INTERVENTIONAL CARDIOLOGY

M. Gilard (Brest, France)

Conflicts of Interest
INTERVENTIONAL CARDIOLOGY

NORSTENT: drug-eluting vs. bare metal stents

DOCTORS: Optical Coherence Tomography and Stenting

BBK II: comparison of stenting techniques for coronary bifurcation lesions

PRAGUE-18: ticagrelor vs. prasugrel in STEMI

ANTARTIC: comparison of normal versus tailored dose of prasugrel after stenting
NORSTENT

**Design**

Multicenter RCT in Norway
9013 patients (73 % of the eligible)
Investigator initiated
Funded by not-for-profit organizations
Inclusion period 2008-2011
5 years follow-up (median)

**Main enrolment criteria**

Stable CAD or ACS
All lesions may be treated with DES only or BMS only
No previous stent
No bifurcation lesion requiring 2-stent technique
No intolerance or contraindications to DAPT
No indication for anticoagulation

K. H. Bønaa, (Trondheim, NO), FP 5713
## Type of Stents Used

### DES group

<table>
<thead>
<tr>
<th>Stent Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promus</td>
<td>67%</td>
</tr>
<tr>
<td>Xience</td>
<td>16%</td>
</tr>
<tr>
<td>Endeavor Resolute</td>
<td>12%</td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
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</table>

95% newer generation DES

### BMS group

<table>
<thead>
<tr>
<th>Stent Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Driver</td>
<td>43%</td>
</tr>
<tr>
<td>Integrity</td>
<td>22%</td>
</tr>
<tr>
<td>Liberte</td>
<td>18%</td>
</tr>
<tr>
<td>Multilink Vision</td>
<td>9%</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
</tr>
</tbody>
</table>

K. H. Bønaa, (Trondheim, NO), FP 5713
PRIMARY EP – Death and Nonfatal Spontaneous MI

HR 0.98 P=0.66

K. H. Bønaa, (Trondheim, NO), FP 5713
All Cause Mortality

HR 1.10 P=0.22
Any Revascularization

HR 0.76 P<0.001

6 year rates:
- DES 16.5 %
- BMS 19.8 %

ARR 3.3%, NNT 30

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Definite stent thrombosis - ARC

HR 0.64 P=0.0498

6 year rates:
→ DES 0.8 %
→ BMS 1.2 %

ARR 0.4%, NNT 250

K. H. Bønaa, (Trondheim, NO), FP 5713
Surprise, surprise...really? 4 Questions

1. What can/should we expect in terms of **efficacy** from new stent technology (i.e. from improvements in the treatment of a coronary segment)?
   - Improved survival? **NO**
   - Reduction in (non-lesion related) MI? **NO**
   - Reduction in (non-lesion related) revascularization? **NO**
   - Reduction in lesion related events? **YES**

2. Did DES meet the expectations compared with BMS in NORSTENT?
   **YES**
   YES. Target lesion revascularization↓ (RRR 53%, ARR 5%, NNT=20; P<0.001)

3. What can/should we expect in terms of **safety** from new stent technology?
   **NO**
   No increase in device related complications (stent thrombosis)

4. Did DES meet the expectations compared with BMS in NORSTENT?
   **YES**
   Yes DES even surpassed the expectations with a significant reduction in the (very low) rate of definite stent thrombosis
Was the benefit less spectacular than expected?

YES  The comparators (newer generation BMS) performed very well  
New stent designs as well as metal composition, thinner struts  
Advanced coronary disease likely in a minority of patients  
Patients had to be candidate for BMS  
>1 procedure in ~6% of patients, mean number of treated lesions 1.4/patient, mean number of stents 1.7/patient, mean total stent length ~ 28 mm/patient

What are the implications of NORSTENT?

DES remain the devices of choice  
If, for some reason (economical? availability?) DES cannot be used, operators have a valuable alternative, especially in less advanced coronary disease → newer generation BMS
Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease

DOCTORS: Does OCT optimise results of Stenting?

