BATTLE

A RCT comparing bare metal stent vs. Paclitaxel polymer free eluting stent: 2-year outcomes

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Disclosures

Y. Gouëffic reports:

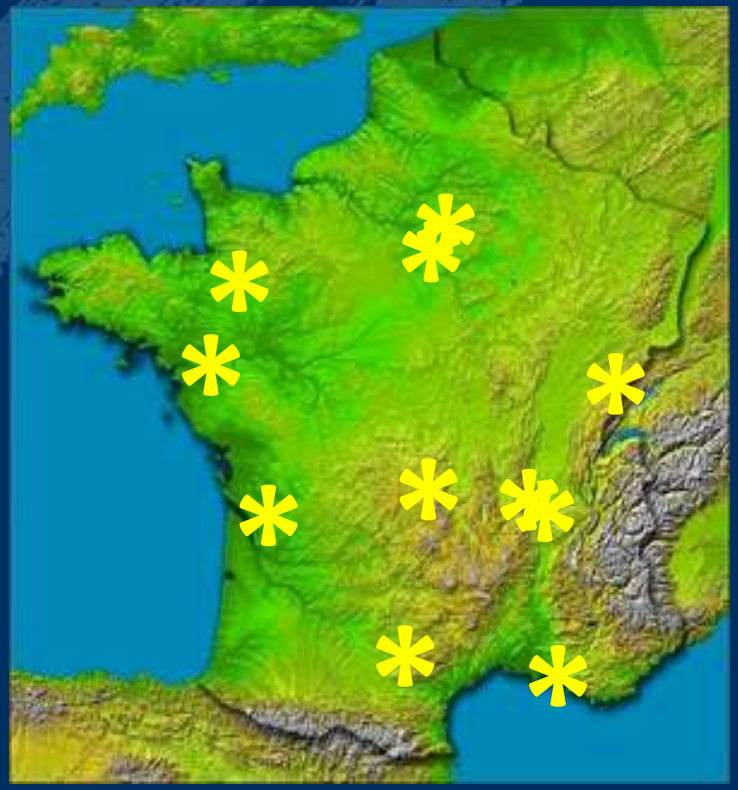
- **Research funding** from Bard, Medtronic, Terumo, WL Gore

- **Personal fees and grants** from Abbott, Bard, Biotronik, Boston Scientic, Medtronic, Terumo, Vygon, WL Gore (medical advisory board, educational course, speaking)

BATTLE trial

French multicentric randomized clinical trial comparing MISAGO® vs. ZILVER® PTX® for the treatment of intermediate femoropopliteal lesions

(ClinicalTrials.gov number, NCT02004951)



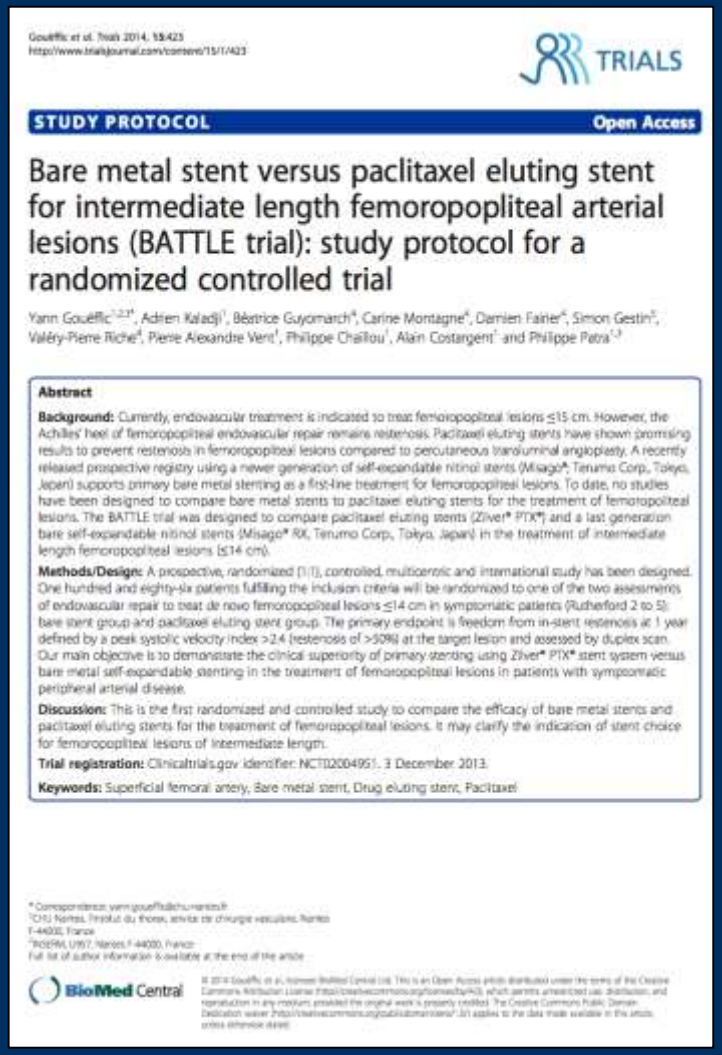
10 centers: Clinique d'Antony (Jean-Marc PERNES); CHU de Besançon (Simon RINCKENBACH); CHU de Bordeaux (Eric DUCASSE) ; CHU de Clermont Ferrand (Eugenio ROSSET) ; AP-HP, Hôpital Henri Mondor (Pascal DESGRANGES) ; CHU de Lyon (Patrick FEUGIER) ; CH de Bourgouin (Patrick LERMUSIAUX); Clinique Ollioules (Philippe COMMEAU) ; CHU de Rennes (Alain CARDON) ; Clinique Pasteur (Antoine SAUGUET); CHU de Nantes (Yann GOUËFFIC)

