

One-Year Clinical Follow up of Patients with Drug-Eluting stents

**Thesis Submitted for partial fulfillment of the M.D. degree in
cardiology**

By

Ahmed Abbas Ahmed Abdel Bary
Master degree of cardiology

Under supervision of

Professor Dr: Assem Mohamed Fathey
Professor of cardiology - Ain Shams University

Professor Dr: Nabil Mahmoud Farag
Professor of cardiology - Ain Shams University

**Professor Dr: Salah Eldinn Hamdy
Demerdash**
Professor of cardiology - Ain Shams University

Doctor: Sameh Saleh Sabet
Assistant professor of cardiology - Ain Shams University

Doctor: Walid Abdel Azim El Hamady
Assistant professor of cardiology - Ain Shams University

**Cairo
Ain Shams University
2010**

Acknowledgement

Thanks to **ALLAH** who gave us the capability to continue this work.

Thanks to **Prof. Dr. Assem Fathey**, I always owe him much. Words are not sufficient to express my deep gratitude for him for his extraordinary support and help.

Thanks to **Prof. Dr. Nabil Farag** who helped me achieving progress in this thesis through his major contribution in the interventional part, clarifying all details and offering me hand on training in the Cath. Lab.

Many thanks to **Prof. Dr. Salah Eldinn Demerdash**, for his guidance, support, major contribution in the Nuclear part of this work and giving me experience in the field. He was always helpful and understanding.

Many thanks to **Dr. Sameh Sabet** for his contribution in the interventional part of this work. He was helpful and supportive and trusting all the way.

Many thanks to **Dr. Walid El Hamady** for his contribution in the interventional part of this work. He was helpful and supportive.

Thank to the Cath. lab team and Nuclear medicine team in Ain Shams University Specialized Hospital and DAF.

AHMED ABBAS

2010

LIST OF STUDIES ABBREVIATIONS

ABSORB	A Continuation in the Clinical Evaluation of the BVS Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions
ARTIST	Angioplasty versus rotational atherectomy for treatment of diffuse in-stent restenosis trial.
ARTS II	Sirolimus eluting stent implantation for patients with multivessel disease: rationale for the arterial revascularisation therapies study part II
BASKET-LATE :	The BASel Stent Kosten Effektivitäts Trial - LAte Thrombotic Events
C-SIRIUS	The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries
E-Five Registry	A World-Wide Registry With The Endeavor Zotarolimus Eluting Coronary Stent (eFive Registry)
E-SIRIUS	Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial
ENDEAVOR	The Medtronic Endeavor Drug Eluting Coronary Stent System in Coronary Artery Lesions
EVASTENT	Cost-effectiveness analysis of the sirolimus active stent in diabetic and non-diabetic patients
FIM	First In Man Study Of SES
FREEDOM	Future Revascularization Evaluation in Patients With Diabetes Mellitus—Optimal Management of Multivessel Disease

LIST OF STUDIES ABBREVIATIONS (Cont...)

FUTURE	First Use To Underscore restenosis Reduction with Everolimus
PROTECT Trial	Patient Related Outcomes With Endeavor Versus Cypher Stenting Trial
RAVEL	Randomized comparison of SES with standard stents for treatment of in-stent restenosis
REALITY	Prospective randomized, multicenter comparison study of the CYPHER sirolimus eluting and TAXUS paclitaxel eluting stent systems.
RESEARCH	Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital
SCAAR	Swedish Angiography and Angioplasty Registry
SIRIUS	Sirolimus eluting stents vs standard stents in patients with stenosis in native coronary arteries
SPIRIT First	A Clinical Evaluation of an Investigational Device. The Abbott XIENCE V® Everolimus Eluting Coronary Stent System in the Treatment of Patients With de Novo Native Coronary Artery Lesions
SPIRIT II:	Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions
SPIRIT V	Post-Marketing Evaluation of the XIENCE V® Everolimus Eluting Coronary Stent System in Europe
SYNTAX	Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery

LIST OF STUDIES ABBREVIATIONS (Cont...)

