CIRSE 2018

The ILLUMINA Study

NiTiDES First In Human Trial

Pr. D. Scheinert

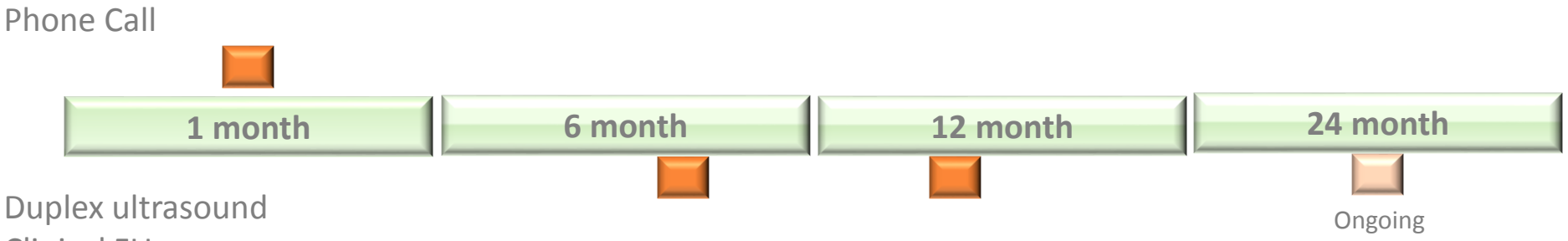
Alvimedica

ILLUMINA study design

Innovative siroLimus seLf expanding drUg-eluting stent for the treatMent of perIpheral disease: evaluation of safety aNd efficAcy

Patients over 18 years with ischemic obstruction of superficial femoral arteries and proximal popliteal arteries due to de novo or restenotic lesion(s) and no prior stent in the target lesion

Prospective, Single arm
10 centers in Europe (n= 100 pts)
Prof. Dierk Scheinert (Coordinating Clinical Investigator, Leipzig-Germany)
eCRFs; Core Lab; CEC



ILLUMINA study design

Innovative siroLimus seLf expanding drUg-eluting stent for the treatMent of perIpheral disease: evaluation of safety aNd effic**A**cy

Primary Endpoint:

- **SAFETY: Composite event –free survival at 12 months:** Freedom from CEC adjudicated MAE (death, target limb amputation, target limb ischemia requiring surgical intervention or surgical repair of target vessel or clinically-driven target lesion revascularization) and freedom from worsening of the Rutherford score by 2 classes, or to class 5 or 6
- **EFFICACY: Primary patency at 12 months.** Primary patency is defined as absence of clinically-driven target lesion revascularization or binary restenosis. Binary restenosis is defined as a peak systolic velocity ratio (PSVR) >2.4 (duplex evaluation)

ILLUMINA study design

Secondary Endpoints:

- Technical Success
- Death within 30 days of the index procedure
- Composite event-free survival and primary patency rate at 6 and 24 months follow-up
- Clinically driven TLR at 6, 12 and 24 months
- Target limb ischemia requiring surgical intervention or surgical repair of target vessel rate at 6 and 24 months
- Rutherford class, Walking impairment test and ABI at 6, 12 and 24 months

ILLUMINA study key inclusion criteria

Clinical

- Patient has symptoms of peripheral arterial disease classified as Rutherford Category (2-4); patients with Rutherford Category 2 can be included only if a conservative and/or medication therapy was unsuccessful.
- Patient has a resting ABI <0.9 or at exercise if resting ABI is normal; patient with incompressible arteries (ABI >1.2) at rest or at exercise must have a TBI <0.8.

Angiographic

- Patient has one documented stenotic or occluded atherosclerotic lesion (lesion length ≤ 14 cm) of the above-the-knee femoropopliteal artery, in one limb, that meet all of the inclusion criteria and none of the exclusion criteria;
- Patient has a de novo or restenotic lesion with >50% stenosis documented angiographically and no prior stent in the target lesion;
- The target lesion must be appropriately covered (margin of 5.0 mm on both sides of the stent) by one or two study stents (NiTiDES). Any occurred dissection of the target vessel must be treated with an additional stent (NiTiDES);
- Tandem lesions are allowed if the distance between 2 lesions is ≤ 3 cm and the total length of all lesions ≤ 14 cm;
- Guidewire successfully passed the lesion through the lumen.

