The Sorin JANUS Flex Tacrolimus-Eluting Carbostent Clinical Trials: Results from a Large Observational Registry

e-JANUS interim analysis for
1, 6 and 12 months

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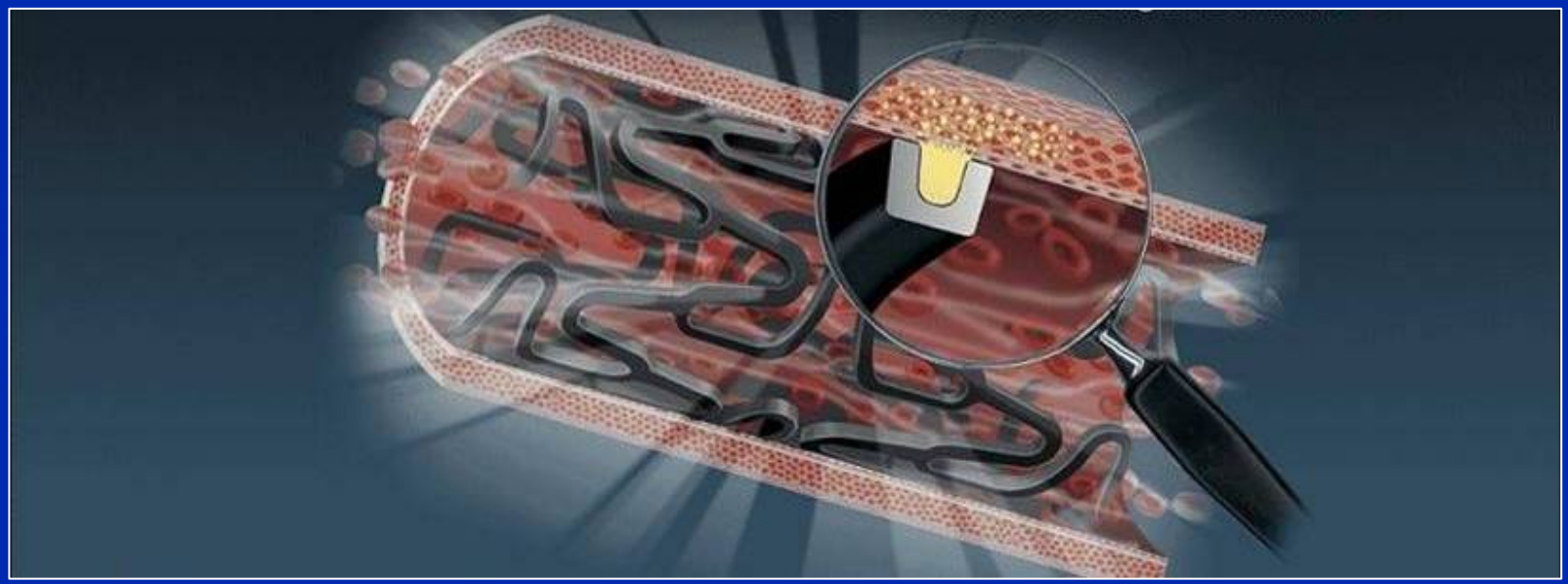
Important Issues that Confront DES today

- 1st generation polymeric DES reduce incidence of restenosis when compared to bare metal stents.
- Late stent thrombosis and hypersensitivity reactions are problems which limit the safety of these stents.
- In most of the above mentioned situations either the polymer or the drug is implicated, therefore it is believed that next generation polymers (bioerodable polymers) or no polymer may be safer for drug delivery from stents.

