EXCITE ISR: Initial Results

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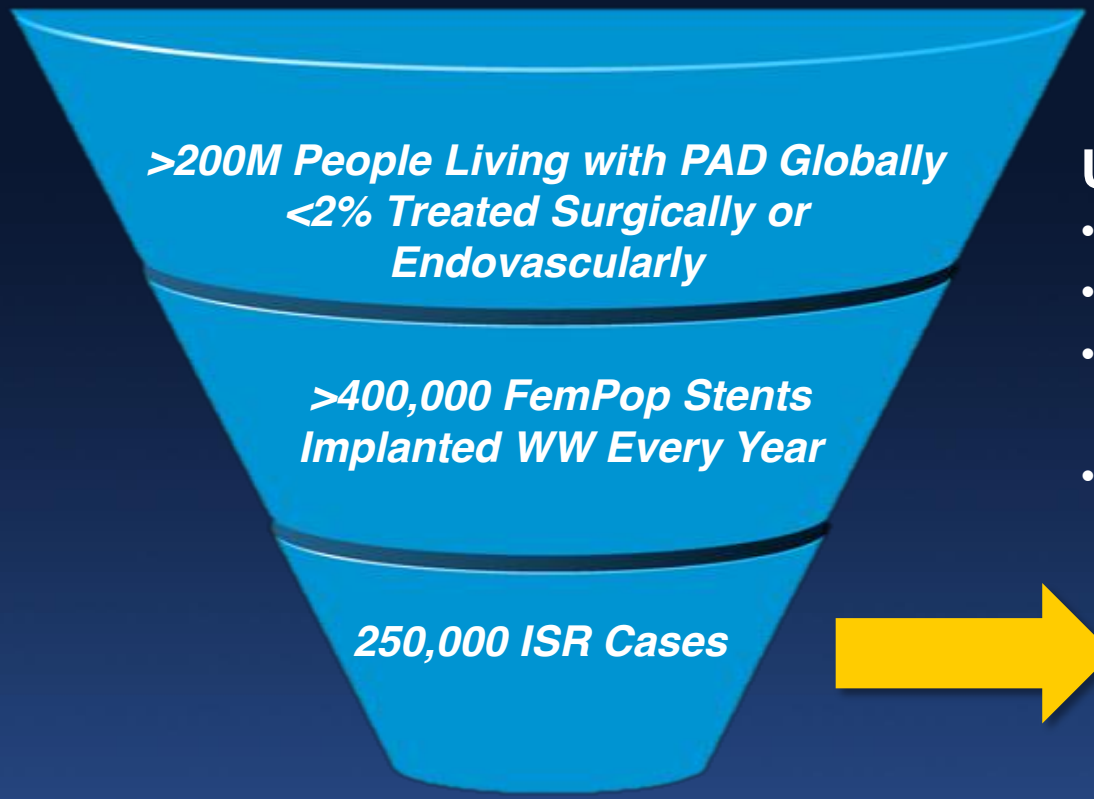
On behalf of the EXCITE ISR Investigators

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• N/A
• Consulting Fees/Honoraria	• Abbott Vascular, Boston Scientific, Covidien, Spectranetics
• Major Stock Shareholder/Equity	• Spectranetics
• Royalty Income	• N/A
• Ownership/Founder	• N/A
• Intellectual Property Rights	• N/A
• Other Financial Benefit	• N/A

GLOBAL PAD/ISR SCOPE OF PROBLEM



U.S. ISR Incidence

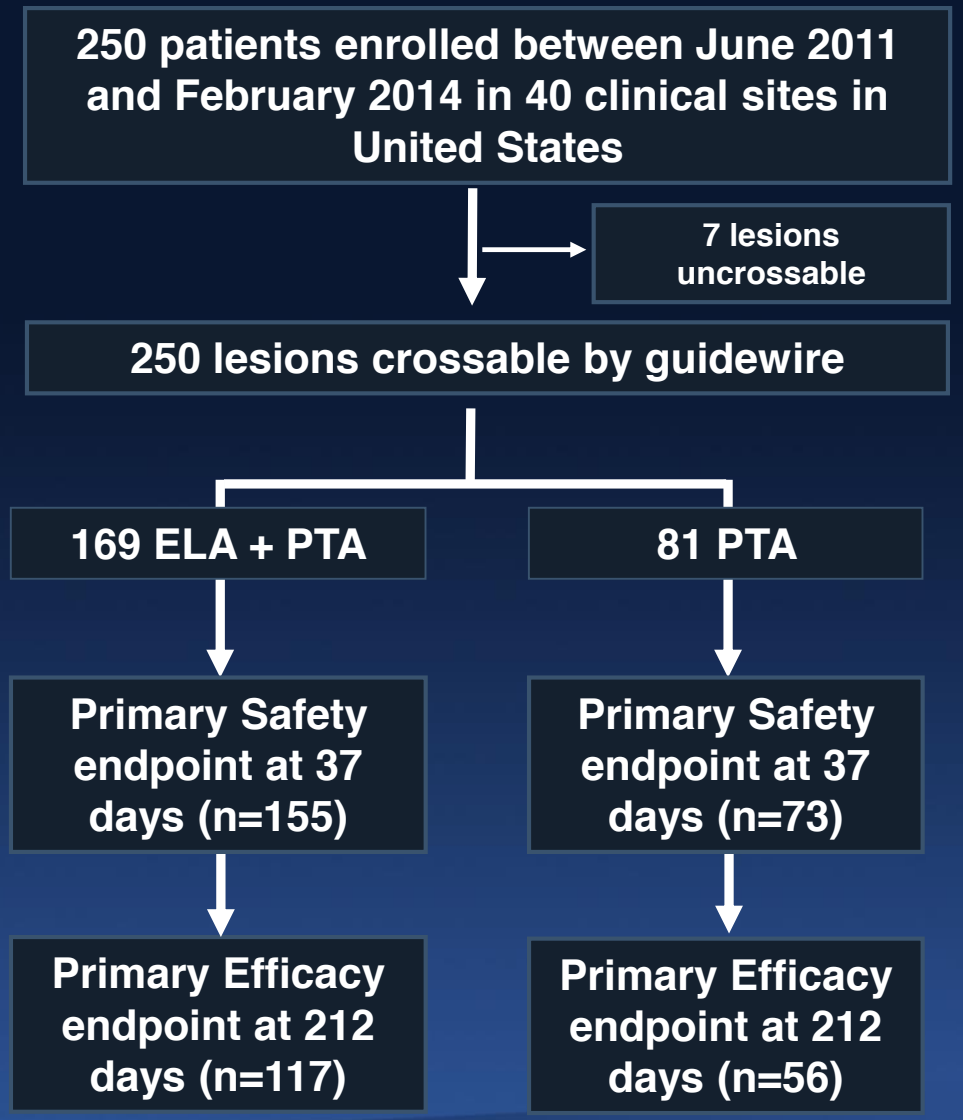
- >200,000 Stents / Year implanted
- Stent volume growing 6-7% annually
- 30-40% 1st time ISR Incidence within 2 years of implant
- ~65% of ISR will recur post-PTA treatment within 2 years

