JUPITER II

double blind randomized comparison of Janus Tacrolimus eluting stent with the Tecnic Carbostent

T. Lefèvre

angioplasty Summit 2006
TCT Asia Pacific

EuroIntervention

Direct stenting of *de novo* coronary stenoses with tacrolimus-eluting versus carbon-coated carbostents. The randomized JUPITER II trial

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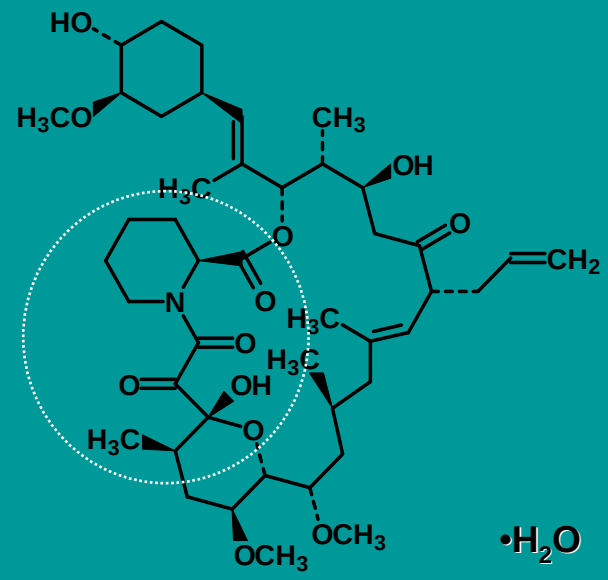
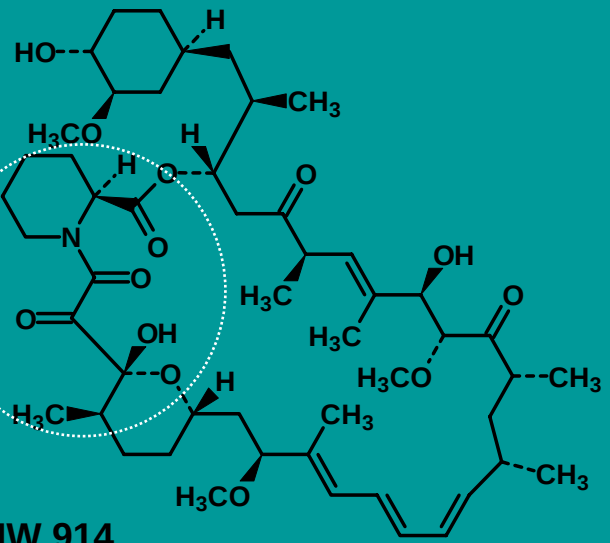
Tacrolimus vs Sirolimus

Tacrolimus (FK506)



