

My Initial Experience with the Dual Therapy Stents

COMBO™ Dual Therapy Stent | by OrbusNeich

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Disclosure Statement of Financial Interest

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

- Grant/Research Support
- Lecture honoraria
- Advisory board

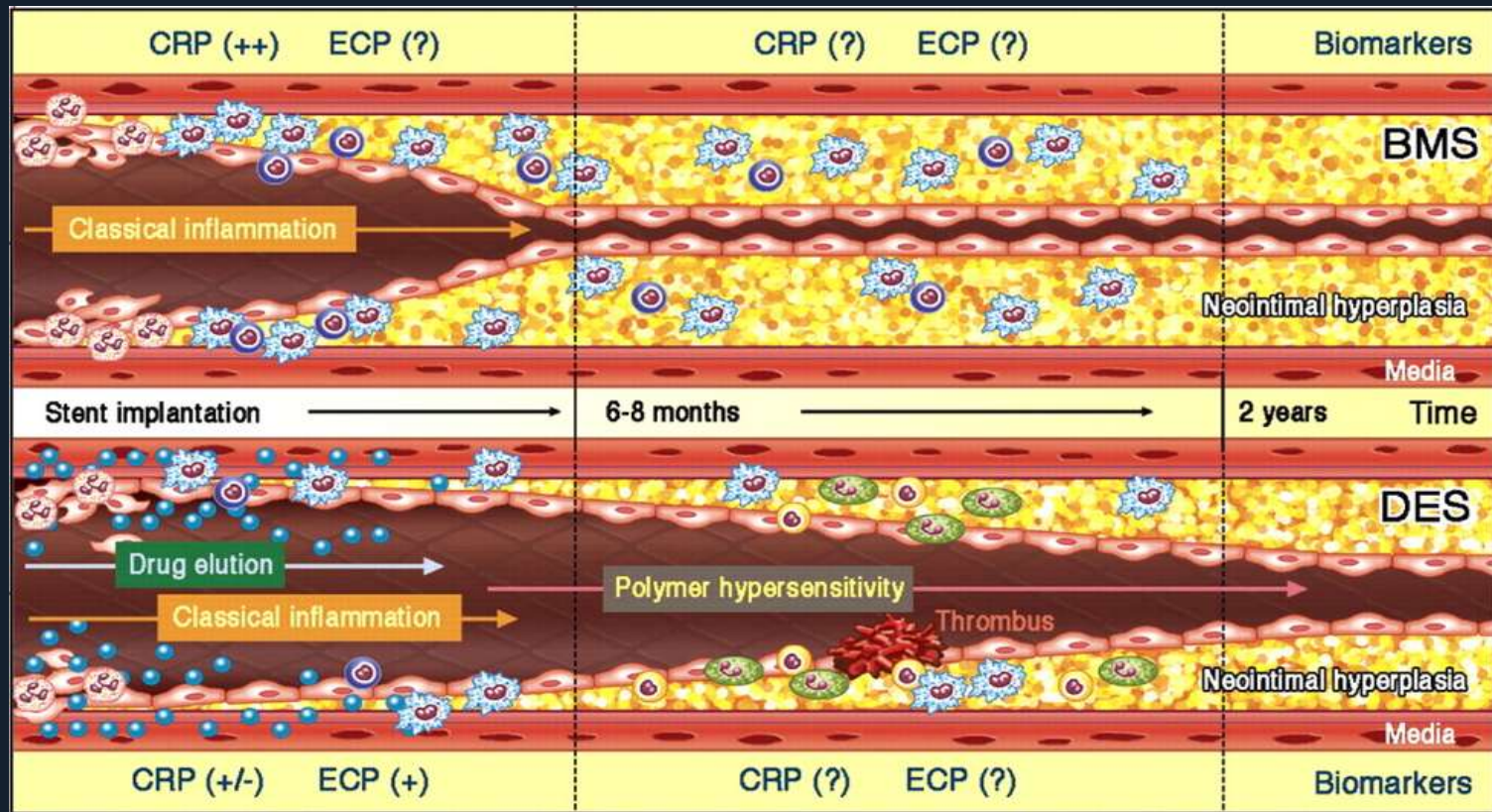
Company

- Medtronic
- Abbott Vascular
- Meril Lifesciences
- OrbusNeich
- Balton
- Medicines

Current Status of DES

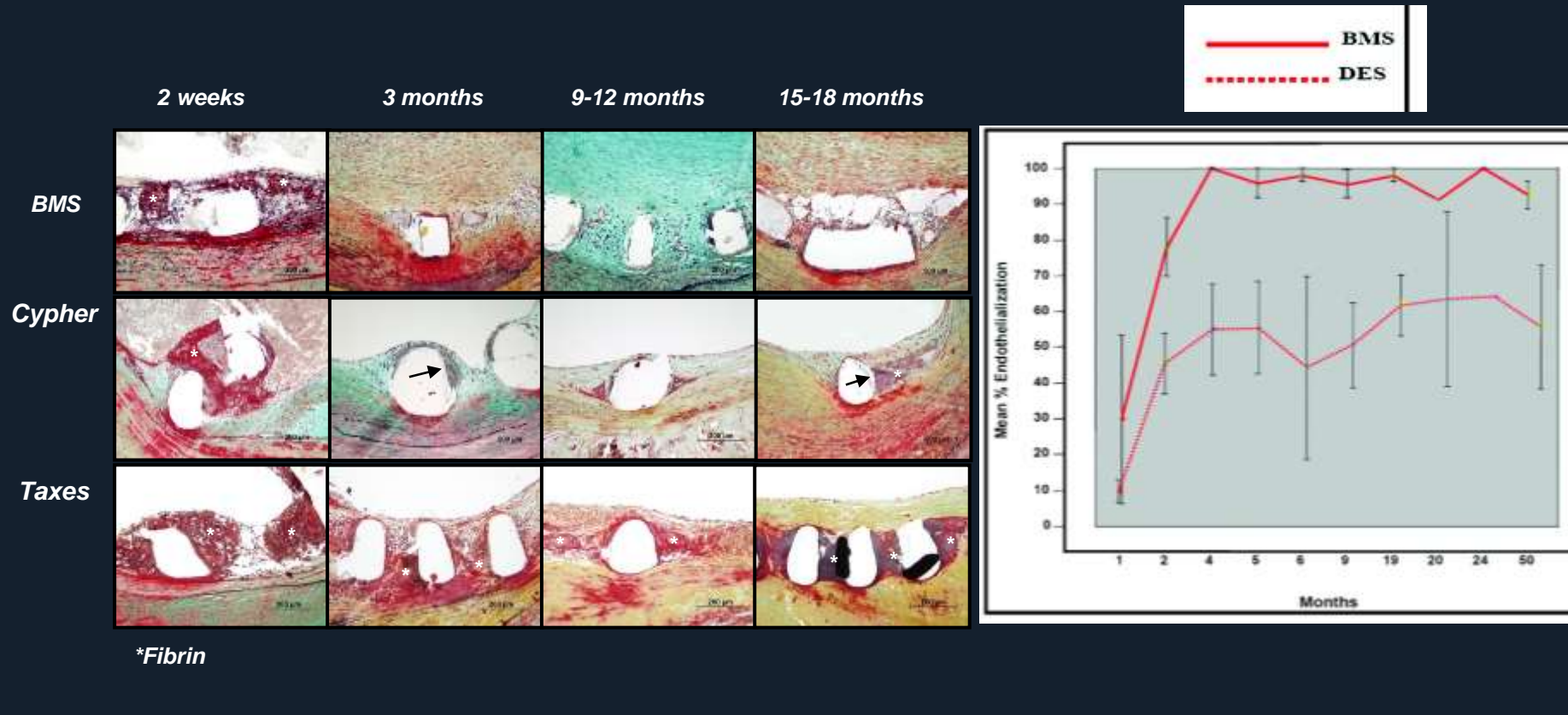
- All-comer registries showed superiority of newer gen DES over BMS and 1st gen DES
- New DES based on abluminally-coated biodegradable drug carrier showed non-inferiority to durable polymer DES
- Biodegradable polymer and pro-healing platforms might overcome the issue of bio-incompatibility and vasomotor abnormalities
- Pro-healing surface might lead to shorter DAT and less DAT-related complications

Adverse Reaction to DES



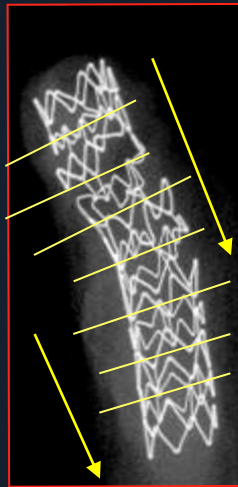
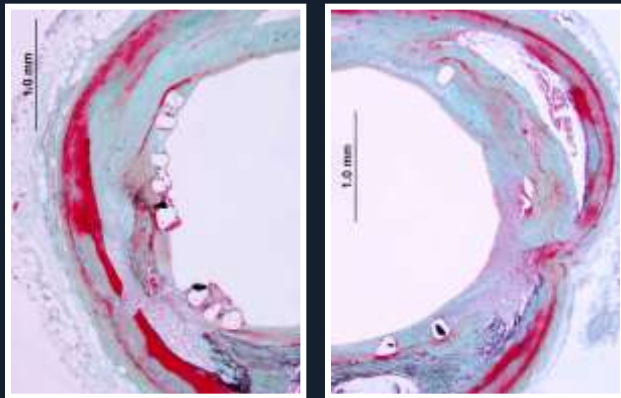
- endoluminal mural thrombi/old thrombi
- prevalence of eosinophils, giant cells, and fibrin
- development of yellow plaque and plaque rupture
- different SMC phenotype
- different optical properties of neointima
- elevated plasma CRP and ECP