115,000 US ISR Cases

EXCITE ISR Trial

Design

- **DESIGN:** Prospective, randomized, multi-center clinical evaluation of excimer laser atherectomy (ELA)
- **OBJECTIVE:** To evaluate safety and efficacy of ELA with adjunctive PTA (ELA+PTA) versus PTA alone for treating femoropopliteal in-stent restenosis
- **PRINCIPAL INVESTIGATORS**
  Eric J Dippel, MD
  Craig Walker, MD



Study Sites

Co-Principal Investigators

Eric J Dippel, MD
Craig Walker, MD

Angiographic Core Lab

Synvacor, Springfield, IL

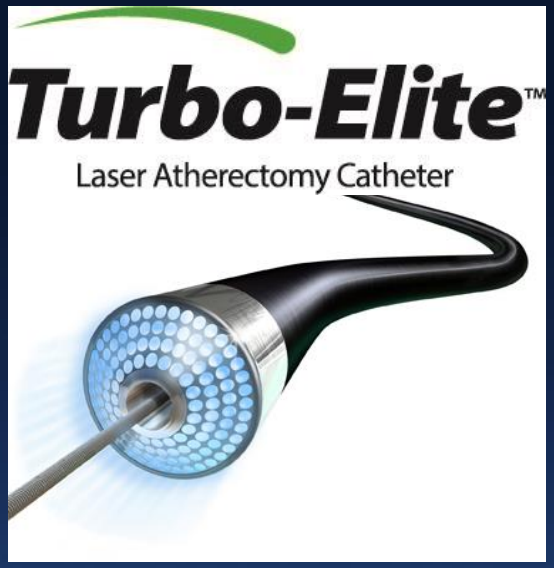
Vascular Ultrasound Core Lab

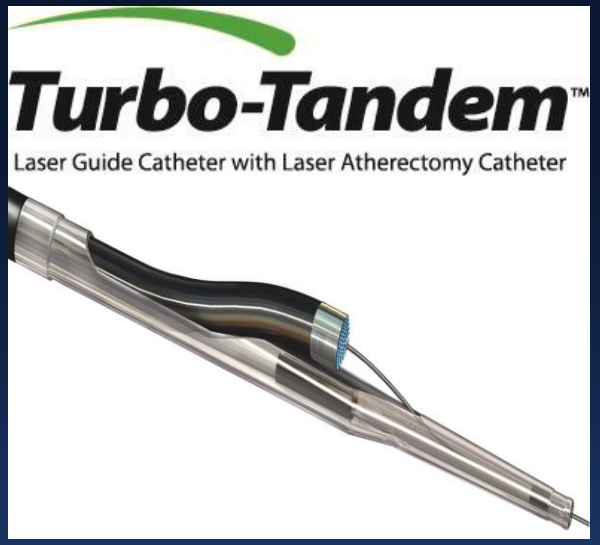
Vascore, Boston, MA

Investigative Sites

Dr. Babaev	New York University Hospital Center (New York NY)
Dr. Beasley	Mt. Sinai Medical Center Miami (Miami FL)
Dr. Bernardo	Washington Hospital Center (Washington D.C.)
Dr. Bunch	Thomas Hospital (Fairhope AL)
Dr. Carr	Cardiovascular Associates of East Texas (Tyler TX)
Dr. Chamberlin	Alexian Brothers Medical Center (Elk Grove Village IL)
Dr. Colleran	St. Vincent Heart Clinic Arkansas (Little Rock AR)
Dr. Colon-Hernandez	Transcatheter Medical Inc. (Rio Piedras Puerto Rico)
Dr. Das	Presbyterian (Dallas TX)
Dr. Eaves	Cardiovascular Consultants (Bossier LA)
Dr. Falcone	Providence Health Center (Waco TX)
Dr. Foster	St. Vincent's East (Birmingham AL)
Dr. Gallino	Montgomery General Hospital (Olney MD)
Dr. Goldstein	St. John's Hospital (Springfield IL)
Dr. Gupta	Aurora Cardiovascular Services (Milwaukee WI)
Dr. Jacobs	St. Louis University Hospital (St. Louis MO)
Dr. Kollmeyer	Methodist Hospital Center (Dallas TX)
Dr. Kovach	Deborah Heart & Lung Center (Browns Mills NJ)
Dr. Laird	UC Davis Medical Center (Sacramento CA)
Dr. Lee	Cardiovascular Research of North Florida LLC (Gainsville FL)
Dr. Lookstein	Mount Sinai Medical Center (New York NY)
Dr. Makam	Cardiovascular Research of Northwest Indiana, (Munster IN)
Dr. Mena-Hurtado	Yale Medical Group (New Haven CT)
Dr. Metzger	Wellmont Holston Valley Medical Center (Kingsport TN)
Dr. Mustapha	Metro Health (Wyoming MI)
Dr. Nelson	Wheaton Franciscan Healthcare (Milwaukee WI)
Dr. Panneton	Sentara Careplex Hospital (Norfolk VA)
Dr. Pastor	Research Physician's Network Alliance (Hollywood FL)
Dr. Patlola	Cardiovascular Institute of the South (Lafayette LA)
Dr. Pratsos	Bryn Mawr Hospital (Bryn Mawr PA)
Dr. Raja	El Paso Cardiac & Endovascular Center (El Paso TX)
Dr. Rossbach	Mission Research Institute (New Braunfels TX)
Dr. Shimshak	Wheaton Franciscan Healthcare - All Saints (Racine WI)
Dr. Soukas	Miriam Hospital (Providence RI)
Dr. Stewart	Arkansas Heart Hospital (Little Rock AR)
Dr. Veerina	Cardiovascular Institute of the South Opelousas(Opelousas LA)
Dr. Weatherford	Coastal Surgery Specialists (Wilmington NC)
Dr. Wheatley	Arizona Heart (Phoenix AZ)
Dr. Wilkins	Hattiesburg Clinic (Hattiesburg MS)
Dr. Zughaib	St. John Providence Hospital (Southfield MI)

