Long-term Outcome of Biodegradable Compared to Durable Polymer Drug-Eluting Stents and Bare Metal Stents – Main Results of a Prospective Randomized Trial

- the BASKET PROspective Validation Examination II-

(BASKET-PROVE II)

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on behalf of the BASKET-PROVE II Investigators

supported by the Basel Cardiovascular Research Foundation

➔ **no industry involvement in design, analysis or interpretation of data**

Register NCT01166685

BASKET-PROVE II

BASKET-PROVE II Organigram

(number of patients randomized)

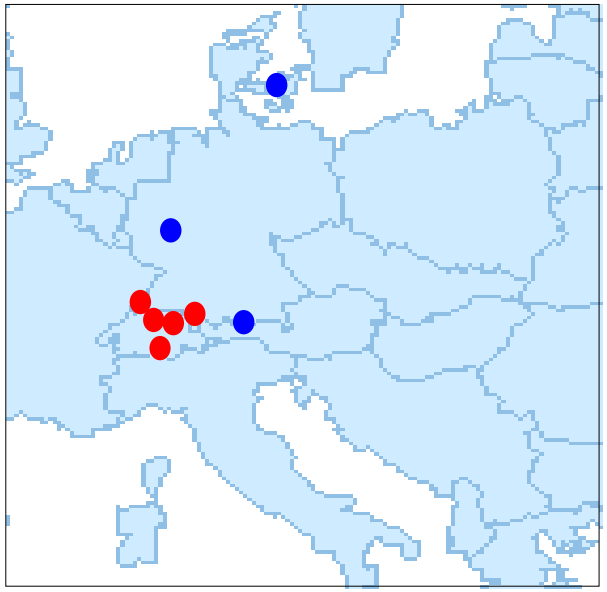
University Hospital Basel, Switzerland (n=398)
R. Jeger

Gentofte University Hospital, Copenhagen, Denmark (n=522)
S. Galatius

University Hospital Innsbruck, Austria (n=331)
H. Alber

Elisabeth-Krankenhaus Essen, Germany (n= 331)
C. Naber

Independent CEC
P.Rickenbacher



Co-PI. C. Kaiser
Co-PI: M. Pfisterer

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
Online November 19th, 2014!

Triemli Hospital Zürich, Switzerland (n=229)
F. Eberli

Cardiocentro Lugano, Switzerland (n=160)
G.Pedrazzini

State Hospital St. Gallen, Switzerland (n=114)
H. Rickli

State Hospital Aarau, Switzerland (n=104)
A. Vuilliomenet

Independent Statistics
CTU University Basel

Background

⇒ **Promise of biodegradable-polymer drug-eluting stents (BP-DES) to be as:**

- ***effective*** **as 2nd generation durable-polymer drug-eluting stents (DP-DES)**
- ***safe*** **>1 year as bare-metal stents (BMS), i.e. very late stent thrombosis (VLST) due to persistent polymers should no longer appear**

Aims

⇒ **To compare the long-term performance of a BP-DES to**

- **the most widely used 2nd generation DP-DES**
- **a last-generation thin-strut coated BMS**

Study Design I

Inclusion: 2'291 patients in need of ≥3.0mm stents irrespective of clinical indication for PCI/stent (April 2010 until May 2012)

Exclusions: shock, in-stent restenosis, stent thrombosis, unprotected LM or SVG, planned surgery < 12 months, oral anticoagulation / increased bleeding risk, history of TIA or stroke, stents >4mm, no compliance

Randomization 1:1:1 to

Biolimus-eluting BP-DES (Nobori ®)
vs
Everolimus-eluting DP-DES (Xience-PRIME ®)
vs
thin-strut coated Cobalt-Chromium BMS (Prokinetik ®)

Study Design II

Assumptions: - 2-year primary EP for DP-DES: 7.6% (*BASKET-PROVE, NEJM 2010*)

- Non-inferiority margin: 3.8%

Sample Size : - 2x800 patients (incl. 10% lost-to-follow-up) for non-inferiority, power 80%, at one-sided type I error of 0.05

DAPT : - ASS and Prasugrel for all patients

12 months after DES or ACS, 4 weeks after elective BMS

- Prasugrel: 60mg loading-dose, 10mg daily (5mg >75 years or <60kg)

Follow-up : - 24 months, angio for clinical indication only

Endpoints : - 1° EP: *Efficacy*: MACE (cardiac death/MI/TVR) within 2 years

a) BP-DES vs DP-DES (non-inferiority)

b) BP-DES vs BMS (superiority)