MW 822

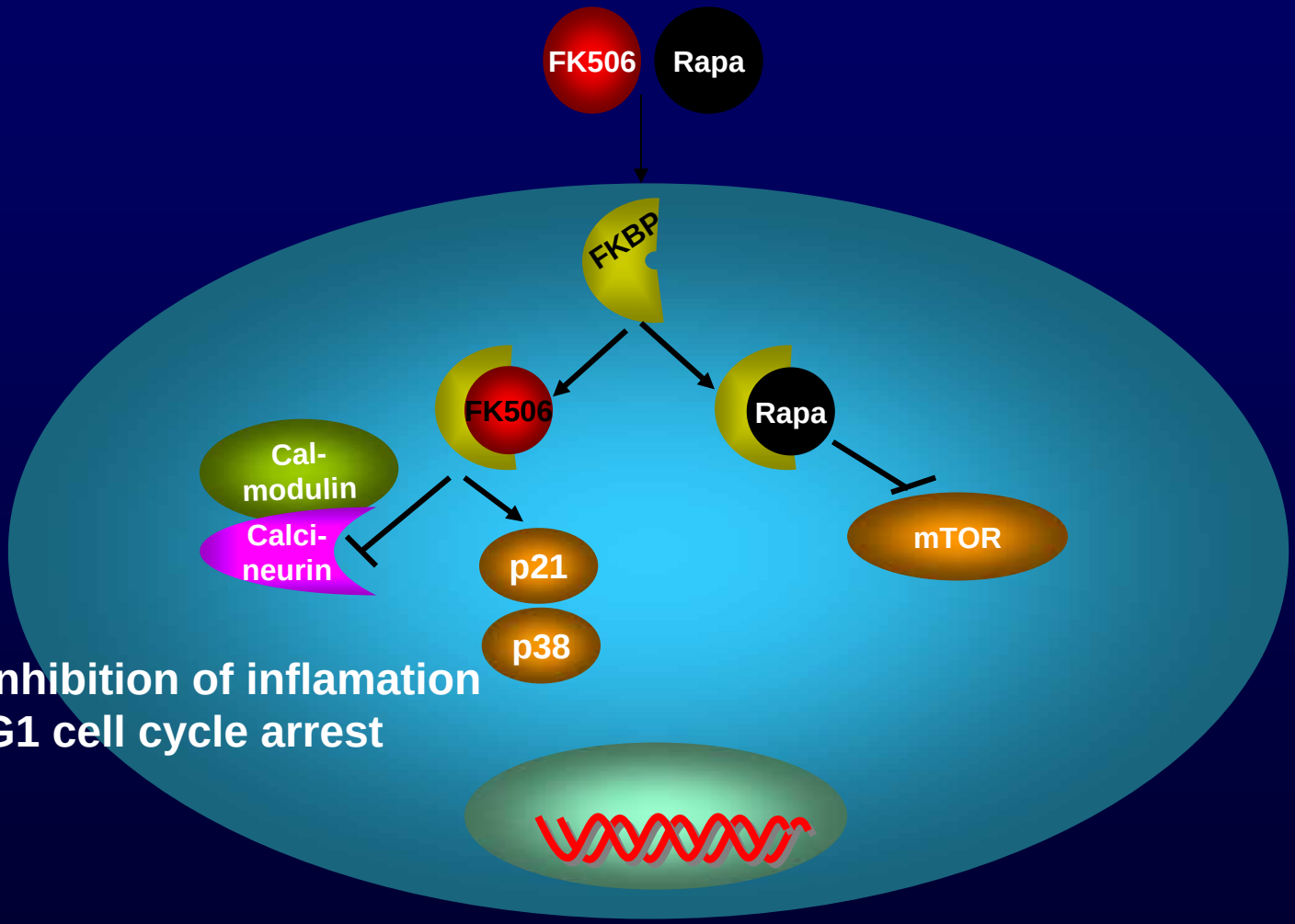
Sirolimus (Rapamycin)



MW 914

Although structurally related to Rapamycin and also binding to intracellular protein FKBP12, mechanism of action is different

