How The Data From BEST-CLI And BASIL-2 Can Be Combined To Produce Conclusions Superior To Those Of Either Trial Alone

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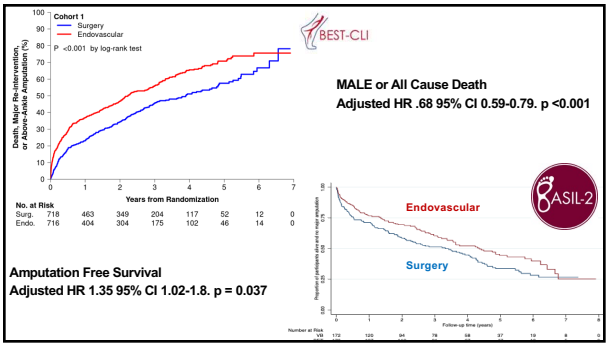
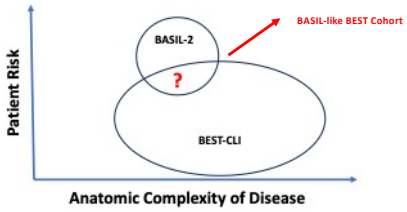
Disclosures

Novo Nordisk Foundation	*Grant recipient*
LeMaitre	*Consultant*
BioGenCell	*Consultant*
Dialysis-X	*Advisory Board*
iThera Medical	*Advisory Board*
Anges	*Advisory Board*



How do we harmonize BEST-CLI and BASIL 2?

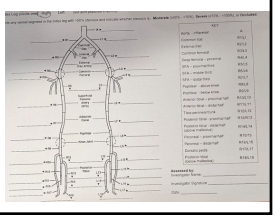


Anatomical Complexity of Arterial Disease

- **BEST-CLI dataset (19 anatomical segments)**

	Segments
SFA - proximal, mid, distal	3
Popliteal – proximal, distal	2
Tibioperoneal trunk	1
Tibials - proximal, distal	6
	12

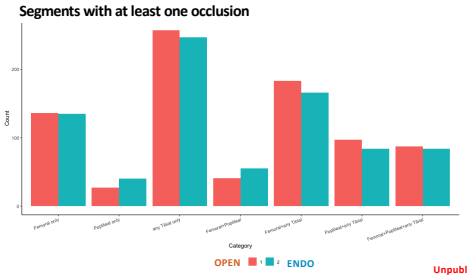
*Exclude aortic, iliac and pedal



Stenosis Grading

	% stenosis
Mild	< 50
Moderate	50-69
Severe	70-99
Occlusion	100

Anatomical Complexity of Open and ENDO



Unpublished Data

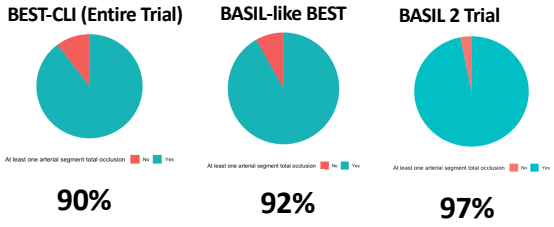
BASIL-like BEST

1,830

1,211 with significant tibial disease

833 underwent tibial revascularization

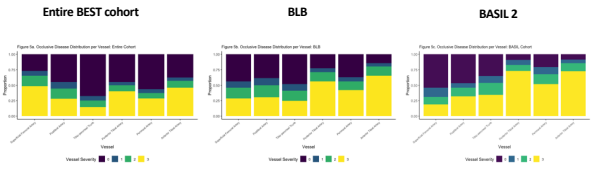
Occlusions



90% 92% 97%

Unpublished Data

Occlusive disease distribution per vessel severity



Unpublished Data

Modified GLASS Anatomic Scoring

BEST-CLI anatomic details	GLASS segment
Superficial femoral - proximal third	fem-pop segment

NOTES

GLASS FP grade 4 occurs if either pop segment =3, or if both pop=1 or 2, or if 2/3 of SFA segments =3

GLASS FP grade 3 occurs if 2/3 of contiguous SFA segments = 1 or 2 or if only 1 segment = 3 or if either pop segment =1 or 2

GLASS FP grade 2 occurs if only 1 SFA segment = 1, 2, or 3, and other SFA segments = 0, 1 and both pop segments = 0,1

GLASS FP grade 1 occurs if only 1 SFA segment = 1, 2, or 3, but other SFA segments and pop segments =0

GLASS IP grade 4 occurs if any single segment in TPT, PTA, peroneal, or ATA =3 or if both segments in PTA, peroneal, or ATA = 1, 2... this does not account for target

GLASS IP grade 3 occurs if TPT = 0,1, 2 and any single segment of PTA, peroneal, ATA = 3 or if TPT = 0,1, 2 and both segments of PTA, personeal, or ATA = 1, 2

GLASS IP grade 2 occurs if TPT = 0 and any single segment of PTA, peroneal, ATA = 1, 2

