IDEAL-LM

Improved Drug Eluting stent for All-comers Left Main: *IDEAL-LM*

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Disclosure Statement of Financial Interest

IDEAL-LM

Within the past 12 months, I or my spouse/partner have had a financial interest, arrangement, or affiliation with the organization(s) listed below:

Affiliation/Financial Relationship	Company
Grant/Research Support	
Consulting Fees/Honoraria	BostonScientific, Abbott Vascular, Astra Zeneca
Major Stock Shareholder/Equity	
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	

Rationale and Aims I

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- The use of PCI for LMCA disease is increasing worldwide
  - SYNTAX, EXCEL, NOBLE
  - European and US Guidelines
- The optimal duration of post-procedural DAPT after LM PCI remains undetermined
  - Ischaemia vs bleeding

A novel DES design with a bioabsorbable polymer and thin struts may facilitate faster healing and allow a shorter duration of DAPT without compromising clinical outcomes

Rationale and Aims II

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- **LM PCI specialties:**
  - **Large amount of myocardium at risk**
  - **High frequency of bifurcation disease (63% of LM in Syntax)**
    - **1 stent with overlap or 2 stent at bifurcation (39% in Syntax LM)**
    - **Inclusion of aortic-ostial disease** (“prone to stent recoil due to the fibroelastic properties of the aortic wall”[1])
  - **Vessel diameter frequently beyond labeled max. stent expansion**

A novel DES design with thinner struts, increased radial strength, and larger over-expansion capabilities may reduce early and late revascularisations

1. Topol EJ J Am Coll Cardiol. 1987;9:1214-8

Novel (Improved) Drug Eluting stent

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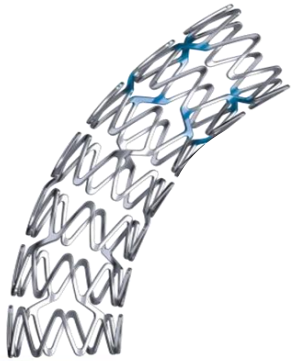
Synergy:

- **Platinum-Chromium** backbone
- Strut thickness: **74**µm
- **Biodegradable** polymer
- **Abluminal** coating

+ Short DAPT (4 months)



Over expansion study of 4 mm stent in 6mm tubing

FKBD

MA: 6.20mm², EI 1.5	MA: 8.20mm², EI 1.2	MA: 1.80mm², EI 1.2
Max SOA 22.80mm² Max SOD 6.50mm	Max SOA 20.90mm² Max SOD 5.70mm	Max SOA 27.20mm² Max SOD 6.90mm
D	D	F
3.5 + 4.0 12 ATM SC 6 ATM	4.0 + 5.0 4 ATM SC 14 ATM	4.0 + 5.0 12 ATM NC: 24 ATM

POT 6mm

MA: 8.40mm², EI 1.0	MA: 1.10mm², EI 1.0	MA: 0mm2, EI 1.0
Max SOA 20.80mm² Max SOD 5.10mm	Max SOA 28.60mm² Max SOD 6.00mm	Max SOA 30.30mm² Max SOD 6.22mm
A	B	C

J.M. Fam, AsiaIntervention 2017;3:111-120
J. Ng et al. Int J of Cardiology 2016;22: 171–179

Novel (Improved) Drug Eluting stent

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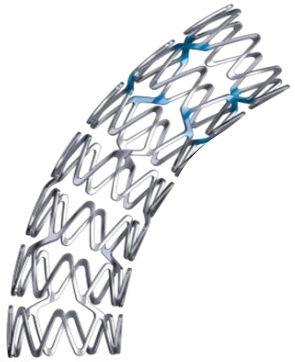
Synergy:
- **Platinum-Chromium** backbone
- Strut thickness: **74**µm
- **Biodegradable** polymer
- **Abluminal** coating

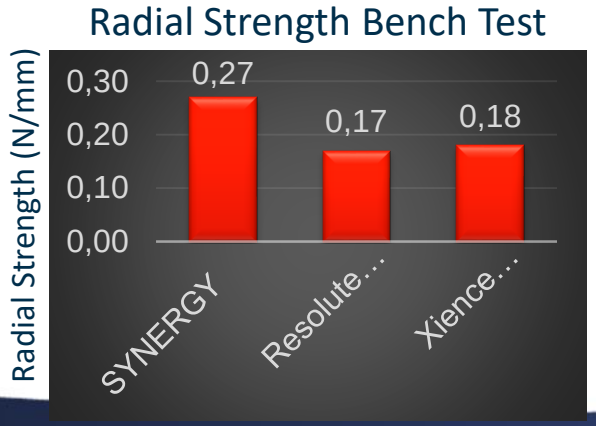
+ Short DAPT (4 months)

RCT

Xience:
- **Cobalt-Chromium** backbone
- Strut thickness: **81**µm
- **Permanent** polymer
- **Circumferential** coating

+ Standard DAPT (12 months)





Primary Endpoint:
2 year MACE (death, MI, ischemic driven TVR)

M.E. Lemmert, Keith Oldroyd Am Heart J 2017;187:104-11

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Patients with LMCA disease who are accepted by the Heart Team for PCI

All-comers:
- Syntax > 32
- ACS
- All EF

29 sites, 5 Countries Dec 2014-Sept 2016

818 patients randomized to LM PCI with either BP-PtCr-EES or PP-CoCr-EES

Synergy + 4 months DAPT

Xience + 12 months DAPT

3 months OCT (n=50) and clinical follow-up (all patients)

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PCR 2017

Strut coverage (>20 µm): 97.7 vs 98.0%

Clinical follow-up: 6,12,24 months

Primary Endpoint: 2 year MACE (death, MI, ischemic driven TVR)

M.E. Lemmert, Keith Oldroyd Am Heart J 2017;187:104-11
Chang Chun Chin JACC: CI September 2019 DOI: 10.1016/j.jcin.2019.09.012