**Design**

- Multicenter RCT in France
- 240 patients
- Investigator initiated
- Funded by not-for-profit organizations
- Inclusion period 2008-2011
- 1 years follow-up (median)

**Main enrolment criteria**

**ACS**

- **Chest pain at rest** lasting for ≥ 10 min in the previous 72 hrs
- and ≥ 1 of the following two criteria:
  - (i) new ST segment depression ≥1 mm or transitory ST segment elevation;
  - or (ii) elevation of cardiac enzymes (CK-MB, Troponin I or T);
- and presenting an **indication for PCI with stent implantation of the target lesion**
Study Design

- NSTE-ACS patient (N=1935)
  - NSTE-ACS patient (N=240)
    - OCT-guided (N=120)
    - Angiography-guided (N=120)

Key inclusion criteria:
- Single lesion on the culprit artery
- without diffuse disease within the same vessel
PRIMARY Endpoint – FFR

![Box plot showing FFR measurements for Angiography-guided and OCT-guided groups.]

- Angiography-guided group: 0.92 ± 0.05
- OCT-guided group: 0.94 ± 0.04

p = 0.005

**Edge dissection**

**Stent malapposition**

**Tissue prolapse**
Number of Patients with post-PCI FFR > 0.90

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography-guided</td>
<td>77 (64.2%)</td>
<td></td>
</tr>
<tr>
<td>OCT-guided</td>
<td>99 (82.5%)</td>
<td></td>
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</table>

p = 0.0001
<table>
<thead>
<tr>
<th>Variable</th>
<th>Angio-guided group (n=119*)</th>
<th>OCT-guided group (n=120)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause</td>
<td>0</td>
<td>1 (0.8%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (0.8%)†</td>
<td>1 (0.8%)†</td>
<td>1</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>1 (0.8%)</td>
<td>2 (1.6%)</td>
<td>0.57</td>
</tr>
<tr>
<td>≥1 of the above</td>
<td>2 (1.6%)</td>
<td>3 (2.5%)</td>
<td>0.66</td>
</tr>
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</table>
What are the implications of DOCTORS?

It is the 1\textsuperscript{st} randomized trial to investigate the use of OCT in ACS patients.

The OCT findings affected physician decision-making directly, and was associated with a higher FFR at the end of the procedure than PCI guided by fluoroscopy alone.

The benefit was obtained at the cost of a longer procedure with higher fluoroscopy time and more contrast medium, but without an increase in periprocedural MI or kidney dysfunction.
Optical Coherence Tomography to Optimize Results of Percutaneous Coronary Intervention in Patients with Non–ST-Elevation Acute Coronary Syndrome

Results of the Multicenter, Randomized DOCTORS (Does Optical Coherence Tomography Optimize Results of Stenting) Study
### Planned and Ongoing OCT Guided PCI Trials

<table>
<thead>
<tr>
<th></th>
<th>Clinicaltrials.gov</th>
<th>Device</th>
<th>Control</th>
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<tbody>
<tr>
<td>OPTICO BVS</td>
<td>NCT02683356</td>
<td>BVS</td>
<td>Angio</td>
</tr>
<tr>
<td>OCTOPUS-3</td>
<td>NCT02607241</td>
<td>BVS</td>
<td>FFR-guided DCB</td>
</tr>
<tr>
<td>DETECT-OCT</td>
<td>NCT01752894</td>
<td>EES/BES</td>
<td>Angio</td>
</tr>
<tr>
<td>OPINION</td>
<td>NCT01873027</td>
<td>Any DES</td>
<td>IVUS</td>
</tr>
<tr>
<td>Yonsei Univ.</td>
<td>NCT02384629</td>
<td>BES</td>
<td>Angio</td>
</tr>
<tr>
<td>Yonsei Univ.</td>
<td>NCT02466282</td>
<td>BVS</td>
<td>Angio</td>
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<tr>
<td>Yonsei Univ.</td>
<td>NCT01869842</td>
<td>ZES</td>
<td>Angio</td>
</tr>
<tr>
<td>ILUMIEN III</td>
<td>NCT02471586</td>
<td>Any DES</td>
<td>IVUS/Angio</td>
</tr>
<tr>
<td>TOBIAS</td>
<td>NCT01914055</td>
<td>Thrombus aspiration</td>
<td>w/o aspiration</td>
</tr>
<tr>
<td>FORZA</td>
<td>NCT01824030</td>
<td>OCT</td>
<td>FFR</td>
</tr>
</tbody>
</table>
BBK II intended two-stent techniques

