Impact of LIFE-BTK on Implications of BEST-CLI or BASIL-2

Lawrence A. Garcia, MD
Chief, Vascular Services
Catholic Health Systems
St. Francis Hospital
Roslyn, NY

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	• Abbott, Medtronic, BSC
• Consulting (non-compensated)	• Medtronic, Boston Scientific, Abbott, Phillips
• Major Stock Shareholder/Equity	• Primacea, TissueGen, Orchestra, R3 Vascular, Transit Medical, Syntervention, Cagent
• Royalty Income	• None
• Ownership/Founder	• Innovation Vascular Partners, LLC
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

Why is this difficult?

- Unfortunately, the outcomes for ATK seem dependent upon patency and walking difficulties
- BTK data are mired in endpoints, heterogeneity of subjects, non-uniform nature of wound care and type of patient enrolled (RB3 in RB 4-5-6)

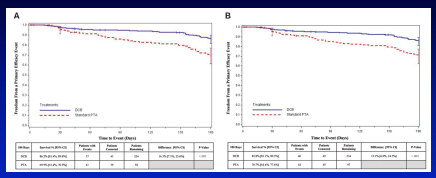
Primary IN.PACT DEEP Outcomes

Primary Efficacy	DEB	PTA	*p*
12-month LLL (mm) [1]	0.61 ± 0.78	0.62 ± 0.78	*0.950*
12-month CD-TLR [2]	9.2% (18/196)	13.1% (14/107)	*0.291*

Primary Safety	DEB	PTA	*p*
6-month Death Major Amputation or CD TLR	17.7% (41/232)	15.8% (18/114)	*0.021* (non-inferiority) *0.662 (superiority)*

Zeller T et al JACC 2014
Zeller T et al JACC Interv 2020

LEVANT BTK



FDA panel voted 2-15 with one abstention regarding effictiveness

SAVAL

Primary Endpoints

12 Months | Subject-based | Intention-to-treat

- Primary effectiveness endpoint of superior 12-month primary patency rate was not met
  - Lower bound of one-sided 97.5% CI < 0

	DES (N=130 Patients)	PTA (N=71 Patients)	Difference (95% CI)	One-sided lower 97.5% CI	Superiority p-value
Primary Patency	**68.0%** (70/103)	**76.0%** (38/50)	-8.0% (-22.9%, 6.8%)	**-22.92%**	0.8552

Primary patency defined as core lab-adjudicated duplex ultrasound flow at 12 months in the absence of clinically-driven TLR or surgical bypass of the target lesion. The effectiveness endpoint was pre-specified to be met if the lower bound of the one-sided 97.5% CI on the difference was greater than zero.

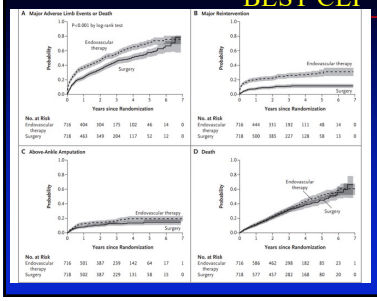
- Primary safety endpoint of non-inferior 12-month MAE-free rate was not met
  - Lower bound of one-sided 97.5% CI < -10%

	DES (N=130 Patients)	PTA (N=71 Patients)	Difference (95% CI)	One-sided lower 97.5% CI	Noninferiority p-value
MAE-free Rate	**91.6%** (109/119)	**95.3%** (61/64)	-3.7% (-10.9%, 3.5%)	**-10.90%**	0.0433

MAEs defined as a composite of above-ankle amputation of the index limb, major re-interventions, and 30-day mortality. Success criterion for the safety endpoint hypothesis was that the lower bound of the one-sided 97.5% CI on the difference was greater than the non-inferiority margin of -10%. P-value is 1-sided adjusted for non-inferiority margin of -10%.

