EBC Main Update: Clinical Evidence with Resolute Onxy DES

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Disclosure

- **None**

Bifurcation PCIs, including the left main, are prevalent and complex

BIFURCATION PCI

~30% of PCIs involve a bifurcation[1]

Bifurcation lesions have **COMPLEX GEOMETRY**[2]

SIDE BRANCH OCCLUSION is a common complication[3]

STENT OPTIMISATION in the main branch, without compromising the side branch, is required[3]

LEFT MAIN (LM) BIFURCATION

70% of left main diameters are 4.5–5.75mm[4]

More than **80%** of LM disease involves the bifurcation[5]

UNIQUE CHALLENGES including wider bifurcation angles, large side branches, and additional calcification and fibrosis[6]

LIMITED EVIDENCE EXISTS to inform best treatment strategies[6]

The optimal treatment strategy for true left main bifurcations remains a highly debated topic

[1]Von Birgelen C, et al. *Lancet*. 2018;392:1235-1245. [2]Onuma et al. *EuroIntervention* 2019;14:e1568-e1577.
[3]Gwon, Hyeon-Cheol. *Korean Circ J*. 2018;48:481-491. [4]Estimations adapted from an analysis of 125 patients, Shand CCI 2014; 84:351-358.
[5]Rab T, et al. *JACC Cardiovasc Interv*. 2017;10:849-865. [6]Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

2018 ESC/EACTS Guidelines

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 87–165
doi:10.1093/eurheartj/ehy394

2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

16.3 Specific lesion subsets

16.3.1 Bifurcation stenosis

A number of RCTs have investigated the optimal intervention strategy in patients with bifurcation lesions and showed no benefit for the systematic two-stent approach vs. main branch-only stenting with provisional stenting of the side branch in terms of clinical outcomes.[617] A recent pooled analysis of two RCTs showed lower 5 year survival in patients randomized to a systematic two-stent approach.[618] In addition, procedure time, contrast volume, radiation exposure, and cost are higher with a two-stent approach.[618] The EBC TWO (European Bifurcation Coronary TWO) trial found no difference between a provisional T-stent strategy and a systematic two-stent strategy (culotte technique) in terms of the composite endpoint of death, MI, and TVR at 12 months among 200 patients with large-calibre true bifurcation lesions (side branch diameter ≥2.5 mm) and significant ostial disease length (≥5 mm).[619] Thus, main branch-only stenting with provisional stenting of the side branch should be the preferred approach for most bifurcation lesions. Exceptions to this rule, where upfront side branch stenting may be preferable, include the presence of a large side branch (≥2.75 mm) with a long ostial side branch lesion (>5 mm) or anticipated difficulty in accessing an important side branch after main branch stenting, and true distal LM bifurcations.

Recently, a multicentre trial conducted in China directly compared a double-kissing crush two-stent strategy with provisional stenting of the main branch in 482 patients with distal LM bifurcation disease. Double-kissing crush resulted in a lower risk of the primary endpoint target lesion failure at 1 year compared with provisional stenting.[620]

When a two-stent strategy is necessary, which two-stent technique should be preferred is debated. The three most widely used contemporary two-stent techniques are culotte, crush (classic or double-kissing crush), and T and protrusion (TAP).[621,622] Several RCTs have compared these techniques. In non-LM bifurcation lesions, there is no compelling evidence that one technique is superior to the others in terms of major clinical endpoints.[621,622] In LM true bifurcation lesions, double-kissing crush has the most favourable outcome data.[623]

Recommendations on specific lesion subsets

Recommendations	Class[a]	Level[b]
Stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch, is recommended for PCI of bifurcation lesions.[654–658]	I	A
Percutaneous revascularization of CTOs should be considered in patients with angina resistant to medical therapy or with a large area of documented ischaemia in the territory of the occluded vessel.[629,659–663]	IIa	B
In true bifurcation lesions of the left main, the double-kissing crush technique may be preferred over provisional T-stenting.[620]	IIb	B

2018 ESC/EACTS Guideline on Myocardial Revascularization

DKCRUSH-V Trial

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ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2017.09.1066

