



# **PROSPECTIVE ANALYSIS OF FIRST LINE CHEMOTHERAPY OUTCOMES IN METASTATIC COLORECTAL CANCER CASES**

## **THESIS**

Submitted for partial fulfillment of master degree in Clinical  
Oncology and Nuclear Medicine

BY

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## عنوان

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# List of abbreviations

5,10-CH <sub>2</sub> -THF:	5,10-Methylenetetrahydrofolate
5-FU:	5 fluorouracil
ACS:	American Cancer Society
ADCC:	Antibody-dependent cell-mediated cytotoxicity
AgNORs:	Argyrophilic nucleolar organizing regions
AJCC:	American Joint Committee on Cancer
ALK:	Alkaline phosphatase
ALP:	Alkaline phosphatase
ASCO:	American Society of Clinical Oncology
ASR:	Age-standardized incidence rate
AUC:	Area under the curve
BSC:	Best supportive care
CAP:	College of American Pathologists
CEA:	Carcinoembryonic antigen
CEA:	Carcinoembryonic antigen

CES:	Carboxylesterase
CI:	Confidence interval
CR:	Complete response
CRC:	Colorectal cancer
CRM:	Circumferential resection margins
CT scan:	Computed tomography
CTCAE:	Common Terminology Criteria for Adverse Events
DCC:	Deleted in Colon Cancer gene
DFS:	Disease-free survival
dMMR:	Defective mismatch repair
dUTPase:	Deoxyuridine triphosphate nucleotidohydrolase
DNA:	Deoxyribonucleic acid
DPD:	Dihydropyrimidine dehydrogenase
ECOG:	Eastern Cooperative Oncology Group
EGFR:	Epidermal growth factor receptor
ECCO:	European Cancer Organization

## Appendix

EORTC:	European Organisation for Research and Treatment of Cancer
ESMO:	European Society for Medical Oncology
FDA:	Food and Drug Administration
FdUMP:	Fluorodeoxyuridine monophosphate
FP:	Fluoropyrimidines
FUDP:	Fluorouracil diphosphate
FUDR:	Floxuridine
GERCOR:	Groupe Coopérateur Multidisciplinaire en Oncologie
GI:	Gastrointestinal
GIT:	Gastrointestinal tract
GPCR:	Gharbiah Population-based Cancer Registry
HAI:	Hepatic artery infusion
HFS:	Hand-foot syndrome
HNPCC:	Hereditary non-polyposis colorectal cancer
HR:	Hazard ratio
IHC:	Immunohistochemistry

## Appendix

IMRT:	Intensity-modulated radioation therapy
INT-0089:	Intergroup trial-0089
IQR:	Interquartile range
IRR:	Incidence rate ratio
ITT:	Intent-to-treat
KRAS:	Kirsten ras oncogene homolog
LDH:	Lactate dehydrogenase
LDH:	Lactate dehydrogenase
LI:	Labeling index
LOH:	Loss of heterozygosity
LNR:	Lymph node ratio
LN:	Lymph nodes
LV:	Lecuvorin
M:	Distant metastasis
MAPK:	Mitogen-Activated Protein Kinases
mCRC:	Metastatic colorectal cancer
MECC:	Middle East Cancer Consortium



Mets:	Metastases
MIS:	Microsatellite instability
MMR:	Mismatch repair
MoAbs:	Monoclonal antibodies
MRF:	Mesorectal fascia
MRI:	Magnetic resonance imaging
MSI:	Microsatellite instability
MSI-H:	High-level microsatellite instability
MSI-L:	Low-level microsatellite instability
MSS:	Microsatellite stable
MTHFR:	Methylenetetrahydrofolate reductase
MVD:	Microvessel density
N:	Regional lymph node
NCCN:	National Comprehensive Cancer Network
NCCTG:	North Central Cancer Treatment Group
NCI:	National Cancer Institute
NCRPE:	National Cancer Registry Program of Egypt

## Appendix

NRAS:	Neuroblastoma RAS Viral Oncogene homolog
No:	Number
NOS:	Not otherwise specified
OPRT:	Orotate phosphoribosyl transferase
ORR:	Objective response rate
OS:	Overall survival
PCNA:	Proliferating cell nuclear antigen
PD:	Progressive disease
PDGF:	Platelet-derived growth factor
PDGFRs:	Platelet-derived growth factor receptors
PFS:	Progression-free survival
PIK3:	Phosphoinositol-3-kinase catalytic alpha subunit
PNI:	Perineural invasion
PR:	Partial response
PS:	Performance status
Pts:	Patients

## Appendix

RFA:	Radiofrequency ablation
SBRT:	Stereotactic body radiation therapy
SD:	Stable disease
SD:	Mean standard deviation
SEER:	Surveillance, Epidemiology, and End Results
T:	Tumor
Topo 1:	Topoisomerase-1
TP:	Thymidine phosphorylase
TGF- $\beta$ -RII:	Transforming growth factor— beta-RII
TS:	Thymidylate synthase
TTP:	Time to progression
UICC:	Union Internationale Contre le Cancer
UGT:	Uridine diphosphate glucuronosyltransferase
US:	The United States of America
VEGF:	Vascular endothelial growth factor
VEGFR:	Vascular endothelial growth factor receptor
WHO:	World Health Organization

Wt: Wild type

$^{90}\text{Y}$ : Yttrium 90

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Aim of  
work

## **Aim of work**

The aim of this work is to retrospectively analyze the various chemotherapeutic agents involved in the armamentarium of first line treatment of metastatic colorectal cancer in terms of: Overall survival, progression-free survival and toxicities; to explore the best options across the continuum of care for patients at Ain Shams University Hospitals.

# Chapter 1

## Epidemiology

### Incidence and mortality

Colorectal cancer (CRC) is the third most common cancer in men (746,000 cases, 10% of the total) and the second in women (614,000 cases, 9.2% of the total) worldwide. Almost 55% of the cases occur in more developed regions. There is wide geographical variation in incidence across the world and the geographical patterns are very similar in men and women: incidence rates vary ten-fold in both sexes worldwide, the highest estimated rates being in Australia/New Zealand (ASR “Age-standardized incidence rate” 44.8 and 32.2 per 100,000 in men and women respectively), and the lowest in Western Africa (4.5 and 3.8 per 100,000). **(Globocan 2012)**

Mortality is lower (694,000 deaths, 8.5% of the total) with more deaths (52%) in the less developed regions of the world, reflecting a poorer survival in these regions. There is less variability in mortality rates worldwide (six-fold in men, four-fold in women), with highest estimated mortality rates in both sexes in Central and Eastern Europe (20.3 per 100,000 for men, 11.7 per 100,000 for women), and the lowest in Western Africa (3.5 and 3.0 respectively). **(Globocan 2012)**