Trial Organisation

IDEAL-LM

- **Investigator initiated multi-centre international RCT**
  - coPIs: Prof RJ van Geuns, Prof KG Oldroyd
  - UK, Netherlands, France, Poland, Russia
- **Funder:** Boston Scientific
- **Sponsor:** Golden Jubilee National Hospital, Glasgow, UK
- **CRO:** Venn Life Sciences, Belfast, UK
- **Data management and statistical analysis:** Diagram, Zwolle, NL
- **Angiographic and OCT core-lab:** Cardialysis, Rotterdam, NL.
- **Independent DSMB:** Chair Prof Jan Tijssen
- **Independent CEC:** Chair Dr E McFadden

M.E. Lemmert, Keith Oldroyd Am Heart J 2017;187:104-11

INCLUSION CRITERIA

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- All comers LM: Patient has an indication for revascularisation of the left main artery in accordance with the ESC guidelines (2014)
- Patient has been discussed with the cardiac surgeon prior to PCI procedure

EXCLUSION CRITERIA

- Not able to receive APT due to contraindications or allergy
- Cardiogenic shock
- STEMI within the last 5 days
- Major surgery within previous 15 days or planned surgery within 12 months
- History of bleeding diathesis or active major bleeding
- Life expectancy < 12 months

M.E. Lemmert, Keith Oldroyd Am Heart J 2017;187:104-11

EFFICACY and SAFETY

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PRIMARY END-POINT

- Rate of MACE defined as death from any cause or MI or ischemia-driven target vessel revascularization (TVR) at 2 years after the procedure

SECONDARY END-POINTS

- Individual components of the primary end-point
- Procedural success (<30% residual stenosis of the target lesion and no in-hospital device-oriented composite endpoints (DOCE)
- DOCE: cardiac death, MI not clearly attributable to a non-treated vessel, and clinically-indicated target lesion revascularization at 1 month, 6 months and annually to 3 years and its individual components
- Stent thrombosis according to ARC definition at all time points
- Composite of BARC 3 or 5 bleeding at 24 months
- Individual BARC bleeding events (BARC 1, 2, 3, 4 and 5)

M.E. Lemmert, Keith Oldroyd. Am Heart J 2017;187:104-11

Power Calculation and Sample Size

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The aim of the study was to demonstrate that PCI with the Synergy stent followed by 4-months DAPT (experimental arm) is non-inferior to PCI with the XIENCE stent followed by 12-months DAPT (active control arm)

- Two-side α error = 5%
- Non-inferiority margin = 7.5%;
- Predicted rate of primary endpoint (MACE) at 2 years = 20.0%
- 1:1 randomization
- Power = 0.85

Using these assumptions, sample size was 409 patients per arm

- 29 sites, 5 countries

M.E. Lemmert, Keith Oldroyd Am Heart J 2017;187:104-11

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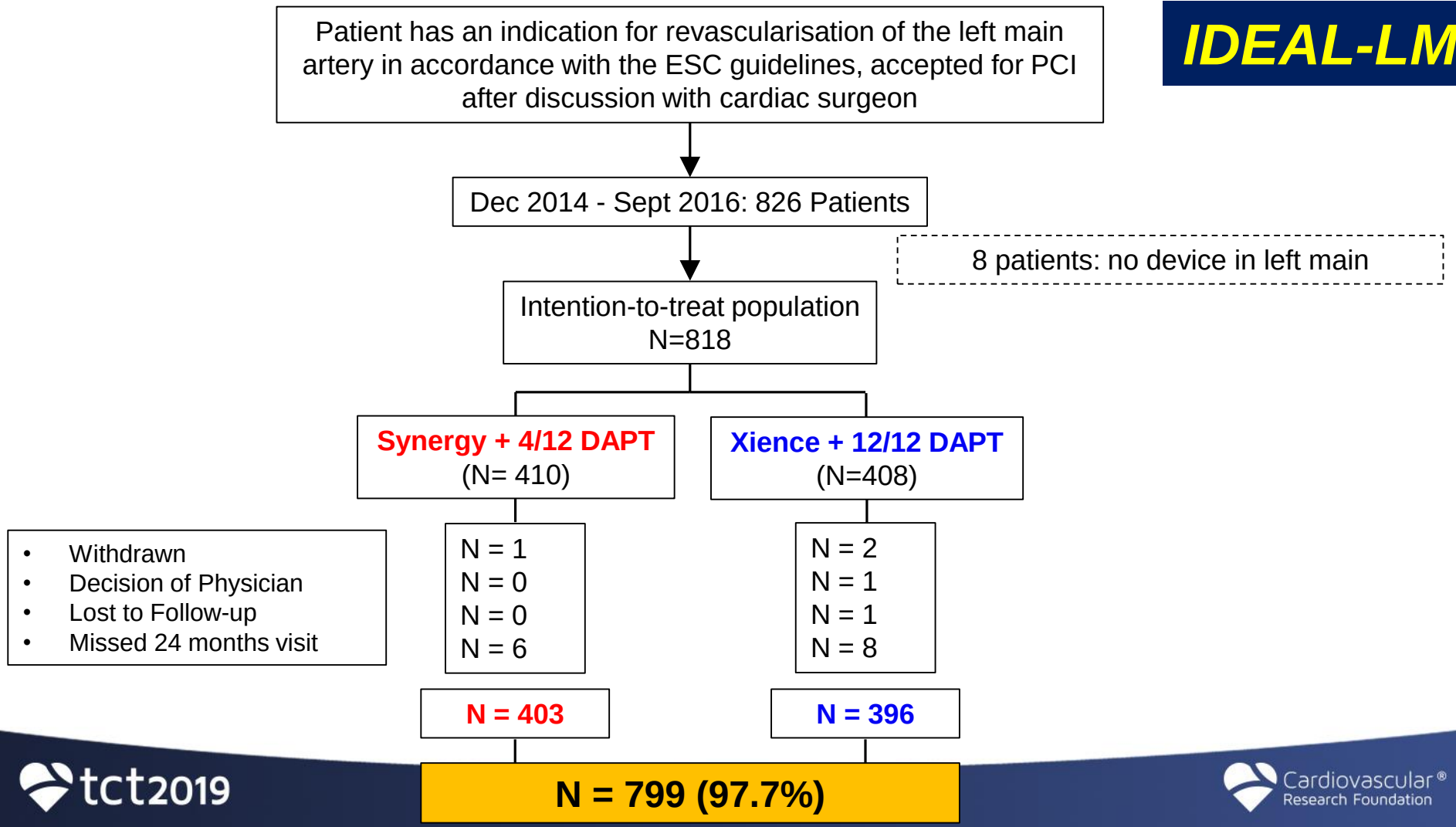
Patient has an indication for revascularisation of the left main artery in accordance with the ESC guidelines, accepted for PCI after discussion with cardiac surgeon
Dec 2014 - Sept 2016: 826 Patients
8 patients: no device in left main
Intention-to-treat population N=818
Synergy + 4/12 DAPT (N= 410)
Xience + 12/12 DAPT (N=408)
• Withdrawn
• Decision of Physician
• Lost to Follow-up
• Missed 24 months visit
N = 1
N = 0
N = 0
N = 6
N = 2
N = 1
N = 1
N = 8
N = 403
N = 396
N = 799 (97.7%)

