BioMimics 3D: the latest clinical evidence from the MIMICS Clinical Programme

Michael Lichtenberg, M.D.
Klinikum Arnsberg
Germany

Conflict of Interest Disclosure

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

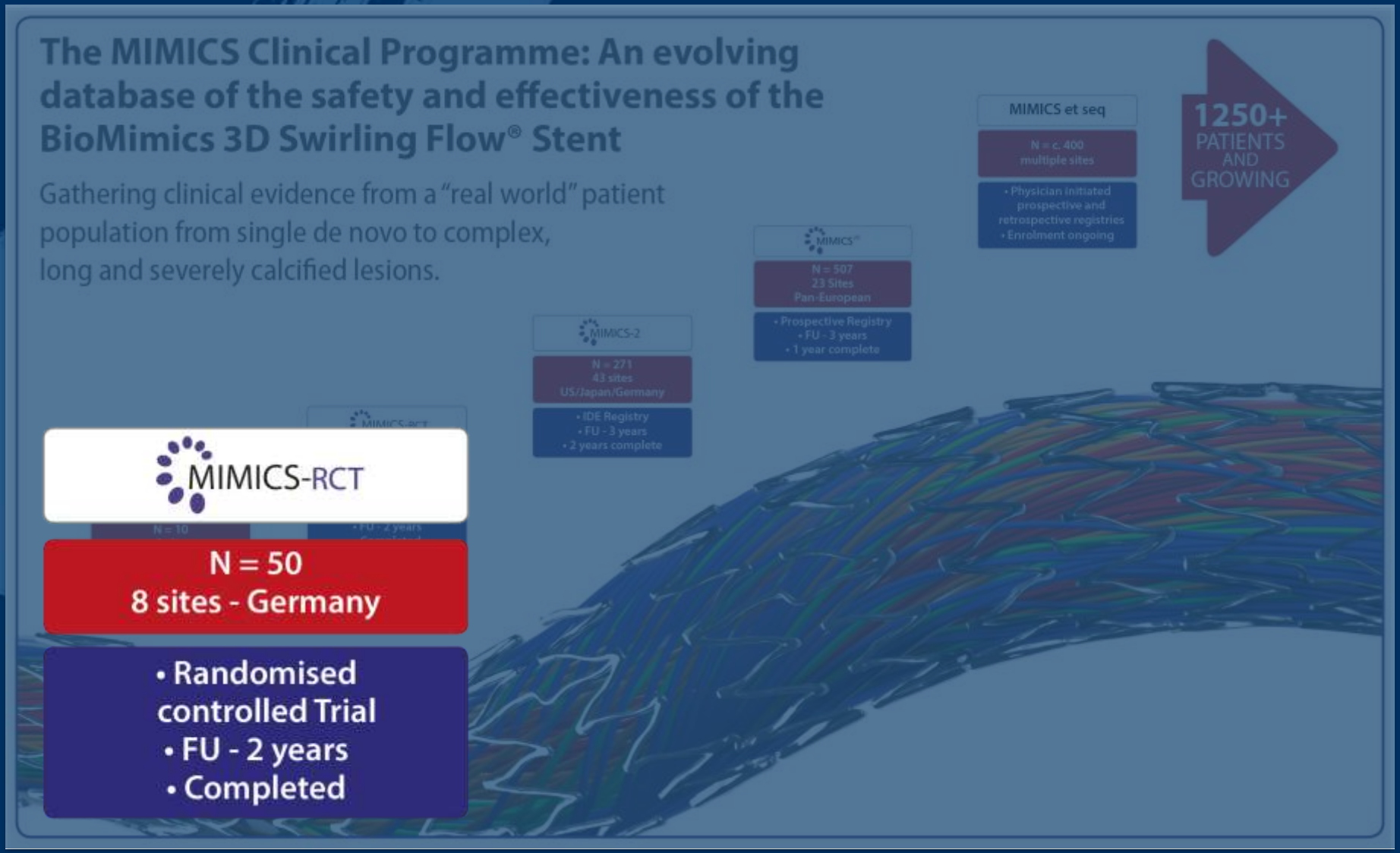
1. Honoraria for lectures: CR Bard, Veniti, AB Medica, Volcano, Optimed GmbH, Straub Medical, Terumo, Biotronik, Veryan

2. Honoraria for advisory board activities: Veniti, Optimed GmbH, Straub Medical, Biotronik, Veryan, Boston Scientific

3. Participation in clinical trials: Biotronik, CR Bard, Veryan, Straub Medical, Veniti, TVA Medical, Boston Scientific, LimFlow

4. Research funding: Biotronik, Boston Scientific, Veryan, Veniti, AB Medica

MIMICS Clinical Programme

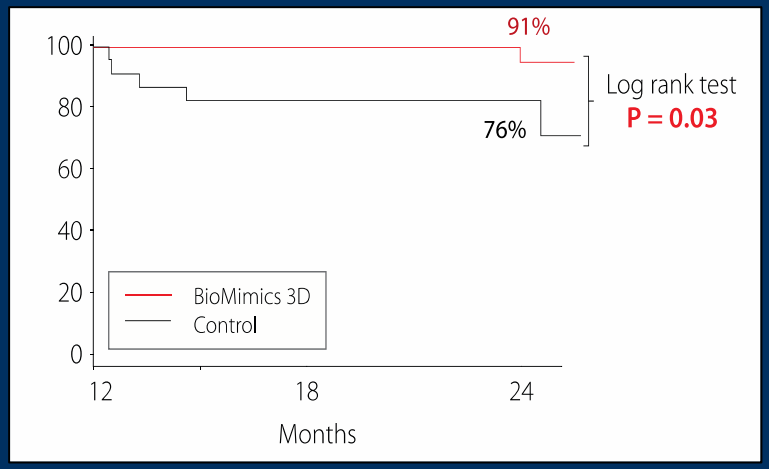


Mimics Randomized Controlled Trial

8 Investigational Sites *Corelab (DUS; angiography; Xray)*		
FIM Lead-in	N=10 BioMimics 3D	
Prospective Randomisation	BioMimics 3D N=50	Straight nitinol stent N=26
24-Month Primary Patency (p=0.05)	**72%**	**55%**
Freedom from CDTLR 12-24 months (p=0.03)	**91%**	**76%**

