# EVOLVE Short DAPT: A Single Arm Study of 3-Month DAPT in Patients at High Bleeding Risk Treated with a Bioabsorbable Polymer-Based Everolimus-Eluting Stent


***Ajay J. Kirtane, MD, SM***

*Columbia University Irving Medical Center /New York-Presbyterian Hospital and the Cardiovascular Research Foundation, New York, NY, USA*

Robert Stoler, Robert Feldman, Franz-Josef Neumann, Loukas Boutis, Naeem Tahirkheli, Ralph Tölg, Islam Othman, Bernardo Stein, James Choi, Stephan Windecker, Robert Yeh, Harold Dauerman, Matthew Price, Paul Underwood, Dominic Allocco, Ian Meredith, Dean Kereiakes

# Disclosure Statement of Financial Interest

I, Ajay J. Kirtane, have the following potential conflicts of interest to report:

Institutional funding to Columbia University and/or Cardiovascular Research Foundation from Medtronic, Boston Scientific Corporation, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, ReCor Medical

# Background

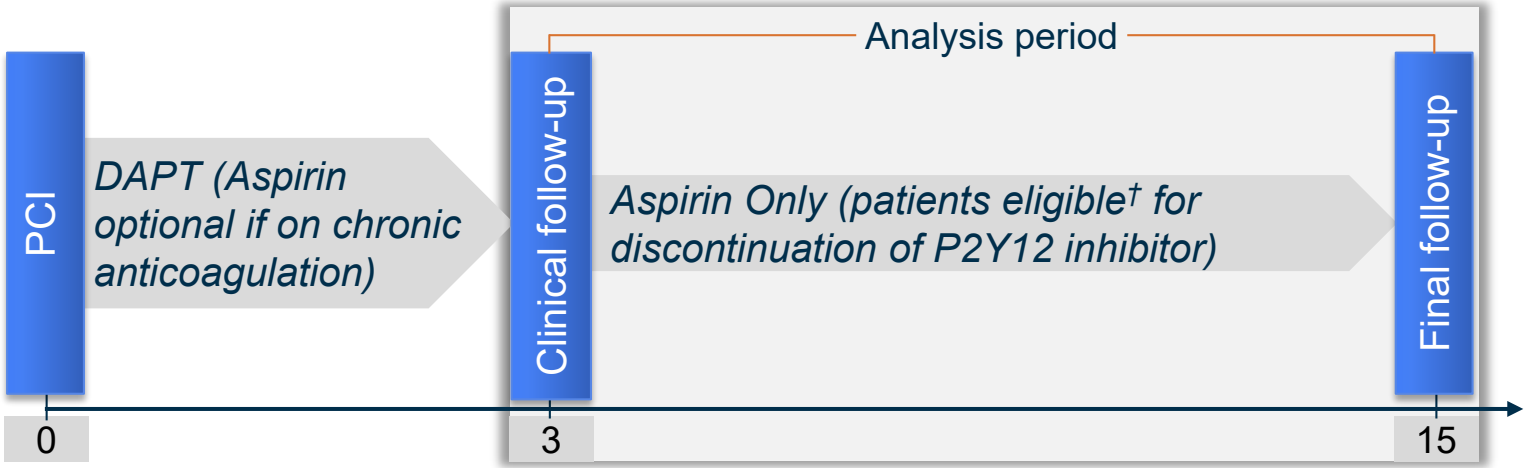
- International guidelines[1,2] recommend extended durations of DAPT in patients undergoing PCI with DES
  - Initial recommendations to extend DAPT based upon observational analyses and concern for late ST with earlier generation DES a decade ago
  - Extended DAPT is associated with higher bleeding rates, despite lower rates of MI and ST, and a net neutral to negative effect upon mortality[3]
- SYNERGY is a thin-strut everolimus-eluting stent with an ultrathin abluminal bioabsorbable polymer coating designed to facilitate healing
  - Drug release and polymer degradation in ≤4 months[4]
  - SYNERGY demonstrated low ST rates (≤0.7%) through 5 years in normal bleeding risk patients on standard DAPT duration[5,6]
  - Optimized platform to test shorter durations of DAPT



[1]Valgimigli et al. *EHJ* 2018; [2]Levine et al. *JACC* 2016; [3]Mauri et. Al. *NEJM* 2014; [4]Wilson, G. J., et al. *Cathet. Cardiovasc. Intervent.* 2015; [5]Meredith TM et al. *EuroIntervention* 2017; [6]Kereiakes et al. *ACC* 2019

# EVOLVE Short DAPT Study Design

Prospective, multicenter, single-arm study powered to define safety of 3-month DAPT in high bleeding risk (HBR) patients treated with SYNERGY