- 2° EP: *Safety*: = definite/probable ST/ MI/cardiac death

- late = > 1 year

BASKET-PROVE II

Patient Flow

2'299 patients randomized

8 refused definite consent

2'291 patients included

765 allocated to BP-DES

765 allocated to DP-DES

761 allocated to BMS

746 FU-information for primary EP available
- 19 censored at time-point of refusal or loss to follow-up

748 FU-information for primary EP available
- 17 censored at time-point of refusal or loss to follow-up

745 FU-information for primary EP available
- 16 censored at time-point of refusal or loss to follow-up

765 analyzed for primary EP

765 analyzed for primary EP

761 analyzed for primary EP

- **Survival status known after 2 years: 98.5%**
- **Complete follow-up after 2 years: 97.7%**

Baseline Characteristics

	BP-DES	DP-DES	BMS
Patients n	765	765	761
Male (%)	78	80	75
Age (years)	62±11	62±11	63±11
Diabetes (%)	21	17	19
Hypertension (%)	66	66	67
Hypercholesterol. (%)	65	63	62
Current Smoker (%)	35	35	37
Prior MI (%)	9	9	10
Prior PCI (%)	13	12	15
Prior CABG (%)	3	3	2
Stable Angina (%)	36	35	39
UA/NSTEMI (%)	34	35	33
STEMI (%)	30	29	27

(No significant differences between groups)

Baseline Vessel Disease and Intervention

	BP-DES	DP-DES	BMS
Patients (n)	765	765	761
MV- disease (%)	37	39	39
LAD treated (%)	62	63	65
Bifurcations treated (%)	4	6	6
CTO treated (%)	4	4	3
GP IIb/IIIa blockers (%)	12	13	12
# of stented lesions/patient	1.2±0.5	1.3±0.6	1.3±0.5
# of stents/patient	1.5±0.8	1.5±0.9	1.5±0.8
total stent length/pat. (mm)	26±17	27±18	25±16
Angiographic success (%)	96	96	95

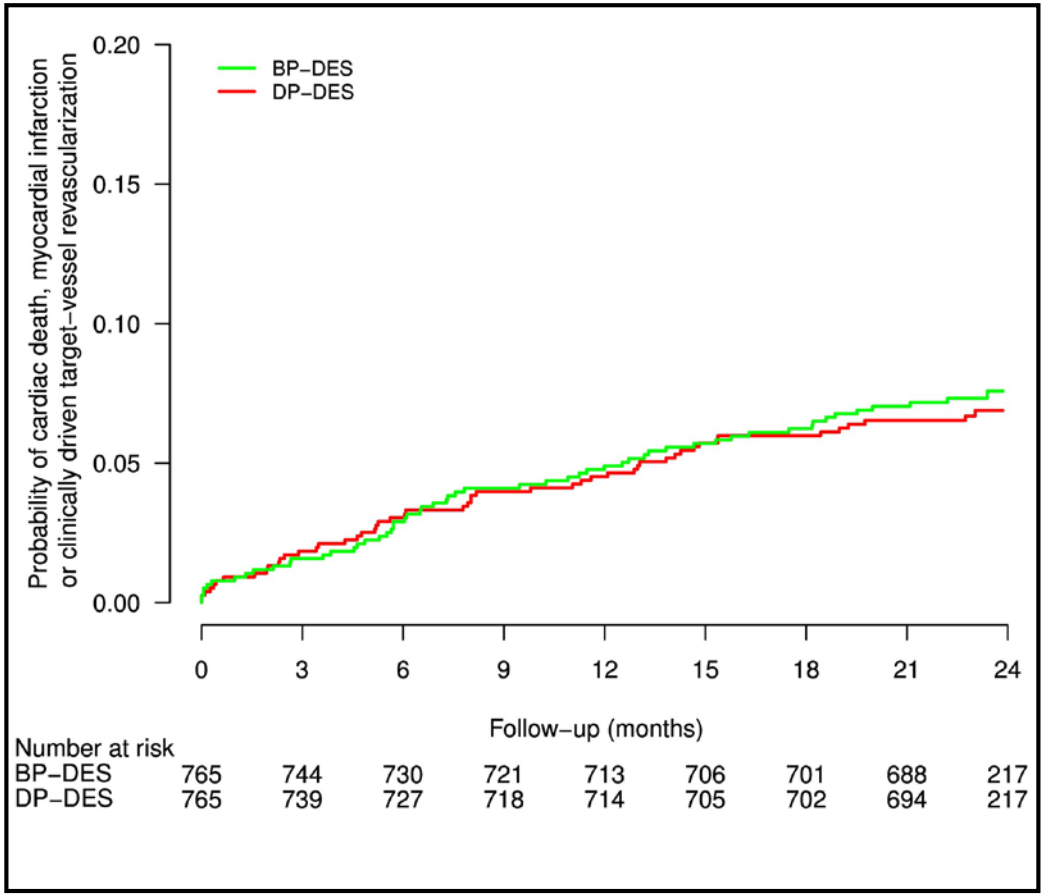
(No significant differences between groups)