Excimer Laser Atherectomy Catheters





- *Turbo Elite → Pilot channel creation*
- *Turbo Tandem → Biased laser catheter for large lumen ablation*

Primary Endpoints

Primary Safety Endpoint

- Major Adverse Events through 30 days:
  - Death
  - Unplanned Major Amputation
  - Target Lesion Revascularization (TLR)

Primary Efficacy Endpoint

- Freedom from clinically driven TLR at 6 months
  - DUS binary restenosis
  - Return of clinical symptoms
  - Deteriorated ABI or Rutherford Classification

Sample Size Determination

- **Efficacy**
  - 80% power one-sided $\alpha = 0.025$ requires 285 patients assuming 70% vs 53%, ELA+PTA vs PTA alone.
- **Safety**
  - 80% power one-sided $\alpha = 0.025$ requires 267 patients with 30 day follow up assuming 91% vs 80%, ELA+PTA vs PTA alone.
- **Prospective Bayesian hierarchical modeling at 200, 250 and 300 patients enrolled with pre-determined alpha spend.**

"Real World" Patients

- *No lesion length limit*
- *Multiple stents allowed*
- *Common stent fractures (Grades 1-3)*
- *Popliteal stents included*

- **Key Inclusion Criteria**
  - ISR lesion ≥ 4 cm
  - Rutherford classification 1-4
  - RVD ≥ 5.0 mm and ≤ 7.0 mm
  - ≥ 1 patent tibial artery
- **Key Exclusion Criteria**
  - Target lesion extends >3 cm beyond stent margin
  - Untreated inflow lesion
  - Grade 4 or 5 stent fracture
- **Follow-up**
  - Discharge, 30 days, 6 months and 1 year post-procedure

Patient Demographics

	ELA + PTA (N=169)	PTA Alone (N=81)	P- Value
Age (mean)	68.5	67.8	0.60
Male	62.7 %	61.7 %	0.89
Hypertension	95.8 %	93.8 %	0.53
Hyperlipidemia	96.4 %	95.0 %	0.73
Diabetes Mellitus	47.0 %	47.5 %	1.00
CAD	64.3 %	68.8 %	0.57
Previous ISR	32.7 %	30.0%	0.77
Smoking History	85%	91.3%	0.23
Rutherford Class			0.54
1	3.0%	3.7%	
2	18.9%	14.8%	
3	62.1%	69.1%	
4	15.4%	11.1%	
5	0.6%	0.0%	
6	0.0%	0.6%	

Baseline Lesion Characteristics

Angiographic Core Lab Assessment

	ELA + PTA (N=169)	PTA Alone (N=81)	P- Value
Mean Lesion Length (cm)	19.6	19.3	0.85
Diameter Stenosis (%)	81.7%	83.5%	0.42
Popliteal Lesion	21.3%	23.4%	0.93
Total Occlusion	30.5%	36.8%	0.37
Calcium (Mod/Sev)	27.1%	9.1%	0.002
Stent Fracture			0.16
0	85.8%	95.8%	
1	5.0%	0.0%	
2	6.4%	4.2%	
3	2.1%	0.0%	
4	0.0%	0.0%	
5	0.7%	0.0%	