Temporal Sequence of Endothelialisation

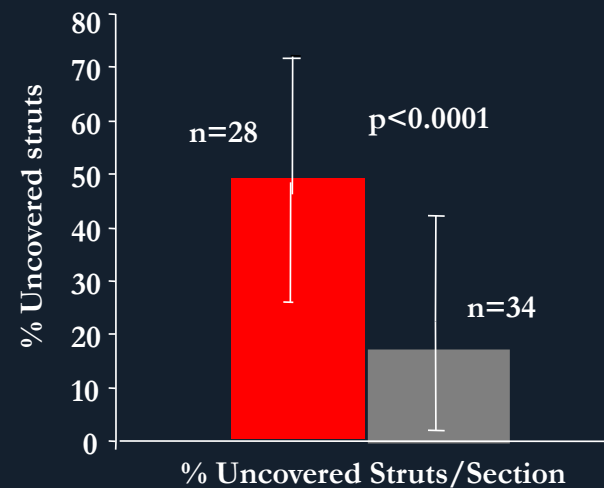
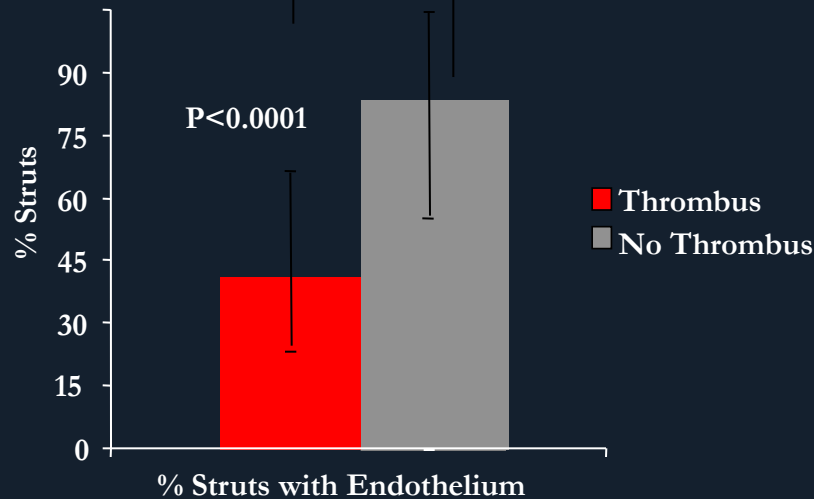
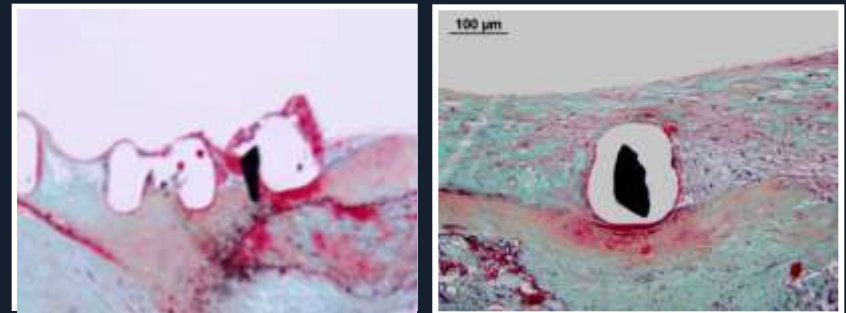


Pathological Correlates of VLST Strut Coverage

> 30 Days Implants
Uncovered Covered



> 30 Days Implants
Uncovered Covered



Mechanisms

Impaired stent healing

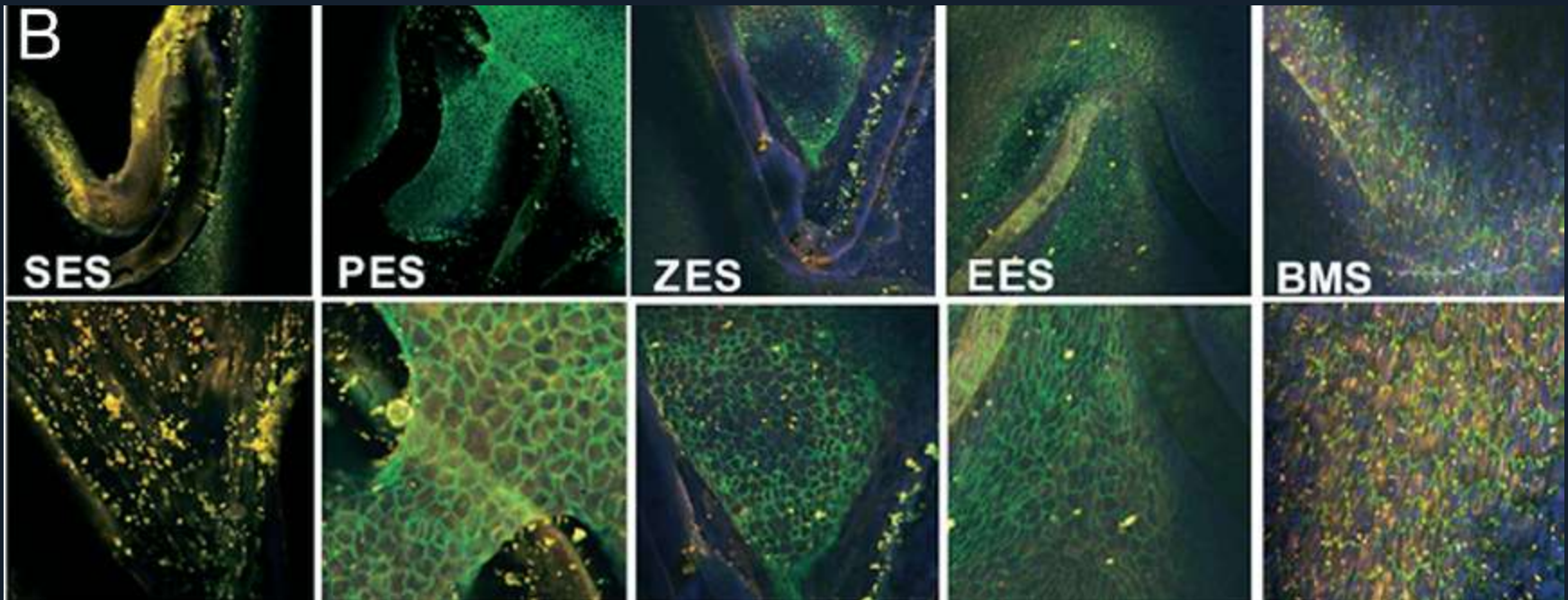
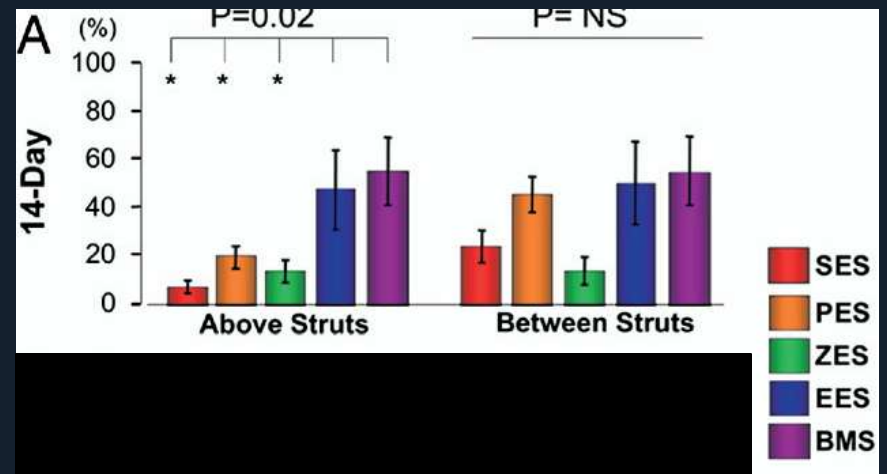
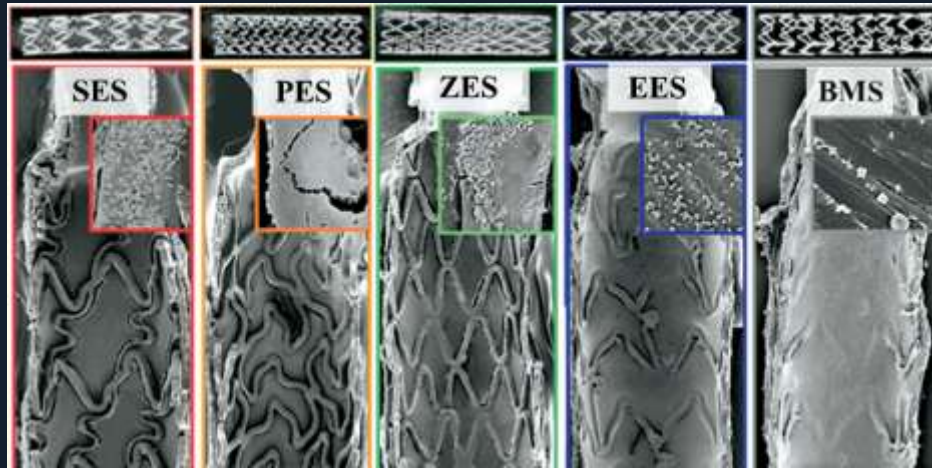
- **Drug toxicity**
 - Reservoir in the vascular wall
 - Diffusion/transport via vasa vasorum
 - Increased recruitment after high-pressure postdilatation
 - Increased number of vasa vasorum after SES vs. BMS
- **Polymer toxicity**
 - Hypersensitivity (acute or delayed)
 - Structural defects (cracks, webbing, delamination)
- Persistent inflammatory reaction
- **Incomplete reendothelialization**
- Neointimal hyperplasia (?)

Mechanisms

Imbalance of vasoactive substances

- Decreased production/availability of NO
- Modulation of NO availability in high shear stress regions
- Desensitization to NO-donors/eNOS uncoupling
- High bioavailability of vasoconstrictors (ET-1, Ang II)
- Reduced sensitivity to vasorelaxants (Ach, Bk, 5-HT)
- Increase of vascular oxidative stress Induction of rho kinase (ROCK) and SMC hypercontraction (paclitaxel)