Modified T stenting
T-and-protrusion = TAP

Culotte stenting

Final «kissing» balloon angioplasty

M. Ferenc, (Bad Krozingen, DE), FP 5034
Primary endpoint: Maximal in-stent percent diameter stenosis of the bifurcation at 9 months
Secondary endpoints: In-stent percent diameter stenosis of each branch
Binary restenosis rate

300 patients, 26 lost to angiographic FU (9%)
Second generation DES >90% of patients

Inclusion criteria
Stable or unstable angina and/or positive stress test
PCI of de novo bifurcation lesion with -olimus-eluting stents
Need for side-branch stent
Amenable to both techniques

Exclusion criteria
STEMI
Contraindication to aspirin, heparin, clopidogrel, stent alloy, -olimus
History of bleeding or coagulopathy
Intraluminal thrombus, heavy calcification and/or severe tortuosity
Primary endpoint: maximal percent diameter stenosis

Mean ±SD:
21 ± 20 % vs. 27 ±25 %

P = 0.038
adjusted P = 0.017

M. Ferenc, (Bad Krozingen, DE), FP 5034
Percent diameter stenosis of main and side branch

Mean ±SD side branch:
16 ± 20 % vs. 22 ±25 %
P = 0.029
Binary in-stent restenosis

- **Restenosis (%)**
  - Any branch $\geq 50\%$: 6.5 (Culotte), 17.0 (TAP), $P=0.006$
  - Side branch $\geq 50\%$: 6.5 (Culotte), 16.5 (TAP), $P=0.029$
  - Main branch $\geq 50\%$: 1.4 (Culotte), 4.4 (TAP), $P=0.434$

M. Ferenc, (Bad Krozingen, DE), FP 5034

ESC CONGRESS
ROME 2016

Congress Highlights

www.escardio.org/ESC2016
Conclusions BBK II

In experienced hands (100% final kissing), culotte technique was superior to T-and-protrusion (TAP) with respect to angiographic endpoints in 2-stent-intended PCI for bifurcation lesions.

Binary restenosis rate of the main branch was low, and no different, in both arms, while in the side branch culotte lowered the restenosis rate.

Stent thrombosis rate at 1 year was exceedingly low in both groups.

BROADER PERSPECTIVE

Provisional stenting is the technique of choice for most patients with bifurcation lesions.

Stent the main branch and, only if needed, the side-branch.
Interventional cardiology

Culotte stenting vs. TAP stenting for treatment of de-novo coronary bifurcation lesions with the need for side-branch stenting: the Bifurcations Bad Krozingen (BBK) II angiographic trial

PRAGUE-18: ticagrelor vs. prasugrel in STEMI

Randomized patients: n = 1230

**Prasugrel n = 634**

- Prasugrel switched to clopidogrel before day 7: n = 89 (14%)
- Prasugrel continued beyond day 30 or until death: n = 458 (72%)
- Prasugrel switched to clopidogrel between days 7-30: n = 87 (14%)

**Ticagrelor n = 596**

- Ticagrelor switched to clopidogrel before day 7: n = 112 (19%)
- Ticagrelor continued beyond day 30 or until death: n = 367 (61%)
- Ticagrelor switched to clopidogrel between days 7-30: n = 117 (20%)

→ Study terminated earlier (planned 2500 patients) for slow enrolment and futility
→ Allocated P2Y12 inhibitor discontinued within 7 and 30 days in 16% and 33% of the patients, respectively

P. WIDIMSKY, (Prague, CZ), FP 5028
PRIMARY ENDPOINT (7 DAYS)

Death, re-infarction, stroke, major bleeding, urgent IRA revascularization

P = 0.935 (log rank test)