Trial Recruitment by Centre

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Moscow	**Merkulov**	**105**	Clinique-Saint Hilaire Rouen	Berland	19
Novosibirsk Research Institute	**Kretov**	**103**	Morriston Hospital	Chase	18
Golden Jubilee National Hospital	Oldroyd	83	Erasmus MC Rotterdam	van Geuns	13
Szpital Kliniczny Przemienienia Panskiego UM w Poznaniu	Lesiak	71	Polyclinique Les Fleurs Ollioules	Barragan	13
Royal Bournemouth Hospital	O Kane	47	Clinique St Martin à Caen	Morelle	13
Belfast City Hospital	Hanratty	46	Northern General Hospital	Gunn	10
Clinique des Nouvelles Cliniques Nantaises	Bressollette	42	Clinique Rhone Durance Avignon	Sainsous	10
Clinique Axium	Silvestri	37	CHU Rangueil	Carrie	10
Krasnoyarsk Regional Vascular Centre	Wlodarczak	30	Polsko Amerykanskie Kliniki Serca	Buszman	7
University Hospital of Wales	Anderson	25	State Budegatery Healthcare Institution	Osiev	5
Miedziowe Centrum Zdrowia	Protopopov	24	Clinique St Augustin	Darremont	4
Altnagelvin Hospital	Peace	23	Royal Infirmary of Edinburgh	Behan	3
Craigavon Hospital	Menown	22	Wielospecjalistyczny Szpital Miejski im. J. Strusia w Poznaniu	Rzezniczak	2
John Radcliffe Hospital	Banning	20	Onze Lieve Vrouwe Gasthuis	Slagboom	2
Essex CTC	Kelly	19			826

Baseline Demographics (1)

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Characteristic	All (n=818)	Synergy + 4/12 DAPT (n=410)	Xience + 12/12 DAPT (n=408)	P-value
Age	**66.4 ± 10.3**	66.8 ± 10.2	66.0 ± 10.5	0.242
Male	**79.6%**	82.4%	76.7%	**0.046**
Current smoker	**22.0%**	21.0%	23.0%	0.500
Diabetes mellitus	**22.0%**	21.2%	22.8%	0.613
Hypertension	**76.2%**	76.8%	75.5%	0.682
Hypercholesterolemia	**74.8%**	77.8%	71.8%	0.053
Previous ACS	**38.9%**	39.9%	38·1%	0.616
Previous PCI	**33.1%**	36.6%	29·7%	0.037
Previous CABG	**7.1%**	7.1%	7.1%	1
Previous cerebrovascular accident	**8.0%**	8.3%	7.6%	0.796
Clinical presentation				0.794
Stable CAD	**50.9%**	50.5%	51.2%	
ACS	**37.3%**	36.6%	38.0%	
Non-ST elevation MI	**15.7%**	14.4%	16.9%	
ST elevation MI	**17.1%**	19.0%	15.2%	
Other (Heart failure, silent ischemia)	**11.9%**	12.9%	10.8%	

Baseline Demographics (2)

IDEAL-LM

Characteristic	All (n=818)	Synergy + 4/12 DAPT (n=410)	Xience + 12/12 DAPT (n=408)	P-value
Eligible for surgery	**93.2%**	91.9%	94.4%	0.21
Reason for choosing PCI over CABG				
Co-morbidities	**23.8%**	23.3%	24.2%	0.80
Low SYNTAX Score	**57.9%**	57.8%	57.9%	1.00
ACS	**16.8%**	14.5%	19.0%	0.12
Other	**34.7%**	35.2%	34.0%	0.76

Characteristic	All (n=818)	Synergy + 4/12 DAPT (n=410)	Xience + 12/12 DAPT (n=408)	P-value
Access site				1.000
Radial	**81.8%**	81.7%	81.9%	
Femoral	**17.0%**	17.1%	16.9%	
Number of diseased vessels				0.470
Left main only	**24.3%**	23.2%	25.5%	
Left main + 1VD	**42.3%**	41.7%	42.9%	
Left main + 2VD	**23.6%**	25.9%	21.3%	
Left main + 3VD	**9.8%**	9.3%	10.3%	
Syntax score				0.552
Low	**63.4%**	61.8%	65.1%	
Intermediate	**24.4%**	25.98%	22.9%	
High	**12.2%**	12.3%	12.0%	
Syntax mean	**21.3 (9.1)**	21.6 (9.0)	20.9 (9.1)	0.311
Number of stents used in LM	**1.3 (0.5)**	1.3 (0.6)	1.2 (0.5)	0.148
1	**79.6%**	77.3%	81.9%	
2	**16.5%**	18.5%	14.5%	
Number of stents outsite LM	**1.1 (0.6)**	1.2 (0.6)	1.1(0.5)	
IVUS performed post procedure	**40.8%**	39.5%	42.2%	0.476