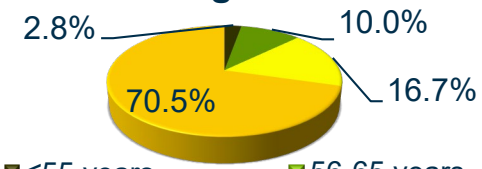

Co-Primary endpoints: Death/MI and ARC definite/probable ST between 3-15 months
Secondary endpoint: BARC 2/3/5 bleeding between 3-15 months (patients not on chronic anticoagulation)



†Subjects free from stroke, MI, revascularization and ST between 0-3 months eligible to discontinue; Mauri et al. *AHJ* 2018

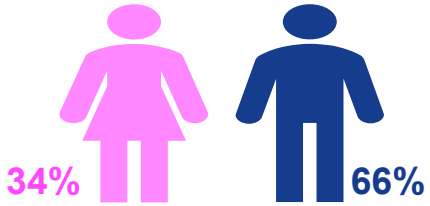
# EVOLVE Short DAPT – Analysis Population

**Age**

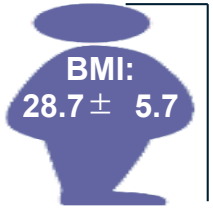



**75.7 ± 8.5 years**

**Gender**




**BMI**




**Height: 170.0 ± 10.9 cm**

**Weight: 83.5 ± 20.6 kg**

| HBR patients with SYNERGY stent implanted | N=1487 |
|---|---|
| Age ≥ 75 yrs, and, risk of major bleeding associated with >3m DAPT outweighs the benefit | 67.5% (1003) |
| Need for chronic or lifelong anticoagulation therapy | 30.6% (455) |
| Major bleeding* within 12 months of index procedure | 2.7% (40) |
| History of stroke (ischemic or hemorrhagic) | 13.4% (200) |
| Renal insufficiency (creatinine ≥ 2.0 mg/dl) or failure (dialysis dependent) | 9.1% (136) |
| Platelet count ≤ 100,000/μL | 2.0% (29) |

*Subjects met more than one HBR criteria: 22.9%*

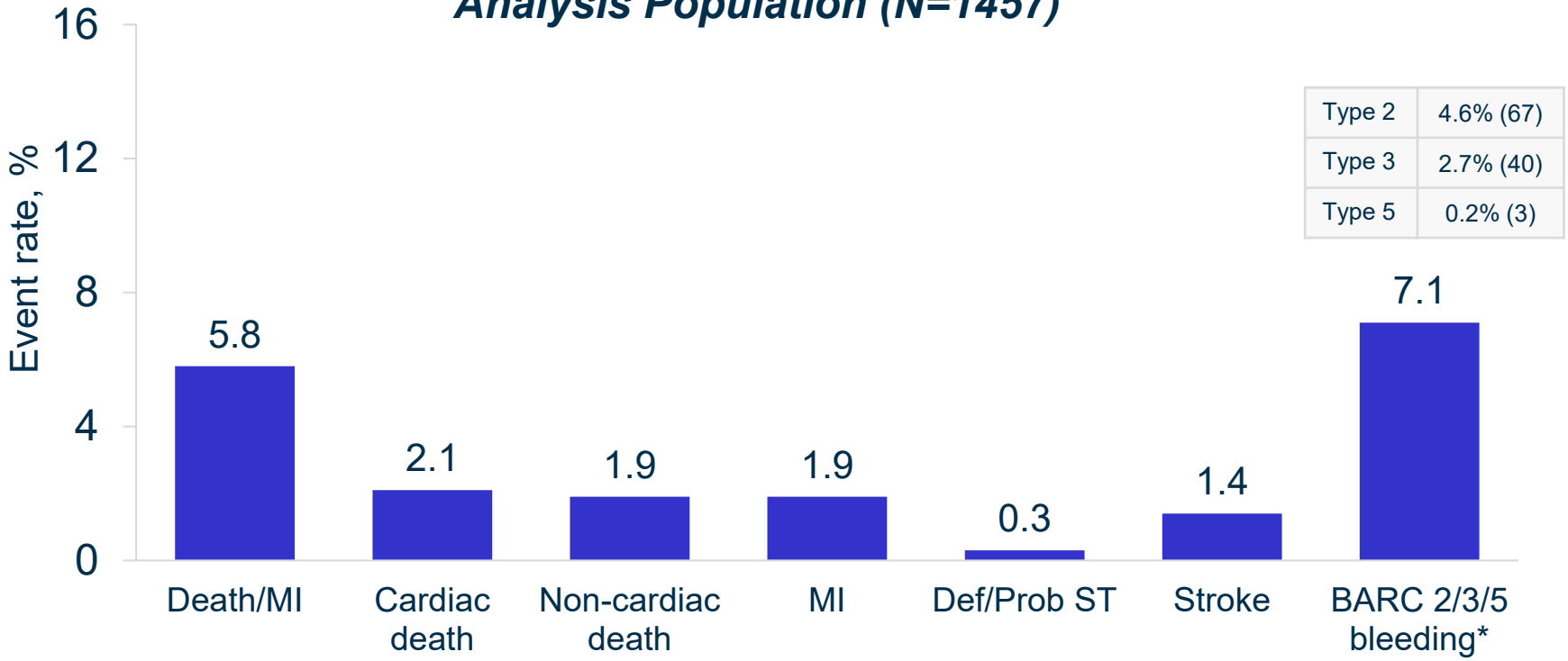
*# of HBR criteria met/subject: 1.3 ± 0.5*