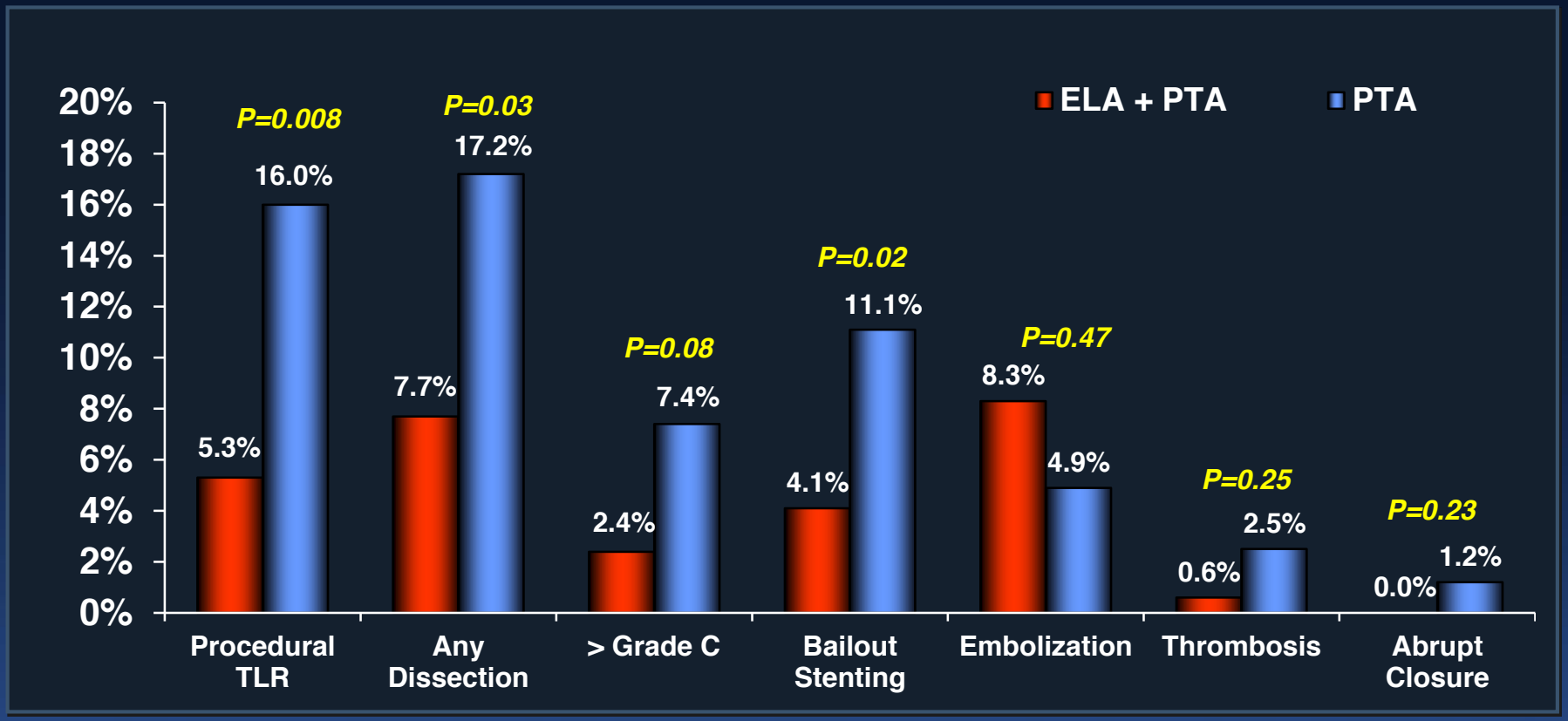
- ***20% of lesions > 30 cm***

Procedural Success

	ELA+PTA n = 169	PTA n = 81	P Value
Turbo Elite use	79.9		na
Distal protection	40.2	30.9	0.16
% Diameter Stenosis	23.9±9.3	25.1±10.9	0.24
Residual Stenosis >30%	4.7	13.6	0.02
Procedural Success	93.5	82.7	0.03

