UNIVERSITI TEKNOLOGI MARA

IMPACT OF CHEMOTHERAPY AND OTHER PROGNOSTIC FACTORS ON SURVIVAL IN ADVANCED NON-SMALL CELL LUNG CANCER AT HOSPITAL KUALA LUMPUR, MALAYSIA

NIDA SAJID ALI BANGASH

Thesis submitted in fulfilment
of the requirement for the degree of
Master of Science

Faculty of Pharmacy

January 2017

ABSTRACT

Determining vital prognostic factors of survival including appropriate chemotherapy regimens in patients with non-small cell lung cancer (NSCLC) is challenging due to increased prevalence and progressive nature of disease. The main objectives of this present study were to describe the prognostic factors of adult NSCLC patients via their demographic and medical data, to investigate the relationship (association and prediction) of NSCLC stage, epidermal growth factor receptor (EGFR) status and Eastern Cooperative Oncology Group (ECOG) performance status (PS) among independent variables from patients' demographic and medical data, to determine the impact of treatment groups, CT groups and lines of CT groups on survival in adult NSCLC patients, to compare survival among treatment groups, CT groups and lines of CT groups in adult NSCLC patients and to assess the impact of study predictor variables on death. This retrospective cohort study included adult (≥ 18 years old) NSCLC patients (n = 235) using purposive sampling method. The study was conducted in the Radiotherapy and Oncology Clinic and ward at Hospital Kuala Lumpur (HKL), Malaysia. The mean (± SD) age of adult NSCLC patients was 56.7 (±10.1) years old. Majority were males, Chinese, had adenocarcinoma, stage IV NSCLC, non-smokers with unknown EGFR status and ECOG PS score of 2. The most common site of metastasis was lung followed by bone, and most prevalent co-morbidity was hypertension (HTN). Using Chi-square test, only sites of metastasis had significant association with NSCLC stage. For EGFR status, independent study variables that had significant association were age, gender, histopathology, smoking status and ECOG PS. Furthermore, ECOG PS was significantly associated with age, body weight and EGFR status. Using multinomial logistic regression analysis, the site of metastasis was the only significant predictor to NSCLC stage. Gender and histology were the significant predictors for EGFR status. The findings of binary logistic regression showed that histopathology was the only significant predictor for EGFR status. The Kaplan Meier (K-M) survival test and log-rank test suggested that for treatment groups, CT improved overall survival (OS); for CT groups, non-platinum based (NPB) therapy showed better OS; and for lines of CT groups, only first-line tyrosine kinase inhibitors (TKIs) showed superiority for OS. The results of Cox proportional hazard (PH) regression model for treatment groups, lines of CT groups and selected study independent variables from demographic and medical data concluded that CT, RT (treatment groups), first-line TKIs, Indian (ethnicity), stage IIIA NSCLC, adenocarcinoma lung cancer (histopathology), positive-negative EGFR status and ECOG PS score of 0 and 2 were significant predictors forbetter survival, whereas PB therapy (chemotherapy groups), Malay and Chinese (ethnicity) and smokers (smoking status) were significant predictors for worse survival in locally advanced or metastatic NSCLC patients. The present study suggested the CT administered and various prognostic factors are capable of influencing survival in adult NSCLC patients.

ACKNOWLEDGMENT

Praise to ALLAH, the Majesty; for His uncountable blessings and best prayers that He bestowed on me throughout the journey of MSc (Clinical Pharmacy) completion. I would like to express the deepest admiration to my main supervisor, Professor Dr. Nahlah Elkudssiah Ismail, who has the attitude and the substance of a genius; she continuously and convincingly conveyed a spirit of adventure in regard to research and an excitement in regard to teaching. Her assistance that will not be forgotten throughout my life stands as a benchmark for my future career. Without her leadership, assistance and management this thesis would not have been possible. Next, I would like to thank my co-supervisor, Dr. Natasha Hashim, for her help and valuable time throughout the research.

My appreciation goes to the Research Management Institute (RMI), Universiti Teknologi MARA (UiTM), Clinical Research Centre (CRC) and staff of Radiotherapy and Oncology Clinic of Hospital Kuala Lumpur, Malaysia, for their support in research ethics approval and data collection process. Thank-you to the Faculty of Pharmacy and Institute of Postgraduate Studies (IPSIS), UiTM, for the monetary support to attend conferences held locally.

I owe my greatest gratitude to all colleagues and friends especially Nurfarahana Binti Abdul Malik who supported me throughout this journey. Last but not least, I am indebted to my parents, brother and sisters for their encouragement and support. Each member of my family truly deserves my deepest appreciation for their continuous supplications for me. Their much needed motivation, assistance, love and sacrifices have been the pillar for me during the study and that's what made to achieve more than I ever thought possible.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 OVERVIEW

Lung cancer is a malignant tumour that develops in tissues of the lungs, usually in the cells lining air passages. Lung cancer is broadly divided into two major types which are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) (National Cancer Institute (NCI) USA, 2016). NSCLC is a group of lung cancers in which the cells found in the tumour do not look small under a microscope as opposed to another less common type of SCLC, which is characterised by the small size of the cells that it is composed of. NSCLC is more frequent and was reported in 80 % to 85 % of all lung cancer cases (European Society for Medical Oncology (ESMO), 2014).

Lung cancer is a major public health problem. Lung cancer was the most common cancer worldwide contributing 13 % of the total number of new cases diagnosed in 2012, 58 % of which occurred in the less developed regions (World Cancer Research Fund (WCRF) International, 2015). Lung cancer is on the rise in the context of mortality worldwide (Jemal et al., 2002). Lung cancer is also the leading cause of cancer related mortality in both genders. According to World Health Organization (WHO) (2009), mortality of lung cancer increased worldwide from 1.3 million deaths in 2004 to 1.4 million deaths in 2008. In 2012, world lung cancer mortality was estimated to be 1.59 million deaths approximately, 19.4 % of the total reported death related cancer (GLOBOCAN, 2012). By 2035, it is expected that people suffering from lung cancer will increase up to 24 million worldwide (Jemal et al., 2011).

The prevalence of lung cancer showed variable trends across disparate populations worldwide. According to American Cancer Society (ACS), in the United States of America (USA) in 2016, 224 390 estimated new cases of lung cancer were reported in both genders with 117 920 (52.6 %) new cases among males and 106 470 (47.4 %) new cases among females. The estimated deaths due to lung cancer in both genders were 158 080 with 85 920 (54.4 %) deaths among males and 72 160 (45.6 %)