BASKET-PROVE II

Primary Endpoint

cardiac death/MI/TVR

BP-DES versus DP-DES



7.6%

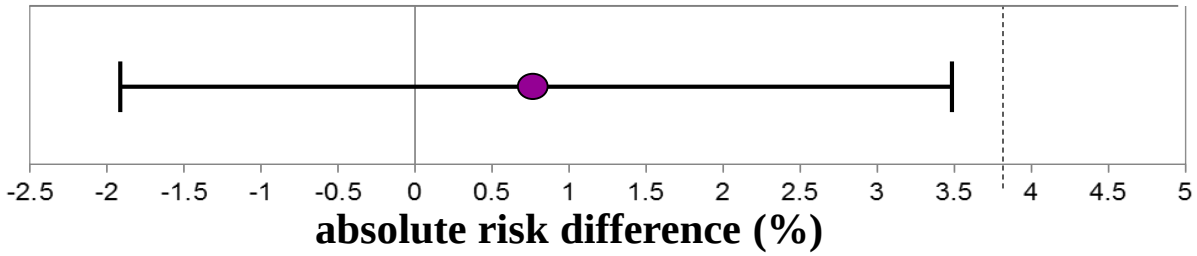
6.8%

HR 1.11; CI 0.77-1.62, p=0.58

Non-Inferiority Analysis

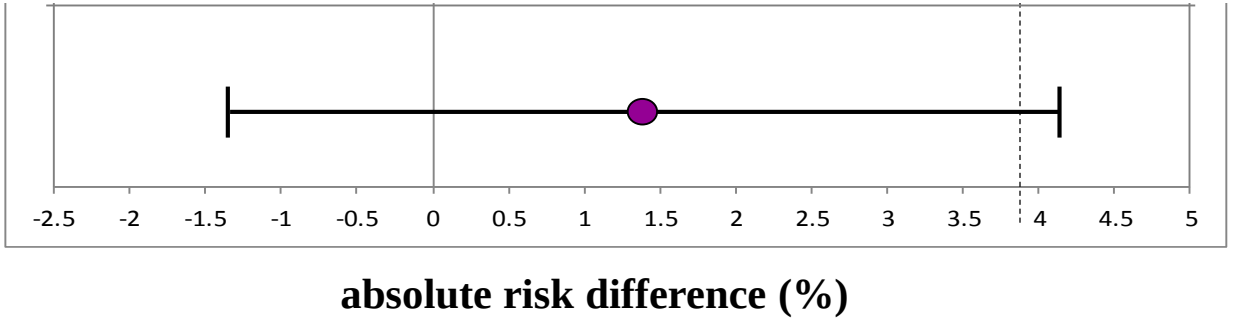
BP-DES versus DP-DES

ITT-Population



- **Intention to treat: absolute risk difference 0.75% (95%CI -1.93% to 3.50%, p for non-inferiority: 0.04)**