GLASS IP grade 1 cannot be calculated with current BEST-CLI data

Modified GLASS Score

	BLB	BASIL 2
Stage 1:	6%	28%
Stage 2:	26%	17%
Stage 3:	68%	55%

Unpublished Data

Infrapopliteal Subgroup Analysis in BEST-CLI

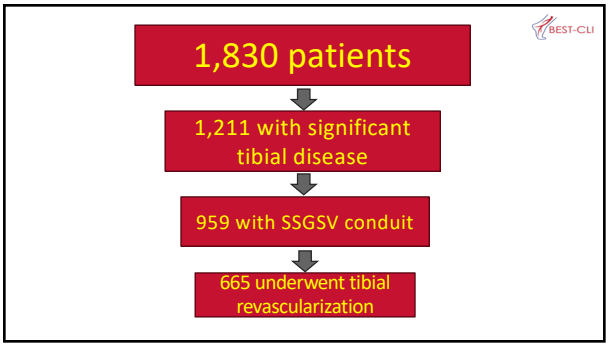
- BEST-CLI patients with

single segment great saphenous vein and

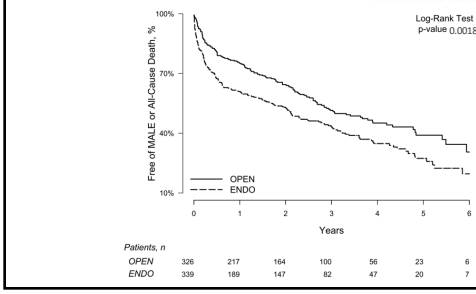
significant *infrapopliteal disease* who

underwent open tibial bypass or endovascular tibial interventions

…to formulate a more precise comparative study for BASIL-2



Freedom from MALE or All-Cause Death



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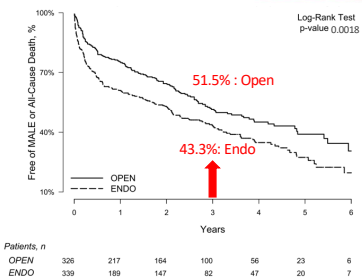
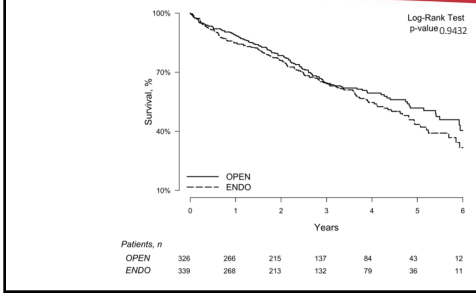


Survival



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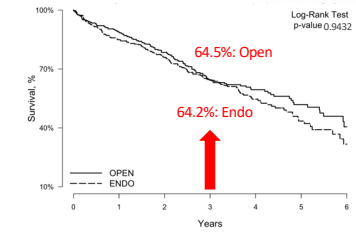
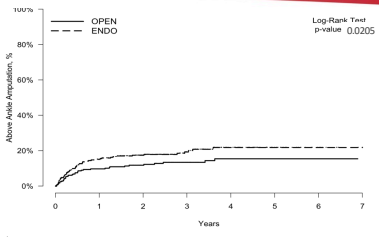


Patients, n

OPEN	326	266	215	137	84	43	12
ENDO	339	268	213	132	79	36	11

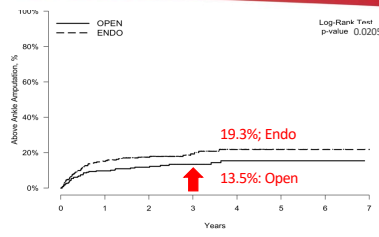
Above-Ankle Amputation



Patients, n

OPEN	326	232	181	111	65	29	9
ENDO	339	231	180	107	61	24	8

Above-Ankle Amputation



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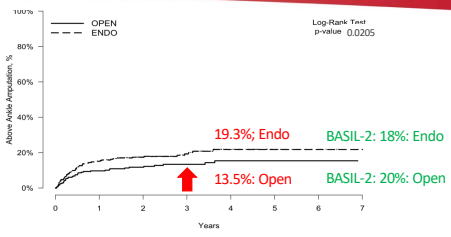

Patients, n

OPEN	326	232	181	111	65	29	9
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Adjusted Outcomes