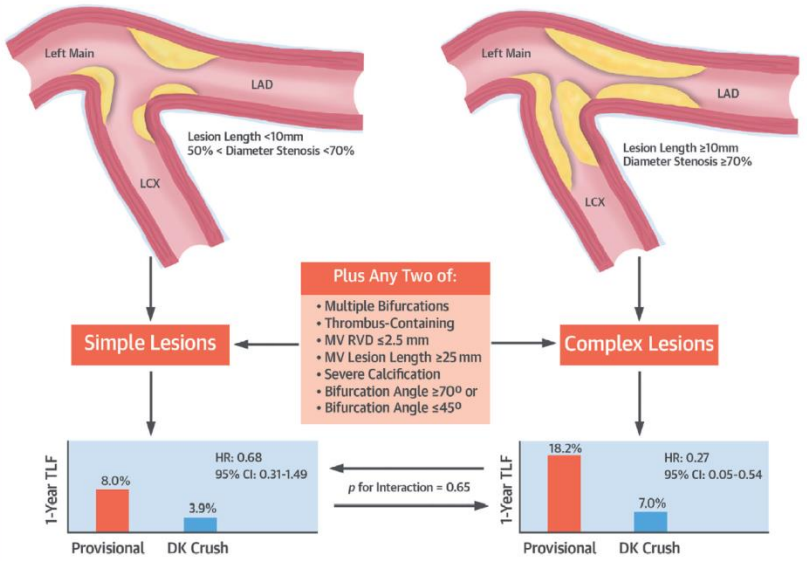
ORIGINAL INVESTIGATIONS

Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions

DKCRUSH-V Randomized Trial

Shao-Liang Chen, MD,[a] Jue-Jie Zhang, PHD,[a] Yaling Han, MD,[b] Jing Kan, MBBS,[a] Lianglong Chen, MD,[c] Chunguang Qiu, MD,[d] Tiemin Jiang, MD,[e] Ling Tao, MD,[f] Hesong Zeng, MD,[g] Li Li, MD,[h] Yong Xia, MD,[i] Chuanyu Gao, MD,[j] Teguh Santoso, MD,[k] Chootopol Paiboon, MD,[l] Yan Wang, MD,[m] Tak W. Kwan, MD,[n] Fei Ye, MD,[o] Nailiang Tian, MD,[o] Zhizhong Liu, PHD,[a] Song Lin, MD,[o] Chengzhi Lu, MD,[p] Shangyu Wen, MD,[q] Lang Hong, MD,[r] Qi Zhang, MD,[s] Imad Sheiban, MD,[t] Yawei Xu, MD,[u] Lefeng Wang, MD,[v] Tanveer S. Rab, MD,[w] Zhanquan Li, MD,[x] Guanchang Cheng, MD,[y] Lianqun Cui, MD,[z] Martin B. Leon, MD,[aa] Gregg W. Stone, MD[aa]

CENTRAL ILLUSTRATION Stenting for LM Bifurcations



Chen, S.-L. et al. J Am Coll Cardiol. 2017;70(21):2605-17.

EBC MAIN

ESC European Society of Cardiology

European Heart Journal (2021) **42**, 3829–3839
doi:10.1093/eurheartj/ehab283

FASTTRACK CLINICAL RESEARCH
Ischaemic heart disease

The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN)

David Hildick-Smith [1,*], Mohaned Egred [2], Adrian Banning [3], Philippe Brunel[4], Miroslaw Ferenc [5], Thomas Hovasse[6], Adrian Wlodarczak [7], Manuel Pan[8], Thomas Schmitz[9], Marc Silvestri[10], Andreis Erglis[11], Evgeny Kretov[12], Jens Flensted Lassen[13], Alaide Chieffo [14], Thierry Lefèvre[6], Francesco Burzotta [15], James Cockburn[1], Olivier Darremont[16], Goran Stankovic [17], Marie-Claude Morice[6], and Yves Louvard[6]