Gouëffic, JACC Intrv, in press

BATTLE trial protocol

Sponsor Nantes University Hospital - *BATTLE ClinicalTrials.gov number, NCT02004951*

- **Investigator initiated study**
- **RCT and multicenter (1:1)**
- **Rigorous data collection process, independent**
- **Adjudication by:**
  - *Duplex ultrasound core laboratory*
  - *Clinical events committee*
  - *Data safety monitoring board*
- **Follow-up includes**
  - 1, 6, 12, and 24-month clinical assessment
  - 1, 12 and 24-month stent x-ray
- **Monitoring with 100% source data verification**



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TRIALS

STUDY PROTOCOL Open Access

Bare metal stent versus paclitaxel eluting stent for intermediate length femoropopliteal arterial lesions (BATTLE trial): study protocol for a randomized controlled trial

Yann Gouëffic[1,2,3*], Adrien Kaladji[1], Béatrice Guyomarch[4], Carine Montagne[4], Damien Fairier[4], Simon Gestin[1], Valéry-Pierre Riche[4], Pierre Alexandre Vent[1], Philippe Chaillou[1], Alain Costargent[1] and Philippe Patra[1,3]

Abstract

Background: Currently, endovascular treatment is indicated to treat femoropopliteal lesions ≤15 cm. However, the Achilles' heel of femoropopliteal endovascular repair remains restenosis. Paclitaxel eluting stents have shown promising results to prevent restenosis in femoropopliteal lesions compared to percutaneous transluminal angioplasty. A recently released prospective registry using a newer generation of self-expandable nitinol stents (Misago®, Terumo Corp., Tokyo, Japan) supports primary bare metal stenting as a first-line treatment for femoropopliteal lesions. To date, no studies have been designed to compare bare metal stents to paclitaxel eluting stents for the treatment of femoropopliteal lesions. The BATTLE trial was designed to compare paclitaxel eluting stents (Zilver® PTX®) and a last generation bare self-expandable nitinol stents (Misago® RX, Terumo Corp., Tokyo, Japan) in the treatment of intermediate length femoropopliteal lesions (≤14 cm).

Methods/Design: A prospective, randomized (1:1), controlled, multicentric and international study has been designed. One hundred and eighty-six patients fulfilling the inclusion criteria will be randomized to one of the two assessments of endovascular repair to treat de novo femoropopliteal lesions ≤14 cm in symptomatic patients (Rutherford 2 to 5): bare stent group and paclitaxel eluting stent group. The primary endpoint is freedom from in-stent restenosis at 1 year defined by a peak systolic velocity index >2.4 (restenosis of >50%) at the target lesion and assessed by duplex scan. Our main objective is to demonstrate the clinical superiority of primary stenting using Zilver® PTX® stent system versus bare metal self-expandable stenting in the treatment of femoropopliteal lesions in patients with symptomatic peripheral arterial disease.

Discussion: This is the first randomized and controlled study to compare the efficacy of bare metal stents and paclitaxel eluting stents for the treatment of femoropopliteal lesions. It may clarify the indication of stent choice for femoropopliteal lesions of intermediate length.

Trial registration: Clinicaltrials.gov identifier: NCT02004951. 3 December 2013.

