APERTO REGISTRY

First large-scale clinical data confirm long-term effectiveness and safety of the Aperto® drug-coated balloon for angioplasty of dysfunctional vascular access

Significantly reduced restenosis and revascularisation of AV fistula stenosis could improve clinical outcomes and treatment cost effectiveness

Principal Investigator:
Matteo Tozzi MD

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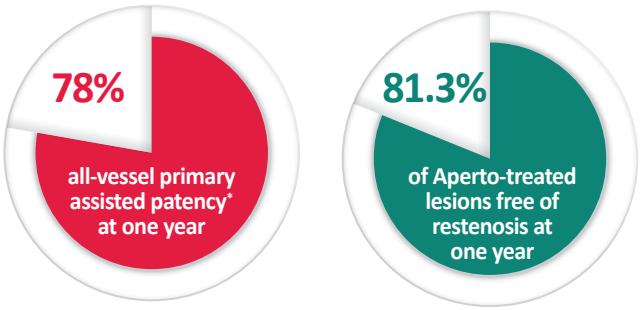
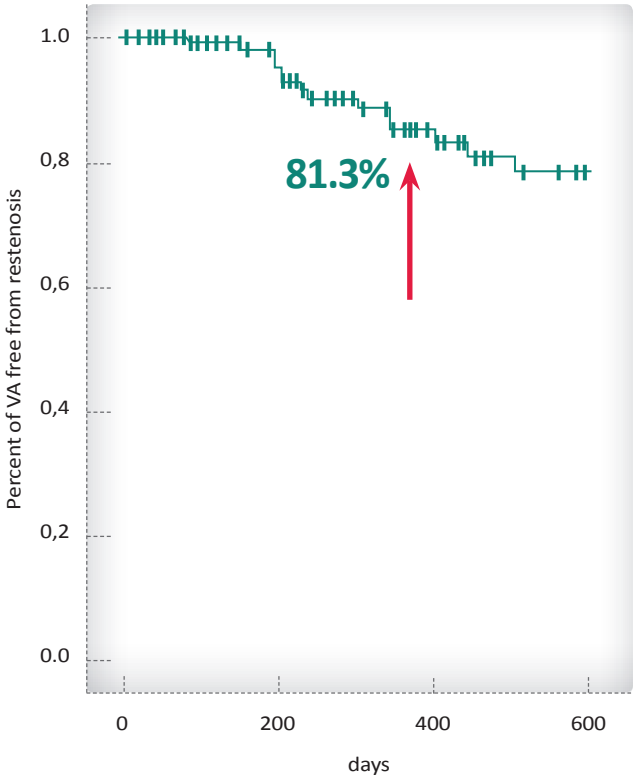
APERTO® Registry

Key results

The first long-term results with Aperto in a large population of patients with AV fistula from the APERTO Italian registry[1] were presented by the primary investigator Prof. Matteo Tozzi at the 2017 Charing Cross Symposium in London in April 2017.[2]
The results confirm the excellent effectiveness and safety profile of Aperto from a total of 150 patients and 176 stenosis treated under conditions of actual clinical practice.

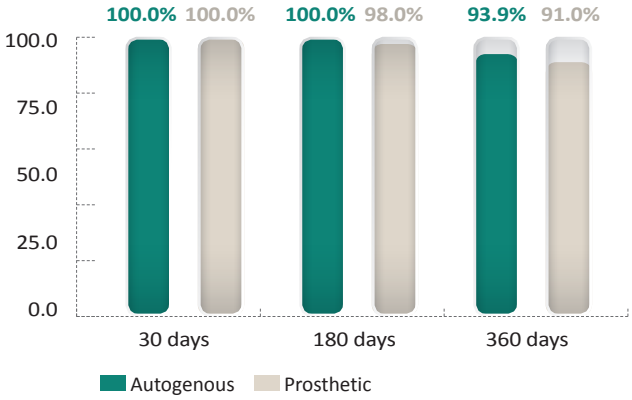


Kaplan-Meyer plot of rates of freedom from restenosis after Aperto angioplasty



Restenosis rates at 360 days were <10% for each access type, whether prosthetic (9.0%) or autogenous (6.1%)