Different Pathways of Rapamycin and Tacrolimus

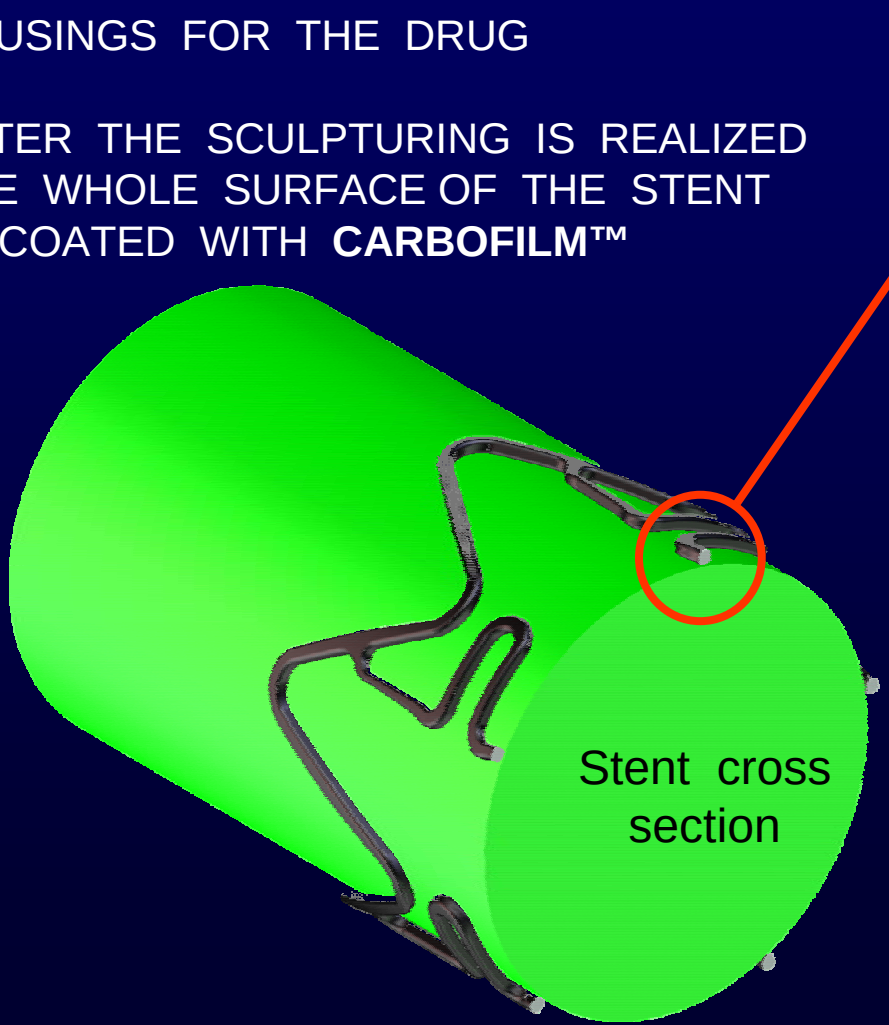


- Inhibition of inflamation
- G1 cell cycle arrest

Sculptured Surface to Embed the Drug

THE EXTERNAL SURFACE OF **JANUS CARBOSTENT** IS SUITABLY SCULPTURED TO PROVIDE DEEP HOUSINGS FOR THE DRUG

AFTER THE SCULPTURING IS REALIZED THE WHOLE SURFACE OF THE STENT IS COATED WITH **CARBOFILM™**



Strut cross section

External surface sculpturing

Integral Carbofilm™ coating

Study Management

Principal Investigator:

- Marie-Claude Morice

Independent DSMB and CEC:

- Bartorelli, MD
- Badano, MD
- Naftel, MD

Angiographic Core Lab:

- Bio Imaging
  Leiden, Netherlands
- **Cardialysis**
  Rotterdam, Netherlands

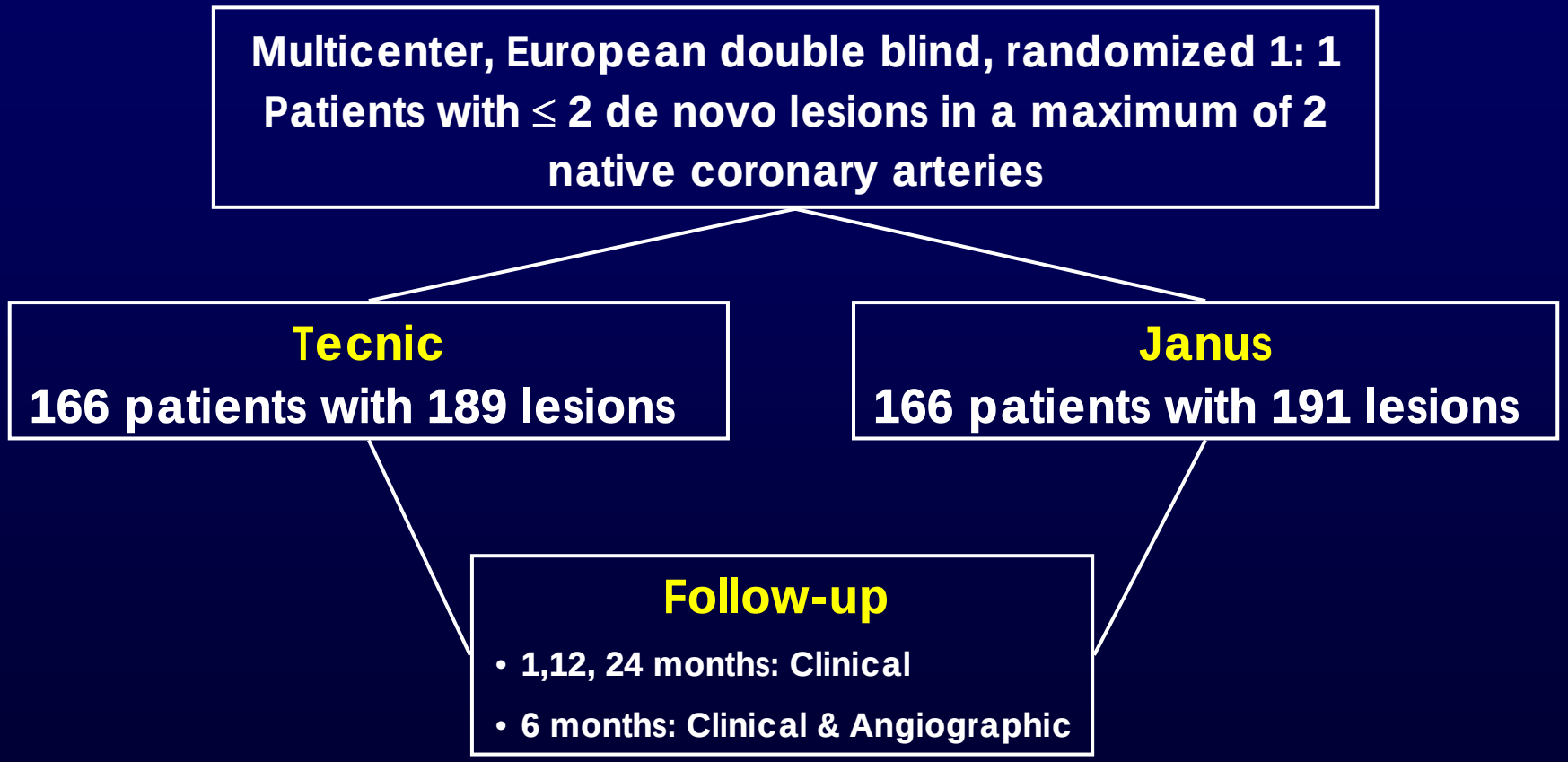
Industry sponsor:

- Sorin Biomedica Cardio
  Saluggia, Italy

Investigators by Country

COUNTRY	INVESTIGATOR
FRANCE (2)	Dr. Morice (PI) – Massy Prof. Carrié - Toulouse
THE NETHERLANDS (3)	Dr. Aengevaeren-Nijmegen Prof. Serruys - Rotterdam Dr. De Winter - Amsterdam
BELGIUM (3)	Dr. De Bruyne, Dr. Wijns - Aalst Dr. Verheye – Antwerp Dr. Dubois - Leuven
GERMANY (3)	Prof.Neumann, Prof. Bestehorn – Bad Krozingen Dr. Hoffmann - Berlin Dr. Hempel - Dresden
SPAIN (1)	Prof. Macaya - Madrid
U.K. (2)	Prof. Di Mario, Prof. Ilsey - London
ITALY (1)	Dr. Cremonesi – Cotignola
AUSTRIA (1)	Prof. Pachinger - Innsbruck
SWITZERLAND (1)	Prof. Amann - Zurich