Keywords: Superficial femoral artery, Bare metal stent, Drug eluting stent, Paclitaxel

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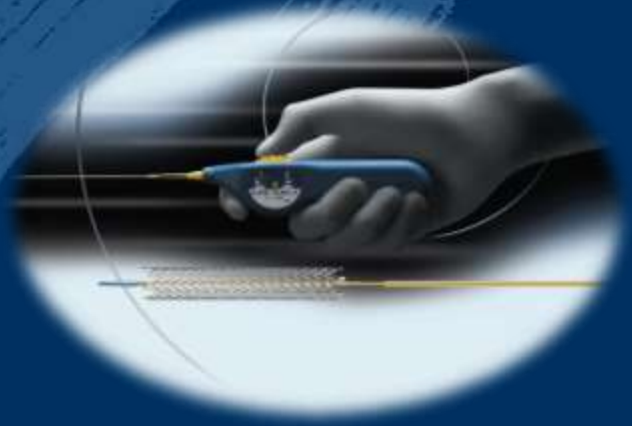
Gouëffic, Trials, 2014

Study devices

MISAGO®



- Bare nitinol stent
- Moderate radial force
- RX system

ZILVER® PTX®

- Self expendable nitinol stent with a polymer-free paclitaxel coating
- Over-the-wire system

BATTLE objective

To demonstrate the clinical superiority of primary stenting using Zilver® PTX® stent system versus bare metal self-expandable stenting (MISAGO®, TERUMO) in the treatment of intermediate length femoropopliteal lesions in patients with symptomatic peripheral arterial disease (Rutherford 2-5).

BATTLE primary endpoint

Freedom from in-stent restenosis @ 1 year

Defined by restenosis of >50% and by a peak systolic velocity index >2.4 at the target lesion. Assessment by an independent core laboratory (thromboses were excluded)

*We calculated that **a sample of 186 patients** (10% dropout included) , randomly assigned in a 1:1 ratio, with an 80% power at a 2 sided alpha level of 0.05.*

