Four-year clinical outcomes in the EVOLVE trial: A randomised evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting stent

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EVOLVE

Session: DES - Impact of biodegradable vs durable polymer on outcomes
Date: Tuesday, May 19th, 2015
Time: 13:40 – 13:47
Location: Room 343

Disclosures

- Honoraria for speaking/consultancy from Boston Scientific

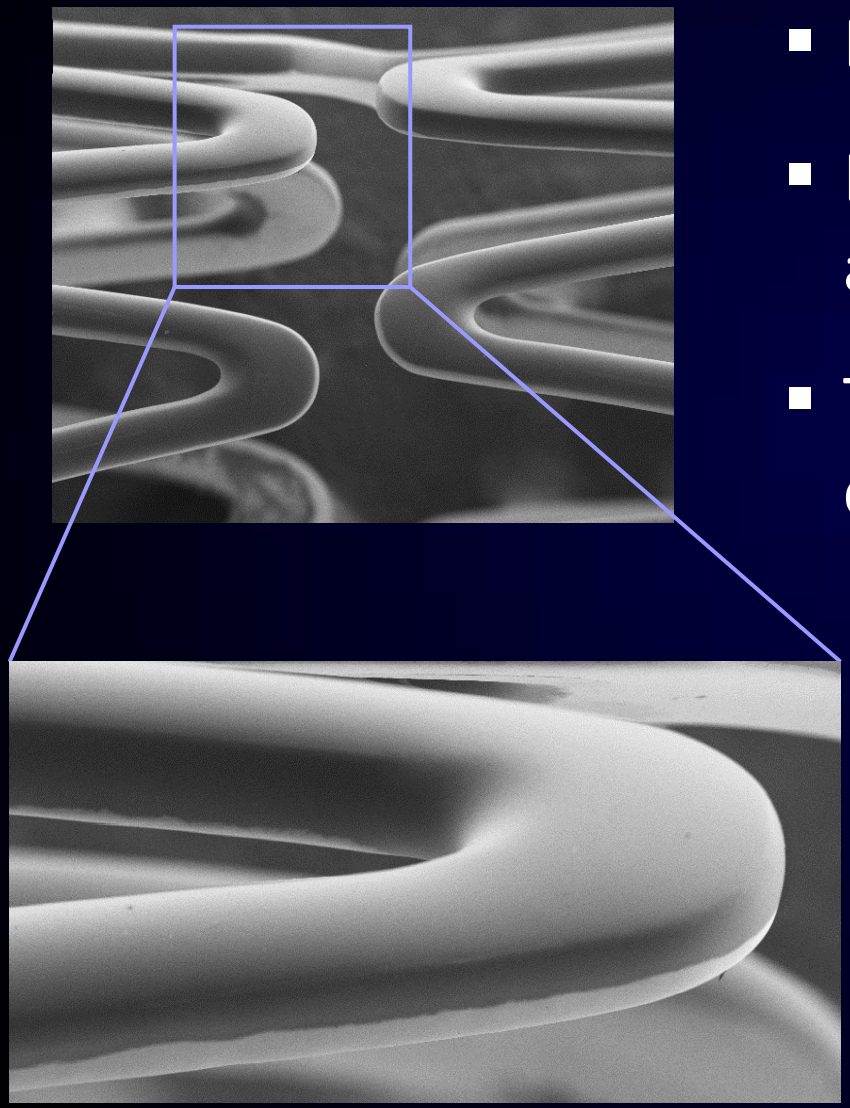
Introduction: Bioabsorbable polymer

- Durable polymer coatings on drug-eluting stents have been associated with chronic inflammation and impaired healing.
  - Potential advantages of bioabsorbable polymer stents:

Reduced polymer load & short-term polymer exposure may:

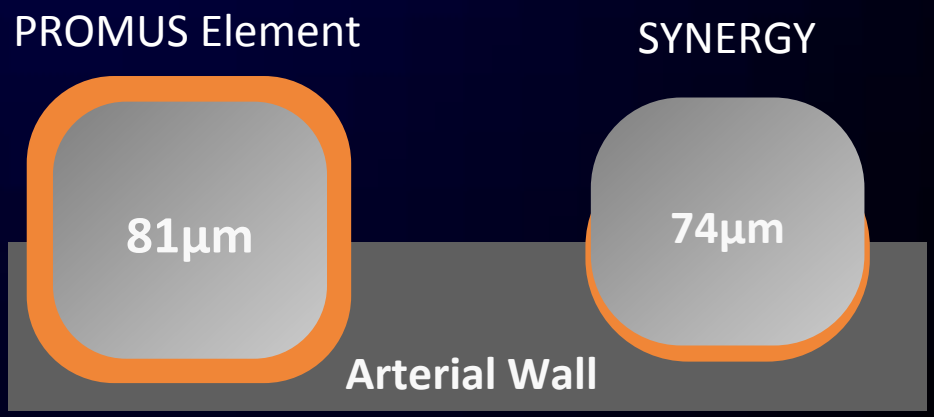
- Decrease risk of late events including ST and TLR
- Reduce required duration of DAPT and risk if interrupted

