

# Late Breaking Clinical Trials: The Celtic Bifurcation Study

## 2-year clinical outcomes

Dr Colm Hanratty MD FRCP  
On behalf of the Celtic Bifurcation Study Investigators

Speaker's name : Colm Hanratty

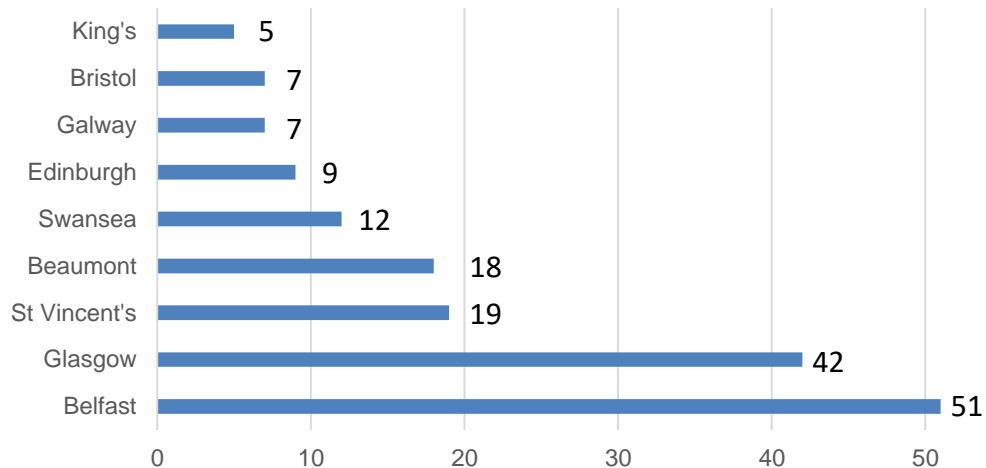
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- Honorarium: Boston Scientific, Abbott Vascular

- There is still controversy over 2-stent bifurcation techniques versus provisional PCI for these lesions
- Recommendations are usually made on anatomy, rather than side branch ischaemic burden
- A single stent strategy may not be the appropriate approach for many patients
- Outcomes with all PCI are improving with the modern generation of stents

- Multicentre RCT
- 9 centres in UK and Republic of Ireland
- Patients with non-LMS bifurcation lesions with planned culotte stenting were randomised to treatment with 2-connector (Synergy) or 3-connector (Xience) EES

# Investigators, Enrolment & Organisation

- Prof David Foley, Beaumont Hospital Dublin, Co-CI
- Dr Simon Walsh, Belfast Trust; Co-CI
- Dr Colm Hanratty, Belfast Trust; PI
- Dr Stuart Watkins, Golden Jubilee Glasgow, PI
- Prof Niall Mulvahill, St Vincent's Hospital Dublin, PI
- Prof Alex Chase, Morriston Hospital Swansea, Co-PI
- Dr Dave Smith, Morriston Hospital Swansea, Co-PI
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- Dr Darren Mylotte, Galway University Hospitals, PI
- Dr Tom Johnson, Bristol Royal Infirmary, PI
- Dr Jonathan Hill, Kings College London, PI



CRO – Data oversight, CEC, DSMB, Angiographic Core Laboratory

Project Lead: Jessica Heringer

NCT 02232815

Indication for PCI and  
Medina 1,1,1 disease



Indication for 2-stent culotte strategy  
(operator determined) and both branches  
 $\geq 2.5\text{mm}$  in diameter



Randomise 1:1  
Xience (n=85) vs Synergy(n=85)

