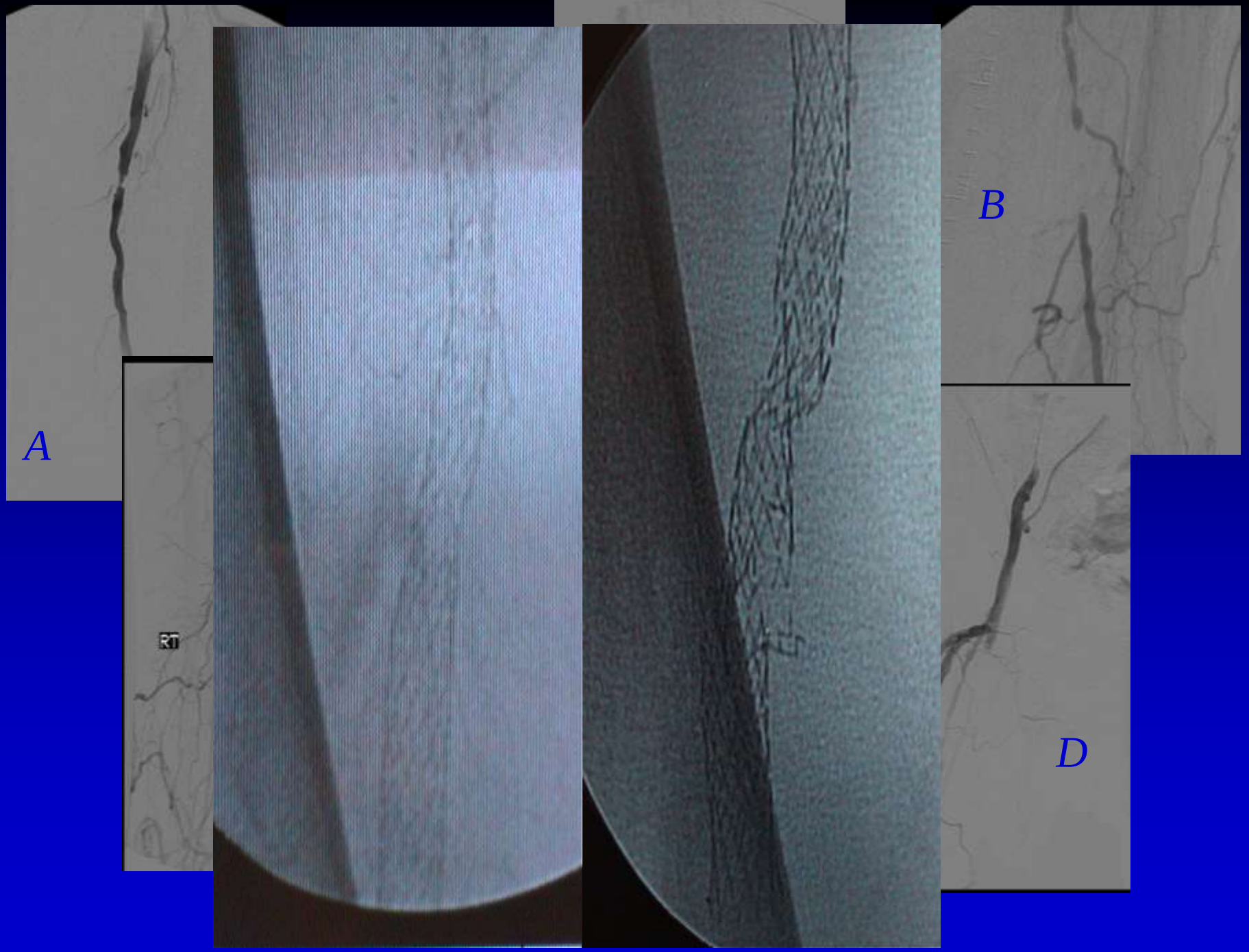
# Stents NOT so fast for lower limb revascularization!

Lawrence A. Garcia, MD
*Chief, Section Interventional Cardiology*
*and Vascular Interventions*
*Director, Vascular Medicine*
*St. Elizabeth's Medical Center*
*Tufts University School of Medicine*
*Boston, MA*

# 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 | • iDev, Covidien, TriReme |
| • Consulting Fees/Honoraria | • Covidien, Boston Scientific, Angiosculpt, Pathway(MedRad) |
| • Major Stock Shareholder/Equity | • Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular |
| • Royalty Income | • None |
| • Ownership/Founder | • None |
| • Intellectual Property Rights | • None |
| • Other Financial Benefit | • None |


A
RT
B
D

# Why not?

- To date the current default technology is stenting
- To date the meaningful studies have evaluated 5-6 cm lesions and only 2 studies have tested long lesions closer to 20 cms that we consider “real world” cases
- The gorilla in the room is restenosis
  - In-stent restenosis vs de-novo restenosis
  - Focal vs diffuse
  - Recurrent vs recurrent
- Alternative therapies have been shown to be just as durable and safe as DES and in some cases better!