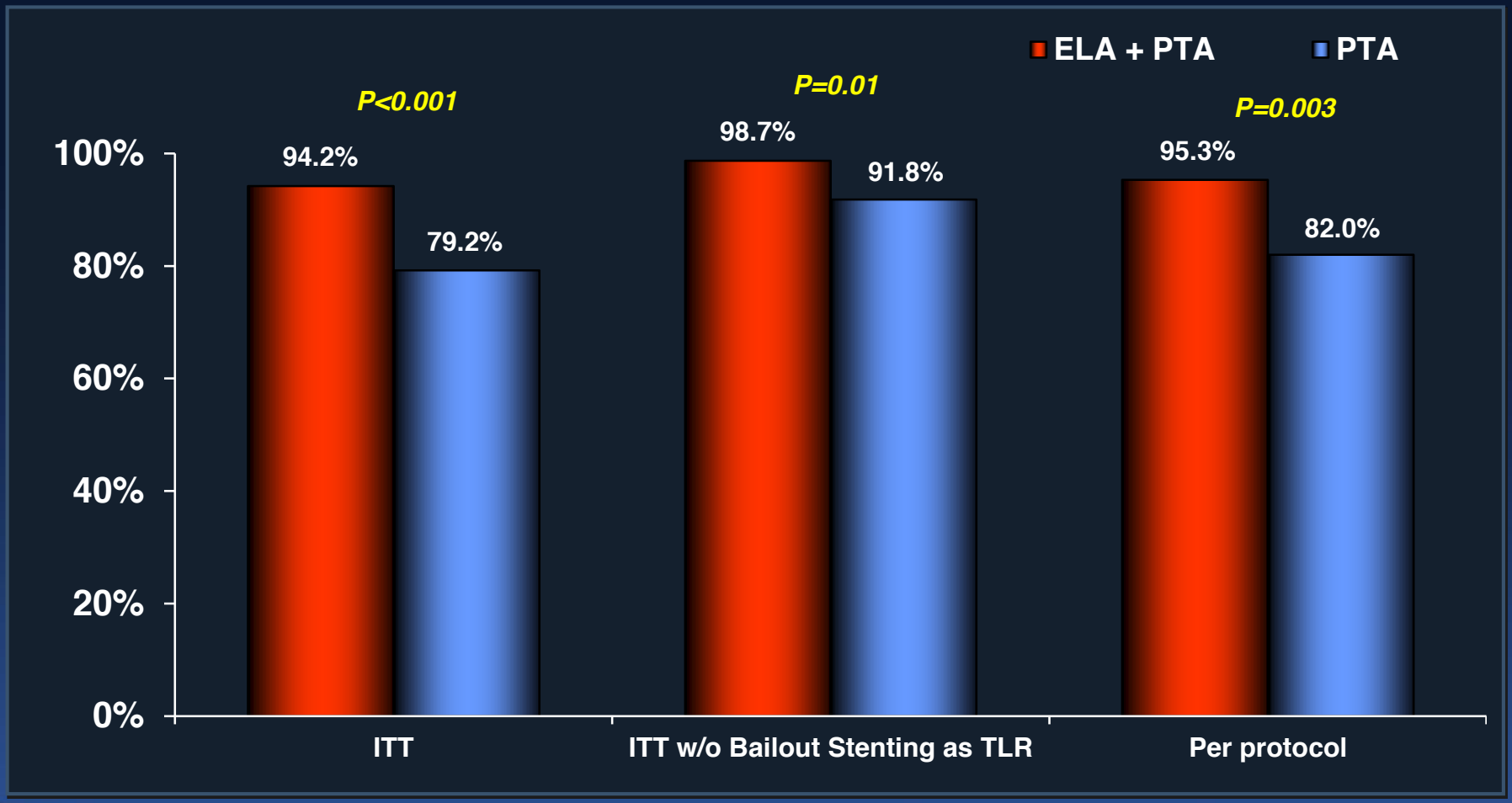
Procedural Complications

All events adjudicated by CEC



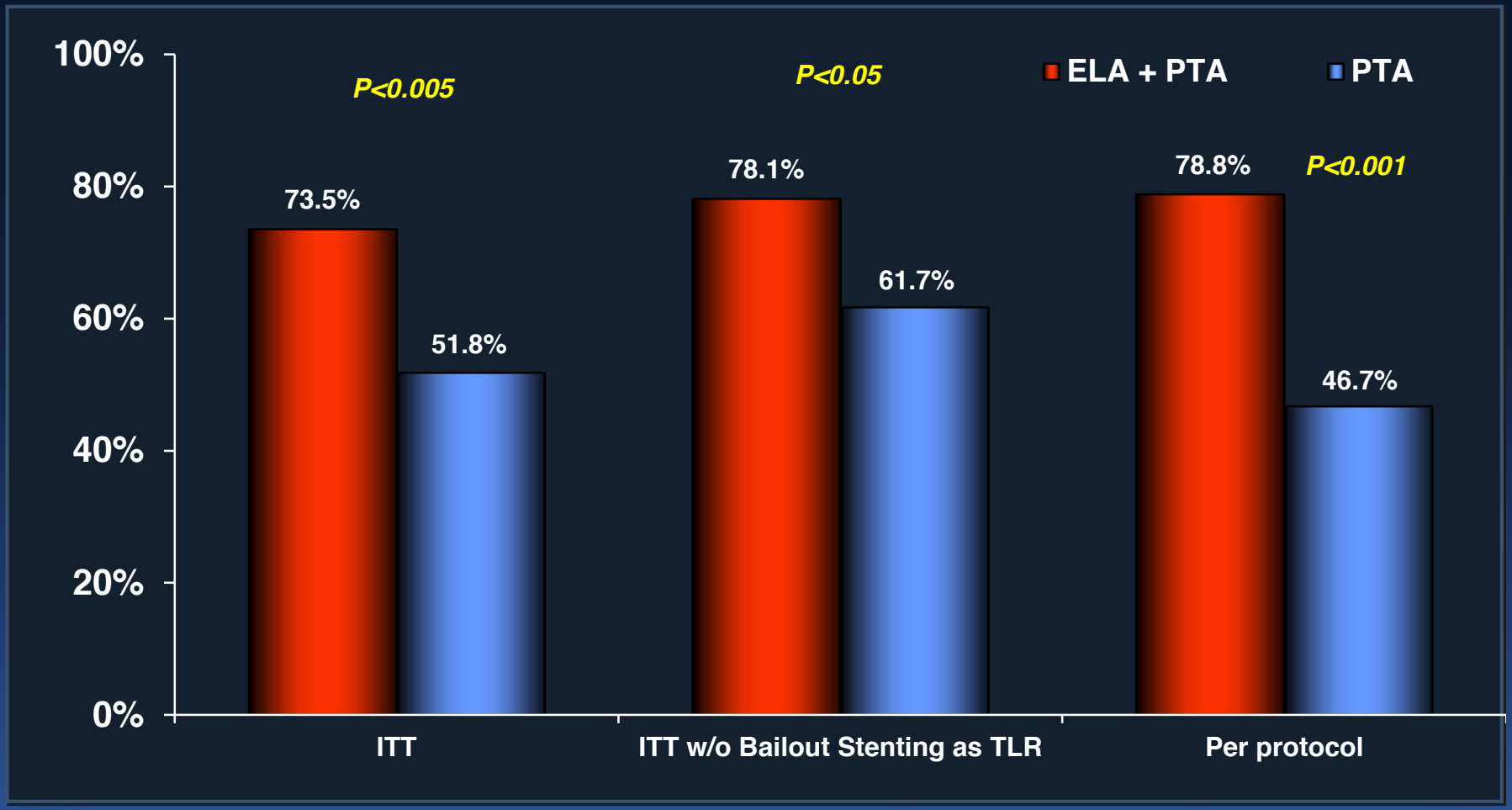
Primary Safety Endpoint

