

# The Titan stent, just a good bare metal stent or more?

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Titanium-nitride-oxide-coated stents have intriguing biological properties. They are more biocompatible than bare metal stents and reduced neointimal hyperplasia after implantation could be demonstrated in a pig model<sup>1</sup>. This positive effect could be confirmed in men in a small angiographic follow-up study<sup>2</sup>. The better tissue acceptance may lead to a faster and more complete endothelialisation after implantation as demonstrated by optical coherence tomography<sup>3</sup>.

Clinical experience with these devices has shown impressive results in real-life trials (Table 1). In many clinical studies this stent fared better than bare metal stents (BMS) and even paclitaxel-eluting stents in low- and high-risk patient groups<sup>4-18</sup>. However, in a single centre trial with an angiographic endpoint, late loss after six months was higher in titanium stents than in zotarolimus-eluting stents<sup>9</sup>.

The multicentre trial published in this journal represents an important addition to our knowledge, providing evidence that titanium stents show clinical results comparable to second generation drug-eluting stents (DES) during a follow-up of 12 months, at least in patients with acute coronary syndromes<sup>19</sup>.

## Article see page 306

This trial has admittedly been flawed by some methodological inconsistencies including protocol changes, relatively small number of patients, restricted stent length used, non-standardised drug treatment during percutaneous coronary interventions (PCI) and in the follow-up period, especially, the length of double antiplatelet

therapy. Nonetheless, it represents an important step in the clinical evaluation of this stent.

The number of trials conducted so far does not suffice to conclude that the Titan stent does have the same safety and efficacy as second generation DES. There are no long-term angiographic results available. Nevertheless, its performance has been encouraging and it might represent a good alternative to DES, because it does not fall into the category that is associated with the need for DAPT.

Further research is needed to define the definite role of this stent in clinical practice and to compare its long-term clinical and angiographic performance with newer generation DES.

## References

1. Windecker S, Mayer I, De Pasquale G, Maier W, Dirsch O, De Groot P, Wu YP, Noll G, Leskosek B, Meier B, Hess OM; Working Group on Novel Surface Coating of Biomedical Devices (SCOL). Stent coating with titanium-nitride-oxide for reduction of neointimal hyperplasia. *Circulation*. 2001;104:928-33.
2. Windecker S, Simon R, Lins M, Klauss V, Eberli FR, Roffi M, Pedrazzini G, Moccetti T, Wenaweser P, Togni M, Tüller D, Zbinden R, Seiler C, Mehilli J, Kastrati A, Meier B, Hess OM. Randomized comparison of a titanium-nitride-oxide-coated stent with a stainless steel stent for coronary revascularization: the TiNOX trial. *Circulation*. 2005;111:2617-22.

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**Table 1. Clinical experience with titanium-nitride-oxide-coated stents.**