The SYNERGY Stent



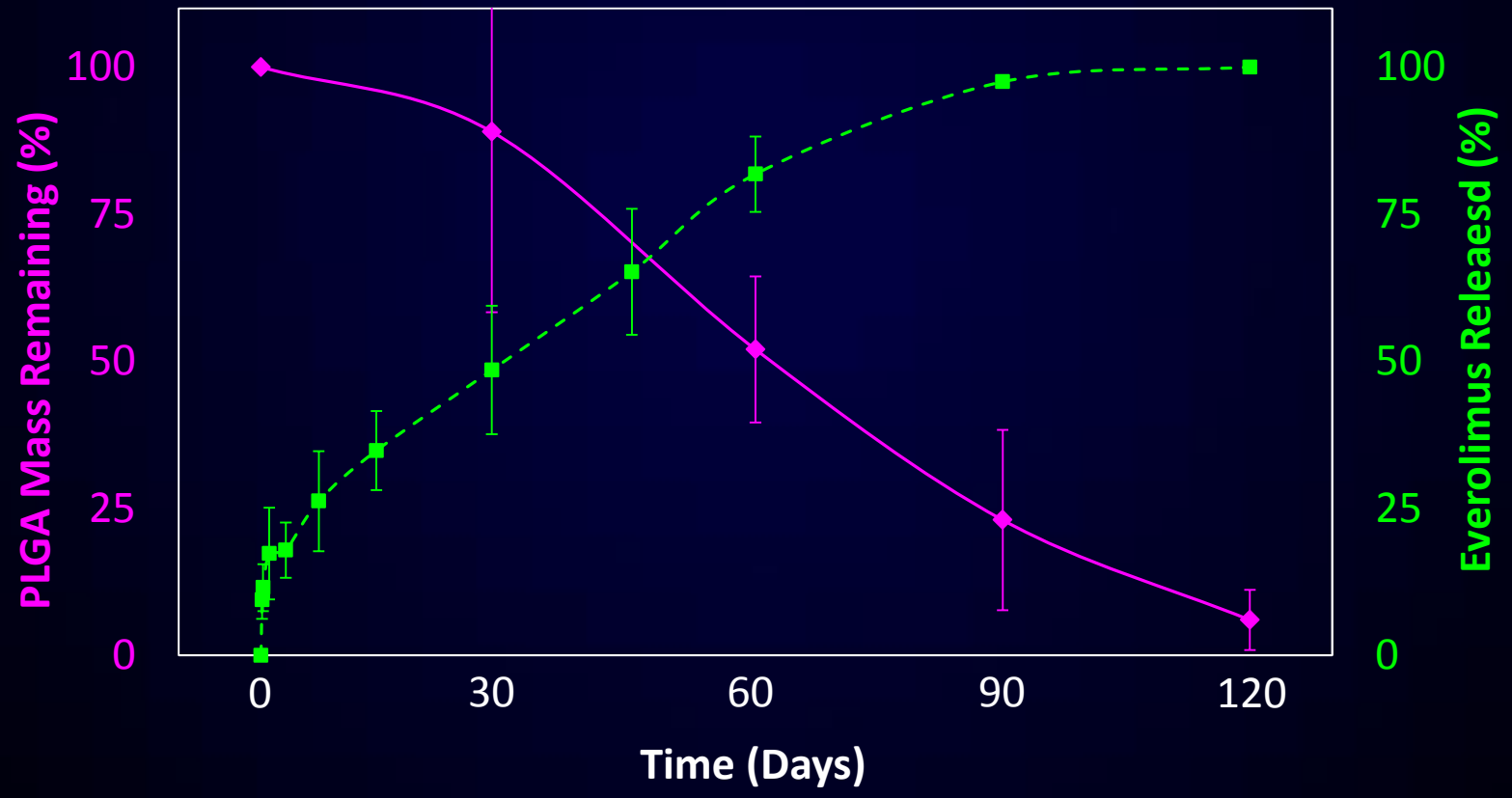
- Bioabsorbable polymer (PLGA)
- Everolimus applied only to the abluminal surface (rollcoat)
- Thin strut (74µm) platinum chromium stent