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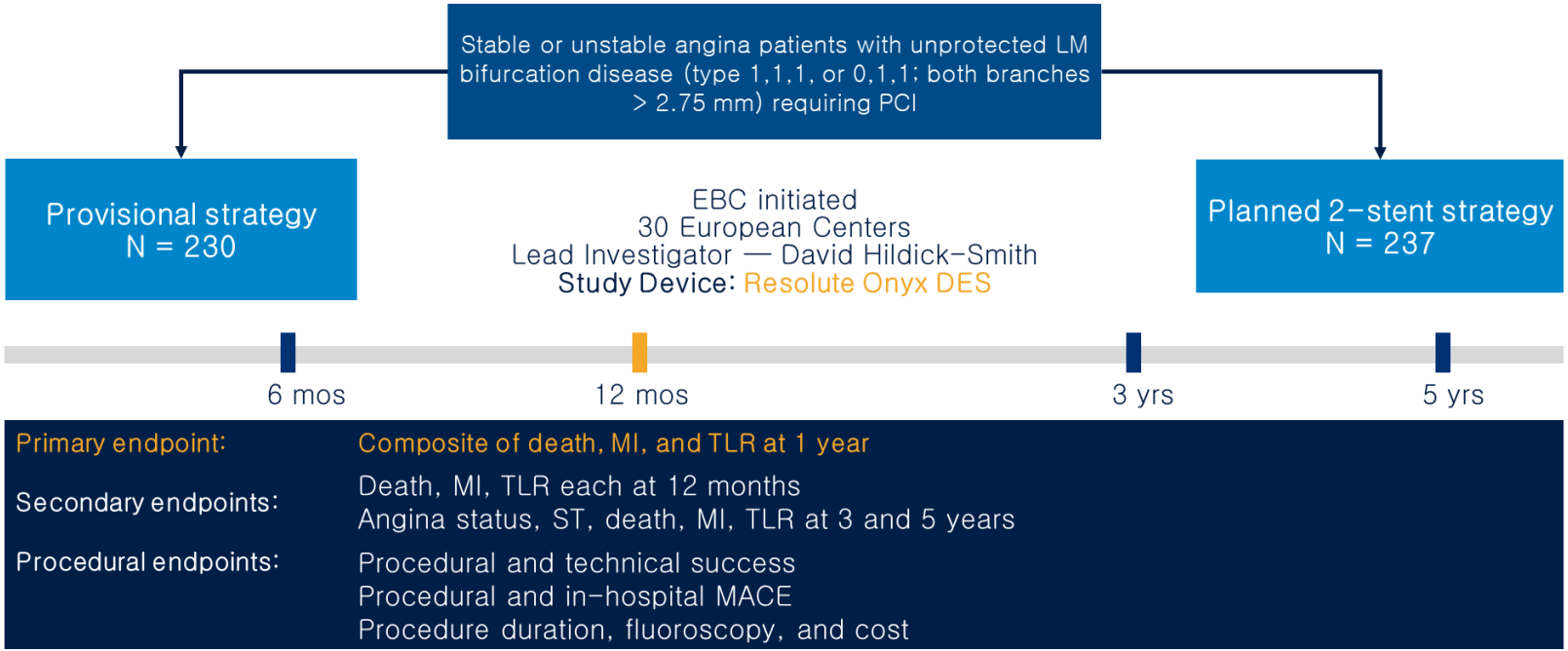
Study Design

PROVISIONAL STRATEGY VS. DUAL-STENT STRATEGY USING RESOLUTE ONYX™ DES IN TRUE BIFURCATION LM DISEASE EBC MAIN STUDY



Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

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Study Design

Main inclusion criteria

- Bifurcation distal left main stem stenosis > 50%
- True bifurcation lesion type 1,1,1 or 0,1,1
- LAD and LCx diameter both ≥ 2.75mm
- Unprotected left main

Main exclusion criteria

- Acute STEMI
- Cardiogenic shock
- CTO of either vessel
- Trifurcation, LM stem > 5.75mm
- Allergy, terminal stage

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

Definition of the provisional and systematic dual stent Strategies

Provisional Strategy:

- Step-by-step layered technique
- According to EBC Consensus (2009-15)
- POT mandated
- Kiss mandated

Systematic Dual-Stent Strategy:

- Operator choice of technique (T, TAP, Culotte, DK Crush)
- Step-by-step approach
- According to EBC Consensus (2009-15)
- High pressure “ostial” bifurcation dilatations
- Kiss mandated after second stent, final POT optional