P. WIDIMSKY, (Prague, CZ), FP 5028
KEY SECONDARY ENDPOINT (30 DAYS)

CV Death, non-fatal MI, or stroke

P = 0.665 (log rank test)

Prasugrel
Ticagrelor

P. WIDIMSKY, (Prague, CZ), FP 5028
Limitations

Study underpowered
25% difference/4% event rate/90% power: 14,190 patients (Keith AA Fox)
Prematurely stopped

P2Y12 inhibitor treatment modified in 1/3 of the patients within 30 days

Perspective

PRAGUE-18 does not allow to establish safety/efficacy of ticagrelor vs. prasugrel in STEMI
Very large study would be needed
Prasugrel versus Ticagrelor in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention.

Multicenter Randomized PRAGUE-18 Study

Zuzana Motovska, MD, PhD1; Ota Hlinomaz, MD, CSc5; Roman Miklik, MD, PhD3; Milan Hromadka, MD, PhD4; Ivo Varvarovsky, MD, PhD2; Jaroslav Dusek, MD, PhD6; Jiri Knot, MD, PhD3; Jiri Jarkovsky, MSc, PhD7; Petr Kala, MD, PhD3; Richard Rokyta, MD, PhD4; Frantisek Toucek, MD8; Petra Kramarikova, Mgr7; Bohumil Majtan, MD6,10; Stanislav Simek, MD, CSc11; Marian Branny, MD, PhD12; Jan Mrozek, MD13; Pavel Cervinka, MD, PhD14; Jiri Ostransky, MD15; Petr Widimsky, MD, DrSc1; PRAGUE-18 Study Group.
ANTARTIC: normal vs tailored dose of prasugrel after stenting

Group 1
Conventional Arm: Prasugrel 5 mg
No monitoring

Group 2
Monitoring Arm: Prasugrel 5 mg

1st assessment: VerifyNow P2Y12: 2 weeks ± 2 d
- PRU ≥ 208 → Prasugrel 10 mg/day
- 85 < PRU < 208 → Prasugrel 5 mg
- PRU ≤ 85 → Clopidogrel 75 mg/day

2nd assessment and adjustment:
VerifyNow P2Y12: 2 weeks ± 2 d

Primary endpoint (net clinical benefit) over 12 months: Bleeding type 2, 3, 5 of the BARC definition and MACE (CV death, MI, urgent revascularisation, stent thrombosis, stroke)
PRIMARY Endpoint – CV death, Stroke, ST, TR or BARC 2,3 or 5

HR (95% CI) P=0.98
Ischemic Endpoint

Bleeding Endpoint

HR (95% CI)  P=0.80

HR (95% CI)  P=0.77
Conclusions ANTARTIC

Largest randomized PCI study in the Elderly

Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an ACS does not improve their clinical outcomes

ANTARCTIC after ARCTIC, confirms failure to improve the prognosis of patients by monitoring platelet function to individualize antiplatelet therapy. Failure is not related to the risk level of the population or type of P2Y12 antagonist.
Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an acute coronary syndrome (ANTARCTIC): an open-label, blinded-endpoint, randomised controlled superiority trial

NORSTENT  DES remain superior to BMS but newer generation BMS convey favorable outcomes and are valid alternatives, if DES are not available, especially in less advanced disease.

DOCTORS  1st randomized trial to investigate the use of OCT in ACS patients. The OCT findings affected physician decision-making directly, and was associated with a higher FFR at the end of PCI.

BBK II  In experienced hands, both culotte and T-and-protrusion (TAP) techniques for PCI of bifurcation lesions requiring 2-stents are associated with low restenosis rates in the main branch, while culotte appears to have an advantage in terms restenosis rate in the side branch.
PRAGUE-18  First, but not conclusive, attempt to compare ticagrelor and prasugrel in STEMI

ANTARTIC  Largest randomized PCI study in the Elderly. Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an ACS does not improve their clinical outcomes