Endothelial healing in DES

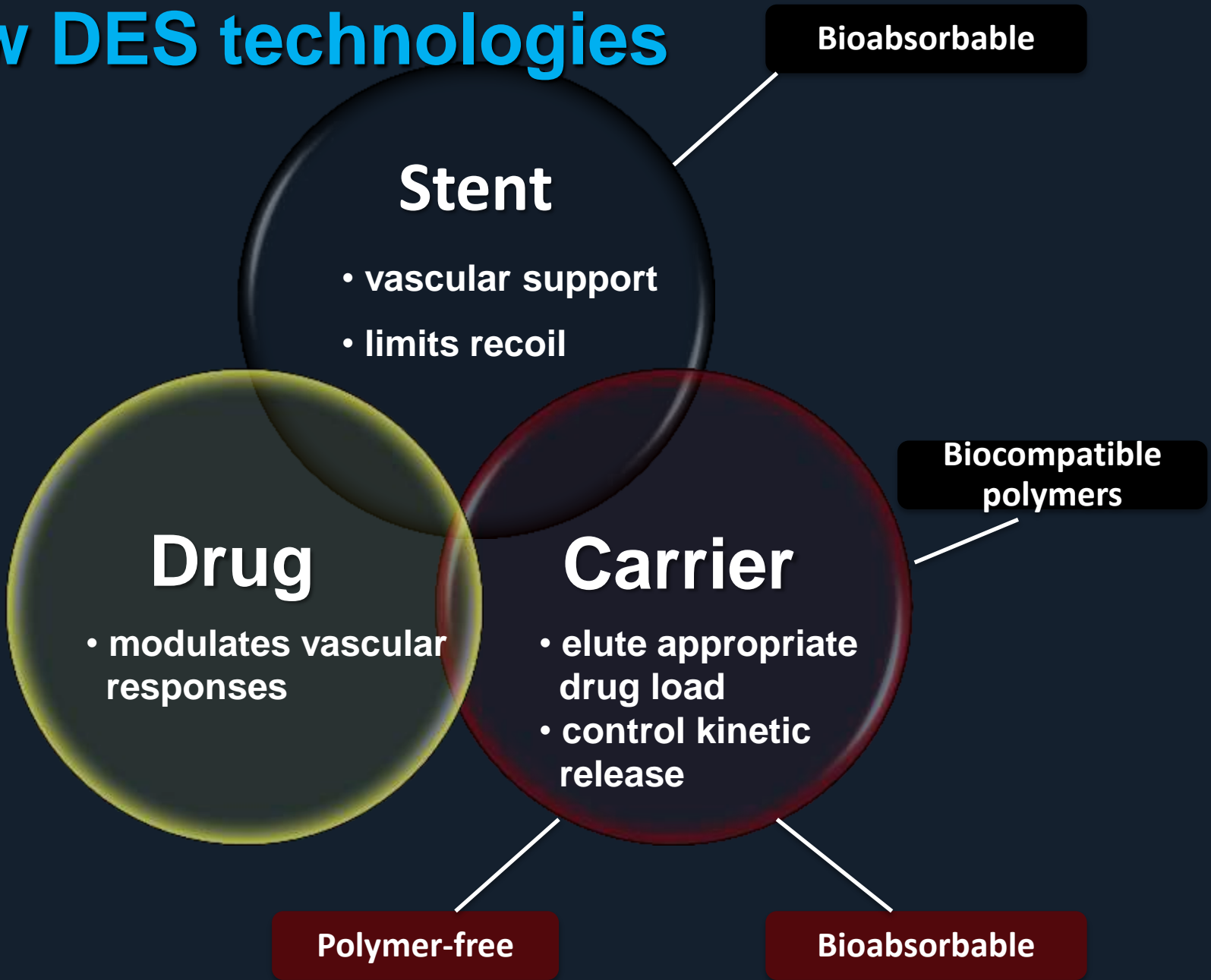


Impaired endothelialization

Most common location of uncovered stent struts:

- Middle section
- Stent overlap
- Penetration into the necrotic core of plaques
- Malapposition,
- Bifurcations
- Thrombus

New DES technologies



Dual Therapy Stent

Drug to control neo-intimal proliferation

- Abluminal sirolimus elution
- Drug eluted by 30 days
- Full and complete polymer degradation within 90 days

Sirolimus in a Biodegradable Polymer Matrix

Abluminal effect

Stent Strut

Anti CD34 Antibody Coating for EPC Capture

EPCs captured for accelerated endothelial coverage

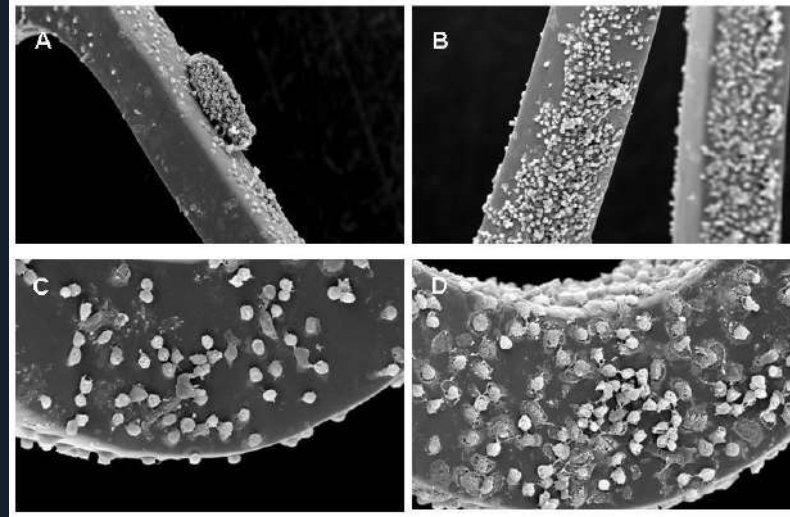
- EPCs are captured by antibodies
- EPCs differentiate into endothelial cells
- A mature, functional endothelium is formed

Luminal effect

Stent platform Unique Dual Helix Design for Unsurpassed Sidebranchability and Natural Conformability

Dual Therapy Stent

Improved endothelialization



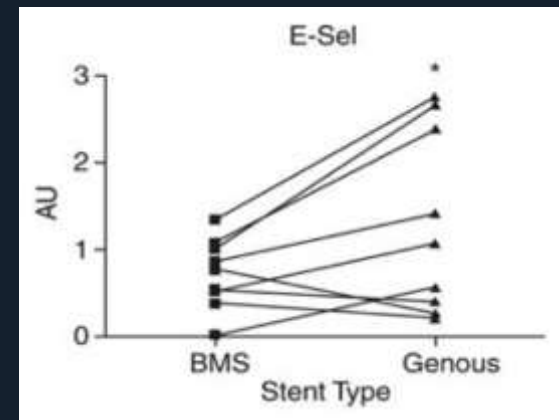
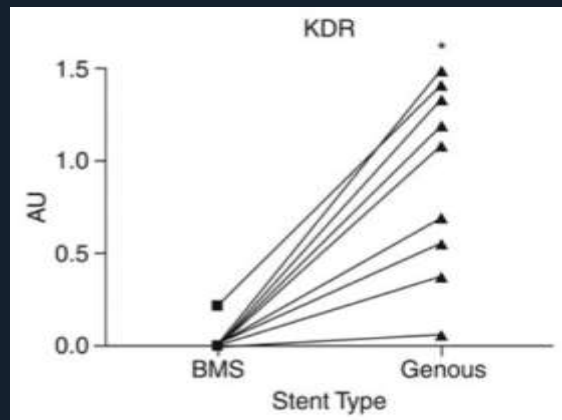
Hallmarks of functional endothelial cells

KDR:

Kinase insert Domain Receptor is a vascular endothelial growth factor receptor

E-Selectin:

Cell adhesion molecule produced by endothelial cells



Dual Therapy Stent

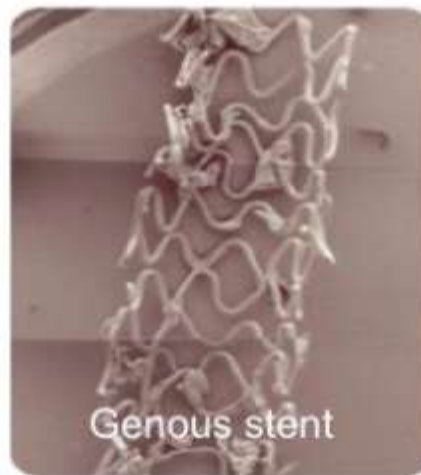
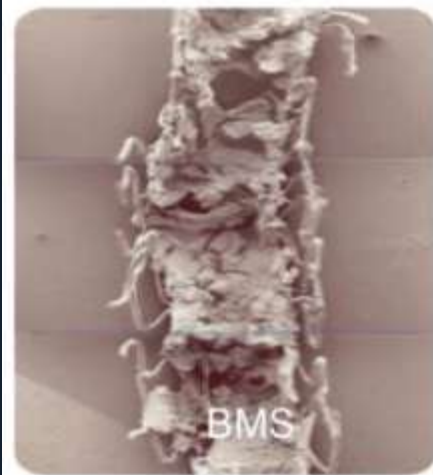
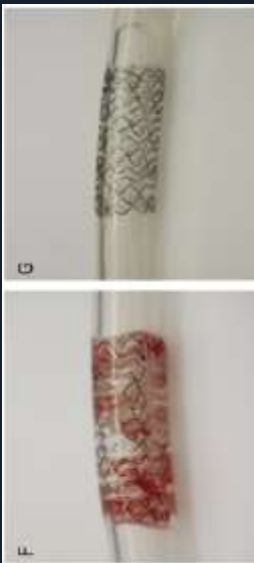
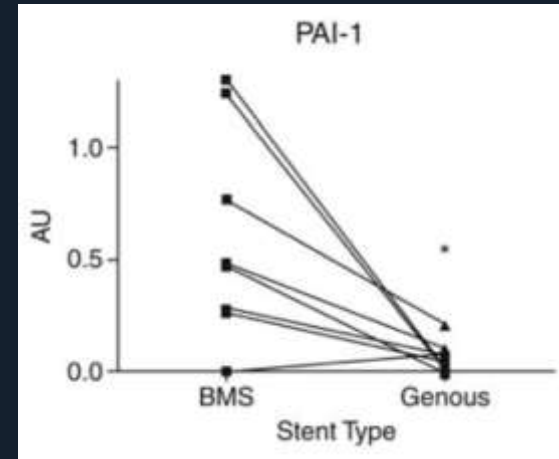
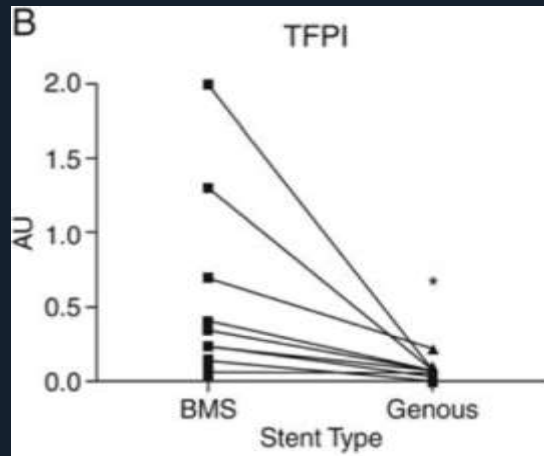
Improved antithrombotic balance

TFPI:

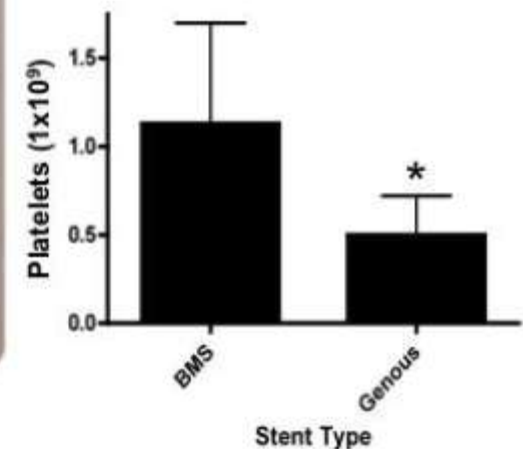
Tissue Factor Pathway Inhibitor is associated with coagulation