ILLUMINA study key exclusion criteria

Clinical

- Clinical conditions, disorders or allergies that limit the participation; serum creatinine >2.5 mg/dl;
- Myocardial infarction within the 90 days or stroke within the 180 days prior to enrollment;
- Hypercoagulable state; gastrointestinal bleeding; uncontrollable hypertension;
- Aneurysmal disease of abdominal aorta, iliac artery and popliteal artery;
- Concomitant therapies such as: atherectomy, cryoplasty, scoring / cutting balloons.

Angiographic

- Significant stenosis or occlusion of inflow tract not successfully treated before this procedure;
- Previous stenting of target vessel;
- Patient lacks at least one patent vessel of runoff with <50% stenosis throughout its course;
- Patient has untreated angiographically-evident thrombus in the target lesion;
- Inflow lesion ≥15 cm long or occlusion (any length) in the ipsilateral iliac artery;
- Not successfully treated <15 cm long inflow lesion in the ipsilateral iliac artery;
- Lesions in contralateral SFA that require intervention during the index procedure (lesions in contralateral SFA can be treated either >30 days prior to or >30 days after the index procedure);
- Patient with stenosis adjacent to an aneurysmal lesion of diameter at least twice the lumen of the native vessel.

ILLUMINA study centers and enrolled pts.

Sites		N
• Universitätsklinikum Leipzig	Scheinert	3
• Universitäts-Herzzentrum Freiburg Bad Krozingen	Zeller	13
• Regiomed GefäBzentrum Sonneberg	Thieme	13
• St. Gertrauden Krankenhaus GmbH - Berlin	Langhoff	17
Total Germany		**46**
• San Raffaele Hospital - Milan	Chiesa/Kahlberg	15
• Maria Cecilia Hospital - Cotignola	Cremonesi	2
• Fondazione IRCCS Policlinico San Matteo - Pavia	Marone	2
Total Italy		**19**
• Clinique Pasteur - Toulouse	Sauguet	24
• Polyclinique Les Fleurs - Ollioules	Commeau	3
• Centre Prive Claude Galien - Quincy	Garot	8
Total France		**35**
GRAND TOTAL		**100**

ILLUMINA study baseline

Baseline Characteristics	
Patients enrolled (n)	100
Mean age (y)	67
Male (n)	78
Smoker (n)	39
Diabetic (n)	35
Hypertension (n)	69
Hypercholesterolemia (n)	54
Reference Vessel Diameter (mm): Mean (SD)	5.11 ± 0.72
Average lesion length (mm)	72.54 ± 37.99

ILLUMINA study pre-procedure information (i)

Calcifications	
None (%)	25
Little (%)	20
Moderate (%)	35
Heavy (%)	20
Lesions Location	
Proximal SFA (%)	8
Middle SFA (%)	49
Distal SFA (%)	38
Popliteal P1 (%)	5

