 3.3 | <.001 | 2.3 | 6.5 | <.001 |
| # of Lesions Treated with Endeavor | 1.23±0.51 | 1.27±0.56 | 0.002 | 1.27±0.57 | 1.26±0.51 | 0.45 |
| # of Endeavor Stents Implanted | 1.46±0.79 | 1.49±0.83 | 0.10 | 1.49±0.82 | 1.50±0.86 | 0.94 |

* serum creatinine 140 – 220 mol/l

† serum creatinine > 220 mol/l

E-Five

Clinical Outcomes at 1 Year: *DM vs non-DM*

| | DM n = 2563 | Non-DM n = 5269 | P value |
|---|----------------|--------------------|---------|
| Death (all) – % (n) | 4.1 (104) | 1.7 (87) | <.001 |
| Cardiac | 2.7 (70) | 1.2 (65) | <.001 |
| MI (all) – % (n) | 1.8 (47) | 1.5 (81) | 0.34 |
| Q Wave | 0.5 (12) | 0.4 (19) | 0.56 |
| Non Q wave | 1.4 (35) | 1.2 (63) | 0.52 |
| Death (cardiac) + MI (all) - % (n) | 4.1 (104) | 2.5 (134) | <.001 |
| ARC Stent Thrombosis (def/prob) – % (n) | 1.5 (39) | 0.9 (49) | 0.09 |
| 0-30 days | 1.1 (29) | 0.6 (30) | 0.07 |
| 31-365 days | 0.4 (11) | 0.4 (20) | 0.51 |
| TLR – % (n) | 5.3 (136) | 4.0 (213) | 0.01 |
| TVR (non-TL) – % (n) | 0.6 (15) | 0.7 (37) | 0.66 |
| TVR – % (n) | 5.7 (147) | 4.6 (240) | 0.03 |
| MACE – % (n) | 9.7 (248) | 6.4 (339) | <.001 |
| TVF – % (n) | 8.7 (224) | 6.5 (341) | <.001 |

