HYBRID: A Prospective, Randomized Trial of Hybrid Coronary Revascularization Versus Standard Surgical Revascularization in Multivessel Disease

Michal Hawranek, MD

on behalf of the

HYBRID Trial Investigators

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Balton

Hybrid Revascularization for Multivessel Coronary Artery Disease

POL-MIDES

Cardiac surgery PI: ***Marian Zembala***

Cardiology PI: ***Mariusz Gasior***

Study Investigators:

Cardiac surgery: M. Zembala Jr., T. Hrapkowicz, K. Filipiak

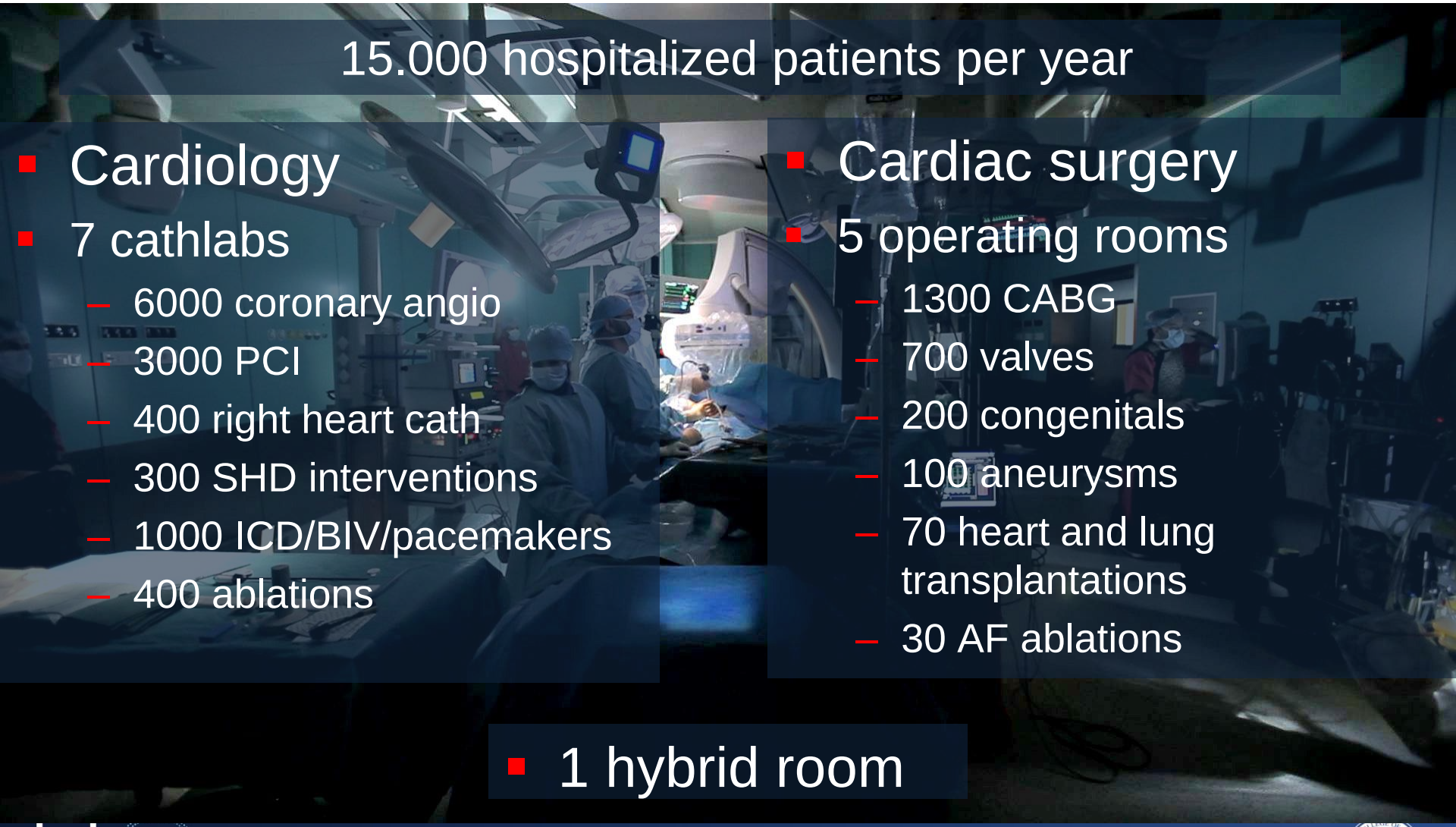
Cardiology: M. Tajstra, M. Hawranek, M. Gierlotka, L. Poloński

Prospective Randomized PilOt Study
EvaLuating the Safety and Efficacy of Hybrid
Revascularization in MultIvessel Coronary
Artery DisEaSe (POLMIDES)

ClinicalTrials.gov number, NCT01035567

POLMIDES study is granting by Ministry of Science and Higher Education of Poland.

