

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

بسم الله الرحمن الرحيم





MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



Cost Effectiveness Analysis of Adding Sofosbuvir to Pegylated Interferon plus Ribavirin in Treatment of Chronic Hepatitis C Patients

A Thesis

Submitted for Fulfillment of

Doctor of Philosophy Degree

In Pharmaceutical Sciences (Clinical Pharmacy)

By

Heba Ali Abdel-Aziz ElRamly
M.Sc. Pharm. Sci. (Clinical Pharmacy), 2011



Cost Effectiveness Analysis of Adding Sofosbuvir to Pegylated Interferon plus Ribavirin in Treatment of Chronic Hepatitis C Patients

A Thesis

Submitted for Fulfillment of

Doctor of philosophy degreeIn Pharmaceutical Sciences

(Clinical Pharmacy)

By

Heba Ali Abdel-Aziz ElRamly

M.Sc. Pharm.Sci. (Clinical Pharmacy), 2011

Under Supervision of:

Prof. Dr. Manal Hamed El-Hamamsy

Professor of Clinical Pharmacy, Faculty of Pharmacy, Ain Shams University

Prof. Dr. Gouda Kamel Helal

Prof. of Pharmacology, and Dean of the Faculty of Pharmacy, Heliopolis University

Prof. Dr. Soheir Abol Azm

Prof. of Pharmacology

Faculty of Medicine, Cairo University

Prof. Dr. Mohamed Mahmoud Al- Kassas

Professor of Endemic Medicine, Faculty of Medicine, Helwan University

Assoc. Prof. Sara Mahmoud Zaki

Associate Professor of Clinical Pharmacy, Faculty of Pharmacy, Ain-Shams University

2021

Acknowledgments

I thank "Allah" for granting me the power to accomplish this work.

First and foremost, I am extremely grateful for *Prof. Dr. Manal El Hamamsy*, Professor of Clinical Pharmacy, Faculty of Pharmacy, Ain Shams University, for her valuable scientific supervision, constructive advice, and continuous guidance throughout the work and for always having the time to help in every possible mean. I am forever indebted for giving me the opportunity and for believing in me.

My deepest gratitude and appreciation are expressed to *Prof. Dr. Gouda Kamel Helal*, Professor of Pharmacology, Faculty of Pharmacy, Al-Azhar University, Head of the Clinical Pharmacy Department and Dean of the Faculty of pharmacy, Heliopolis University for his divine support and for kindly supplying help whenever needed. His immense knowledge and plentiful experience guided me immensely throughout the work. I am really thankful for his aspiring guidance that helped me in all the time of research through this work and before. Couldn't ask for better mentor.

I would like to acknowledge my indebtedness and render my warmest thanks to *Prof. Dr. Soheir Abo El-Azm* for her encouragement and support. She was very generous with her time, effort ready to help in any and every way always with a kind smile and motherly feelings.

I would like to say a special thank you to *Prof. Dr. Mohamed ElKassas*, Professor of Endemic medicine, Faculty of Medicine, Helwan University. His research, and overall insights in this field have been of tremendous help throughout this work.

From the bottom of my heart, I would like to say a very Big Thank You for *Dr. Sara Shaheen*, Associate Professor of Clinical Pharmacy, Faculty of Ain Shams University. No words are enough to say how grateful I am for providing me time, guidance, and enlightening comments. I am thankful for her treasured support which was really influential in shaping my work and critiquing my results. Her valuable help and big effort are greatly appreciated. I also thank her for being a sounding board when required.

Furthermore, I would like to thank *Pharmacist Ahmed Kamal* whose tremendous help and efforts specially during the practical part are beyond description. I'm also grateful for all the patients who participated in this study.

I would like to thank my colleagues, friends and every person who contributed to this thesis in direct or indirect ways. I also thank the Clinical Pharmacy Department, Ain Shams University.

My deepest everlasting thanks and appreciation are for my beloved *Father*, *Mother* and *Brother* for their continuous support and encouragement throughout my life. Nouran, Jana and Yasseen, Thanks for being there, for bearing with me and for pushing me to do my best.

Finally, I owe more than Thanks to my Husband, *Dr. Khaled AbuZeid*, Ass. Professor of Pharmaceutics. I am beyond thankful for his continuous support and understanding, but also for more concrete things during this work. He has been the ultimate role model and I could not have done it without him.

