

Recent Trends in Management of Gastrointestinal Stromal Tumors

Essay

*Submitted for partial fulfillment of master degree in
General Surgery*

By

Mohammed Yousuf M. El Sayed Khalil

M.B., B.Ch
Faculty of Medicine
Ain Shams University

Under supervision of

Prof. Dr. Mahmoud Ahmed El Shafei

*Professor of General Surgery
Faculty of Medicine
Ain shams University*

Dr. Mohamed Moh. Matar

*Lecturer of General Surgery
Faculty of Medicine
Ain Shams University*

**Faculty of Medicine
Ain Shams University
2015**



*First of all, I should express my deep thanks to **Allah**, without his great blessing, I would never accomplish my work, and to whom I relate any success in achieving any work in my life.*

*I would like to express my sincere appreciation and deepest gratitude to **Prof. Dr. Mahmoud Ahmed El Shafei** professor of General Surgery, Ain-Shams University, for his meticulous advice, continuous encouragement and valuable instructions, help, all through this work, honest assistance and active guidance and the precious time he had given in follow up of this work,*

*I am deeply grateful to **Dr. Mohamed Moh. Matar**, lecturer of General surgery, Ain Shams University ,of every word and every step in this work have been kindly arranged by his sincere effort, care .*

My truthful affection and love to My Family, who were and will always be, by my side all my life.



Contents

List of Abbreviations	i
List of Tables	ii
List of Figures	iii
Introduction and Aim of the Work	1
Pathophysiology of GIST.....	5
Presentation of GIST	45
Diagnosis of GIST	50
Current methods of treatment of GIST	88
Recent methods of treatment of GIST	110
Summary	148
References	151
Arabic Summary	--

List of Abbreviations

<i>Abbrev.</i>	<i>Full Term</i>
AIDS	Aquired immunodeficiency syndrome.
BID	Twice daily.
CB	Clinical benefit .
CGH	Comparative genomic hybridization.
CML	Chronic myeloid leukemia or Chronic myelogenous leukemia.
C_{min}	Plasma concentration.
CR	Complete response.
DFS	Disease free survival.
DOG 1	Discovered on GIST 1.
EUS	Endoscopic ultrasonography.
GANTs	Gastrointestinal autonomic tumors.
GI	Gastrointestinal.
GIT	Gastrointestinal tract.
GISTs	Gastrointestinal stromal tumors.
GIST/Ls	Gastrointestinal stromal tumors and leiomyomas,
GIPACTs	Gastrointestinal pacemaker cell tumors.
JM	Juxtamembrane.
HAE	Hepatic arterial embolization.
HPF	High power field.
HTERT	Human telomerase reverse transcriptase.
HTR	Human telomerase RNA component.
ICCs	Interstitial cells of Cajal.

List of Abbreviations (cont.)

IM	Imatinib Mesylate.
LMP	Low malignant potential.
MVD	Microvessel density.
OD	Once daily.
OS	Overall survival.
PD	Progressive disease.
PDGFRα	Platelet-derived growth factor receptor alpha.
PFS	Progression-free survival.
PR	Partial response.
RECIST	Response Evaluation Criteria in Solid Tumors .
RR	Response rate.
SD	Stable disease.
SMemb	Embryonic isoform of myosin heavy chain.
SMA	Smooth muscle actin.
SU	Sunitinib.
SUV_{max}	Maximum standardized uptake value.
TAP1	Telomerase-associated protein 1.
VEGFRs	Vascular endothelial growth factor receptors.

List of tables

<i>Table</i>	<i>Title</i>	<i>Page</i>
1	NIH risk stratification of primary GIST	33
2	Risk classification of progressive disease	35
3	Risk classification of progressive disease according to Joensuu	36
4	TNM classification of GIST	38
5	GISTs and their differential diagnosis	81
6	Differential Diagnosis for GIST	87
7	Treatment in localized and advanced phase of the different molecular subtypes of GIST	119
8	Tyrosine kinase inhibitors approved and in development for the treatment of GIST	129
9	Modified CT Response Evaluation Criteria	139

List of Figures

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
1	Distribution of GIST in the various portions of the gastrointestinal tract	12
2	A and B, Large gastrointestinal stromal tumor (GIST) gross pathology	13
3a	Histology of GIST	17
3b	Histology of GIST	19
4	Immunohistochemical staining for KIT in GIST	21
5	Mutations in GIST	22
6	Positive E2F1 immunostaining in malignant GIST	24
7	P27KIP1 expression in LMP GIST	26
8	P16 immunostaining in LMP GIST	27
9	Immunopositivity demonstration	29
10	Nomogram	37
11	Gastric GIST arises from the lesser curvature	52
12	Gastric GIST arises from greater curve	52
13	a large exophytic gastric GIST arises from the greater curve	54
14	Gastric GIST over the lesser curve	55
15	Jejunal GIST	57
16	A large intraluminal mass is seen in the stomach, with heterogeneous liver metastases	59
17	Benign GIST of gastric body	60
18	CT of GIST of the gastric antrum and body	61

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
19	CT of duodenal GIST	62
20	CT of GIST of gastric fundus	63
21	CT of GIST of the small bowel mesentery	64
22	CT of posterior gastric wall GIST	65
23	Gastric GIST arises from greater curve	65
24	Angiographic GIST	71
25	Endoscopic images of GIST	72
26	Endoscopic ultrasound of GIST	74
27	Spindle cell-type histologic pattern of GIST	79
28	Outlines a proposed treatment algorithm	89
29	Gastric Gist excision	93
30	Laparoscopic excision of Gist of lesser curvature of stomach	97
31	GIST of the antrum of the stomach	98
32	GIST of small intestine	100
33	Gist of Large intestine	101
34	Trans rectal approach of rectal Gist	102
35	Procedure of gastroscopic resection of GIST	106
36	Suggested algorithm for management of suspected gastrointestinal stromal tumors	112
37	Responding hepatic and peritoneal metastases in a patient with advanced gastrointestinal stromal tumor	120

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
38	hepatic artery embolization of GIST	133
39	Intraoperative photograph in the initial phase of a RFA of a liver metastasis from GIST	135
40	Responding hepatic metastasis with pseudoprogression in a patient with duodenal gastrointestinal stromal tumor	140
41	Recurrence with new intratumoral nodules in a patient with small bowel gastrointestinal stromal tumor	141

الطرق الحديثة في علاج أورام الجهاز الهضمي السدودية

رسالة

مقدمة للحصول على درجة الماجستير

في الجراحة العامة

مقدمة من

الطبيب / محمد يوسف محمد السيد خليل

بكالوريوس الطب و الجراحة
كلية الطب - جامعة عين شمس

تحت إشراف

الأستاذ الدكتور / محمود أحمد الشافعي

أستاذ الجراحة العامة
كلية الطب - جامعة عين شمس

الدكتور / محمد محمد مطر

مدرس الجراحة العامة
كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٥



Introduction and Aim of the Work





Pathophysiology of GIST





Diagnosis of GIST





Recent methods in treatment of GIST





Summary