*Severe/life threatening or moderate bleeding

# Clinical Outcomes between 3-15 Months

***Analysis Population (N=1457)***

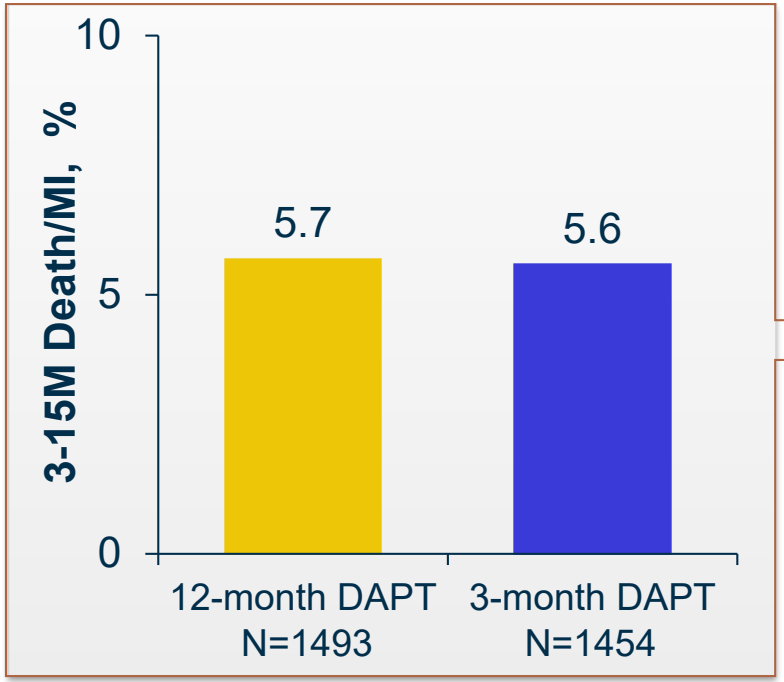


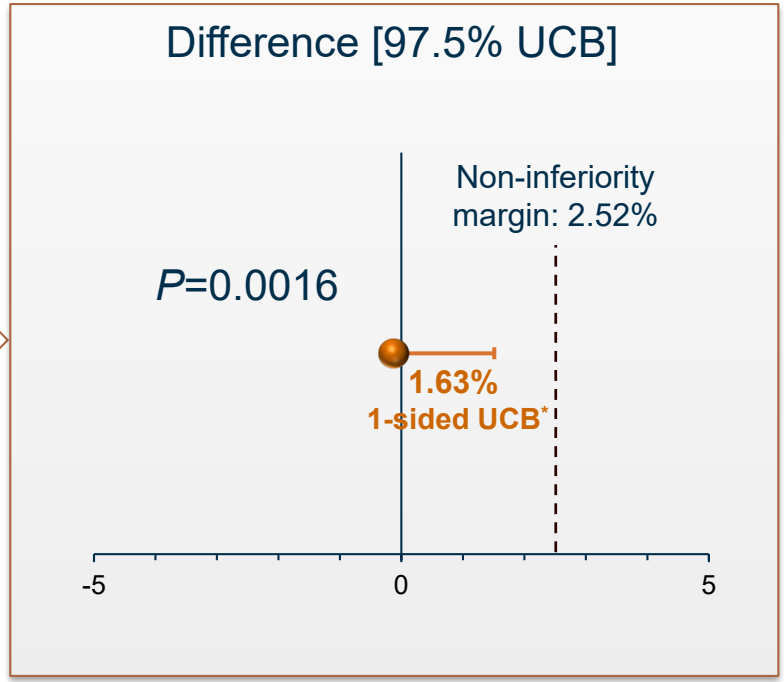

| | |
|---|---|
| Type 2 | 4.6% (67) |
| Type 3 | 2.7% (40) |
| Type 5 | 0.2% (3) |



Binary rates; denominator includes patients with sufficient f/u or having a CEC event; *Non-hierarchical