Study Design



Study Endpoint

Primary endpoint & Sample size calculation:

- In-stent and in segment "Late Lumen Loss (LLL)" at 6 month follow-up by QCA.
- Assumed 6-month in segment LLL of 0.70 mm for TECNIC and 0.45 mm for JANUS (36% reduction), 150 patients for each arm to be enrolled (one sided α = 0.05 and 80% power to reject null hypothesis that 2 treatment groups are equal)
- + 10% "drop-out" $\rightarrow$ 330 pts in total

Study Secondary Endpoints

- Assessment of binary angiographic restenosis at 6 month angiographic follow-up
- MACE at discharge, 30 days, 6, 12 and 24 months
- TLR within 6, 12 and 24 month follow-up
- Incidence of stent thrombosis at discharge, 30 days, 6, 12 and 24 months

Major Inclusion/ Exclusion Criteria

Inclusion Criteria:

- Patients > 18 years willing to participate in the study, after signature of informed consent
- Angina CCS class I, II, III, IV
- Angina Braunwald Class B & C I-II-III
- Documented Silent ischemia
- Lesions suitable for direct stenting stenting
- Target vessel ∅ 2.7 to 4.0 mm
- Lesion length ≤ 20 mm
- Target lesion stenosis ≥ 50% and ≤ 100% (TIMI I)

Exclusion Criteria:

- Acute Q-wave MI within 7 days
- LVEF ≤40%
- Less than 1 year life expectancy
- Angiographic evidence of massive thrombus in the target lesion
- Ostial lesion
- Unprotected Left Main > 50%
- Total occlusion
- In-stent restenosis
- Lesions involving bifurcation with a side branch ∅ >2 mm

Study Medications

Pre-Procedure

Clopidogrel: 300 mg the day of procedure as loading dose

Aspirin: >100 mg (Patients without oral aspirin treatment should receive 500 mg i.v. of soluble aspirin before procedure)

During Procedure

Heparin: IV boluses (ACT 250 sec)

GPIIb/IIIa receptor antagonist: under judgment of the Investigator

Post Procedure

Clopidogrel: 75 mg once daily For at least 2 months

Aspirin: ≥75 mg indefinitely

Baseline Clinical Characteristics (I)

	TECNIC	JANUS	*p*-Value
Patients (n)	166	166	
Male (%)	75.9	74.7	NS
Age (yrs)	63.9 ± 10.0	63.9 ± 9.6	NS
Clinical Status (%)			
Asymptomatic	5.4	4.2	NS
Silent Ischemia	9.6	6.6	NS
Stable Angina	63.9	62.1	NS
Unstable Angina	15.1	18.7	NS
Post MI	6.0	8.4	NS
CAD (%)			
Single vessel disease	60.8	60.2	NS
Multivessel disease	39.2	39.8	NS