DES

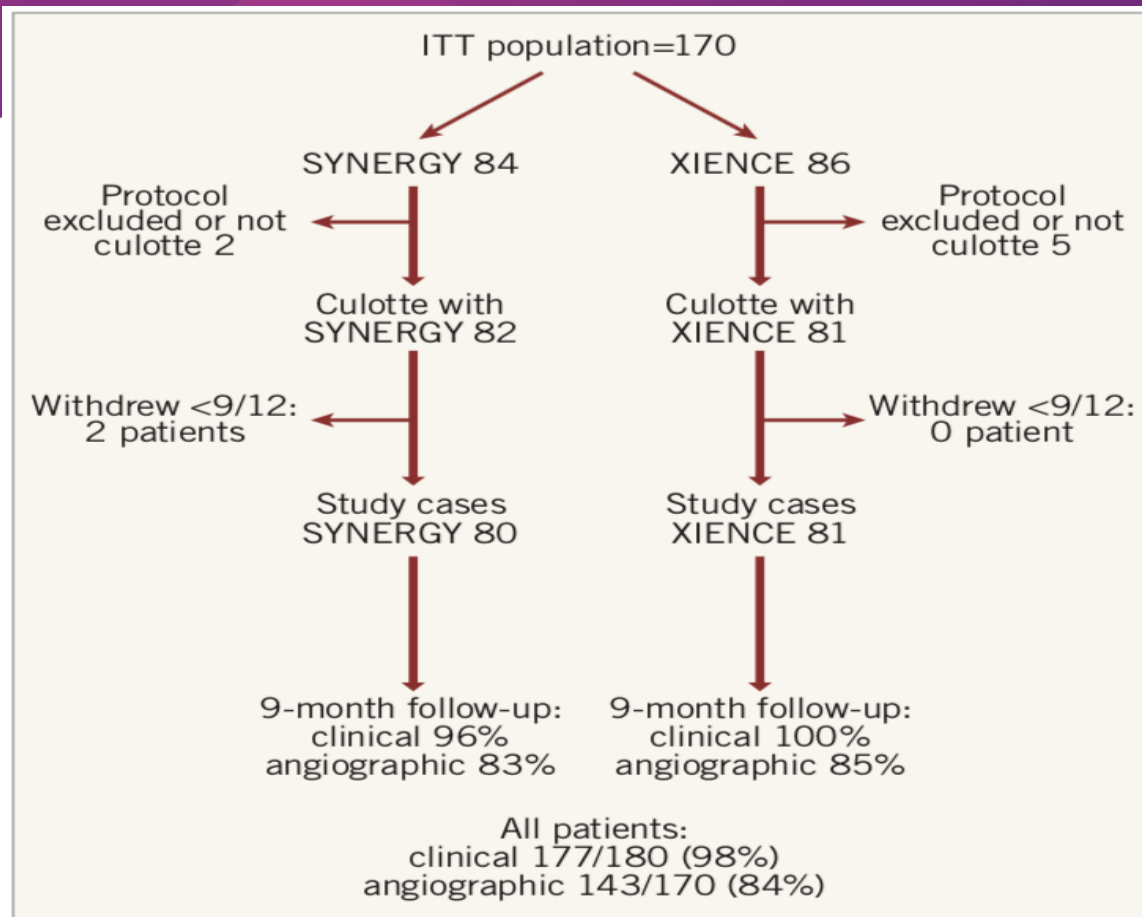


9-month hospital visit: Angiogram  
and clinical follow-up



Telephone follow-up to 2 years

- 24 month composite of:
  - Death
  - MI
  - CVA
  - Target Vessel Failure
  - Binary Angiographic Restenosis at 9 months
- **Primarily exploratory** – estimated event rate 10% at 9 months
- Exploratory power calculation: 85 patients per group with  $\alpha$  of 5% and  $1-\beta$  of 90% to assess non-inferiority limit of 15% for Synergy vs Xience