# Co-Primary Endpoint: Adjusted Death/MI between 3-15 months with 3-Month DAPT Compared to Historical Control



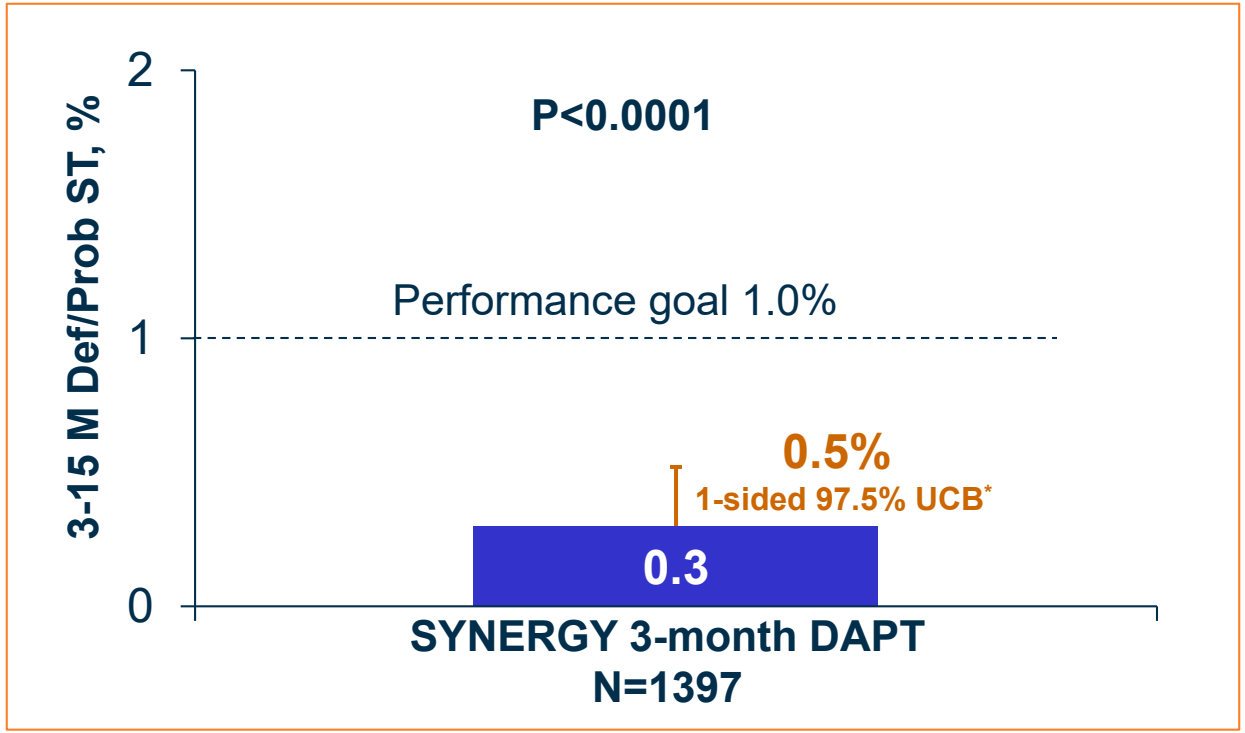




**Patients with respective event or sufficient follow-up included in the denominator**



*One-sided 97.5% Upper Confidence Bound (Z-test);
Worst-case scenario analysis: site-reported MI in control group between 0-12m assumed within 0-3m if not CEC adjudicated

# Co-Primary Endpoint: ARC Definite/Probable ST between 3-15 months




**Patients with respective event or sufficient follow-up included in the denominator**

*One-sided 97.5% Upper Confidence Bound (Exact test)

# Secondary Endpoint: Adjusted BARC 2,3,5 Bleeding Between 3-15 Months

| | 12-Month DAPT (N=947) | 3-Month DAPT (N=974) | Difference [95% CI] | Superiority Test P value |
|---|---|---|---|---|
| BARC 2,3,5 Bleeding | 4.17% | 6.26% | 2.10% [-0.10%, 4.29%] | 0.98 |
| Type 2 | 2.12% | 3.64% | 1.52% [-0.16%, 3.19%] | - |
| Type 3 | 2.32% | 2.67% | 0.35% [-1.17%, 1.87%] | - |
| Type 5 | 0.00% | 0.27% | 0.27% [-0.05%, 0.60%] | - |

**Patients with respective event or sufficient follow-up included in the denominator**

# Conclusions

- EVOLVE Short DAPT was designed to evaluate the safety of DAPT discontinuation at 3 months in HBR subjects treated with SYNERGY
  - Bleeding risk was significant, and key subgroups (age≥75 with risk/benefit favoring shorter DAPT, need for anticoagulation) were well-represented
- The study met both co-primary endpoints despite incomplete event adjudication in the control group, with favorable rates of ischemic outcomes from 3-15 months after discontinuation of P2Y12 inhibitor
  - Death/MI: 5.6%; Definite/probable ST: 0.3%; MI: 1.8%
- Although bleeding endpoint was not met, these data illustrate the truly high-bleeding risk nature of the enrolled population and the challenges of non-randomized comparisons