JANUS Flex platform

- **Embedded reservoirs** on the outer stent surface
- **No inflammatory polymer coating required**
- **Targeted & precise drug release:** 100% drug release towards the vessel wall
- **Integral Carbofilm™ coating:** Proven highly biocompatible and non-thrombogenic coating
- **Tacrolimus*:** Cytostatic immunosuppressant drug with both anti-proliferative and anti-inflammatory activities



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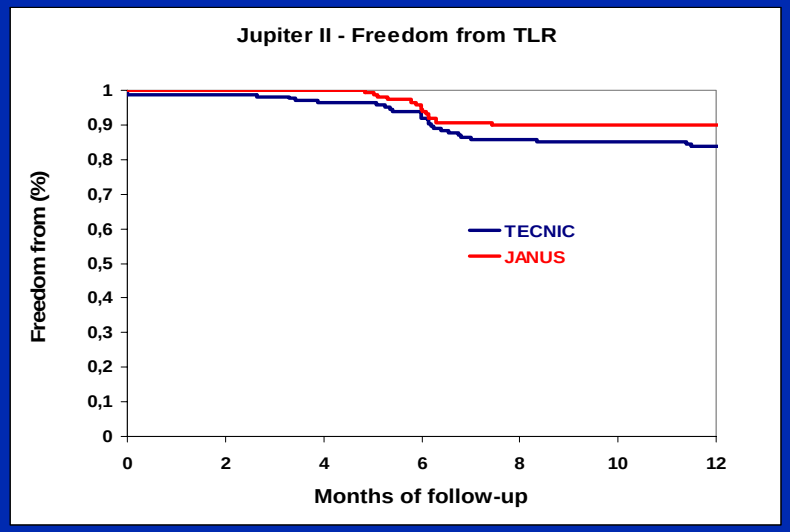
Clinical results of the Jupiter II randomized trial*

	6-month clinical events			12-month clinical events		
	TECNIC 163 pts (compl. 98.2%)	JANUS 161 pts (compl. 96.9%)	*p*	TECNIC 159 patients (compl. 95.8%)	JANUS 155 patients (compl. 95.1%)	*p*
ALL MACE (n)	17.2% (28)	13.0% (21)	*Ns*	19.5% (31)	14.8% (23)	*Ns*
TLR (n)	14.1% (23)	9.9% (16)	*Ns*	16.4% (26)	10.3% (16)	*Ns*
TLR Clinical	6.7% (11)	3.7% (6)	*Ns*	8.8% (14)	3.9% (6)	.07
Reduction clinical TLR		-44.8%			-55.7%	



- No new TLRs between 6 and 12 months in Janus arm
  - ➢ Long term data stability
- 0% acute, sub-acute and late stent thrombosis in Janus arm with an extremely short dual antiplatelet therapy (≤6months)
  - ➢ Extremely safe device profile

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International “real world” electronic registry

99 Sites

Phase I – European sites:

Austria 6	Italy 31
Benelux 4	Portugal 2
France 17	Spain 20
Germany 9	Sweden 1
Greece 3	Switzerland 1
	United Kingdom 1

Opening PHASE II – Worldwide centers:

- Brazil 2
- China 1
- Iran 1
- Other centers underway

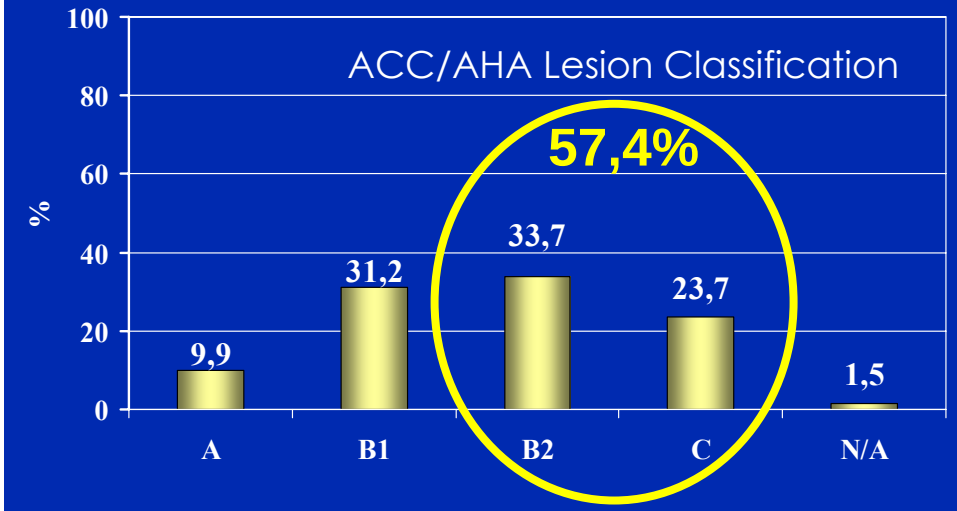
Prospective electronic registry – 3% monitoring