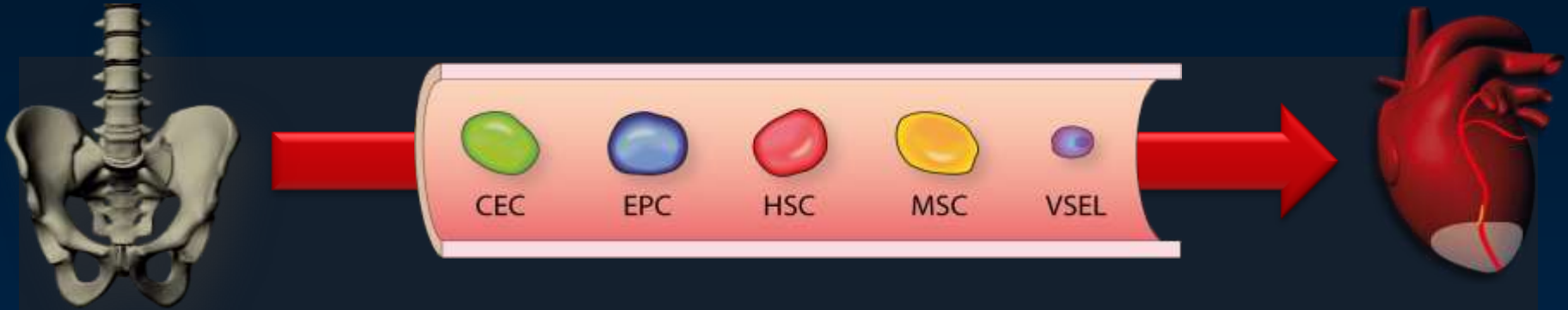
PAI-1:

Plasminogen Activator Inhibitor - 1 is associated with fibrin

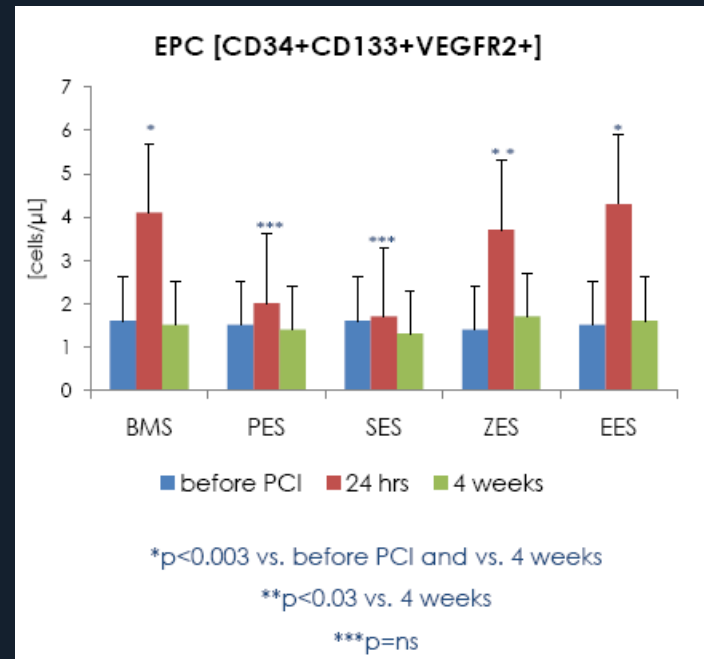
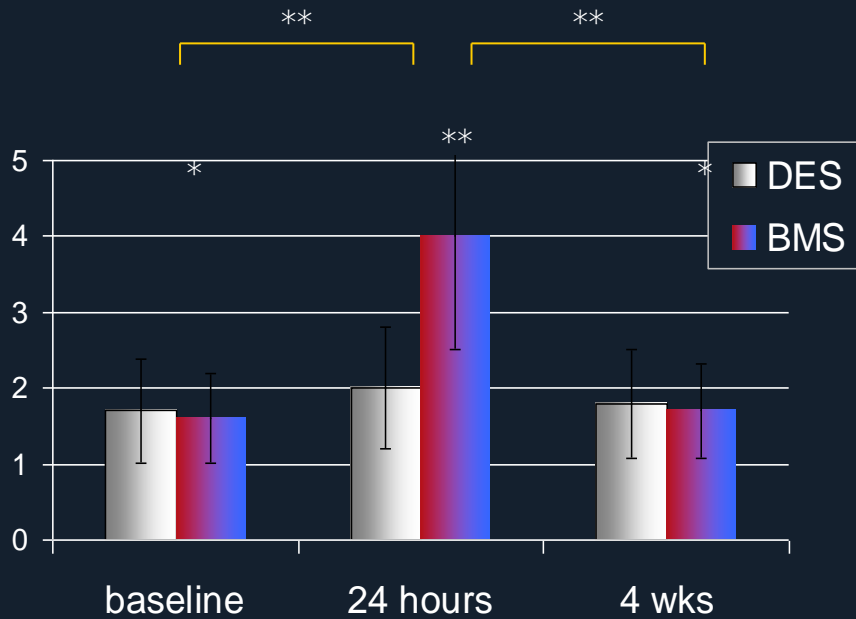


Platelet Accumulation on Stents Struts in Baboons





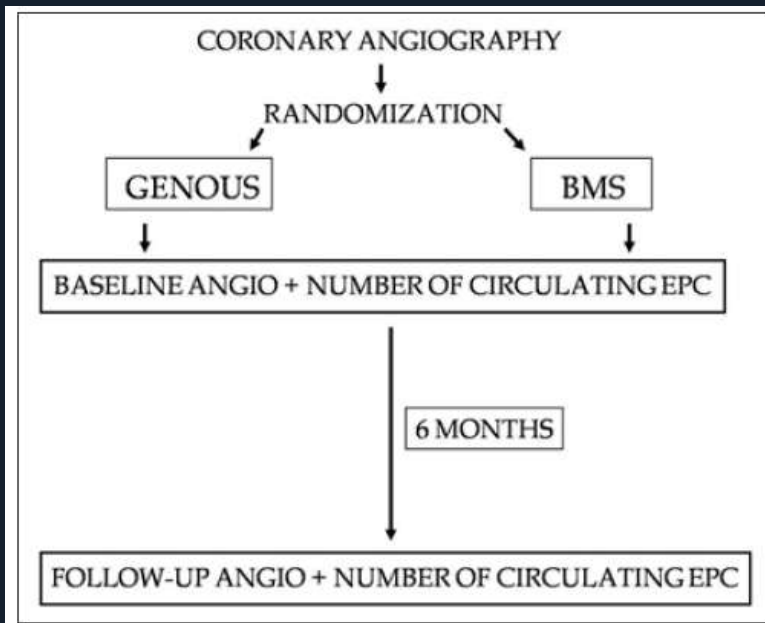
CD34+VEGFR+CD133+ [cells/ μ l]



**P < 0.02

*P = ns

Circulating endothelial progenitor cells are inversely correlated with in-stent restenosis in patients with non-ST-segment elevation acute coronary syndromes treated with EPC-capture stents (JACK-EPC trial)

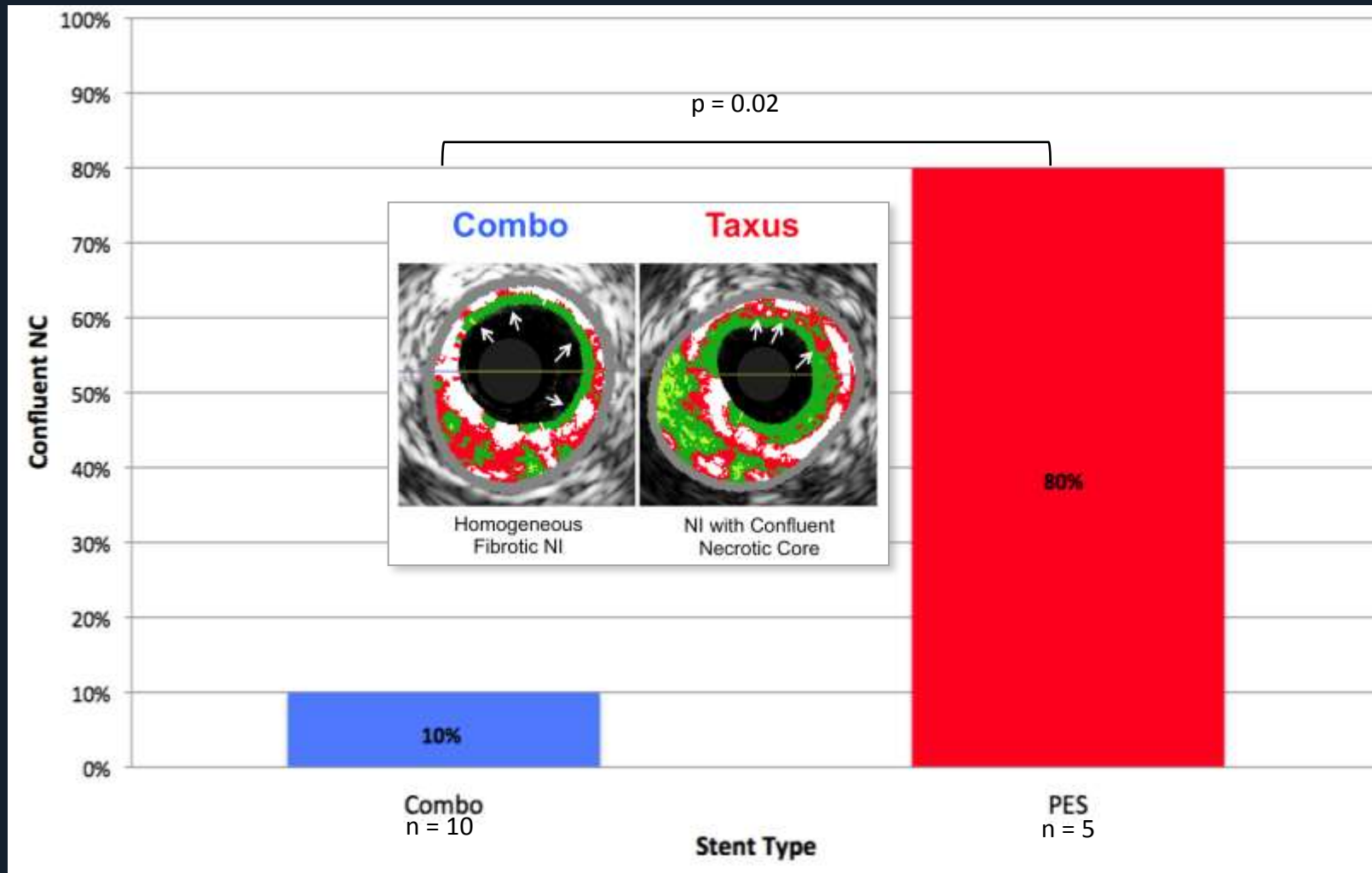


- **Non ST-segment elevation acute coronary syndromes (NSTEMI and unstable angina)**
- **de novo lesion >70% in native coronary artery**
- **target vessel diameter 2.5-4.0mm**
- **target lesion length \leq 30mm which can be covered with single stent.**