Stent Strut Cross Sections



SYNERGY Stent
Synchronous Drug Release & Polymer Absorption

Kinetics of Drug Release and Polymer Absorption in a Preclinical Porcine Model



Bennett and Dubois. *Biologics: Targets and Therapy.* 2013; 7: 149-159.

Trial Design and Methods

Patients with *de novo* native coronary lesions
≤ 28 mm in length, RVD ≥2.25 mm ≤3.5, %DS>50
(excluded LM disease, CTO, AMI or recent MI)

Randomized 1:1:1 at 29 sites
(Europe, Australia, New Zealand)

- PROMUS Element N=98
- SYNERGY N=94
- SYNERGY ½ Dose N=99

Single-blind, noninferiority design

Primary Clinical Endpoint: TLF (TV-CD, TV-MI, or TLR) at 30 days

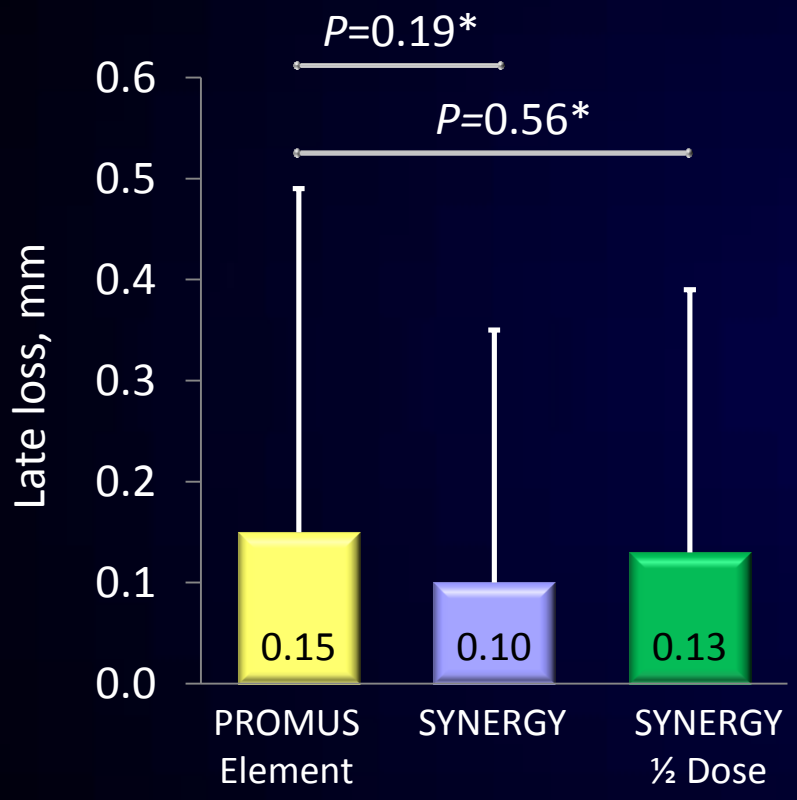
Primary Angiographic Endpoint: In-stent late loss at 6 months

Per protocol patients were treated with clopidogrel, ticlopidine or prasugrel for at least 6 months following the index procedure