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

Detailed Description for stepwise provisional single stent

The protocol specified the procedural steps for this group of patients. Coronary guide wires were passed to the left anterior descending (LAD) and circumflex (Cx)/intermediate arteries, respectively. One was designated the main vessel and one the side vessel. Lesion preparation was undertaken as required but side vessel predilatation was discouraged unless considered essential by the operator, to reduce the risk of an unsecured dissection. Stenting of the main vessel was undertaken with a wire jailed in the side vessel to preserve side vessel flow and access. Stent diameter was chosen according to the diameter of the main vessel immediately distal to the bifurcation. Following stenting of the left main into the main vessel, the left main stent was dilated to the carina with a short non-compliant balloon of appropriate size for the left main stem (proximal optimization technique, POT). Following this, the side vessel was rewired through a distal stent strut where possible, and a kissing balloon inflation was undertaken. Kissing balloon sizes were chosen according to the diameter of the distal main and side vessel respectively, with individual higher pressure inflation followed by a final lower pressure kiss dilatation. The left main stent was then dilated using either low pressure dilatation of the kissing balloon pair or a separate individual balloon. For these dilatations, non-compliant balloons were preferred to limit the risk of dissection through uneven expansion. Following kissing dilatation, the side vessel was not to be treated further unless there was one of the following: <TIMI 3 flow in the side vessel, severe (>90%) ostial pinching of the side vessel, threatened side-vessel closure or side-vessel dissection >type A. Under these circumstances, the operator could choose to implant a side vessel stent in a manner of their choosing (e.g. T, TAP, culotte). Following implantation of a second stent, repeat POT followed by recrossing and repeat kissing balloon inflation was mandatory, again using non-compliant balloons as above, with individual very high pressure inflations at the stent bifurcations followed by final kissing balloons at lower pressures. Further treatment to proximal or distal aspects of the main vessel or side vessel could be continued at the discretion of the operator in the event of, for example, proximal or distal dissections.

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

COMPLEX patients and lesions reflective of real-WORLD, left main BIFURCATION PCI

PATIENT CHARACTERISTICS

Patient characteristics	Provisional (n = 230)	Planned 2–Stent (n = 237)
Age	70.8	71.4
Male	79%	74%
Diabetes	29%	27%
Hypertension	79%	82%
Hypercholesterolemia	70%	72%
Ischaemic symptoms	97%	95%
Previous MI	26%	28%
Previous PCI	41%	43%
Acute coronary syndrome	**33%**	**40%**
Syntax score, mean	22.6	23.2

LESION CHARACTERISTICS

Lesion characteristics	Provisional (n = 230)	Planned 2–Stent (n = 237)
Moderate/severe calcification	**44%**	**54%**
Moderate/severe tortuosity	19%	24%
Lesion location	29%	27%
LM/LAD	77%	77%
LM/LCX	23%	23%
Medina classification	20%	20%
1.1.1	**90%**	**89%**
0.1.1	10%	11%

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

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High procedural success with provisional and dual-stent strategy performed according to EBC consensus

PROCEDURAL CHARACTERISTICS

Procedural characteristics	Provisional (n = 230)	Planned 2–Stent (n = 237)
Imaging		
IVUS	36%	31%
FFR	4%	7%
OCT	4%	1%
POT after first stent	85%	87%
KBT after first stent	89%	6%
Side branch stented	**22%**	**94%**
Implantation technique		
Provisional single stent	99%	5%
Culotte	N/A	53%
T or TAP	N/A	33%
DK Crush	N/A	5%

Procedural characteristics	Provisional (n = 230)	Planned 2–Stent (n = 237)	P value
Stented length	25 mm	32 mm	< 0.001
No. stents at bifurcation	1.6	2.3	< 0.001
Procedure duration, min	74	80	0.049
Fluoroscopy duration, min	21	24	0.02
Technical success*	88%	89%	
Procedural success†	**97%**	**92%**	

*Technical success: Completion of stent placement, balloon dilatation, rewiring, and final kissing balloon therapy as required by the protocol.
†Procedure success: Placement of stents as per randomisation with TIMI 3 flow and < 30% stenosis in any stented vessel and TIMI 3 flow in any unstented vessel.

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No Difference between two strategies