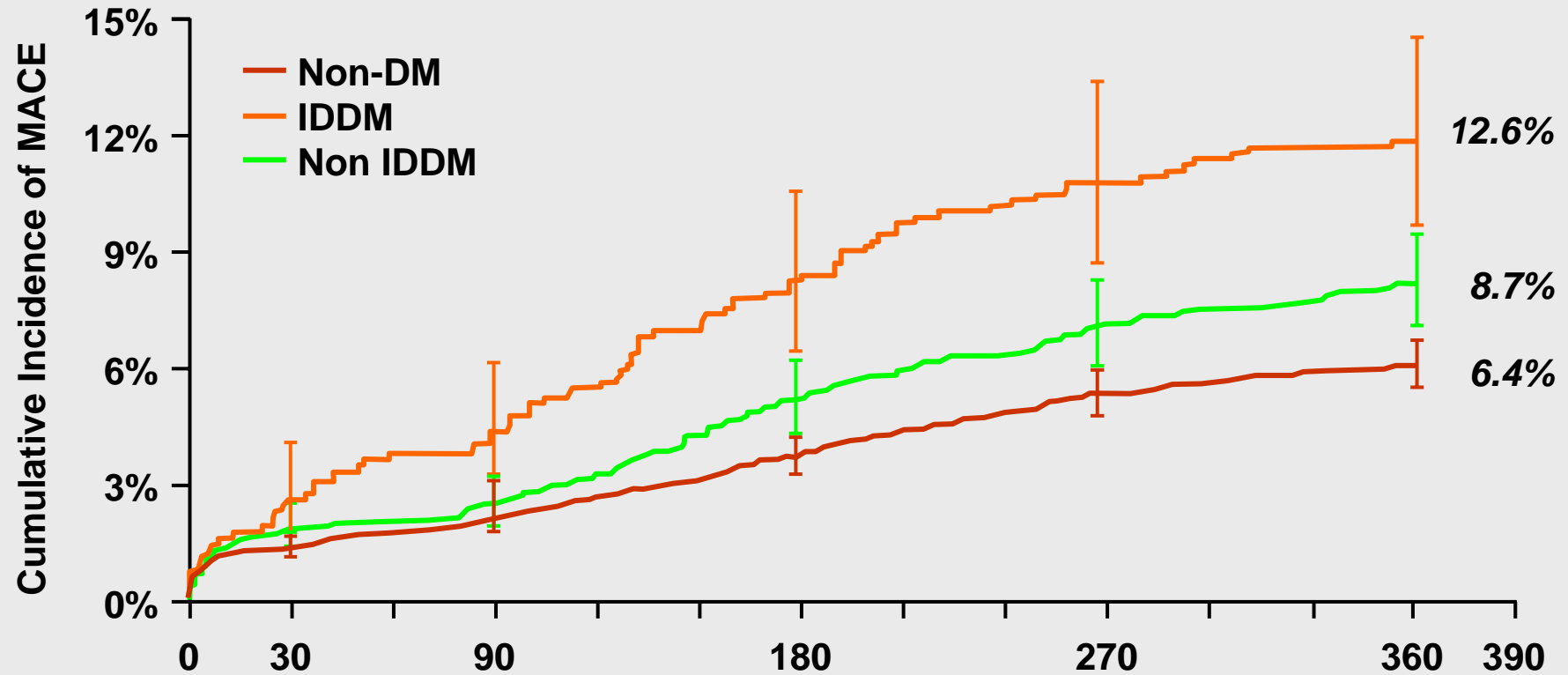
E-Five

Clinical Outcomes at 1 Year: *IDDM vs non-IDDM*

| | IDDM n = 644 | NIDDM n = 1919 | P value |
|---|-----------------|-------------------|---------|
| Death (all) – % (n) | 6.7 (43) | 3.2 (61) | <.001 |
| Cardiac | 4.5 (29) | 2.1 (41) | 0.003 |
| MI (all) – % (n) | 1.7 (11) | 1.9 (36) | 0.87 |
| Q Wave | 0.2 (1) | 0.6 (11) | 0.31 |
| Non Q wave | 1.6 (10) | 1.3 (25) | 0.70 |
| Death (cardiac) + MI (all) - % (n) | 5.3 (34) | 3.6 (70) | 0.08 |
| ARC Stent Thrombosis (def/prob) – % (n) | 2.2 (14) | 1.3 (25) | 0.14 |
| 0-30 days | 1.6 (10) | 1.0 (19) | 0.28 |
| 31-365 days | 0.8 (5) | 0.3 (6) | 0.16 |
| TLR – % (n) | 6.5 (42) | 4.9 (94) | 0.13 |
| TVR (non-TL) – % (n) | 0.5 (3) | 0.6 (12) | 0.77 |
| TVR – % (n) | 7.0 (45) | 5.3 (102) | 0.12 |
| MACE – % (n) | 12.6 (81) | 8.7 (167) | 0.005 |
| TVF – % (n) | 11.0 (71) | 8.0 (153) | 0.02 |

