Pivotal Trial to Evaluate the Safety and Efficacy of the Diamondback 360° Orbital Atherectomy System in Treating *De Novo*, Severely Calcified Coronary Lesions (ORBIT II)

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Potential conflicts of interest

Speaker's name: Jeff Chambers, M.D.

☑ I have the following potential conflicts of interest to report:

Consultant: Cardiovascular Systems Inc., MN, USA

CEC: Boston Scientific

ORBIT II Study Design

- To evaluate safety and efficacy of coronary OAS to prepare *de novo,* severely calcified coronary lesions for stent placement
  - Prospective, multi-center trial
  - Single arm - FDA recommendation as there are no FDA-approved percutaneous treatments for patients with severely calcified lesions

443 patients enrolled in 49 US sites

↓

30 day follow-up

↓

Complete in 99.3% (N=437/440)

Primary Safety Endpoint: 30-Day MACE

- MI (CK-MB >3x ULN), TVR, cardiac death

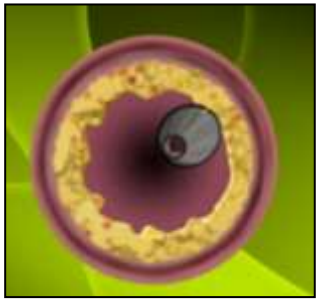
Primary Efficacy Endpoint: Procedural Success

- Success in facilitating stent delivery with a final residual stenosis of <50% (as determined by Angiographic Core Lab) and without in-hospital MACE

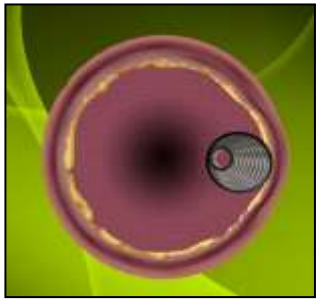
Unique Mechanism of Action

Differential Sanding

Crown will only sand the hard components of plaque

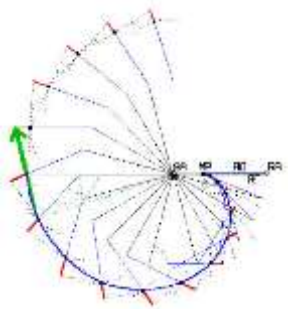


Soft components (plaque/tissue) flex away from crown



Differential Orbital Sanding

- **Orbital mechanism[1]:**
  - Increased speed = Increased centrifugal force
  - Greater centrifugal force = Larger orbital diameter
- **One crown treats different vessel diameters based on speed[1]**
- **Continuous flow of blood and saline**
  - Potentially minimizes thermal injury[1,2]
  - Potentially decreases no-reflow[3]



1. Himmelstein, et al., 2008. Supplement to Endovascular Today, Summer.
2. Adams, et al., 2011. J Cardiovasc Transl Res. 2011 Apr;4(2):220-9.
3. Orbit II data on file at CSI.

Actual results may vary depending on device-to-lumen ratio, run time and speed, and plaque morphology.

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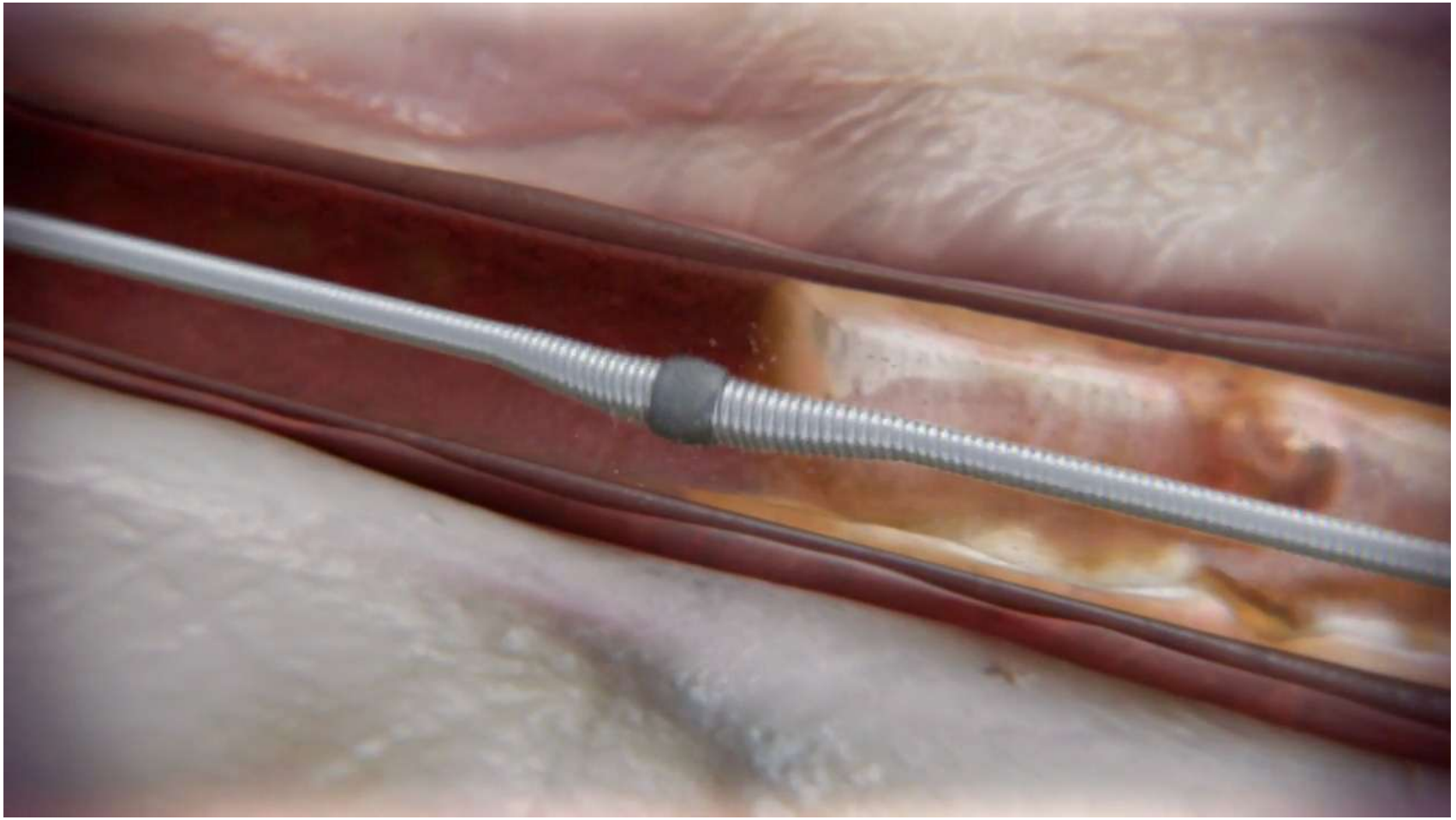
Coronary OAS Mechanism Of Action