Freedom from CDTLR

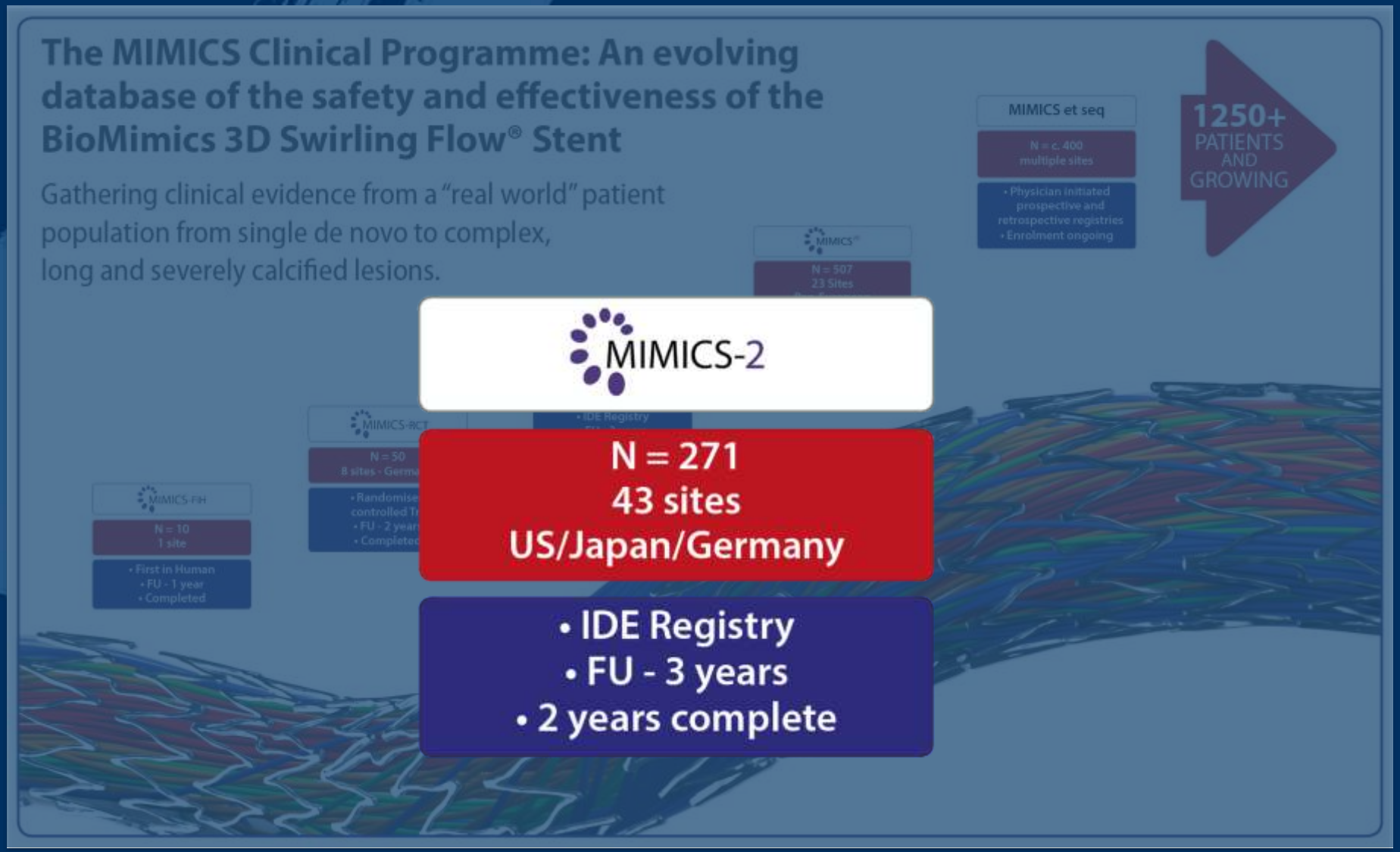
Landmark Analysis[2]



- Provided the first clinical proof supporting the durable outcome benefit arising from the BioMimics 3D Swirling Flow stent compared to a straight nitinol stent[1]

1. Zeller T et al; Circ Cardiovasc Interv. 2016
2. Sullivan TM et al; Int J Vasc Med. 2018

MIMICS Clinical Programme



MIMICS-2 (Multinational IDE Study)

Evaluation of Safety and Effectiveness of the BioMimics 3D Stent System in the Femoropopliteal Arteries of Patients with Symptomatic Peripheral Arterial Disease

- **Primary Endpoints**
  - Safety: composite of death, major amputation or CDTLR through 30 days
  - Effectiveness: primary patency at 12-months
- **Follow-up**: 3 years
- 43 investigational sites enrolled 271 subjects
  - US: 31 sites N = 162
  - Germany: 6 sites N = 78
  - Japan: 6 sites N = 31
- Core labs: ultrasound; angiography; X-ray
- Clinical Event Committee adjudication
- **Study Principal Investigators**
  - Timothy M. Sullivan, MD Minneapolis, MN, USA
  - Thomas Zeller, MD Bad Krozingen, Germany
  - Masato Nakamura, MD Tokyo, Japan

ClinicalTrials.gov Identifier: NCT02400905

MIMICS-2 (Multinational IDE Study)

