Drug Eluting Stent Summit-II

The Program of DES of SORIN

Gian B. Danzi
Poliambulanza Hospital
Brescia- ITALY

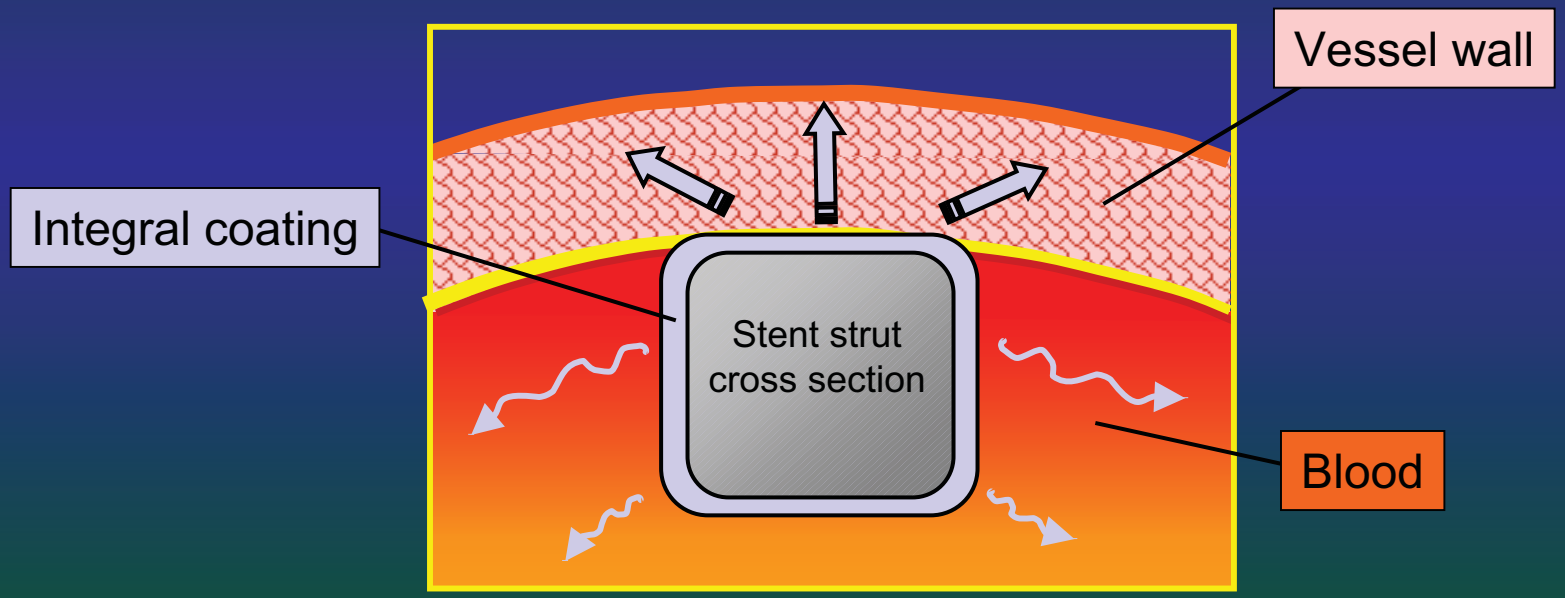
The Program of DES of SORIN

- The platform
- The drug
- Animal data
- Clinical studies

Drug Eluting Stent Technologies STATE OF THE ART

Presently available drug eluting stents are characterized by surfaces *integrally coated* with:

- ***polymer matrices containing the drug***
- ***drugs directly linked to the stent surface***
- ***ceramic coatings embedding the drug***



They proved to be effective, but also showed potential limitations

DES with integral coating: POTENTIAL LIMITATIONS

1) Relatively low drug loading capability

2) Non-targeted drug release

3) Significant drug loss in the blood stream

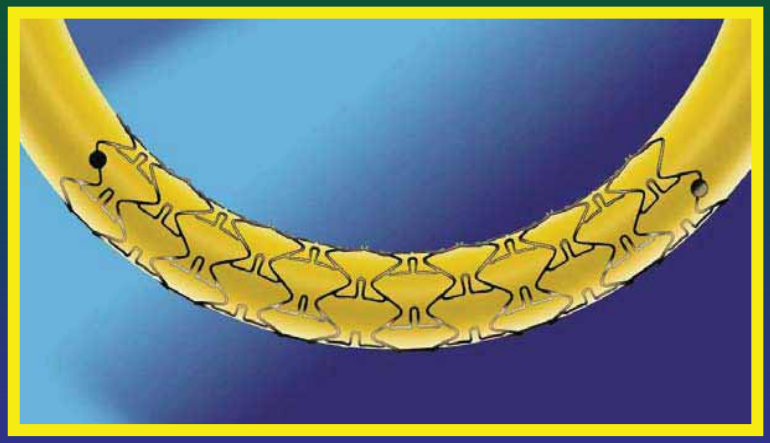
4) Potential suboptimal biocompatibility of the surface (at the end of release)

5) Potentially delayed endothelialization

6) Limitations in Direct Stenting approach

JANUS CARBOSTENT : The releasing platform

The releasing platform of the Sorin DES is CARBOSTENT. This device, in clinical use from more than five years, is characterized by a number of distinctive features important to be preserved on a DES.