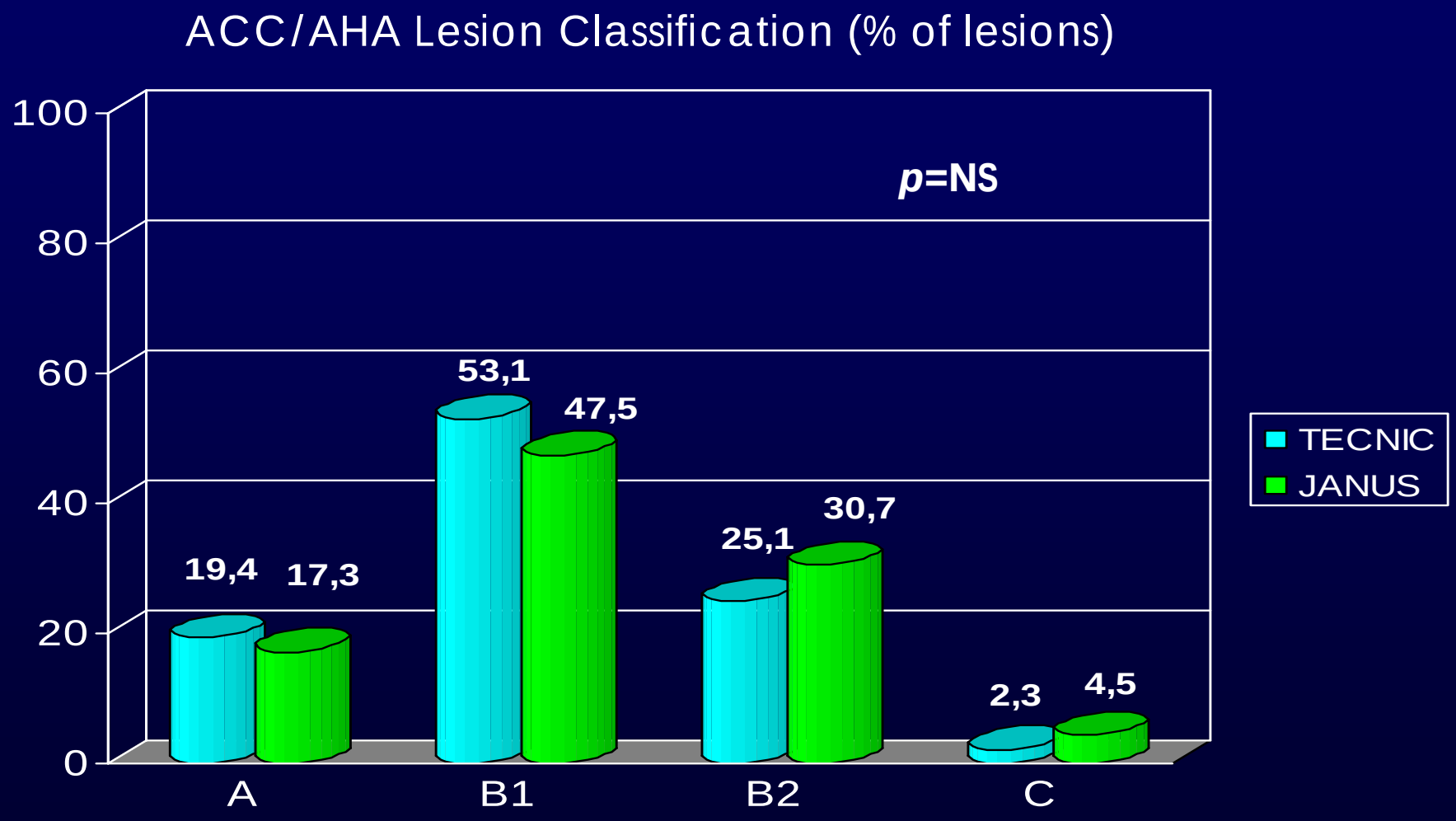
Baseline Clinical Characteristics (II)

	TECNIC	JANUS	p-Value
Patients (n)	166	166	
Risk factors (%)			
Smokers	38.5	44.0	NS
Diabetes	20.5	18.1	NS
ID Diabetes	6.0	3.0	NS
NID Diabetes	14.5	15.1	NS
Hypertension	63.2	57.8	NS
Hypercholesterolemia	69.9	67.5	NS
Family history of CAD	27.7	28.9	NS