Baseline Patient Demographics

		N= 271 Subjects
Age	Mean years ± SD (N)	68.4 ± 9.5 (271/271)
Gender	Male / Female	180 (66.4%) / 91 (33.6%)
Risk Factors	Diabetes Mellitus	45.4% (123/271)
	Hypertension	90.0% (244/271)
	Hypercholesterolemia	81.9% (222/271)
	Smoker Current / Former	80.8% (219/271)
Coronary Revascularization	Previous Percutaneous or Surgical	43.2% (117/271)
Previous Peripheral Intervention	None in target vessel	98.2% (266/271)
Rutherford Category	1	0% (0/271)
	2	26.9% (73/271)
	3	67.5% (183/271)
	4	5.2% (14/271)
	5	0.4% (1/271)
Ankle Brachial Index	Mean ± SD (N)	0.70 ± 0.20 (257/271)

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

Baseline Angiography and QVA

Core Laboratory Data		N= 271 Subjects
Reference Vessel Diameter (mm)	Mean ± SD	5.2 ± 0.9 (269/271)
Lesion Type[1]	De novo	100% (271/271)
Lesion Location in Femoropopliteal Artery	Prox	11.5% (31/270)
	Mid	48.1% (130/270)
	Distal	40.4% (109/270)
Diameter Stenosis (%)	Mean ± SD	77.8 ± 18.3 (269/271)
Lesion Length (mm)	Mean ± SD	81.2 ± 38.4 (269/271)
Total Occlusion (%)		30.0 (81/270)
Calcification (%)	None - Mild	54.1 (146/270)
	Moderate - Severe	45.9 (124/270)
Run-off (%) - 1 or more patent tibial artery (<50% stenosis)		98.8 (237/240)

[1] *Investigator-reported*

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

Index Procedure Data

		N= 271 Subjects
BioMimics 3D Stents placed[1]	# Stents / N	305 / 271
	# Subjects with 1 stent	87.5% (237/271)
	# Subjects with 2 stents	12.5% (34/271)
Stented Segment Length[2]	Mean ± SD (mm)	112.3 ± 36.3 (269/271)
Diameter Stenosis[2]	Pre-stent % ± SD	77.8 ± 18.3 (269/271)
	Post-stent % ± SD	12.6 ± 7.5 (269/271)
Dissections[2]	No Dissection	97.8% (263/269)
	Type A-C	2.2% (6/269)
	Type D-F	0% (0/269)
Device Success		100% (271/271)
Technical Success		100% (269/269)

[1] Investigator-reported

[2] CoreLab-reported

Technical Success: Core Lab determined ≤50% residual diameter stenosis (in-stent) at end of index procedure

Device Success: Successful delivery of System; placement of stent and retrieval of System

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

Primary Endpoint: **Safety**

Composite of CEC-adjudicated Major Adverse Events through 30 days, including death, any major amputation performed on the target limb, or Clinically-Driven Target Lesion Revascularisation

	Performance Goal	Rate (n/N) [95% CI]
Freedom from MAE through 30 days	>88%	**99.6%** (268/269) [97.7%, 100%]
Primary safety endpoint		**Achieved**

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

Primary Endpoint: **Effectiveness**

Primary stent patency rate at 12 months.

	Performance Goal	Rate (n/N) [95% CI]
Primary stent patency	>66%	**73.1%** (182/249) [67.3%, 78.2%]
Primary effectiveness endpoint		**Achieved**

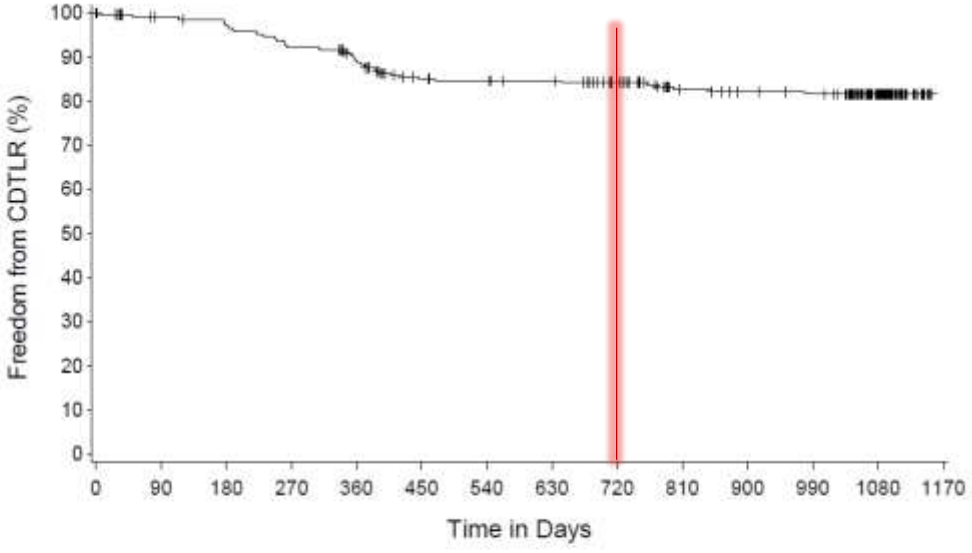
Patency was defined as no significant reduction in luminal diameter (< 50% diameter stenosis) since the index procedure.

Loss of patency was determined by an independent core laboratory when the peak systolic velocity ratio (PSVR) exceeds 2.0, or where angiography revealed > 50% diameter stenosis, or where the subject had a CDTLR.