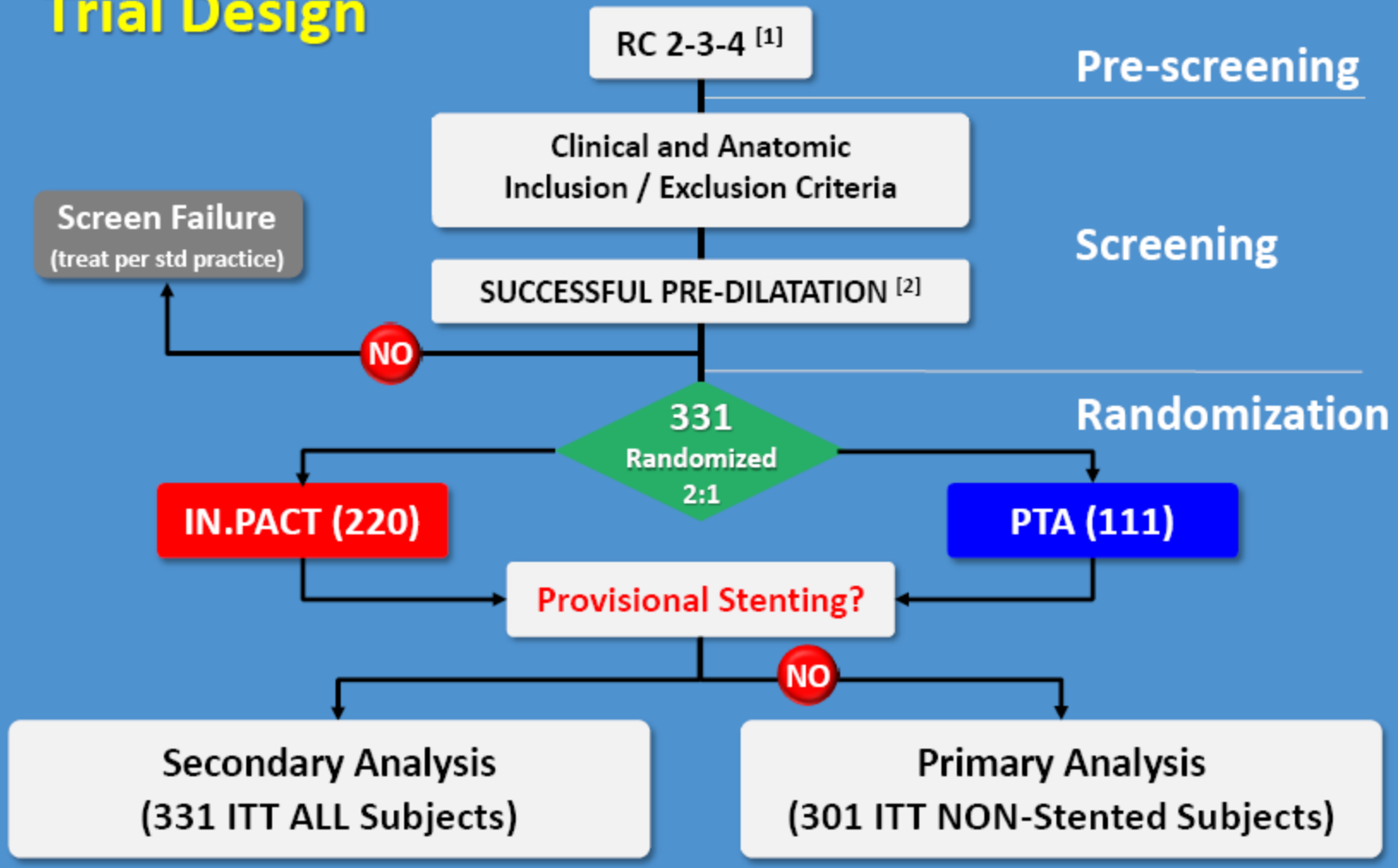
# Current endovascular data

| | Patients (n) | Device | Lesion length (cm) | 1 year primary patency (%) (PSVR) |
|---|---|---|---|---|
| MIMIC | 81 | PTA | NA | NA |
| ABSOLUTE | 104 | Stent | 10.2 | 63 (2.5) |
| RESILIENT | 137 | Stent | 6.3 | 81 (2.4) |
| VIBRANT | 76 | Stent graft | 19.6 | 53 (2.5) |
| VIPER | 119 | Stent graft | 19.0 | 73(2.5) |
| ZilverPTX | 240 | DES-SES | 5.4 | 83 (2.0) |
| THUNDER | 54 | DCB | 7.4 | 74 (2.4) |
| LEVANT | 50 | DCB | 8.1 | 78 (2.5) |
| IN-PACT | 301/220 | DCB | 8.9 | 90 (2.4) |

# IN-PACT

- 2:1 randomized single blinded study DCB vs PTA alone
- 1 year results presented of 5 year study
- Lesions under 18 cm
  - Occlusions under 10 cm
  - RB 2-4 enrolled
- 331 randomized (all subjects) ITT 301 patients
- Provisional stenting listed in all subjects