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Compliance with DAPT Regimen

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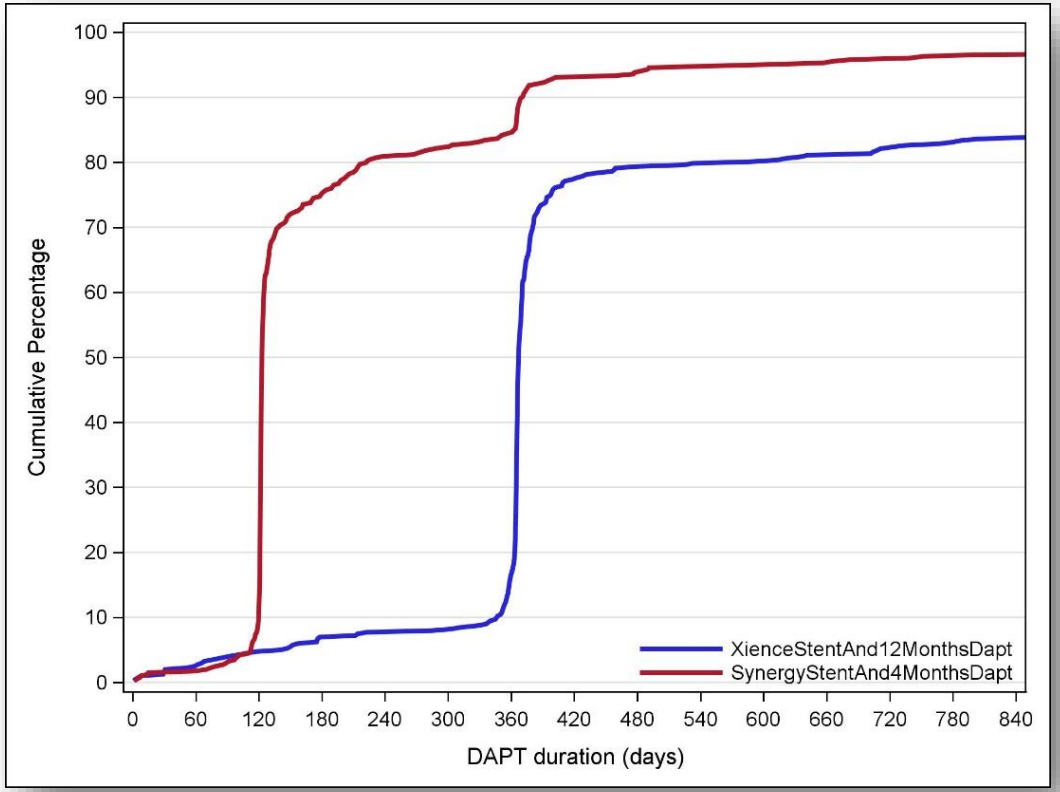
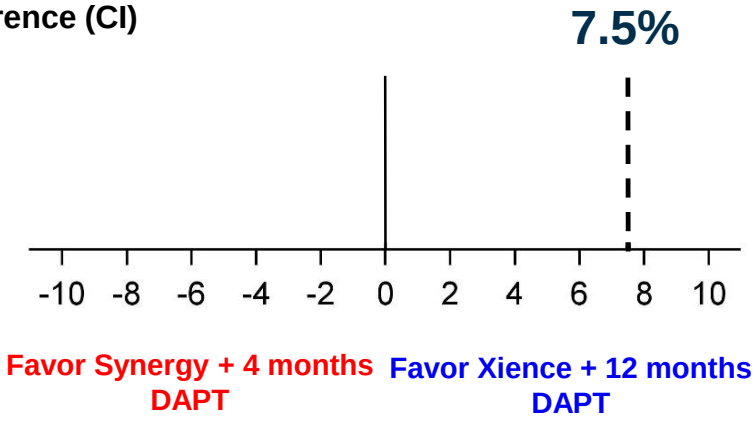


Primary Outcome Measure

IDEAL-LM

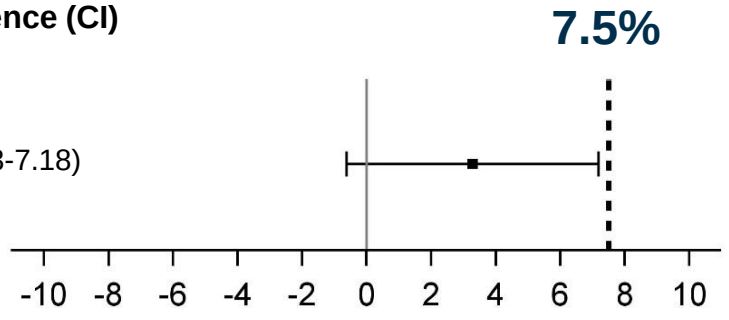
Synergy + 4 months DAPT	Xience + 12 months DAPT	Risk Difference (CI)
Events/N (%)	Events/N (%)	
59/403 (14.6)	**45/396 (11.4)**	3.28



Primary Outcome Measure

IDEAL-LM

Confidential Interval	Synergy + 4 months DAPT	Xience + 12 months DAPT	Risk Difference (CI)
	Events/N (%)	Events/N (%)	
90% CI	59/403 (14.6)	45/396 (11.4)	3.28 (-0.63-7.18)



