ZOMAXX I

A Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the ZoMaxx™ Drug-Eluting Coronary Stent System Compared to the TAXUS™ Express²™ Paclitaxel-Eluting Coronary Stent System in *de novo* Coronary Artery Lesions

B Chevalier

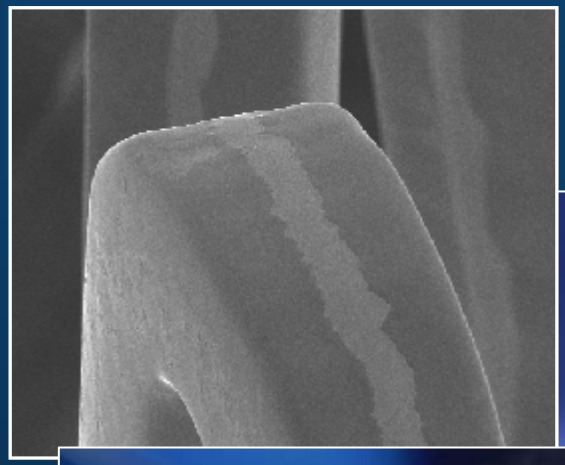
For the ZOMAXX I Investigators

Conflict of Interest

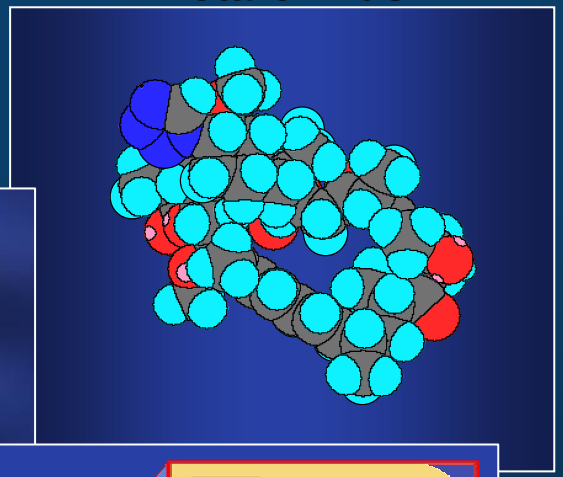
- Consultant to Abbott Vascular

ZoMaxx

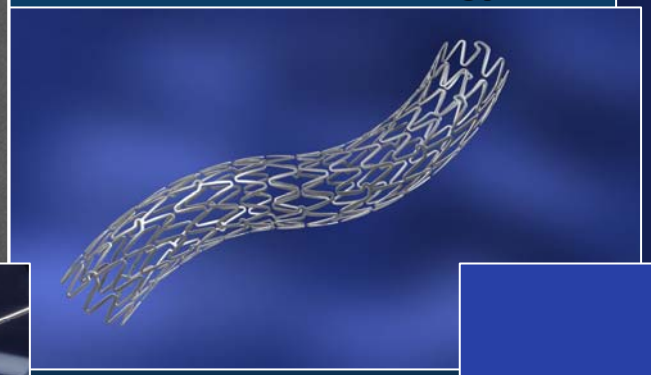
Triplex Material*



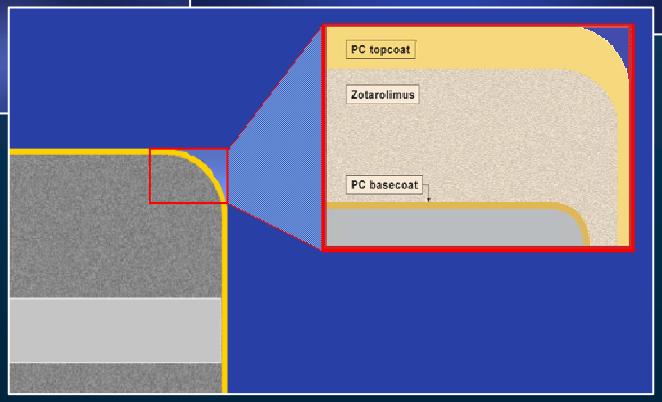
Zotarolimus



O.C.C. Technology



Stent Delivery Catheter

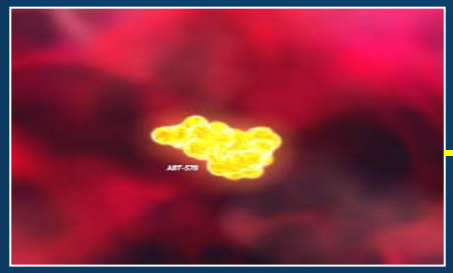


Phosphorylcholine (PC)