Silesian Center for Heart Diseases
Zabrze, Poland



15.000 hospitalized patients per year

- Cardiology
- 7 cathlabs
  - 6000 coronary angio
  - 3000 PCI
  - 400 right heart cath
  - 300 SHD interventions
  - 1000 ICD/BIV/pacemakers
  - 400 ablations

- Cardiac surgery
- 5 operating rooms
  - 1300 CABG
  - 700 valves
  - 200 congenitals
  - 100 aneurysms
  - 70 heart and lung transplantations
  - 30 AF ablations

- 1 hybrid room

BACKGROUND

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Subset of CAD by anatomy	Favours CABG	Favours PCI	Ref.
1VD or 2VD - non-proximal LAD	IIb C	I C	—
1VD or 2VD - proximal LAD	I A	IIa B	30, 31, 50, 51
3VD simple lesions, full functional revascularization achievable with PCI, SYNTAX score ≤22	I A	IIa B	4, 30–37, 53
3VD complex lesions, incomplete revascularization achievable with PCI, SYNTAX score >22	I A	III A	4, 30–37, 53
Left main (isolated or 1VD ostium/shaft)	I A	IIa B	4, 54
Left main (isolated or 1VD, distal bifurcation)	I A	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≤32	I A	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≥33	I A	III B	4, 54

In almost all variations of MVD with involvement of LM/proximal LAD CABG is the method of choice

but…

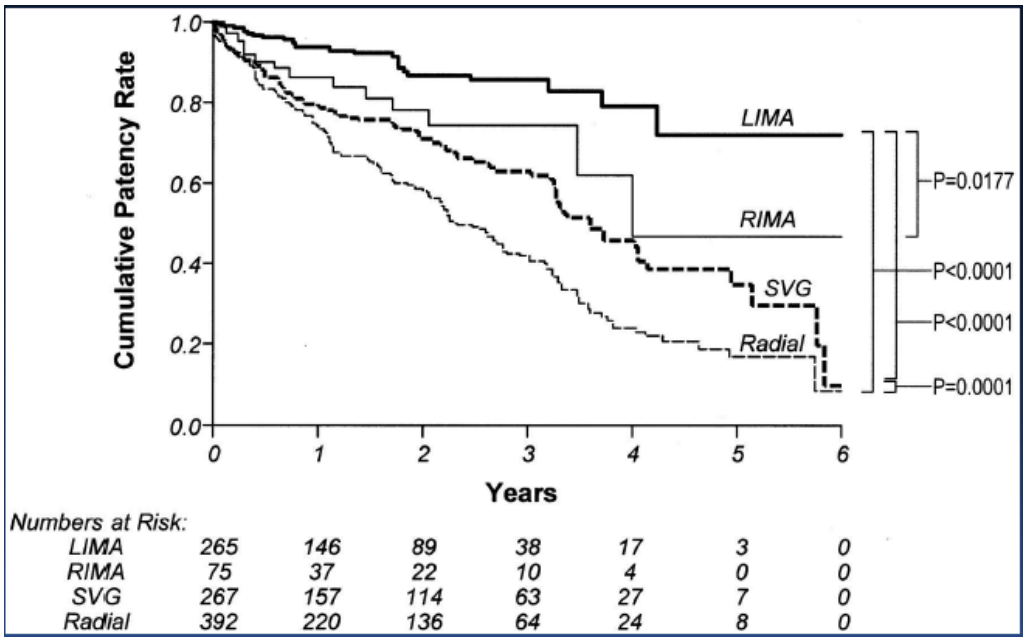
Wijns, W et al. *European Heart Journal* 2010

BACKGROUND

We know that…

- Excellent short and long term results for LIMA graft
- Occlusion rate of SVG at 12 months
  - 13 – 21%
    (Yun, J Thorac Cardiovasc Surg 2005)
- TVR rate of DES in MVD at 12 months
  - 14,2% (Serruys, NEJM 2009)
- Equivalence in short term patency between DES and SVG