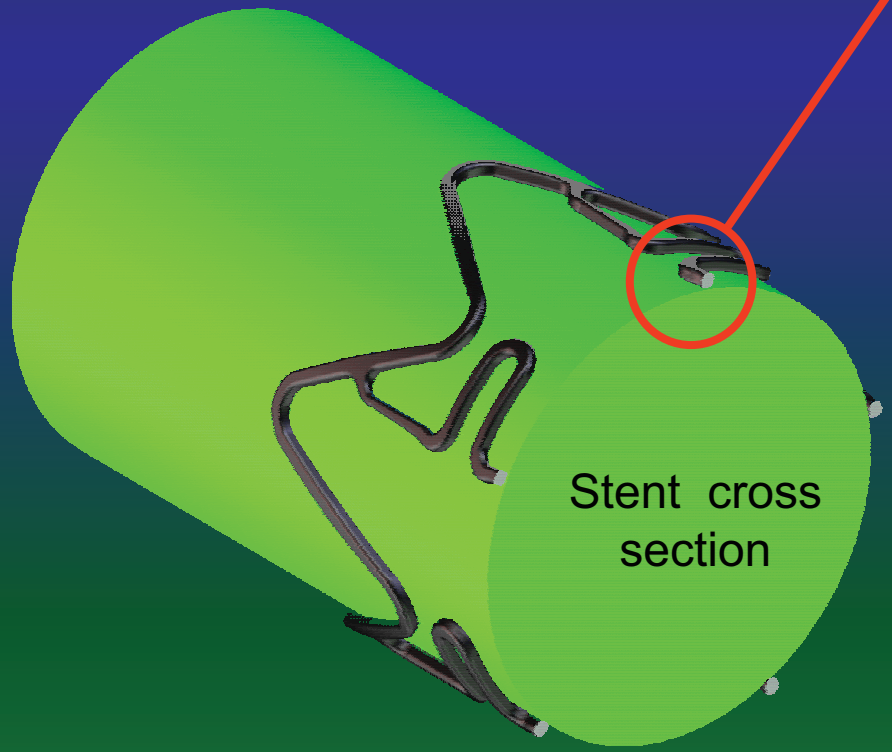


Distinctive Feature	Benefit
1) CLOSED CELL ARCHITECTURE	HOMOGENEOUS EXPANSION
2) MIRROR POLISHING	THROMBORESISTANCE
3) CARBOFILM COATING	BIO- & HEMOCOMPATIBILITY

SCULPTURED SURFACE TO LOAD 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™**



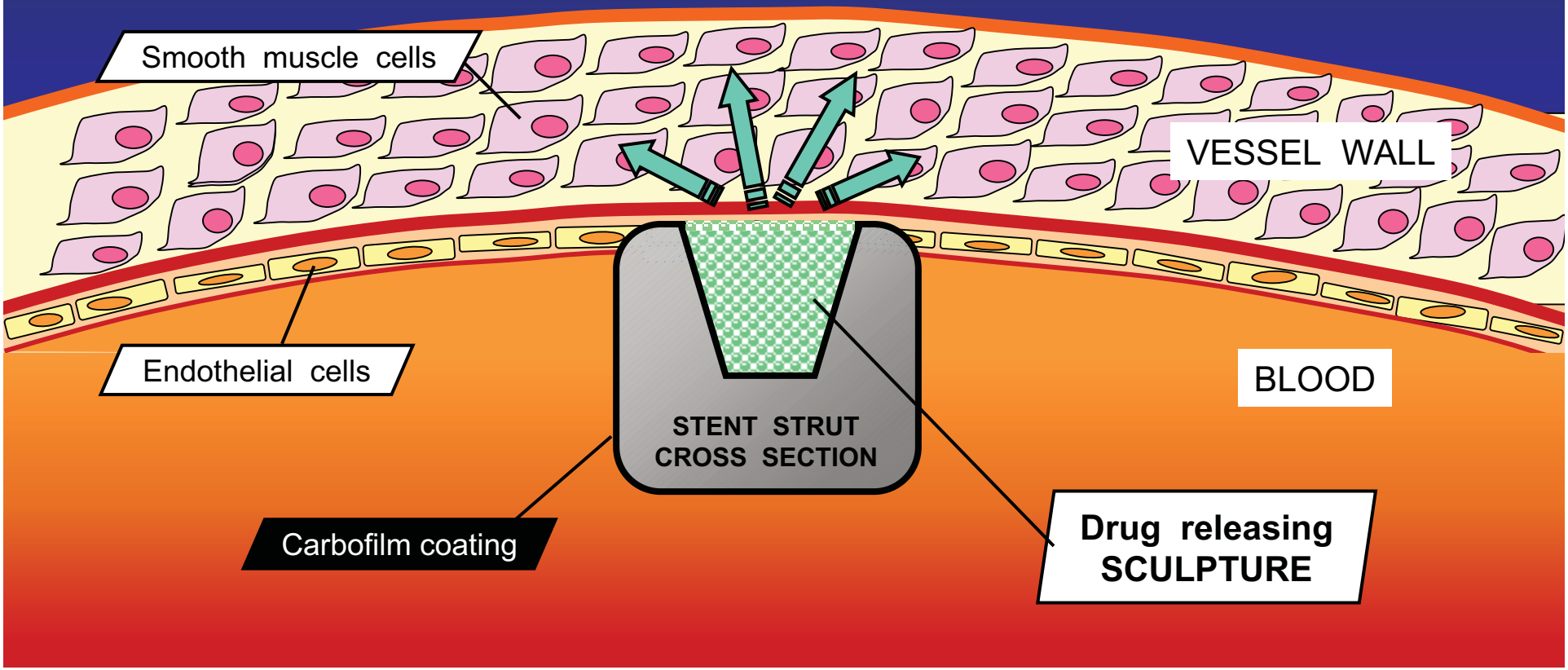
Strut cross section

External surface sculpturing

Integral Carbofilm™ coating

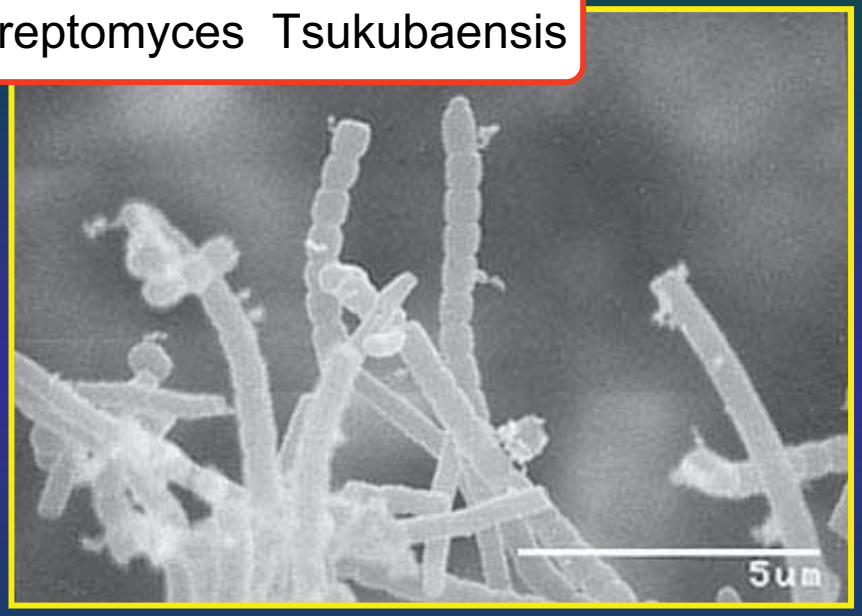
JANUS CARBOSTENT RELEASING MECHANISM

- DEEP SCULPTURES ON THE OUTER STENT SURFACE CONTAIN AND RELEASE THE DRUG ONLY TOWARDS THE VESSEL WALL
- NO DRUG IS LOST INTO THE BLOOD STREAM