Study	Number of pts	Control group	Selection of pts	FU time	Primary endpoint	MACE (%)	MI (%)	TLR (%)	ST (%)	Death (%)	Late loss
[2]	92	BMS	All-comers	6 months	Late loss	Titan: 7 BMS: 27	Titan: 0 BMS: 2	Titan: 7 BMS: 23	Titan: 0 BMS: 2	Titan: 0 BMS: 2	Titan: 0.55 BMS: 0.9 $p=0.03$
[9]	302	ZES	All-comers	6 months	Late loss	Titan: 21.1 ZES: 18.0	Titan: 5.3 ZES: 6.7	Titan: 17.8 ZES: 13.3	Titan: 0.7 ZES: 0	Titan: 0.7 ZES: 0.7	Titan: 0.64 ZES: 0.47 Titan: inferior
[6]	92	BMS	All-comers	5 years	Clinical MACE	Titan: 16 BMS: 39 $p=0.03$	Titan: 2 BMS: 7	Titan: 9 BMS: 25	Titan: 0 BMS: 2	Titan: 5 BMS: 9	
[10]	405	PES	All-comers	1 year	Clinical MACE	Titan: 10.9 PES: 13.7 $p=ns$	Titan: 4.5 PES: 10.3	Titan: 5.0 PES: 4.9	Titan: 0 PES: 3.4	Titan: 0.5 PES: 2.5	
[8]	405	PES	All-comers	3 years	Clinical MACE	Titan: 13.9 PES: 23.5 $p=0.006$	Titan: 7.5 PES: 19.1	Titan: 5.5 PES: 9.3	Titan: 0 PES: 7.4	Titan: 1.0 PES: 3.4	
[4]	405	PES	All-comers	5 years	Clinical MACE	Titan: 16.9 PES: 26 $p=0.03$	Titan: 9.5 PES: 20.6	Titan: 6.0 PES: 10.3	Titan: 0 PES: 7.8	Titan: 2.0 PES: 4.4	
[11]	425	PES	Myocardial infarction	1 year	Clinical MACE	Titan: 10.3 PES: 12.8 $p=ns$	Titan: 4.2 PES: 8.1	Titan: 9.3 PES: 7.1	Titan: 0.9 PES: 4.3	Titan: 2.3 PES: 2.8	
[7]	425	PES	Myocardial infarction	2 years	Clinical MACE	Titan: 11.2 PES: 21.8 $p=0.004$	Titan: 5.1 PES: 15.6	Titan: 9.3 PES: 10.0	Titan: 0.5 PES: 6.2	Titan: 0.9 PES: 4.7	
[5]	1774	PES	All-comers	1 year	Clinical MACE	Titan: 8.9 PES: 12.6 $p=0.02$	Titan: 2.7 PES: 5.6				
[12]	1607	PES SES	All-comers	3 years	Clinical MACE	Titan: 20 SES: 19 PES: 22 $p=ns$	Titan: 3 SES: 4.4 PES: 4.8	Titan: 7 SES: 6.9 PES: 7.7	Titan: 1 SES: 1.9 PES: 1.5	Titan: 8 SES: 8.2 PES: 9.8	
[13]	356	no	All-comers	1 year	Clinical MACE	7.2	1.5	5.1	0.3	1.2	
[14]	296	no	All-comers	6 months	Clinical MACE	6.3	0.7	5.4	0.7	0.7	
[15]	193	no	All-comers	9 months	Clinical MACE	10.4	4.1	8.3	0	0	
[16]	100	no	All-comers	6 months	Clinical MACE	6	0	6	0	0	
[17]	156	no	Diabetic	6 months	Clinical MACE	10.3	1.3	7.1	0	1.9	
[18]	311	no	Small vessels	6 months	Clinical MACE	6.9	2.1	4.2	0.3	0.7	
[19]	827	EES	ACS	1 year	Clinical MACE	Titan: 9.6 EES: 9.0 $p=ns$	Titan: 2.2 EES: 5.9	Titan: 6.5 EES: 4.9	Titan: 0.7 EES: 2.2	Titan: 1.9 EES: 1.0	

BMS: bare metal stent; EES: everolimus-eluting stent; MACE: major adverse cardiac event; MI: myocardial infarction; PES: paclitaxel-eluting stent; SES: sirolimus-eluting stent; ST: stent thrombosis; TLR: target lesion revascularisation; ZES: zotarolimus-eluting stent

3. Lehtinen T, Airaksinen KE, Ylitalo A, Karjalainen PP. Stent strut coverage of titanium-nitride-oxide coated stent compared to paclitaxel-eluting stent in acute myocardial infarction: TITAX-OCT study. *Int J Cardiovasc Imaging*. 2012 Feb 24. [Epub ahead of print].

4. Karjalainen PP, Ylitalo A, Airaksinen JK, Nammas W. Five-year clinical outcome of titanium-nitride-oxide-coated bioactive stent implantation in a real-world population: a comparison with

paclitaxel-eluting stents: the PORI registry. *J Interv Cardiol*. 2011;24:1-8.

5. Karjalainen PP, Biancari F, Ylitalo A, Raeber L, Billinger M, Hess O, Airaksinen KE. Pooled analysis of trials comparing titanium-nitride-oxide-coated stents with paclitaxel-eluting stents in patients undergoing coronary stenting. *J Invasive Cardiol*. 2010;22:322-6.