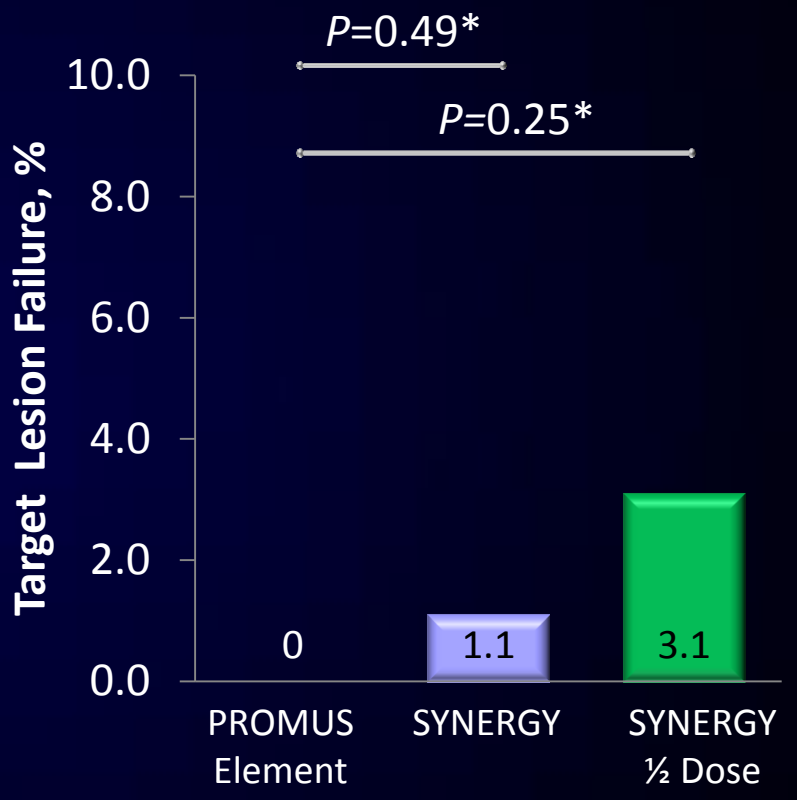
Meredith et al. *JACC* 2012; 59 (15): 1362-70