# Trial Design



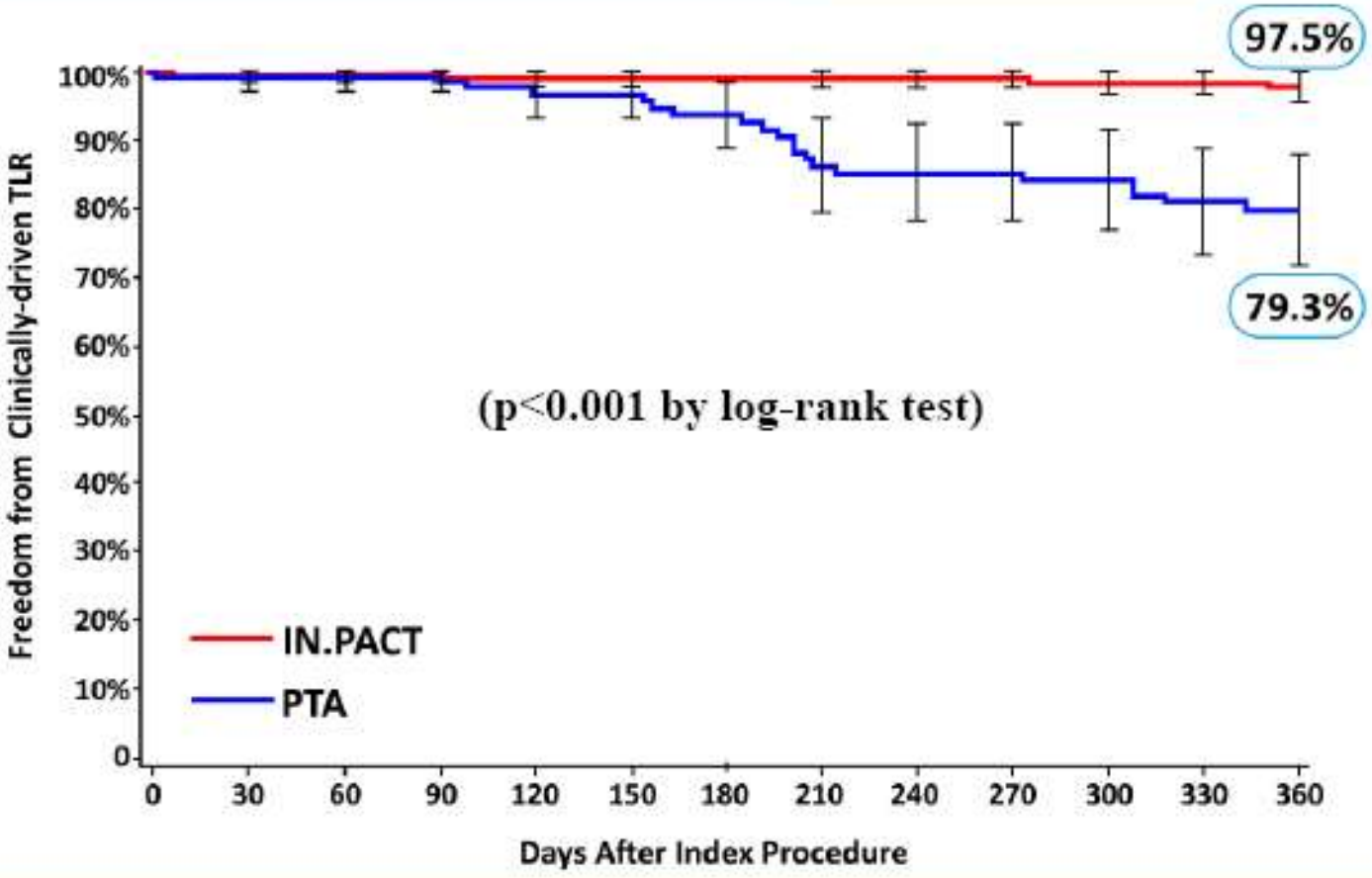

1. With symptoms of claudication and/or rest pain and angiographic evidence of SFA/PPA stenosis
2. Pre-dilatation mandatory for all subjects in IN.PACT SFA II phase only

# Baseline characteristics

| | | IN-PACT | PTA | P |
|---|---|---|---|---|
| | | n=220 subjects (221 lesions) | n=111 subjects (113 lesions) | |
| Lesion Type | De-novo | 95.0% (209/220) | 94.6% (105/11) | 0.875 |
| | Restenotic | 5.0% (11/220) | 5.4% (6/111) | |
| Run off vessels | 0 | 3.3% (7/212) | 4.5% (5/112) | 0.76 |
| | 1 | 13.7% (29/212) | 26.8% (30/112) | <0.05 |
| | 2 | 41.5% (88/212) | 33.0% )37/112) | 0.15 |
| | 3 | 41.5% (88/212) | 35.7% (40/112) | 0.34 |
| Prox popliteal involvement (%) | | 6.8% (15/221) | 7.1% (8/113) | 1.00 |
| Lesion length (cm) | | 8.94±4.89 | 8.81±5.12 | 0.81 |
| Total occlusions (%) | | 25.8% (57/221) | 19.5% (22/113) | 0.22 |
| Severe calcification (%) | | 8.1% (18/221) | 6.2% (7/113) | 0.66 |
| RVD (mm) | | 4.65±0.84 | 4.68±0.83 | 0.73 |
| MLD pre (mm) | | 0.90±0.78 | 0.93±0.77 | 0.71 |
| Diameter stenosis pre (%) | | 81.1±15.5 | 81.3±13.7 | 0.95 |

# All ITT, 12 month patency

| | IN.PACT | PTA | *p* |
|---|---|---|---|
| Clinically-driven TLR [1] | 2.4% | 20.6% | *<0.001* [2] |