Freedom from MAE thru 30 days

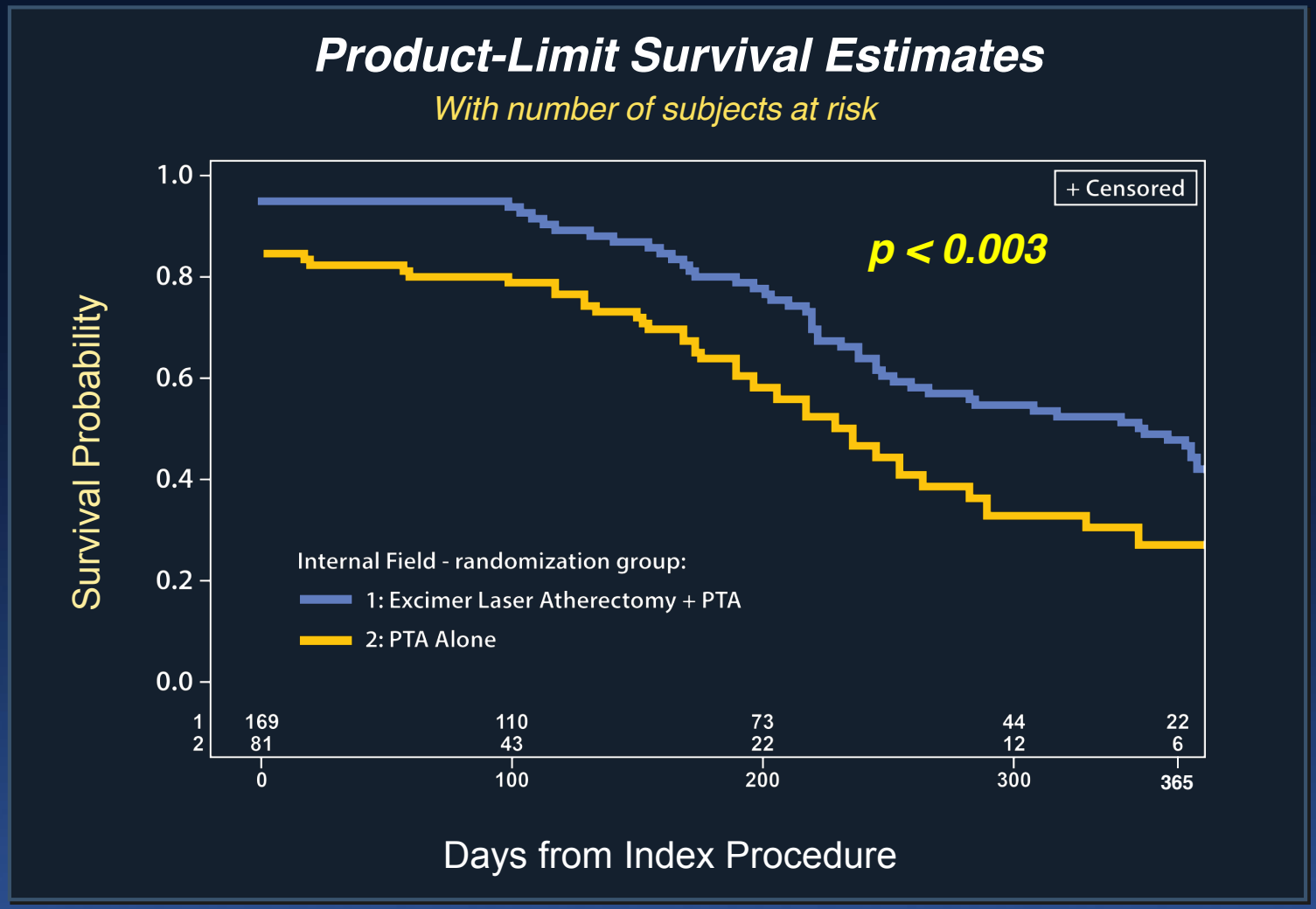


Primary Efficacy Endpoint

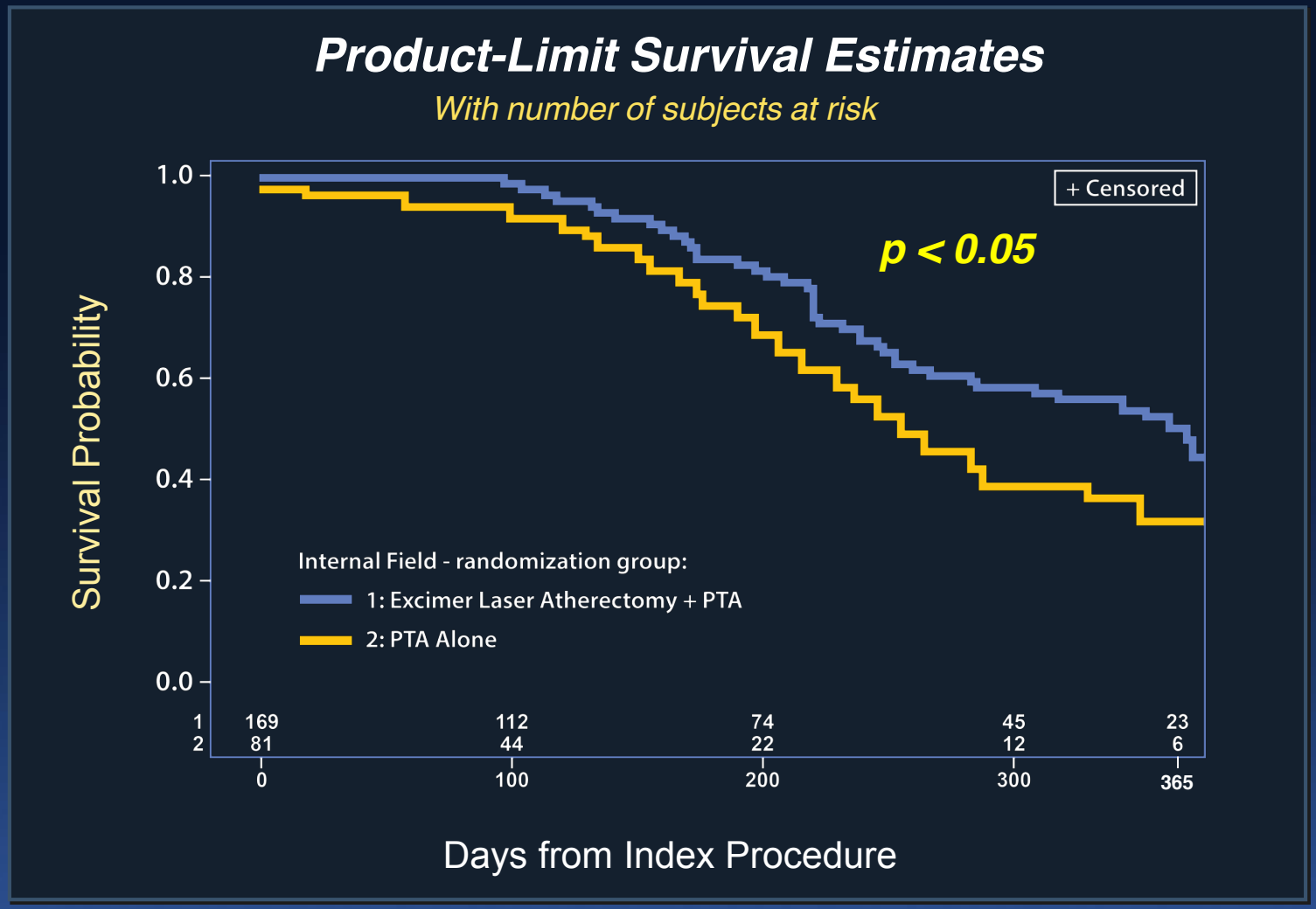
Freedom from TLR thru 6 months