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Inclusion/Exclusion Criteria

Key Inclusion:

- The target lesion must have fluoroscopic or IVUS evidence of **severe calcium**:
  - Presence of radiopacities noted without cardiac motion prior to contrast injection involving both sides of the arterial wall with calcification length of **at least 15 mm** and extend partially into the target lesion
  - OR presence of **≥ 270° of calcium** at one cross section via IVUS
- The target vessel reference diameter **≥ 2.5 mm and ≤ 4.0 mm** and lesion must not exceed **40 mm** in length

Key Exclusion:

- Diagnosed with chronic renal failure (CR >2.5 mg/dl) **unless under hemodialysis**
- Evidence of current **LVEF ≤25%**
- More than 1 lesion requiring intervention unless the lesions are staged
- In-stent treatment
- Target lesion is an **ostial location, bifurcation or has a ≥ 1.5 mm side branch**
- Target lesion has **thrombus or dissection**

ORBIT II: Demographics & Characteristics

Demographics	N=443
Male	64.6%
Age (yrs)	71.4
History of diabetes mellitus	36.2%
History of CABG	14.7%
History of dislipidemia	91.9%
History of hypertension	91.6%
Smoker (current or previous)	66.1%
Vessel & Lesion Characteristics	**N=440**
Mean pre-procedure target lesion length	18.9 mm
Mean pre-procedure minimum lumen diameter	0.5 mm
Mean pre-procedure percent stenosis	84.4%
Subjects with severely calcified lesions	99.3%
Subjects with calcification determined by IVUS	8.0%

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Procedural Results

Parameter	Result
Subjects treated with Pre-OAS balloon dilations	1.8%
Subjects treated with Post-OAS/Pre-Stent balloon dilations	41.1%
Mean maximum inflation pressure	12.1 ± 0.3 atm
Subjects with stent placed	98.2%
Mean stents used per subject	1.3 ± 0.0
Mean maximum deployment pressure	**13.8 ± 0.2 atm**
Subjects treated with post stent balloon dilitation	51.6%
Total mean interventional fluoroscopy time (includes diagnostic)	18.2 ± 0.6 mins
Total mean interventional volume of contrast used (includes diagnostic)	173.9 ± 4.1 ml
Core lab assessed final procedure mean minimum lumen diameter	**2.9 ± 0.0 mm**
Core lab assessed final procedure mean stenosis	**4.7 ± 0.7 %**

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Angiographic Complications

Criteria	Prior to OAS	Post OAS	Post Balloon/Stent	Unknown	Overall N=443
Subjects with severe angiographic complications					**7.2%**
Dissection Type C- F	0.2%	**2.3%**	0.9%	0.0%	**3.4%**
Perforation	0.0%	**0.9%**	0.9%	0.0%	**1.8%**
Slow flow & Persistent no reflow	0.2%	**0.2%**	0.5%	0.0%	**0.9%**
Abrupt closure	0.2%	**0.9%**	0.2%	0.5%	**1.8%**

Factors analyzed for predictors of angiographic complications:

- Total OAD run time
- Average reference vessel diameter
- Percent stenosis
- OAD size used (OR for 0.1 unit increase)
- Number of balloon/stent inflations used (post OAD)
- Size of the balloon/stent used relative to the average reference vessel diameter (post OAD)- (OR for 0.1 unit increase)
- Length of calcium
- Highest stent deployment pressure used (post OAD)

Univariable Analysis	OR [95% CI]	P-value
Lesion length (investigator assessed)	**1.04 [1.00, 1.08]**	**0.0298**
Highest deployment pressure during stent procedure	**1.16 [0.99, 1.35]**	**0.0710**
Length of calcium	**1.02 [1.00, 1.04]**	**0.0717**
OR>1: Increase in the odds of angiographic complication with an increase of one unit in predictor.		