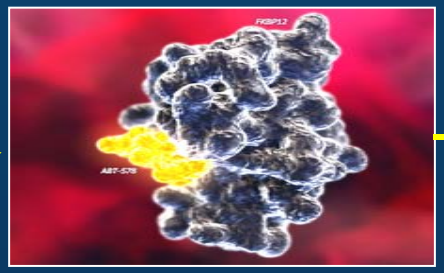
*Triplex is a trademark of Uniform Tubing, Inc

Zotarolimus

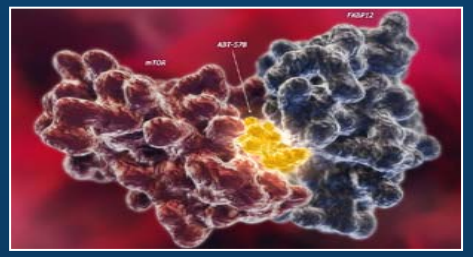
Mode of Action



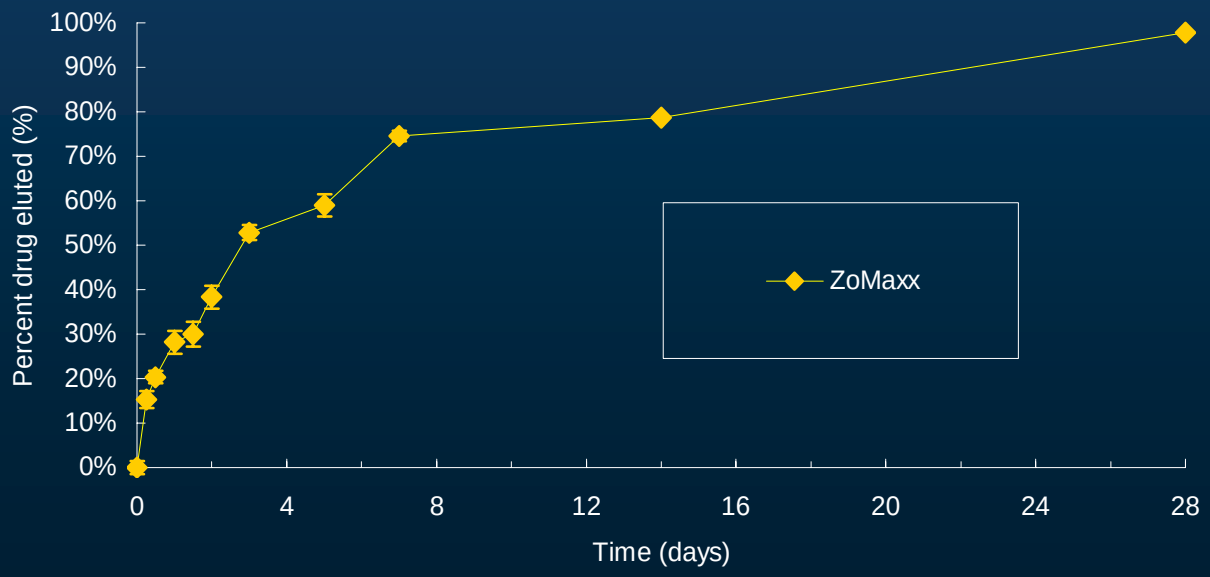
Zotarolimus



Zotarolimus binds with FKBP-12 protein



Complex blocks mTOR signal transduction



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ZOMAXX Clinical Program

TRIMAXX study	FIM study 100 patients, single arm, clinical endpoint
ZOMAXX IVUS	FIM study 40 patients, single arm, IVUS endpoint
ZOMAXX I	International pivotal study 400 patients, RCT, angiographic endpoint
ZOMAXX II	US pivotal study 1670 patients, RCT, clinical endpoint
ZOMAXX EUROPE	European single/double vessel 900 patients, single arm, clinical endpoint