JANUS CARBOSTENT - The DRUG

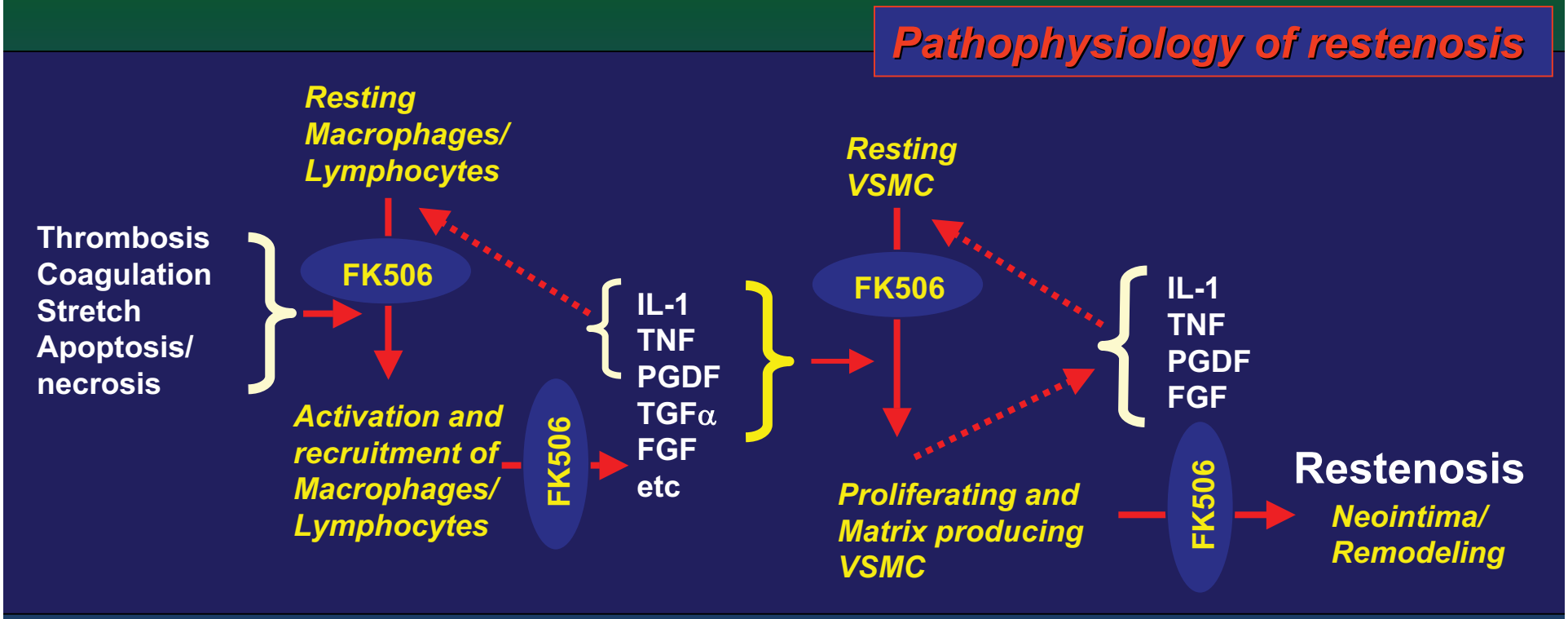
Streptomyces Tsukubaensis



The first drug which has been selected and tested in combination with Janus Carbostent is *Tacrolimus (FK 506)*, produced by Fujisawa Pharmaceutical Co. (Japan).

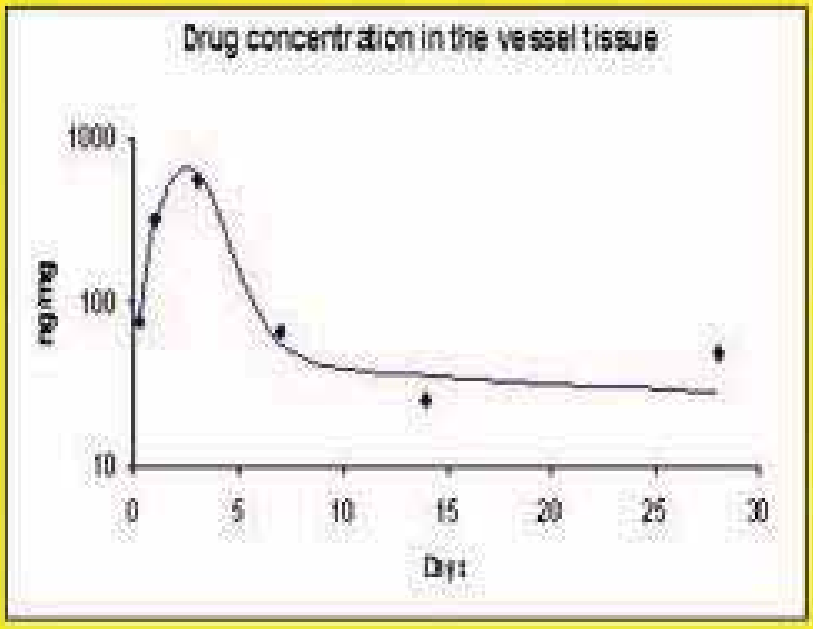
Tacrolimus is the active ingredient of two pharmaceutical products registered in all the main countries of the world: the immunosuppressant Prograf®, used in the treatment of patients after kidney or liver transplantation, and the Protopic®, used in the treatment of atopic dermatitis.

TACROLIMUS (FK506) MODE OF ACTION



- Number two renal transplant immunosuppressive macrolide, structurally related to sirolimus.
- Binds to the intracellular protein FKPB12, suppressing T-cell proliferation and inhibiting release of pro-inflammatory cytokines(IL2, IL3, IL4 and IFN).
- Inhibits four key steps of the restenosis pathway.