55%

ILLUMINA study procedure results

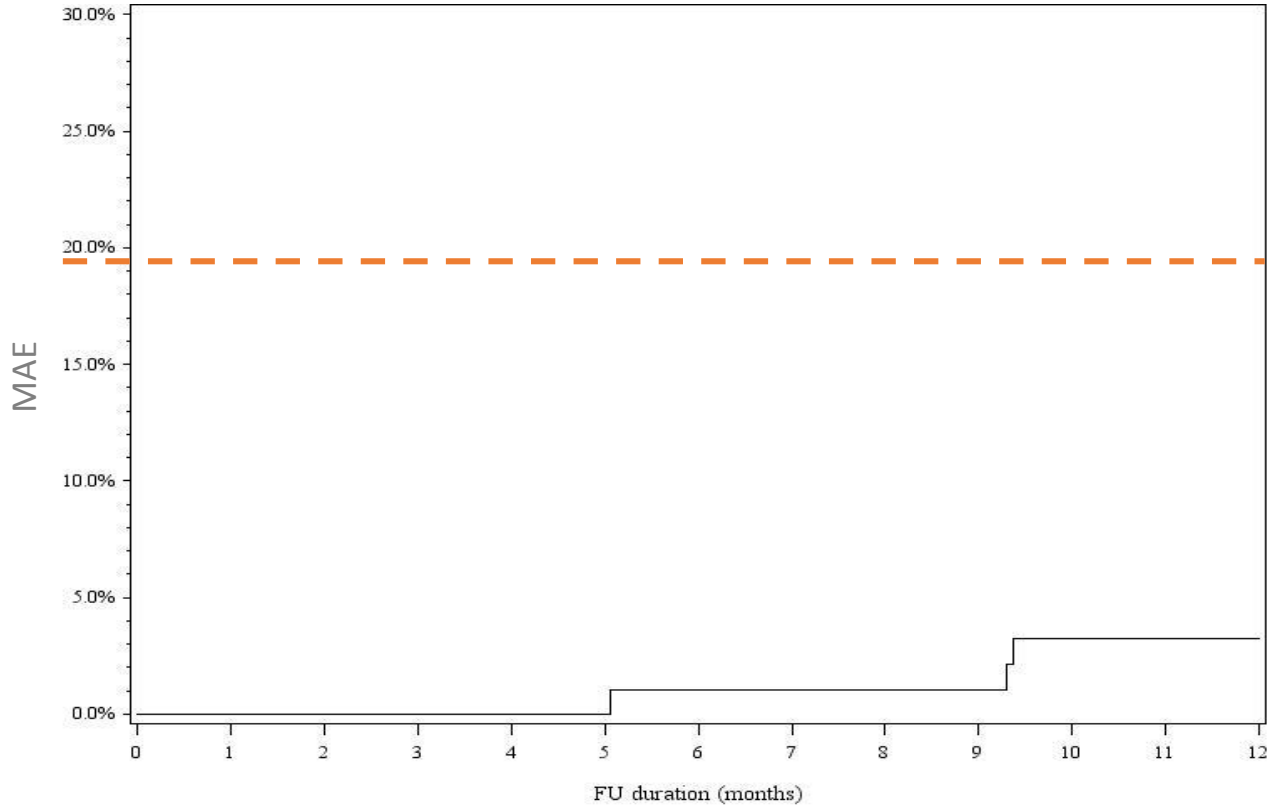
Procedure results	
Stent deployment success	100%
Procedural success	100%
Stent per patient (n)	1.09 ± 0.32
Total mean length of stent (mm)	86.7 ± 40.8

ILLUMINA 12 months study results: safety

Major Adverse Event (MAE)	
Clinically driven Target Lesion Revascularization (TLR)	2
Death*	1
Target limb amputation	0
Target limb ischemia requiring surgical intervention or surgical repair of the target vessel	0
Worsening of the Rutherford score by two classes, or class 5 and 6	0
MAE	**3**