E-Five

Cumulative Incidence of MACE to 1 Year

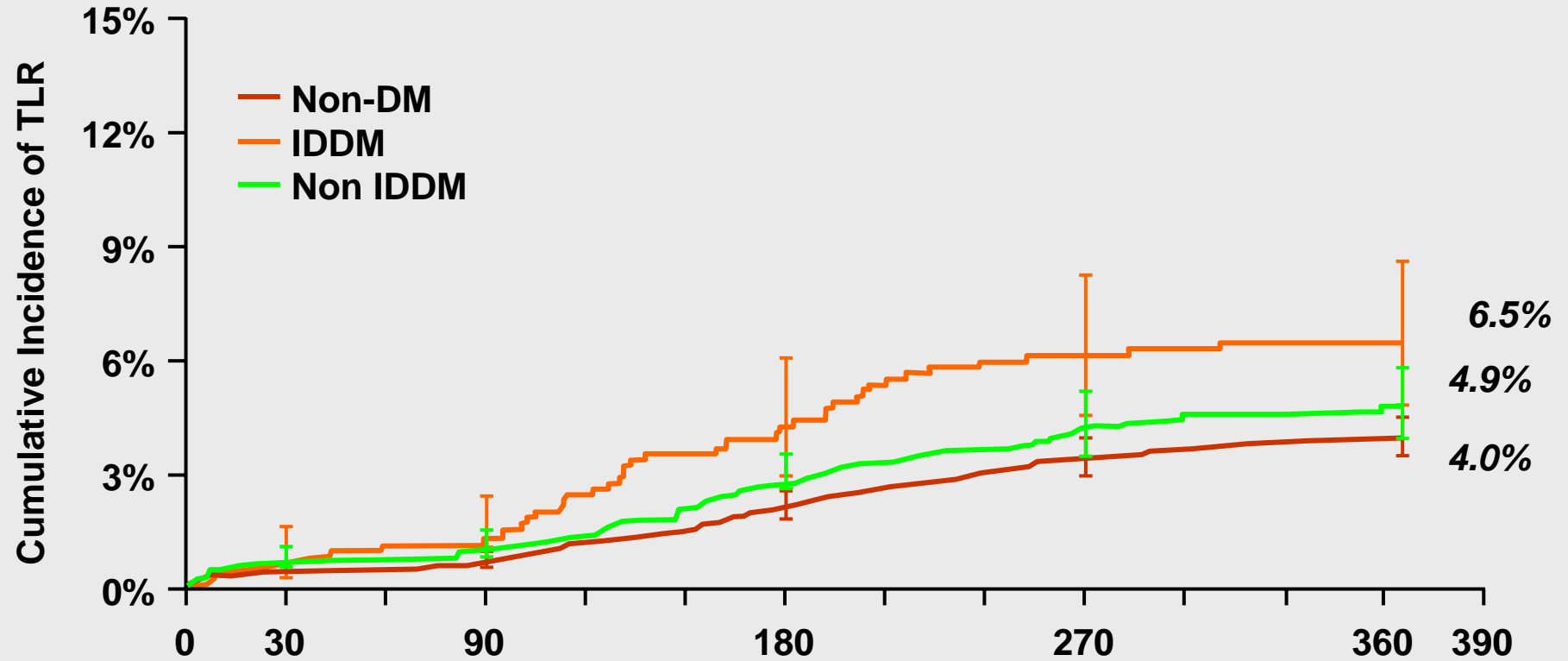


| MACE | 0 | 30 | 180 | 270 | 360 |
|----------|------|------|------|------|------|
| Non-DM | 5593 | 5552 | 5383 | 5271 | 5077 |
| IDDM | 682 | 677 | 641 | 612 | 577 |
| Non IDDM | 2039 | 2031 | 1957 | 1894 | 1871 |