QUANTITATIVE CORONARY ANGIOGRAPHY

	GENOUS	BMS	P-VALUE
BEFORE PROCEDURE (n=60)			
REFERENCE DIAMETER, mm	2.87±0.47	2.96±0.51	P=ns
LESION LENGTH, mm	18,2±6.3	18,6±7.4	P=ns
DIAMETER STENOSIS, %	74.9±18.5	73.7±14.7	P=ns
MLD, mm	0.77±0.45	0.84±0.5	P=ns
AFTER PROCEDURE (n=60)			
DIAMETER STENOSIS, %	14.5±1.7	15.5±1.4	P=ns
MLD, mm	2.75±0.72	2,54±0.91	P=ns
6 MONTHS FOLLOW-UP (n=49)			
DIAMETER STENOSIS, %	28.2±15.4	37,63±13.7	P=0.03
MLD, mm	2.34 ±0.51	2.01±0.64	P=0.06
BINARY RESTENOSIS RATE, %	4 (13)	8 (26.6)	P=0.04
IN-STENT LATE LOSS, mm	0.45±0.54	0.86±0.77	P=0.03

Confluent Necrotic Core in NI (IVUS-VH) REMEDEE (9-month FU)



Dual Therapy Stent

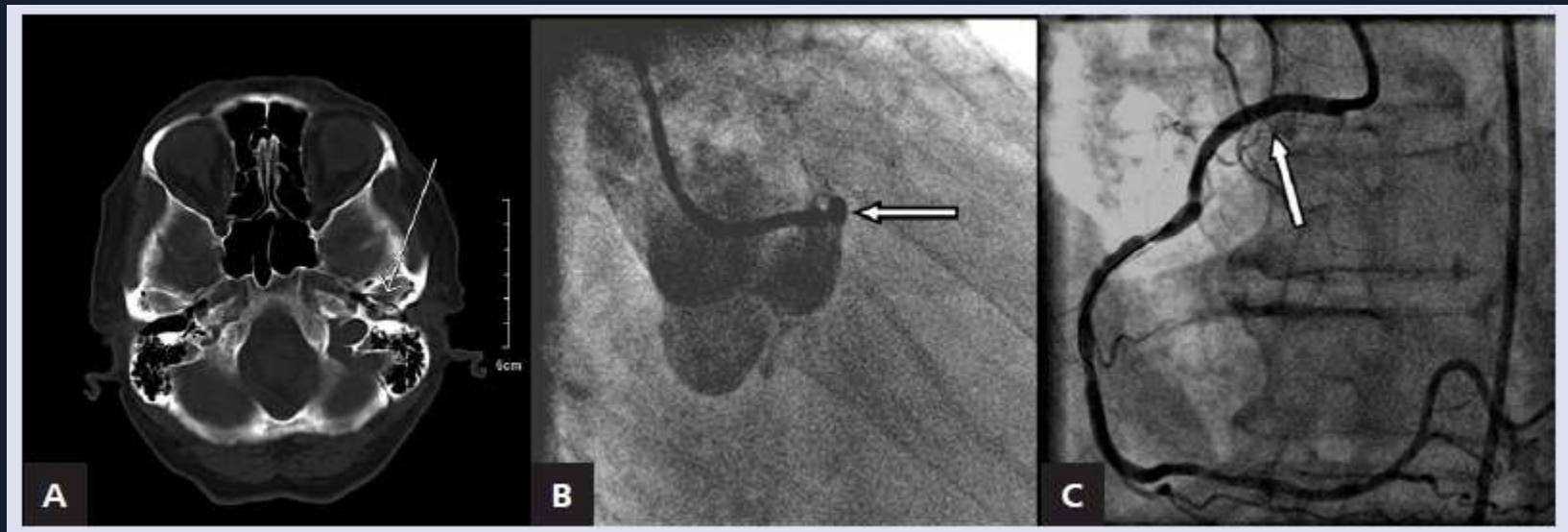
- **Patients with high bleeding risk**
 - **Non-compliant with DAT**
 - **DAT contraindicated (active bleeding, surgery, diathesis, thrombocytopenia, etc)**
 - **Allergy**
- **High thrombotic risk**
 - **STEMI**
- **Other populations**

Dual Therapy Stent

- **Patients with high bleeding risk**
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 - **Allergy**
- **High thrombotic risk**
 - **STEMI, NSTEMI**
- **Other populations**

Dual Therapy Stent

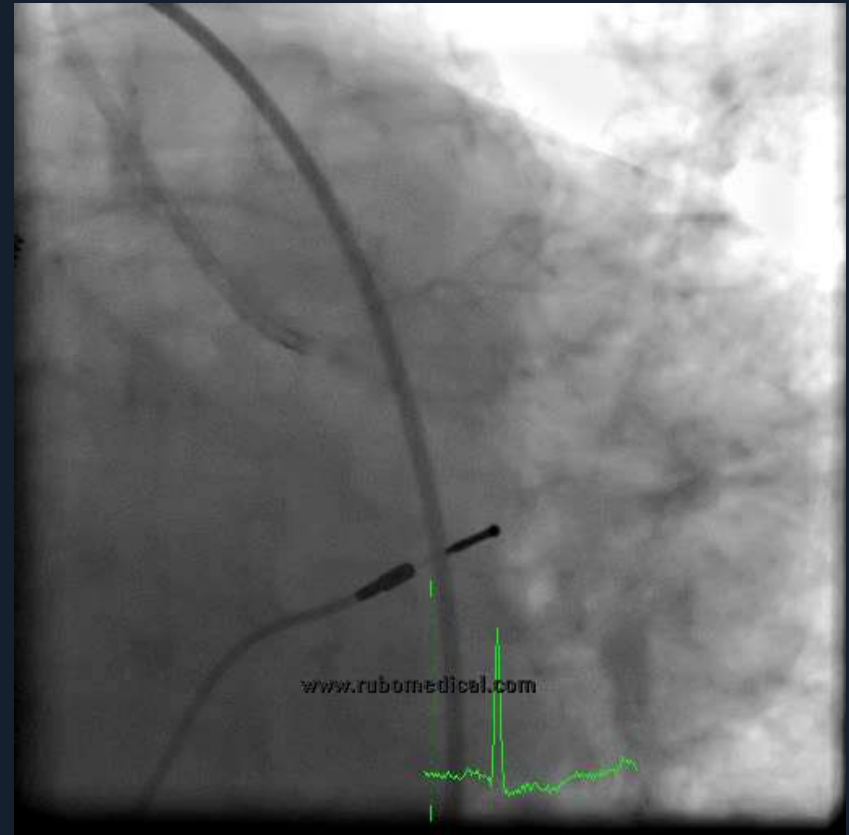
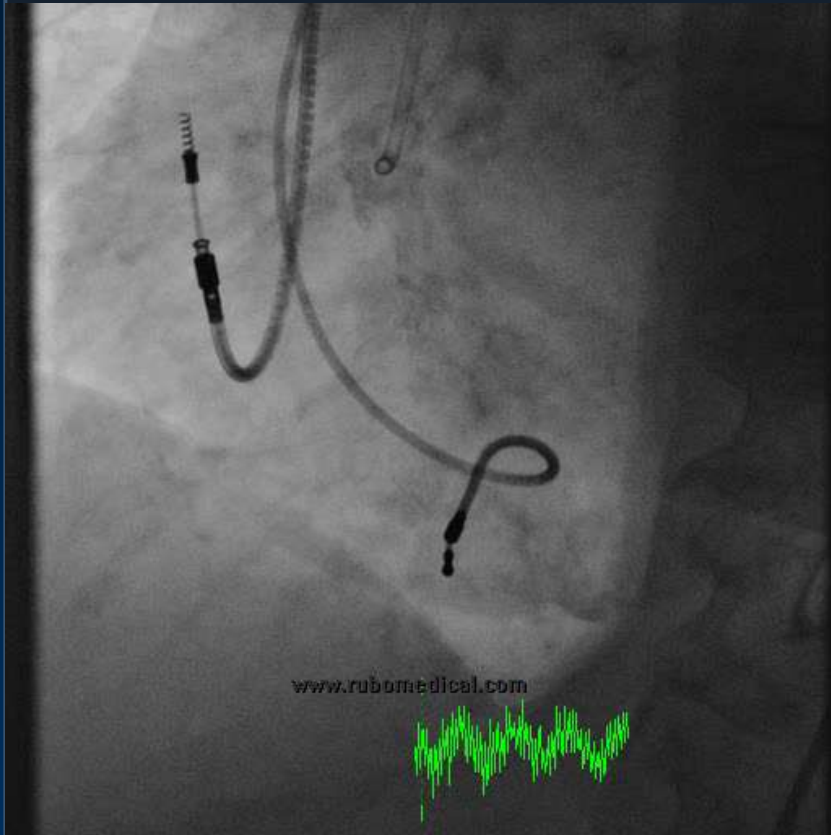
Primary PCI with endothelial progenitor cell-capture stent in patient with skull base fracture and aspirin allergy



Dual Therapy Stent

- Patients with high bleeding risk
 - Non-compliant with DAT
 - DAT contraindicated (active bleeding, surgery, diathesis, thrombocytopenia, etc)
 - Allergy
- High thrombotic risk
 - STEMI, NSTEMI
- Other populations

