Asymptomatic Carotid Stenosis Stenting v. Endarterectomy Trial (ACT I)

Lawrence R. Wechsler, MD on behalf of the
ACT I Steering Committee and Investigators

Presenter Disclosure Information

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Disclosures:

- ACT I steering committee: Abbott Vascular - Modest
- Scientific Advisory Board: Silk Road Medical - Modest

Background

- RCTs 1980s, 90s suggested CEA superior to medical therapy for asymptomatic stenosis
- Early 2000s comparison of CEA and CAS for mostly symptomatic stenosis – variable results
- CREST study initiated to randomize CEA and CAS for symptomatic stenosis – added asymptomatic stenosis
- ACT I trial initiated in 2005 to randomize only asymptomatic stenosis CEA v. CAS

ACT I Study Design

- Randomized non-inferiority trial of asymptomatic carotid stenosis CAS v. CEA 3:1
- Funded by Abbott Vascular
- 1453 patients enrolled from 2005 – 2013 at 62 sites in US (1089 CAS, 364 CEA)
- Original goal 1658 pts, study halted due to slow enrollment
- Xact stent and Emboshield protection device,
- Patients in both arms received intensive risk factor control
- Prespecified non-inferiority margin based on one-sided upper limit of 95% CI for difference in event rates $\leq$ 3%

ACT I Study Design

- Surgeons and interventionalists reviewed by SMC and IMC
- Lead-in enrollment prior to randomization
- Operations committee to review performance of sites
- All endpoints adjudicated by clinical events committee

Patient Selection

- Age < 80
- No symptoms for at least 180 days
- Asymptomatic status verified by neurologist prior to enrollment
- Standard medical and anatomic risk for surgery
- Stenosis ≥ 70% by ultrasound or angiography
- Stenosis assessed by ultrasound according to core lab standards

Endpoints

- Primary Endpoint
  - ***Stroke, MI, death within 30 days of procedure and ipsilateral stroke 31d – 1 year***

- Secondary Endpoints
  - Device success within 30 d
  - Procedural success within 30 d
  - Composite morbidity measure (CN injury, vasc or wound injury, bleeding, surgical complications)
  - Freedom from clinically driven TLR 6, 12 mo
  - Freedom from ipsilateral stroke yr 2,3,4,5

Demographics

	CAS (N=1089)	CEA (N=364)
Age (mean)	67.7 ± 7.0	67.9 ± 6.9
Male	61.2%	56.9%
Caucasian	90.4%	89.8%
Hypertension	90.6%	89.6%
Hyperlipidemia	90.0%	87.9%
Diabetes	35.6%	32.4%
Smoking	73.7%	71.2%
CAD	53.4%	51.1%
Hx of stroke	6.7%	4.7%
Stenosis (mean)	73.7% ± 8.8	73.9% ± 10.2
Ulcerated	16.2%	14.5%

Primary Endpoint: ITT

- Stroke, MI, death within 30 days of procedure and ipsilateral stroke 31d – 1 year