Area left of reference line representative of Non Inferiority

Non-inferiority confirmed

End-Points

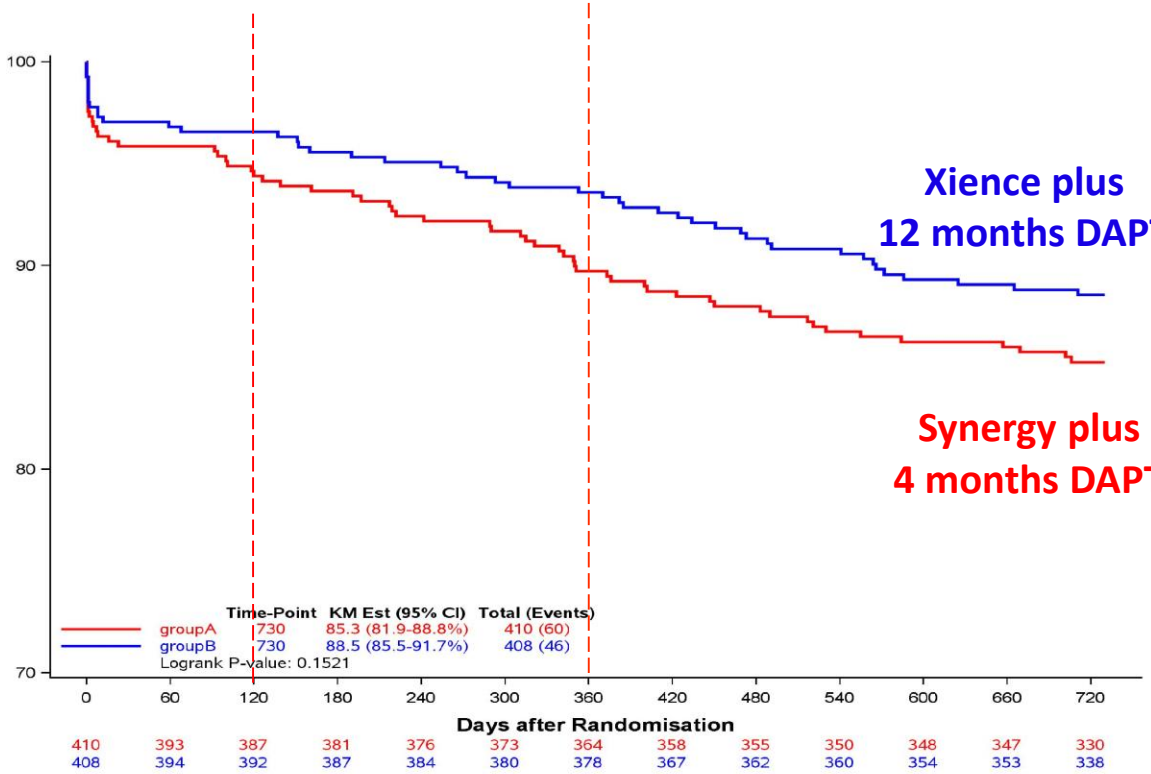
IDEAL-LM

	Synergy + 4/12 DAPT (n=410)	Xience + 12/12 DAPT (n=408)	*P* value
Primary end-point			
MACE (All cause death, MI, idTVR)	59/403 (14.6%)	45/396 (11.4%)	0.17
Secondary end-points			
All cause death	5.2%	5.3%	1.00
All MI	6.0%	3.5%	0.13
Ischaemia driven TVR	7.4%	4.8%	0.14
Ischaemia driven TLR	6.0%	4.6%	0.43
LM + 5mm	*5.7%*	*3.3%*	*0.12*
DOCE	11.9%	9.6%	0.31
Definite/Probable Stent Thrombosis	2.7%	1.3%	0.21
BARC 3 or 5 bleeding	2.7%	0.5%	0.02

DOCE (cardiac death, MI not clearly attributable to a non-treated vessel, and idTVR).
MI: SCAI for periprocedural, 3rd Universial for spontaneous

Kaplan-Meier: MACE

IDEAL-LM



Xience plus
12 months DAPT

88.5%

85.3%

Synergy plus
4 months DAPT

Δ 3.2%

Log-Rank p=0.152

Landmark analysis: MACE

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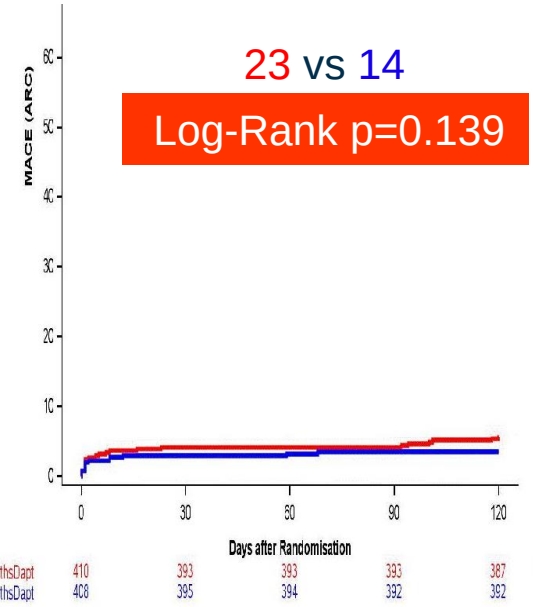
0-4 months