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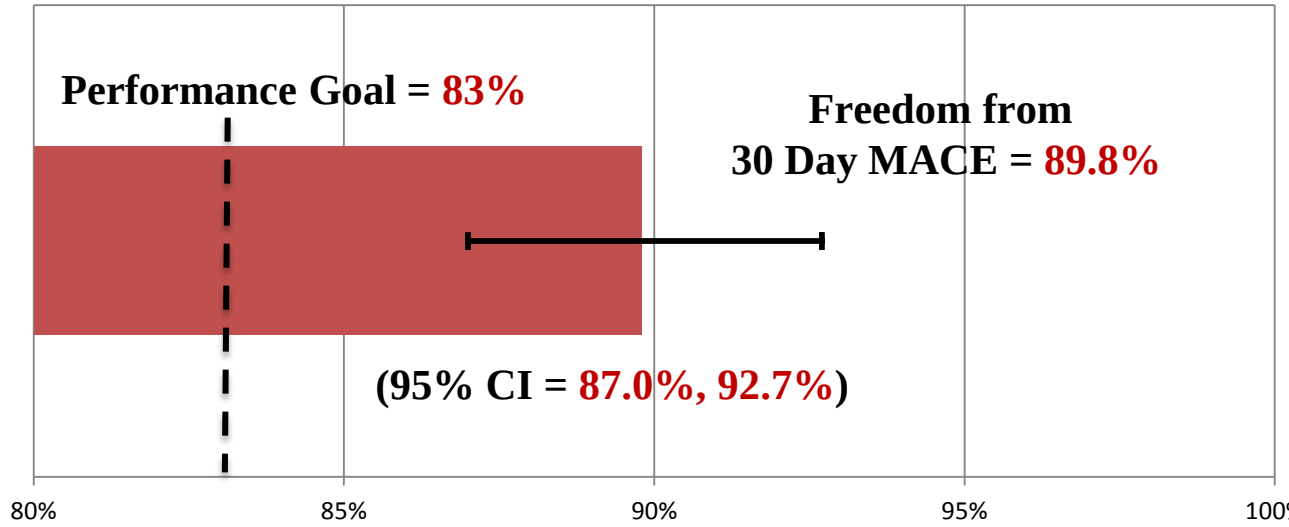
ORBIT II: Primary Safety Endpoint

30 Day MACE Rate Components:

MI (CK-MB >3x ULN):	**9.7%**
Non Q-wave	8.8%
Q-wave	0.9%
TVR/TLR:	**1.4%**
TVR	0.7%
TLR	0.7%
Cardiac death:	**0.2%**



Results based on Clinical Events Committee adjudication

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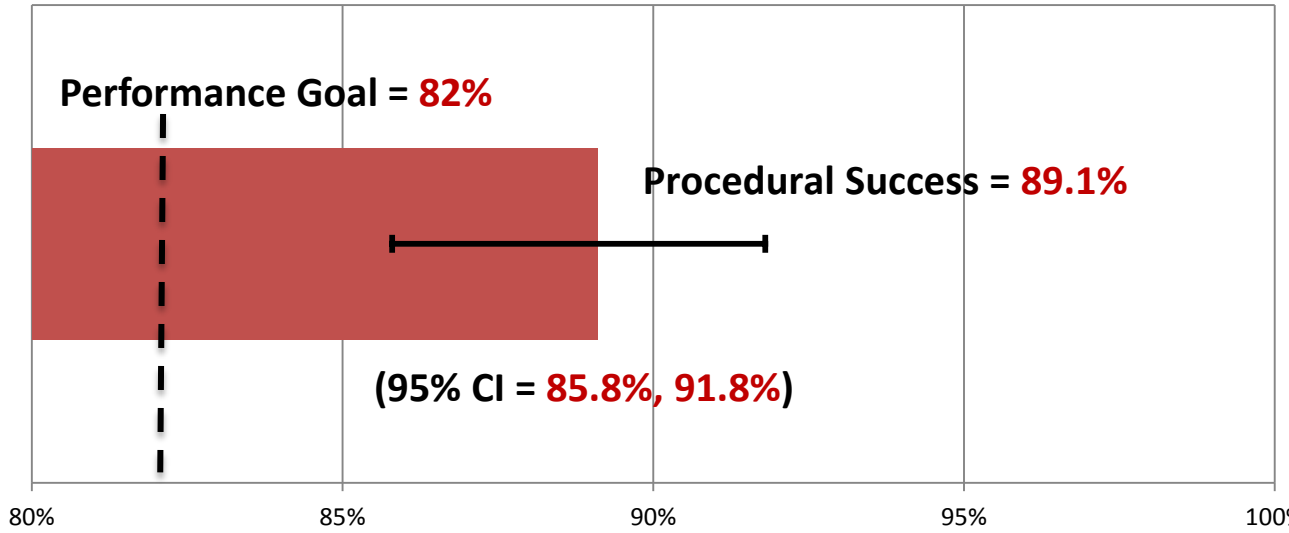
ORBIT II: Primary Efficacy Endpoint