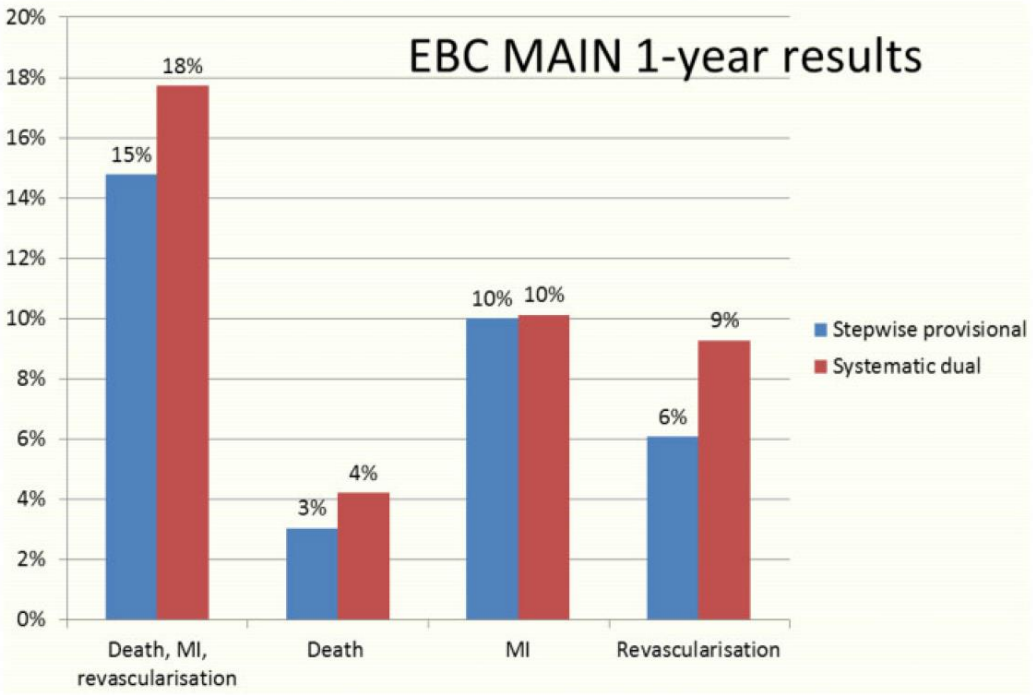

Figure 1 Graphical representation of the primary endpoint. MI, myocardial infarction.

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

No Difference between two strategies

Table 5 **Trial endpoints**

	Stepwise provisional ($n = 230$)	Systematic dual ($n = 237$)	Hazard ratio (95% CI) and *P*-value
Primary endpoint			
Death, myocardial infarction or target lesion revascularization at 12 months	34 (14.7%)	42 (17.7%)	HR 0.8 (0.5–1.3), $P = 0.34$
Secondary endpoints			
Death	7 (3.0%)	10 (4.2%)	HR 0.7 (0.3–1.9), $P = 0.48$
Myocardial infarction	23 (10.0%)	24 (10.1%)	
Peri-procedural	9 (4%)	11 (5%)	HR 0.9 (0.5–1.7), $P = 0.9$
Subsequent	12 (5%)	13 (6%)	
Target lesion revascularization	14 (6.1%)	22 (9.3%)	
PCI	13	19	HR 0.6 (0.3–1.2), $P = 0.16$
CABG	1	3	
Stent thrombosis (definite/probable)	4 (1.7%)	3 (1.3%)	
Acute	1	0	
Subacute	1	1	HR 0.9 (0.4–1.9), $P = 0.9$
Late	2	2	

CABG, coronary artery bypass grafting; CI, confidence interval; HR, hazard ratio; PCI, percutaneous coronary intervention.

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

Why the difference with DKCRUSH-V? Authors say…

1. The definitions in the studies were different. The DKCRUSH-V study used cardiac death and target vessel-related myocardial infarction rather than death and myocardial infarction and this will have reduced the overall number of events

2. The coronary anatomy was different. The respective SYNTAX scores were 31 (DK crush) vs. 23 (EBC MAIN) and the side-vessel lesion lengths were 16mm (DK crush) vs. 7mm

- the extent of disease was greater in the DKCRUSH-V study and indeed 45% of patients in the provisional group had implantation of two stents vs. 22% in EBCMAIN.

3. The philosophical approach varied between the two trials.

- The DK crush technique was pioneered by the Chinese Cardiology vs. the stepwise provisional approach has been championed by the European Bifurcation Club
- unconscious biases are likely to have played a part in both trials.
- Attention to detail with regard to the specific technical aspects of each procedure likely differed

Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11

Why the difference between EBC Main and DKCRUSH-V

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3840–3843
doi:10.1093/eurheartj/ehab363

EDITORIAL

Left main coronary disease at the bifurcation: should the pendulum swing back towards the provisional stenting approach?