RABBIT STUDY
Release Kinetic



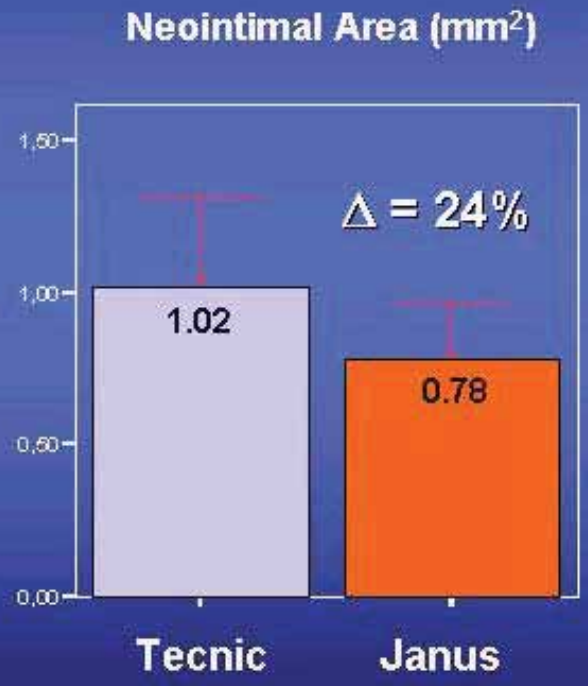
- **The drug concentration in the iliac artery tissue reached its maximum few days after implantation**
- **This peak corresponds to that of the vessel inflammatory response**
- **A steady tissue concentration was present over the following weeks**

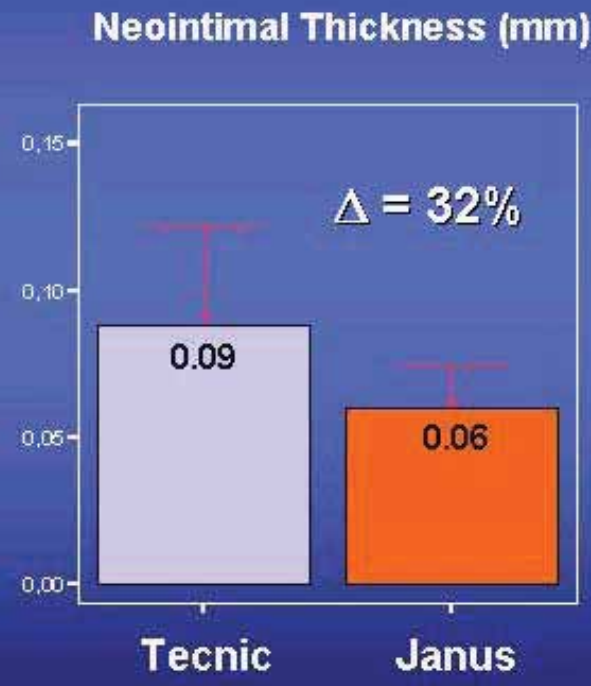
- One month after stent implantation, about 50% of the drug was released
- The drug concentration in the blood was always below the HPLC sensitivity threshold, confirming that no drug was released into the blood stream