Key eligible criteria

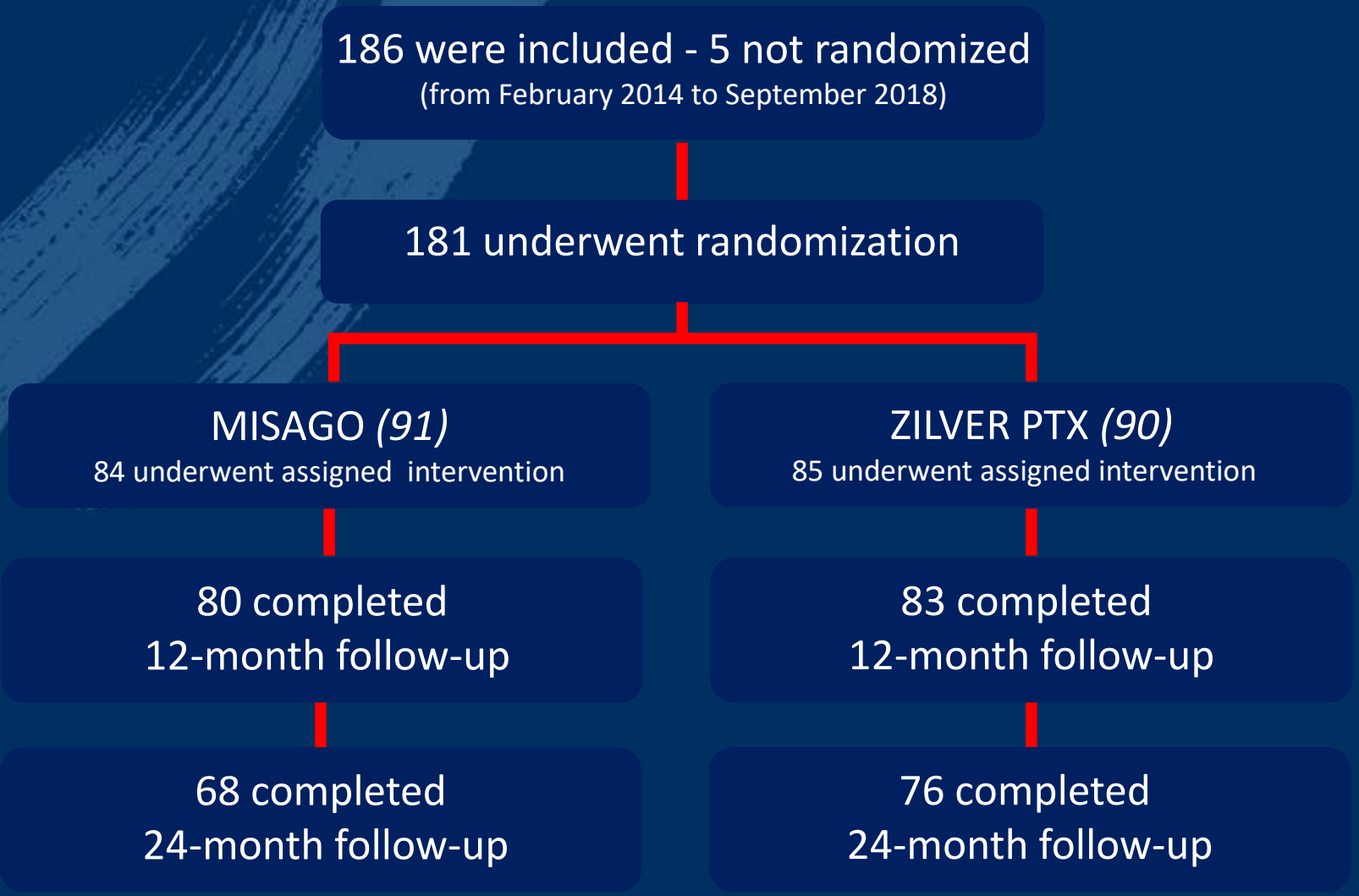
Main inclusion criteria

- Rutherford stages 2-5
- De novo atherosclerotic lesions (stenosis and/or occlusion) of the SFA, the proximal popliteal artery (P1), or both
- Target lesion has a length ≥2-cm and ≤14-cm
- RVD 4 to 7-mm

Main exclusion criteria

- Asymptomatic lesion
- Restenosis
- No atheromatous disease

BATTLE flow chart



**ITTm: modified intention-to-treat analysis on the primary endpoint was performed to include only patients who had undergone randomization and met the major inclusion criteria.*

***6 patients were lost of FU at 1-year.*

Baseline clinical characterisctics

	MISAGO® (n= 85)	ZILVER® PTX® (n=86)
Age (y)	68±12	71±12
Sex ♂, n (%)	62 (73)	62 (72)
Smoking, n (%)	28 (33)	20 (23)
Hypertension, n (%)	52 (61)	59 (69)
Diabetes mellitus, n (%)	22 (26)	41 (48)
Dyslipidemia, n (%)	61 (73)	55 (65)
Renal failure, n (%)	6 (7)	8 (9)
CAD, n (%)	34 (40)	27 (31)
Statines, n (%)	66 (78)	67 (78)
Antiplatelet drug, n (%)	78 (92)	80 (93)
ACE inhibitors, n (%)	32(38)	22 (26)

Intermittent claudication:

MISAGO®: 82% / ZILVER® PTX®: 79%

Baseline lesions characteristics

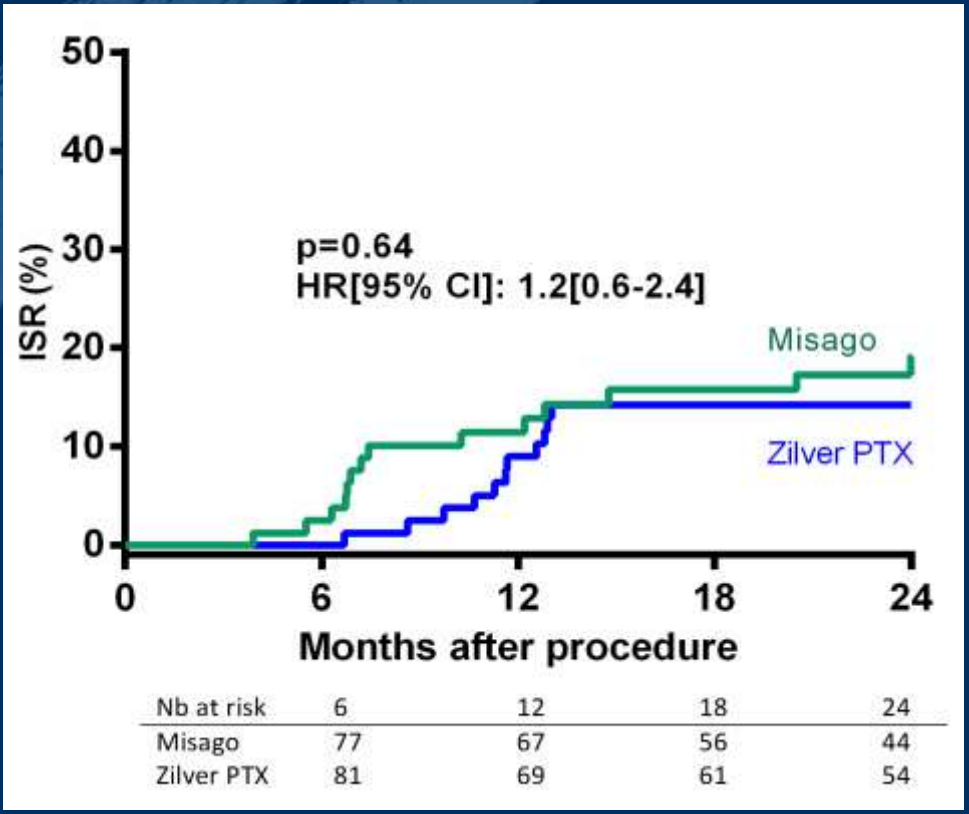
	MISAGO® (n= 85)	ZILVER® PTX® (n=86)
Mean treated lesion length (cm)	7.6 ± 4.1	6.9 ± 3.5
Reference vessel diameter (mm)	5.8 ± 0.5	5.8 ± 0.6
# of patent run-off vessel **1, n (%)** **2 or 3, n(%)**	 13 (15) 72 (85)	 11 (13) 75 (87)

