# EGFR MUTATIONS IN NON SMALL CELL LUNG CANCER PATIENTS IN SOUTH AFRICA

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## DECLARATION

I, Sze Wai Chan declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Internal Medicine / Medical Oncology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

SZE WAI CHAN

1st Sept. 2014

DATE

## DEDICATION

This work is dedicated to my loving parents

## ABSTRACT

**Introduction:** Tyrosine kinase inhibitors and EGFR mutations has changed the treatment approach to lung cancer globally. This retrospective study will look at factors associated with EGFR mutations and define the EGFR mutation rate in South Africa.

**Methods:** Retrospective record review from NSCLC patients in South Africa who were tested for EGFR mutations at Lancet Laboratories during 1st September 2009 to 30th June 2012. Chi-squared test was used to determine association with categorical variables. Kaplan- Meier survival analysis was done for OS and PFS between EGFR mutation positive and negative patients. Cox proportional hazards were used for subgroup analysis. Treatment practices and response were described.

**Results:** 170 lung cancer samples were evaluable for EGFR mutation and 37 were EGFR mutation positive (21.8%). There were 22 (59.5%) exon 19 deletions, 11 (29.7%) L858R mutations, two G719X mutations, one S768I mutation and one exon 20 insertion. The median age was 63 (range 27-85). There were more females (55.6%) than males (44.4%) sent for mutation testing. Most patients were whites (71%), followed by blacks (18.3%), and other race (10.7%). 85% of all NSCLC samples tested were adenocarcinoma. None of the squamous cell carcinoma tested was positive for EGFR mutation. Smoking status was inversely proportional to EGFR mutation status ($p<0.001$). Over 60% patients received chemotherapy first and second line and responses decreased with each line of chemotherapy. Median PFS and OS were not different between the EGFR mutation positive and negative groups (6.85 versus 6.8 months; HR 1.6; 95% CI 0.70-3.65; p=0.2543 and 11.5 versus 12.9 months; HR 0.70;

95% CI 0.28-1.75; p=0.44, respectively). On multivariate analysis, only non-white race was associated with decrease in OS (HR 6.66; 95% CI 2.31-19.19; p=0.0004).

**Conclusion:** EGFR mutation rate in South African lung cancer patients was 21.8%. 89% of all EGFR mutations were either exon 19 deletions or L858R point mutations. Most EGFR mutations were associated with adenocarcinoma of the lung in non-smokers. These findings were consistent with current literature in western countries. Treatment practice remained chemotherapy based, with few patients receiving EGFR TKIs. Efforts should be made to prioritized targeted treatment approach in lung cancer in South Africa.

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## DEFINITION OF TERMS

Smoking status was defined according to the IPASS and the Spanish screening study from Rosell et al (21, 23).

NEVER SMOKERS: < 100 lifetime cigarettes

FORMER SMOKERS: ≥ 1 year since cessation

CURRENT SMOKERS: Still smoking, or < 1 year since cessation

FORMER LIGHT SMOKERS: stopped smoking at least 15 years previously and had a total of ≤ 10 pack-years of smoking

RESPONSE RATE: Measured by Response Evaluation Criteria in Solid Tumours (RECIST) 1.0 criteria (99)

PROGRESSION FREE SURVIVAL (PFS): From the date of first treatment to the earliest sign of disease progression, as determined by means of the RECIST 1.0

OVERALL SURVIVAL (OS): From the date of first treatment until death from any cause

LOST TO FOLLOW UP: Patient did not return for follow up visits AND unable to contact patient by telephonic means in 3 separate consecutive occasions

## ABBREVIATIONS

ALK: Anaplastic Lymphoma Kinase

ASR: Age Standardized incidence Rate (per 100,000 population)

DCR: Disease Control Rate

ECOG: Eastern Cooperative Oncology Group

EGFR: Epidermal Growth Factor Receptor

EMA: European Medicines Agency

ESMO: European Society for Medical Oncology

FACT-L: Functional Assessment of Cancer Therapy-Lung (100)

FDA: Food and Drug Administration of USA

HR: Hazard Ratio

IARC: International Agency for Research on Cancer

IHC: Immunohistochemistry

ITT: Intention To Treat

LCINS: Lung Cancer In Never Smokers

LR: Lifetime Risk of developing a cancer before the age of 74 years

NSCLC: Non-Small Cell Lung Cancer

OR: Odds Ratio

OS: Overall Survival

PFS: Progression Free Survival

PM: Particulate Matter

RR / ORR: Response rate / Overall Response Rate

SASCRO: South African Society of Clinical and Radiation Oncology

SASMO: South African Society of Medical Oncology

SEER: Surveillance, Epidemiology, and End Results

TKI: Tyrosine Kinase Inhibitors

TTP: Time To Progression

WHO: World Health Organization