The Program of DES of SORIN

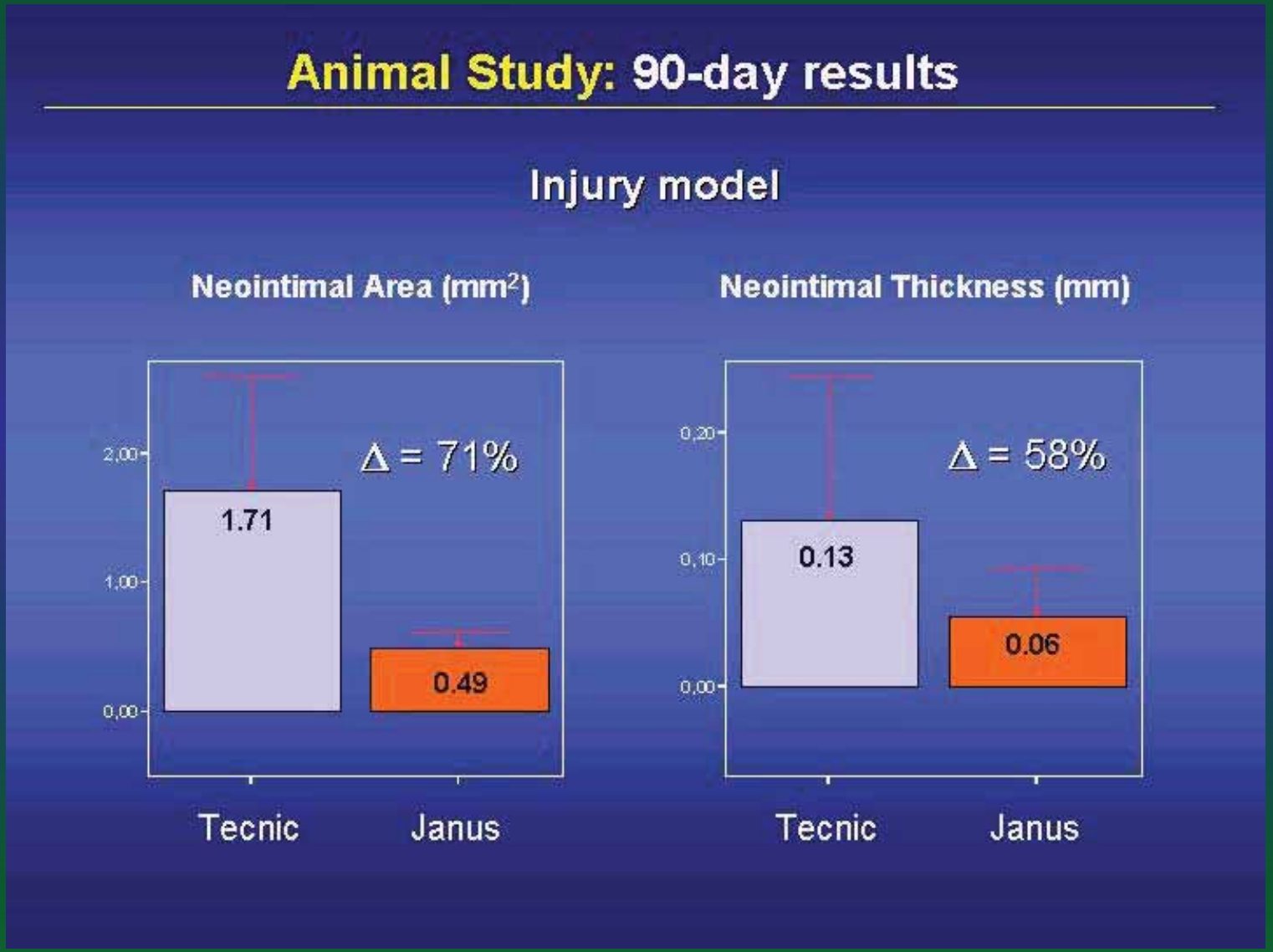
Animal Study: 28-day results

Non Injury model



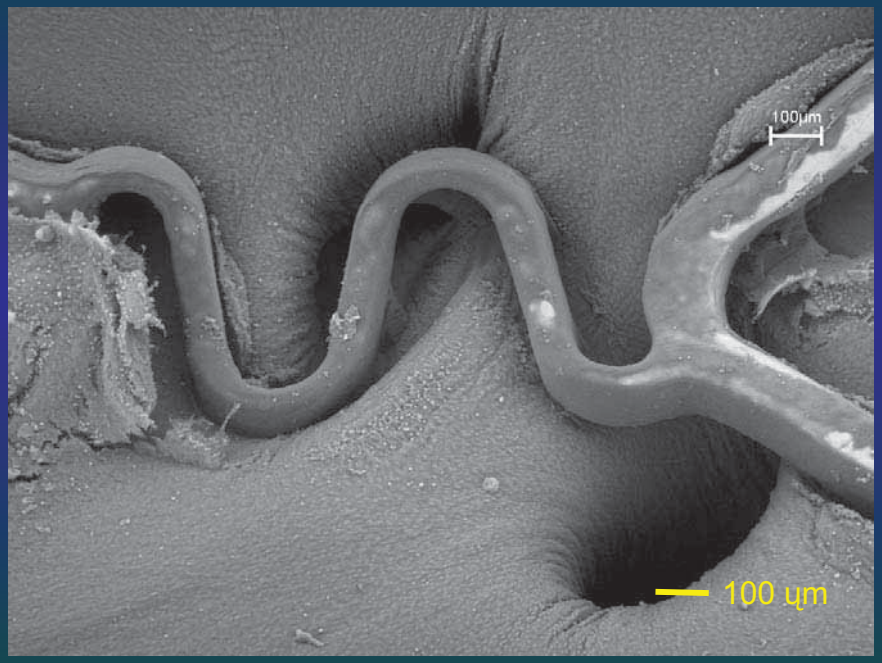


The Program of DES of SORIN



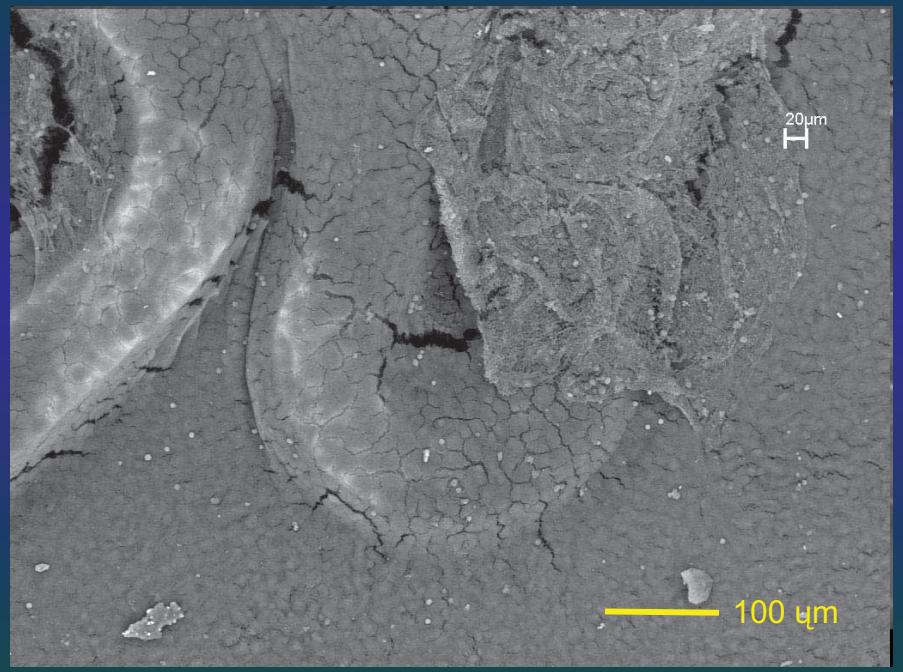
ENDOTHELIALIZATION STUDY IN ANIMAL MODEL

SEM – porcine coronary arteries – 7 day follow-up



LAD

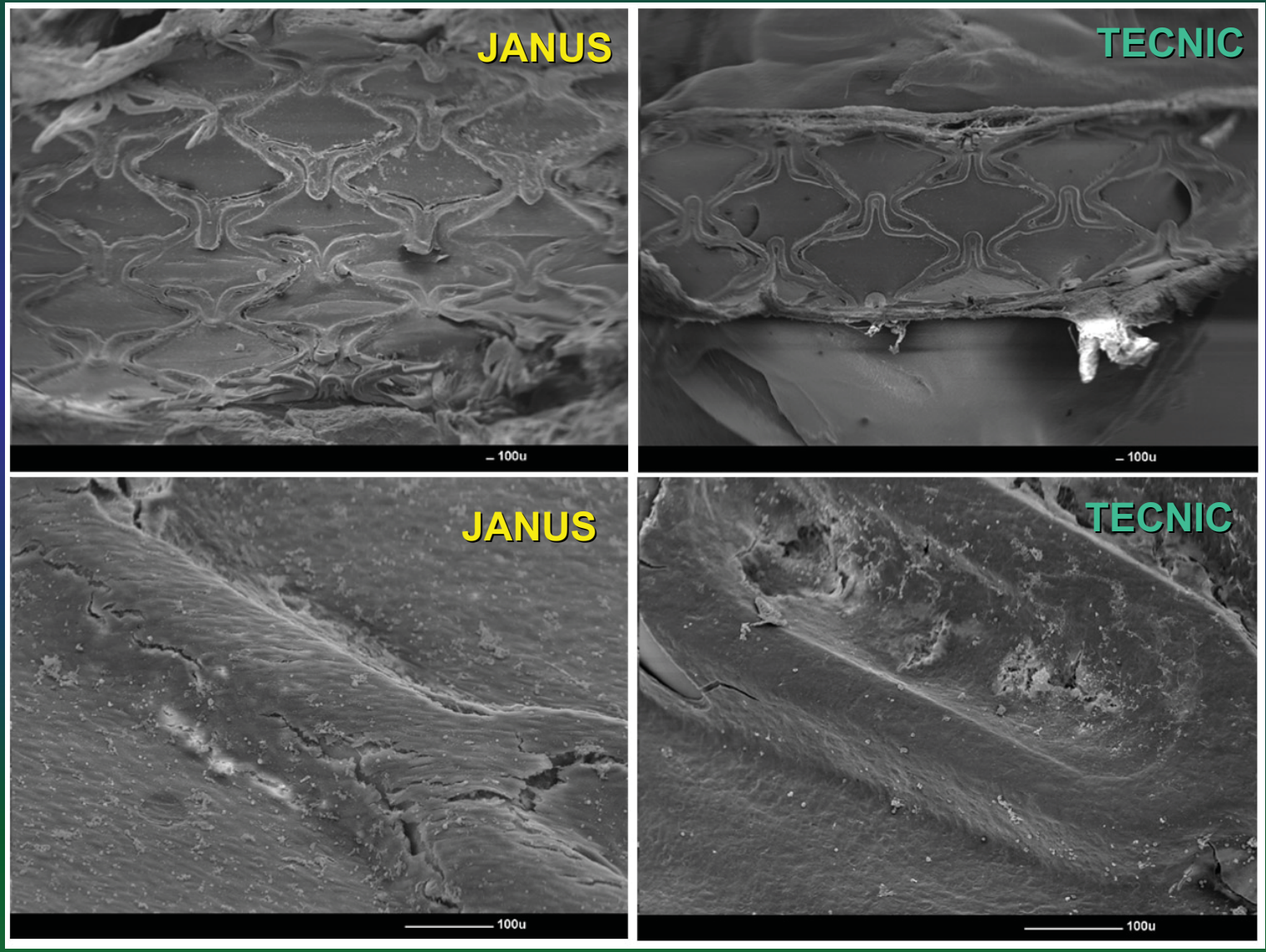
Control DES



LAD

Janus Carbostent

Endothealization at 15 days