CABG: long term graft patency



Khot,UN et al. *Circulation* 2004;109:2086-2091

BACKGROUND

Practice Guideline

2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

5.11. Hybrid Coronary Revascularization: Recommendations

Class IIa

1. Hybrid coronary revascularization (defined as the planned combination of LIMA-to-LAD artery grafting and PCI of ≥1 non-LAD coronary arteries) is reasonable in patients with 1 or more of the following[1116–1122] (*Level of Evidence: B*):
   a. Limitations to traditional CABG, such as heavily calcified proximal aorta or poor target vessels for CABG (but amenable to PCI);
   b. Lack of suitable graft conduits;
   c. Unfavorable LAD artery for PCI (ie, excessive vessel tortuosity or chronic total occlusion).

Class IIb

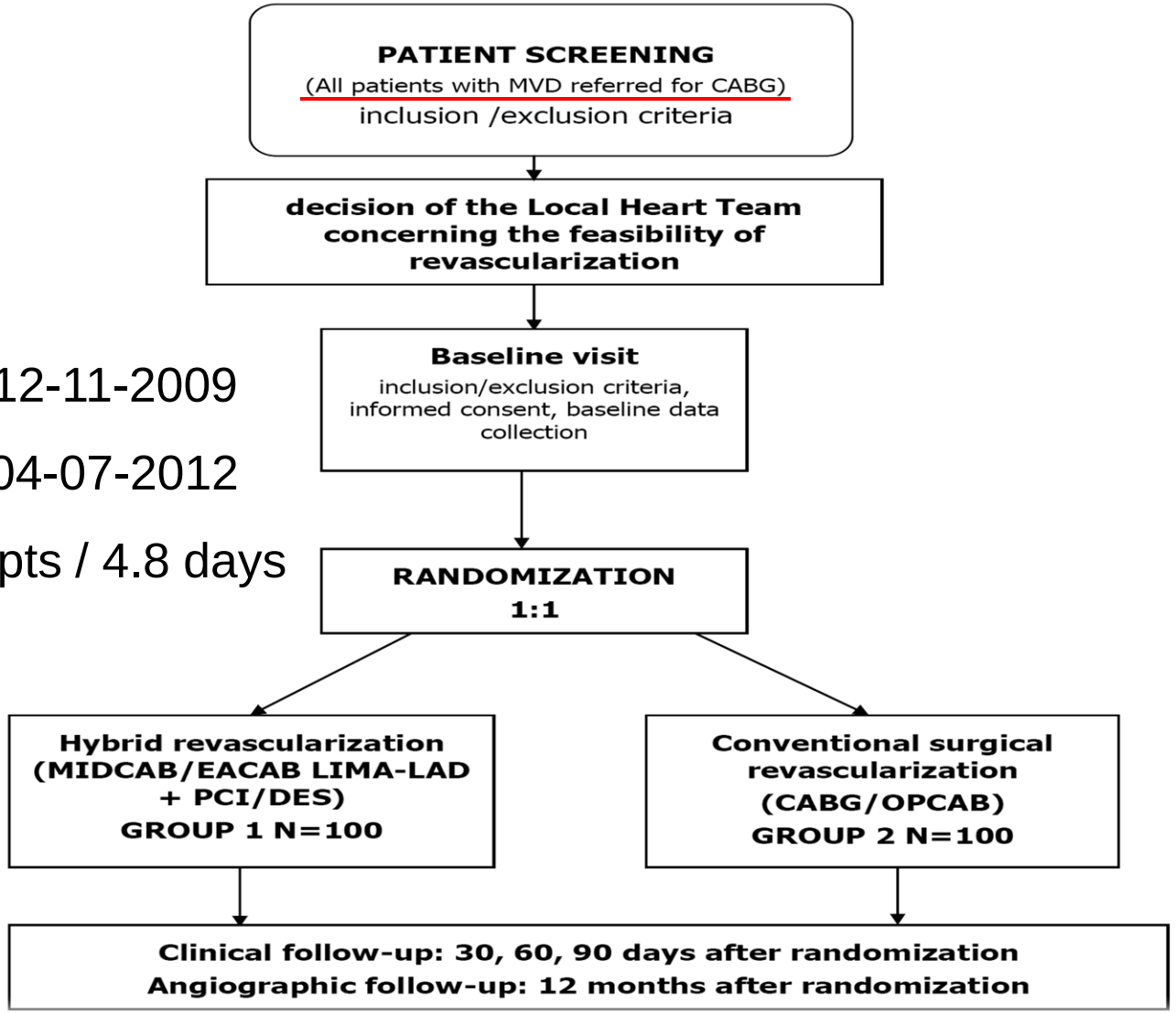
1. Hybrid coronary revascularization (defined as the planned combination of LIMA-to-LAD artery grafting and PCI of ≥1 non-LAD coronary arteries) may be reasonable as an alternative to multivessel PCI or CABG in an attempt to improve the overall risk–benefit ratio of the procedures. (*Level of Evidence: C*)

