Vascular Closure Devices Versus Manual Compression After Femoral Artery Access

– the ISAR-CLOSURE Randomized Trial

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Disclosure Statement of Financial Interest

I, Stefanie Schüpke, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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Background

- The role of vascular closure devices (VCD) for the achievement of hemostasis after femoral artery puncture remains controversial

- Increased efficacy, i.e. reduced time to hemostasis and earlier ambulation, has been a consistent finding across different trials of VCDs

- However, meta-analyses suggest an increased risk of vascular complications with VCD compared to manual compression

Koreny et al. JAMA 2004;1:350-357

Background

- Size of most RCTs has generally been modest, permitting evaluation of efficacy but precluding definitive assessment of safety

- Moreover, comparative efficacy studies between devices used in contemporary practice remain a scientific gap

Objectives

- **Primary objective**

  Comparison of 2 hemostasis strategies:

  Vascular closure device (VCD) vs. manual compression

- **Secondary objective**

  Comparison of 2 types of VCD:

  Femoseal vs. Exoseal

… in pts undergoing transfemoral coronary angiography

Hypothesis

In patients undergoing transfemoral coronary angiography, VCD are **non-inferior** to manual compression to terms of vascular access site complications

Design

- Investigator-initiated, randomized, large-scale, multicenter, open-label trial

- Recruitment period: 04/2011 – 05/2014

Study Organisation

Participating Centers:

Deutsches Herzzentrum Munich
Klinikum rechts der Isar, Munich
Krankenhaus der Barmherzigen Brüder, Munich
Klinikum Landkreis Erding

Steering Committee:

Adnan Kastrati (Study Chair)
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Coordinating Center:

ISAResearch Center Munich

Event Adjudication Committee:

Olga Bruskina (Chair)
Gjin Ndrepepa
Andreas Stein

Imaging Core Lab:

Corinna Böttiger

Eligibility Criteria

Major Inclusion Criteria:

Pts undergoing coronary angiography with a 6 French sheath via the common femoral artery
Diameter of common femoral artery of > 5 mm

Major Exclusion Criteria:

Implantation of a VCD within the last 30 days
Symptomatic leg ischemia
Prior TEA or patch plastic of the common femoral artery
Planned invasive diagnostic/interventional procedure in the following 90 days
Heavily calcified vessel
Active bleeding or bleeding diathesis
Severe arterial hypertension (>220/110 mmHg)
Local infection
Autoimmune disease
Allergy to resorbable suture
Pregnancy

Endpoints

- **Primary endpoint:**

  Vascular access site complications at 30 days after randomisation

  i.e. the composite of hematoma ≥ 5 cm, arterio-venous fistula, pseudoaneurysm, access-site related bleeding*, acute ipsilateral leg ischemia, need for vascular surgical or interventional treatment or local infection