 العالمين	ر ب ا	لله	الحمد	9

Table of Contents

Item	Page No.
List of Abbreviations	I
List of Figures	III
List of Tables	IV
Abstract	1
Introduction	3
Literature Review	5
1. Basic Virology	5
2. Transmission, Natural History and Manifestations of HCV	7
3. Symptomatology	8
4. Disease Progression	9
5. Global Prevalence and Economic Burden of HCV	11
6. Prevalence and Economic Burden in Egypt	13
7. Impact of HCV infection	15
8. Treatment and management of Hepatitis C	18
9. Pharmacoeconomics	28
10. Cost-effectiveness Analysis	30
Aim of Work	33
Methodology	34
Results	39
Discussion	70
Conclusions	82
Limitations and Recommendations	83
Summary	84
References	86
الملخص العريى	

List of Abbreviations

Abbreviation	Words	
1 st	First	
3rd	Third	
ANC	Absolute neutrophil count	
ANOVA	Analysis of Variance	
CEA	Cost-Effectiveness Analysis	
CER	Cost-Effectiveness Ratio	
СНС	Chronic Hepatitis C	
CI	Confidence Interval	
CTLs	Cytotoxic T-Lymphocytes	
CYP3A/4	Cytochrome P450 3A/4	
DAAs	Direct-Acting Antivirals	
DC	Decompensated Cirrhosis	
DCV	Daclatasvir	
DHS	Demographic Health Survey	
FDA	Food and Drug Administration	
GDP	Gross Domestic Product	
GT	Genotype	
HBV	Hepatitis B Virus	
НСС	Hepatocellular Carcinoma	
HCV	Hepatitis C Virus	
ICER	Incremental Cost-Effectiveness Ratio	
INC	Incremental	
IMPDII	Inhibitor of Inosine 5' Monophosphate	
IMPDH	Dehydrogenase	

Ph.D. Thesis 2021

Max	Maximum		
Min	Minimum		
МНС	Major Histocompatibility		
NHL	Non-Hodgkin's Lymphoma		
NIs	Nucleos(T)Ide Analogue Inhibitors		
NK	Natural Killer		
NNIs	Nonnucleos(T)Ide Analogue Inhibitors		
NRTI	Nucleoside Reverse Transcriptase Inhibitor		
NS	Non-Structural		
NS5B	Non-Structural Protein 5B		
OR	Odds Ratio		
pegIFN	Pegylated Interferon		
PSA	Probabilistic Sensitivity Analysis		
Q	Quadrant		
QALY	Quality-Adjusted Life-Years		
RASs	Resistance Substitutions		
RBV	Ribavirin		
SOF	Sofosbuvir		
SVR	Sustained Virologic Response		
WHO	World Health Organization		
WTP	Willingness to Pay		

Ph.D. Thesis 2021

List of Figures

No	Figure	Page
1	HCV Genome and Proteins	6
2	Disease progression in hepatitis C	11
3	Frequency distribution of different hepatitis C virus genotypes in Egypt	13
4	Timeline of hepatitis C virus prevalence in Egypt among adults	14
5	Replication cycle of hepatitis C virus and therapeutic targets	23
6	Cost-effectiveness plane	32
7	Overall Virological Response (SVR12) in All Treatment Groups	41
8	Baseline characteristics of patients based on SVR12	43
9	Association of Baseline characteristics with SVR12 in patients of Group1	45
10	Association of Baseline characteristics with SVR12 in patients of Group2	47
11	Association of Baseline characteristics with SVR12 in patients of Group 3	49
12	Cost effectiveness plane for group 1	57
13	Cost effectiveness plane for group 2	58
14	Cost effectiveness plane for group 3	59
15	Distribution of ICER for Group 1 (SOF/RBV/pegINF)	61
16	Distribution of ICER for group 2 (SOF / RBV)	62
17	Distribution of ICER for group 3 (SOF / DCV)	63
18	Contribution of Input Variables to the change in ICER for Group 1	64
19	Sensitivity of ICER for Group 1 to the change in input variables	65
20	Contribution of Input Variables to the change in ICER for Group 2	66
21	Sensitivity of ICER for Group 2 to the change in input variables	67
22	Contribution of Input Variables to the change in ICER for Group 3	68
23	Sensitivity of ICER for Group 3 to the change in input variables	69

Ph.D. Thesis 2021