TAXI	Randomized comparison between paclitaxel and sirolimus stents in the real world of interventional cardiology
TAXUS I	Six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel eluting stent for de novo coronary lesions
TAXUS III	In-stent restenosis treated with stent-based delivery of paclitaxel incorporated in a slow-release polymer formulation.
TAXUS IV	One-year clinical results with the slow-release, polymer-based, paclitaxel-eluting TAXUS stent
ZEST	Zotarolimus-Eluting Stent Versus Sirolimus-Eluting Stent and PacliTaxel-Eluting Stent for Coronary Lesions

LIST OF ABBREVIATIONS

%DS	:	Percent Diameter Stenosis
ARC	:	Academic Research Consortium
BMS	:	Bare metal Stents
CABG	:	Coronary Artery Bypass Grafting
CAD	:	Coronary Artery Disease.
CD34	:	Cluster Determinant 34
CFR	:	Coronary Flow Reserve
cSNP	:	Coding Region SNP.
CTO	:	Chronic Total Occlusion
CXP	:	Cytochrome P
DCA	:	Directional Coronary Atherectomy
DES	:	Drug eluting stents
DM	:	Diabetes Mellitus
DNA	:	Deoxyribonucleic Acid.
ELCA	:	Excimer Laser-Assisted Coronary Angioplasty
FFR	:	Fractional Flow Reserve
FKBP	:	FK Binding Protein
G1	:	Gap 1 Phase Of Mitotic Cell Cycle/
ICAM	:	Intracellular Adhesion Molecules
IHD	:	Ischemic Heart Disease.
IL-1	:	Interleukin-1
IL-6	:	Interleukin-6
IPST	:	Intraprocedural Stent Thrombosis
ISNP	:	Intergenic SNP.
ISR	:	In-stent Restenosis
IVUS	:	Intravascular Ultrasound
LAD	:	Left Anterior Descending Artery
LCX	:	Left circumflex Artery
LST	:	Late Stent Thrombosis
LV	:	Left ventricle
LVEF	:	Left Ventricular Ejection Fraction
M	:	Mitosis Phase Of Mitotic Cell Cycle
MACE	:	Major Adverse Cardiac Events.
MCP	:	Macrophage Chemotaxis Protein
MCP	:	Monocyte Chemoattractant Protein
MI	:	Myocardial Infarction

LIST OF ABBREVIATIONS (Cont...)

MIP	:	Macrophage Inflammatory Protein
MLD	:	Minimum Lumen Diameter
MMP	:	Matrix Metalloproteinase
MPA	:	Mycophenolic Acid
MPI	:	Myocardial Perfusion Imaging
mRNA	:	Messenger Ribonucleic Acid
MSCT	:	Multi-slice CT
mTOR	:	Mammalian Target Of Rapamycin
NIH	:	Neointimal Hyperplasia
NQMI	:	Non Q myocardial infarction.
PBMA	:	Poly-N-Butyl Methacrylate (PBMA)
PCI	:	Percutaneous Coronary Intervention
PCR	:	Paris Course Of Revascularization
PDGF	:	Platelet Derived Growth Factor
PET	:	Position Emission Tomography
PEVA	:	Polyethylene-Vinyl-ncetate
PTCA	:	Percutaneous Transluminal Coronary Angioplasty
Pts	:	Patients
QCA	:	Qantitative Coronary Angiography
RVD	:	Reference Vessel Diameter
S	:	Synthesis Phase Of C Mitotoic Cell Cycle/
SES	:	Sirolimus Eluting Stent
SMC	:	Smooth Muscle Cell
SNPs	:	Single nucleotide Polymorphisms.
SPECT	:	Single Photon Emission Computed Tomography
Tc99m	:	Technetium 99
TNF	:	Tumor Necrosis Factor
TLR	:	Target Lesion Revascularization
TVR	:	Target Vessel Revascularization
US	:	United States
VCAM	:	Vascular Cell Adhesion Molecule
VEGF	:	Vascular Endothelial Growth Factor.