EVOLVE Primary Endpoint

Late Loss at 6 Months



TLF at 30 days

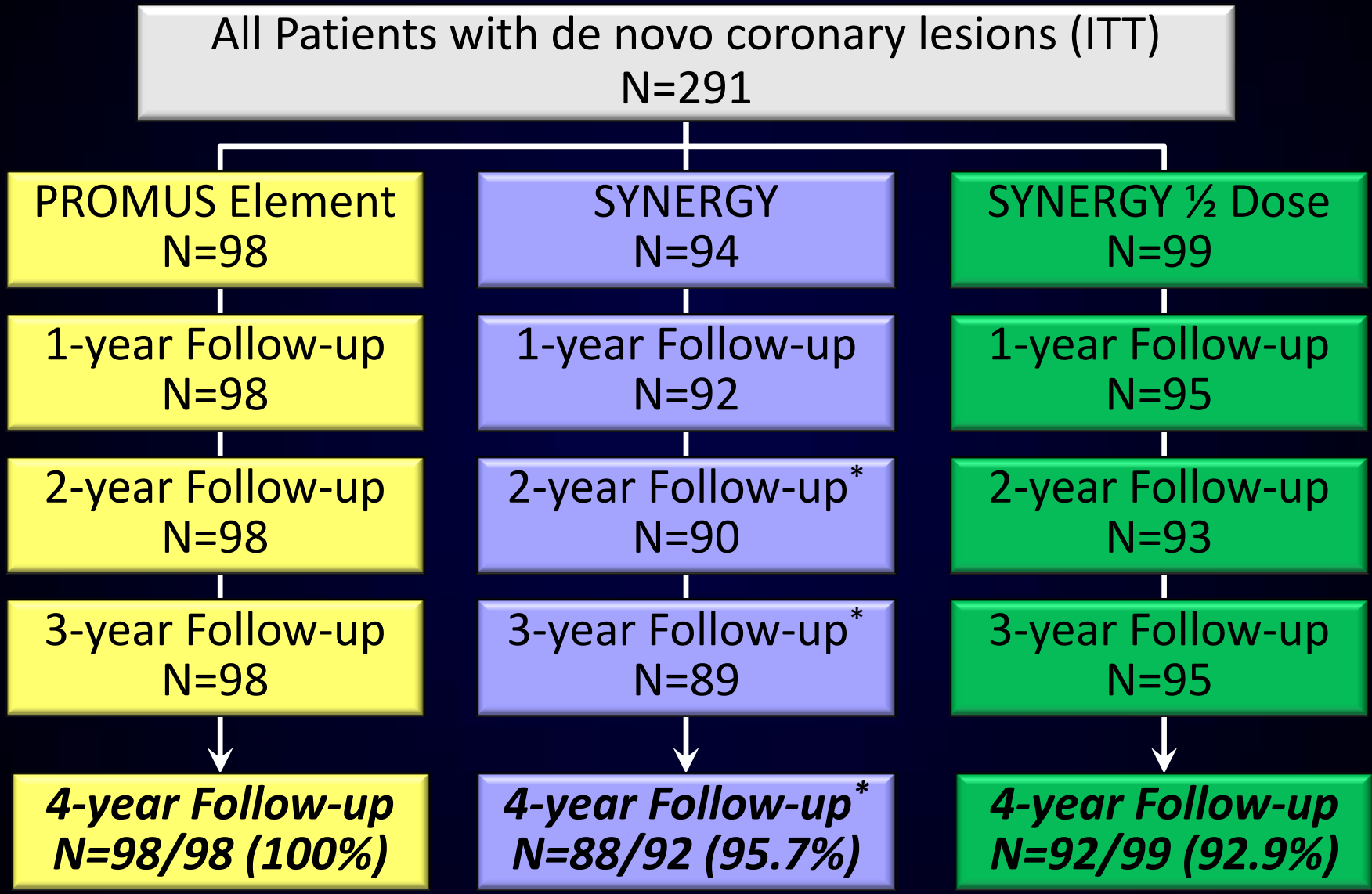


Noninferiority was proven *because the upper 95.2% confidence bound of the difference in 6-month late loss is <0.20 for both SYNERGY stents*

Meredith et al. *JACC* 2012; 59 (15): 1362-70

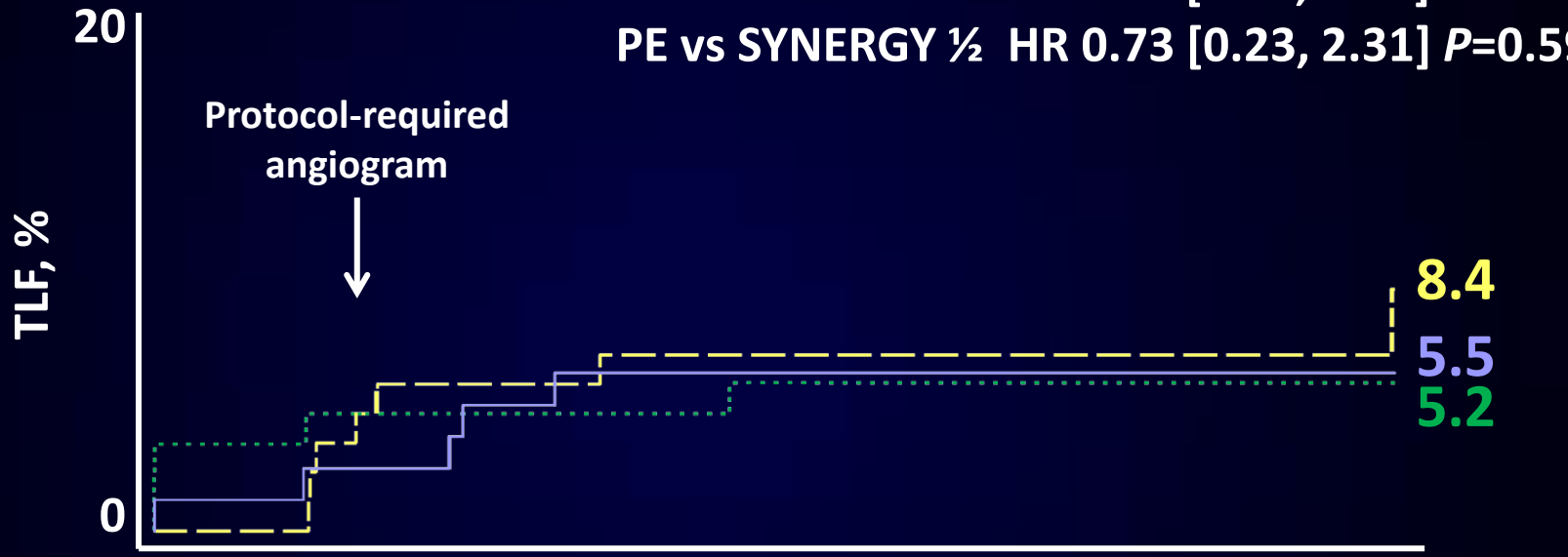
Intent-to-treat; Mean + Standard Deviation; **P* values for superiority comparison

Patient Disposition



*After 1-year follow-up, the prespecified safety analysis patient population, including only those patients treated with a study stent, was analysed. Two SYNERGY patients who did not receive the study stent were not included in the safety analysis.