Case#1

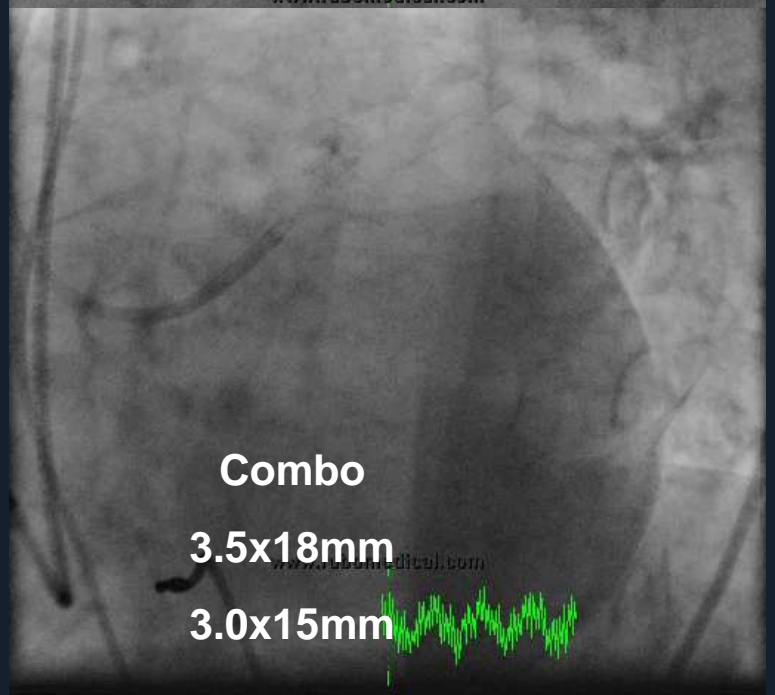
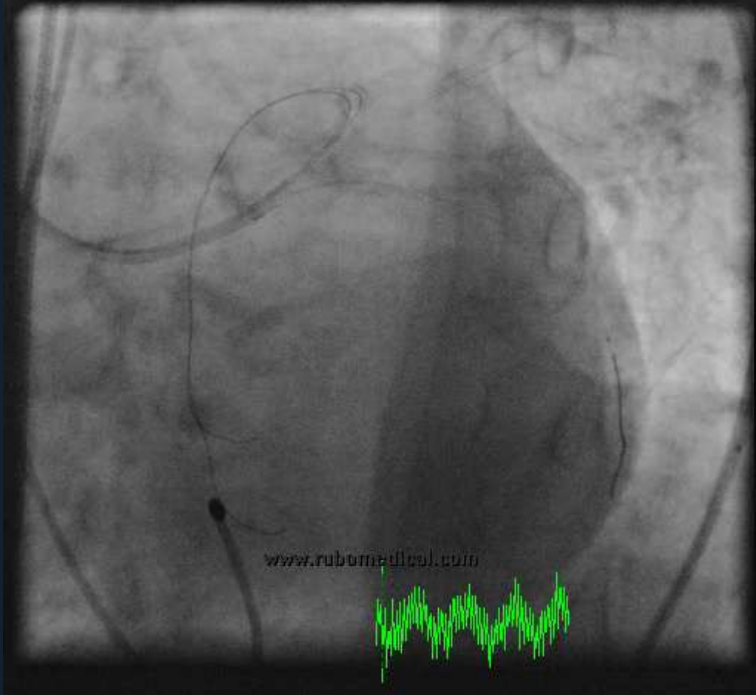
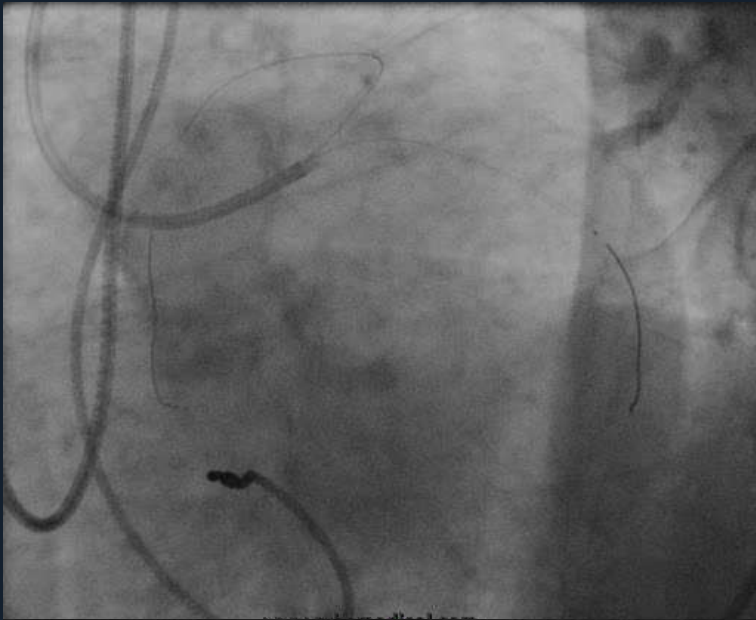


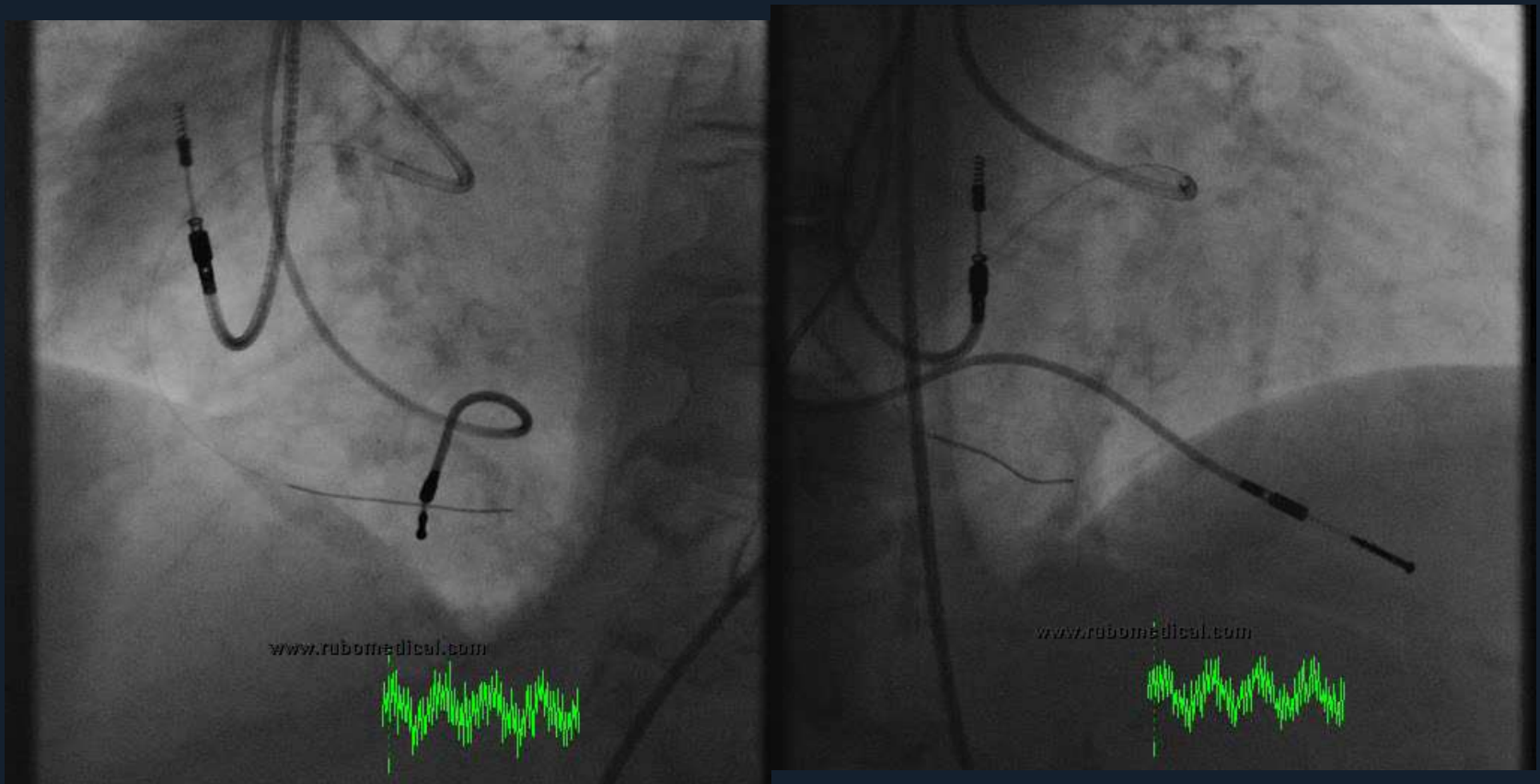
57 yo male, CCS IV, cardiogenic shock

NSTEMI

LVEF 40%

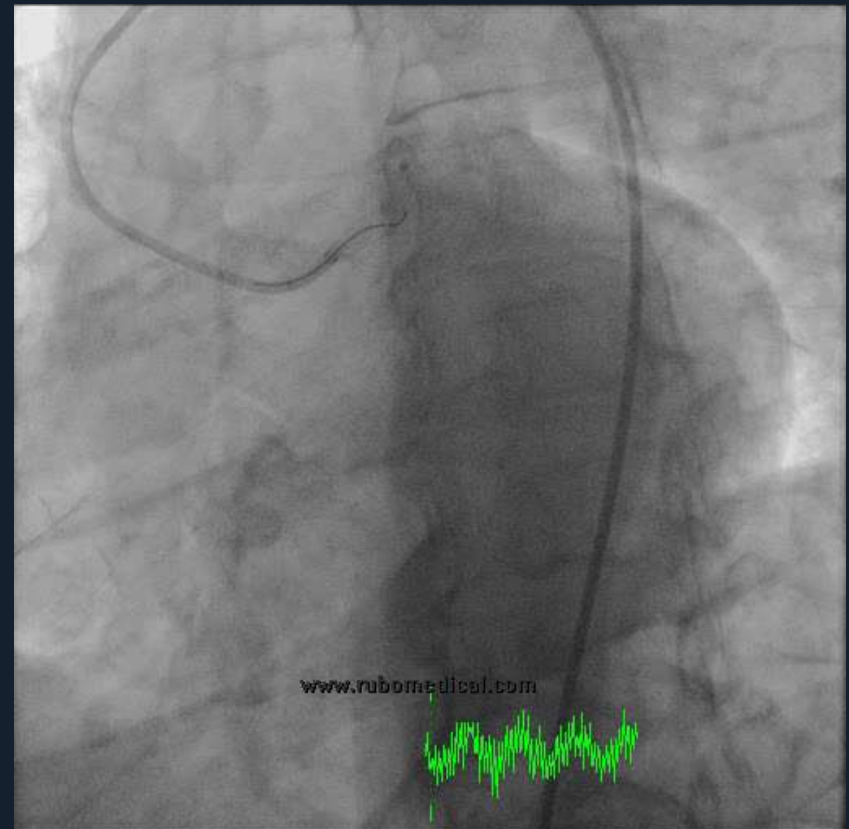
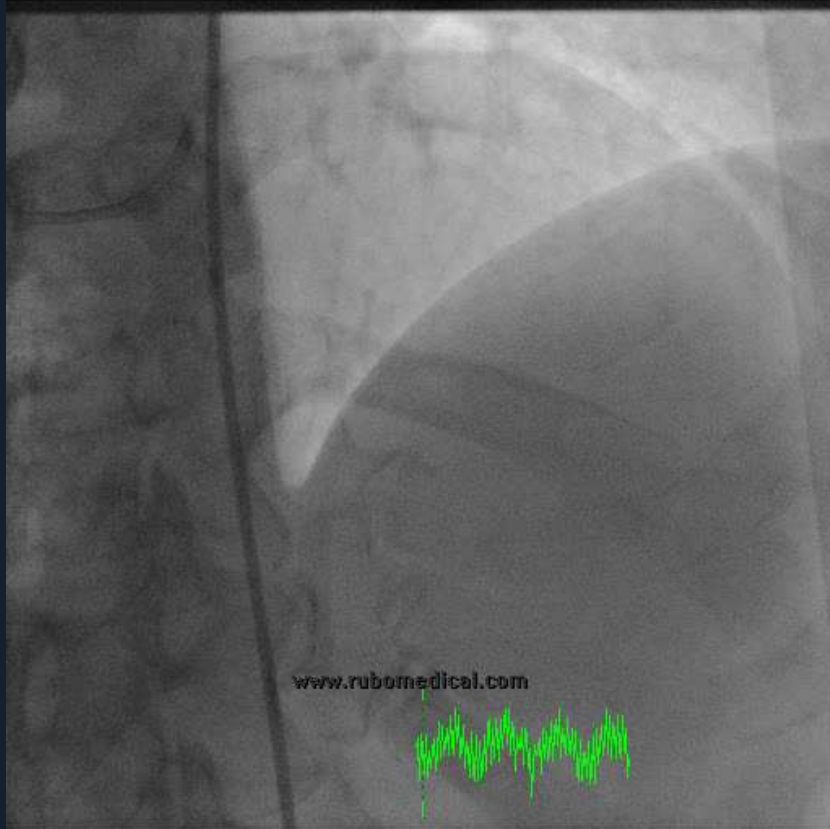
History of PCI 2011





