Comparison of the Supraflex Cruz 60 micron stent strut versus the Ultimaster Tansei 80 micron stent strut in High Bleeding Risk PCI population

SITE INITIATION VISIT

STUDY MANAGEMENT

- **Sahajanad Medical Technologies (SMT):** Grant-giver

- **Research Maatschap Cardiologen Rotterdam Zuid**

  Maasstad Ziekenhuis, Rotterdam:
  - Study Sponsor
  - Overall Project Management
  - Regulatory Submission
  - Site Management and Monitoring
  - Safety reporting
  - Central Data Management

- **CERC (Cardiovascular European Research Center)**
  - CEC
  - DMC
  - Statistics
  - Angiographic Corelab activities for events

- **Medwave Clinical Research**
  - CRF development
  - Monitoring of Maasstad Ziekenhuis

STUDY TEAM

Research Maatschap Cardiologie Cardiologen Rotterdam Zuid, Maasstad Ziekenhuis

Pieter Smits
Coordinating Principal **Investigator**

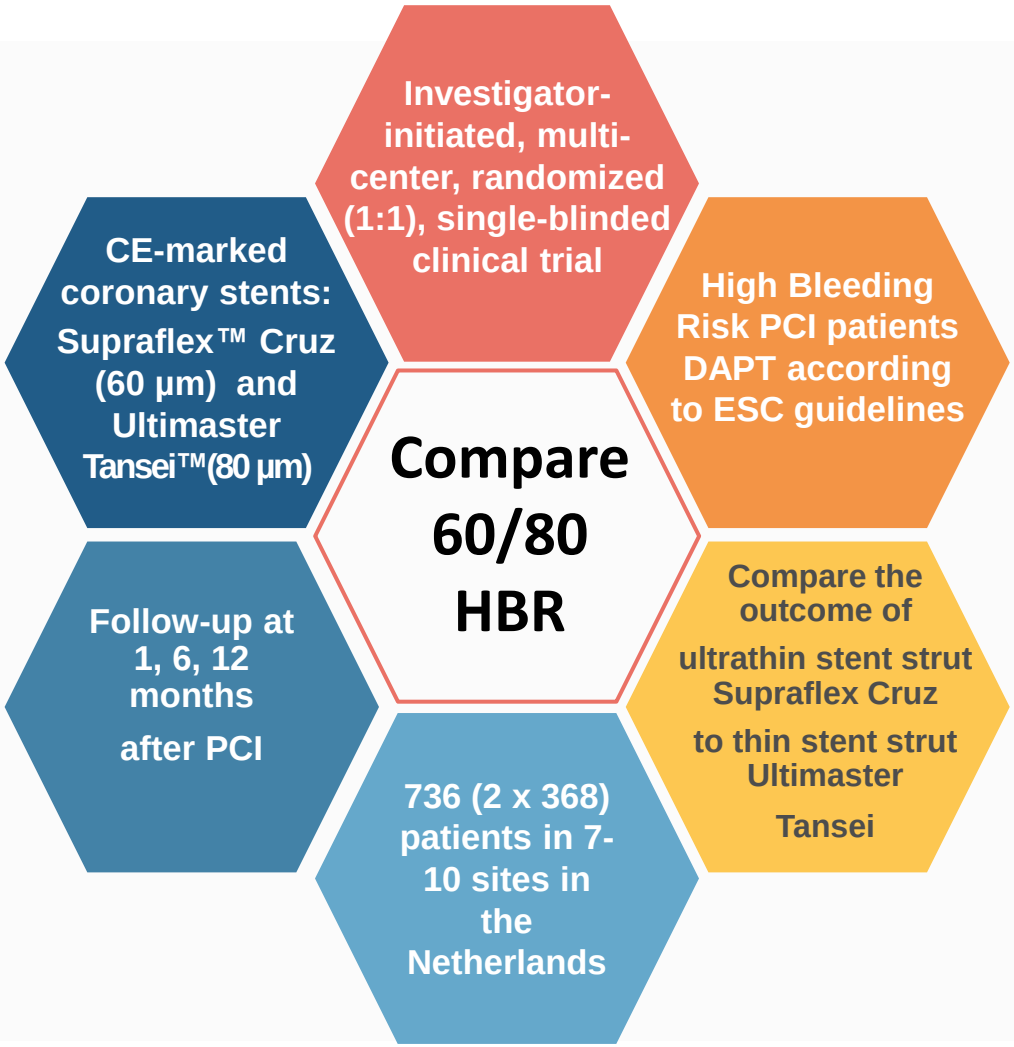
Claudia van Vliet
Clinical Research Associate