LIST OF CONTENTS

Title	Page No.
- Introduction and Aim of the work.....	1
- Review of literature	5
Restenosis	5
Drug eluting stents	44
- Patients and Methods	98
- Results	106
- Discussion	123
- conclusion	131
- Recommendation	132
- Summary	133
- References.....	137
- Arabic Summary.....	—

LIST OF FIGURES

Fig. No.	Title	Page No.
1-	Pathophysiological mechanisms of restenosis	18
2-	The Glagov phenomenon.....	19
3-	Divergent processes of vascular repair after balloon angioplasty and stenting of an atherosclerotic vessel	20
4-	Neointimal proliferation following arterial injury	30
5-	Patterns of ISR	32
6-	Schematic representation of different modalities of drug-eluting stent platforms	53
7-	The leading processes of restenosis and correspondent inhibitory effects of different biological agents	57
8-	The Three components of Cypher Stent	59
9-	The Bx VELOCITY Stent	59
10-	The Cypher Stent	60
11-	The Drug Carrier Vehicle for Cypher Stent	61
12-	Controlled Sirolimus Elution From Cypher Stent	62
13-	Mechanism of Action of Sirolimus.....	63
14-	Sirolimus – FKBP Binds to TOR and Inhibits Proliferation	64
15-	FIM: 4 -year Angiographic Follow-up	66
16-	FIM: 2-year Angiographic Follow-up	67
17-	IVUS Analysis (3-D)	71
18-	The cell cycle can be blocked at different phases to prevent the exaggerated cell division and proliferation in the stented artery	73
19-	Comparison between both groups as regarding number of diseased vessels.....	114
20-	Comparison between both groups as regarding diseased vessel.....	115

LIST OF FIGURES (cont...)

Fig. No.	Title	Page No.
21-	Comparison between both groups as regarding stent length, diameter, deployment pressures and stent/lesion length ratio	116
22-	Comparison between both groups as regarding stent deployment technique either direct stenting or PTCA first.....	117
23-	Comparison between both groups as regarding lesion types	118
24-	Comparison between both groups as regarding stress test and positive result in relation to instant restenosis.....	119
25-	Comparison between both groups as regarding TLR in relation to follow up time.....	120
26-	Comparison between incidence (ISR)TLR and DM.....	122
27-	Comparison between both groups as regard QMI	123
28-	Comparison between both groups as regarding frequency of NQMI and timing of follow up.	124
29-	Comparison between both groups as regard Positive symptomatology.....	125
30-	Comaprison between both groups as regarding repeated hospitalization for a cardiac cause	126

LIST OF TABLES

Tab. No.	Title	Page No.
1-	Definitions used for angiographic restenosis	37
2-	Risk Score for late stent thrombosis.....	91
3-	Comparison between both groups as regarding Demographic & Clinical Data	111
4-	Comparison between both groups as regarding Angiographic Data.....	113
5-	Comparison between both groups as regarding Stent data & Technique of deployment	116
6-	Comparison between both groups as regarding Lesion types.....	118
7-	Comparison between both groups as regarding stress test and positive result in relation to instent restenosis	119
8-	Comparison between both groups as regarding Target lesion revascularization.....	120
9-	Comparison between DM and association with clinical Instent restenosis(TLR) in group B	121
10-	Comparison between both groups as regarding QMI.	122
11-	Comparison between both groups as regarding Non QMI	123
12-	Comparison between both groups as regarding Positive symptomatology	124
13-	Comparison between both groups as regarding repeated hospitalization for a cardiac cause.....	125
14-	Comparison between both groups as regarding cardiac mortality.....	126

LIST OF TABLES (cont...)

Tab. No.	Title ⁱⁱⁱ	Page No.
15-	Prevalence of risk factors favouring instent restenosis in our study compared to others	129
16-	In-stent restenosis rate in different series	130

INTRODUCTION
AND AIM OF THE WORK

REVIEW OF LITERATURE

PATIENTS AND METHODS