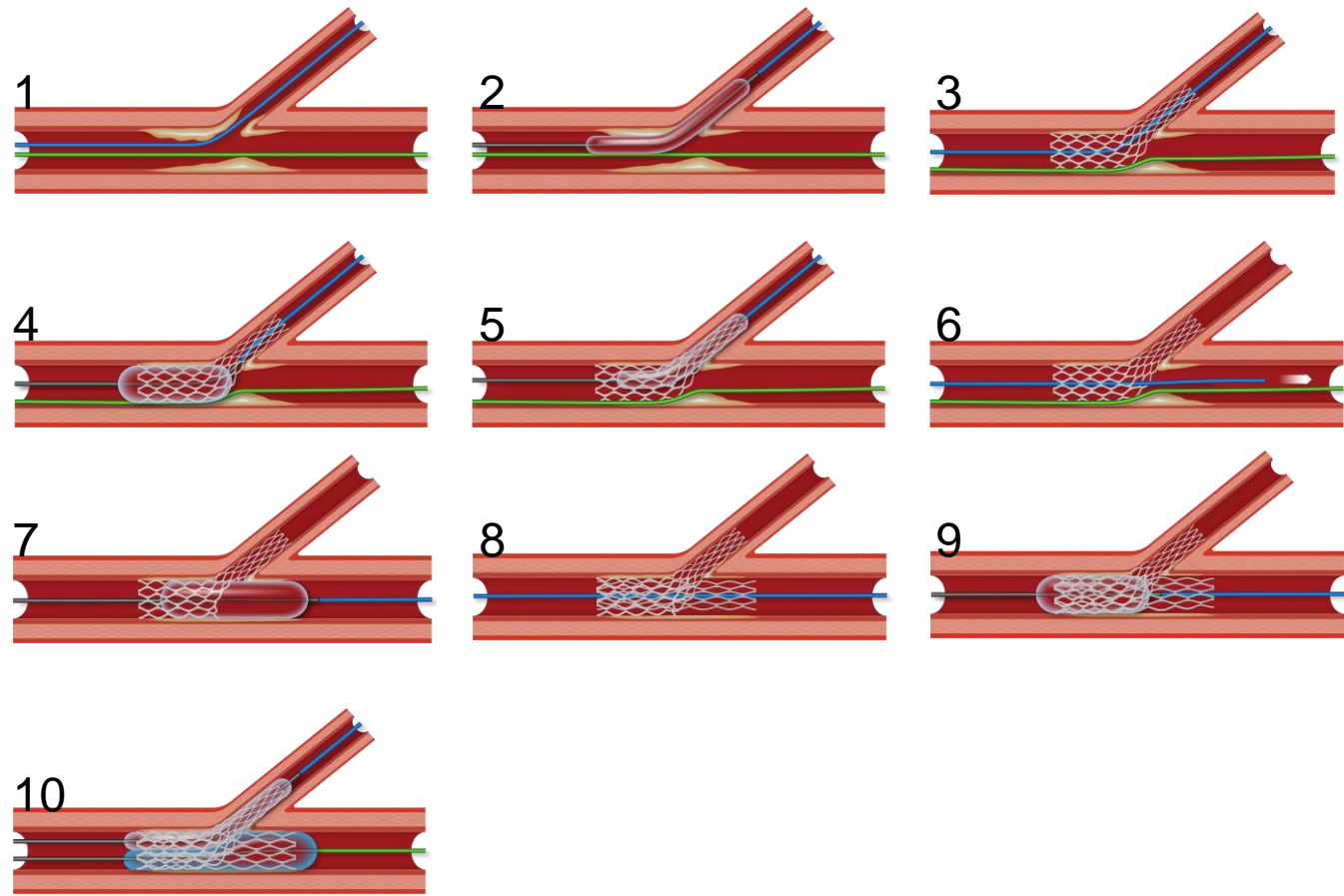


Variable	Statistic	SYNERGY	XIENCE	p-value	Variable	Statistic	SYNERGY	XIENCE	p-value
Total number of patients	N	84	86		NSTEMI	%	20.5	16.7	
Age (years)	Mean (SD)	64 (10.2)	66 (9.3)	0.169	STEMI (stabilised)	%	1.2	0.0	
Male	%	81.0	86.1	0.371	Other	%	3.6	8.3	
BMI (kg/cm <sup>2</sup> )	Mean (SD)	29 (6.4)	29 (4.9)	0.861	Extent of CAD				
LVEF (%)	Mean (SD)	53 (8.9)	53 (6.7)	0.951	LAD >70%	%	81.9	88.1	0.264
Medical history					LCx >70%	%	24.1	19.1	0.428
Cardiac					RCA >70%	%	16.9	13.1	0.495
Myocardial infarction	%	21.0	31.3	0.132					
CABG	%	3.6	3.6	0.988					
PCI	%	37.8	44.1	0.414					
Non-cardiac									
Peripheral vascular disease	%	7.7	6.3	0.722					
Renal insufficiency	%	12.1	6.0	0.168					
Stroke	%	3.6	2.4	0.640					
Risk factor									
Current smoker	%	19.0	15.9	0.600					
Diabetes mellitus	%	22.8	13.4	0.122					
Hypercholesterolaemia	%	73.4	75.6	0.750					
Hypertension	%	63.3	61.0	0.762					
Family history	%	65.8	69.5	0.617					
Indication for PCI									
Silent ischaemia	%	1.2	3.6	0.518					
Stable angina	%	65.1	60.7						
Unstable angina	%	8.4	10.7						