ZOMAXX I

ZOMAXX I Trial

PI: Bernard Chevalier

Single, *de novo* coronary lesions
lesion length ≥ 10 mm and ≤ 30 mm,
RVD 2.5-3.5 mm.
Pre-dilatation required

ZoMaxx Stent N=200	TAXUS Stent N=200

Clinical follow-up

30d | 6mo | 9mo | 12mo | 2yr | 3yr | 4yr | 5yr

Angio & IVUS follow-up

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Trial Management

Steering Committee

Bernard Chevalier MD (Chairman),Carlo DiMario MD, Franz-Josef Neumann MD, Flavio Ribichini MD, Philip Urban MD

QCA Core Lab

Brigham and Women's Angiographic Core Lab, Boston, MA, Jeffrey J. Popma, MD

IVUS Core Lab

Cardiovascular Core Analysis Lab (CCAL), Stanford, CA, Peter J. Fitzgerald, MD, PhD

Data Management / Clinical Events Committee

Harvard Clinical Research Institute (HCRI), Boston, MA, Donald Cutlip, MD

DSMB

David Williams MD, Chairman

Sponsor

Abbott Vascular

Investigational Centers

Investigator	Hospital	Patients
Robert Whitbourn	St. Vincent's Hospital	40
John Ormiston	Auckland City Hospital	40
Eberhard Grube	Heart Center Siegburg	39
Franz-Josef Neumann	Herz-Zentrum Bad Krozingen	34
Hubertus Heuer	St. Johannes Hospital	28
Didier Carrié	Hôpital de Rangueil-CHU	28
Thomas Heitzer	Universitätsklinikum Eppendorf	21
Ian Meredith	Monash Medical Centre	19
Olivier Bar	Clinique Saint Gatien	14
Bernard Chevalier	Centre Cardiologique du Nord	13
Joseph Dens	Ku Leuven-UZ Gasthuisberg	12
Kari Saunamäki	Heart Centre Rigshospitalet	12
Philippe Commeau	Polyclinique les Fleurs	11
Peter Sick	Leipzig Heart Center	10
Carlo DiMario	Royal Brompton Hospital	10

Investigational Centers

Investigator	Hospital	Patients
Paul Vermeersch	Middelheim Algemeen Ziekenhuis	9
Raimund Erbel	Universitätsklinikum Essen	7
Gerry Wilkins	Dunedin Hospital	7
Leif Thuesen	Skejby Sygehus	7
Sigmund Silber	Hospital Prof. Silber	7
Victor M.G. Legrand	C. H. U. Sart Tilman	6
Bernard de Bruyne	Onze Lieve Vrouw Hospital	5
Ricardo Seabra-Gomes	Hospital de Santa Cruz	4
Jean Fajadet	Clinique Pasteur	3
Philip Urban	La Tour Hospital	3
Martin Rothman	London Chest Hospital	3
Franz R. Eberli	University Hospital	2
Michael Pieper	Herzzentrum Bodensee	1
Patrick Serruys	Erasmus MC Rotterdam	1

Study Endpoints

- **Primary Endpoint**
  - 9-month in-segment late loss
    - One-sided 95% upper confidence bound for the difference in means between treatment groups
    - Margin of difference to support non-inferiority was 0.25mm
    - SD = 0.40
    - Alpha = 0.05
    - Power = >90%