Farouc A. Jaffer[1]*, **Julinda Mehilli**[2,3,4] and **Javier Escaned**[5]

Table 1 Comparison of the EBC MAIN, DEFINITION II, and DKCRUSH-V trials

RCTs: two-stent vs. provisional	No. of patients/ centres	Years enrolled	Primary endpoint	%Medina 1,1,1	Mean SS score	Average SB length	PPMI definition	%SB stent provisional group	%without SB stent in two-stent group	%DK in two-stent group	%IVUS or OCT	Final KBI
EBC MAIN	467/31	2016–2019	ACD + MI + cTLR	90%	23	7 mm	SCAI	22%	6%	5% (culotte 53%, T/TAP 33%)	39%	94% vs. 89%
DEFINITION II (29% LM)	188/49	2015–2018	TLF (CD + TVMI + cTLR)	84%	25	20 mm	SCAI + additional criteria	23%	8%	78% (culotte 18%, TAP 3%	28%	99% vs. 96%
DK Crush V	482/26	2011–2016	TLF (CD + TVMI + cTLR)	81%	31	16 mm	SCAI + additional criteria	47%	0%	100%	41%	99.6% vs. 78.9%

Farouc A. Jaffer, European Heart Journal (2021) 42, 3840–3843

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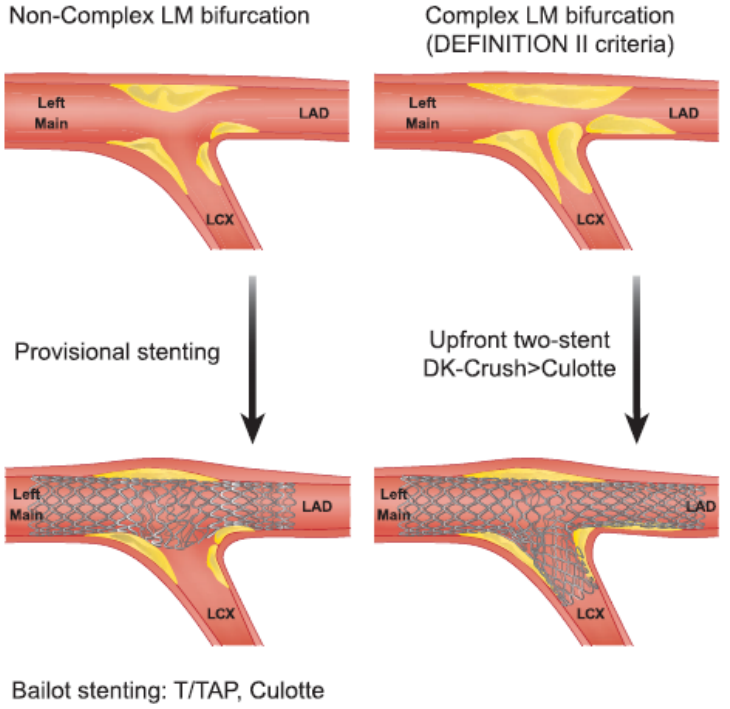
Proposed strategy for left main bifurcation stenting



KEY CONCEPTS FOR LM PCI

- 7F>6F guide when possible
- Image-guidance: IVUS or OCT
- Bifurcation angle
- Side branch diameter
- Plaque preparation (scoring, atherectomy, lithotripsy)
- MCS options, provisional or up-front
- POT with high-pressure NC balloon
- KBI with high-pressure NC balloons
- DK-Crush: Re-wire proximal strut
- Provisional: Re-wire distal strut
- Stent expansion limits
- Computational flow dynamic simulations

Graphical Abstract Proposed strategy for left main bifurcation stenting.

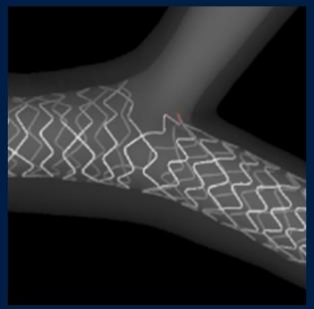
Farouc A. Jaffer, European Heart Journal (2021) 42, 3840–3843

Resolute Onyx™ DES

BIFURCATION PCI

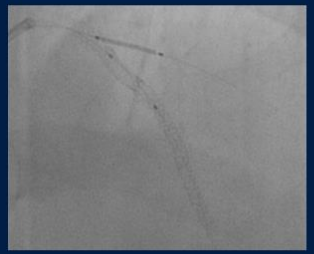
LEFT MAIN BIFURCATION PCI

Single wire design increases flexibility and conformability to achieve optimal strut apposition



Round struts create a smooth passage when accessing the side branch and lower the propensity to catch

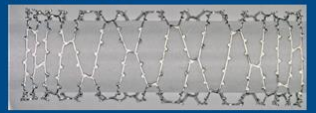
Platinum iridium core increases visibility for accurate stent placement without compromising strut thickness



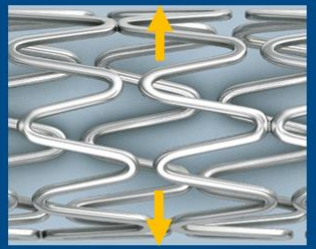
4.5 and 5.0 mm diameters expand to 6.00 mm† for optimal deployment with even scaffolding

Resolute Onyx DES

Synergy Megatron * DES



Sustained radial strength needed to handle the left main artery's elasticity



Data on file at Medtronic.