BEST-CLI

	Surgery (N = 326)		Endovascular (N = 339)			
	N (%)	3-Year	N (%)	3-Year	HR (95% CI) [Open vs Endo]	p-value
MALE or All-Cause Death	**136 (41.72%)**	**48.51%**	**176 (51.92%)**	**56.71%**	**0.69 (0.54, 0.87)**	*0.0018*
MALE	62 (19.0%)	22.9%	109 (32.2%)	35.2%	0.49 (0.35, 0.69)	*<.0001*
All-Cause Death	99 (30.37%)	35.48%	105 (30.97%)	35.76%	1.01 (0.77, 1.33)	0.9432
Major Amputation or All-Cause Death	**120 (36.8%)**	**43.6%**	**136 (40.1%)**	**45.3%**	**0.87 (0.68, 1.13)**	**0.2957**
Major Limb Amputation	37 (11.35%)	13.45%	56 (16.52%)	19.32%	0.59 (0.38, 0.92)	*0.0205*
Reintervention (any), Amputation, or All-Cause Death	177 (54.3%)	60.6%	216 (63.7%)	68.7%	0.71 (0.57, 0.88)	*0.0018*
Major Reintervention	30 (9.20%)	10.93%	63 (18.58%)	20.18%	0.44 (0.27, 0.70)	*0.0006*
MACE	119 (36.5%)	43.2%	123 (36.3%)	43.4%	1.05 (0.81, 1.36)	0.6977

*(Adjusted for age, sex, race, diabetes, ESRD, prior infrainguinal revascularization of index limb, and smoking history)
^ Similar results were obtained using "as treated" methodology for confirmatory analysis

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From the Society for Clinical Vascular Surgery

Surgery or endovascular therapy for patients with chronic limb-threatening ischemia requiring infrapopliteal interventions

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ABSTRACT

Objective: The recent publication of randomized trials comparing open bypass surgery to endovascular therapy in patients with chronic limb-threatening ischemia, namely, Best Endovascular vs Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI) and Bypass versus Angioplasty in Severe Ischaemia of the Leg-2 (BASIL-2), has resulted in potentially contradictory findings. The trials differed significantly with respect to anatomical disease patterns and primary end points. We performed an analysis of patients in BEST-CLI with significant infrapopliteal disease undergoing open tibial bypass or endovascular tibial interventions to formulate a relevant comparator with the outcomes reported from BASIL-2.

Methods: The study population consisted of patients in BEST-CLI with adequate single segment saphenous vein conduit randomized to open bypass or endovascular intervention (cohort 1) who additionally had significant infrapopliteal disease and underwent tibial level intervention. The primary outcome was major adverse limb event (MALE) or all-cause death. MALE included any major limb amputation or major reintervention. Outcomes were evaluated using Cox proportional regression models.

Results: The analyzed subgroup included a total of 665 patients with 326 in the open tibial bypass group and 339 in the tibial endovascular intervention group. The primary outcome of MALE or all-cause death at 3 years was significantly lower in the surgical group at 48.5% compared with 56.7% in the endovascular group ($P = .0018$). Mortality was similar between groups (35.5% open vs 35.8% endovascular; $P = .94$), whereas MALE events were lower in the surgical group (37.3% vs 55.0%; $P < .0001$). This difference included a lower rate of major reinterventions in the surgical group (10.9%) compared with the endovascular group (20.2%; $P = .0006$). Freedom from above ankle amputation or all-cause death was similar between treatment arms at 43.8% in the surgical group compared with 45.3% the endovascular group ($P = .30$); however, there were fewer above ankle amputations in the surgical group (11.5%) compared with the endovascular group (19.5%; $P = .0205$). Perioperative (30-day) death rates were similar between treatment groups (2.5% open vs 2.4% endovascular; $P = .93$), as was 30-day major adverse cardiovascular events (5.3% open vs 2.7% endovascular; $P = .12$).

Conclusions: Among patients with suitable single segment great saphenous vein who underwent infrapopliteal revascularization for chronic limb-threatening ischemia, open bypass surgery was associated with a lower incidence of MALE or death and fewer major amputation compared with endovascular intervention. Amputation-free survival was similar between the groups. Further investigations into differences in comorbidities, anatomical extent, and lesion complexity are needed to explain differences between the BEST-CLI and BASIL-2 reported outcomes. (J Vasc Surg 2024;■:1-10.)

Keywords: Chronic limb-threatening ischemia; Infrapopliteal disease; Tibial bypass; Tibial endovascular intervention; BEST-CLI; BASIL-2; Major adverse limb events; Amputation free survival

Comparison of BEST-CLI and BASIL 2

How do we harmonize BEST-CLI and BASIL 2?

- **Simply combining ITT groups from both trials and comparing OPEN vs ENDO is methodologically flawed**
  - **Populations are different**
    - **Entry life expectancy different**
    - **Comorbidities are different**
    - **Risk of bypass is inordinately high in BASIL 2**
  - **Entry criteria into trials are different**
  - **Primary and secondary endpoints are different**
  - **Ascertainment of endpoints different**

What can we do?

Next Steps

- Prospective, *as-treated*, meta-analysis of BASIL-2 and BEST-CLI
- Using Individual Patient Data and common endpoint (MALE/Death)
  - Assess heterogeneity
  - Try to identify patient/anatomical/procedural factors that drive mortality and limb loss outcomes across both trials
  - Show where there is consistency

Future Efforts

- Obtain actual baseline images from BEST-CLI
- Validate GLASS for BEST-CLI
- Compare performance of Modified GLASS to GLASS in BEST-CLI/BASIL
- GLASS 2.0?