Combo
3.0x15mm

Case#2

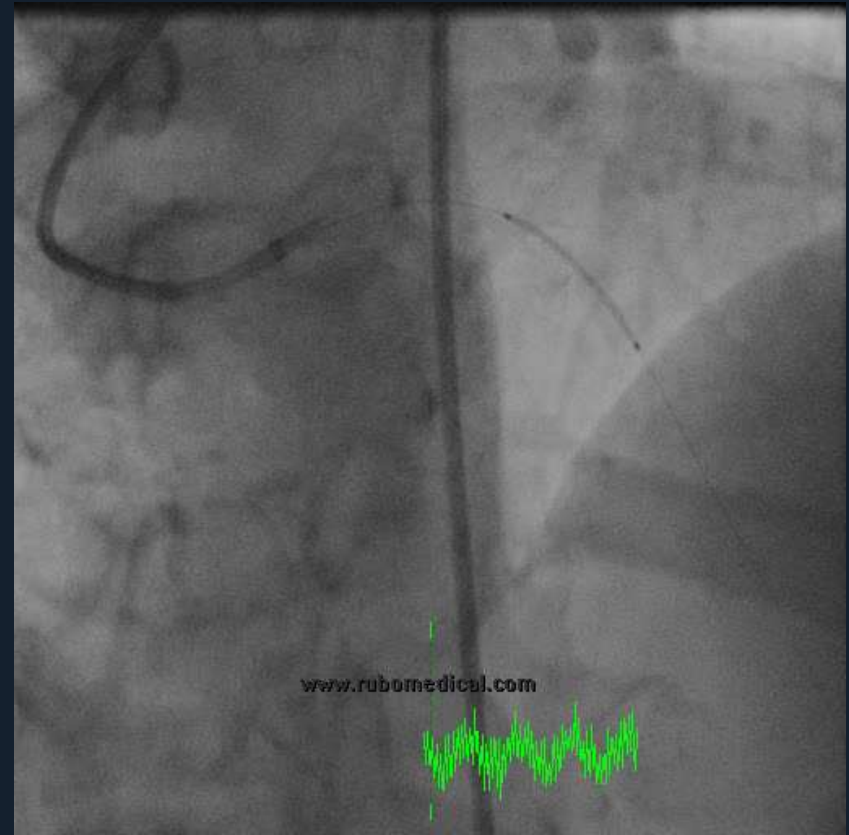
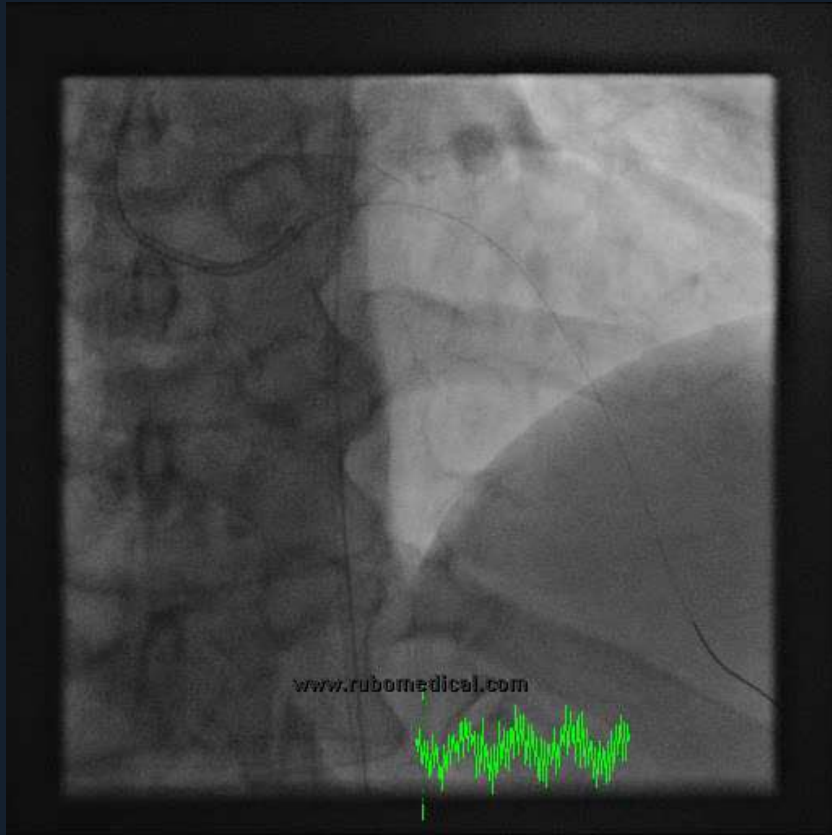


72 yo female, STEMI

LVEF 35%

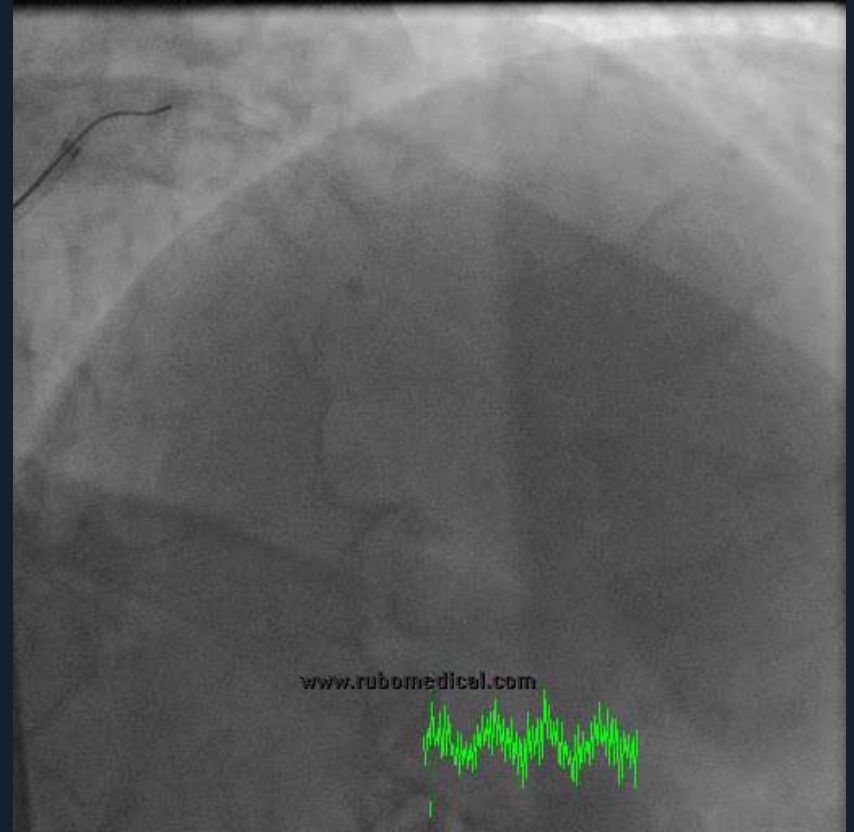
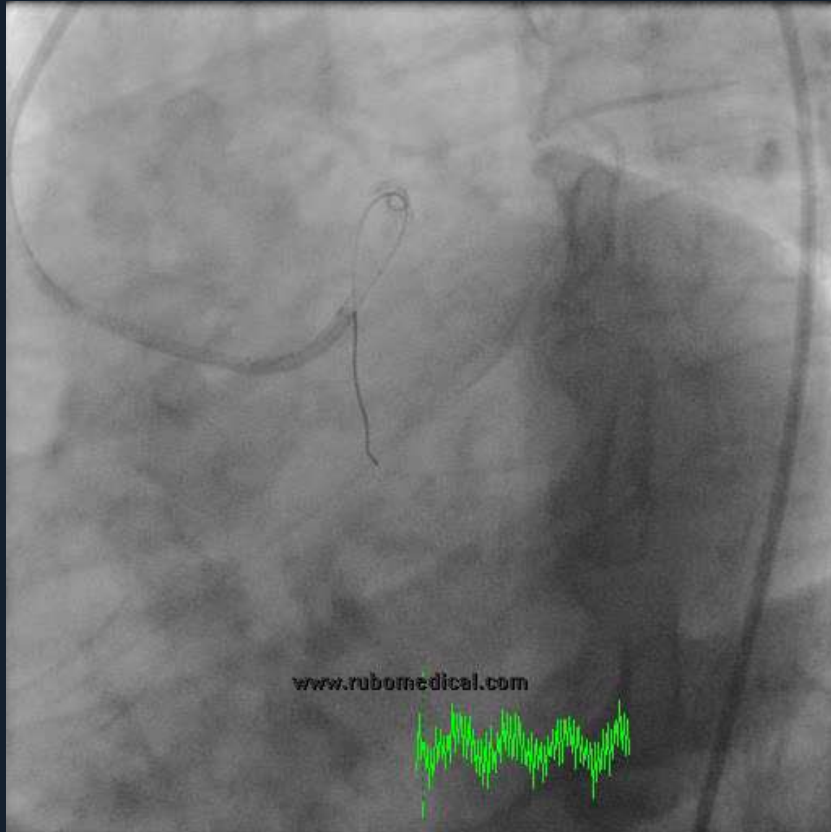
History of diabetes and hypertension