(SEM- coronary arteries in porcine model)



Jupiter I Study

Clinical Experience with the Tacrolimus-eluting Janus Carbostent in de-novo coronary arteries

JUPITER I Study: *Principal Investigators*

1. **Antonio Bartorelli, MD**
   Centro Cardiologico Monzino (Milano)

2. **David Antoniucci, MD**
   Ospedale Careggi (Firenze)

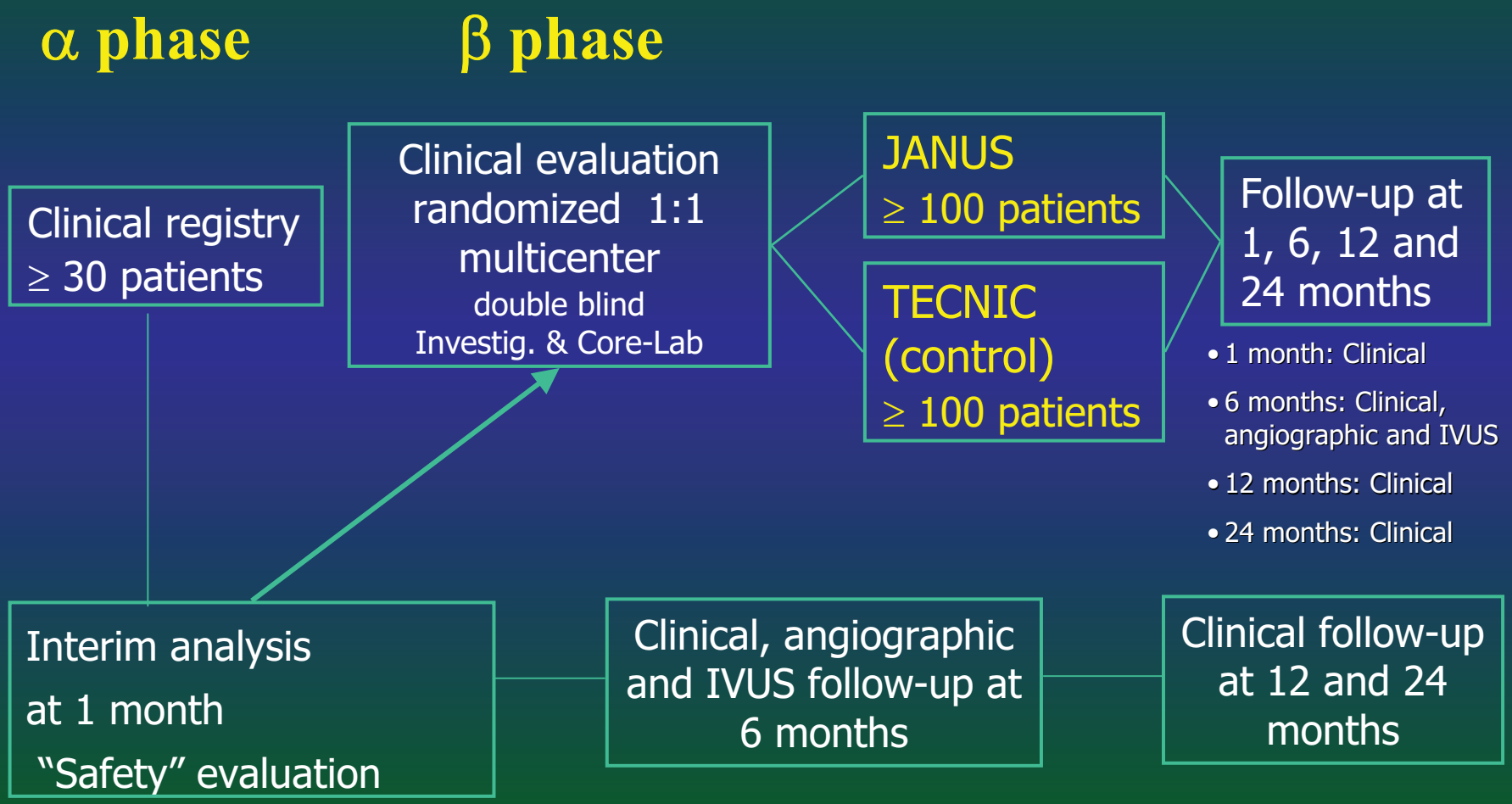
3. **Giancarlo Piovaccari, MD**
   Ospedale degli Infermi (Rimini)