Freedom from restenosis



The procedural and follow-up safety associated with Aperto was confirmed:
- Procedural success rates were 100%
- Nine cases of acute thrombosis (6%) and 12 cases of residual astenosis (8%) were recorded
- No permanent graft failure was recorded at 12 months

"Aperto is an appealing alternative to plain balloon angioplasty, reducing the yearly number of retreatment, both angioplasty and surgical interventions"

"The Aperto design reduces the strain on the access vessels and saves them for potentially important procedures later"
Matteo Tozzi

APERTO Italian registry results in context

The results from the registry validate the superiority of drug-coated balloons over angioplasty with conventional or cutting balloons for vascular access stenosis.
Compared with other technologies, the one-year 78% rates of primary patency with Aperto are notably higher than rates with alternative drug-coated balloon in patients with AV fistula:

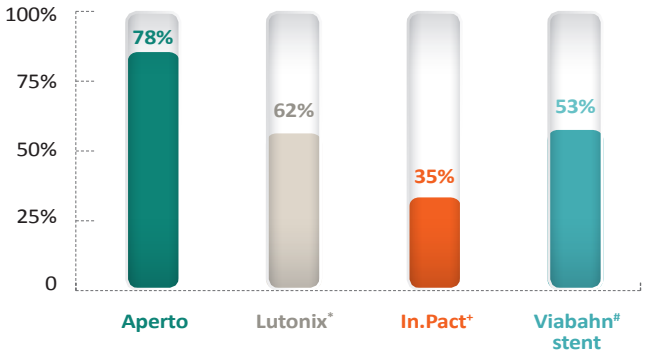
- The LUTONIX AV Clinical Trial with the Lutonix drug-coated balloon reported 62% at 8 months,[3] meaning rates at 12 months are expect-ed to be even lower.

* *Primary assisted patency was defined as absence of restenosis and revascularization*

» APERTO® Registry

- A small-scale study with the In.Pact balloon reported 35% patency rates (n=20) at 12 months.[4]
- The Aperto patency rates also compare favourably with the rates at 6 months with the Viabahn stent graft in the REVISE study.[5]

» Patency rates at 12 months



* 260 days follow-up
\+ n=20
\# 6 months follow-up

Note: *comparisons are not perfect since the trials vary in design, patient populations and follow-up. Specifically designed head-to-head comparisons are not available at present.*

Aperto is the only drug-coated balloon with strong positive data in patients with prostethic vascular access.

"Aperto is the first drug-coated balloon that compares favourably with stent graft in patients with AV fistula, supported by large-scale data"
Matteo Tozzi

The APERTO Italian registry results go some way towards filling the lack of "clear evidence-based data" on drug-coated balloons noted by the European Society of Cardiology experts in their Positioning Document in 2004.[6]
Long-term data in large patient groups will be needed to confirm the potential for improved effectiveness and safety of Aperto in AVF patients compared with other technologies.

"...not all drug-coated balloons are created equal" [6]
ESC Expert Group

» Methods

Predilatation angioplasty was performed routinely with cutting balloons or with focal-force angioplasty balloons. The Aperto OTW® balloon was inflated for 120/180 seconds at 15 atm. Postoperatively, all patients started anticoagulant therapy using enoxaparin sodium 2,000 IU once daily plus antiplatelet therapy for 12 days after the procedure.
Average follow-up was 300 days ranging from 180 to 886 days (2.4 years). The performance was evaluated on the risk of primary assisted patency, critical restenosis target lesions (primary end point) and on rates of non critical restenosis (secondary end point).

