UNIVERSITI TEKNOLOGI MARA

IMMUNOHISTOCHEMICAL STAINING PATTERN OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) PROTEIN OVEREXPRESSION IN NON SMALL CELL LUNG CANCER.

MUHAMAD ASRI BIN ABD RAHMAN

AUGUST 2012

1] ACKNOWLEDGEMENT

TABLE OF CONTENTS

4] ABSTRACT

Lung cancer is the leading cause of cancer death worldwide and non-small cell lung cancer (NSCLC) accounts for almost 80% of such deaths. Non–small cell lung cancer (NSCLC) is considered as a heterogeneous disease; where patients with similar clinical and pathologic features show different outcomes: some are cured, whereas in others, the cancer recurs. Hence, some patients may receive potentially toxic chemotherapy unnecessarily. The discovery of the epidermal growth factor receptor (EGFR) signaling pathway as a therapeutic target leads to the development of small molecule tyrosine kinase inhibitors (TKIs). However, EGFR protein overexpression in NSCLC varies in previous studies with some contradicting results. The aim of this study is to determine the expression pattern (membranous vs. cytoplasmic) and heterogeneity (percentage of positive tumour cells) of EGFR immunohistochemical staining in adenocarcinoma type of non small cell lung carcinoma. The samples were formalin-fixed and paraffin-embedded tissue. The tissues were sectioned at 3 to 5μ thick and pre-treated according to the protocoal. Tissue specimens were stained with EGFR marker using the validated EGFR pharmDx™ (Dako, Denmark) assay, which utilizes a standard staining protocol (Dako, EGFR pharmDx™). The pattern of membrane and cytoplasmic staining were assessed in each tumor sample. Statistical analyses were used to analyze the association of EGFR expression patterns with each of the pathologic and clinical characteristics, respectively. This study provides pilot local data for identification of high risk groups in which the likely clinical behaviour may be predicted and also in the identification of high risk groups of patients for whom specific therapy might be necessary. The results showed that over expression of EGFR protein is associated with

5] INTRODUCTION

Lung cancer is the leading cause of cancer death worldwide and non-small cell lung cancer (NSCLC) accounts for almost 80% of such deaths (Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM, 2010). In Malaysia, lung cancer became the third most common cause of cancer death. (O Zainal Ariffin 2011). Lung cancer is the most frequent cancer among male (Ferlay et al. 2010; O Zainal Ariffin, 2011), and Chinese in Malaysia (O Zainal Ariffin 2011). Most of the patients were diagnosed at older age and at stage 4 (O Zainal Ariffin 2011).

Non–small cell lung cancers (NSCLC) such as lung adenocarcinoma, squamous cell carcinoma and large cell carcinoma are considered as heterogeneous diseases; where patients with similar clinical and pathologic features show different outcomes: some are cured, whereas in others, the cancer recurs (Brundage, Davies, Mackillop WJ. 2002). Only 15% from the diagnosed patients survive for 5 years (http://seer.cancer.gov/statfacts/html/lungb.html, cited date: 01 December 2012). According to the World health Organization (WHO) 2004, lung adenocarcinoma also shows heterogenous histological growth pattern: , acinar, papillary, solid with mucin production and bronchioloalveolar pattern (Travis 2004).

A few biomarkers have been studied on to comprehend the pathology and physiology of lung cancer and finding cure for treatment. One of them is epidermal growth factor receptor protein which is believed to be over expressed along the way of cancer progress. The discovery of the epidermal growth factor receptor (EGFR) signaling pathway enhanced the development of personalized target therapy of small molecule tyrosine kinase inhibitors (TKIs). However, EGFR protein over expression in NSCLC varies in previous studies with some contradicting results.