4. **Gianbattista Danzi, MD**
   Poliambulanza Hospital (Brescia)

5. **Alberto Benassi, MD**
   Hesperia Hospital Modena (Modena)

6. **Roberto Serdoz, MD**
   Ospedale San Pietro FBF (Roma)

Study design



Inclusion Criteria (α *phase*)

The JUPITER I study

Angiographic criteria:

- De-novo coronary lesions in native vessels
- Lesion located in target vessel with a diameter ≥3 and ≤4 mm
- Target lesion length ≤12 mm
- The stented target vessel segment must be 3 mm longer than the target lesion
- Target lesion with a %DS ≥ 50% and ≤ 100% (TIMI I)
- ≤ Two target vessels for each patient
- One target lesion for each target coronary vessel
- One Janus stent only (15-mm x 3.0-3.5 mm) for each target lesion

Exclusion Criteria
(α *phase*)

Clinical

- **Oral anticoagulation unrelated to stent procedure**
- **Contraindication / allergy to aspirin, ticlopidine or clopidogrel**
- **Depressed LV function (EF≤ 40%)**
- **AMI**

Anatomic

- **Bifurcation lesions**
- **Lesions located in the only remaining vessel or LM**
- **Grafts**
- **CTO**
- **Massive thrombus**
- **Heavily calcified lesions**

Patient Population (α Phase)

- N° patients 50
- N° lesions 54
- N° stent 58
- Male gender: 72.9%
- Age (years) 63.9 ± 9.0
- Diabetes: 22%
  - *ID* *10%*
  - *NID* *12%*
- Hypercholesterol: 48%
- Previous MI: 31.2%

Antiplatelet Treatment

- Pretreatment with aspirin (325 mg/day or 500 mg i.v.)
- Heparin bolus to mantain the ACT > 300 seconds throughout the procedure
- **Aspirin (325 mg/day) + Clopidogrel loading dose followed by 75 mg/day for 2 months**

Short & long-term in-stent thrombosis

The JUPITER I study

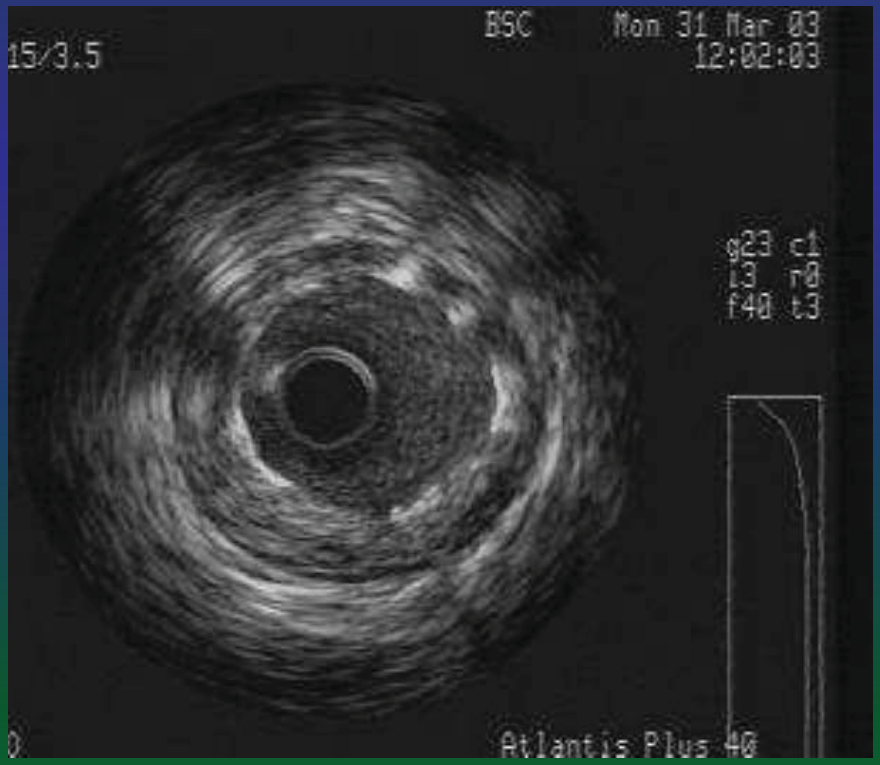
	α Phase	β Phase	Total
Thrombosis at 30 days	0/50	0/23	0/73
Thrombosis at 3 months	0/50	0/9	0/59
Thrombosis at 6 months	0/45	-	0/45
Thrombosis at 12 months	0/4	-	0/4

The JUPITER I study

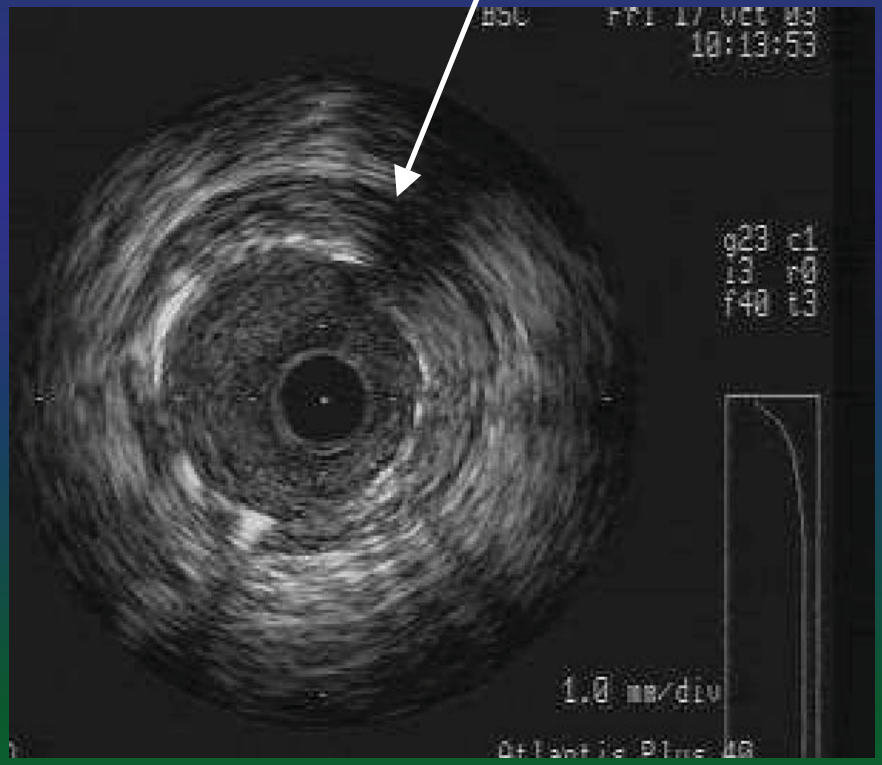
IVUS ANALYSIS

JUPITER I – alfa phase

No post-procedural and late malapposition (0/20)