Ria van Vliet
Project Manager

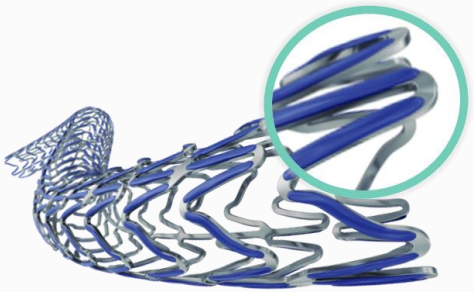
CERC (Cardiovascular European Research Center)

Trang NGUYEN
Project Manager

STUDY DESIGN



STUDY DEVICES



	Supraflex™ Cruz (SMT)	Ultimaster™ Tansei™ (Terumo)
Stent strut thickness	**60 µm (ultrathin)**	**80 µm (thin)**
Drug and dose	Sirolimus 1.4 µg/mm²	Sirolimus 3.9 µg/mm stent length
Stent material	L-605 Co-Cr Alloy	L-605 Co-Cr Alloy
Polymer type	Biodegradable polymer	Biodegradable polymer

STUDY DESIGN

Study Hypothesis:

The Supraflex Cruz stent is non-inferior to Ultimaster Tansei stent in terms of Net Adverse Clinical Endpoint (NACE) at 12 months follow-up.

Study Population:

High Bleeding Risk Population (according to HBR ARC criteria) eligible for PCI with stents for treatment of native coronary artery lesions (no stent thrombosis)

Inclusion Criteria

Patients are eligible for inclusion if the following criteria are met:

- Patients of 18 years and above
- Written or witnessed oral consent to participate in the study
- Native coronary artery lesions eligible for PCI with stents with no restrictions in number of lesions and stents, vessel size or lesion complexity, apart from stent thrombosis.
- Patients at high risk for bleeding according to the HBR ARC criteria.
  Patients meet the HBR ARC criteria if ≥1 major or ≥2 minor criteria are met.

Major HBR criteria are the following:

- Clinical indication for treatment with oral anticoagulants (OAC/NOAC) for at least 12 months
- Severe or end-stage chronic kidney failure (GFR $\leq$ 30 ml/min)
- Hemoglobin (Hb) level at screening < 11g/dl or < 6.8 mmol/l
- Spontaneous bleeding requiring hospitalization or transfusion in the past 6 months or at any time, if recurrent
- Moderate or severe baseline true thrombocytopenia (platelet count <100 *109/L)
- History of chronic bleeding diathesis, like: leukemia, haemophilia, vitamin K deficiency, Factor V or VII deficiency etc.
- Liver cirrhosis with portal hypertension
- Active malignancy (other than skin) within the past 12 months
- Spontaneous intracranial haemorrhage ICH (at any time)
- Traumatic intracranial haemorrhage ICH within 12 months
- Presence of a brain arterio-venous malformation (AVM)
- Moderate or severe ischemic stroke within the past 6 months
- Non-deferrable major surgery on DAPT after PCI
- Recent major surgery or major trauma within 30 d before PCI

Minor HBR criteria are the following:

- Age ≥ 75 years
- Moderate chronic kidney disease (GFR >30 and <60 ml/min)
- Hemoglobin (Hb) 11–12.9 g/dL / 6.8-8.0 mmol/l for men and 11–11.9 g/dL / 6.8-7.4 mmol/l for women
- Any ischemic stroke at any time not meeting the major criterion
- Spontaneous bleeding requiring hospitalization or transfusion within the past 12 months
- Need for chronic treatment with steroids or non-steroidal anti-inflammatory drugs

Exclusion criteria

- Treated with stents other than Supraflex Cruz or Ultimaster < 6 months prior to index PCI
- Treatment of lesions with stent thrombosis
- Treatment of venous or arterial coronary grafts
- Treated for stent thrombosis in 12 months prior to index PCI procedure
- Treated with a bio-resorbable scaffold 3 years before index PCI procedure
- Cardiogenic shock at index procedure
- Active SARS-CoV-2 infection or suspicion of SARS-CoV-2 infection
- Cannot provide written informed consent
- Under judicial protection, tutorship or curatorship
- Unable to understand and follow study-related instructions or to comply with study protocol
- Active bleeding requiring medical attention (BARC≥2) at index PCI
- Life expectancy less than one year
- Known hypersensitivity or allergy for aspirin, clopidogrel, ticagrelor, prasugrel, cobalt chromium or sirolimus
- Any anticipated PCI after index PCI, unless planned and scheduled at index PCI
- Participation in another stent or drug trial

STUDY ENDPOINTs

Primary endpoint: Net Adverse Clinical Endpoint (NACE)

COMPOSITE OF:

- Cardiovascular death
- Myocardial infarction
- Target vessel revascularization
- Stroke
- Major Bleeding (BARC 3 or 5)

at 12 months follow-up after the index PCI.