PP-Population

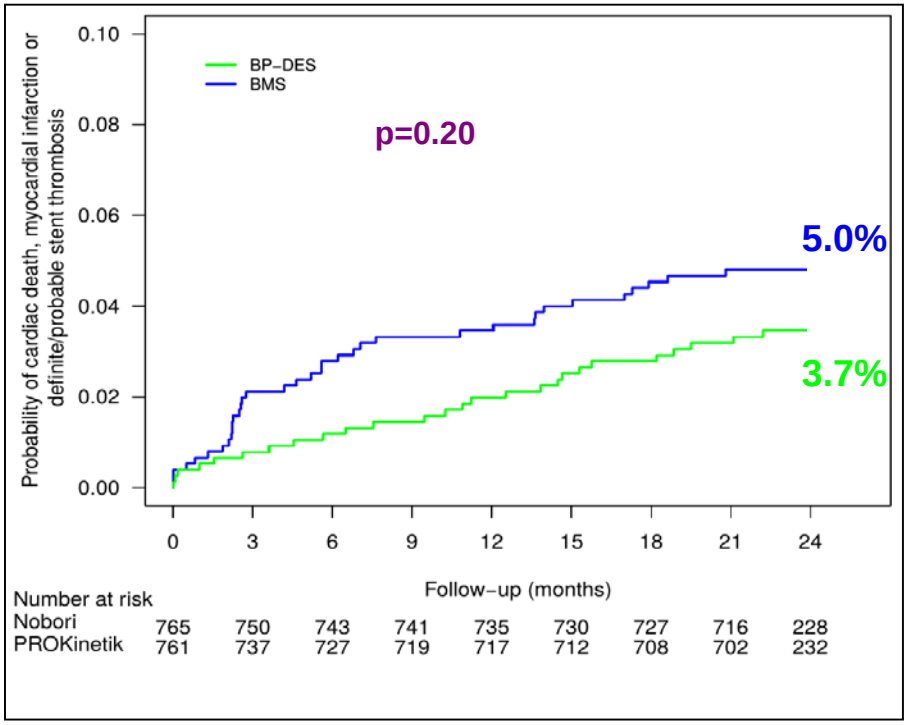


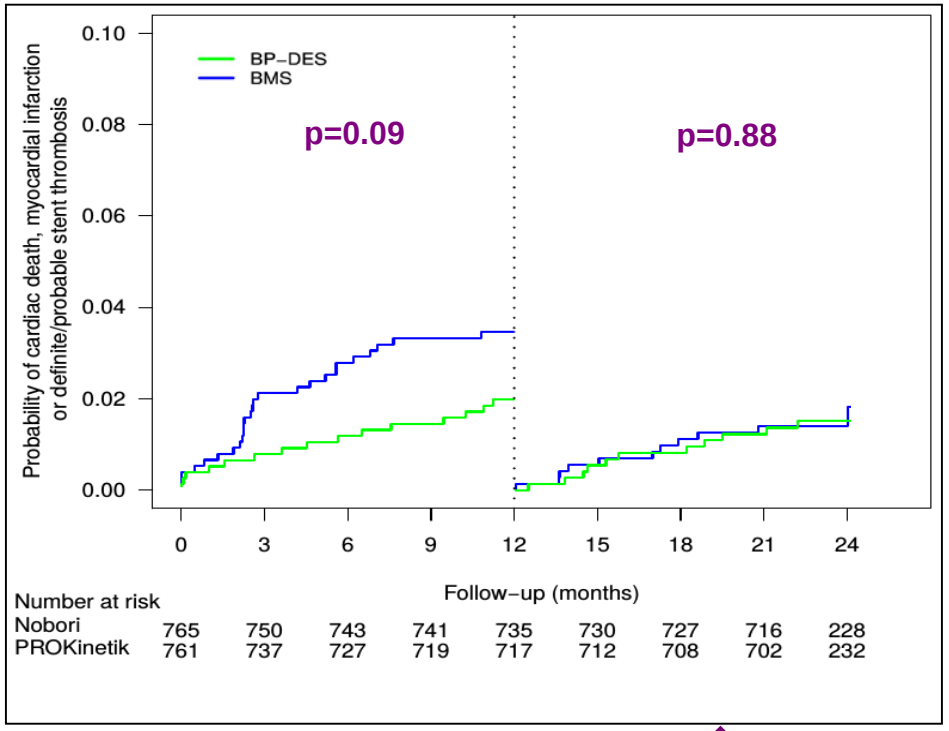
- **Per protocol: absolute risk difference 1.41% (95%CI 1.33% to 4.15%, p for non-inferiority: 0.09)**
  - ***Difference due to exclusion of 6 events in patients with protocol violations: 4 due to DAPT violations, 2 no stent***