Standard error was estimated by Peto formula

E-Five

Cumulative Incidence of TLR to 1 Year

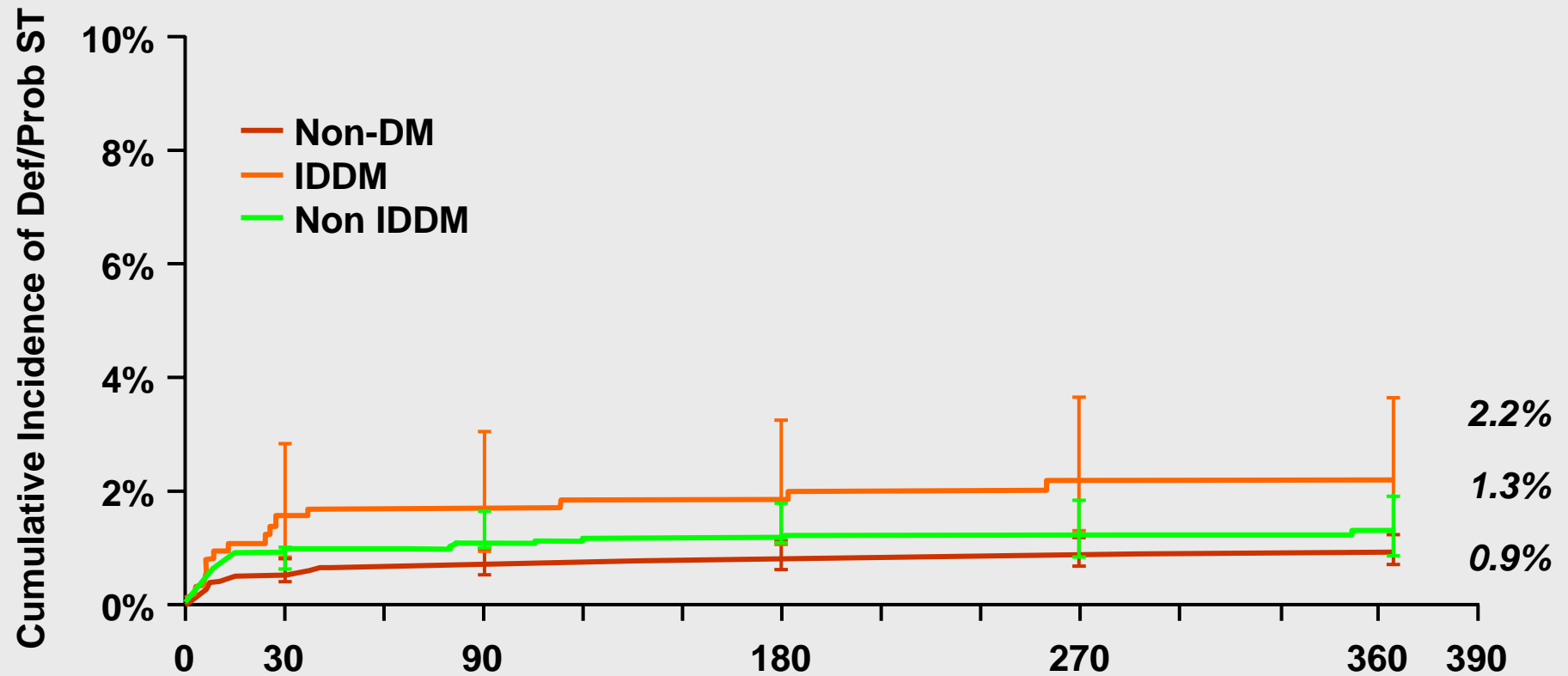


| TLR | 0 | 30 | 180 | 270 | 360 |
|----------|------|------|------|------|------|
| Non-DM | 5593 | 5583 | 5440 | 5328 | 5131 |
| IDDM | 682 | 680 | 652 | 624 | 582 |
| Non-IDDM | 2039 | 2036 | 1974 | 1925 | 1836 |