Secondary Endpoints

- Major adverse cardiac and cerebral events (MACCE) defined as a composite of cardiac death, myocardial infarction, target vessel revascularization and stroke
- Major or clinically relevant non-major bleeding (MCB) defined as a composite of type 2, 3 and 5 BARC bleeding events
- Target Lesion Failure (TLF) is defined as cardiac death, myocardial infarction attributed to the target vessel and clinically indicated target lesion revascularization
- Target Vessel Failure (TVF) is defined as cardiac death, myocardial infarction attributed to the target vessel and clinically indicated target vessel revascularization
- The individual components of the composite primary endpoint
- The composite of cardiovascular death, myocardial infarction and stroke
- The composite of cardiovascular death, myocardial infarction, stroke and major bleed according to BARC 3 and 5
- Stent thrombosis according to the ARC definitions
- Myocardial infarction
- Urgent target vessel revascularization
- Non-target vessel revascularization (urgent and non-urgent)
- Clinically indicated target vessel revascularization
- Bleeding events according to the BARC, TIMI and GUSTO classification
- Transfusion rates both in patients with and/or without clinically detected over bleeding
- Event rates according to the PRECISE-DAPT score
- Procedural success & Device success

STUDY PROCEDURES

Index PCI: is either the single procedure or the first procedure of planned staged procedures

Informed consent:

- Elective patients should sign ICF before index PCI
- In case of STEMI: (verbal) consent to short version of ICF→ long version of PIF signed after PCI

Randomization: is performed after successful wiring of the first target lesion during the index procedure.

Treatment regimen and procedure:

- Patients are treated according to the randomized regimen from the day of randomization till the last planned staged PCI procedure
- In case of unsuccessful delivery or deployment of one of the randomized stents, **cross-over to the usage of the opposite stent type is required after optimal attempts to deliver the designated stent** type per randomization.
- In case of unsuccessful delivery or deployment of any study stent, any other stent type can be used according to the discretion of the operator.

STUDY PROCEDURES

Cardiac Markers: to be measured before and after PCI

DAPT regimen: DAPT treatment (combination and duration) is according to the Guidelines of the European Society of Cardiology for Myocardial Revascularization *(Neuman et al. EHJ 2019).* (Precise Dapt score)

Referring hospitals: in case patients are discharged to a referring hospital, please obtain also the discharge letters form referring hospitals.

Baseline Angios: will be collected from all patients

SUMMARY OF VISITS

	Before index PCI	Index PCI	Post PCI	1 M (30± 14 days post randomization)	6 M (180± 14 days post randomization)	12M (365± 14 days post randomization)
Type of contact	Visit/ Admission	Admission	Admission	Visit/ Telephone	Visit/ Telephone	Visit
Inclusion/ Exclusion criteria	X					
Informed consent	X	X				
Physical examination	X					
Medical and cardiac history	X			X	X	X
Randomization		X				
Blood sampling	X	X	X			
Peri-procedural PCI data			X			
12-lead ECG	X		X			X
Medication regimen	X		X	X	X	X
Anginal status	X		X	X	X	X
Adverse event monitoring		X	X	X	X	X

Study Committees

Steering Committee

- Peter Smits
- Pim Tonino
- Sjoerd Hofma
- Jeroen Vos
- Jan-Peter van Kuijk

Clinical Event Committee

- Stefan Cook
- Emanuelle Barbato
- Fina Mauri

Data Monitoring Committee

- Eric Boersma
- Thomas Cuisset
- Giuseppe Tarantini

PARTICIPATING SITES

Maasstad - Rotterdam	Valeria Paradies
Catharina - Eindhoven	Pim Tonino
MCL - Leeuwarden	Sjoerd Hofma
Albert Schweitzer - Dordrecht	Rohit Oemrawsingh
St. Antonius - Nieuwegein	Jan-Peter van Kuijk
Zorgsaam Terneuzen	Amar Al Mafragi
Rijnstate - Arnhem	Ron Pisters
Amphia - Breda	Sander Ijsselmuiden
Meander - Amersfoort	Fabrizio Spano
Tergooi - Blaricum	Maribel Madeira Camba