* Death due to Myocardial Infarction - non stent or procedural related

ILLUMINA 12 months study results K-M: safety



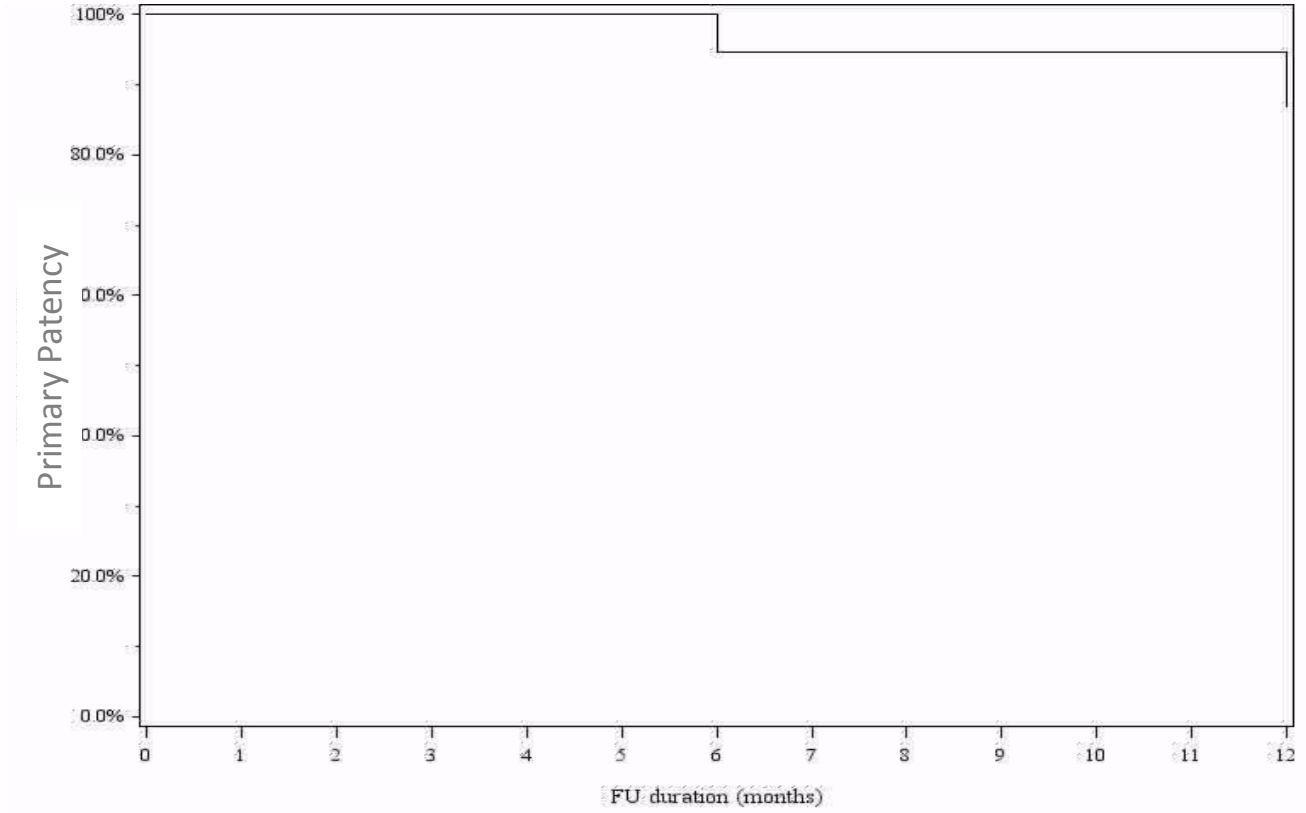
Objective Performance Goal

	Safety endpoint	Lower 95.00% CL	Upper 95.00% CL	Remaining at Risk
0-month	0.0%	0.0%	0.0%	100
1-month	0.0%	0.0%	0.0%	99
6-month	1.1%	0.1%	7.2%	94
12-month	3.2%	1.1%	9.7%	88