Procedural characteristics

	MISAGO® (n= 85)	ZILVER® PTX® (n=86)	P-value
Pre-dilatation performed, n (%)	70 (83)	69 (80)	0.60
Number of implanted stents, n	102	117	
1, n(%)	68 (80)	57 (66)	0.07
2, n(%)	17 (20)	27 (31)	
3, n(%)	0 (0)	2(2)	
Stents localisation			-
Proximal SFA, n	14	10	
Mid SFA, n	55	56	
Distal SFA, n	44	46	
P1, n	15	11	
Mean stent length (per stent)(mm)	91±40 (40-120)	72±40 (40-100)	-
Mean stent length (per patient)(mm)	90.3±38.1 (40-150)	71.2±22.2 (40-105)	<0.001
Diameter 4/5/6/7/8, n	0/1/75/23/3	1/0/87/27/0	-
Post dilatation performed, n(%)	73 (86)	79 (92)	0.14
Technical success, n(%) [1]	85 (100)	86 (100)	-

Technical success defined as achievement of a final residual diameter stenosis of <30% on the procedural completion angiogram

Freedom from in-stent restenosis* @ 12 months (primary endpoint) *(Kaplan Meier estimates)*



Nb at risk	6	12	18	24
Misago	77	67	56	44
Zilver PTX	81	69	61	54

@ 12 months:

MISAGO®: 85.7%

ZILVER® PTX®: 90.3%

P=0.36

@ 24 months:

MISAGO®: 80.9%

ZILVER® PTX®: 85.8%

P=0.64

*Defined by restenosis of >50% and by a peak systolic velocity index >2.4 at the target lesion. Assessment by an independent core laboratory (thromboses were excluded)

BATTLE trial
Safety outcomes through 2-years *(Kaplan Meier estimates)*

	MISAGO® (n= 85)	ZILVER® PTX® (n=86)	HR [95% CI]	p
MACEs, n (%) [1]	7 (6.4)	1 (1.2)	7.3 [0.9–59.3]	0.06
All-cause Death, n (%)	7 (6.4)	1 (1.2)	7.3 [0.9–59.3]	0.06
Major amputation, n (%)[2]	0	0	-	-
Device- or Procedure-related Death, n (%)	0	0	-	-

1- Major adverse clinical events (MACEs) at 12 post-procedure defined as MACEs including all deaths and major amputation; 2- Limb salvage defined as freedom from major ipsilateral amputations (above the ankle) at 12 months postprocedure

Causes of death

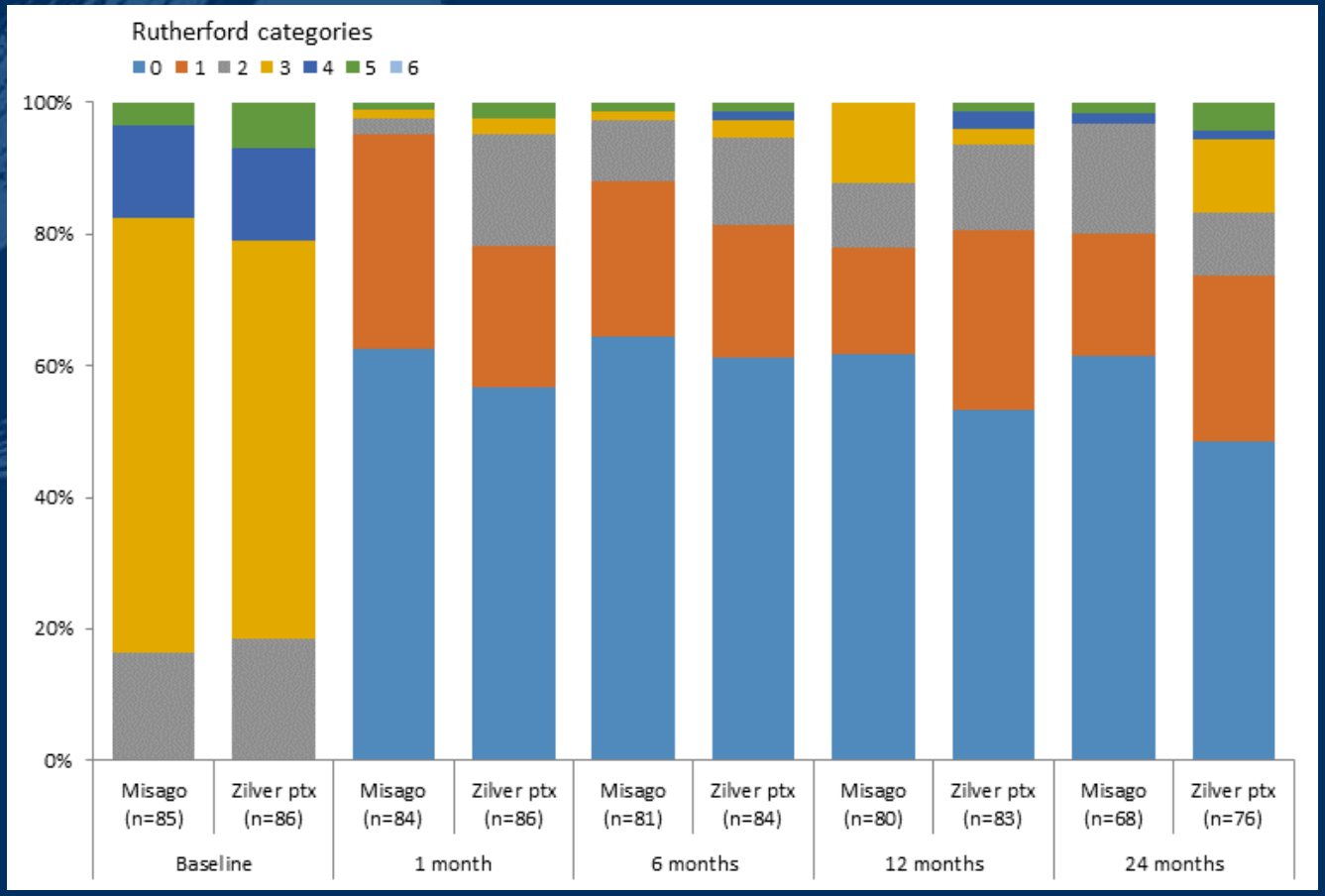
Misago® group (n=7):