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

Freedom from clinically-driven TLR* at 24 months = **84.2%**



Time (days):	0-0	1-30	31-360	361-365	366-720	721-730	731-1080	1081-1095
# at Risk (interval start):	271	266	223	222	179	177	91	60
# Subjects with Events:	0	1	27	1	11	0	5	0
# Censored:	0	4	16	0	32	2	81	31
Event-free % cumulative:	100%	99.6%	89.1%	88.7%	84.2%	84.2%	81.6%	81.6%
Standard error:	0.0%	0.4%	1.9%	2.0%	2.3%	2.3%	2.5%	2.5%
95% Confidence Interval:								76.7%, 86.5%

**Core Lab adjudicated, clinically-driven TLR with objective evidence*
Subjects are censored at their last known follow-up, or at time of study exit (withdrawal or lost to follow-up) or death

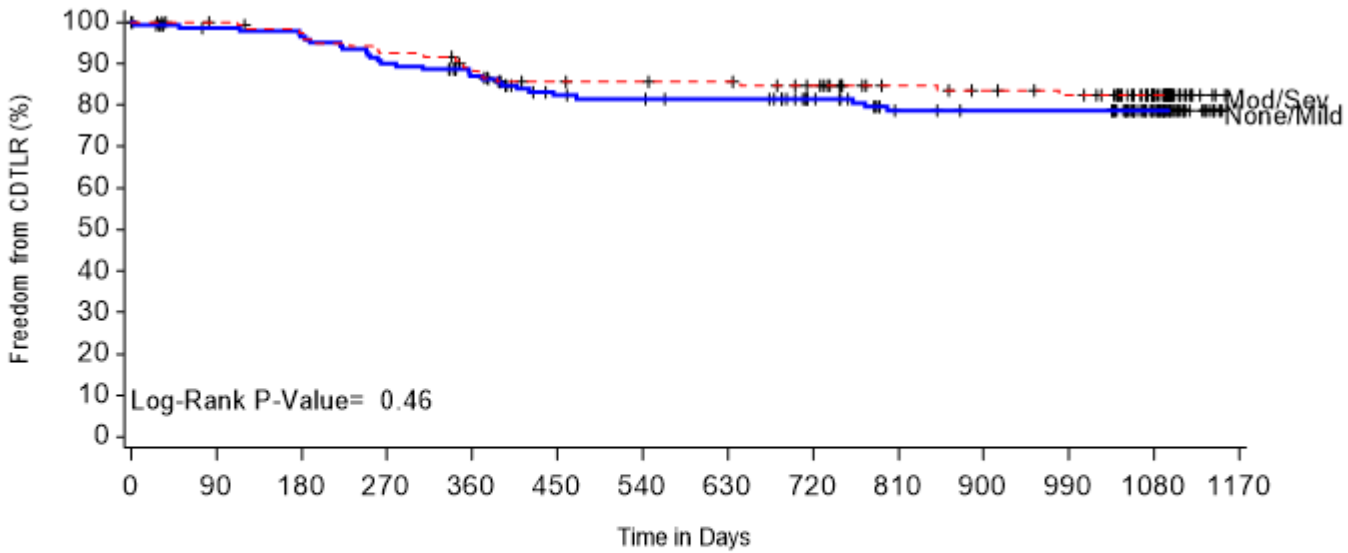
The Swirling Flow® Stent: delivering continuing benefit at **2 Years**, even in challenging cases

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

*Kaplan Meier survival estimates of freedom from clinically-driven TLR**

***Lesion Calcification** (CoreLab)*



Time (days):	0-0	1-30	31-360	361-365	366-720	721-730	731-1080	1081-1095
None/Mild								
# at Risk (interval start):	146	142	115	115	88	87	43	28
# Subjects with Events:	0	1	17	0	7	0	3	0
Event-free % :	100%	99.3%	87.0%	87.0%	81.5%	81.5%	78.6%	78.6%
Mod/Sev								
# at Risk (interval start):	124	123	104	103	87	86	45	29
# Subjects with Events:	0	0	13	1	4	0	2	0
Event-free % :	100%	100%	89.1%	88.2%	84.7%	84.7%	82.4%	82.4%

**CEC adjudicated, clinically-driven TLR with objective evidence*

Subjects are censored at their last known follow-up, or at time of study exit (withdrawal or lost to follow-up) or death

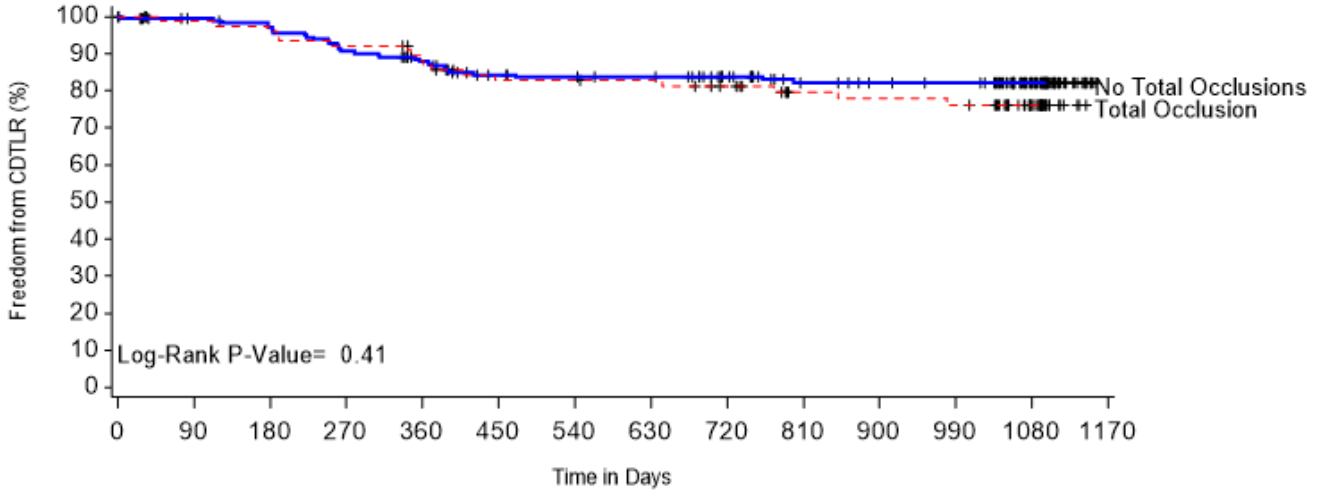
The Swirling Flow® Stent: delivering continuing benefit at **2 Years**, even in challenging cases