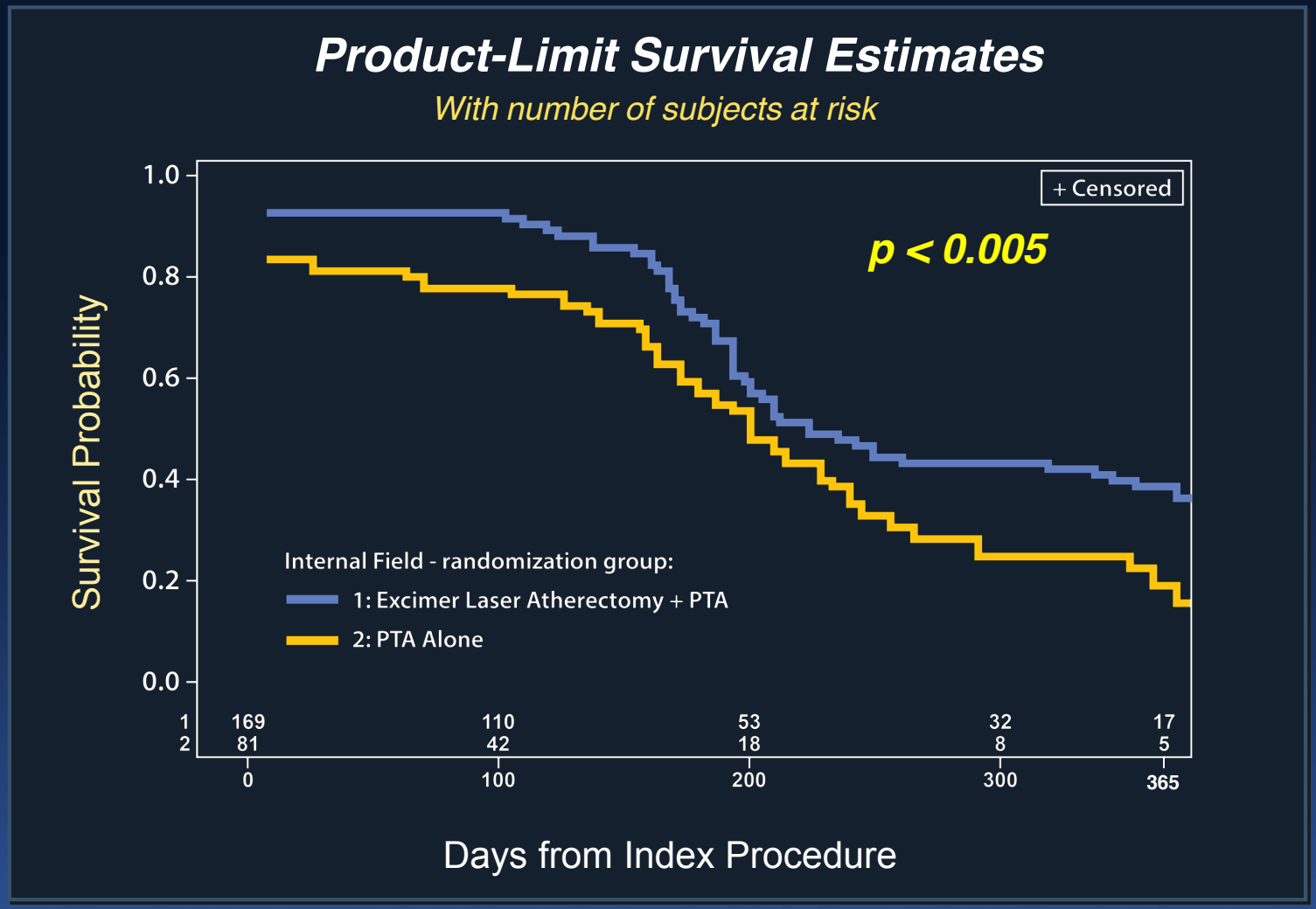
Freedom from TLR



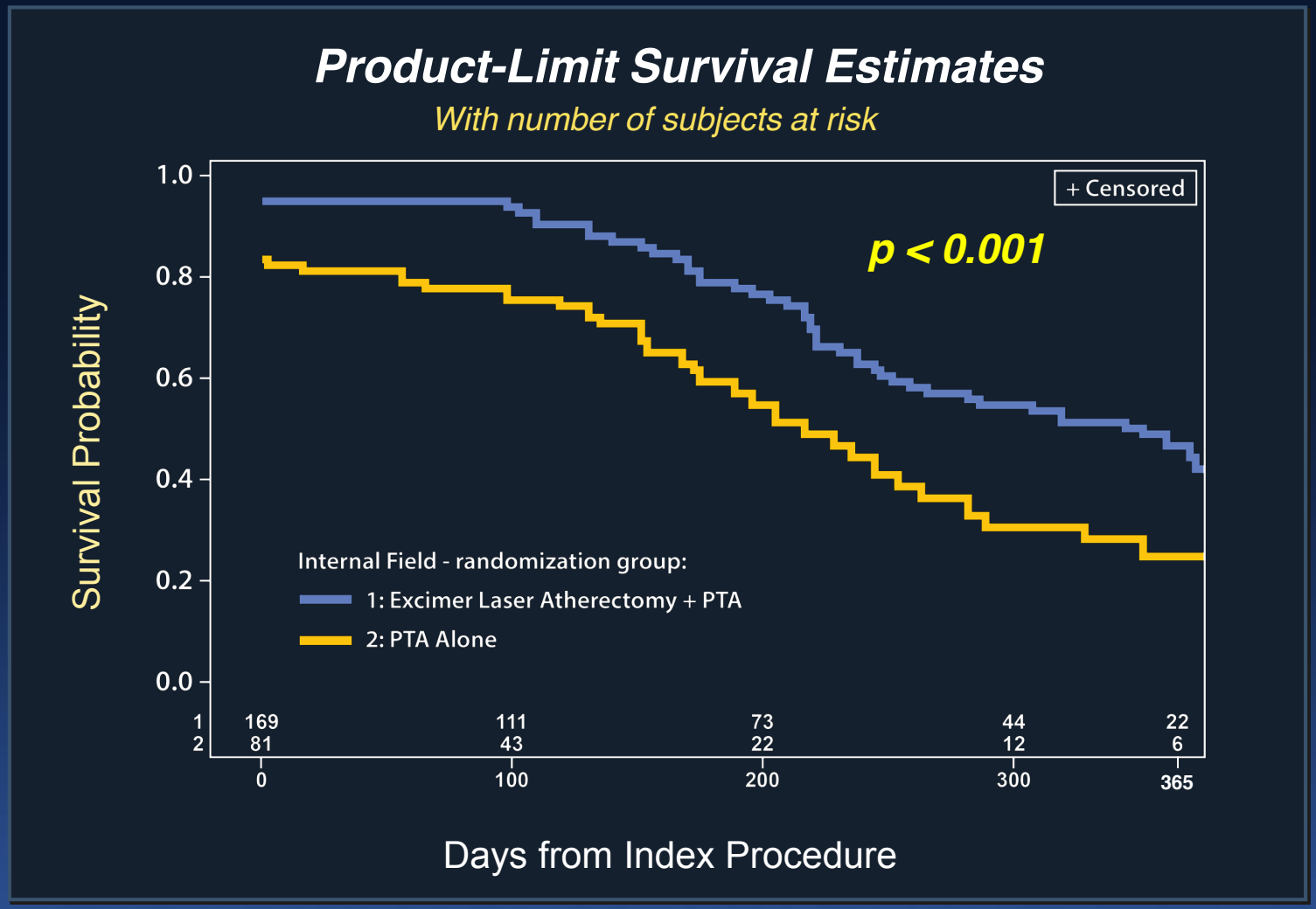
Freedom from TLR without Bailout Stenting