- **Secondary endpoints:**

  - Time to hemostasis
  - Repeat manual compression
  - VCD failure

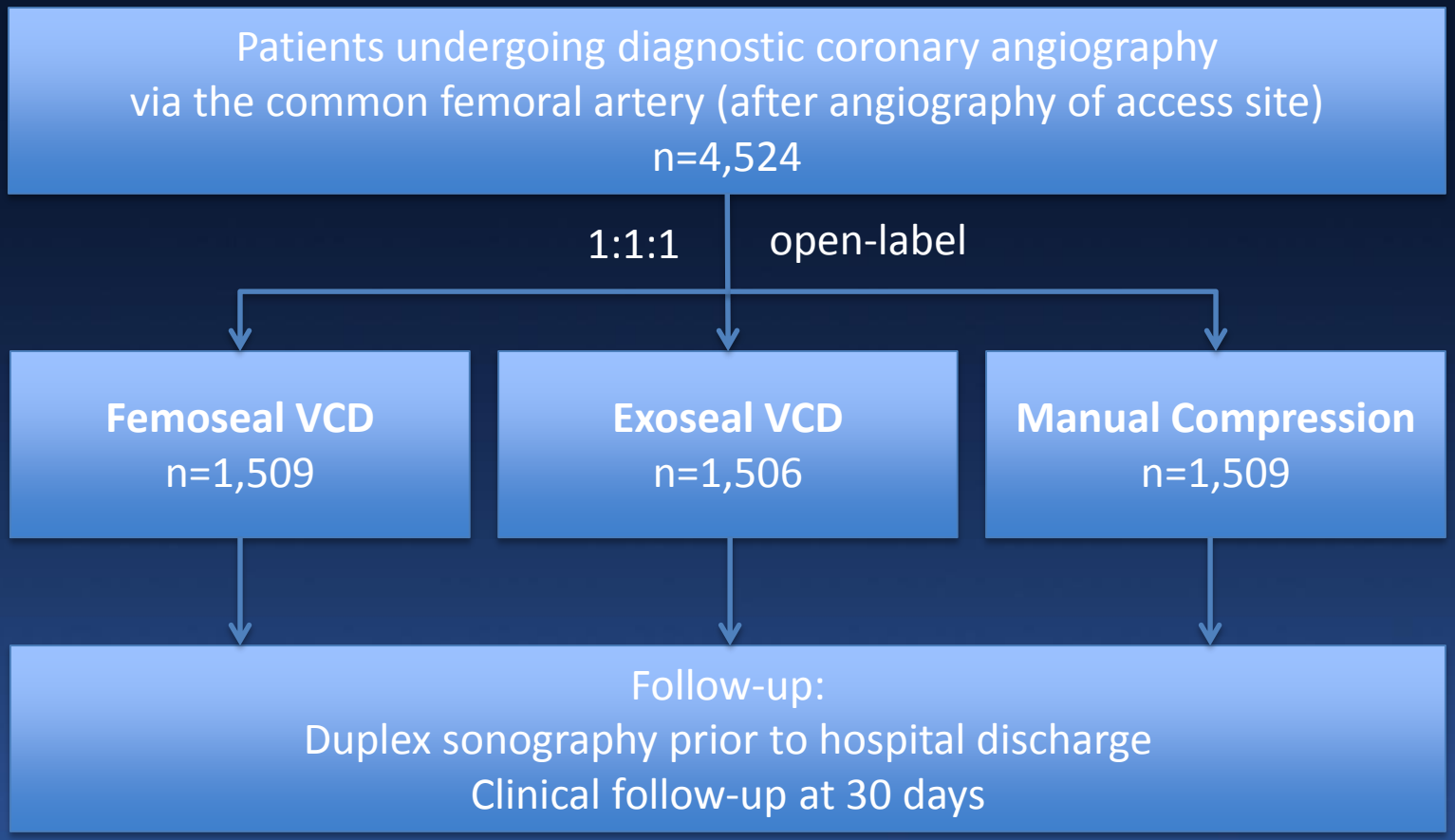
*Adapted from REPLACE-2 criteria:
Hb drop ≥ 3 g/dl with evident bleeding, Hb drop ≥ 4 g/dl with/without evident bleeding or bleeding requiring blood transfusion

Sample Size Calculation

- Assumptions:
  - Incidence of the primary endpoint in the manual compression group: 5%
  - Margin of non-inferiority: 2% (absolute)
  - Power 80%
  - 1-sided α-Level 0.025

→ Enrolment of 4,500 patients required

Study Flow


Patients undergoing diagnostic coronary angiography
via the common femoral artery (after angiography of access site)
n=4,524
1:1:1
open-label
Femoseal VCD
n=1,509
Exoseal VCD
n=1,506
Manual Compression
n=1,509
Follow-up:
Duplex sonography prior to hospital discharge
Clinical follow-up at 30 days

Baseline Characteristics (1/2)

	Vascular Closure Device (n=3015)	Manual Compression (n=1509)
Age, years	67.4 [58.4-74.7]	68.4 [59.5-74.8]
Female	917 (30)	478 (32)
Arterial Hypertension	2599 (86.2)	1319 (87.4)
Hypercholesterolemia	1942 (64)	997 (66)
Diabetes Mellitus	584 (19.4)	321 (21.3)
- Insulin-Requiring	142 (4.7)	65 (4.3)
Family History	944 (31)	471 (31)
Active or Former Smoker	1249 (41)	602 (40)

Baseline Characteristics (2/2)

	Vascular Closure Device (n=3015)	Manual Compression (n=1509)
History of Prior MI	813 (27.0)	393 (26.0)
History of Prior PCI	1785 (59)	882 (58)
History of Prior CABG	255 (8.5)	135 (8.9)
Body Mass Index, kg/m^2	27.1 [24.5-29.8]	27.0 [24.5-30.2]
Renal Failure		
- Not Dialysis Dependent	312 (10.3)	161 (10.7)
- Dialysis Dependent	11 (0.4)	3 (0.2)
Platelet Count, $x10^9$/Liter	208 [176-245]	206 [174-246]