Target Lesion Failure
4-year Follow-up

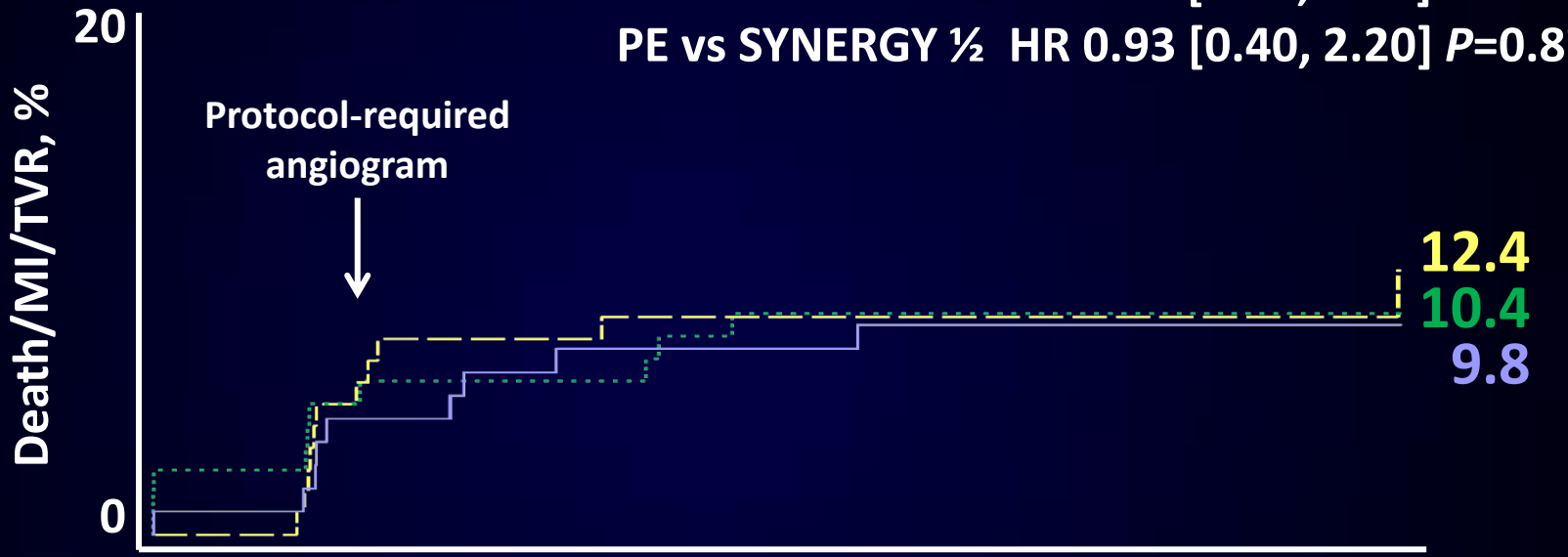


Numbers at risk	0	1	2	3	4
PE	98	98	93	92	64
SYNERGY	92	90	86	83	59
SYNERGY ½ Dose	99	92	90	87	62