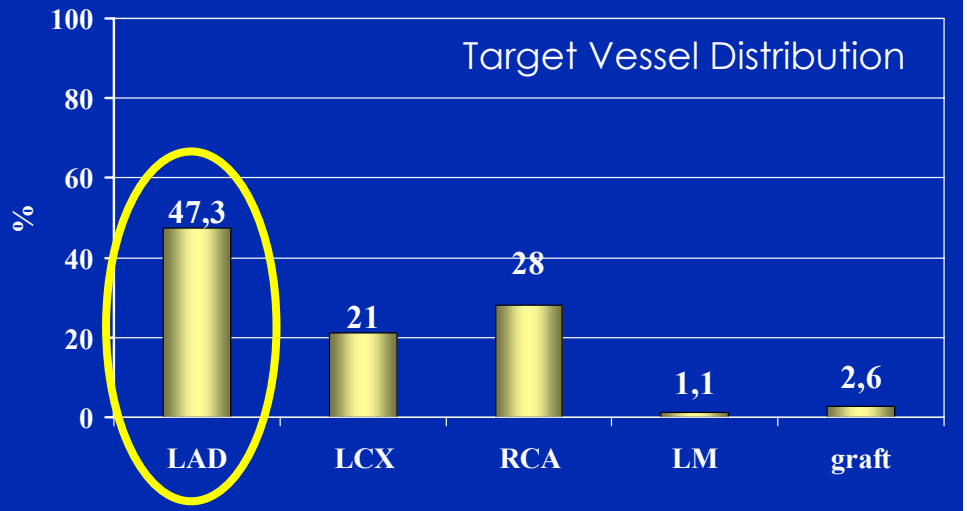
Baseline Clinical Characteristics

• N° of enrolled pts	2927
• Interim Analysis on	2927 pts
• Male	76.8%
• Age (yrs)	63.5 ± 11.1
• Diabetes	28.2% (825 pts)
ID Diabetes	7.1% (209 pts)
NID Diabetes	21.1% (616 pts)
• AMI	24.9% (729 pts)
• Multivessel disease	51.1% (1493 pts)

Target Lesion Characteristics

- N° of lesions 3388
- Bifurcations 16.9% (573/3388)
- Ostial Lesions 10.9% (368/3388)
- Total Chronic Occlusions 6.3% (212/3388)
- Lesion Lenght 16.7± 8.5





e-Janus Interim Analysis on 2927 pts

Procedural Characteristics

Direct stenting technique	**43.9%**
# Stent/patient	**1.32 ± 0.63**
# Stent/lesion	**1.13 ± 0.42**
Stent size ≤ 3.0 mm	**70.1%**
Mean Stent Length (mm)	**18.6 ± 5.5**
Stent delivery pressure (atm)	**14.0 ± 3.2**

Procedure Success*	**99.1% (3358/3388 les)**

*Residual diameter stenosis ≤ 20% (by visual estimate) after stenting procedure

Clinical Events from discharge to 1 month follow-up*

on 2359 pts.	Total
MACE (n)	**3.2% (77)**
Death (n)	**1.3% (30)**
Cardiac Death	1.3% (30)
MI (n)	**1.1% (27)**
Q-Wave	0.6% (15)
Non Q-Wave	0.5% (12)
TLR (n)	**0.8% (20)**
CABG	0%
Re-PTCA	0.2% (6)
Re-PTCA + stent	0.6% (14)
TVR* (n) *includes TLR and non-TLR TVR	1.4% (34)