*Third-party brands are trademarks of their respective owners.

† Resolute Onyx DES received CE and FDA approval for increased expansion in 2020.

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PROSPECTIVE, MULTICENTRE, SINGLE-ARM TRIAL
RESOLUTE ONYX BIFURCATION STUDY

Resolute Onyx Post-Approval Study
Coronary lesions treated with Resolute Onyx™ DES
25 U.S. Sites (2.0 mm–5.0 mm)
5 EU Sites (2.0 mm–5.0 mm)
Study Principal Investigator — Dr. Matthew Price

Bifurcation Cohort
Single *de novo* bifurcated lesion amenable to treatment with Resolute Onyx DES using the **provisional stenting technique**
N = 205

Bifurcation Primary endpoint:	**Target Vessel Failure (TVF: cardiac death, tv-MI or TVR) at 1 year**
Secondary endpoints:	Acute success rates, individual components of primary endpoints, definite/probable stent thrombosis All assessed at discharge, 30 days, and 6, 12, 24, and 36 months post-procedure except for acute success

Source: Price M. One year Clinical Outcomes in Patients with coronary bifurcation lesions: results from the Resolute Onyx Bifurcation Study. Presented at ACC.21.

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COMPLEX PATIENTS AND LESIONS REFLECTIVE OF REAL-WORLD BIFURCATION PCI

PATIENT CHARACTERISTICS

Patient characteristics	Bifurcation Cohort (N=205 patients)
Age (yrs)	66.6 ± 10.7
Female	21.5%
Diabetes	30.2%
Hypertension	77.1%
Hyperlipidemia	74.1%
Prior MI	19.5%
Prior PCI	35.1%
Prior CABG	9.3%
Silent ischaemia	14.2%
Stable angina	36.3%
Acute coronary syndrome†	**47.4%**
STEMI	3.7%
Non-STEMI	3.7%
Unstable angina	36.8%

LESION CHARACTERISTICS*

Lesion characteristics	Bifurcation Cohort (N=207 lesions)
Multivessel disease	**37.2%**
Moderate/severe calcification	**35.3%**
Vessel location	
LAD	55.1%
LCX	26.1%
RCA	16.4%
Left main (protected)	2.4%
Main vessel stenting only	96.6%
Side branch (bailout) stenting	3.4%
- Culotte (n)	4/7
- T-stenting (n)	3/7
Total stent length/patient (mm)**	**35.9 ± 21.8**
Medina classification	
1.1.1	22.7%
1.0.1	3.4%
0.1.1	6.3%

Source: Price M. One-year Clinical Outcomes in Patients with coronary bifurcation lesions: results from the Resolute Onyx Bifurcation Study. Presented at ACC.21.

* Based on lesions which met the bifurcation criteria as assessed by the core lab

† ACS includes 3.2% MI > 72 hours.