Primary Patency

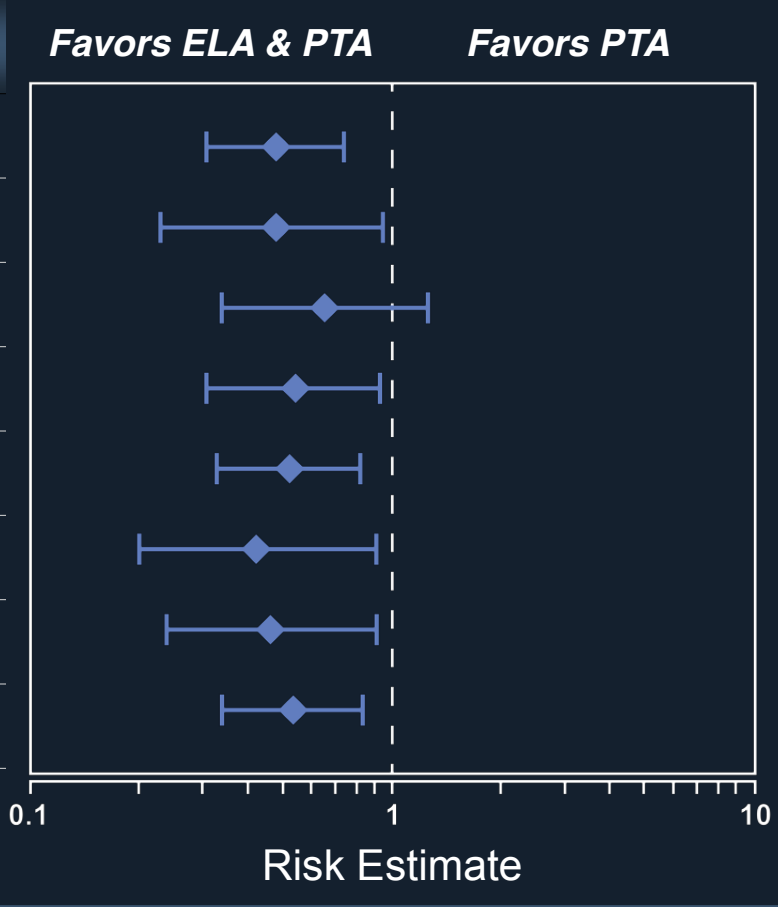


Freedom from MAE



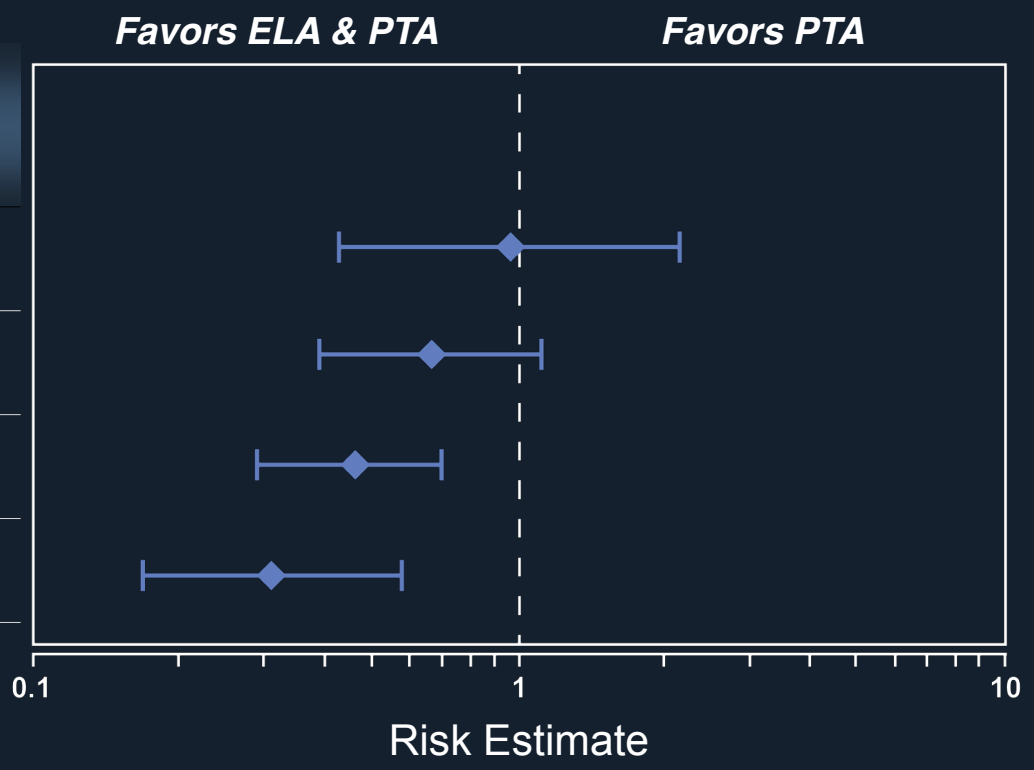
Cox Proportional Hazards Subgroup Analysis

Variable	Estimate	Lower CL	Upper CL	P-value
Overall	0.48	0.31	0.74	0.001
Age > 70	.047	0.23	0.95	0.04
Diabetes	0.65	0.34	1.26	0.20
Previous ISR	0.54	0.31	0.93	0.03
RVD ≤ 5.5	0.52	0.33	0.82	0.005
TASC D	0.42	0.20	0.91	0.03
Occlusion	0.46	0.24	0.91	0.02
> 10 cm	0.53	0.34	0.84	0.007



Lesion Length and TLR

Variable (Lesion Length)	Estimate	Lower CL	Upper CL
5 cm	0.96	0.43	2.14
15 cm	0.66	0.39	1.12
25 cm	0.46	0.29	0.70
35 cm	0.31	0.17	0.58



Conclusions

- **ELA with adjunctive PTA treatment of ISR is superior to PTA alone for the treatment of femoropopliteal ISR:**
  - **Complicated lesions averaging 19 cm in length**
  - **Significantly higher procedural success rate (ELA 93.5% vs PTA alone 82.7%, P=0.02)**
  - **Significantly higher safety rate (freedom from MAE: ELA 94.2% vs. PTA alone 79.2%, P<0.001)**
  - **Significantly lower rate of TLR for ELA throughout study**
- **1st FDA approved IDE randomized control study demonstrating the benefits of atherectomy in the lower extremities**
- **ELA with PTA should be considered the standard care for femoropopliteal ISR**