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

*Kaplan Meier survival estimates of freedom from clinically-driven TLR**

Occlusion vs. No Occlusion



Time (days):	0-0	1-30	31-360	361-365	366-720	721-730	731-1080	1081-1095
No Total Occlusions								
# at Risk (interval start):	189	185	153	153	121	119	62	45
# Subjects with Events:	0	1	21	0	7	0	2	0
Event-free % :	100%	99.5%	87.8%	87.8%	83.7%	83.7%	82.2%	82.2%
Total Occlusion								
# at Risk (interval start):	81	80	66	65	54	54	26	12
# Subjects with Events:	0	0	9	1	4	0	3	0
Event-free % :	100%	100%	88.2%	86.9%	81.3%	81.3%	76.2%	76.2%

**Core Lab adjudicated, clinically-driven TLR with objective evidence*

Subjects are censored at their last known follow-up, or at time of study exit (withdrawal or lost to follow-up) or death

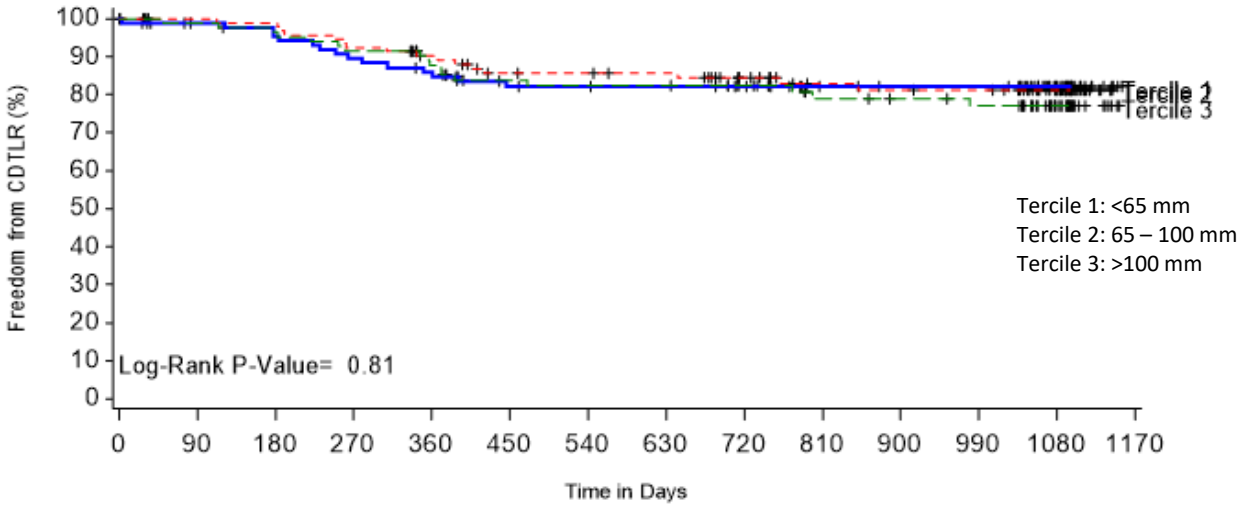
The Swirling Flow® Stent: delivering continuing benefit at **2 Years**, even in challenging cases

Data on file at Veryan Medical

MIMICS-2 (Multinational IDE Study)

*Kaplan Meier survival estimates of freedom from clinically-driven TLR**

Tercile of Lesion Length



Time (days):	0-0	1-30	31-360	361-365	366-720	721-730	731-1080	1081-1095
Tercile 1								
# at Risk (interval start):	90	87	72	71	62	61	31	21
# Subjects with Events:	0	1	11	1	2	0	0	0
Event-free % :	100%	98.9%	85.9%	84.7%	82.2%	82.2%	82.2%	82.2%
Tercile 2								
# at Risk (interval start):	95	94	80	80	60	59	34	22
# Subjects with Events:	0	0	9	0	5	0	2	0
Event-free % :	100%	100%	90.2%	90.2%	84.4%	84.4%	81.2%	81.2%
Tercile 3								
# at Risk (interval start):	86	85	68	68	54	54	24	15
# Subjects with Events:	0	0	10	0	4	0	3	0
Event-free % :	100%	100%	87.6%	87.6%	82.3%	82.3%	77.1%	77.1%

**Core Lab adjudicated, clinically-driven TLR with objective evidence*
Subjects are censored at their last known follow-up, or at time of study exit (withdrawal or lost to follow-up) or death

The Swirling Flow® Stent: delivering continuing benefit at **2 Years**, even in challenging cases