Antithrombotic Medication On Admission

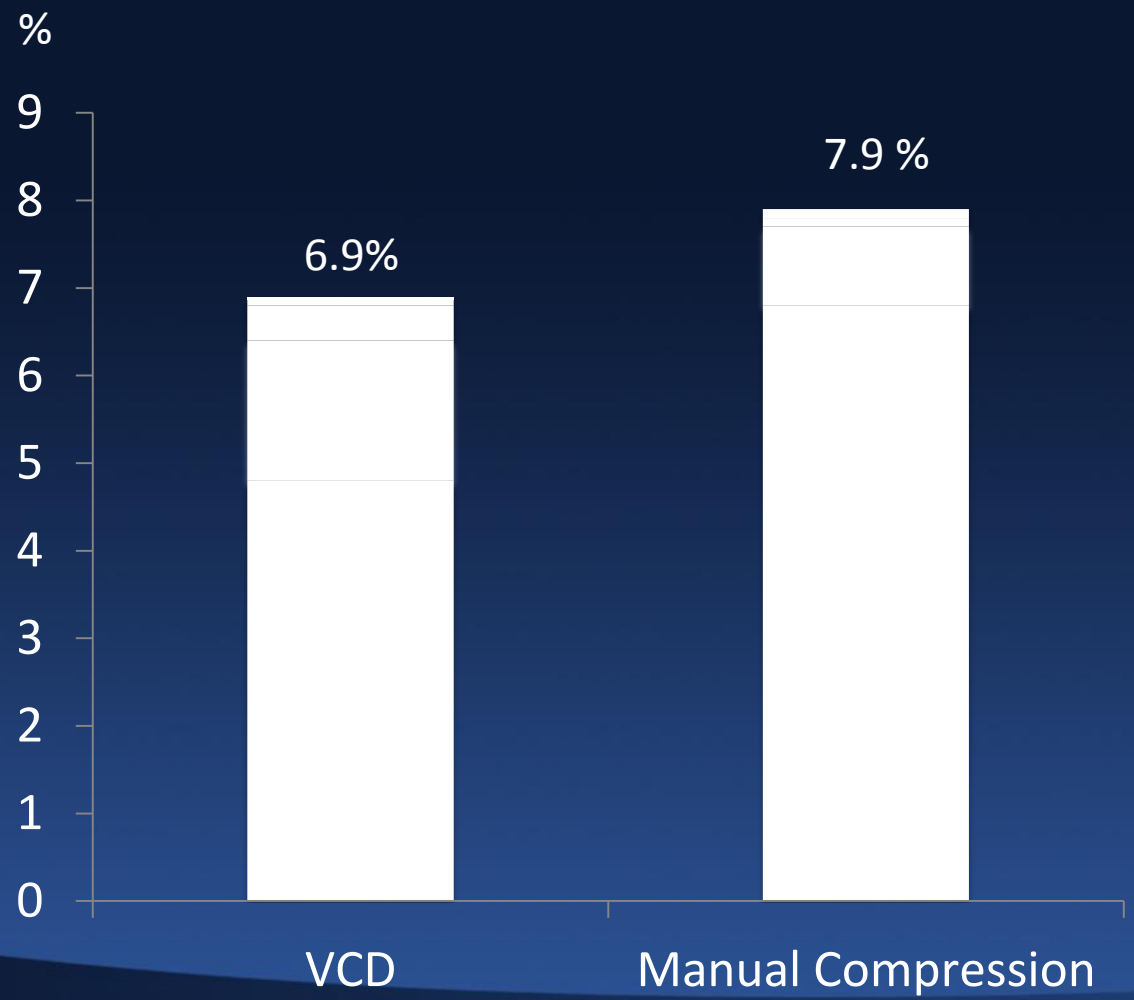
	Vascular Closure Device (n=3015)	Manual Compression (n=1509)
Acetylsalicylic acid	2072 (67)	1025 (68)
ADP-Receptor Blocker		
- **Clopidogrel**	1058 (35.1)	503 (33.3)
- **Prasugrel**	131 (4.3)	48 (3.2)
- **Ticagrelor**	29 (1.0)	16 (1.1)
Oral Anticoagulation		
- **Coumadins**	330 (10.9)	175 (11.6)
- **Rivaroxaban**	42 (1.4)	33 (2.2)
- **Dabigatran**	14 (0.5)	6 (0.4)
- **Apixaban**	2 (0.1)	2 (0.1)