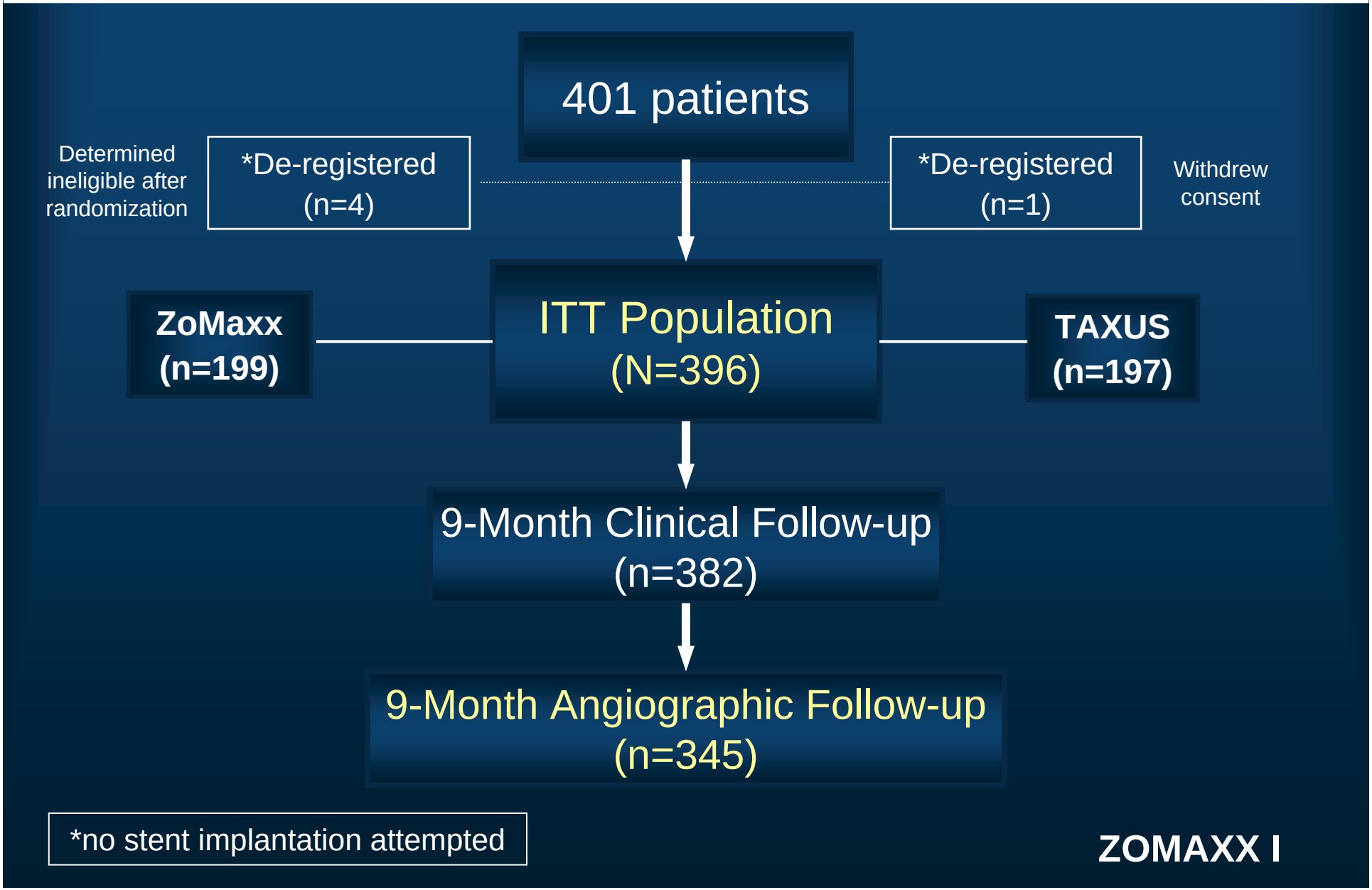
Study Endpoints

- **Key Secondary Endpoints**
  - Clinical
    - MACE, TLR, TVR, TVF, Stent Thrombosis
  - Angiographic
    - In-Stent Late Loss, In-Stent & In-Segment Binary Restenosis
  - IVUS
    - % Neointimal Volume Obstruction

Key Exclusion Criteria

- AMI within 72 hours of procedure
- Creatinine > 2.0 mg/dL
- Stroke or TIA within 6-months
- Ostial lesion location
- Planned or prior
  - Brachytherapy
  - PCI within 30-days in any vessel
  - DES within 60-days in any vessel