*** Clinical data from the interim statistical analysis up to 1 month can not be used to calculate the cumulative 12 months events rate.**

Clinical Events at 6-month follow-up*

on 1877 pts.	Total
MACE (n)	**9.4% (178)**
Death (n)	**1.0% (19)**
Cardiac Death	1.0% (19)
MI (n)	**1.2% (24)**
Q-Wave	0.6% (12)
Non Q-Wave	0.6% (12)
TLR (n)	**7.2% (135)**
CABG	1.1% (21)
Re-PTCA	1.8% (34)
Re-PTCA + stent	4.3% (80)
TVR* (n) *includes TLR and non-TLR TVR	9.3% (175)

*** Clinical data from the interim statistical analysis at 6 months can not be used to calculate the cumulative 12 months events rate.**

Clinical Events at 12-month follow-up*

on 970 pts.	Total
MACE (n)	**5.1% (50)**
Death (n)	**0.5% (5)**
Cardiac Death	0.5% (5)
MI (n)	**0.7% (7)**
Q-Wave	0%
Non Q-Wave	0.7% (7)
TLR (n)	**3.9% (38)**
CABG	0.4% (4)
Re-PTCA	0.9% (9)
Re-PTCA + stent	2.6% (25)
TVR* (n) *includes TLR and non-TLR TVR	6.2% (60)

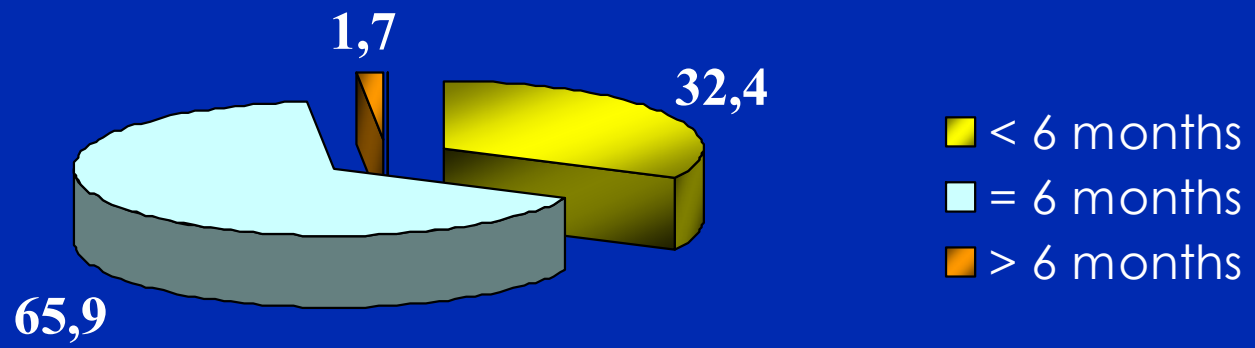
*** Clinical data from the interim statistical analysis at 12 months can not be used to calculate the cumulative 12 months events rate.**

Sub-acute and Late Thrombosis

Sub-acute Thrombosis	**0.8%** (18/2359)
Late Thrombosis	**0.1%** *(2/1877)

* 1 pt stopped dual antiplatelet therapy early.

Dual antiplatelet therapy duration



AMI patients background

- Complicated clinical context
- Actively thrombotic environment
- Higher risks of further cardiac complications
- Un-optimal evaluation of angiographic parameters (i.e. complete stent strut wall apposition)

- Increased incidence of **MACE**
- Increased incidence of **stent thrombosis**

Need to increase SAFETY for AMI patients maintaining good device efficacy

AMI Subgroup

Baseline Clinical Characteristics

• **N° of analyzed pts**	**729 out of 2927**
• **Male**	**80.3%**
• **Age (yrs)**	**61.2 ± 11.9**
• **Diabetes**	**25.7% (187 pts)**
ID Diabetes	6.5% (47 pts)
NID Diabetes	19.2% (140 pts)
• **Multivessel disease**	**48.6% (353 pts)**