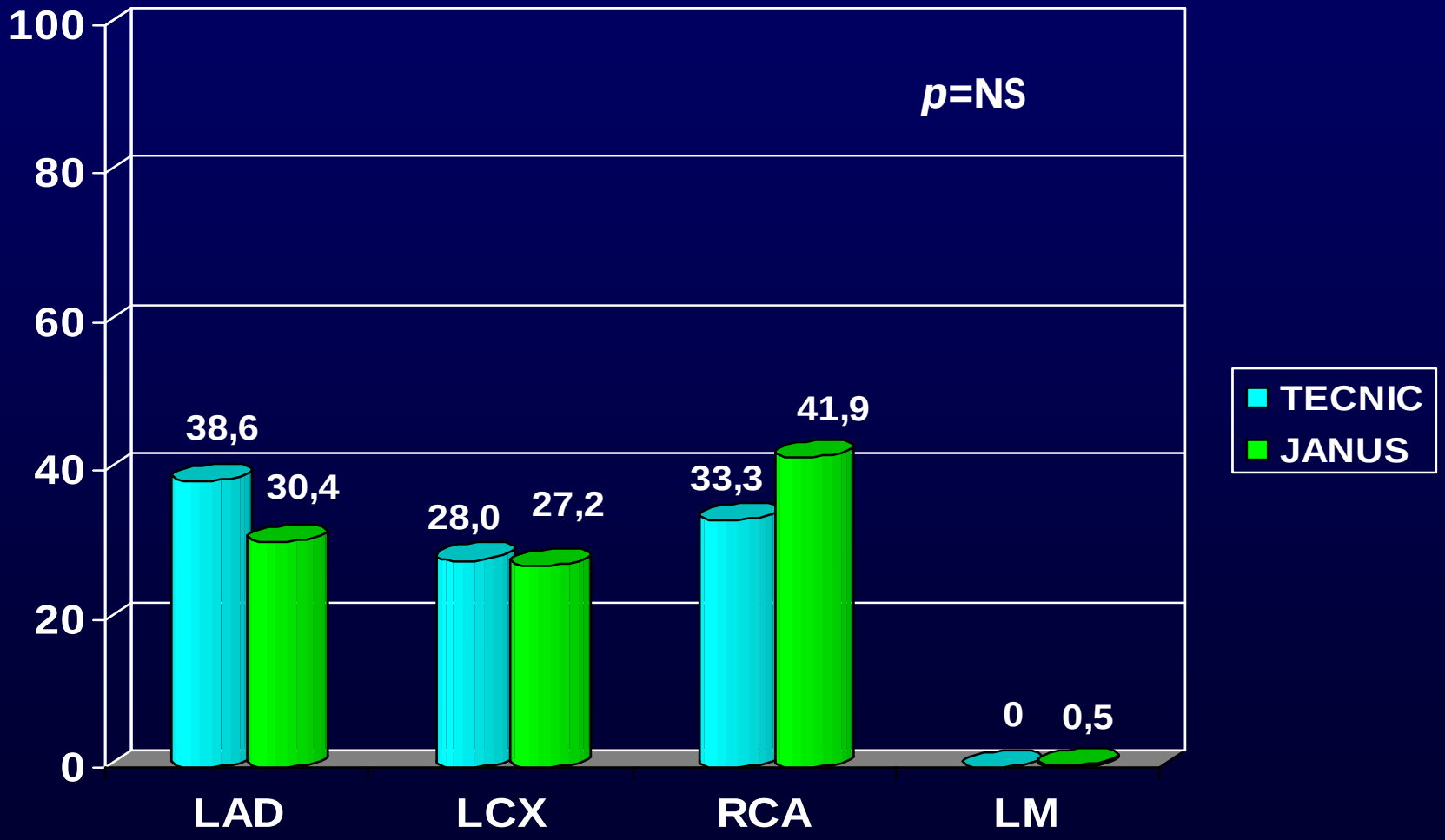
Target lesion Characteristics (I)

	TECNIC	JANUS	p-Value
N° of lesions	189	191	
De Novo (%)	98.9	99.5	NS
Concentric (%)	54.7	47.2	NS
Eccentric (%)	45.3	52.8	NS
Calcification (%)	18.0	23.6	NS
Tortuosity (%)	6.3	13.1	NS
Bifurcation (%)	0.0	3.1	NS
Ostial Lesion (%)	0.5	1.0	NS
Total Chronic Occlusion (%)	0.0	1.0	NS

Target lesion Characteristics (II)



