PREVALENCE OF THE SYNONYMOUS EGFR Q787Q VARIANT IN MEXICAN PATIENTS WITH NON-SMALL CELL LUNG CANCER.


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INTRODUCTION

Epidermal Growth Factor Receptor (EGFR) is the primary target of current molecular therapies in non-small cell lung cancer (NSCLC). The most frequent EGFR mutations (EGFRm) affect exons 18-21, among them exon 19 deletions and L858R in exon 21 are the most common in NSCLC. There are other less identified mutations in the EGFR gene who have oncogenic activity and may limit the response to EGFR TKI treatment. Single nucleotide polymorphisms (SNPs) in the EGFR gene are associated with cancer development. The Q787Q EGFR polymorphism is found in exon 20 and it is considered as a pathogenic variant who affect the catalytic kinase domain of EGFR, increase phosphorylation activity and also modifying EGFR expression. In to account response to therapy, the role of Q787Q is still in controversy. This study aims to know the prevalence of the synonymous EGFR Q787Q variant, assess survival and clinical characteristics of Mexican patients with NSCLC.

RESULTS

One-hundred fourteen patients were analyzed. The median age at diagnosis of NSCLC was 64 years. The majority of patients were female (71.1%), non-smokers (65.8%), had previous wood-smoke exposure (68.4%), were diagnosed with stage IV disease (84.2%) and nearly 83% of the patients had a low and moderate histological grade tumor. The frequency of Q787Q variant was 35% (40 patients). Q787Q co-occurrence partners most frequently were TP53 (77.5%), PDGFRA (37.5%) and MET (25%) (Figure 1). Q787+ patients had more cMET and PDGRA co-mutations compared with Q787- (p = 0.034) and 83.3 vs 16.7% (<0.001) respectively. Almost 67% patients received platinum-based chemotherapy as first-line.

For survival analysis first we analyzed patients with a common EGFRm vs others mutations including uncommon, complex, exon 20 insertions and specific very rare single point mutations (median OS 25 [EGFR-common] vs 8.6 months [EGFR-others]; log rank p=0.001) (Figure 2).

PFS and OS survival was lower when compared to patients with Q787Q (+) vs Q787 (-) (log rank p=0.001 for both).

METHODS

We conducted a retrospective multicenter analysis and included patients with advanced EGFRm NSCLC who performed a Next-Generation Sequencing (NGS). Patients were categorized according Q787Q status: Positive (+) and negative (-). Statistical analysis was performed with SPSS v26. Kaplan-Meier curves were used to evaluate median progression-free survival (PFS) and Overall survival (OS).

CONCLUSION

Also survival was analyzed take into TP53 was the most common co-occurrence with Q787Q+. For patients with Q787+(+)/TP53(-) progression-free survival was 11.5 vs 6.4 months [Q787(+)TP53(+)] (log rank p=0.001), OS was significantly longer in patients with [Q787(+)TP53(+)] 20.5 vs 9.4 months [Q787(+)/TP53(-)] (log rank p=0.024) (Figure 3).

Keywords: EGFR, Q787Q, SNP

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Image 1

Figure 1.

Figure 2.

Figure 3.