Clinical Events from discharge to 1 month follow-up* AMI subgroup

on 570 pts.	Total
MACE (n)	**4.9% (28)**
Death (n)	**3.1% (18)**
Cardiac Death	3.1% (18)
MI (n)	**0.9% (5)**
Q-Wave	0.5% (3)
Non Q-Wave	0.4% (2)
TLR (n)	**0.9% (5)**
CABG	0%
Re-PTCA	0.4% (2)
Re-PTCA + stent	0.5% (3)
TVR* (n) *includes TLR and non-TLR TVR	1.4% (8)

*** Clinical data from the interim statistical analysis up to 1 month can not be used to calculate the cumulative 12 months events rate.**

Clinical Events at 6-month follow-up* AMI subgroup

on 414 pts.	Total
MACE (n)	**8.0% (33)**
Death (n)	**0.5% (2)**
Cardiac Death	0.5% (2)
MI (n)	**1.7% (7)**
Q-Wave	0.5% (2)
Non Q-Wave	1.2% (5)
TLR (n)	**5.8% (24)**
CABG	0.7% (3)
Re-PTCA	1.7% (7)
Re-PTCA + stent	3.4% (14)
TVR* (n) *includes TLR and non-TLR TVR	7.7% (32)

*** Clinical data from the interim statistical analysis at 6 months can not be used to calculate the cumulative 12 months events rate.**

Clinical Events at 12-month follow-up* AMI subgroup

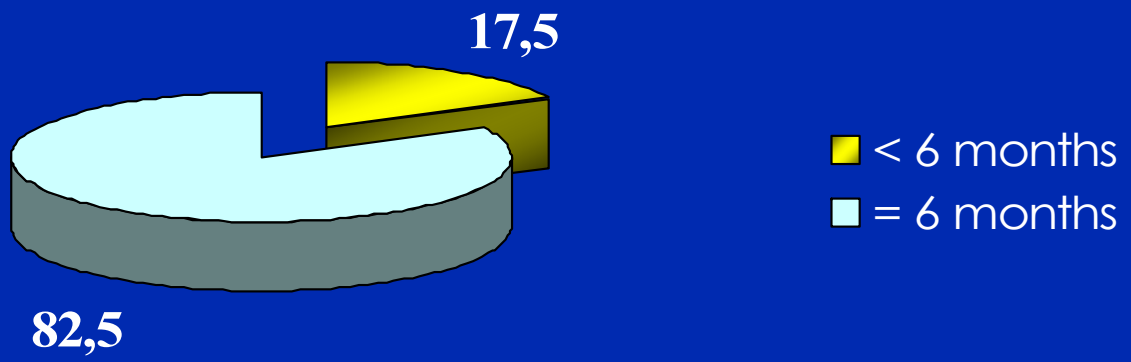
on 199 pts.	Total
MACE (n)	**2.0% (4)**
Death (n)	**0%**
Cardiac Death	0%
MI (n)	**0.5% (1)**
Q-Wave	0%
Non Q-Wave	0.5% (1)
TLR (n)	**1.5% (3)**
CABG	0%
Re-PTCA	1.0% (2)
Re-PTCA + stent	0.5% (1)
TVR* (n) *includes TLR and non-TLR TVR	3.0% (6)

*** Clinical data from the interim statistical analysis at 12 months can not be used to calculate the cumulative 12 months events rate.**

Subacute and Late Thrombosis

Sub-acute Thrombosis	**0.9%** (5/570)
Late Thrombosis	**0%**

Dual antiplatelet therapy duration



Conclusions

- e-Janus “real-world” interim data demonstrated:
  - Positive results in complex patients setting
  - Clinical efficacy with low TLR rate at 6 &12 months in high risk AMI subgroup
  - Outstanding safety profile up to 12 months in the overall cohort (0.1% LST) & AMI patients (0% LST)
- Encouraging values in late stent thrombosis clearly reinforce the strong benefit of JANUS Flex platform’s unique features
- In the future new platform and other drug release pattern have to further reduce TLR rates