# Directional atherectomy

SilverHawk

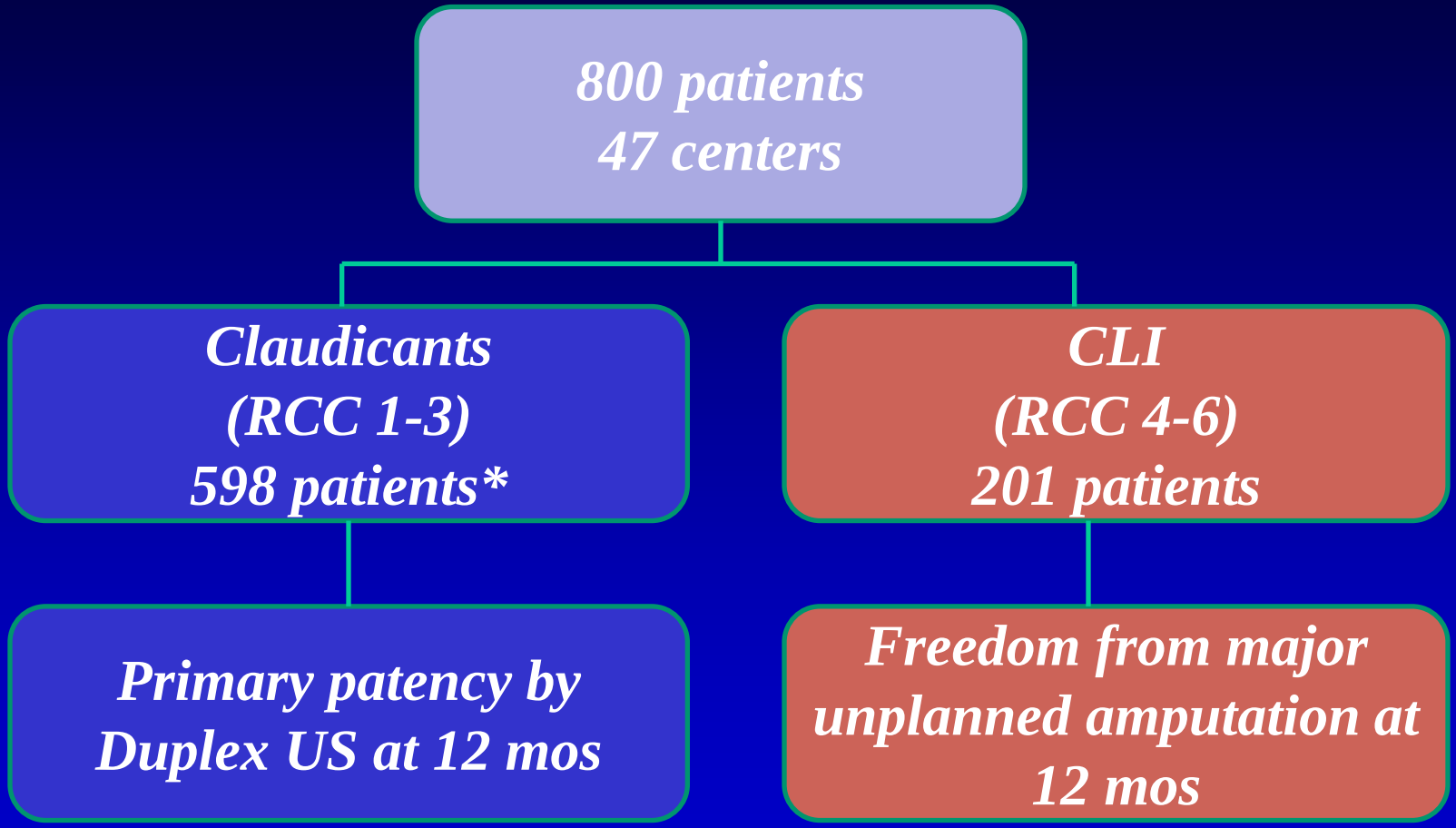
# Key Study Design Elements

- **Study Design and Oversight:**
  - Prospective, non-randomized, global study
  - 800 subjects enrolled at 47 centers
  - CEC and Steering Committee oversight and CEC adjudicaiton
  - Angiographic and Duplex core laboratory analyses

- **Inclusion Criteria**
  - RCC 1-6
  - ≥ 50% stenosis
  - Lesion lengths up to 20cm
  - Reference Vessel ≥ 1.5 mm and ≤ 7.0 mm

- **Exclusion Criteria**
  - Severe calcification
  - In-stent restenosis
  - Aneurysmal target vessel

# Study Design & Primary Endpoints



# Key Study Endpoints

| Claudicants | Primary Endpoint: Primary Patency at 12 Months (PSVR ≤ 3.5) | | Secondary Endpoint: Primary Patency at 12 Months (PSVR ≤ 2.4) | |
|---|---|---|---|---|
| | Patency | LL (cm) | Patency | LL (cm) |
| All (n=743) | 82% | 7.5 | 78% | 7.5 |
| Diabetic (n=345) | 80% | 7.6 | 77% | 7.6 |
| Non-Diabetic (n=398) | 83% | 7.4 | 78% | 7.4 |