STUDY DESIGN

First patient: 12-11-2009

Last patient: 04-07-2012

Enrollment: 1pts / 4.8 days



STUDY DESIGN

INCLUSION CRITERIA

- Age 18 or more
- Angiographically confirmed multivessel CAD with involved LAD and critical (>70%) lesion in at least one (apart LAD) major epicardial vessel amenable to both PCI and CABG
- Indication for revascularization based upon symptoms of angina and/or objective evidence of myocardial ischemia
- Patient is willing to comply with all follow-up visits
- Patient signed an Informed Consent

STUDY DESIGN

EXCLUSION CRITERIA

- Severe congestive heart failure (class III or IV according to NYHA, or pulmonary edema, cardiogenic shock) at the time of enrollment
- Prior surgery with the opening of pericardium or pleura
- Prior stroke (within 6 months)or more than 6 months if there are substantial neurological defects
- Prior history of significant bleeding (within previous 6 months) that might be expected to occur during PCI/CABG related anticoagulation
- More then one chronic total occlusions in major coronary territories except LAD
- LVEF <35%
- Left main stenosis (at least 50% diameter stenosis)
- Acute ST-elevation MI within 72 hours prior to enrollment requiring revascularization
- Planned simultaneous surgical procedure unrelated to coronary revascularization (e.g. valve repair/replacement, aneurysmectomy, carotid endarterectomy or carotid stenting)
- Contraindication to either CABG, MIDCAB or PCI/DES because of a coexisting clinical condition
- Significant leukopenia, neutropenia, thrombocytopenia, anemia, or known bleeding diathesis.
- Intolerance or contraindication to aspirin or both clopidogrel and ticlopidine
- Extra-cardiac illness that is expected to limit survival to less than 5 years e.g. oxygen-dependent chronic obstructive pulmonary disease, active hepatitis or significant hepatic failure, severe renal disease
- Suspected pregnancy. A pregnancy test will be administered prerandomization to all women of child-bearing age
- Concurrent enrollment in another clinical trial
- Patient inaccessible for follow-up visits required by protocol

STUDY DESIGN

STUDY ENDPIONTS

Primary endpoint

- Feasibility defined by means of
  - a % of patients with completed hybrid procedure according to study protocol, and
  - a % of conversion to standard CABG.
- Safety defined as a occurrence of

  MACE such as death, MI, stroke, TVR, or major bleeding within 12 months follow up

Secondary endpoint

- Postprocedure and follow up angiographic measurements as patency of grafts and restenosis in revascularized segments
- Assessment of quality of life of alive study participants according to SF-36 Health Survey version 2
- Cost-effectiveness defined as a cost of revascularization procedure and costs of hospitalizations in both groups.

STUDY DESIGN

Hybrid revascularization – timing of the procedures and medications

- Pre-procedure
- Aspirin 75mg/d starting at least 12h before procedure

1 stage – MIDCAB LIMA - LAD

↓

Assessment of:
- Drainage ≤ 25ml/h within last 2 hours
- HCT > 25%; Plt >80.000

↓

2 stage – PCI with DES

< 36 hours

- Pre-Procedure
- Clopidogrel 600mg <2h before PCI
- Clopidogrel 300mg <6h before PCI
- Procedural
- Heparin initial bolus 100IU/kg i.v., ACT > 250s
- Post-procedure
- Aspirin 75mg indefinitely
- Clopidogrel 75 mg for 12 months

- Co-Cr everolimus eluting stents

RESULTS

BASELINE CHARACTERISTICS

Variable	CABG group (n=102)	Hybrid (n=98)	P value
Age – year (mean ± SD)	63.9 ± 8.4	63.1 ± 8.2	0.43
Female sex (%)	28.4	20.4	0.19
BMI (mean ± SD)	29.1 ± 4.2	28.2 ± 3.3	0.07
Medical history (%)			
Diabetes	30.4	25.5	0.44
Hypertension	82.4	88.8	0.2
Smoking	35.3	30.6	0.48
History of ACS	57.8	53.1	0.49
Prior stroke	4.9	4.1	0.95
Carotid artery disease	11.8	9.2	0.55
Stable CAD	83.3	85.7	0.64
Unstable CAD	16.7	14.3	0.64
LVEF (mean ± SD)	50.7 ± 7	49.8 ± 6.3	0.37
EuroScore (mean ± SD)	3.4 ± 2	3.1 ± 2.1	0.23