23 vs 14

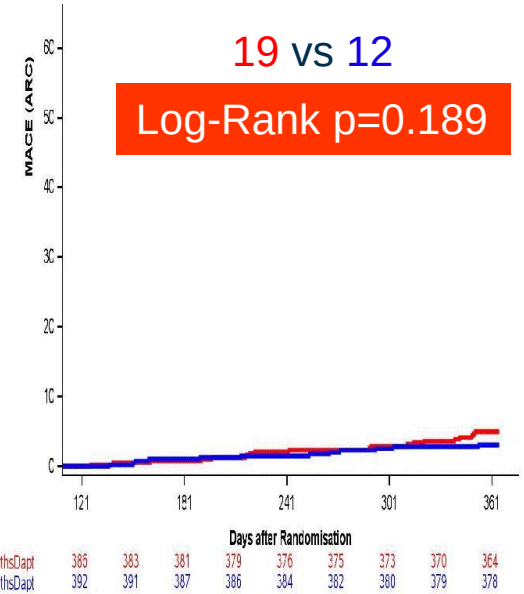
Log-Rank p=0.139



4-12 months

19 vs 12

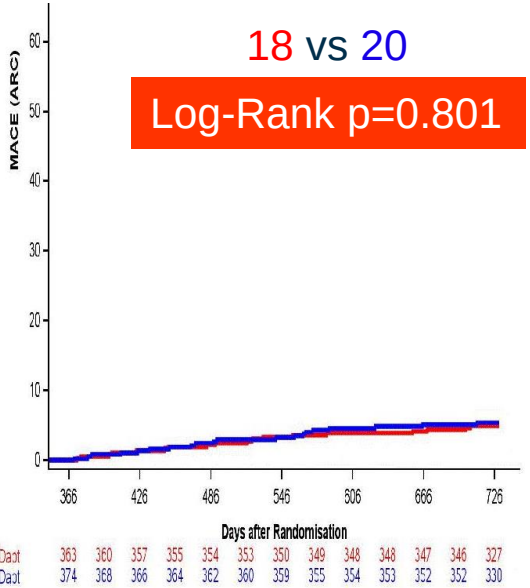
Log-Rank p=0.189



12-24 months

18 vs 20

Log-Rank p=0.801



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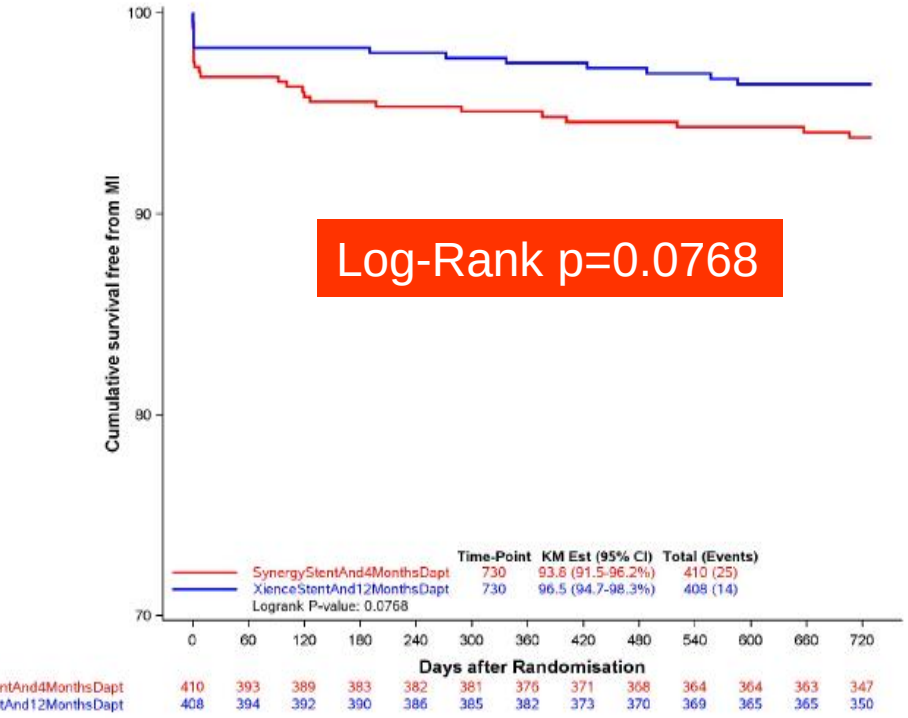
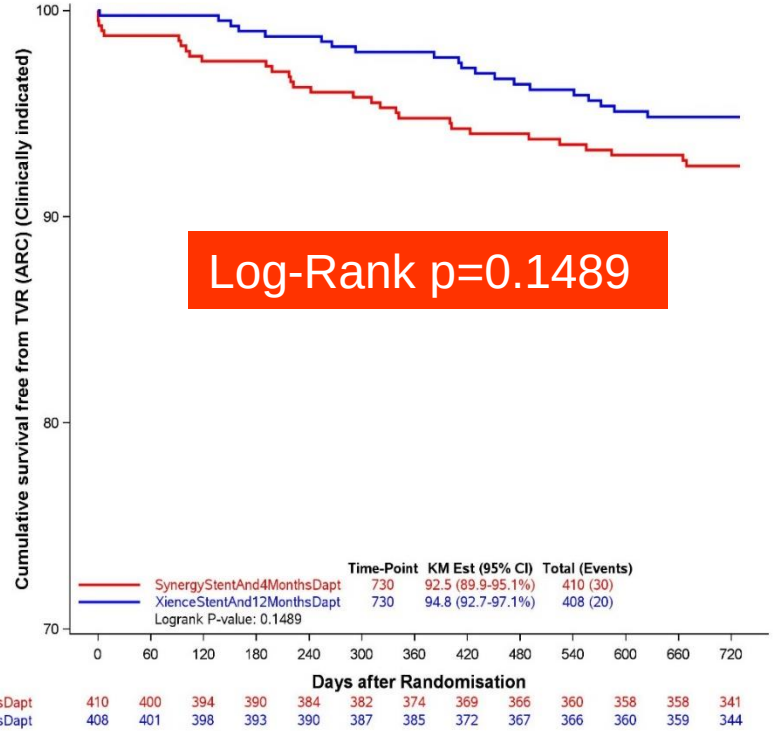
Myocardial Infarction