Data on file at Veryan Medical

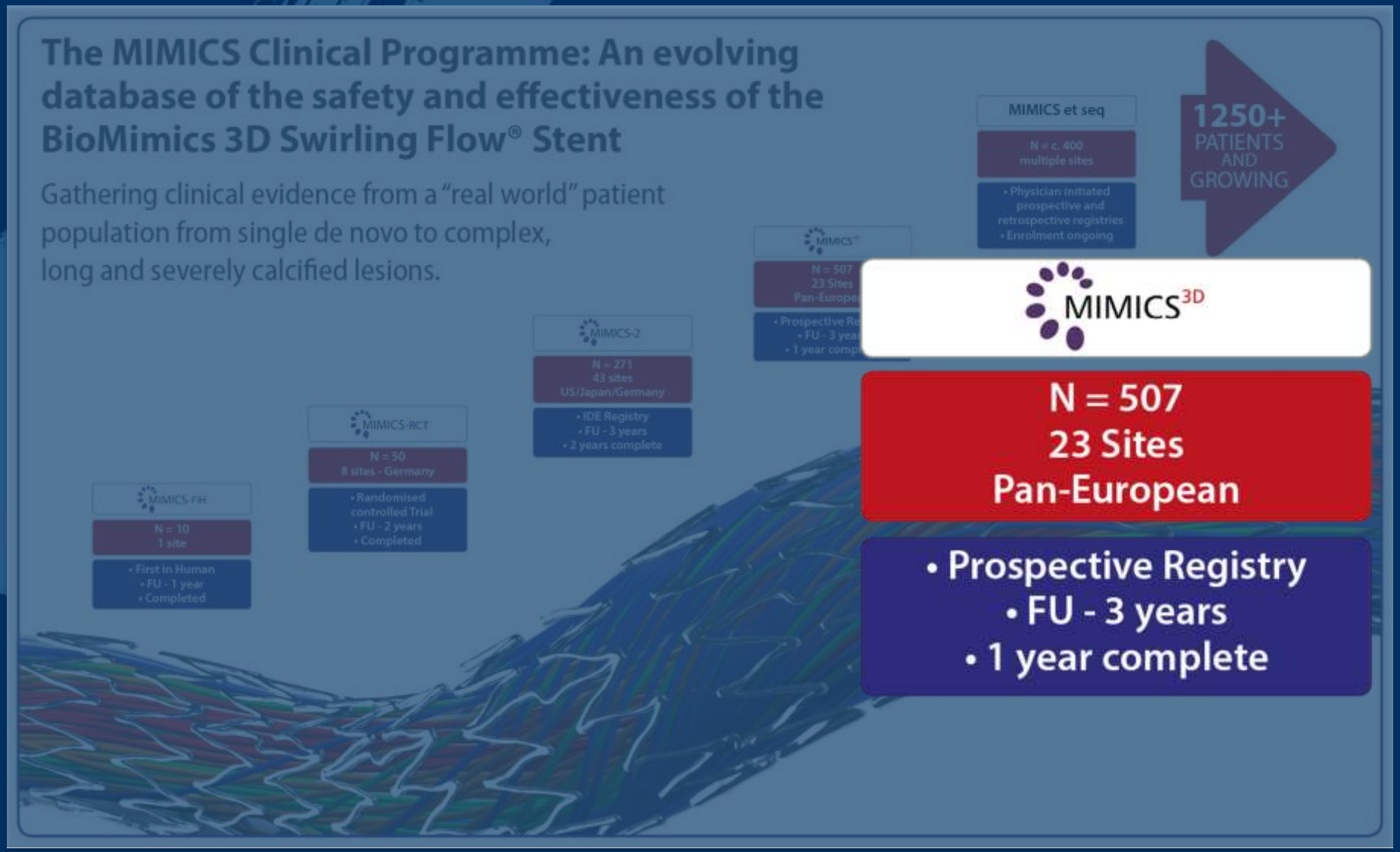
Mimics RCT and MIMICS-2

What have we learned so far about the Swirling Flow stent?

- Randomized data from Mimics RCT showed patency superiority for BioMimics 3D over a straight nitinol stent and no CD-TLR between 12 and 24 months
- MIMICS-2 is an IDE study of 271 subjects with more complex lesions
  - CD-TLR outcomes comparable with drug eluting devices
  - Outcomes not affected by calcification, lesion length or number of stents

The Swirling Flow® Stent: delivering continuing benefit at **2 Years**, even in challenging cases

MIMICS Clinical Programme



MIMICS-3D Registry

A Prospective, Multicentre Observational Study to Evaluate BioMimics 3D Stent in PAD in the Real World

Principal Investigator: Michael Lichtenberg MD, Arnsberg, Germany

- 23 European investigators enrolled 507 subjects
  - 24% critical limb ischemia (RCC 4-6)
  - 38% moderate to severe calcification (PACSS 2 or 4)
  - 50% of lesions concomitantly treated with DCB
- Primary Endpoints:
  - 30-day CEC-adjudicated Safety: death, major amputation or CDTLR
  - 12-month Effectiveness: freedom from CDTLR

Rocha-Singh KJ et al

Longer, more complex lesions

Mean ± SD (mm)	MIMICS-RCT	MIMICS-2	MIMICS-3D
Lesion Length	66 ± 29	81 ± 38	**127 ± 92**
Stented Segment Length	**99** ± 30	**112** ± 36	**131 ± 79**

- Sicker patients, longer and more complex lesions
- BioMimics 3D stent use 50:50 primary or bail-out to DCB
- Highly relevant population for a contemporary registry

MIMICS-3D Study Results

Primary Endpoints

- 30-day Safety:
  - **99%** (486/492) Freedom from MAE
    - 2 TLR (Day 13, 18); 2 Amputations (Day 3, 8); 2 Deaths (closure system failure & leukemia)
- 12-month Effectiveness:
  - **89%** (380/427) Freedom from CDTLR