Van OverHagen, CIRSE 2022

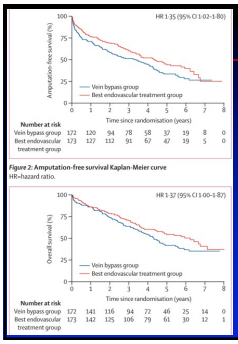
BEST CLI



- *5 years to enroll study*
- *18% non-surgeons in the endovascular group, no IMC*
- *38% cross over in the endo group never defined*
- *Primary outcomes major revision, thrombolysis or revision to graft not restenosis*

Farber A et al NEJM 2022

BASIL 2



- *10 years to enroll study*
- *Similar endpoints MALE etc*
- *However, primary outcome was revision or primary procedural repeat as failure*
- *Endo any restenosis considered failure*
- *Only mortality drove difference between cohorts*

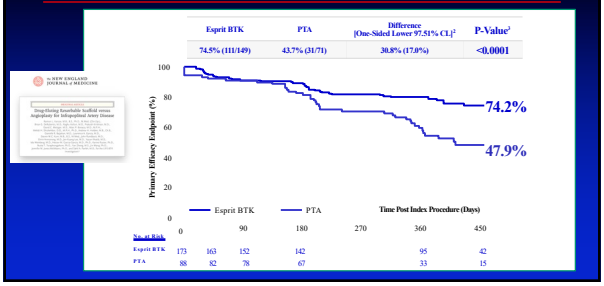
BEST-CLI vs. BASIL-2: trial designs

- BEST-CLI: 150 global centers
  - 1434 subjects over ~5 years (average 2/center/year)
  - Study populations
    - Cohort 1: suitable autologous venous conduit for bypass
    - Cohort 2: need for alternative bypass conduit
  - Excluded if excessive surgical risk
  - Randomized 1:1 in a stratified fashion by anatomy (presence or absence of BTK disease) and clinical (rest pain or tissue loss)
- BASIL-2: 41 primarily UK centers
  - 345 subjects enrolled over 6 years
    - No exclusions for vein suitability
    - No exclusion for bypass suitability
  - Multiple stratifications
  - More bypass:endo cross-over (27%), more reintervention in the endo group (19%)

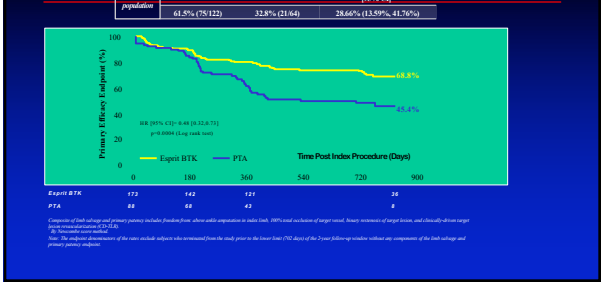
BEST-CLI vs. BASIL-2: Endpoints

- BEST-CLI Primary endpoint:
  - Composite of death and MALE (above ankle amputation, major limb reintervention)
    - ***Reintervention need and timing was determined by site investigator***
    - ***No CD-TLR criteria or independent adjudication***
- BASIL-2 Primary endpoint:
  - Amputation-free survival (AFS) or all-cause death

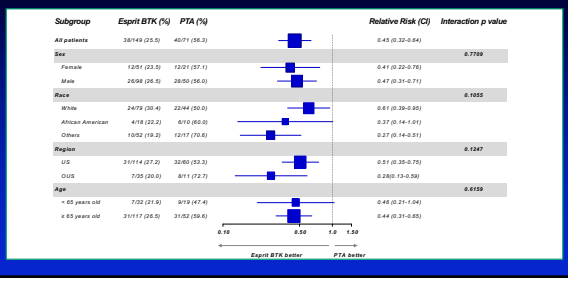
LIFE-BTK



Composite of Limb Salvage & Primary Patency at **2 Years**



Subgroup Analyses of Composite Primary Efficacy Endpoint at 1 Year



What's in the future?

• Serranator (RECOIL)	Cagent
• Magic Touch (LIMES, DEBATE)	Concept Medical
• Luminor DCB (MERLION)	iVASCULAR
• Litos DCB (ACOART II)	Acotec
• IMPACT DEEP redux	Medtronic
• Selution BTK	MedAlliance
• Orchestra	Orchestra

Conclusion(s)

- BTK trials are "in"
- BEST-CLI and BASIL-2 enrolled distinct patients
- LIFE-BTK has been the only significant successful endovascular randomized trial to date
- The cohort of patients enrolled in LIFE-BTK were very specific compared with BEST and BASIL
- Benefit of LIFE BTK augments a victory for BTK endovascular care of pateints with RB4-5