Angiographic And Procedural Characteristics

	Vascular Closure Device (n=3015)	Manual Compression (n=1509)
Ejection Fraction, %	60 [52-62]	60 [52-62]
No. of Diseased Vessels		
- No Obstructive CAD	996 (33.0)	516 (34.2)
- 1	522 (17.3)	269 (17.8)
- 2	567 (18.8)	272 (18.0)
- 3	930 (30.8)	452 (30.0)
Multivessel Disease	1497 (49.7)	724 (48.0)
Arterial Blood Pressure		
- Systolic, mmHg	140 [129-160]	140 [128-160]
- Diastolic, mmHg	75 [65-80]	75 [65-80]

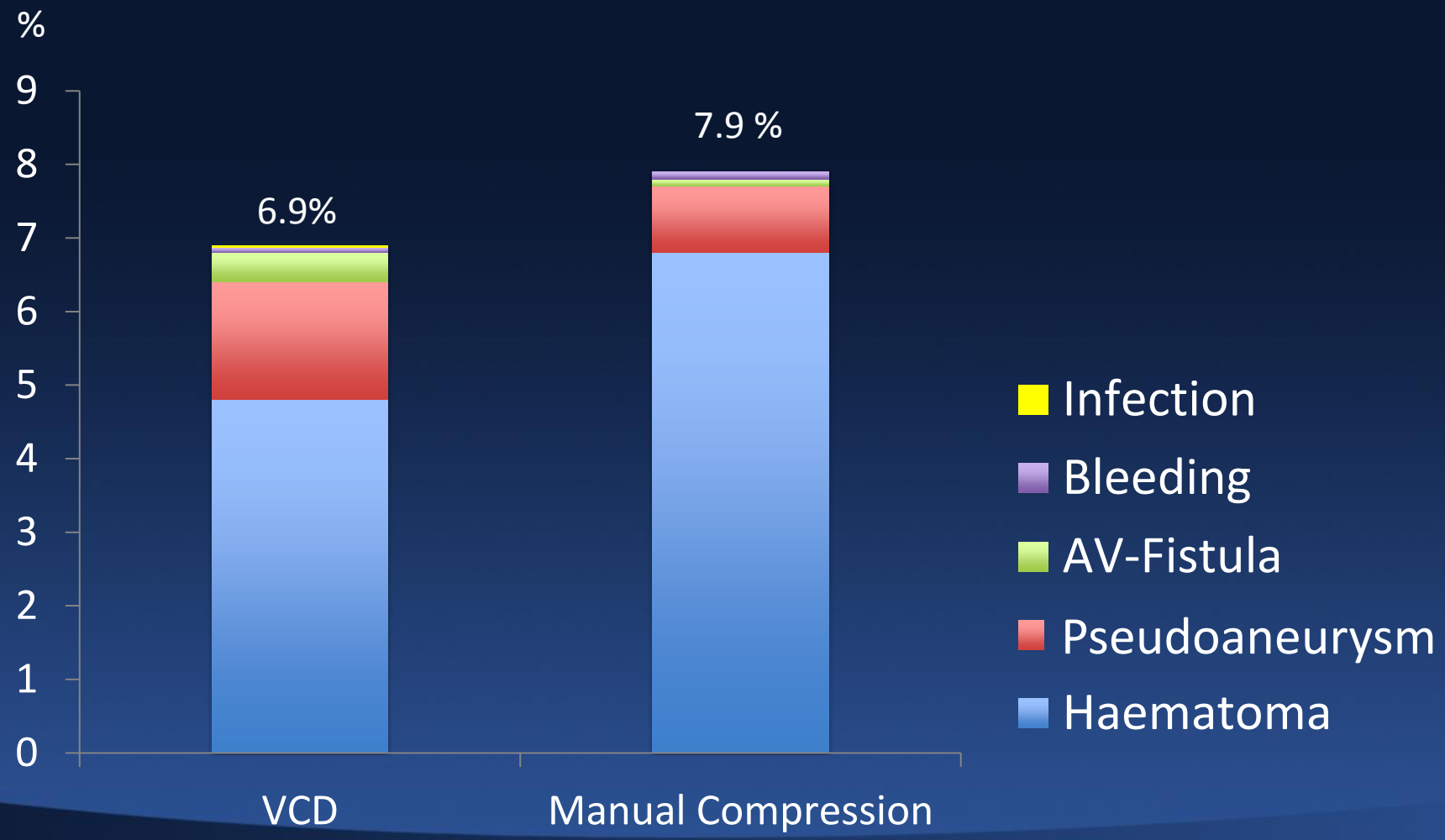
Primary Endpoint:

the Composite of Vascular Access Site Complications



Primary Endpoint:

the Composite of Vascular Access Site Complications

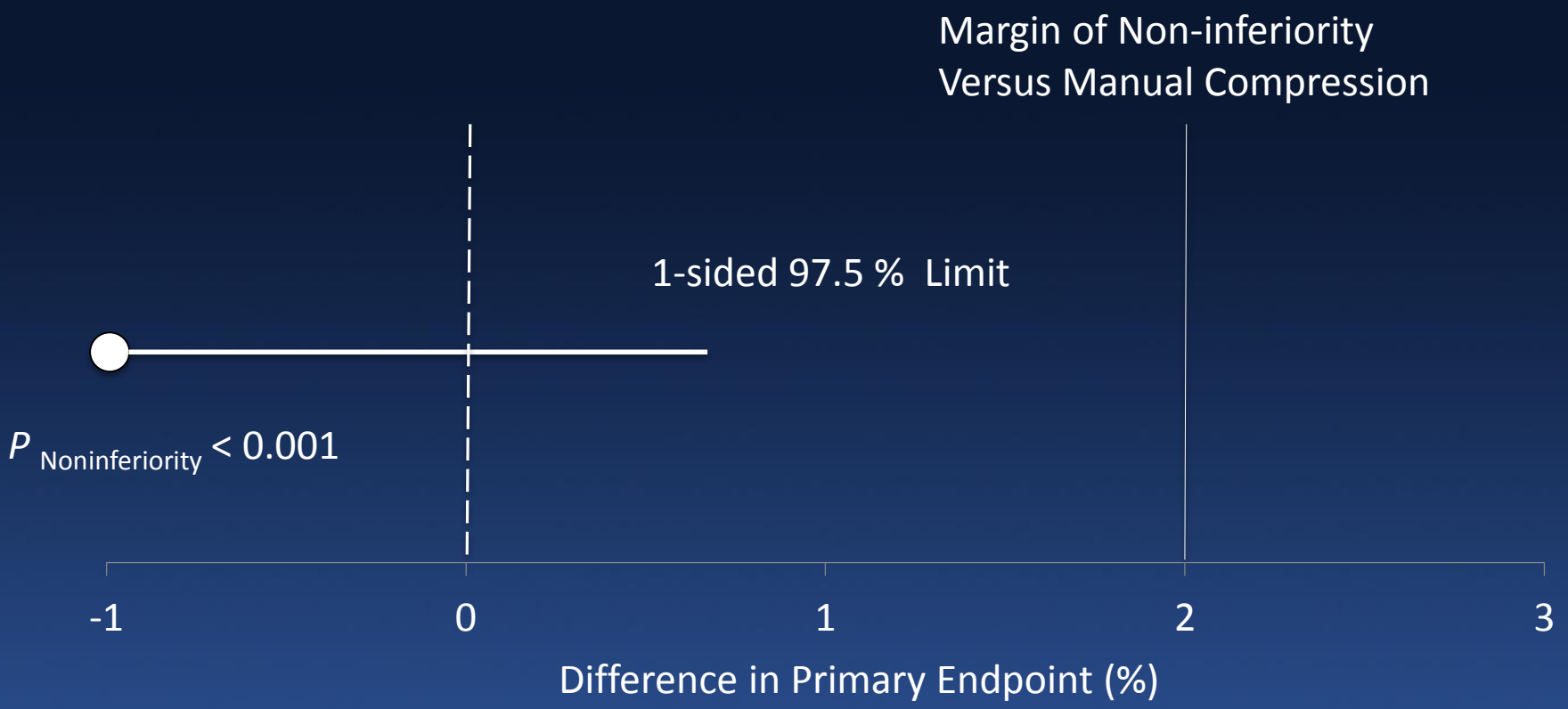


Primary Endpoint
- Individual Components -

	Vascular Closure Device (n=3015)	Manual Compression (n=1509)	*P**
Primary Composite Endpoint	208 (6.9)	119 (7.9)	0.227
- Hematoma ≥5 cm	145 (4.8)	102 (6.8)	0.006
- Pseudoaneurysm	53 (1.8)	23 (1.5)	0.564
- Arteriovenous Fistula	12 (0.4)	2 (0.1)	0.130
- Access Site-Related Major Bleeding	3 (0.1)	3 (0.2)	0.387
- Acute Ipsilateral Leg Ischaemia	0	0	
- Need for Vascular Surgical or Interventional Treatment	0	0	
- Local Infection	1	0	0.479

*Conventional superiority testing with a significance level of p<0.025

Primary Endpoint

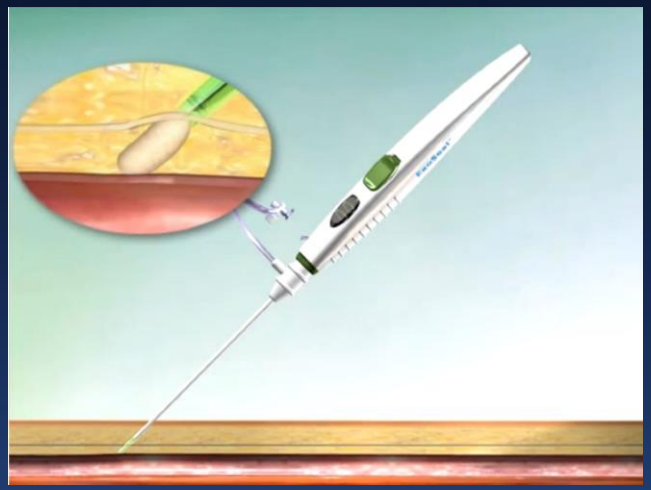


Secondary Endpoints

	Vascular Closure Device (n=3015)	Manual Compression (n=1509)	*P**
Time to Hemostasis, minutes	1 [0.5-2.0]	10 [10-15]	<0.001
Repeat Manual Compression	53 (1.8)	10 (0.7)	0.003

*Conventional superiority testing with a significance level of p<0.025

Secondary Comparison: Femoseal vs. Exoseal



Secondary Comparison: Femoseal vs. Exoseal

	Femoseal (n=1509)	Exoseal (n=1506)	*P**
Primary Endpoint of Vascular Access Site Complications	90 (6.0)	118 (7.8)	0.043
- **Hematoma ≥5 cm**	65 (4.3)	80 (5.3)	0.197
- **Pseudoaneurysm**	22 (1.5)	31 (2.1)	0.210