Safety Population; KM Event Rate; log-rank *P* values

Death/MI/TVR
4-year Follow-up

PE vs SYNERGY HR 0.86 [0.36, 2.08] *P*=0.74
PE vs SYNERGY ½ HR 0.93 [0.40, 2.20] *P*=0.87

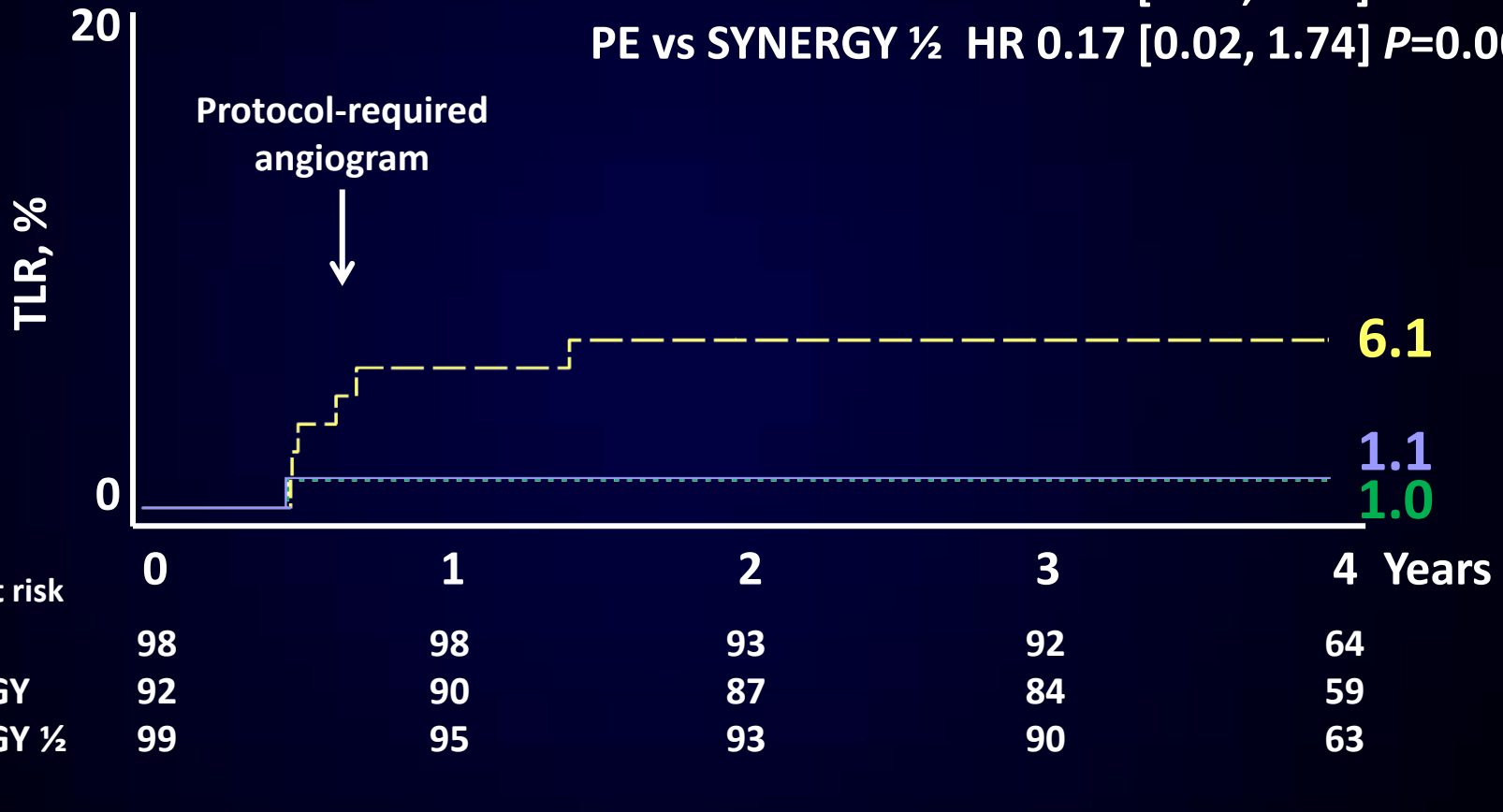


Numbers at risk	0	1	2	3	4
PE	98	96	89	88	62
SYNERGY	92	90	84	81	58
SYNERGY ½ Dose	99	92	88	84	60