**Study population well matched**

- Radial approach almost universal (99% Synergy/93% Xience)
- Majority LAD/Diagonal lesions (82% Synergy/85% Xience)
- Mainly treated with 2 stents (67% Synergy/69% Xience)
- POT > 90% per step
- Kissing inflation almost all cases (99% Synergy/95% Xience)

Variable	Statistic	SYNERGY	XIENCE	p-value	95% CI
Technical success*	%	96.4	96.3	1.000	(-15.3;15.7)
Total procedure time (min)	Mean (SD)	76 (42)	74 (46)	0.706	(-10.0;15.0)
Total radiation dose (cGy.cm <sup>2</sup> )	Mean (SD) Median (Q1-Q3)	6601 (6955) 4757 (2342-7441)	6715 (6534) 4983 (3177-7242)	0.424	(-657.9;1718.8)
Total contrast volume (ml)	Mean (SD)	215 (90)	225 (85)	0.314	(-40.0;10.0)
Need of secondary equipment	%	24.1	24.1	1.000	(-15.7;15.7)
Extra support guidewire	%	4.8	8.4	0.535	(-19.2;12.1)
Anchor balloon	%	22.9	20.5	0.851	(-13.3;18.1)
Mother and daughter catheters	%	6.0	4.8	1.000	(-14.5;16.9)
Longitudinal stent compression	%	1.2	0.0	1.000	(-14.5;16.9)
Stent fracture at angiographic follow-up	%	1.5	2.7	1.000	(-17.7;15.3)



- At 9-months the outcomes for MACCE were similar between the 2-stents

Variable	Statistic	SYNERGY II	XIENCE	p-value	95% CI
Composite of death, MI, CVA, TVF, ST and restenosis*	%	16.3%	18.6%	0.003	(NC;12.7)
Target vessel failure (TVF)	n (%)	1 (1.4)	0	0.472	(-14.8;17.4)
Death	n (%)	3 (3.7)	1 (1.4)	0.404	(-14.0;18.7)
Cardiac	n (%)	2 (2.4)	0	0.252	(-13.6;18.3)
MI	n (%)	4 (4.9)	1 (1.2)	0.201	(-12.3;19.7)
Type 1	n (%)	2 (2.4)	0	0.244	(-13.3;18.0)
Type 2	n (%)	1 (1.2)	0	0.489	(-14.4;16.8)
Type 4a	n (%)	1 (1.3)	1 (1.2)	0.969	(-15.8;16.1)
Q-wave	n (%)	2 (2.5)	0	0.237	(-13.5;18.4)
CVA	n (%)	1 (1.3)	1 (1.2)	0.973	(-16.0;16.2)
ST	n (%)	0	1 (1.2)	0.995	(-17.0;14.9)
Late	n (%)	0	1 (1.2)	0.995	(-17.0;14.9)
Definite	n (%)	0	1 (1.2)	0.995	(-17.0;14.9)
Binary angiographic stenosis	n (%)	5 (7.7%)	10 (13.9%)	0.316	(-25.0;13.5)

\*One-sided non-inferiority test with margin of 15% and one-sided confidence interval (CI). All other tests are two-sided exact tests with a two-sided exact CI. Numbers are observed, percentages, differences and CIs come from a multiple imputation analysis with 100 imputations. CVA: cerebrovascular accident; MI: myocardial infarction; NC: not calculated; ST: stent thrombosis

CLINICAL RESEARCH  
CORONARY INTERVENTION



### Culotte stenting for coronary bifurcation lesions with 2<sup>nd</sup> and 3<sup>rd</sup> generation everolimus-eluting stents: the CELTIC Bifurcation Study