- pulmonary cancer (n=3)
- sepsis (n=2)
- trauma (n=1)
- multi-system organ failure (n=1)

Zilver® PTX® group (n=1):

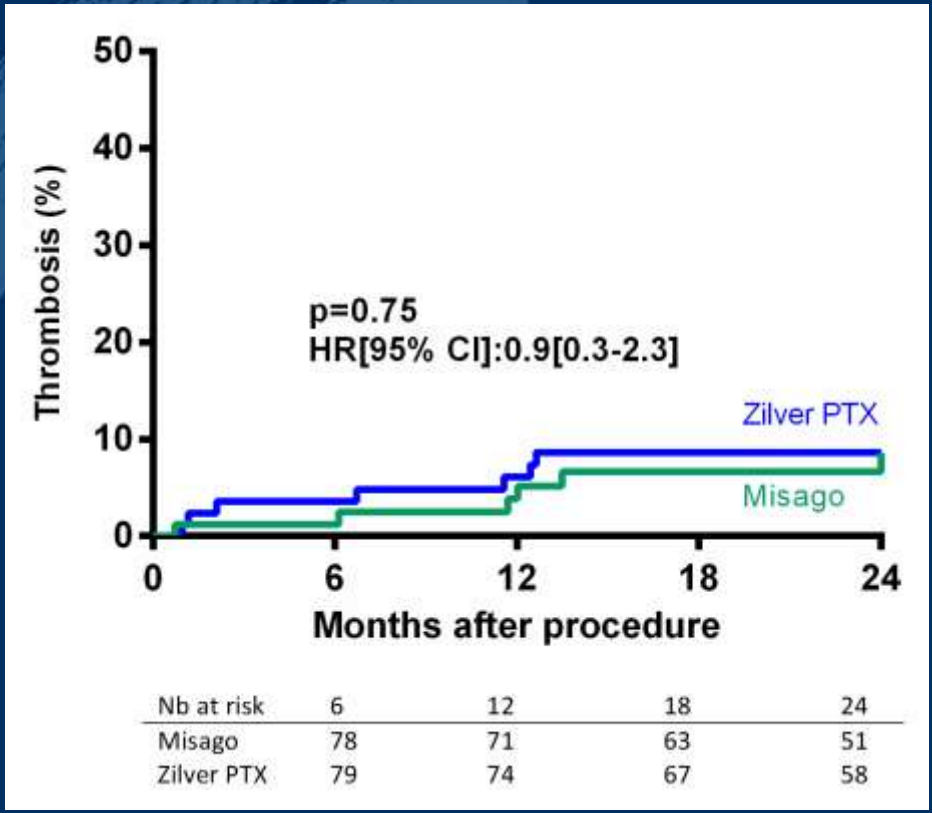
haemorrhagic shock (n=1)

Clinical outcomes



Symptomatology, based on Rutherford status, was improved for both groups at one year but with a difference observed between them at 2 years

In-stent thrombosis *(Kaplan Meier estimates)*



@ 12 months:

MISAGO®: 3.8%

ZILVER® PTX®: 6.1%

P=0.75

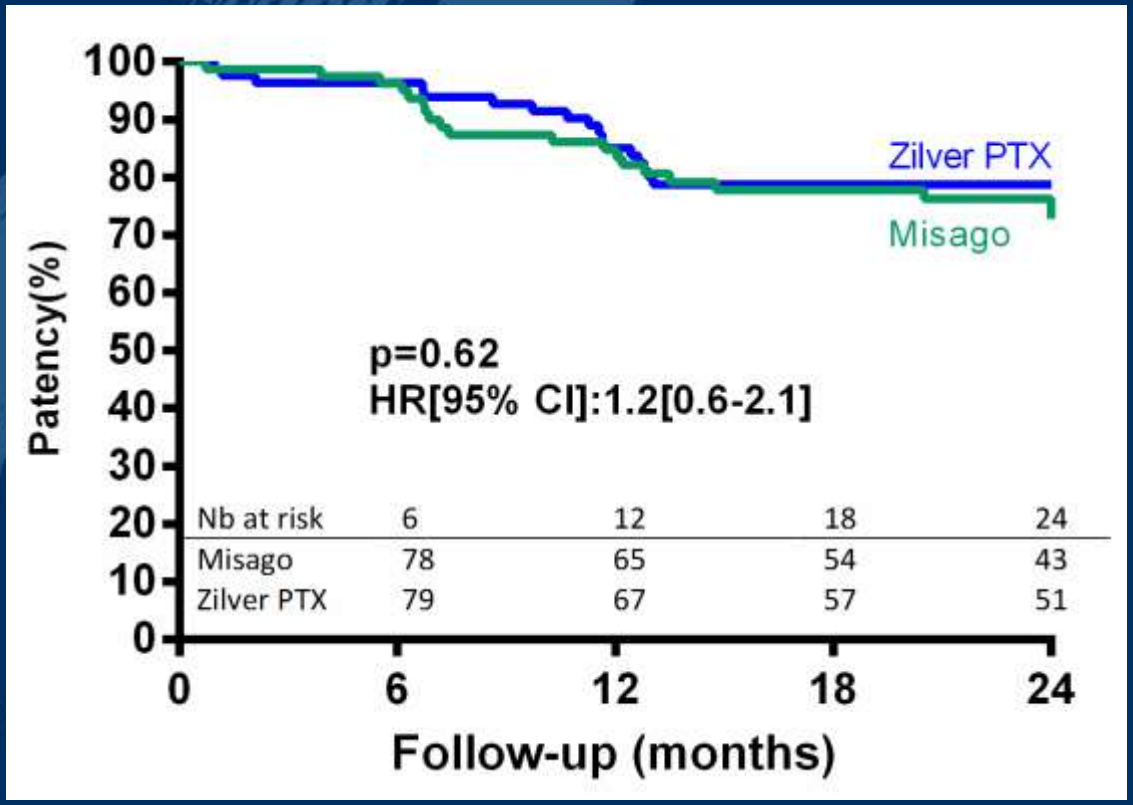
@ 24 months:

MISAGO®: 6.7%

ZILVER® PTX®: 8.6%

P=0.75

Patency* *(Kaplan Meier estimates)*



@ 12 months:

MISAGO®: 84.8%

ZILVER® PTX®: 85.1%

P=0.62

@ 24 months:

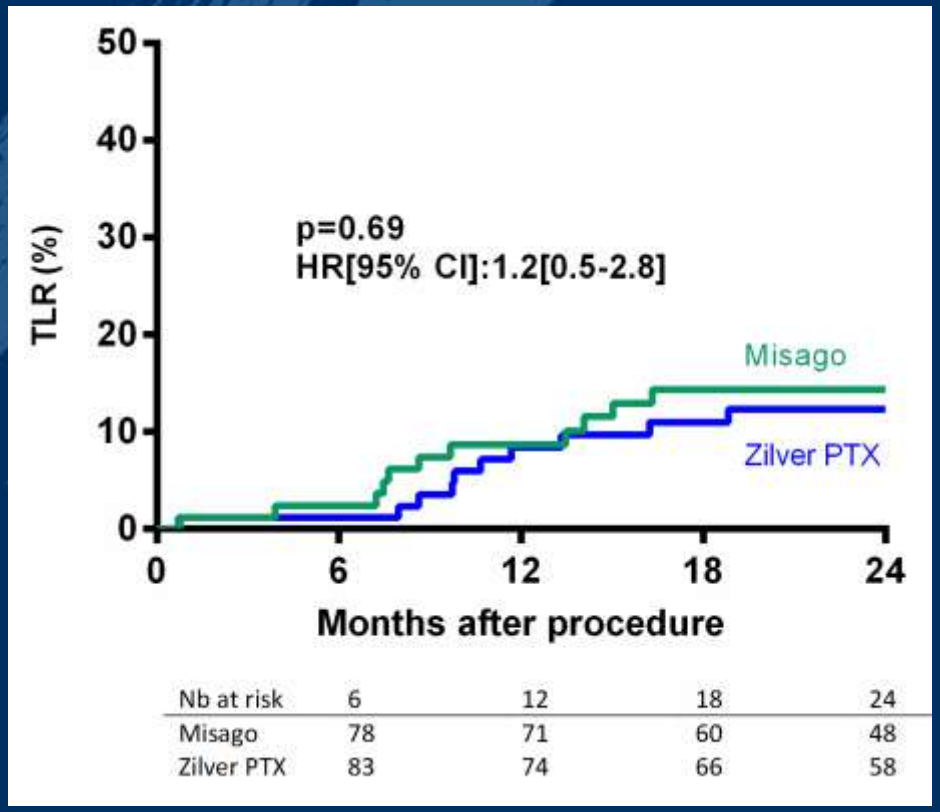
MISAGO®: 74.6%

ZILVER® PTX®: 78.8%

P=0.62

** Primary patency is defined as patency without any percutaneous or surgical intervention in the treated segment or adjacent areas*

Target lesion revascularisation* *(Kaplan estimates)*



@ 12 months:

MISAGO®: 8.7%

ZILVER® PTX®: 8.4%

P=0.69

@ 24 months:

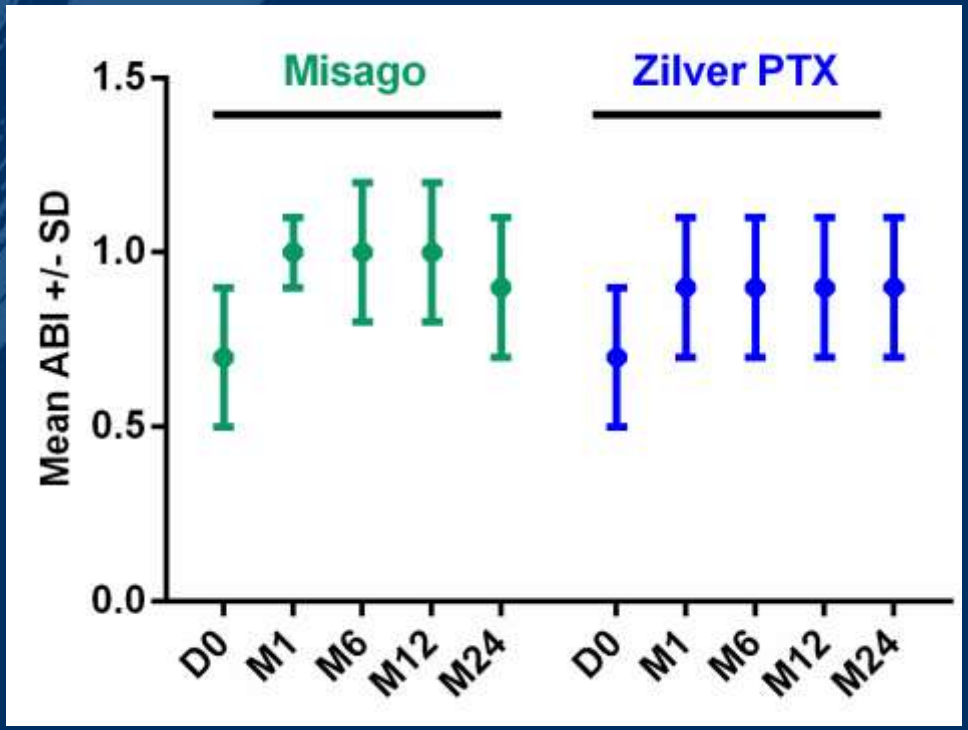
MISAGO®: 14.4%

ZILVER® PTX®: 12.4%

P=0.69

**Target lesion revascularization (TLR) expresses the frequency of the need for repeated procedures (endovascular or surgical) due to a problem arising from the stent (1 cm proximally and distally to include edge phenomena) in surviving patients with preserved limb.*

Hemodynamic outcomes



The resting ABI was significantly improved at one year compared with baseline in both groups (Misago®: 0.71±0.21 versus 0.96±0.19; Zilver® PTX®: 0.68±0.18 versus 0.92±0.19) without any difference between the groups at one year (p=0.33)

Take home message

- In BATTLE trial, Zilver® PTX® (COOK) polymer-free paclitaxel eluting stent failed to show superiority in comparison to MISAGO® (TERUMO), a bare metal stent, in term of ISR @ 1 year.
- Outcomes are sustained at 2-years
- Advantages of drug eluting therapy in comparison to bare metal stent is still required to define the strategy for the treatment of intermediate length femoropopliteal lesions.

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