RESULTS

ANGIOGRAPHIC CHARACTERISTICS

Variable	CABG group (n=102)	Hybrid (n=98)	P value
2 – VD (%)	46.1	45.9	0.98
3 – VD (%)	53.9	54.1	0.98
No. of lesions (mean ± SD)	3.7 ± 1.2	4.0 ± 1.4	0.16
LAD occlusion (%)	29.4	22.4	0.44
No. CTO (%)			
- RCA	6.9	6.1	0.83
- Cx	10.8	8.2	0.28
Syntax Score (mean ± SD)	22.8 ± 5.3	23.4 ± 6.3	0.48

RESULTS
PROCEDURAL CHARACTERISTICS

Variable	CABG group (n=102)	Hybrid (n=98)	P value
Revascularization per protocol (%)	100	93.9	
CABG			
Total grafts (mean ± SD)	2.6 ± 0.7	1.2 ± 0.7	N/A
Arterial grafts (mean ± SD)	1.6 ± 0.9	1.1 ± 0.1	N/A
Complete arterial revascularization (%)	24.5	-	N/A
Postprocedure LIMA patency (%)		97.8	N/A
PCI			
No. treated lesions (mean ± SD)	-	2.0 ± 0.9	N/A
No. stents used (mean ± SD)	-	2.3 ± 1	N/A
Successful PCI (%)	-	92*	N/A
Overall			
Complete revascularization (%)	78.4	78.6	0.84
Total drainage (ml)	1168 ± 486	1018 ± 730	0.1
Time MIDCAB to PCI, h (mean ± SD)	-	21 ± 5.7	N/A
Surgery diuration, h (mean ± SD)	3.68 ± 0.9	2.5 ± 1	0.001

* Includes 6 patients without PCI due to crossover to CABG

RESULTS

IN-HOSPITAL OUTCOME

Variable	CABG group (n=102)	Hybrid (n=98)	P value
Blood transfusion (%)	26.5	19.4	0.23
Renal failure (%)	0	1.0	0.98
MI perioperative (%)	3.9	5.1	0.69
Stroke	0	0	
Death	0	0	
In-hospital stay, days (mean ± SD)	8.9 ± 5.6	8.8 ± 4.3	0.88

RESULTS

FOLLOW UP OUTCOME

Variable	CABG group (n=102)	Hybrid (n=98)	P value
Follow up duration, months (mean ± SD)	12.6 ± 0.4	12.9 ± 0.5	
Angina status			
Freedom from angina, (%)	90.2	86.7	0.44
CCS I (%)	4.9	10.2	0.18
CCS II (%)	4.9	3.1	0.72
Re-hospitalization (%)	4.9	6.1	0.71
LVEF (mean ± SD)	49.2 ± 5.9	50.2 ± 5.9	0.25

RESULTS

PRIMARY ENDPOINT - FEASIBILITY

- % of patients with completed hybrid revascularization procedure

93.9%

- % of conversion to standard CABG

6.1%

Reasons:

- LAD not visible through the minithoracothomy incision – 2 pts.
- Hemodynamically unstable when preparing LAD for grafting. Recurrent VTs. Emergency conversion to full sternotomy – 1 pts.
- LIMA damaged during endoscopic harvesting – 1 pts.
- Patient did not tolerate single lung ventilation – 1 pts.
- Surgeons decision 'on table' – 1 pts.