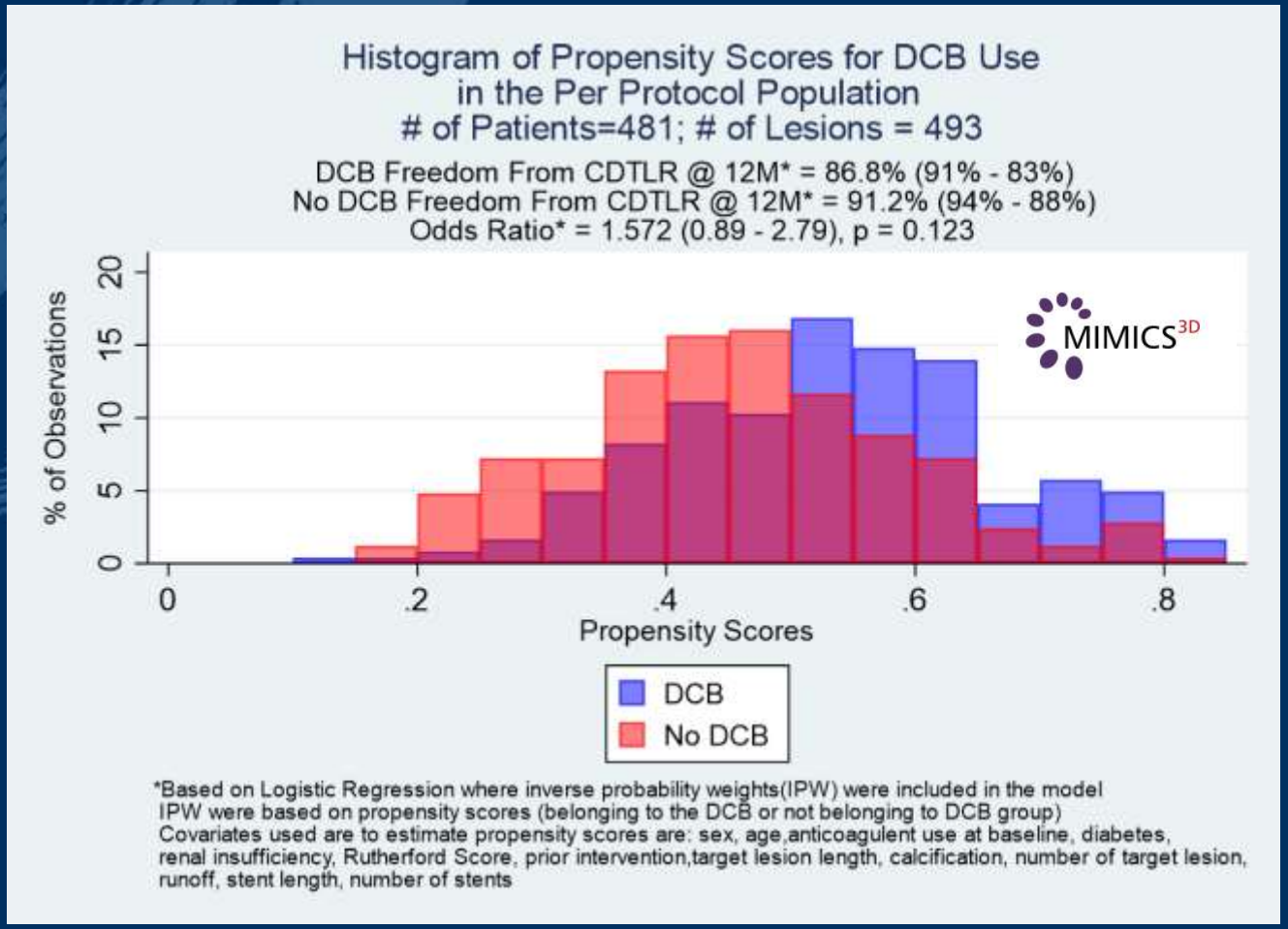
MIMICS-3D: BioMimics 3D The Swirling Flow® Stent ± Drug-Coated Balloon

	BioMimics 3D *with* DCB	BioMimics 3D *without* DCB	Overall result
Freedom from CDTLR at 12 months *(ITT population)*	**89.5%**	**88.5%**	**89.0% [p > .88]**

- Could imbalance in distribution of lesion characteristics or patient demographics be confounding?
- Propensity score analysis of per-protocol population adjusts for the difference between patient-level characteristics within selected subgroups