Case#2

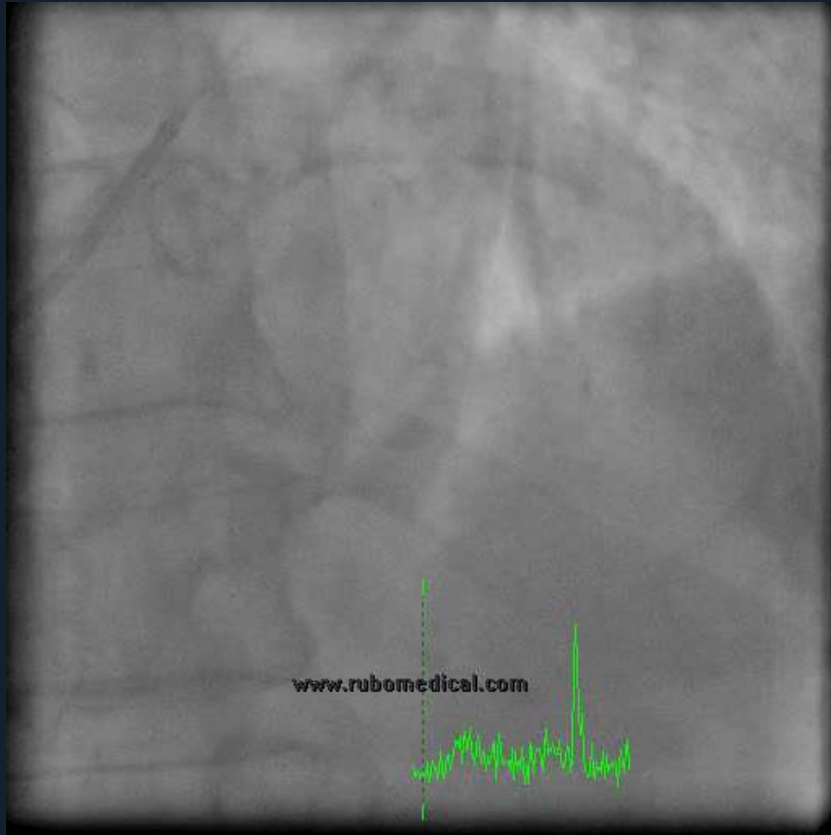


Combo
3.0x23mm

Case#2



Case#3

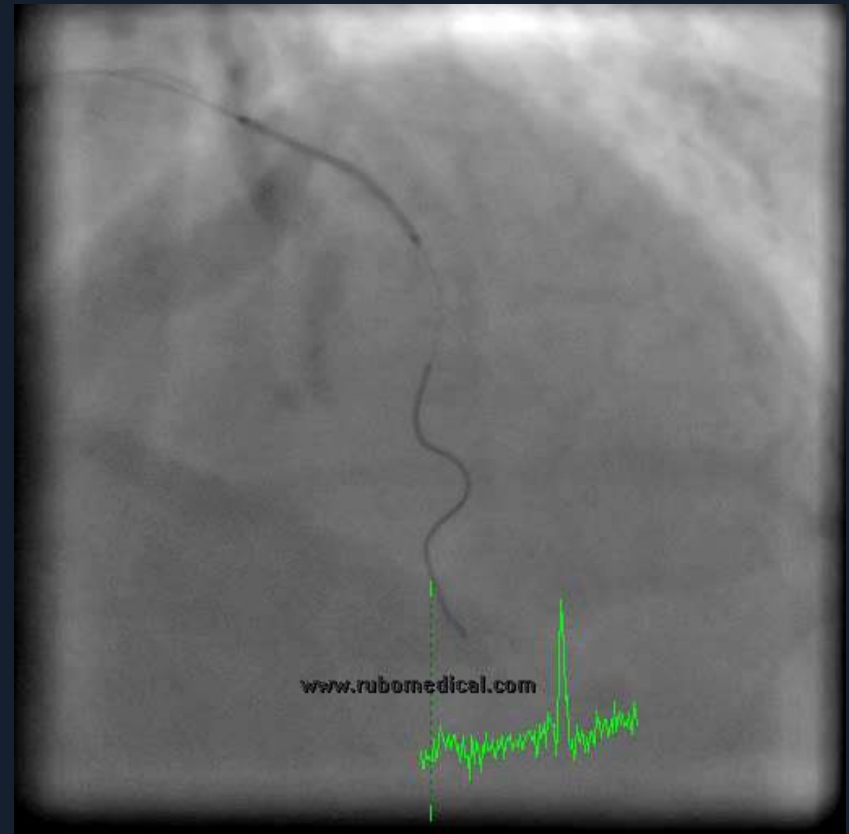
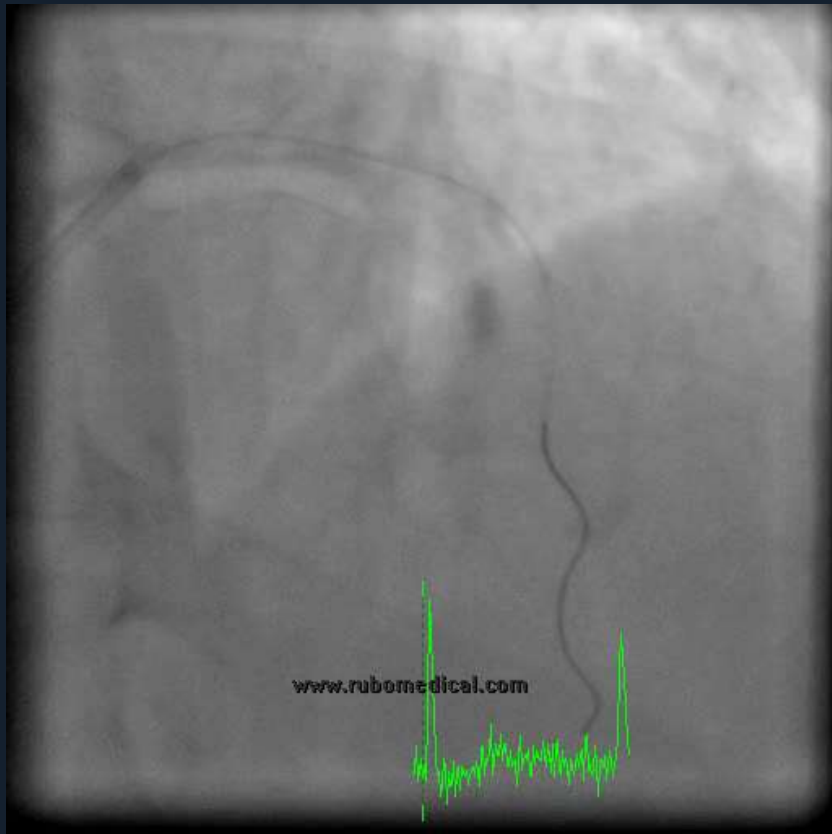


52 yo female, NSTEMI

LVEF 55%

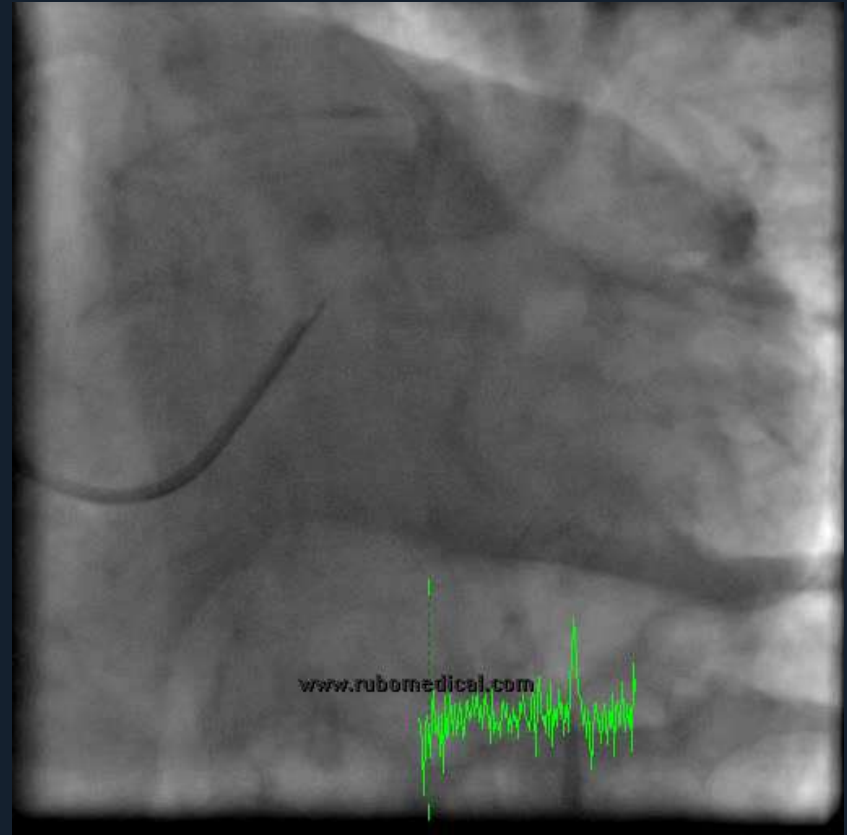
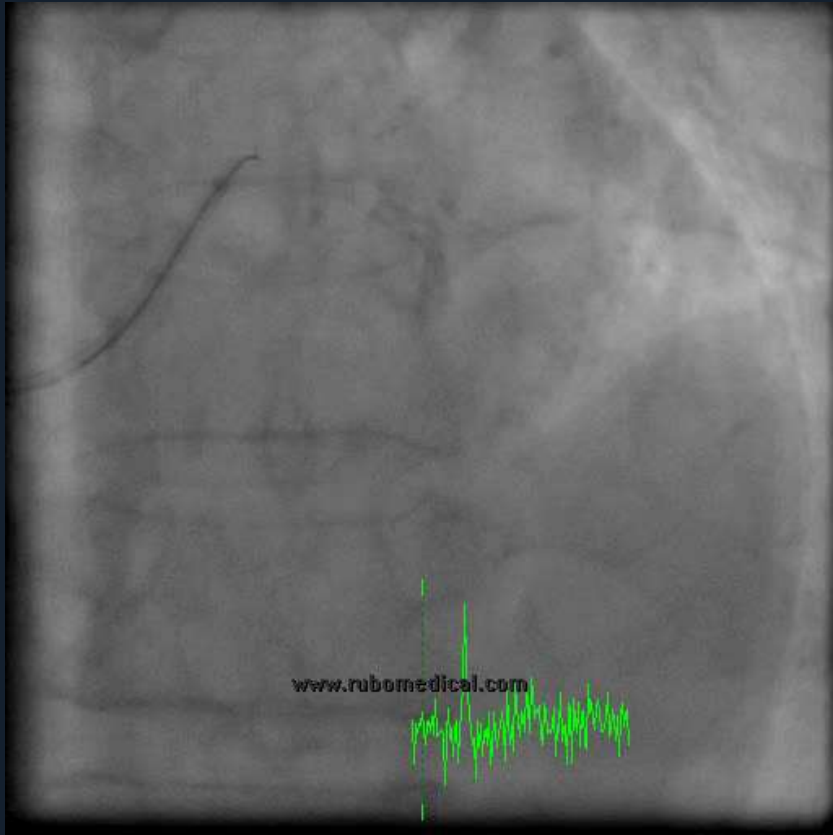
History of hypertension

Case#3



Combo
2.5x23mm

Case#3



Dual Therapy Stent

- Patients with high bleeding risk
 - Non-compliant with DAT
 - DAT contraindicated (active bleeding, surgery, diathesis, thrombocytopenia, etc)
 - Allergy
- High thrombotic risk
 - STEMI
- Other populations

Conclusions

Dual therapy stent (COMBO)

- EPC-capture technology validated in large populations
- Antiestenotic efficacy (abluminal biodegradable polymer + limus)
- Rapid endothelialization
- Favorable safety and clinical efficacy
- Especially indicated for high bleeding risk and majority of ACS patients given its pro-healing properties

Thank you for attention