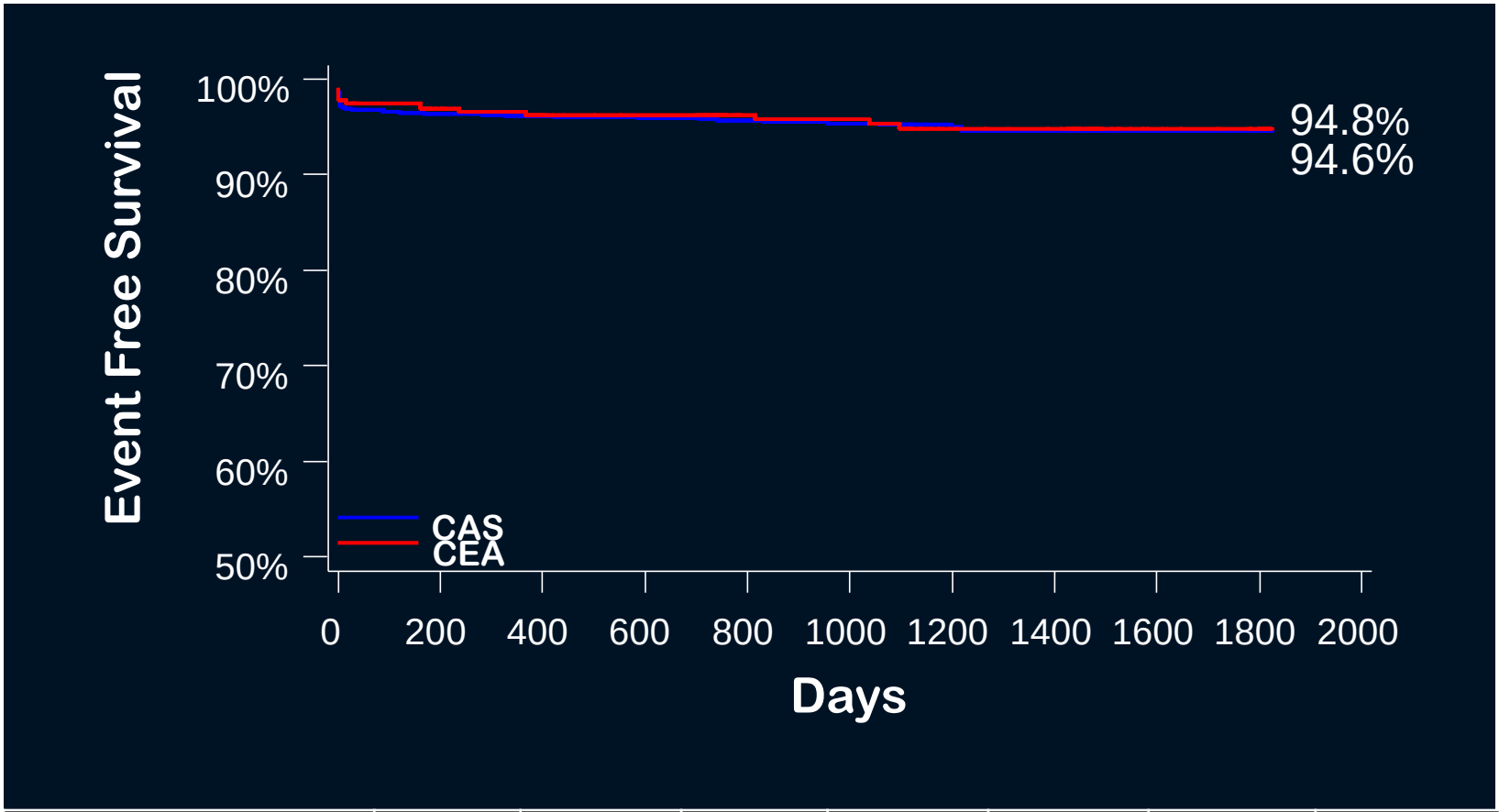
	CAS (N=1089)	CEA (N=364)	Diff	Upper Limit 95% CI	p Value NI
Primary Endpoint	3.8% ± 0.59%	3.4% ± 0.98%	0.4%	2.27 %	0.01

30 Day Outcomes

	CAS	CEA	p
Stroke, MI, Death	3.3%	2.6%	0.60
Stroke, Death	2.9%	1.7%	0.33
Major stroke, Death	0.6%	0.6%	1.00
Major stroke	0.5%	0.3%	1.00
Minor stroke	2.4%	1.1%	0.20
Composite morbidity *	2.8%	4.7%	0.13