Standard error was estimated by Peto formula

E-Five

Cumulative Incidence of Stent Thrombosis to 1 Year

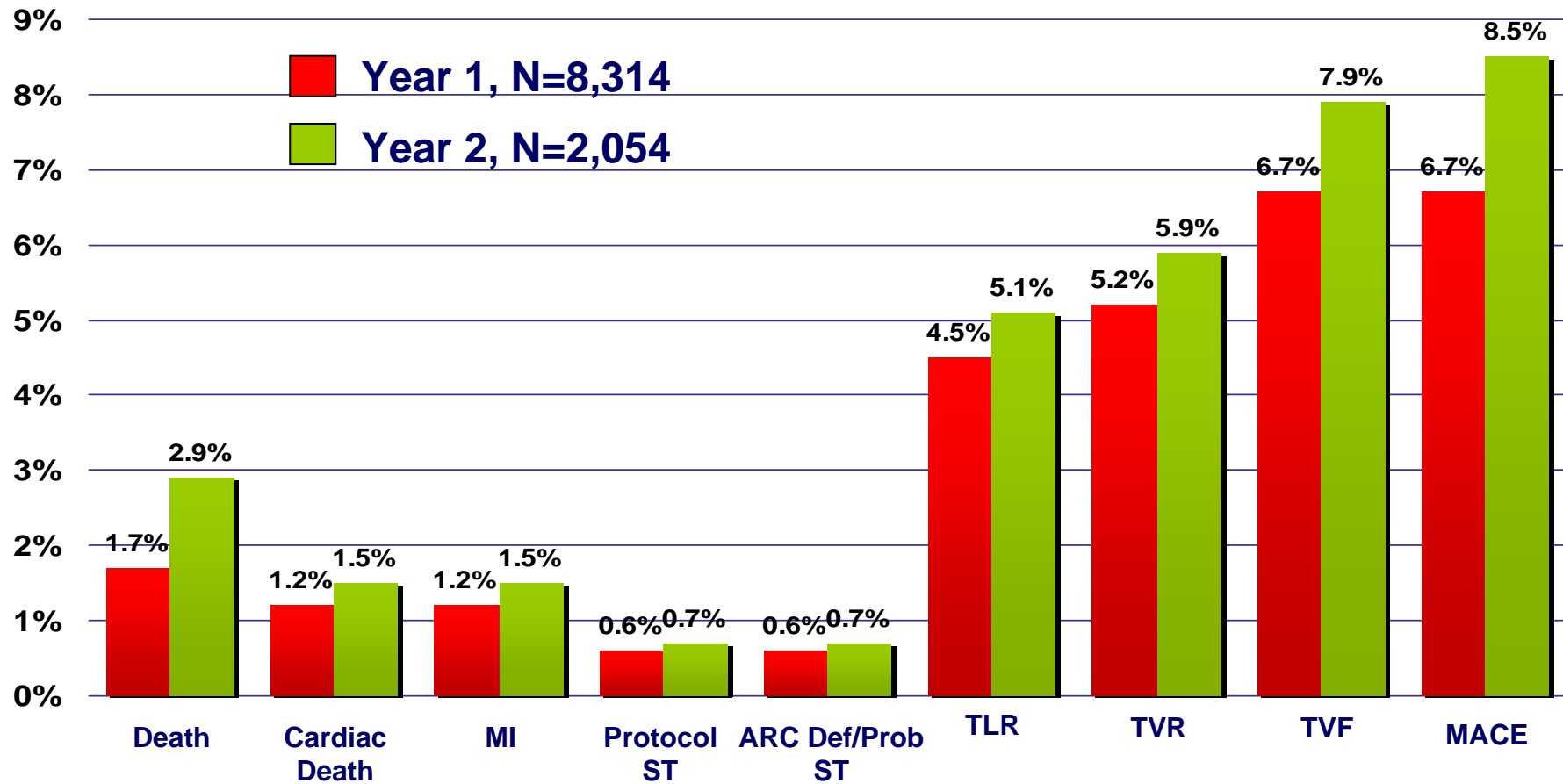


| ARD Def/Prob | 0 | 30 | 180 | 270 | 360 |
|--------------|------|------|------|------|------|
| Non-DM | 5593 | 5584 | 5451 | 5412 | 5284 |
| IDDM | 682 | 680 | 655 | 645 | 615 |
| Non IDDM | 2039 | 2036 | 1981 | 1964 | 1903 |