Data on file at Veryan Medical

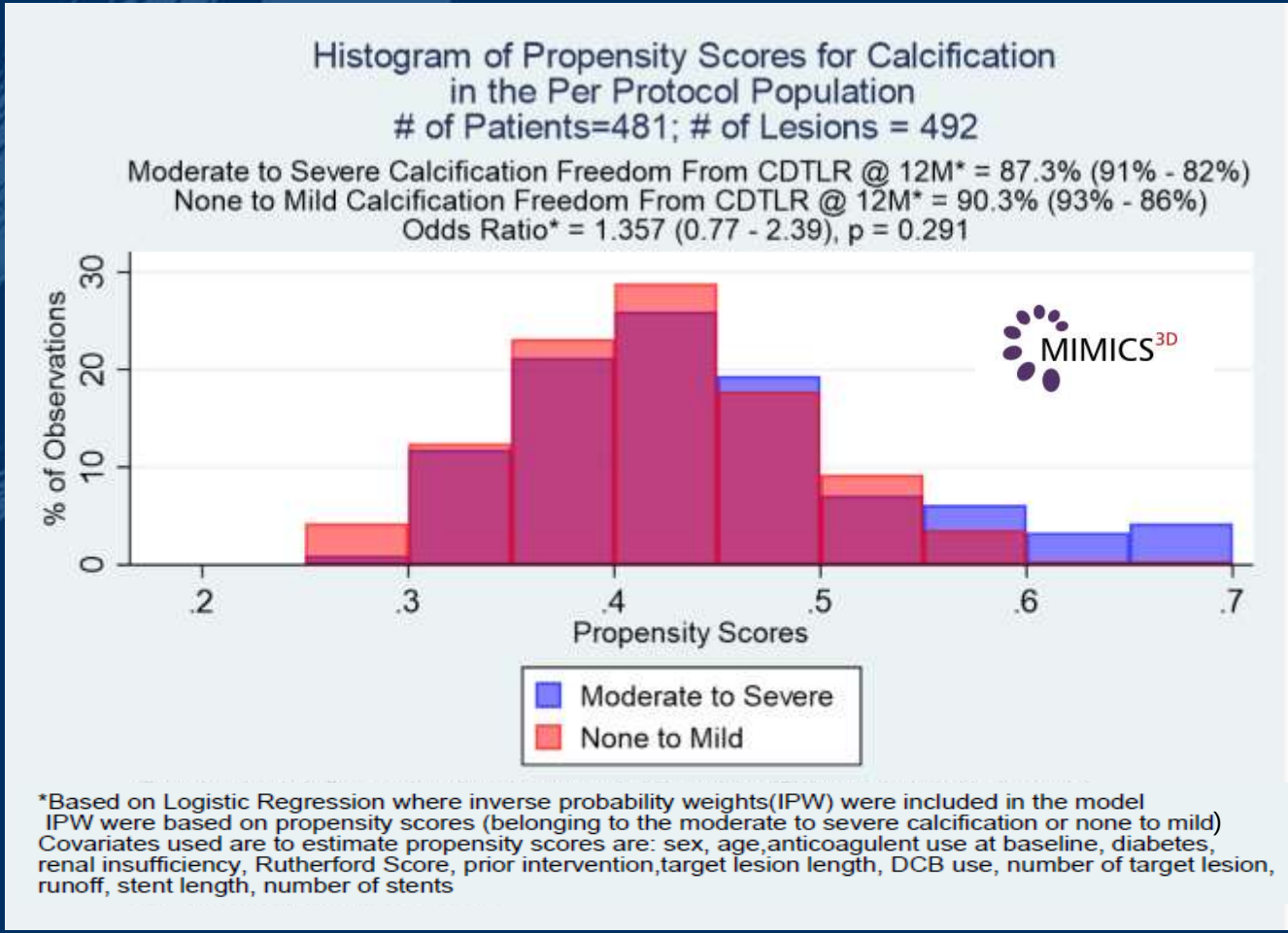
BioMimics 3D With / Without DCB



Propensity matched analysis reveals the rate of CDTLR in MIMICS-3D was independent of DCB use

Data on file at Veryan Medical

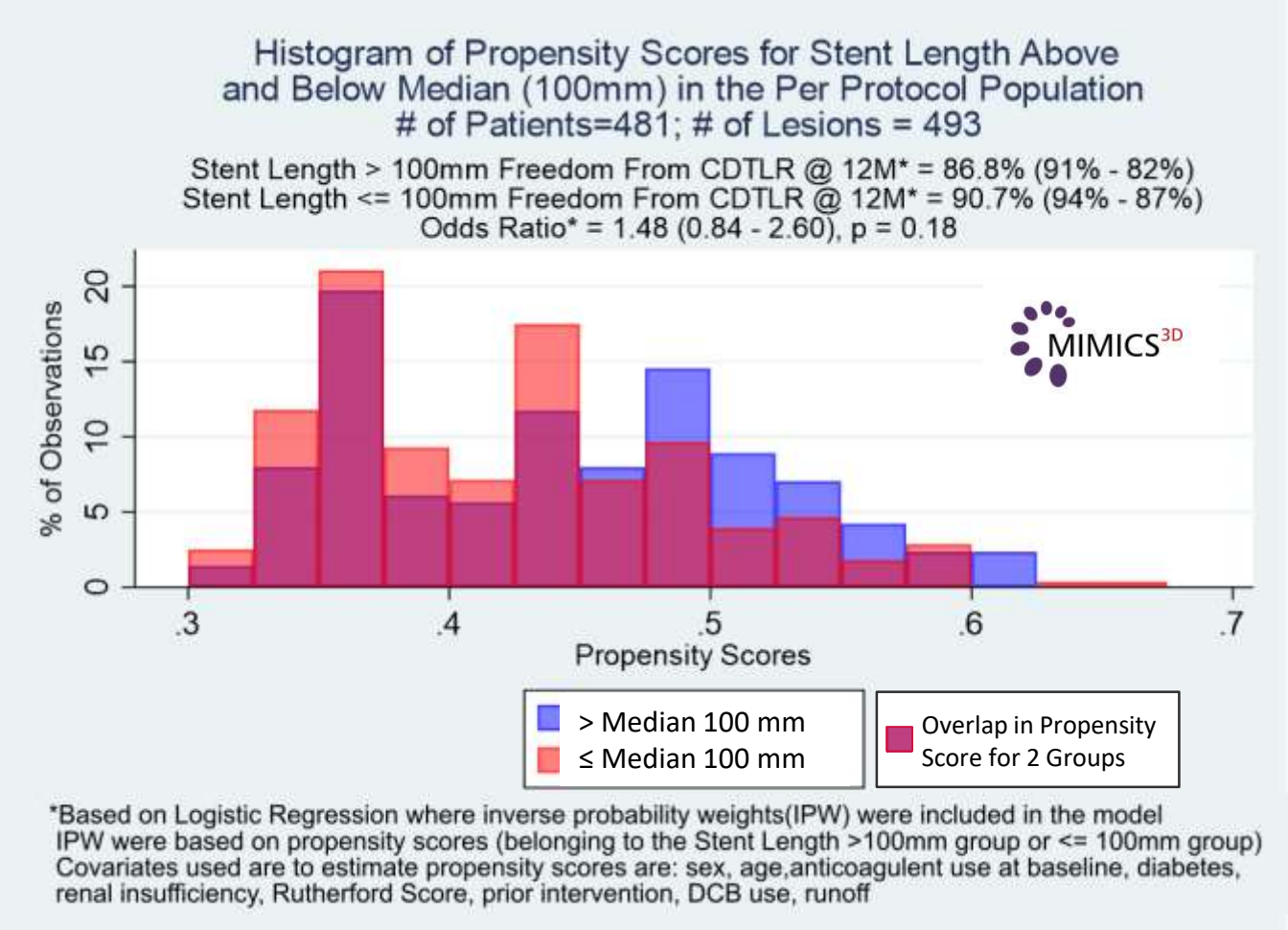
Effect of Lesion Calcification



Propensity matched analysis reveals the rate of CDTLR in MIMICS-3D was independent lesion calcification

Data on file at Veryan Medical

Effect of Stent Length



Propensity matched analysis reveals the rate of CDTLR in MIMICS-3D was independent of stent length

Data on file at Veryan Medical

MIMICS-3D Registry

- 12-month freedom from CD-TLR was 89% in a challenging real-world population
- Rate of CD-TLR was independent of concomitant DCB use, lesion calcification and stent length
- MIMICS-3D data contribute real-world experience to the evolving database supporting the therapeutic value of swirling flow in the BioMimics 3D stent
- 3-year follow-up continues

BioMimics 3D: the latest clinical evidence from the MIMICS Clinical Programme

Michael Lichtenberg, M.D.
Klinikum Arnsberg
Germany