Safety Population; KM Event Rate; log-rank *P* values

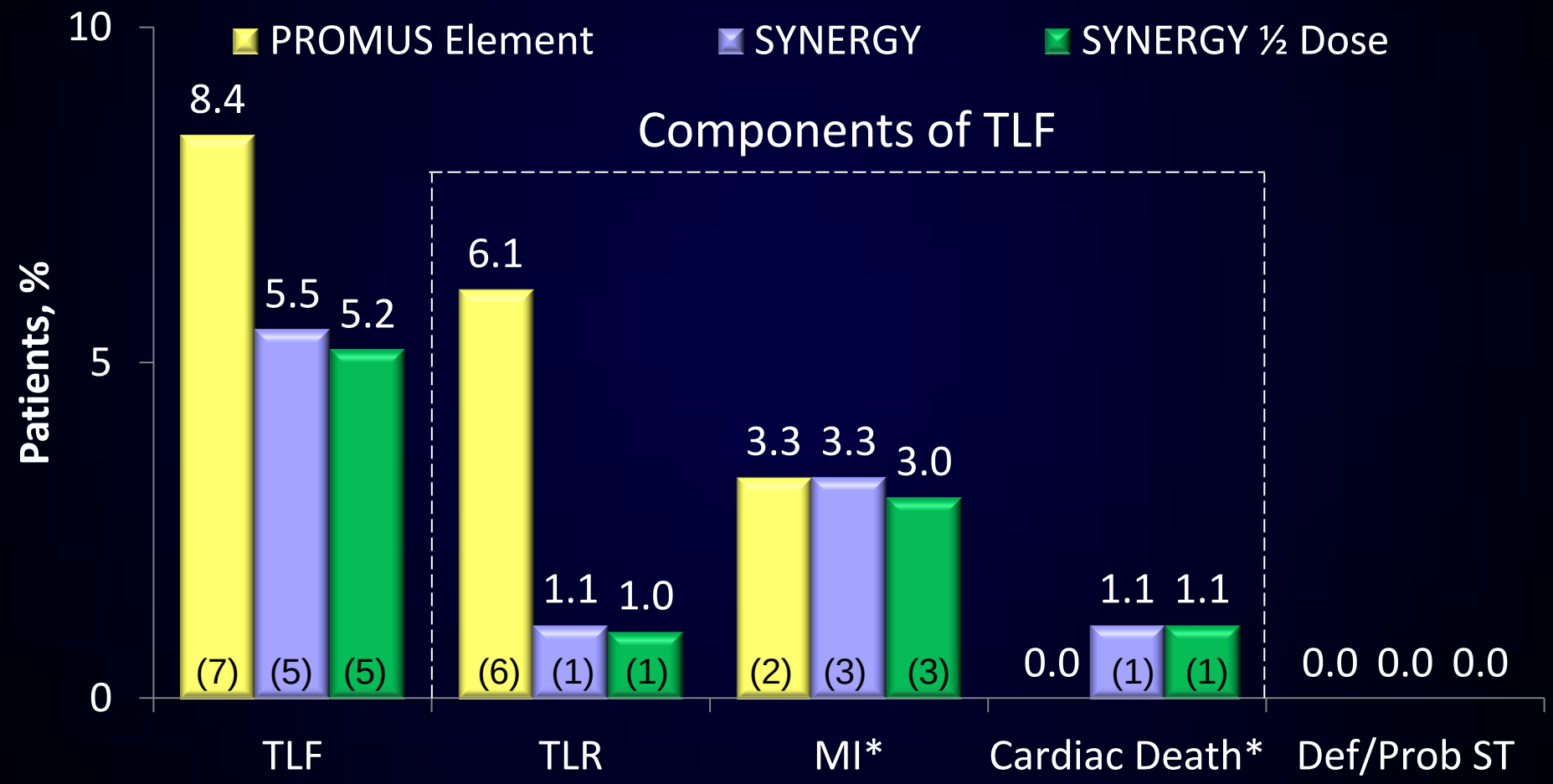
Target Lesion Revascularisation

4-year Follow-up



Safety Population; KM Event Rate; log-rank *P* values

4-Year Clinical Outcomes



Number of Events (N)

Safety Population; KM Event Rates; All *P* values are >0.05; *Target vessel-related

4-year Outcomes

	PROMUS Element n=98	SYNERGY n=92	*P* value	SYNERGY ½ Dose n=99	*P* value
All-cause death	0.0% (0)	5.5% (5)	0.02	4.2% (4)	0.04
- Cardiac	0.0% (0)	1.1% (1)	0.29	1.1% (1)	0.30
- Non-cardiac	0.0% (0)	4.4% (4)	0.04	3.2% (3)	0.08
Any MI	3.3% (2)	3.3% (3)	0.58	3.0% (3)	0.63
- Q-wave	0.0% (0)	0.0% (0)	Undef	0.0% (0)	Undef
- Non-Q-wave	3.3% (2)	3.3% (3)	0.58	3.0% (3)	0.63

Safety Population; KM Event Rates, *P* values are versus PROMUS Element (Fisher exact test)

Deaths in EVOLVE

Day (Post index procedure)	Cause
191	Multiple injuries sustained in motor bike accident
364	Broken ribs and pneumothorax after a fall leading to respiratory failure
373	Diffuse metastatic breast carcinoma
472	Death due to unknown cause (considered a cardiac death)
577	Right lung carcinoma
593	Right middle cerebral artery infarct
678	Death due to unknown cause (considered a cardiac death)
777	Gastric cancer
825	Pancreatic cancer

Conclusions and Significance

- At 4 years, no significant differences were found between groups for TLF, cardiac death or MI
  - Trend toward lower rates of TLR with SYNERGY vs PROMUS Element
  - No incidence of definite/probable stent thrombosis in any group at 4 years
- These results support the medium-term safety and efficacy of the novel abluminal bioabsorbable polymer SYNERGY everolimus-eluting stent for the treatment of patients with *de novo* coronary artery disease
- Additional research is needed to evaluate clinical event rates and the potential for dual antiplatelet therapy reduction with this novel stent