6. Moschovitis A, Simon R, Seidenstücker A, Klauss V, Baylacher M, Lüscher TF, Moccetti T, Windecker S, Meier B, Hess OM. Randomised comparison of titanium-nitride-oxide coated stents with bare metal stents: five year follow-up of the TiNOX trial. *EuroIntervention*. 2010;6:63-8.
7. Karjalainen PP, Ylitalo A, Niemelä M, Kervinen K, Mäkikallio T, Pietilä M, Sia J, Tuomainen P, Nyman K, Airaksinen KE. Two-year follow-up after percutaneous coronary intervention with titanium-nitride-oxide-coated stents versus paclitaxel-eluting stents in acute myocardial infarction. *Ann Med*. 2009;41:599-607.
8. Karjalainen PP, Annala AP, Ylitalo A, Vahlberg T, Airaksinen KE. Long-term clinical outcome with titanium-nitride-oxide-coated stents and paclitaxel-eluting stents for coronary revascularization in an unselected population. *Int J Cardiol*. 2010;144:42-6.
9. Pilgrim T, Räber L, Limacher A, Löffel L, Wenaweser P, Cook S, Stauffer JC, Togni M, Vogel R, Garachemani A, Moschovitis A, Khattab AA, Seiler C, Meier B, Jüni P, Windecker S. Comparison of titanium-nitride-oxide-coated stents with zotarolimus-eluting stents for coronary revascularization a randomized controlled trial. *JACC Cardiovasc Interv*. 2011; 4: 672-82.
10. Karjalainen PP, Ylitalo A, Airaksinen JK. Titanium and nitride oxide-coated stents and paclitaxel-eluting stents for coronary revascularization in an unselected population. *J Invasive Cardiol*. 2006;18:462-8.
11. Karjalainen PP, Ylitalo A, Niemelä M, Kervinen K, Mäkikallio T, Pietilä M, Sia J, Tuomainen P, Nyman K, Airaksinen KE. Titanium-nitride-oxide coated stents versus paclitaxel-eluting stents in acute myocardial infarction: a 12-months follow-up report from the TITAX AMI trial. *EuroIntervention*. 2008; 4:234-41.
12. Limacher A, Räber L, Laube E, Lauterburg A, Löttscher S, Hess N, Moschovitis A, Baldinger SH, Wenaweser P, Meier B, Hess OM, Jüni P. Clinical long-term outcome after implantation of titanium nitride-oxide coated stents compared with paclitaxel- or sirolimus-eluting stents: propensity-score matched analysis. *EuroIntervention*. 2012;7:1043-50.
13. Angioi M, Barragan P, Cattani S, Collet F, Dupouy P, Durand P, Fajadet J, Finet G, Gerardin B, Gommeaux A, Karsenty B, Loubeyre C, Meyer P, Morice MC, Moulichon M<sup>É</sup>, Sayah S, Silvestri M, Tabone X, Untersee H, Wittenberg O, Lablanche JM. French Ministry of Health prospective multicentre study using bioactive stents coated with titanium nitride oxide: the EVIDENCE registry. *Arch Cardiovasc Dis*. 2012;105:60-7.
14. Mosseri M, Miller H, Tamari I, Plich M, Hasin Y, Brizines M, Frimerman A, Jefary J, Guetta V, Solomon M, Lotan C. The Titanium-NO Stent: results of a multicenter registry. *EuroIntervention*. 2006;2:192-6.
15. Karjalainen PP, Ylitalo AS, Juhani Airaksinen KE. Real world experience with the TITAN(R) stent: a 9-month follow-up report from The Titan PORI Registry. *EuroIntervention*. 2006;2: 187-91.
16. Mosseri M, Tamari I, Plich M, Hasin Y, Brizines M, Frimerman A, Miller H, Jafari J, Guetta V, Solomon M, Lotan C. Short- and long-term outcomes of the titanium-NO stent registry. *Cardiovasc Revasc Med*. 2005;6:2-6.
17. Valdés Chavarri M, Bethencourt A, Pinar E, Gomez A, Portales JF, Pomar F, Calvo I, López-Minguez J, Valdesuso R, Moreu J, Martínez A, Namas W. Titanium-nitride-oxide-coated stents multicenter registry in diabetic patients: the TIBET registry. *Heart Vessels*. 2012;27:151-8.
18. Valdesuso R, Karjalainen P, García J, Díaz J, Portales JF, Masotti M, Picó F, Serra A, Burgos JM, Insa L, Mauri F, Collado JR, Namas W. The EXTREME registry: titanium-nitride-oxide coated stents in small coronary arteries. *Catheter Cardiovasc Interv*. 2010;76:281-7.
19. Karjalainen PP, Niemelä M, Airaksinen JKE, Rivero-Crespo F, Romppanen H, Sia J, Lalmand J, de Bruyne B, DeBelder A, Carlier M, Namas W, Ylitalo A, Hess OM on behalf of the BACE-ACS study Investigators. A prospective randomised comparison of titanium-nitride-oxide-coated bioactive stents with everolimus-eluting stents in acute coronary syndrome: the BASE-ACS trial. *EuroIntervention* 2012;8:306-315.