BASELINE



6 MONTHS

MACE at 30 days

	α Phase	β Phase
Death	0/50	0/23
Q-wave MI	0/50	0/23
Non Q-wave MI	0/50	0/23
CABG	0/50	0/23
TLR	0/50	0/23
TLR with stent	0/50	0/23
% MACE	0%	0%
% completion	100	85,2

α Phase

Clinical Follow Up at 6 months

33 patients

• Death	0/33 (0%)
• MI	0/33 (0%)
• TLR	1/33 (3.0%)

JUPITER II

Clinical Investigation

Treatment of Restenosis of Coronary Lesions with Sorin Janus Carbostent in Direct Stenting

Investigators & Centers

- Dr. Aengevaeren
  University Medical Center Radboud
  Nijmegen – Holland

- Prof. Amann
  Herz Gefäss Zentrum Zürich
  Klinik im Park
  Zürich - Switzerland

- Prof. Carrié
  Hospital de Rangueil
  Toulouse – France

- Dr. Cremonesi
  Casa di Cura Villa Maria Cecilia
  Cotignola – Italy

- Prof. De Bruyne, Prof. Wijns
  Onze Lieve Vrouw Ziekenhuif
  Aalst – Belgium

- Prof. Di Mario, Dr. Ilsey
  Royal Brompton Hospital
  London – U.K.

- Prof. Macaya
  Hospital Clinico San Carlos
  Madrid - Spain

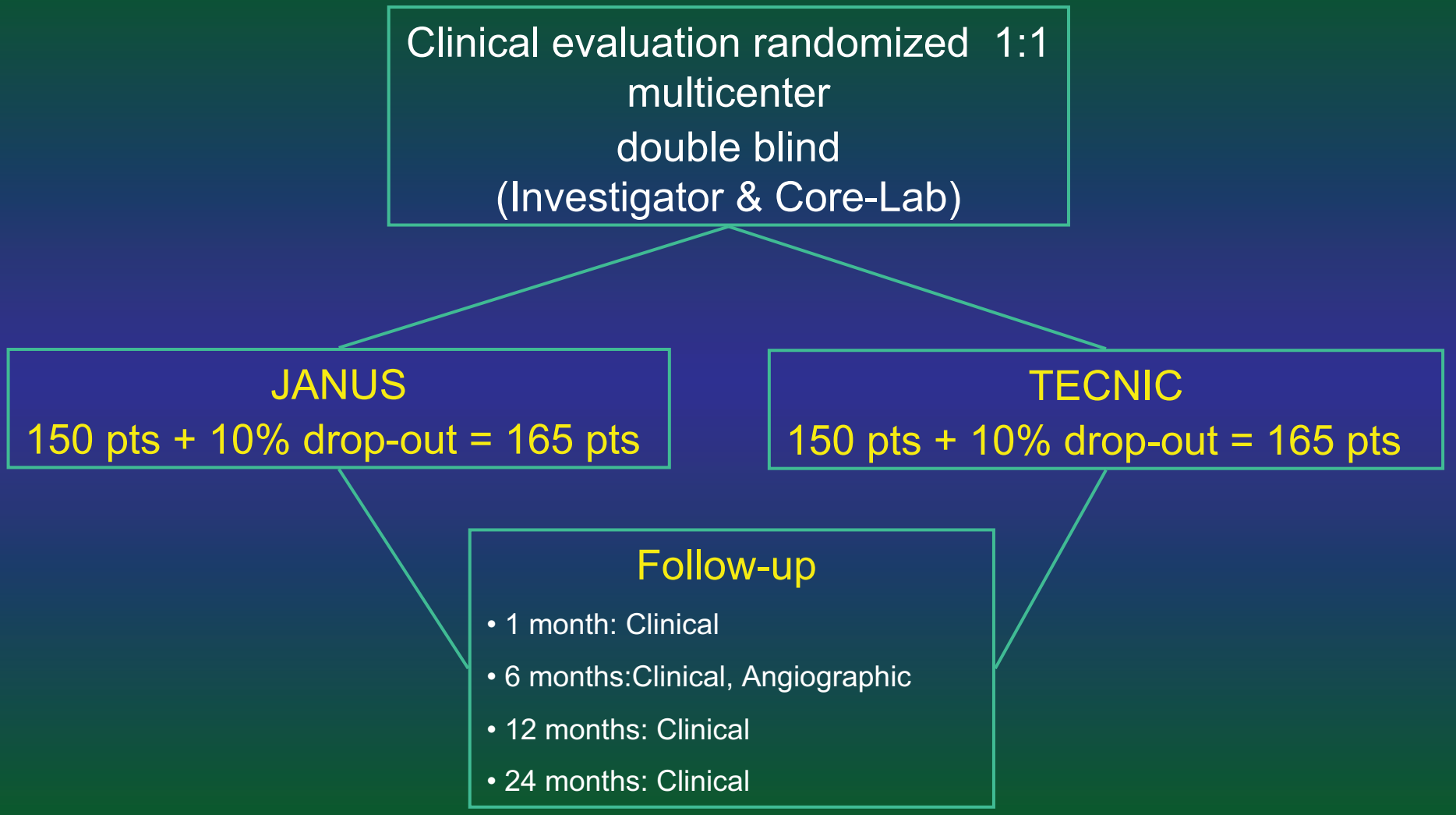
- Dr. Morice
  Institut Hospitalier Jacques Cartier,
  Massy – France

- Prof.Neumann, Prof. Bestehorn
  Bad Krozingen – Germany

- Prof. Pachinger
  University of Innsbruck
  Innsbruck – Austria

- Prof. Bartorelli
  Centro Cardiologico Monzino
  Milan – Italy

Study design



End Point: Angiographic Late Lumen Loss at 6 months