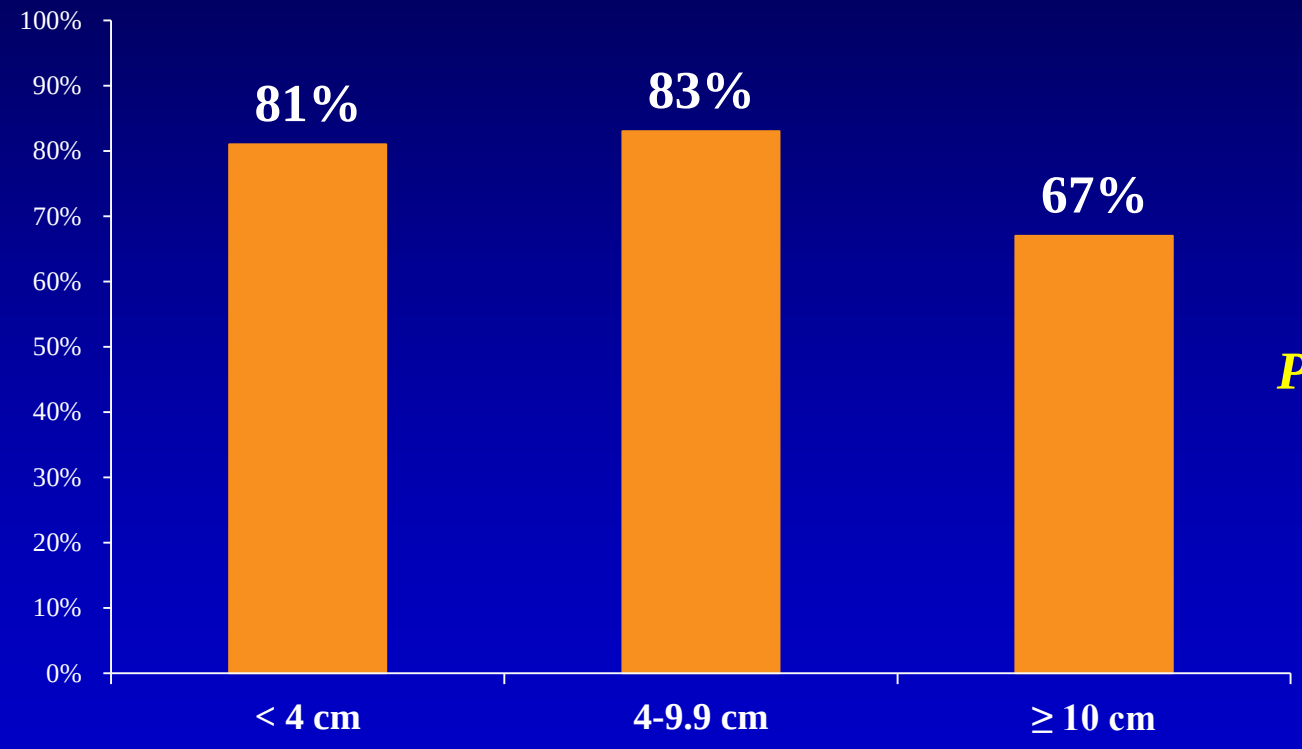
| CLI | Primary Endpoint: Freedom from Major Unplanned Amputation of the Target Limb at 12 Months |
|---|---|
| All (n=201) | 95% |

# Primary Patency in Subgroups

| Subgroup | Claudicants (n=743) | |
|---|---|---|
| | Patency (PSVR ≤ 2.4) | Lesion Length (cm) |
| All (n=1022) | 78% | 7.5 |
| By Lesion Length | | |
| < 4 cm (n=318) | 81% | 2.2 |
| 4-9.9 cm (n=418) | 83% | 6.5 |
| ≥ 10 cm (n=283) | 67% | 14.4 |
| SFA Only By Lesion Length | | |
| < 4 cm (n=184) | 78% | 2.3 |
| 4-9.9 cm (n=253) | 83% | 6.5 |
| ≥ 10 cm (n=232) | 65% | 14.6 |