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This paper also includes supplementary data published online at: [http://www.pcronline.com/eurointervention/136th\\_issue/36](http://www.pcronline.com/eurointervention/136th_issue/36)



**Table. Primary endpoint and components at 2 years**

Variable	Synergy II	Xience	Difference	95% CI	P-value
MACCE, % *	13/70 (17.71%)	15/74 (18.81%)	-1.10%	(NC;14.27)	0.0055
Target vessel failure (TVF), %	1/69 (1.54%)	0/73 (0.03%)	1.50%	(-4.24;9.00)	0.4366
Death, %	3/80 (3.75%)	1/82 (1.59%)	2.16%	(-5.95;10.69)	0.4553
<i>Cardiac</i>	2/80 (2.48%)	0/82 (0.10%)	2.37%	(-3.59;9.68)	0.2668
<i>Non-Cardiac</i>	1/80 (1.27%)	1/82 (1.49%)	-0.21%	(-7.81;6.74)	0.9686
MI, %	5/80 (6.10%)	2/82 (1.19%)	4.91%	(-1.85;13.50)	0.1116
<i>Type 1</i>	2/80 (2.40%)	0/82 (0.01%)	2.39%	(-2.58;9.08)	0.2440
<i>Type 2</i>	1/80 (1.21%)	0/82 (0.00%)	1.21%	(-3.52;7.13)	0.4890
<i>Type 4a</i>	2/80 (2.48%)	1/82 (1.17%)	1.30%	(-4.87;8.47)	0.6017
<i>Q-wave</i>	2/80 (2.48%)	0/82 (0.01%)	2.46%	(-2.74;9.53)	0.2367
<i>Non Q-wave</i>	3/80 (3.62%)	2/82 (1.17%)	2.44%	(-3.55;9.78)	0.3607
CVA, %	1/80 (1.30%)	1/82 (1.33%)	-0.03%	(-7.00;6.84)	0.9732
<i>TIA</i>	0/80 (0.04%)	1/82 (1.27%)	-1.23%	(-7.60;4.21)	0.9574
<i>Stroke</i>	1/80 (1.26%)	0/82 (0.06%)	1.20%	(-4.38;7.75)	0.5066
ST, %	0/80 (0.15%)	1/82 (1.17%)	-1.02%	(-7.06;5.06)	0.9946
<i>Late</i>	0/80 (0.15%)	1/82 (1.17%)	-1.02%	(-7.06;5.06)	0.9946
<i>Definite</i>	0/80 (0.15%)	1/82 (1.17%)	-1.02%	(-7.06;5.06)	0.9946

\* One sided non-inferiority test with margin of 15% and one sided confidence interval (CI). All other test are two sided exact tests.