** Including non-bifurcation lesions.

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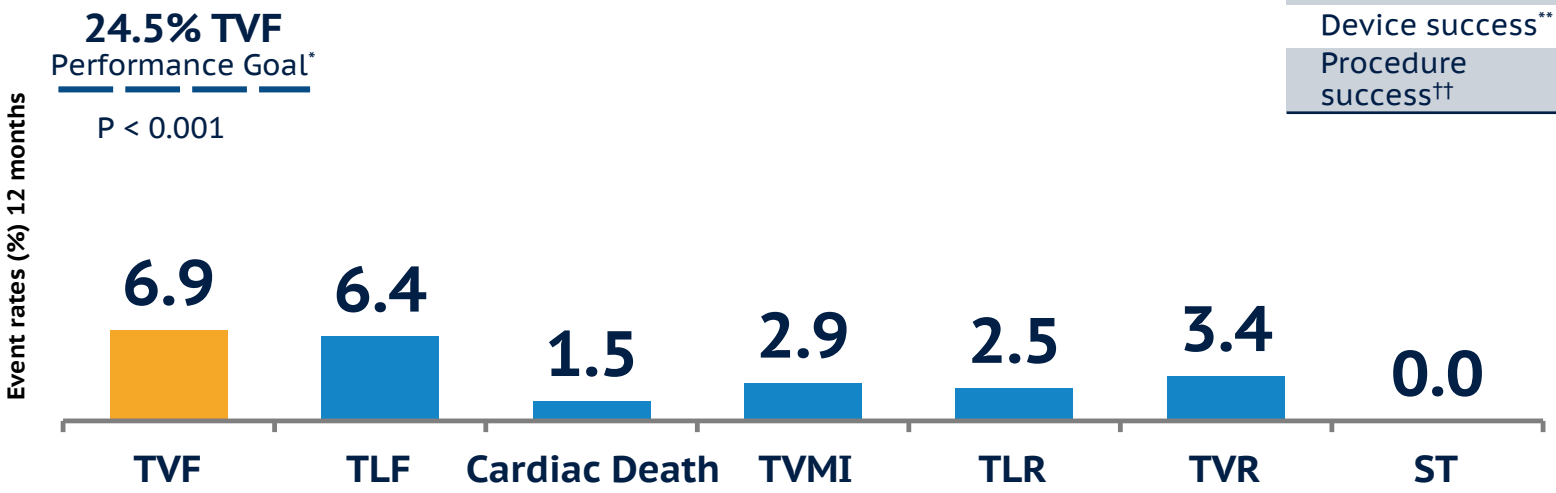
RESOLUTE ONYX™ DES SAFE AND EFFECTIVE IN BIFURCATION LESIONS, WITH HIGH LESION AND DEVICE SUCCESS

Procedural outcomes	
Lesion success†	98.9
Device success**	97.3
Procedure success††	96.6



Beat performance goal derived from contemporary bifurcation trials with low event rates at 1 year, **including 0% ST**

For bifurcation lesions only (corelab assessed)
*Resolute All Comers (RAC) Resolute and Xience V Arms), TRYTON trials.
†The attainment of <30% residual stenosis by QCA (or < 20% by visual assessment) and TIMI flow 3 after the procedure, using any percutaneous method.
** The attainment of <30% residual stenosis by QCA (or < 20% by visual assessment) and TIMI flow 3 after the procedure, using the assigned device only.
††The attainment of <30% residual stenosis by QCA (or < 20% by visual assessment) and TIMI flow 3 after the procedure, using any percutaneous method without the occurrence of MACE during the hospital stay.

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NEW DATA SUPPORTING RESOLUTE ONYX™ DES IN BIFURCATION PCI, INCLUDING THE LEFT MAIN

DEMONSTRATED EXCELLENT OUTCOMES IN THE EBC MAIN STUDY[1]

- EBC MAIN is the first randomised trial based on the EBC* Consensus, comparing provisional to a planned 2-stent strategy in true left main bifurcations.
- Resolute Onyx DES was chosen because of its 4.5- and 5.0-mm diameters, which can now expand to 6.0 mm.†
- Resolute Onyx DES is now the only DES with randomised data supporting adaptability to provisional and planned 2-stent strategies.

DEMONSTRATED EXCELLENT SAFETY AND EFFICACY WITH 0% ST AND 97.3% DEVICE SUCCESS IN THE RESOLUTE ONYX BIFURCATION STUDY[2]

- Bifurcation lesions account for ~30% of PCIs[3] and are one of the most challenging procedures.
- Resolute Onyx beat the performance goal derived from contemporary bifurcation trials.
- Data from the study will support the submission for the first U.S. DES bifurcation indication.

RESOLUTE ONYX DES IS OPTIMISED FOR BIFURCATION PCI, INCLUDING THE LEFT MAIN

*Resolute Onyx DES received CE and FDA approval for increased expansion in 2020.

[1]Hildick-Smith D, et al. *European Heart Journal*.2021;ehab283,00:1-11
[2]Price M. One year Clinical Outcomes in Patients with coronary bifurcation lesions: results from the Resolute Onyx Bifurcation Study. Presented at ACC.21.
[3]Von Birgelen C, et al. *Lancet*. 2018;392:1235-1245.

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Summary

- **Stepwise provisional strategy is a valid option for LM bifurcation stenting**
- **In highly complex cases, systematic dual stenting strategy should be considered**
- **Resolute Onyx™ DES has proven data in bifurcation lesions including left main**

Thank you for your attention!