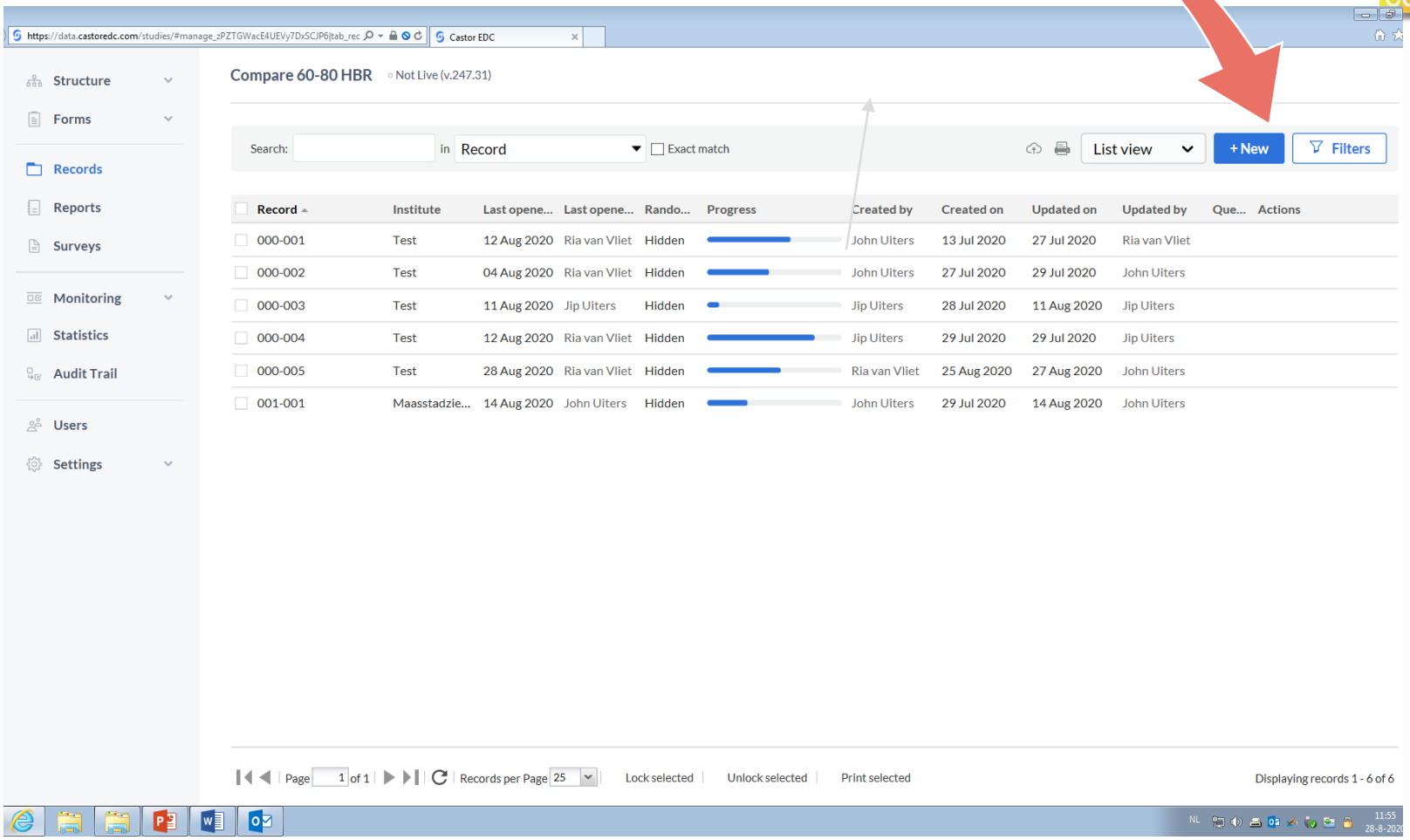
TIMELINES

Item	When
Regulatory Submission	July 2020
Site initiations	Sep - Nov 2020
First patient enrolled	14 Sep 2020
Last patient enrolled	01 Jul 2021
Last patient out	01 Jul 2022
Data lock	01 Sep 2022
Presentation of results	01 Nov 2022

CRF system is CASTOR

https://data.castoredc.com/login

Create a new patient in the system



Randomise a patient

https://data.castoredc.com/studies/#manage_zPZTGWacE4UEVy7DxSCJP6|tab_rec

Castor EDC

Back to records

Record

Study

Reports

Surveys

Monitoring

Randomization

Record ID: 000-005 ◦ Not Live (v.247.31)

Record: 000-005

Progress: 55%

Show Reports

In Progress

Pre-Index PCI

Completed

Randomization

In Progress

Index PCI

In Progress

Discharge

In Progress

1 month Follow-Up

Randomization

21. Randomization

ATTENTION: please ensure to enter the actual time by manually overwriting the default intervals for the minutes in the drop-down!

21.1 Date and start time PCI (i.e time of FIRST wire passage target lesion): 01-08-2020 (dd-mm-yyyy) 12:00 (hh:mm)

21.2 Stratification criterion 1: presence acute coronary syndrome (ACS) at index procedure — Yes / No

This field value cannot be changed as it was used for randomization of this record.

21.3 Stratification criterion 2: presence of Diabetes Mellitus at index procedure — Yes / No

This field value cannot be changed as it was used for randomization of this record.

21.4 Please confirm that patient meets all inclusion and exclusion criteria: Yes / No

21.4.1 Confirm that patient will now be randomized: Yes

PLEASE CONTINUE TO NAVIGATE TO RANDOMISATION BUTTON

Randomise a patient