Patient Flow



Demographics

	ZoMaxx (n=199)	TAXUS (n=197)	P-Value
Age (years)	63 ± 10	63 ± 11	0.98
Male gender	75%	77%	0.64
Unstable angina	26%	24%	0.73
Hypercholesterolemia	78%	72%	0.13
Hypertension	69%	67%	0.67
Diabetes	22%	26%	0.29
Insulin dependent	8.0%	8.6%	0.86
Prior MI	29%	29%	1.00
Prior PCI	20%	25%	0.23
Prior CABG	4.5%	1.0%	0.06

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Baseline Vessel and Lesion Characteristics

	ZoMaxx (n=199)	TAXUS (n=197)	P-Value
Vessel location			**0.025**
LAD	48%	40%	--
LCX	24%	19%	--
RCA	28%	41%	*
Lesion location			**0.031**
Ostial	4.0%	0%	**
Proximal	39%	41%	--
Mid	51%	51%	--
Distal	6.0%	8.6%	--

RCA vs others *p=0.008; Ostial vs others ** p=0.007

Baseline Vessel and Lesion Characteristics

	ZoMaxx (n=199)	TAXUS (N=197)	P-Value
RVD (mm)	2.79 ± 0.43	2.81 ± 0.46	0.66
Lesion length (mm)	14.9 ± 5.7	14.6 ± 5.5	0.61
< 10 mm	19%	19%	-
10 - 19.9 mm	65%	63%	-
≥ 20 mm	16%	18%	-
Total stent length (mm)	21.3 ± 5.9	20.8 ± 5.7	0.35
Stent / lesion ratio	1.57 ± 0.60	1.55 ± 0.55	0.65
Stents / patient	1.10 ± 0.39	1.10 ± 0.32	0.98

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Post-Procedure Results

	ZoMaxx (n=199)	TAXUS (n=197)	P-Value
Lesion success	**99%**	**99%**	**0.62**
Device success	**99%**	**99%**	**0.68**
Procedure success	**95%**	**96%**	**0.64**

Lesion success: <30% residual in-stent diameter stenosis;

Device success: <30% residual in-stent diameter stenosis with assigned stent;

Procedure success: <30% residual in-stent diameter stenosis without in-hospital MACE.

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Post-Procedure Results

	ZoMaxx (n=170)	TAXUS (n=175)	P-Value
In-stent			
MLD (mm)	2.71 ± 0.39	2.72 ± 0.43	0.76
DS (%)	4.6 ± 7.9%	4.4 ± 8.5%	0.80
Acute gain (mm)	1.90 ± 0.41	1.96 ± 0.49	0.29
In-segment			
MLD (mm)	2.29 ± 0.47	2.29 ± 0.49	0.98
DS (%)	20 ± 9.7%	20 ± 9.5%	0.76
Acute gain (mm)	1.49 ± 0.45	1.53 ± 0.51	0.45

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MACE at 30-Days

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
Cardiac death	0%	0%	--
Q-wave MI	0.5%	0.5%	1.00
Non Q-wave MI	4.5%	3.6%	0.80
TVR (ischemia-driven)	0%	1.0%	0.25
MACE*	**5.0%**	**4.1%**	**0.81**

*Hierarchical analysis

Non Q-wave MI – CK > 2.0 x normal with elevated CK-MB in the absence of new pathological Q-waves. (WHO)

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Protocol Specified Parametric Analysis

Primary Endpoint	ZoMaxx Mean±SD	Taxus Mean±SD	Mean Difference	Upper 1-sided confidence interval
In-segment late loss (mm)	0.43 ± 0.60	0.25 ± 0.45	0.17	0.27

Protocol specified 9-month in-segment late loss non-inferiority margin of 0.25 mm was exceeded by 0.02 mm