# Effective treatment for all lesion lengths

***12 Month Primary Patency Rates from DEFINITIVE LE***



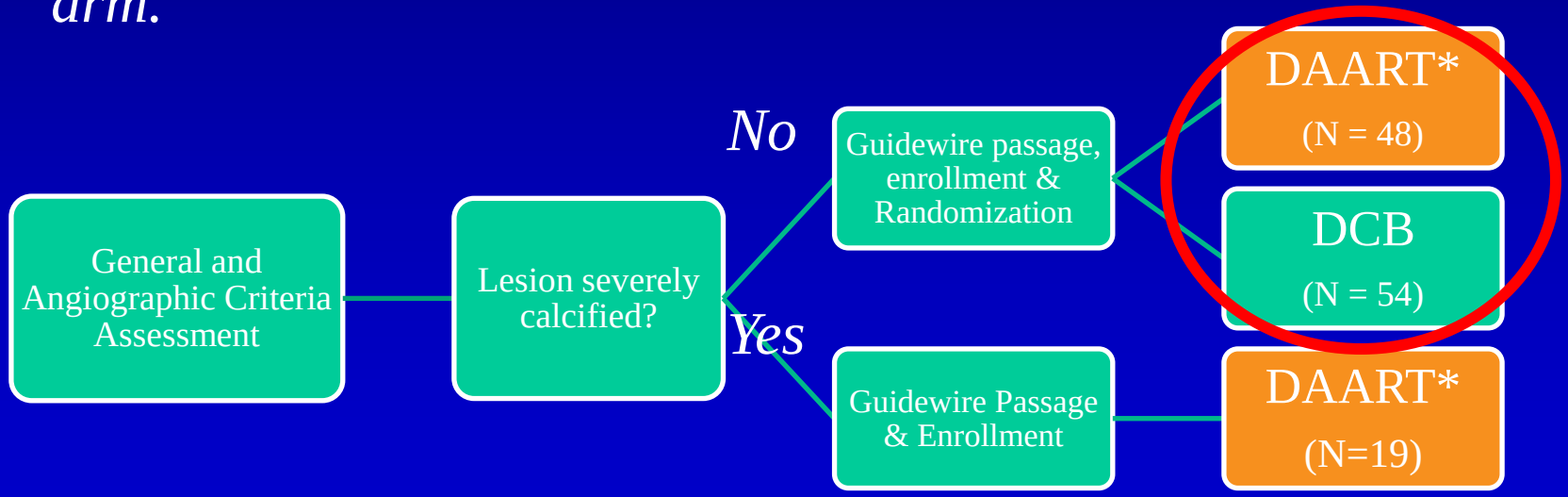

***PSVR ≤ 2.4***

| | | | |
|---|---|---|---|
| ***Mean length :*** | ***2.2 cm*** | ***6.5 cm*** | ***14.4 cm*** |
| ***Number of lesions:*** | ***220*** | ***307*** | ***214*** |

# DEFINITIVE AR Study Design

*Purpose: assess and estimate the effect of treating a vessel with directional atherectomy + DCB (DAART) compared to treatment with DCB alone*

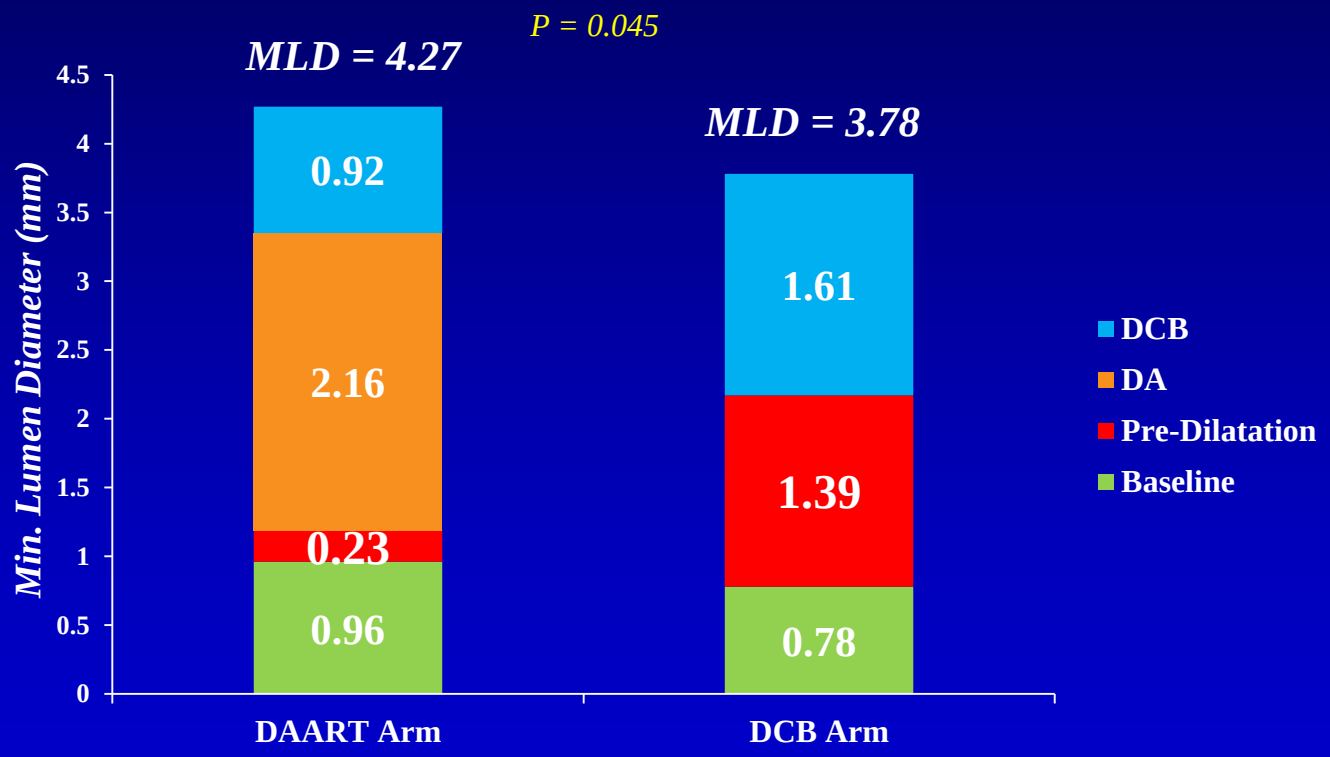
*Registry arm for severely calcified lesions created to limit bail-out stenting (and therefore variables) in randomized arm.*




* ***D****irectional* ***A****therectomy +* ***A****nti-****R****estenotic* ***T****herapy*