Procedural Success Components:

Successful Stent delivered:	**97.7%**
Less than 50% residual stenosis:	**98.6%**
In hospital MACE:	**9.5%**
MI (CK-MB >3x ULN):	**9.3%**
Non Q-wave	8.8%
Q-wave	0.9%
TVR:	**0.7%**
Cardiac death:	**0.2%**



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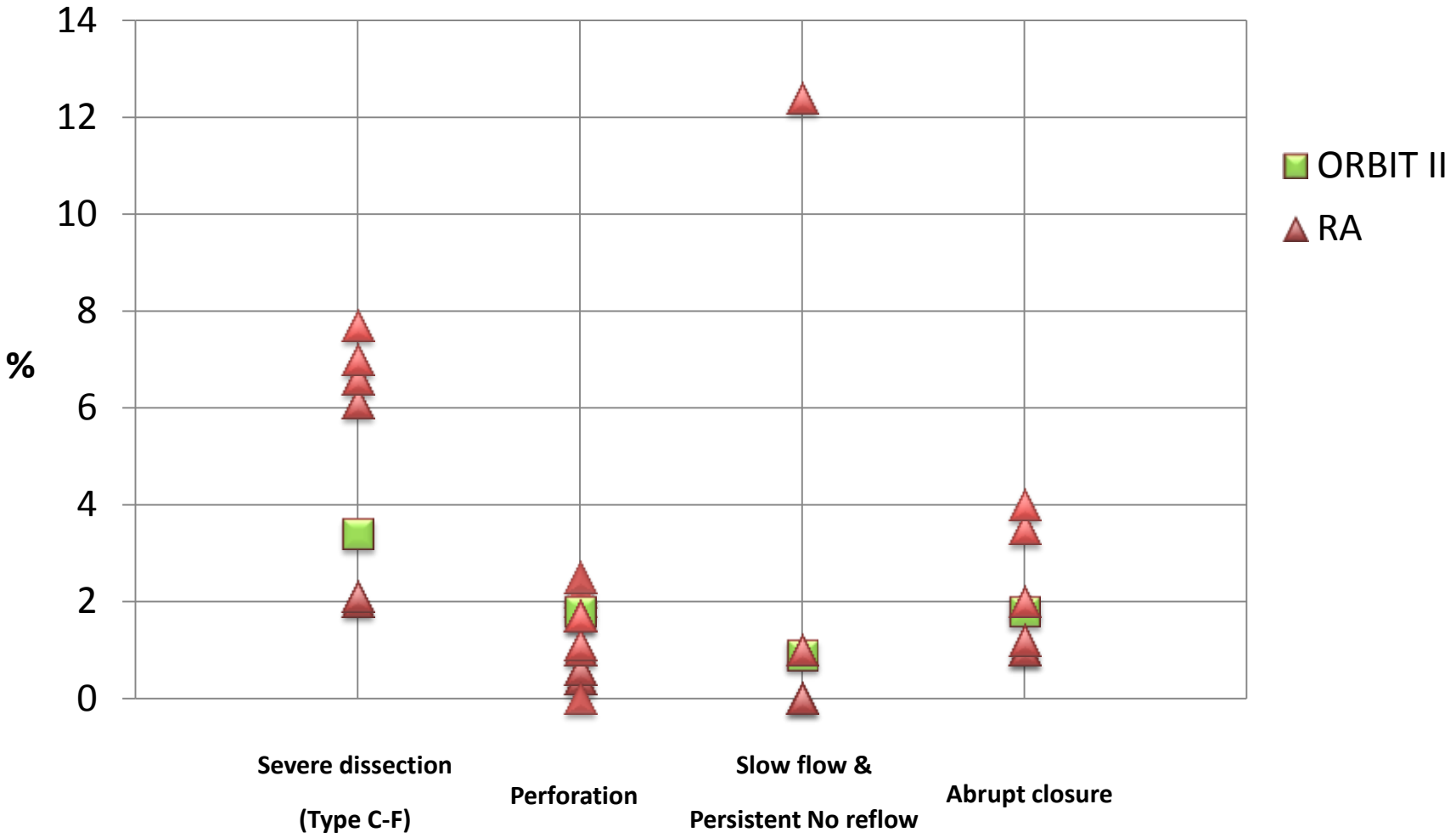
Angiographic Complications Compared to Rotational Atherectomy Literature (RA)[1]



1. RA References: Abdel-Wahab (2013), Albertal (2001), Bersin (1999),Brown (1997),Clavijo (2006), Furuichi (2009), Garcia de Lara (2010), Henneke (1999), Levin (1998), Mauri (2003), Rathore(2010), Reisman (1997), Tsubokawa (2003). Note: some references did not report all complications listed on table.

