Selected success stories from Switzerland in clinical research

Marco Valgimigli, MD, PhD
University Hospital of Bern, Switzerland

COI: no personal disclosure
I have institutional COI which will be clarified during the talk
What defines a success in clinical research?

The study null hypothesis is rejected

The study has identified a winner

“yes...BUT!”

The benefit is small...why bother?

The benefit is too big...is it reproducible?

Why?

...
What defines a success in clinical research?

A study which changes practice in the community

...very few single academic studies achieve this

- Stimulate new research directions
- Conveys reproducible findings
- Changes the guidelines
Outcomes associated with drug-eluting and bare-metal stents: a collaborative meta-analysis

Comparison of Zotarolimus- and Everolimus-Eluting Coronary Stents


March 21, 2006

The NEW ENGLAND JOURNAL OF MEDICINE

Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study


The NEW ENGLAND JOURNAL OF MEDICINE

December 1, 2005

Biomaterials and drug-eluting vs sirolimus-eluting stents with durable coronary revascularisation (LEADER): a randomised, single-blind, non-inferiority trial

Steven Windberg, Patrick W. Serruys, Simon Wallentin, Paola Sciacca, Santiago Rodes-Cabau, Victor Fuster, Volkmar Fieschi, Frank Emmerich, Peter Jüni, John O. Serruys, Patrick Serruys, and the LEADER Investigators

February 10, 2011

Percutaneous coronary interventional strategies for treatment of in-stent restenosis: a network meta-analysis

George A. Serruys, Ludovica Di Filippo, Dimitrios Vlachojannis, Konstantinos Stamatelos, Pietro P. Hoesch, Robert-Jan van Geuns, and the DISRUPT (Disruption of In-stent Restenosis) group

May 31, 2012

Effect of Biomaterials—Eluting Stents With Drug-Coated Polymer vs Bare-Metal Stents on Cardiovascular Events Among Patients With Acute Myocardial Infarction: The COMFORTABLE AMI Randomized Trial

Lorenzo Rubis, MD, Hannes Kellkamp, MD, Marie-Odile Gonneau, MD, Peter Schmermund, MD, and the COMFORTABLE AMI Investigators

July 11, 2013

Ultrastiff biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial

Patrick W. Serruys, Simon Wallentin, Paola Sciacca, Santiago Rodes-Cabau, Victor Fuster, Volkmar Fieschi, Frank Emmerich, Peter Jüni, John O. Serruys, Patrick Serruys, and the BIOMICS (Biodegradable Polymer—Eluted Sirolimus) Investigators

September 18, 2009

Bioresorbable scaffolds: clinical experience

Patrick W. Serruys, Patrick Pribil, and Maximilian M. Nikitin

February 25, 2016

The NEW ENGLAND JOURNAL OF MEDICINE

Pragmatic randomized controlled trials: the new kid on the block

Paul Y. Lee

July 19, 2012
Is Aspirin a still contemporary treatment option?

**Primary Endpoint (Effectiveness): Death or Q wave MI**

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**All-comers PCI population**
(ACS and Stable CAD patients)
(N = 16,000)

**Bivalirudin*-supported**
BioMatrix family stent implantation

1:1 Randomization, Open-Label Design

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**Experimental Treatment Strategy**
- **ASA**
  - 1 month
- **P2Y12 i**
  - 24 months

**Reference Treatment Strategy**
- **ASA**
  - 24 months
- **P2Y12 i**
  - 12 months
"Less is more": Aspirin withdrawal

Post-PCI:
GLOBAL LEADERS (NCT01813435) started on February 2013 (ticagrelor)
TWILIGHT (NCT02270242) started on August 2015 (ticagrelor)
TICO (NCT02494895) started on July 2015 (ticagrelor)

ACS patients:
GEMINI-ACS-1 (NCT02293395) started on April 2015 (rivaroxaban)

Post-ACS:
COMPASS (NCT01776424) started on February 2014 (rivaroxaban)

Post-PCI in AF patients:
PIIONEER AF-PCI (NCT01830543) started on May 2013 (rivaroxaban)
REDUAL-PCI (NCT02164864) started on July 2014 (dabigatran)
AUGUSTUS (NCT02415400) started on June 2015 (apixaban)
ENTRUST AF-PCI going to be registered (edoxaban)

Post-TAVI:
GALILEO (NCT02556203) started on December 2015 (rivaroxaban)
ATLANTIS (NCT02664649) started on February 2016 (apixaban)
Sponsor ECRI

Consortium of Investigators

Biosensors

AstraZeneca

The Medicines Company

Sponsor ECRI

CRO
Cardialysis

CTU
Bern

triggers research, reproducible, affect guidelines
Time to Reveal

Multicenter International trial
levering on our original study idea

Got Funded
by SNF

Excluded:
- Patients with anatomic or clinical contraindications for TAVI or REVEAL implantation
- Patients with previously implanted PPM/ICD/CRT

- Clinical assessment, REVEAL interrogation
- 12-lead ECG after 1, 3, 6, and 12 months
- TTE after 30 days and 1 year (BERN-TAVI)
Study Organization and Sites

Sponsor
Gruppo Italiano Studi Emoemina

Grant suppliers: The Medicines Company and Terumo
Principal Investigator: Marco Valgimigli, MD, PhD
Study Director: Maria Salomone, MD, PhD

78 Sites across 4 EU countries recruited patients

National Coordinating Investigators and CROs
Paolo Calabrò, MD, PhD, Italy; Trial Form Support
Arnoud W J van’t Hof, MD, The Netherlands; Trial Form Support
Manel Sabate’, MD, PhD, Spain; FLS-Research Support
Elmir Omerovic, MD, PhD, Sweden; Gothia Forum

Clinical Event Committee
P. Vranckx, Chair
S. Leonardi Co-Chair
P. Tricoci

Statistical Committee (CTU)
P. Jüni, MD, Chair
M. Rothenbühler
Dik Heg

Data Mng
E. Frigoli, Eustrategy
Project Leader
NSTEACS or STEMI with invasive management

Aspirin + P2Y12 blocker

Heparin ± GPI

Bivalirudin

Mono-Tx

Stop infusion

Prolong ≥ 4 hs infusion

Trans-Radial Access

MATRIX Program

NCT01433627

http://www.cardiostudy.it/matrix
2011 NSTEACS GL  ➔  No formal reco for access site selection

2015 NSTEACS GL

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<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
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<tr>
<td>In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI.</td>
<td>I</td>
<td>A</td>
<td>MATRIX Meta-analysis</td>
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Art is 'I'; science is 'we'.

~ Claude Bernard