ILLUMINA 12 months study results: efficacy

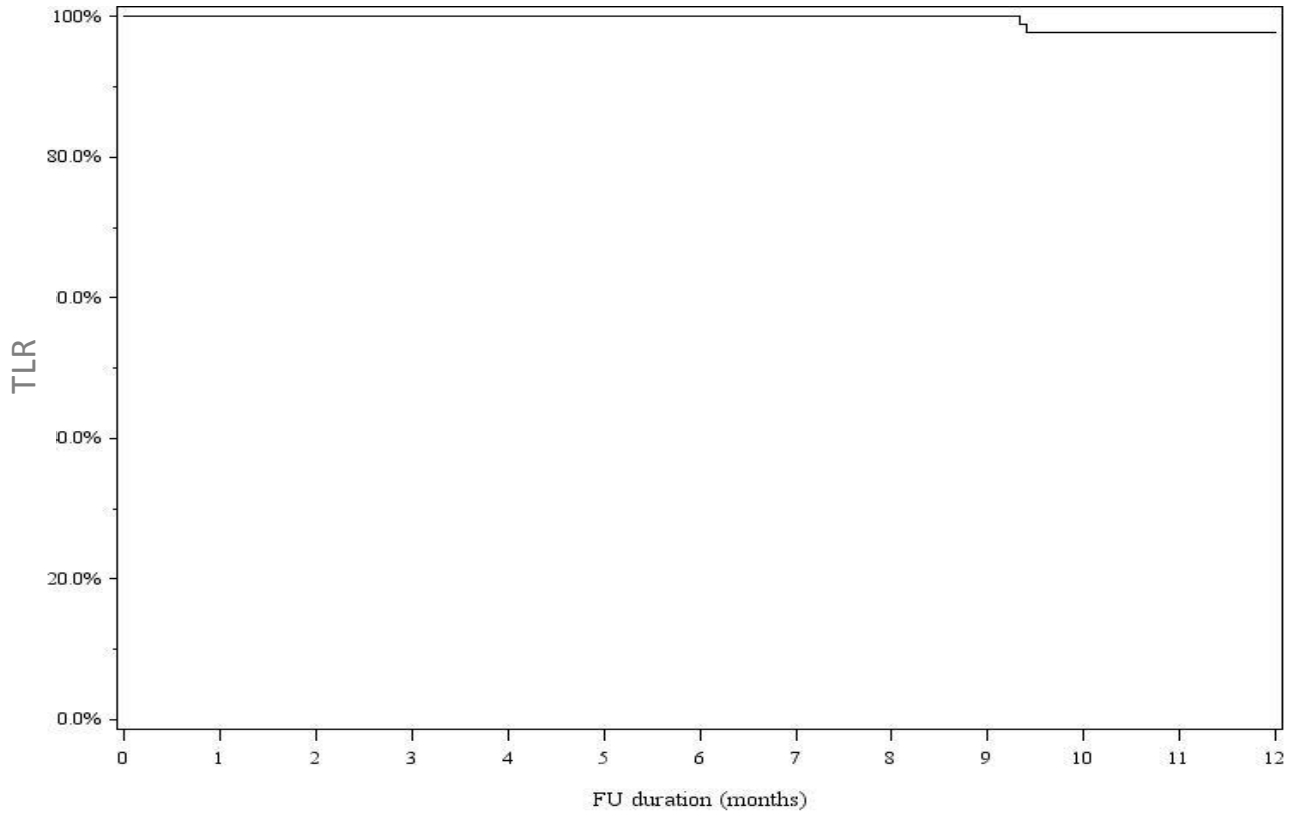
Hierarchical Primary Patency	
Clinically driven target lesion revascularization (TLR)	2
Peak systolic velocity ratio (PSVR) >2.4	10
Primary Patency	**87%**

ILLUMINA 12 months study results K-M: efficacy



	Efficacy endpoint	Lower 95.00% CL	Upper 95.00% CL	Remaining at Risk
0-month	100%	100%	100%	100
1-month	100%	100%	100%	99
6-month	94.7%	87.7%	97.8%	89
12-month	86.9%	78.0%	92.3%	78