# Minimum Lumen Diameters

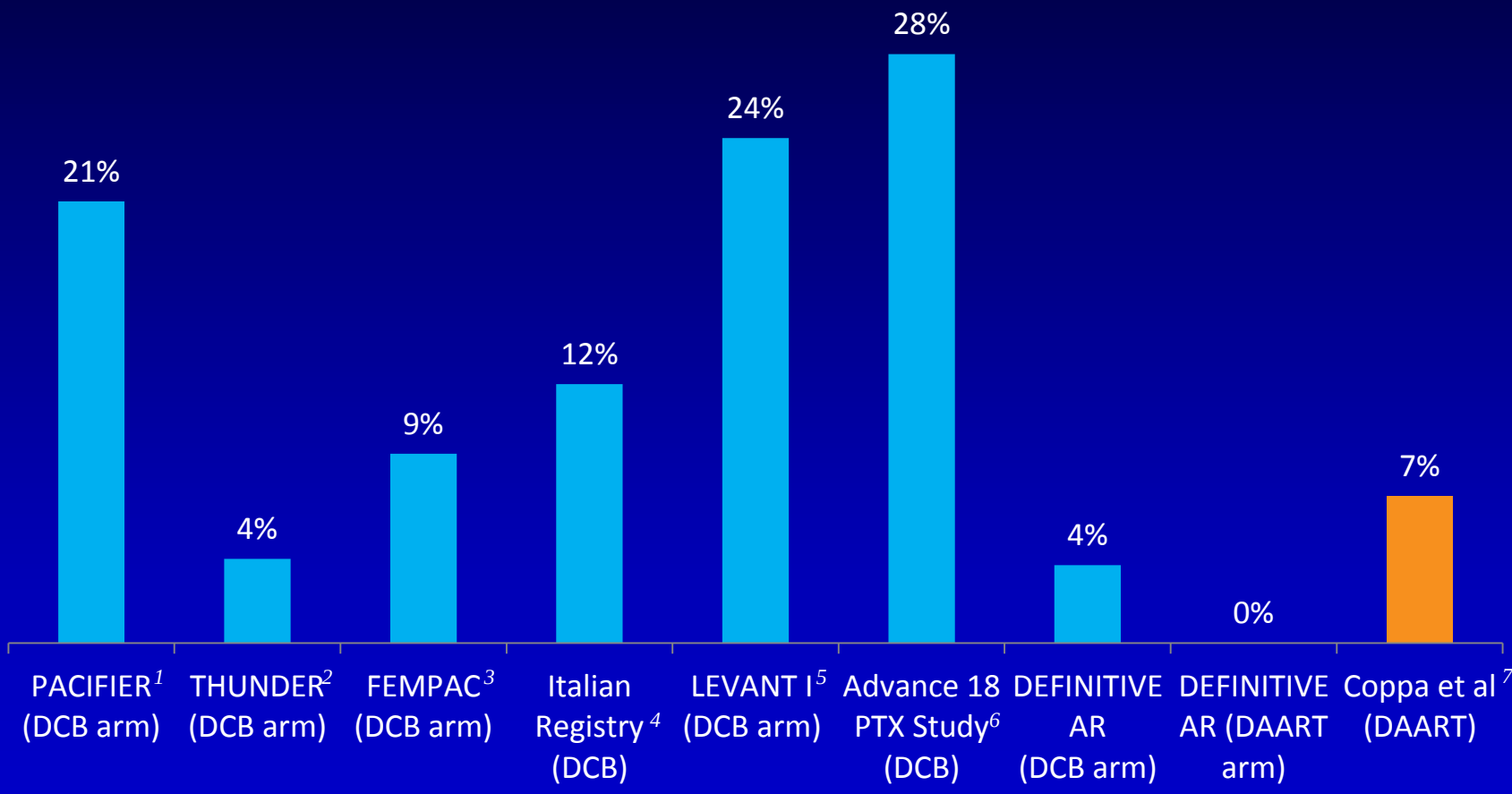
*DAART resulted in a significantly larger minimum lumen diameter (MLD) following the protocol-defined treatment (4.27 mm vs. 3.78 mm, P = 0.045)*






SC1196092013A

# Fewer stents placed with DAART procedure vs. DCB





1. Werk, M., et al., Circ Cardiovasc Interv, 2012. **5**(6): p. 831-40.
2. Tepe, G., et al., N Engl J Med, 2008. **358**(7): p. 689-99.
3. Werk, M., et al., Circulation, 2008. **118**(13): p. 1358-65
4. Micari, A., et al., JACC Cardiovasc Interv, 2012. **5**(3): p. 331-8.
5. Scheinert, D., 56 Month Reesults of the LEVANT I Trial. TCT. 2010. Washington, DC
6. Scheinert, Advance 18 PTX Study 6 Month Resutls. LINC 2013 , Leipzig, Germany
7. Cioppa, A., et al.,Cardiovasc Revasc Med, 2012.