Ischaemia-driven TVR



BARC 3 or 5 bleeding

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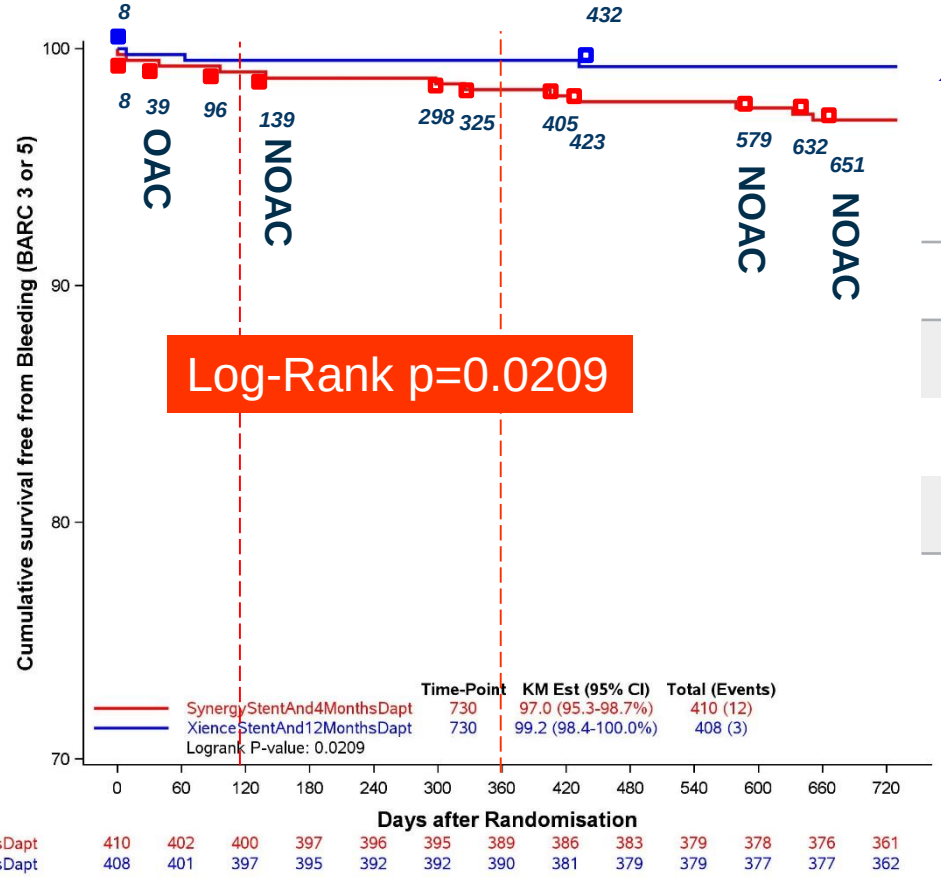

Xience plus 12 months DAPT

Synergy plus 4 months DAPT

	Synergy	Xience
On DAPT	4	1
Off DAPT	7	1
Total	11	2

- **Synergy on**
- **Synergy off**
- **Xience on**
- **Xience off**

Definite/Probable Stent Thrombosis

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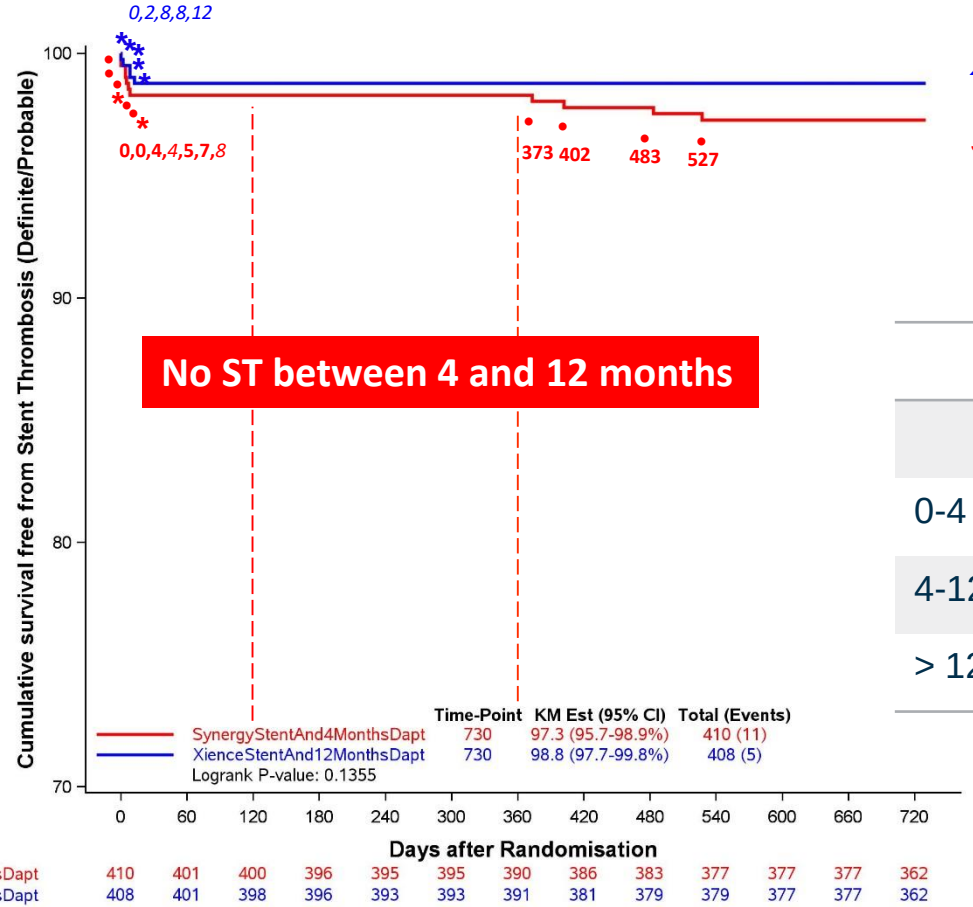