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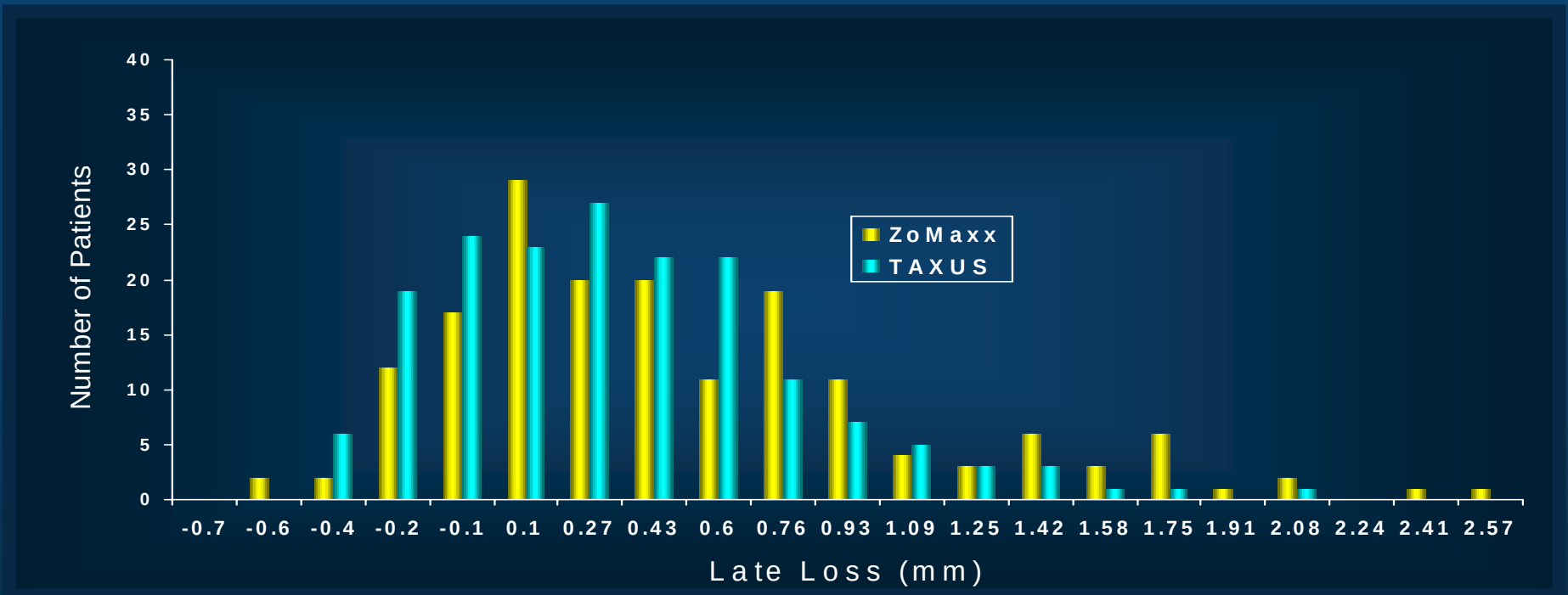
Distribution of In-Segment Late Loss



Assumptions for Parametric Non-inferiority Test

1. Normality: Yes for Taxus ($p \geq 0.05$) and No for ZoMaxx ($p < 0.05$)
2. Homogeneity of Variance: No ($p < 0.05$)

Based on distribution & variance of angiographic data, a non-parametric analysis is the appropriate statistical presentation of the primary endpoint versus the protocol specified parametric analysis

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Non-parametric Analysis

Primary Endpoint	ZoMaxx Median (IQR)	Taxus Median (IQR)	Median difference	Upper 1-sided confidence interval
In-segment late loss (mm)	0.29 (-0.01-0.73)	0.22 (-0.09-0.54)	0.12	0.21

9-month in-segment late loss upper 1-sided confidence interval of 0.21 is less than the non-inferiority margin of 0.25 mm

Non-protocol specified analysis based on Price RM, Bonett DG. Distribution-Free Confidence Intervals for Difference and Ratio of Medians. J Statist Comput Simul. 2002. 72(2):119-124.

Angiographic Results

	ZoMaxx (n=170)	Taxus (n=175)	P-Value
In-stent			
Late loss (mm)	0.67 ± 0.57	0.45 ± 0.48	<0.001
Restenosis	12.9%	5.7%	0.03
In-segment			
Late loss (mm)	0.43 ± 0.60	0.25 ± 0.45	0.003
Restenosis	16.5%	6.9%	0.007