Target Vessels



Procedural Characteristics

	TECNIC	JANUS	p-Value
Lesions (n)	189	191	NS
Stents (n)	195	208	NS
Attempted direct stenting (%)	85.7	75.9	.0339
Direct stenting success (%)	99.3	100	NS
# Stent/patient (n)	1.18 ± 0.44	1.26 ± 0.56	NS
# Stent/lesion (n)	1.04 ± 0.19	1.09 ± 0.37	NS
Stent Diameter (mm)	3.22 ± 0.25	3.22 ± 0.25	NS
Stent max pressure (atm)	13.9 ± 3.2	13.6 ± 3.0	NS

Procedural Success

	TECNIC	JANUS	p-Value
Lesion Success*	99.5	99.5	NS
Procedure Success**	99.4	99.4	NS

* Residual diameter stenosis <20% (visual) after stenting procedure

** Final diameter stenosis <20% (visual) without any MACE

Angiographic Results –overall (Cardialysis)

	TECNIC	JANUS	*p*-Value
Lesions (n)	168	169	NS
Preprocedure RVD (mm)	2.81±0.50	2.77±0.48	NS
Pre procedure MLD (mm)	1.16±0.32	1.11±0.27	NS
Pre Implant %DS (%)	58.5±9.1	59.8±7.4	NS
Post procedure RVD, In-Segment (mm)	2.83±0.47	2.85±0.45	NS
Post procedure RVD, In-Stent (mm)	2.88±0.47	2.89±0.41	NS
Post procedure MLD, In-Segment (mm)	2.19±0.46	2.20±0.43	NS
Post procedure MLD, In-Stent (mm)	2.45±0.39	2.49±0.37	NS
Post procedure % DS, In-Segment (%)	22.6±9.3	22.5±9.3	NS
Post procedure % DS, In-Stent (%)	14.4±7.1	13.4±7.2	NS
6-month %DS, In Segment (%)	38.0±18.1	34.3±16.6	NS
6-month %DS, In Stent (%)	35.6±19.3	32.7±17.5	NS
6-month LLL, In Segment (mm)	0.48±0.52	0.42±0.46	NS
6-month LLL, In Stent (mm)	0.66±0.53	0.65±0.47	NS
6-month BR, In Segment (mm)	19.0	12.4	NS
6-month BR, In Stent (mm)	17.3	11.8	NS

Cumulative Clinical Events at 12-month follow-up

	TECNIC 159 patients (compl. 95.8%)	JANUS 155 patients (compl. 95.1%)	*P*-value
ALL MACE (%)	19.5	16.1	NS
Death (%)	0	1.8	NS
Cardiac Death	0	0.6	NS
MI (%)	2.5	1.3	NS
Q-Wave	1.9	0	NS
Non Q-Wave	0.6	1.3	NS
Q-Wave not reported	0.6	0	NS
TVR (%)	17.0	12.9	NS
TLR (%)	16.4	10.3	NS
Clinically driven	8.8	3.9	NS
Angiographically driven	7.6	6.5	NS
CABG	0.6	1.3	NS
Re-PTCA	16.4	11.6	NS

Stent Thrombosis (Acute, Subacute & Late)

	TECNIC	JANUS	p-Value
Acute Thrombosis (%)	1.2	0	NS
Sub-acute Thrombosis (%)	1.8	0	NS
Late Thrombosis (%)	0	0	NS
Total (%)	3	0	NS

Conclusion

✓ In this randomised trial with direct stenting comparing TES with CCS, favourable angiographic and clinical results were obtained in both groups.

✓ Although the 6-month LLL associated with TES was consistent with that estimated in the planning of the trial, it was not significantly less than that observed with CCS.

Conclusion (cont ..)

✓ The absence of stent thrombosis in the TES group is encouraging from a safety standpoint.

✓ A trend toward a lower TLR rate at 12 months F-up was observed in the TES group, suggesting that the angiographic observations made at 6 months may not reliably predict longer-term clinical outcomes.

✓ These unsettled issues warrant further examination in larger populations over longer periods of observations.