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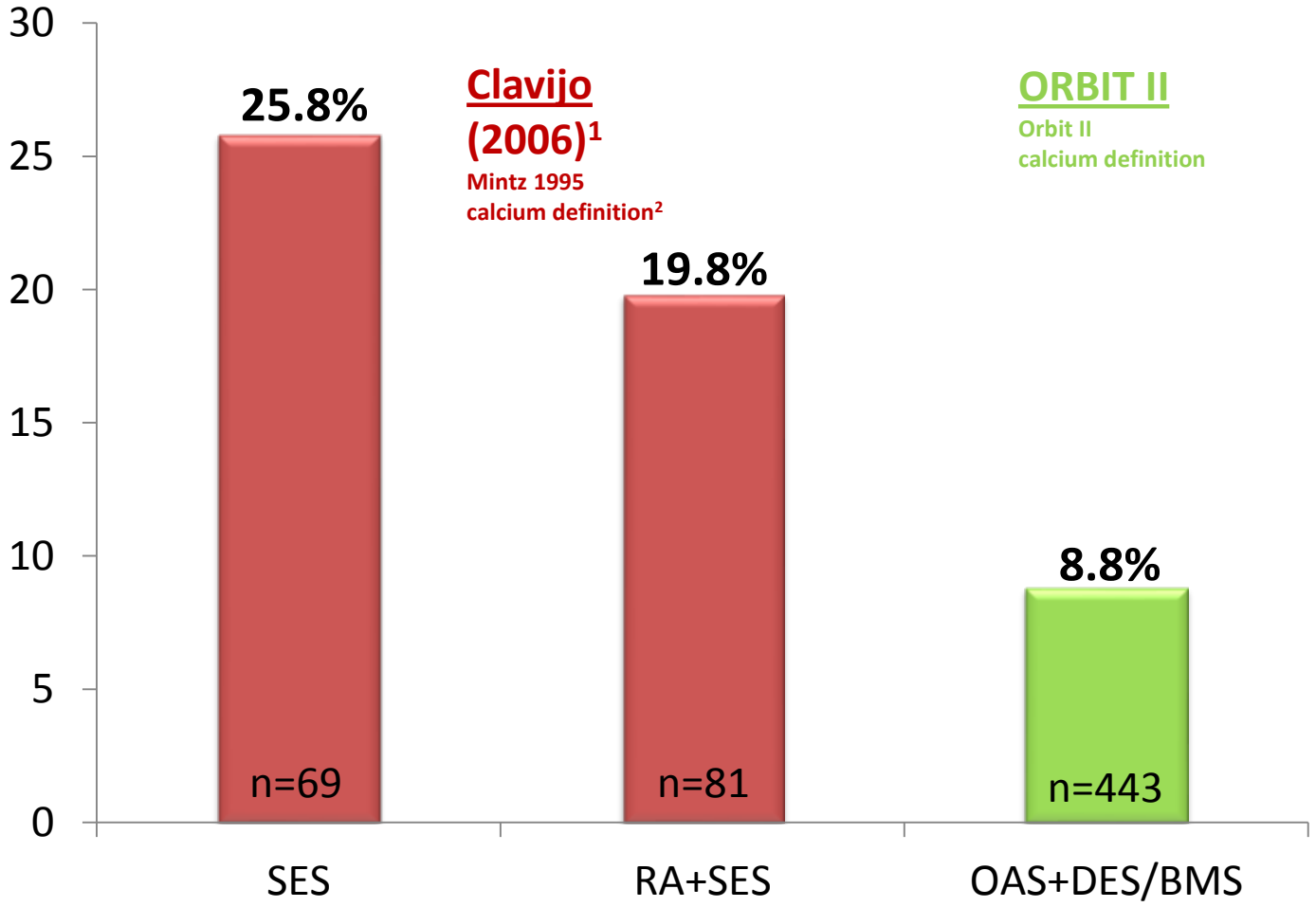
Non-Q-Wave MI in Severely Calcified Lesions (CK-MB>3X ULN)



1. Clavijo, et al. Catheterization and Cardiovascular Interventions. 2006. 68:873–878
2. Mintz G, et al. Patterns of Calcification in Coronary Artery Disease. Circulation. 1995;91(7):1959-1965.