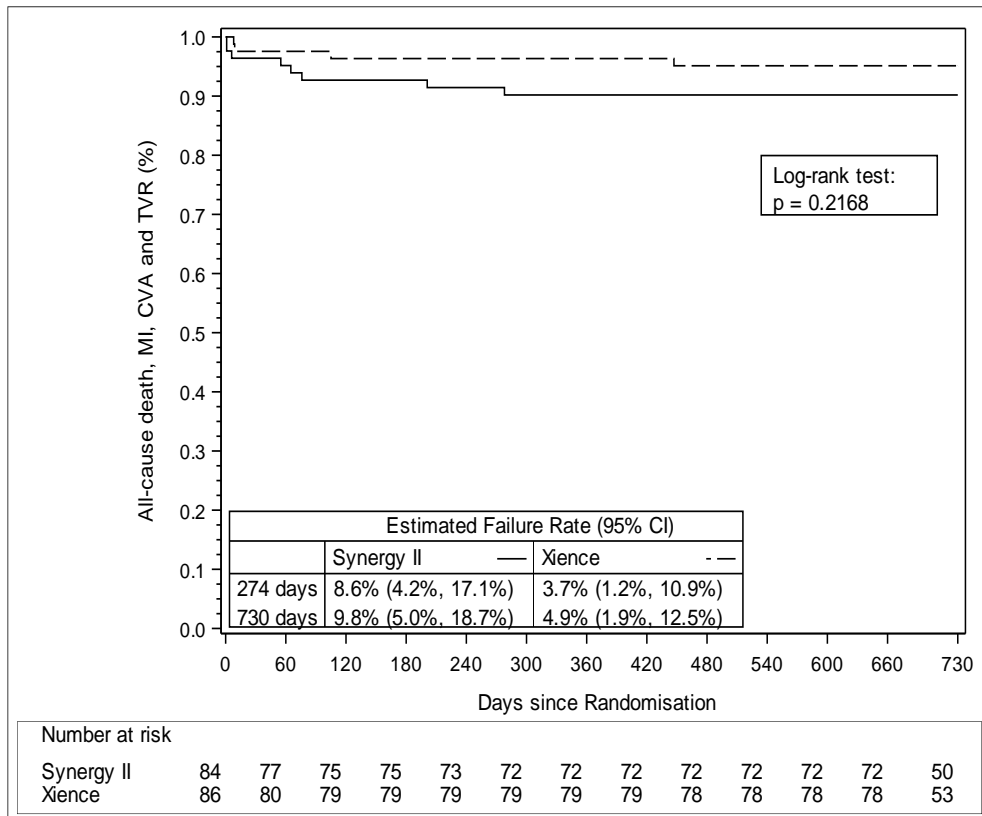
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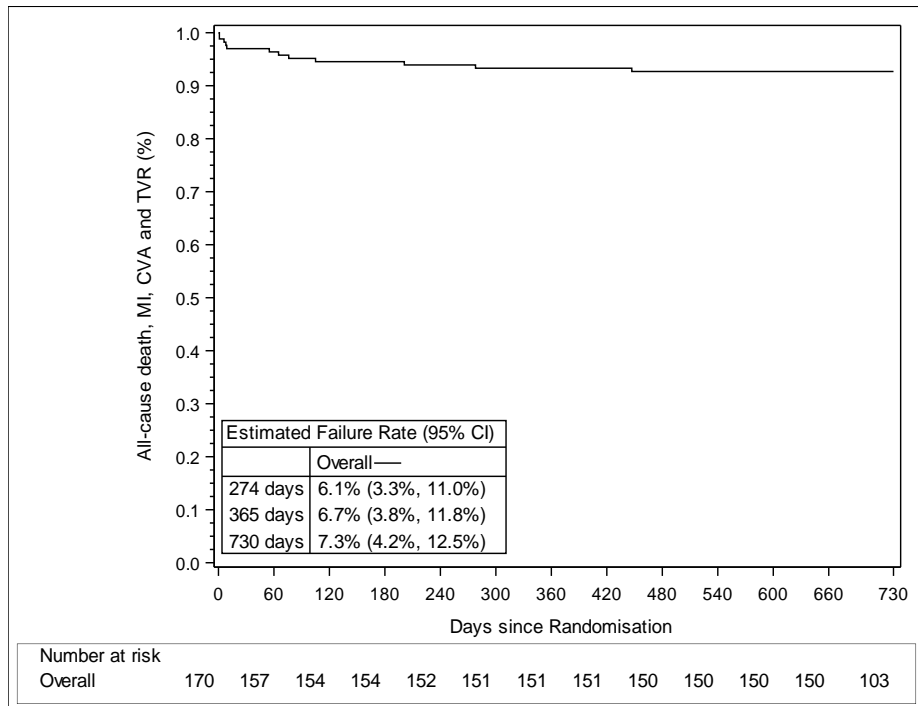
Predominately procedural and angiographic follow up rather than ongoing clinical issues

# What are the essential results?

- At 24-months MACE rates were low for a 2-stent technique in contemporary PCI
- There was very little attrition between 12 and 24 months



- MACE of 5.9% at 12 months with contemporary PCI techniques
- MACE of 7.3% at 24 months illustrates a durable result with contemporary DES



Combined results

- Management of bifurcation lesions remains controversial
- Guidelines & consensus documents still support a provisional approach
- Reassuring clinical outcomes with 7.3% MACE at 24 months are possible with contemporary techniques and stents
- Good procedural technique critical to enable these type of results