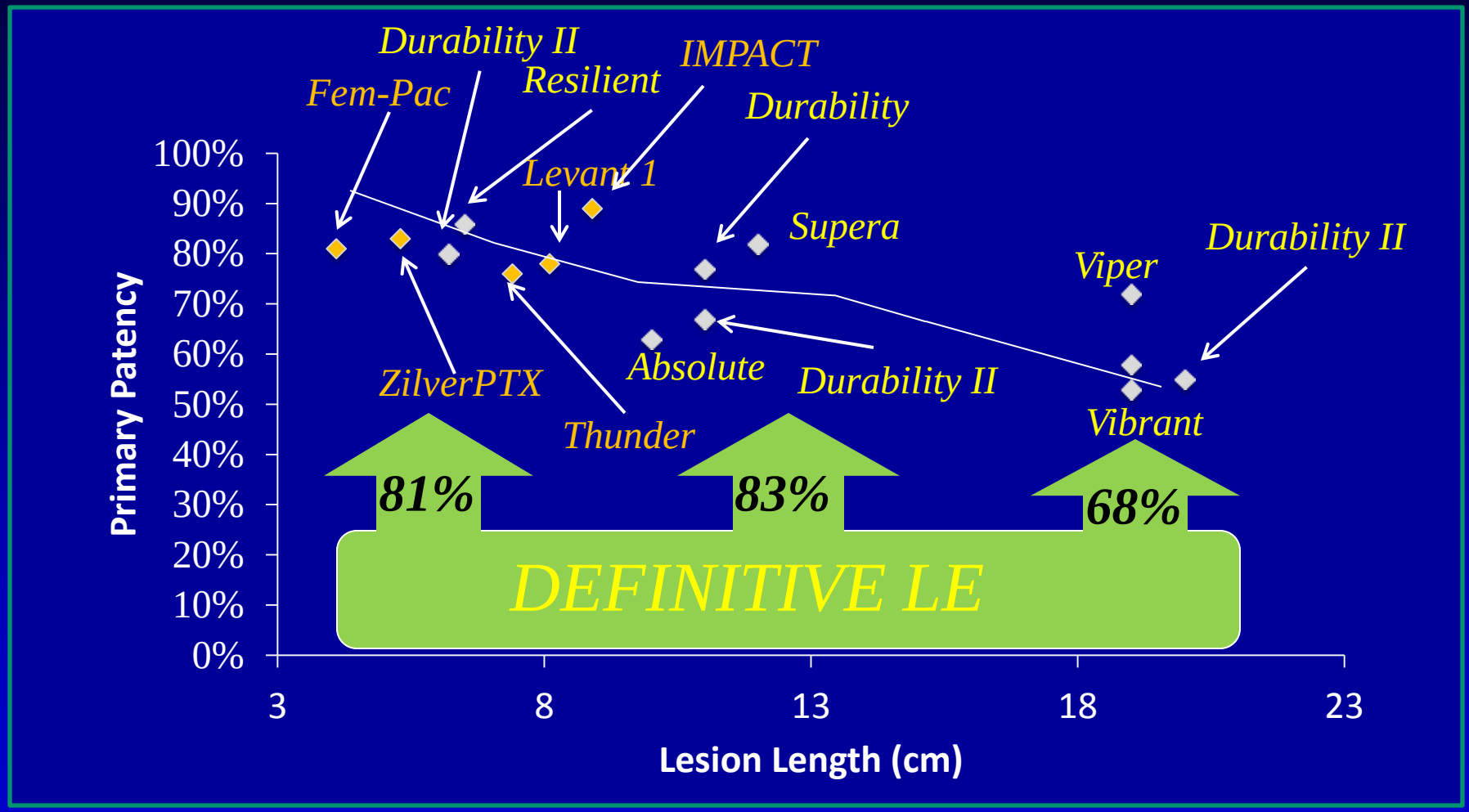
# Comparisons

| | Lesion length (mm) | PSVR | Patency (%) |
|---|---|---|---|
| **RESILIENT** | **63** | **2.5** | **81** |
| **ZILVER PTX** | **54** | **2.0** | **83** |
| **Levant I** | **81** | **2.5** | **78** |
| **THUNDER** | **74** | **2.4** | **74** |
| **IMPACT** | **89** | **2.4** | **89** |
| **DEFINITIVE LE < 4 cm** | **22** | **2.4** | **81** |
| **DEFINITIVE LE 4 – 9.9 cm** | **65** | **2.4** | **83** |

# Comparisons

| | Lesion length (mm) | PSVR | Patency (%) |
|---|---|---|---|
| VIBRANT | 19.6 | 2.5 | 53 |
| VIPER | 19.0 | 2.5 | 72 |
| ZILVER PTX registry | 11.0 | 2.5 | 80 |
| ABSOLUTE | 10.2 | 2.5 | 63 |
| In-Pact | 8.9 | 2.4 | 90 |
| DEFINITIVE LE 10 cm and up | 14.4 | 2.4 | 67 |

# Comparing non-stent technologies at 12 months



# Stents not so fast!

- Drug coated balloon technology is safe and effective
- IN-Pact has shown benefit at 1 year higher than any other trial to date in a level 1 randomized protocol at near 9 cm LL.
- DEFINITIVE LE proved atherectomy safe & effective at 12 months
  - Effective for short, medium and long lesions in claudicants & CLI patients
- DEFINTIVE AR has completed enrollment—data release 2014
- Initial signal suggests an potential role for DCB with atherectomy that may obviate the need for stenting as an upfront need for our patients with complex peripheral vascular disease
- Opportunity for re-therapy remains open to the operator and patient if no endoprosthesis is left behind at the index procedure.
- Overall cost benefit needs assessment but remember repeat revascularization for ISRS may not benign and only once