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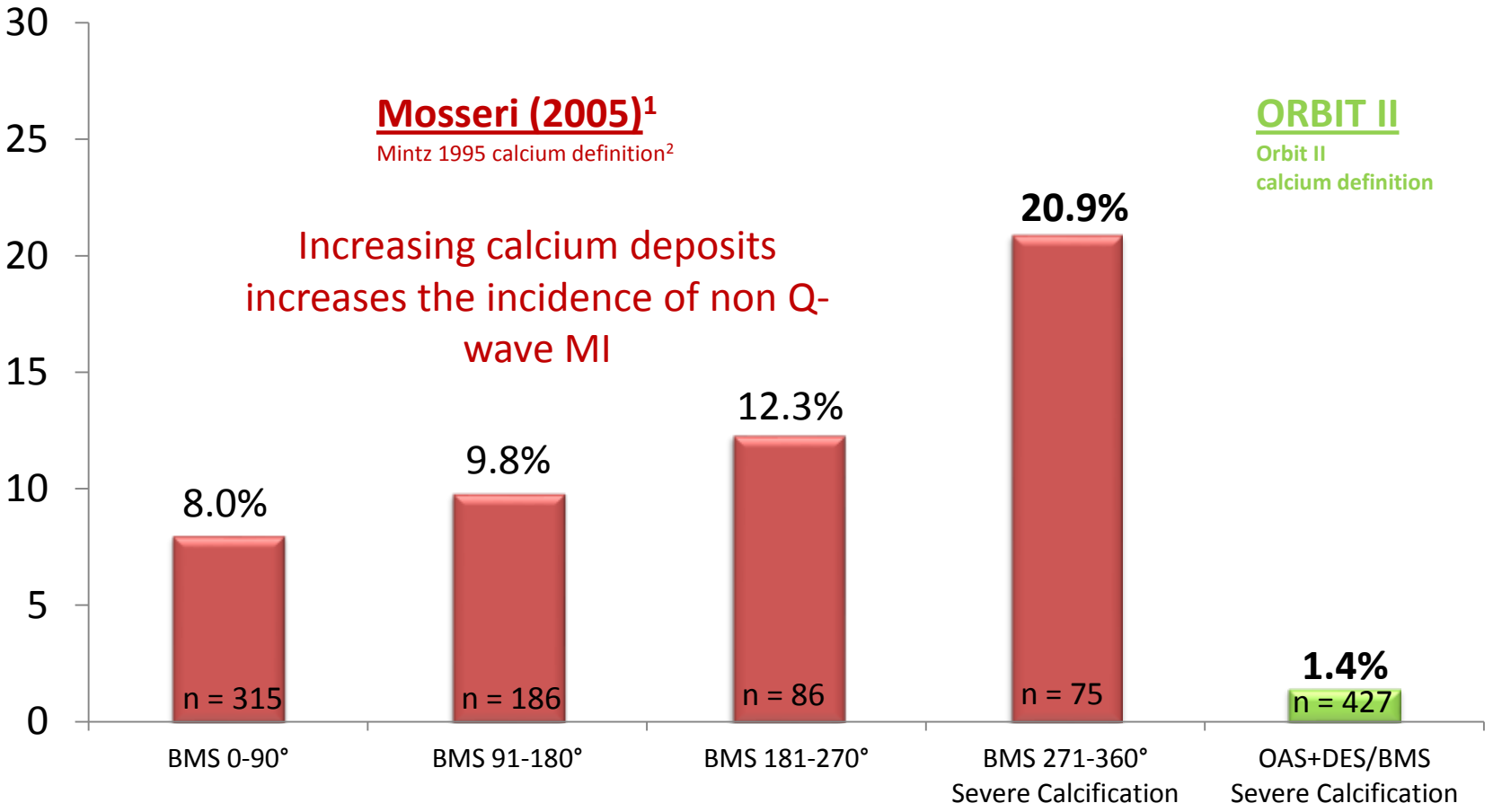
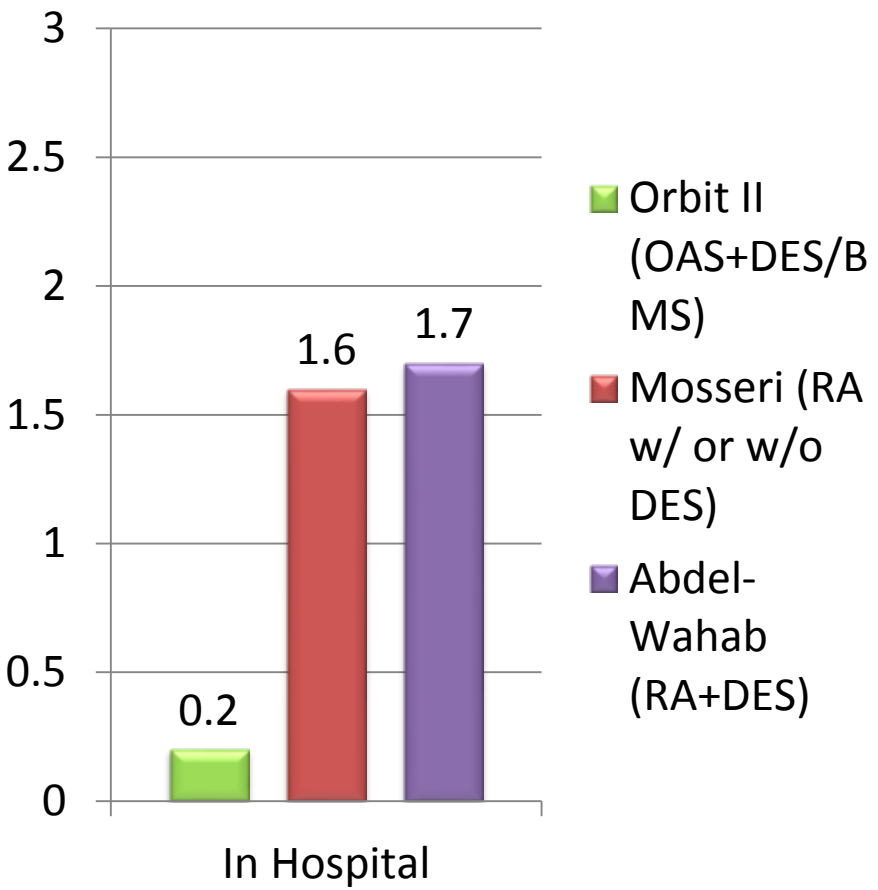