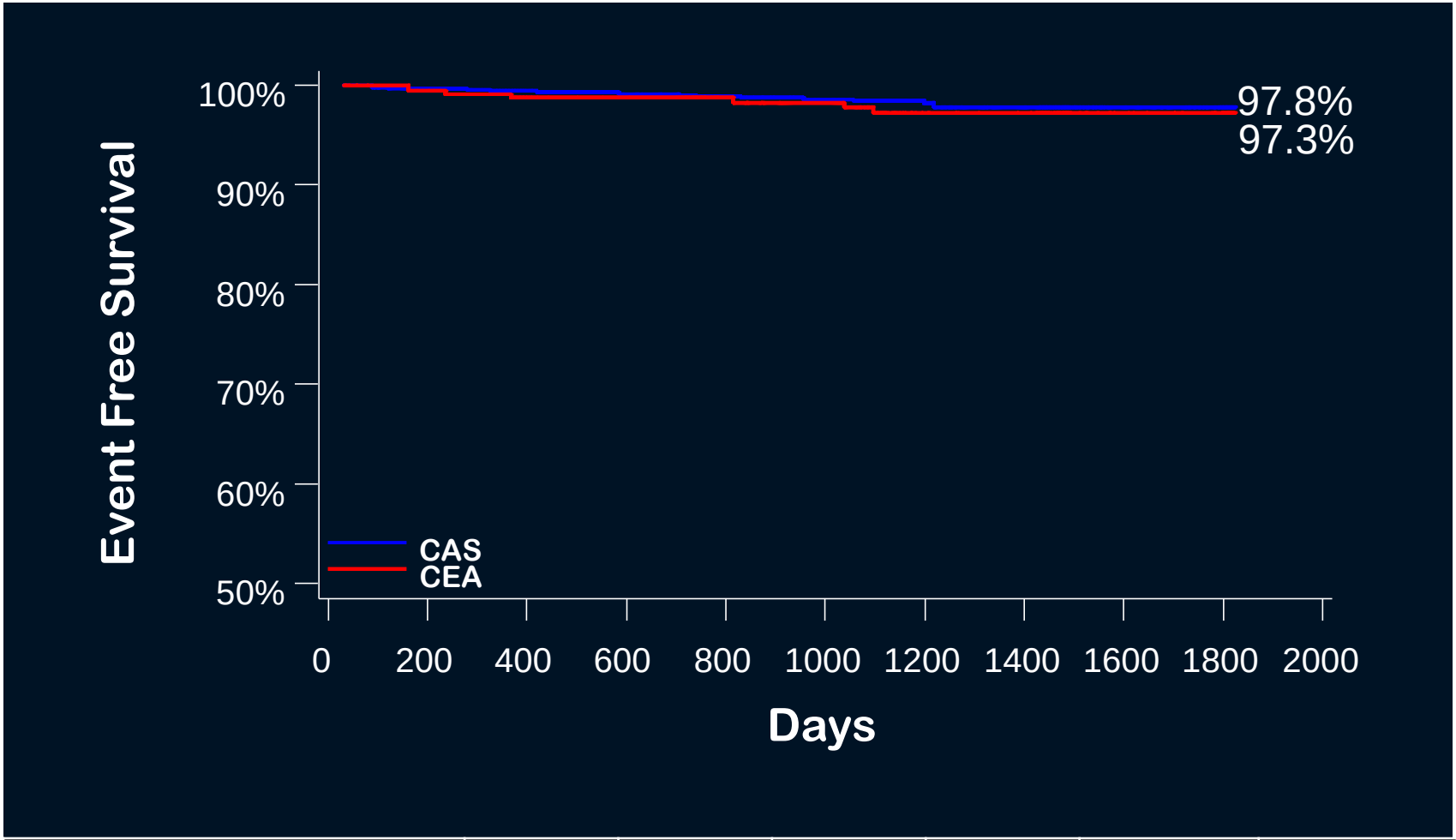
- * Composite morbidity – cranial n. injury, peripheral n. injury, vascular injury, noncerebral bleeding, endarterectomy or puncture site bleeding

Freedom from Death, Stroke and MI within 30 Days and Ipsilateral Stroke 31 Days to 5 Years



Days	0	(0, 30]	(30, 365]	(365, 730]	(730, 1095]	(1095, 1460]	(1460, 1825]
CAS Number at Risk	1089	1067	1016	862	729	544	364
CEA Number at Risk	364	354	325	285	246	182	112

Freedom from Ipsilateral Stroke from 31 Days to 5 Years



Days	31	(31, 365]	(365, 730]	(730, 1095]	(1095, 1460]	(1460, 1825]
CAS Number at Risk	1049	1045	887	751	561	375
CEA Number at Risk	333	333	291	251	185	115

Five Year Outcomes

	CAS	CEA	p[1]
31 d – 5 yr freedom from ipsilateral stroke	97.8%	97.3%	0.51
5 yr freedom from stroke	93.1%	94.7%	0.44
5 yr freedom from clinically driven revascularization	98.4%	96.7%	0.05
5 yr survival	87.1%	89.4%	0.21

[1] Log-rank

ACT I v. CREST (Asymptomatic)

	CAS	CEA	p
ACT I – Primary Endpoint	3.8%	3.4%	0.01[1]
CREST – Primary Endpoint	5.6%	4.9%	0.56[2]
ACT I – 30 d Stroke, MI, Death	3.3%	2.6%	0.60
CREST – 30 d Stroke, MI, Death	3.5%	3.6%	0.96
ACT I – 30 d Stroke, Death	2.9%	1.7%	0.33
CREST – 30 d Stroke, Death	2.5%	1.4%	0.15

[1] 1-sided non-inferiority test
[2] 2-sided superiority test

CREST – 1181 Asx pts: 594 CAS, 587 CEA
ACT I – 1453 Asx pts: 1089 CAS, 364 CEA

Limitations

- Enrollment stopped early due to slow recruitment – power reduced from 80% - 75%
- Medical therapy based on then current guidelines
- No information on patients at participating sites not entered into trial
- Limited data on compliance with medical therapy
- Incomplete long term follow-up

Summary

- For asymptomatic, non-octogenarian, standard surgical and anatomic risk patients with significant carotid stenosis:
  - CAS is non-inferior to CEA for 30 day DSMI and 1 year ipsilateral stroke.
  - CAS and CEA have similar five year rates of stroke and survival.
- CREST 2 addressing question of benefit of revascularization v. medical therapy in asymptomatic stenosis with modern medical management

Thank You

- PIs
  - Kenneth Rosenfield
  - Jon Matsumura
- Steering committee
- Investigators
- Coordinators
- Patients
- Remembering Larry Brass