Key Safety Secondary Endpoint

Cardiac Death / MI / def. or prob. ST

BP-DES versus BMS





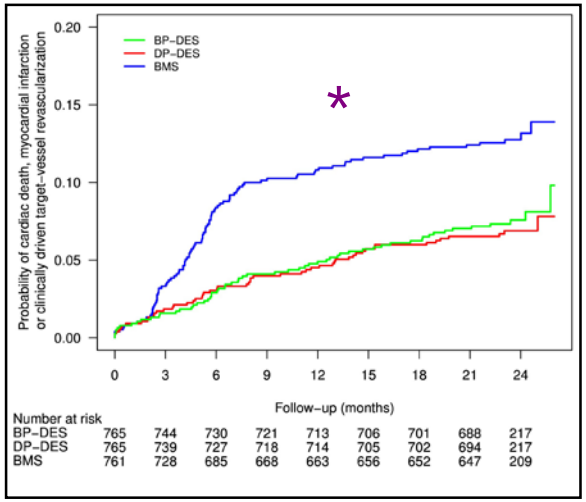
HR: 0.72; CI 0.44-1.18

No difference in late safety

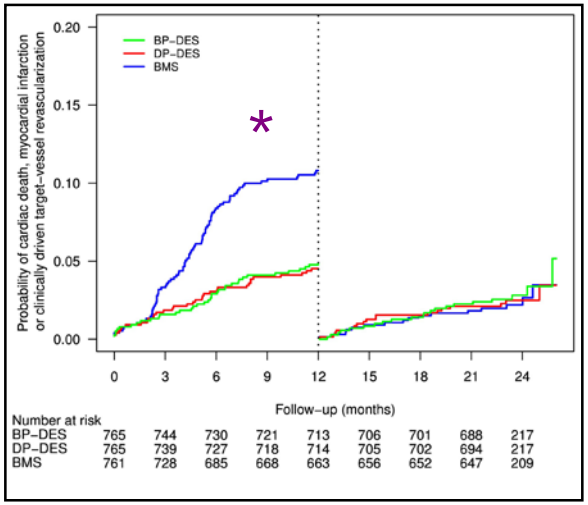
Comparison of all 3 Stent Groups

Early vs Late Events

overall

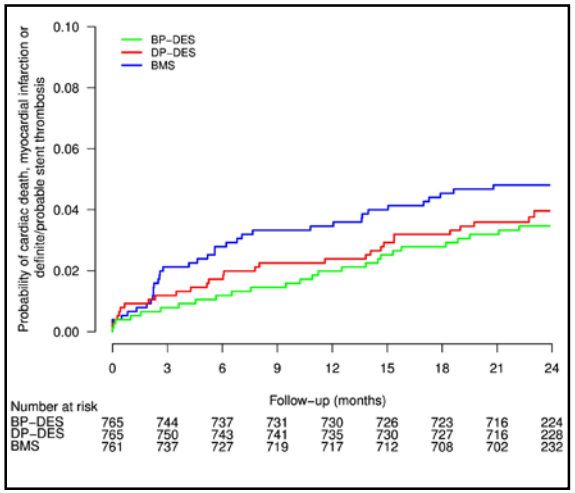


1st year 2nd year



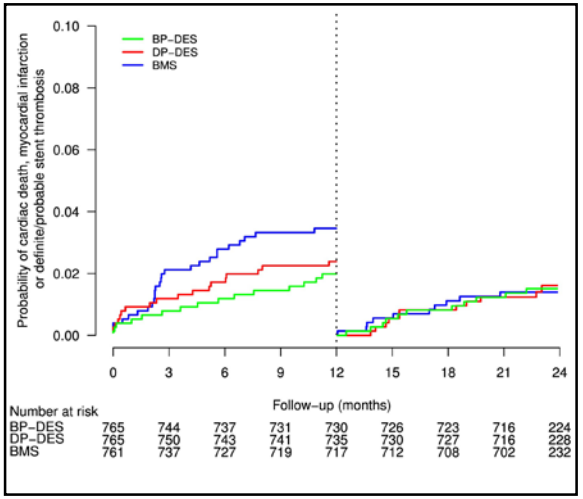
Efficacy

card death/MI/TVR



Safety

card death/ MI/def/prob ST



* p<0.001

Discussion

⇒ **BP-II was powered for *efficacy*, the primary EP (i.e. non-inferiority), not for *late safety***

- **>20'000 patients needed to prove significant differences in VLST**

⇒ **The non-inferiority margin was *3.8%***

- **In accordance with previous trials**

⇒ **All patients were treated with *prasugrel*-based DAPT**

- **May question the generalizability of the results on VLST and ischemic endpoints (separate analysis under review)**

⇒ **Results apply for patients with *large vessel* stenting**

- **Selected for low TVR-, high MI/death-risk**

Conclusions and Implications

⇒ **By intention-to-treat, biolimus-eluting BP-DES were *non-inferior* to everolimus-eluting DP-DES after 2 years in a real-world population of patients in need for large-vessel stenting.**

⇒ **Both DES were *superior* in efficacy (TVR⬇) to thin-strut coated BMS.**

⇒ **There was *no evidence* for a better safety, particularly a lower very late stent thrombosis rate, for BP-DES *beyond 1 year*.**

⇒ **Findings *challenge* the concept that polymers should be key in the perceived late deficiency (VLST⬇) of DP-DES.**