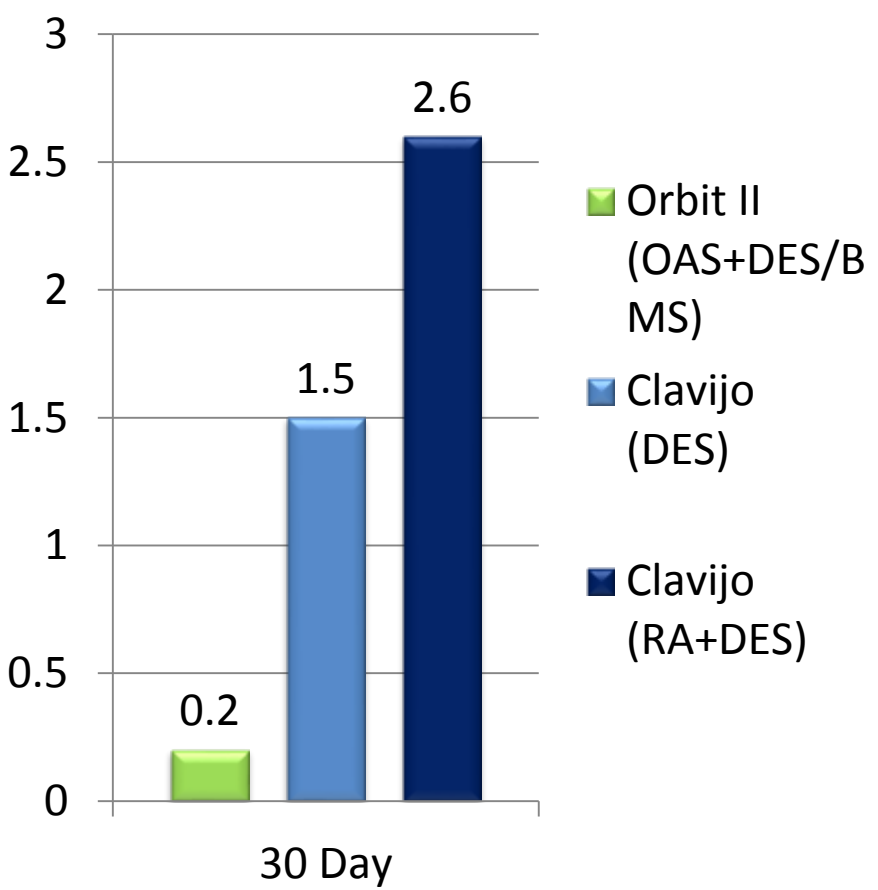
Non-Q-Wave MI in Severely Calcified Lesions (CK-MB>20% of total CK)