Aperto registry patients and procedures	
150 patients and 176 stenoses treated	
Baseline characteristics	
Age ±SD	67 ±12
Male sex	93 (62%)
CVD	61%
Hypertension	38%
Diabetes	35%
Smoking	23%
IHD	35%
COPD	17%
Procedural details	
Autogenous vascular access	73 (41%) ← **6.1%** restenosis at 12 months
Venous side:	17 (23%)
Perianastomotic:	56 (77%)
Prosthetic vascular access	103 (59%) ← **9.0%** restenosis at 12 months
Venous anasthomosis:	41 (40%)
Venous outflow:	27(26%)
Prosthesis:	23 (22%)
Arterial anastomosis:	12 (12%)

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» About the APERTO Italian registry

The APERTO Italian registry was designed to demonstrate the efficacy and safety of Aperto in a real – world scenario. It is a collaborative effort by four centres in Italy. For the current report, 150 patients and 176 stenoses were treated with Aperto for the indications of asymptomatic ≥50% stenosis, uncomplicated symptomatic stenosis causing malfunctions of the vascular access, or symptomatic stenosis complicated by thrombosis. The APERTO Italian registry is continuing to enrol and follow patients, with an interim goal of 200 patients at the four centres. The longest follow-up at present is 2.4 years.

» About Aperto

Aperto is the first drug-coated balloon dedicated to treat AV fistula shunt stenosis.
Aperto is designed to solve unmet clinical needs in treatment of haemodialysis access stenosis and recanalisation of arteriovenous shunt grafts. The high-pressure balloon design reduces the need for pre-dilatation and drives long-term patency.
The unique Safepax delayed-delivery coating incorporates nanocrystalline translucent 0.1 µm paclitaxel particles for improved drug uptake and minimised risk of micro-embolisation.
The use of ammonium salt as excipient renders Safepax uniquely resistant to mechanical influence: in wash-off studies drug losses are consistently <0.3%, which guarantees safe working conditions for physicians and predictable drug delivery to the target lesion site.
By reducing the risk of re-intervention Aperto has the potential to improve patients' quality of life and control healthcare costs.

» About Cardionovum

CARDIONOVUM GmbH is a leading company in innovative coronary and peripheral drug coating technologies improving clinical outcomes and quality of life. Legflow® drug coated balloon for peripheral artery disease treatment as well as Aperto® Drug coated balloon for haemodialysis shunt treatment and Restore® for coronary artery disease treatment are the latest innovations with highest patient safety guarantee.

» References

[1] Ierardi AM, Franchin M, Fontana F, Piffaretti G, Duka E, Tonolini M, *et al.* Usefulness of paclitaxel-releasing high-pressure balloon associated with cutting balloon angioplasty for treatment of outflow stenoses of failing hemodialysis arteriovenous shunts. *La radiologia medica* 2017;122:69–76.

[2] Tozzi, M. Drug- eluting balloons in AV fistulas: APERTO Italian Registry. Presented at the 2017 Charing Cross Symposium, London UK, April 2017.

[3] Trerotola S. Eight-month data from the Lutonix AV trial.Presented at the 2017 Charing Cross Symposium, London UK, April 2017.

[4] Kitrou PM, Katsanos K, Spiliopoulos S, Karnabatidis D, Siablis D. Drug-eluting versus plain balloon angioplasty for the treatment of failing dialysis access: final results and cost-effectiveness analysis from a prospective randomized controlled trial (NCT01174472). *Eur J Radiol* 2015;84:418–423.

[5] Vesely T, DaVanzo W, Behrend T, Dwyer A, Aruny J. Balloon angioplasty versus Viabahn stent graft for treatment of failing or thrombosed prosthetic hemodialysis grafts. *J Vasc Surg* 2016;64:1400–1410.e1.

[6] Cortese B, Granada JF, Scheller B, Schneider PA, Tepe G, Scheinert D, et al. Drug-coated balloon treatment for lower extremity vascular disease intervention: an international positioning document. *Eur Heart J* 2016;37:1096–103.

[7] CardioNovum: Wash-off effect studies of ammonium salt solution/PTX coating. Study report, April 2017; data on file

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