RESULTS

PRIMARY ENDPOINT - SAFETY

- Major Adverse Cardiac Events at 12 months

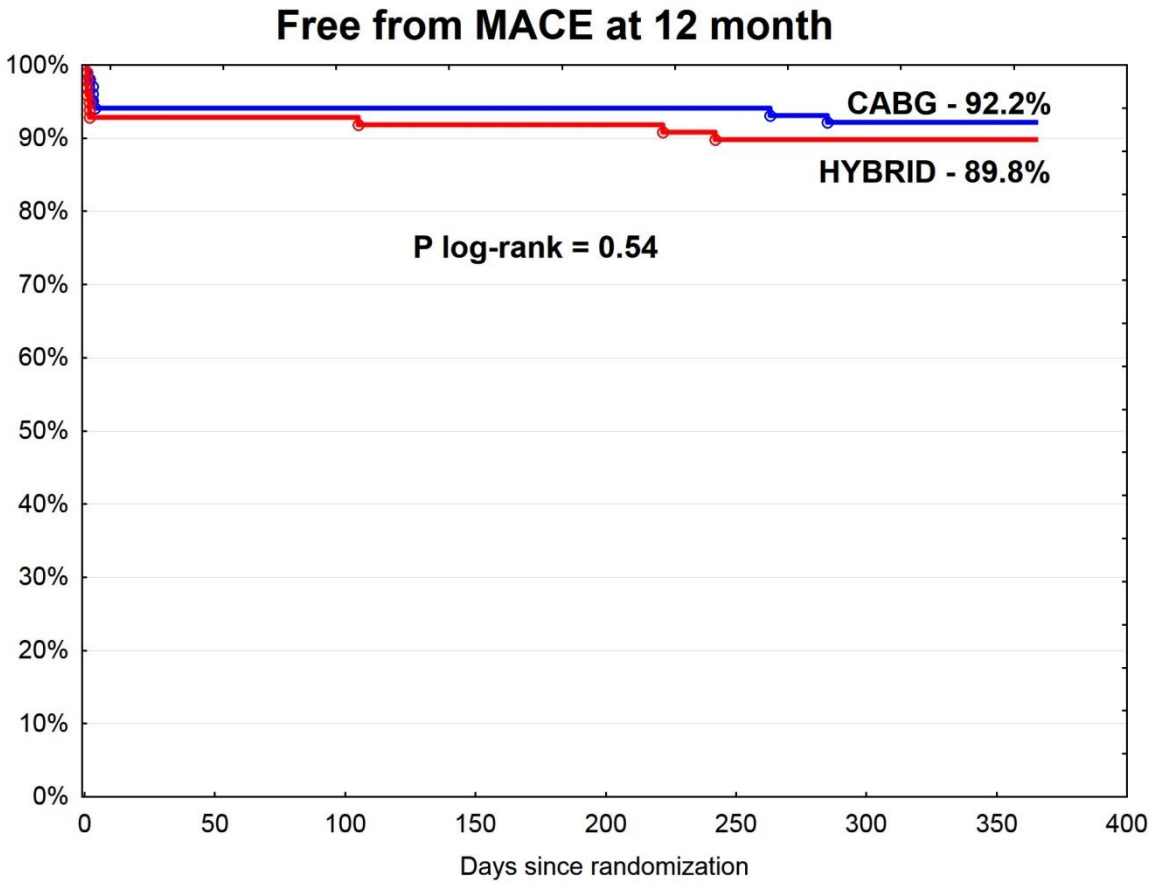
Variable (%)	CABG group (n=102)	Hybrid (n=98)	P value
Death	2.9	2.0	NS
MI*	3.9	6.1	NS
Stroke	0	0	NS
TVR	0	2.0	NS
Major bleedings	2.0	2.0	NS

* Includes perioperative MI

RESULTS

PRIMARY ENDPOINT - SAFETY

- Major Adverse Cardiac Events – death, MI, stroke, TVR, major bleedings



RESULTS

SECONDARY ENDPOINT

- Follow up angiographic measurements as patency of grafts and restenosis in revascularized segments

Variable	CABG group	Hybrid	P value
Angiographic follow up, %	81	85	0.41
LAD arterial graft patency, %	93*	94**	0.74
LAD arterial graft stenosis %	5	1	0.36
Other grafts patency, %	79***	-	N/A
Other grafts stenosis, %	2	-	N/A
In-stent occlusions, %	-	5.1	N/A
In-stent restenosis %		7.5	N/A
HYBRID patency score**** %	81	90	0.01

* 70 LIMA grafts and 13 RIMA grafts, ** Ao – LAD graft in one patient,
***SVG and non-LAD arterial grafts
**** HYBRID patency score = free of stenosis/occlusions grafted or stented arteries to total number of grafted and stented arteries ratio

CONCLUSIONS

- Hybrid coronary revascularization is feasible and safe in selected population of patients with MVD
- MIDCAB as a first stage procedure in patients with MVD considered for hybrid revascularization was not associated with more adverse events
- This first randomized pilot study on hybrid coronary revascularization shows promising results supporting the idea of hybrid coronary revascularization in patients with MVD