- **Arteriovenous Fistula**	4 (0.3)	8 (0.5)	0.246
- **Access-Site-Related Major Bleeding***	2 (0.1)	1 (0.1)	0.565
- **Acute Ipsilateral Leg Ischaemia**	0	0	
- **Need for Vascular Surgical/Interventional Treatment**	0	0	
- **Local Infection**	1 (0.1)	0	0.318

*Conventional superiority testing with a significance level of p<0.025

Secondary Comparison: Femoseal vs. Exoseal

	Femoseal (n=1509)	Exoseal (n=1506)	*P**
Time to Hemostasis	0.5 [0.2-1.0]	2 [1.0-2.0]	<0.001
Repeat Manual Compression	22 (1.5)	31 (2.1)	0.210
Closure Device Failure	80 (5.3)	184 (12.2)	<0.001

*Conventional superiority testing with a significance level of p<0.025

Summary And Conclusion (1/2)

- In patients undergoing transfemoral coronary angiography, VCD are non-inferior to manual compression in terms of vascular access site complications and reduce time-to-hemostasis
- The increase in efficacy of VCD with no trade-off in safety provides a sound rationale for the use of VCD over manual compression in daily routine

Summary And Conclusion (2/2)

- The use of the intravascular Femoseal VCD was associated with a tendency towards less vascular access-site complications as compared to the extravascular Exoseal VCD
- Time-to-hemostasis was shorter and device deployment failures were less frequent with the Femoseal VCD compared to the Exoseal VCD

Thanks for your attention!