Standard error was estimated by Peto formula

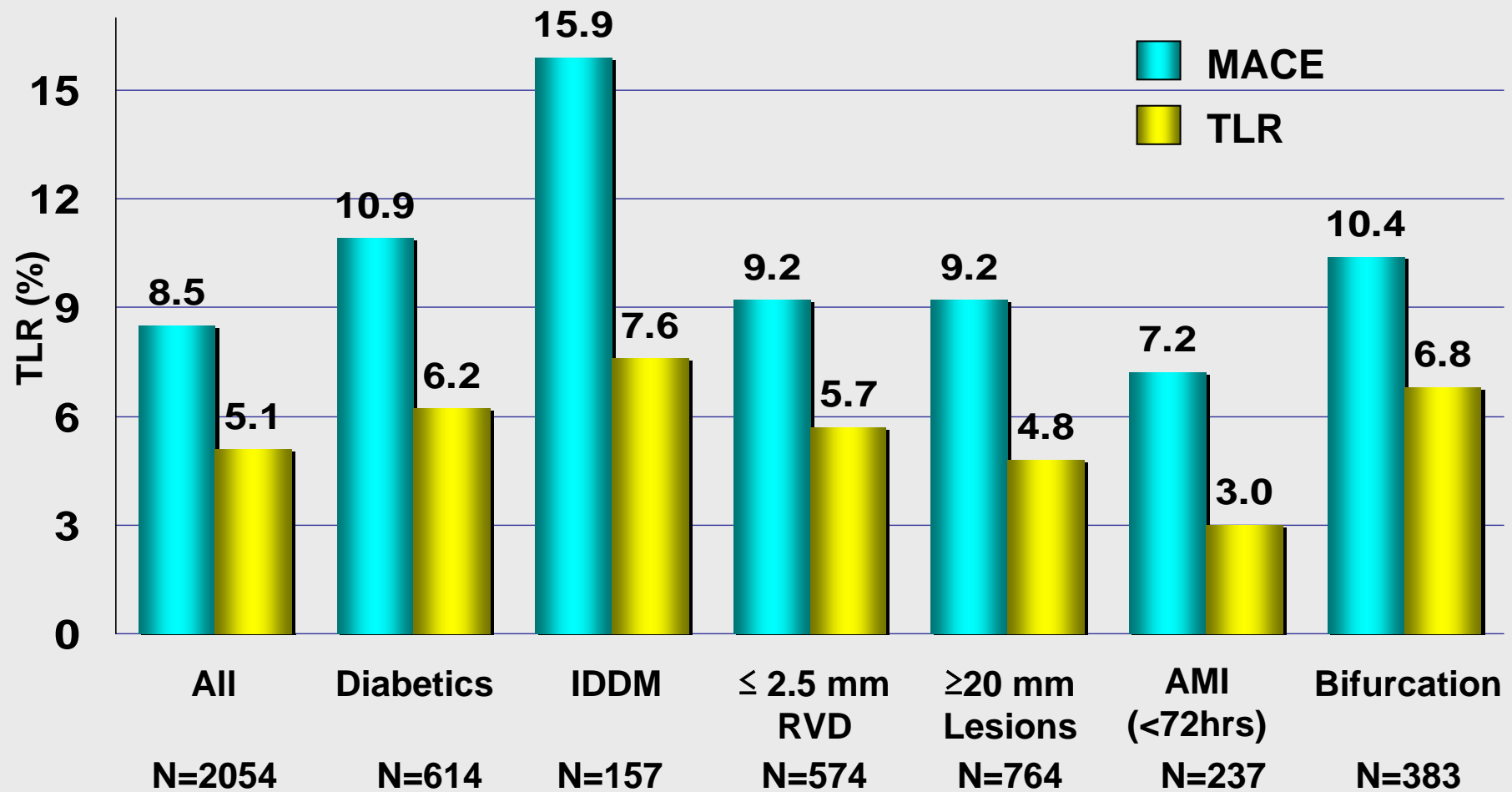
E-Five Registry

Adverse Events at 1 and 2 Years



E-Five

MACE and TLR Across Subgroups at 2 Years



Endeavor in Perspective: Diabetes

Summary

- › Consistent with other DES programs, clinical and angiographic outcomes among the diabetic population are generally less favorable compared with non-DM
- › *ENDEAVOR IV*: Late term (2 year) composite and individual outcomes similar between Endeavor and Taxus
- › *E-Five*
 - In broad, unselected patient population, 1-year Endeavor efficacy outcomes in diabetes (*TLR 5.3%*) similar to those observed in non-diabetic cohort
 - Compared with non-diabetic patients, differences in composite endpoints principally driven by increased cardiovascular death among diabetic patients
 - 2-year diabetic cohort outcomes awaited at EuroPCR 2009