Xience plus 12 months DAPT

Synergy plus 4 months DAPT

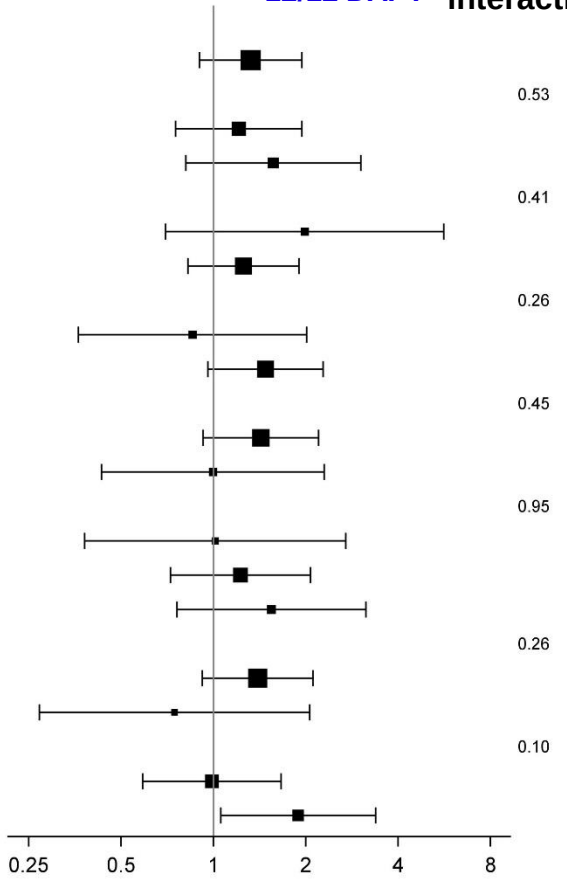
- **Definite ST;** ** Probable ST*

Definite/Probable ST

	Synergy	Xience
0-4 months	7	5
4-12 months	0	0
> 12 months	4	0

Cardiovascular® Research Foundation

Subgroup	Synergy + 4 months DAPT Events/N (%)		Xience + 12 months DAPT Events/N (%)		HR (95% CI)	P for interaction
All	60/ 410	(14.6)	46/ 408	(11.3)	1.32 (0.90 - 1.94)	
ACS						0.53
Non-ACS	38/ 260	(14.6)	31/ 253	(12.3)	1.21 (0.75 - 1.94)	
ACS	22/ 150	(14.7)	15/ 155	(9.7)	1.57 (0.81 - 3.02)	
Stent						0.41
Multiple stents	12/ 93	(12.9)	5/ 74	(6.8)	1.98 (0.70 - 5.63)	
Single stent	48/ 317	(15.1)	41/ 334	(12.3)	1.25 (0.82 - 1.90)	
Sites						0.26
Low recruiting sites	10/ 84	(11.9)	11/ 82	(13.4)	0.85 (0.36 - 2.01)	
High recruiting sites	50/ 326	(15.3)	35/ 326	(10.7)	1.48 (0.96 - 2.28)	
Access site						0.45
Radial access	49/ 335	(14.6)	35/ 334	(10.5)	1.43 (0.92 - 2.20)	
Non-Radial access	11/ 75	(14.7)	11/ 74	(14.9)	1.00 (0.43 - 2.30)	
SYNTAX						0.95
High	8/ 50	(16.0)	8/ 49	(16.3)	1.01 (0.38 - 2.70)	
Low	30/ 252	(11.9)	26/ 265	(9.8)	1.22 (0.72 - 2.07)	
Intermediate	21/ 106	(19.8)	12/ 92	(13.0)	1.54 (0.76 - 3.14)	
Eligible Surgery						0.26
Surgical	52/ 377	(13.8)	39/ 385	(10.1)	1.39 (0.92 - 2.11)	
Non-Surgical	8/ 33	(24.2)	7/ 23	(30.4)	0.75 (0.27 - 2.06)	
IVUS						0.10
No IVUS	29/ 235	(12.3)	28/ 224	(12.5)	0.99 (0.59 - 1.66)	
IVUS	31/ 175	(17.7)	18/ 184	(9.8)	1.89 (1.06 - 3.37)	



Conclusions

IDEAL-LM

- After 2 years, in patients undergoing LM-PCI, a Bioabsorbable Polymer Everolimus-Eluting Platinum Chromium stent (*Synergy*) followed by 4 months DAPT was **non-inferior** to a Permanent Polymer Everolimus-Eluting Cobalt Chromium stent (*Xience*) followed by 12 months DAPT with respect to the composite end point of death from any cause or MI or ischemia-driven target vessel revascularization.
- No difference in ischemic events up to 24 months
  - No difference in definite/probable stent thrombosis
  - No stent thrombosis in either group from 4 to 12 months (Synergy off DAPT)
- Excess BARC 3 or 5 bleeding in short DAPT group but…
  - 4/11 were on OAC/NOAC (2 on triple Rx) and 7/11 were off DAPT
  - Trial not powered for bleeding events

Trial Recruitment by Centre

IDEAL-LM

Moscow	**Merkulov**	**105**	Clinique-Saint Hilaire Rouen	Berland	19
Novosibirsk Research Institute	**Kretov**	**103**	Morriston Hospital	Chase	18
Golden Jubilee National Hospital	Oldroyd	83	Erasmus MC Rotterdam	van Geuns	13
Szpital Kliniczny Przemienienia Panskiego UM w Poznaniu	Lesiak	71	Polyclinique Les Fleurs Ollioules	Barragan	13
Royal Bournemouth Hospital	O Kane	47	Clinique St Martin à Caen	Morelle	13
Belfast City Hospital	Hanratty	46	Northern General Hospital	Gunn	10
Clinique des Nouvelles Cliniques Nantaises	Bressollette	42	Clinique Rhone Durance Avignon	Sainsous	10
Clinique Axium	Silvestri	37	CHU Rangueil	Carrie	10
Krasnoyarsk Regional Vascular Centre	Wlodarczak	30	Polsko Amerykanskie Kliniki Serca	Buszman	7
University Hospital of Wales	Anderson	25	State Budegatery Healthcare Institution	Osiev	5
Miedziowe Centrum Zdrowia	Protopopov	24	Clinique St Augustin	Darremont	4
Altnagelvin Hospital	Peace	23	Royal Infirmary of Edinburgh	Behan	3
Craigavon Hospital	Menown	22	Wielospecjalistyczny Szpital Miejski im. J. Strusia w Poznaniu	Rzezniczak	2
John Radcliffe Hospital	Banning	20	Onze Lieve Vrouwe Gasthuis	Slagboom	2
Essex CTC	Kelly	19			826

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