



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم

# بسم الله الرحمن الرحيم



**HANAA ALY**



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التوثيق الإلكتروني والميكروفيلم



# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# 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



**HANAA ALY**



# **Retrospective Analysis of Folfox versus Folfox and Cetuximab for Patients with Metastatic Cancer Colon**

**Thesis**

*Submitted for Partial Fulfillment of Master Degree in  
Clinical Oncology*

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## *List of Abbreviations*

| Abb.          | Full term                                           |
|---------------|-----------------------------------------------------|
| ACG .....     | American College of Gastroenterology                |
| AFAP .....    | Attenuated FAP                                      |
| AJCC .....    | American Joint Cancer Committee                     |
| ATE.....      | Arterial thromboembolism                            |
| CAPOX .....   | Capecitabine and oxaliplatin                        |
| CEA .....     | Carcinoembryonic antigen                            |
| COX-2.....    | Cyclooxygenase-2                                    |
| CRC .....     | Colorectal cancer                                   |
| CT .....      | Computed tomographic                                |
| EGFR.....     | Epidermal growth factor receptor                    |
| EMA.....      | European Medicines Agency                           |
| FAP .....     | Familial adenomatous polyposis                      |
| FDA .....     | Food and Drug Administration                        |
| FDG .....     | Fluorodeoxyglucose                                  |
| FIT .....     | Fecal immunochemical test                           |
| FOBT .....    | Fecal occult blood test                             |
| FOLFIRI.....  | Irinotecan and infusional 5-FU/folinic acid         |
| FOLFOX-4..... | Oxaliplatin plus infusional (5-FU) and folinic acid |
| GPCR.....     | Gharbiah Population-based Cancer Registry           |
| HNPCC.....    | Hereditary non-polyposis colorectal cancer          |
| IARC .....    | International agency for Research on cancer         |
| IFL .....     | Irinotecan, 5-fluorouracil, and leucovorin          |
| IHCs .....    | Immunohistochemistry techniques                     |
| ITT .....     | Intention-to-treat                                  |
| LAC.....      | Laparoscopic-assisted colectomy                     |
| LVI.....      | Lymphovascular invasion                             |
| MCRC .....    | Metastatic colorectal cancer                        |
| MMR.....      | Mismatch repair                                     |

## *List of Abbreviations Cont...*

| Abb.         | Full term                              |
|--------------|----------------------------------------|
| MSI .....    | Microsatellite instability             |
| NSAIDs ..... | Nonsteroidal anti-inflammatory drugs   |
| OS .....     | Overall survival                       |
| pCR.....     | Pathological complete regression       |
| PFS .....    | Progression-free survival              |
| TEM.....     | Transanal endoscopic microsurgery      |
| TME.....     | Total mesorectal excision              |
| TRUS .....   | Transrectal ultrasound                 |
| UICC .....   | Union for International Cancer Control |
| VEGF .....   | Vascular endothelial growth factor     |

# INTRODUCTION

The epidermal growth factor receptor (EGFR) targeting monoclonal antibody cetuximab improves overall survival when added to standard chemotherapy used in the treatment of metastatic colorectal cancer (mCRC). (Oxaliplatin and Cetuximab in First-Line Treatment of mCRC) study demonstrated that the tumor mutation status of codons 12 and 13 of the *KRAS* gene was predictive for the activity of cetuximab combined with oxaliplatin plus infusional (5-FU) and folinic acid (FOLFOX-4) in the first-line treatment of mCRC (*Bokemeyer et al., 2009*).

Cetuximab activity is limited to patients whose tumors were *RAS* wild type. It was also consistent with retrospective analysis in mCRC involving cetuximab administered as monotherapy in patients who had failed prior chemotherapy and as first-line treatment in combination with irinotecan and infusional 5-FU/folinic acid (FOLFIRI). These analyses demonstrated improved outcome for patients with *RAS* wild-type mCRC who received treatment including cetuximab, with overall survival improved in both studies (*Van Cutsem et al., 2010*).

At the time of initial reporting, overall survival data were not available for the study. In addition, *RAS* tumor mutation data were not completely available for all of patients in the intention-to-treat (ITT) population. Although comparison of the

baseline characteristics and efficacy data suggested that the *RAS* population was essentially representative of the ITT population, it was believed that the accuracy and strength of the conclusions would be increased if tumor *KRAS* mutation status could be determined for a higher proportion of patient samples. This study therefore reports an updated analysis based on the consideration of overall survival and other end points in an increased population of patients for which tumor *RAS* mutation status has been determined (*Lievre et al., 2008*).

Patients were randomly assigned to receive FOLFOX-4 (oxaliplatin 85 mg/m<sup>2</sup>; folinic acid 200 mg/m<sup>2</sup>, followed by 5-FU, as a 400 mg/m<sup>2</sup> intravenous bolus then a 600 mg/m<sup>2</sup> infusion over 22 h, days 1 and 2 of a 14-day cycle) with or without cetuximab (initial dose 400 mg/m<sup>2</sup> and 250 mg/m<sup>2</sup>/week thereafter), until disease progression or unacceptable toxicity, as first-line treatment for mCRC. Response was assessed radiologically, every 12 weeks (*De Roock et al., 2008*).

The addition of cetuximab to first-line FOLFOX chemotherapy statistically significantly improved PFS, OS, and ORR in pts with *RAS* wt mCRC. The TAILOR study met its primary objective and confirms cetuximab in combination with chemotherapy as a standard-of-care first-line treatment regimen for patients with *RAS* wt mCRC (*Qin et al., 2016*).