1. Mosseri, et al. Cardiovascular Revascularization Medicine. 2005. 6:147-153.
2. Mintz G, et al. Patterns of Calcification in Coronary Artery Disease. Circulation. 1995;91(7):1959-1965.

Death Rates in Severely Calcified Lesions





1. Clavijo, et al. Catheterization and Cardiovascular Interventions. 2006. 68:873–878
2.Mosseri, et al. Cardiovascular Revascularization Medicine. 2005. 6:147-153.
3. Abdel-Wahab, et al. JACC Cardiovasc Interv. 2013 Jan;6(1):10-9..

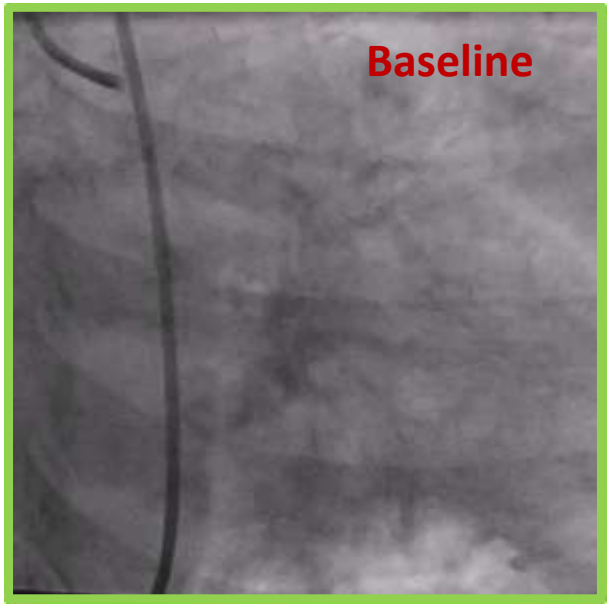
ORBIT II Case Study

euro PCR 2013

Female, 70 years old

History of DM, smoker, dyslipidemia, HTN, EF 50%, Positive stress test

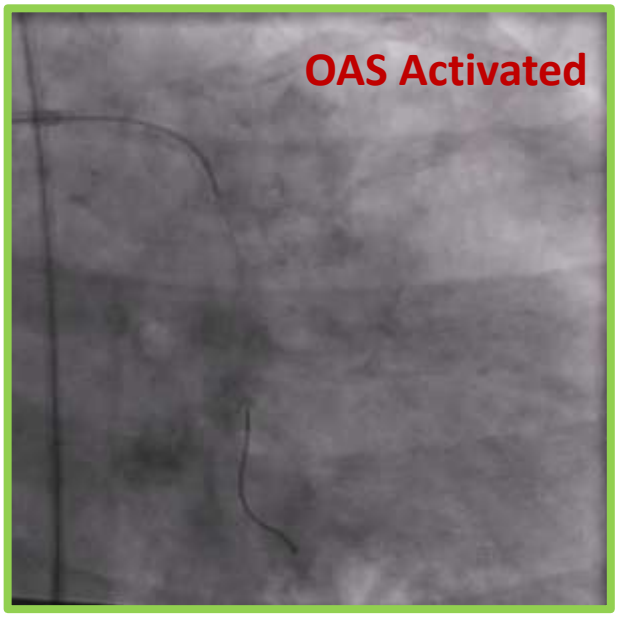
LCX Lesion length 24 mm

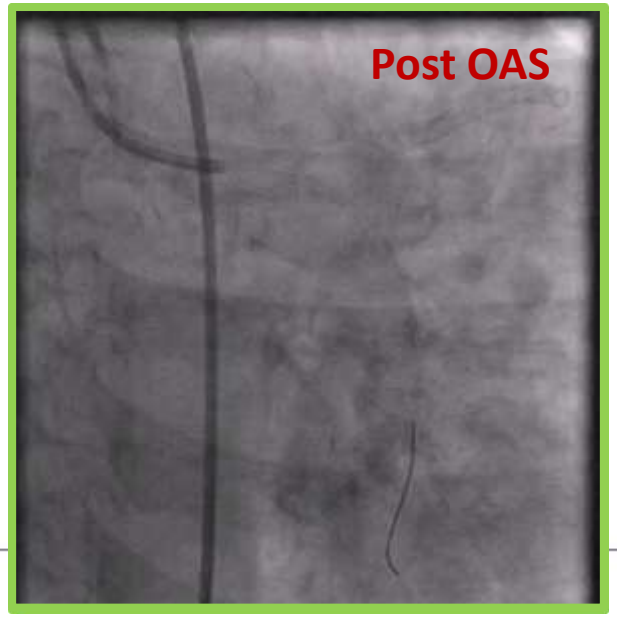


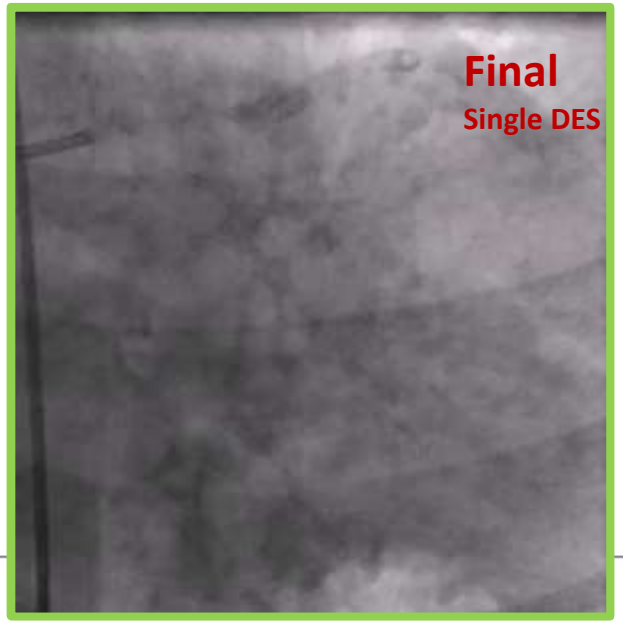
1.25 mm Crown With Electric OAD

Low Speed, 15 Seconds

High Speed, 15 Seconds







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Conclusion

- ORBIT II was unique in enrolling only patients with severely calcified coronary arteries
- The ORBIT II trial met the primary safety and efficacy endpoints by a significant margin
- The improvement in clinical outcomes might be attributed to the unique mechanism of action of OAS
- **OAS is a unique technology that appears to address an unmet need for this difficult to treat patient population**