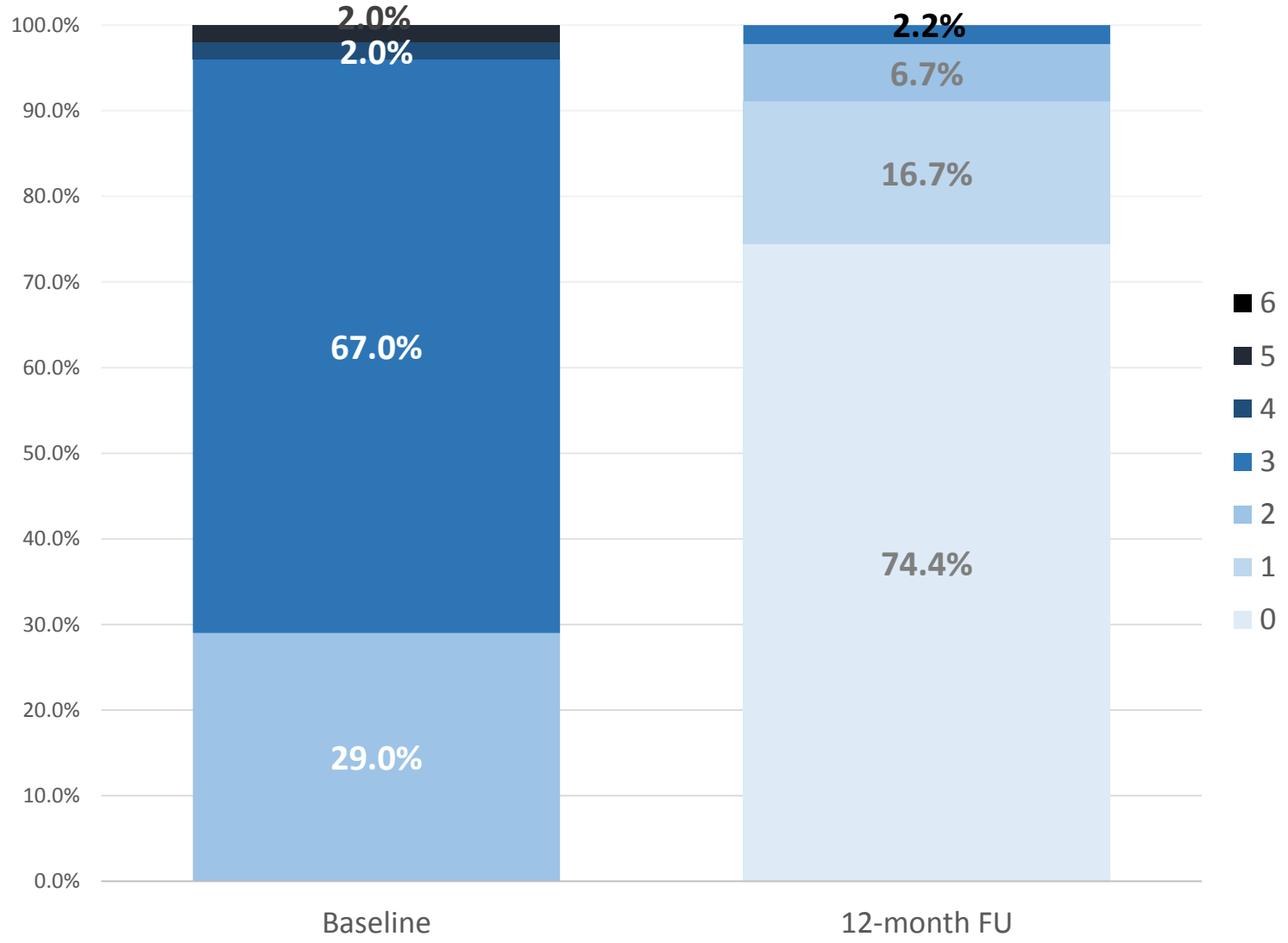
ILLUMINA 12 months study results K-M: TLR



	Freedom from TLR	Lower 95.00% CL	Upper 95.00% CL	Remaining at Risk
0-month	100%	100%	100%	100
1-month	100%	100%	100%	99
6-month	100%	100%	100%	94
12-month	97.8%	91.5%	99.4%	88

ILLUMINA 12 months study clinical results

Rutherford measurements at 12 months improvement



ILLUMINA 12 months study results summary

Even if the ILLUMINA FIM study included complex patients and complex lesions, such as:

- #2 patients in Rutherford 5
- Inclusion of Lesions up to 140mm (stent length 150mm)
- 55% of moderate and heavy calcifications
- RVD of 5.11mm

The study results have been remarkable.

SAFETY:

- MAE, device related, of 2%
- 0% Target limb amputation or target limb ischemia requiring any intervention
- 0% worsening of the Rutherford score by two classes, or patients in class 5 and 6

EFFICACY

- 2% TLR with high rate of Primary Patency

ILLUMINA study conclusions

- The ILLUMINA MAE rate, 3%, was much lower than the target (objective performance goal) set up together with the Notified Body which was 19.3%.

- 2 TLR and a high rate of Primary Patency demonstrated excellent device efficacy.

- Illumina results stand NiTiDES at the top of effectiveness in today DES scenario.