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IVUS Results

	ZoMaxx (n=114)	Taxus (n=120)	P-Value
Stent volume (mm^3)	155 ± 62	143 ± 58	0.20
Lumen volume (mm^3)	132 ± 54	127 ± 55	0.54
Neointimal volume obstruction (%)	14.6 ± 7.9%	11.3 ± 9.6 %	0.02
Stent incomplete apposition (SIA)			
Post-Procedure	20%	19%	0.86
Resolved at Follow-up	10.6%	8.9%	0.81
Persistent at Follow-up	9.6%	9.9%	1.00
New (late acquired)	0.0%	3.0%	0.25

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Compliance to Medication Regimen

Medication	Treatment	Pre	Discharge	30-day	6-month	9-month
Aspirin	ZoMaxx	96.5%	99.0%	98.5%	94.9%	93.4 %
	Taxus	100%	99.5%	97.4%	98.0%	96.9%
Clopidogrel or Ticlopidine	ZoMaxx	93.5%	99.5%	96.5%	81.3%	55.1%
	Taxus	97.0%	99.5%	100%	83.7%	47.4%

Medications:

Loading dose: Clopidogrel 300 mg, Aspirin at least 100 mg

Follow-up: Clopidogrel 75 mg QD for at least 6 months, Aspirin 100 mg QD ≥12 months

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MACE at 9-Months

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
Cardiac death	0%	0%	--
Q-wave MI	1.0%	0.5%	1.00
Non Q-wave MI	4.5%	4.1%	1.00
TVR (ischemia-driven)	8.5%	6.6%	0.57
MACE*	**12.6%**	**9.6%**	**0.43**

*Hierarchical analysis
Analysis includes follow-up angiography through 284 days

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MACE at 12-Months

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
Cardiac death	0.5% (1)	0.0% (0)	NS
Q-wave MI	1.0% (2)	0.5% (1)	NS
Non Q-wave MI	4.5% (9)	4.1% (8)	NS
TVR (ischemia-driven)	10.1% (20)	7.1% (14)	NS
MACE*	15% (29)	10% (20)	NS

*Hierarchical analysis

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Clinical Endpoints at 12-Months

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
All Death	2.0% (4)*	0.0% (0)	NS
Cardiac death	0.5% (1)	0.0% (0)	NS
Myocardial Infarction	5.5% (11)	4.6% (9)	NS
Q-wave MI	1.0% (2)	0.5% (1)	NS
Non Q-wave MI	4.5% (9)	4.1% (8)	NS
TLR	9.5% (19)	4.1% (8)	0.044
TVR (ischemia-driven)	10.1% (20)	7.1% (14)	NS
non-TL TVR	2.5% (5)	3.6% (7)	NS
TVF	15% (29)	10% (20)	NS

*causes of non-cardiac deaths were acute renal & multi-organ failure (day 91), neuroendocrine malignancy (day 212) & intracerebral hemorrhage (day 274)

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Stent Thrombosis at 12-Months

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
Stent thrombosis	0.5% (1)	0.5% (1)	NS
Acute (24 hr)	0.0% (0)	0.0% (0)	NS
Subacute (1-30 days)	0.5% (1)	0.5% (1)	NS
Late (>30 days)	0.0% (0)	0.0% (0)	NS

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Stent Thrombosis at 12-Months
(ARC Definition)

	ZoMaxx (n=199)	Taxus (n=197)	P-Value
Stent thrombosis	1.0% (2)	1.0% (2)	NS
Acute (24 hr)	0.5% (1)[a]	0.5% (1)[b]	NS
Subacute (1-30 days)	0.0% (0)	0.5% (1)[a]	NS
Late (>30 days)	0.5% (1)[c]	0.0% (0)	NS

[a]Definite
[b]Probable
[c]Possible

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Conclusions

- Protocol specified parametric analysis of the primary endpoint exceeded the non-inferiority margin by 0.02 mm
- After 9-months, ZoMaxx stent exhibited less neointimal inhibition than TAXUS as demonstrated by higher in-stent late loss by QCA and neointimal volume obstruction by IVUS
- This biological effect is translated in a higher TLR rate @ 12 months in comparison with Taxus
- There were no instances of late-acquired incomplete stent apposition after ZoMaxx stent implantation
- The safety of ZoMaxx stent was exhibited by the overall low observed stent thrombosis rate, with the absence of late (definite and probable) stent thrombosis (> 30 days)

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