Frequency of *EGFR* mutations in Greek Non-Small-Cell Lung Cancer (NSCLC) patients

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Background

Two small molecule tyrosine kinase (TK) inhibitors of the epidermal growth factor receptor (*EGFR*) have recently received license for the treatment of first line NSCLC patients harboring activating somatic mutations within the TK domain of EGFR. Treatment of patients harboring *EGFR* mutations leads to improved response and survival outcomes, therefore screening for *EGFR* mutations has entered routine clinical practice. Several clinico-pathological factors correlate with these mutations including gender, smoking history, and histology. The frequency of *EGFR* mutations is also ethnicity-dependent, wherein the incidence in Asian populations is ~30%, while in Caucasians (Whites) it is lower, ~15%. However, limited data is available on intra-ethnic differences throughout Europe.

Aim

The aim of this study was to determine the frequency and spectrum of *EGFR* mutations in Greek NSCLC patients.

Methods

We set up High Resolution Melting (HRM) assays to identify mutations in exons 18-21 of the *EGFR* gene. Validation of the sensitivity of the HRM analysis (HRMA) was tested by making serial dilutions of a sample with a known mutation and tumor cell content (TCC) (Fig.1).
Formalin-fixed paraffin embedded (FFPE) tissue samples from 547 patients were analyzed for somatic *EGFR* mutations. Pathological review was obtained for all samples and macro-dissection was used to ensure a tumor cell content (%TCC) of >75% in all possible cases. HRMA was used for initial screening and the mutation status was verified by bi-directional sequencing (Figs. 2 and 3).

Figure 1: HRMA Sensitivity

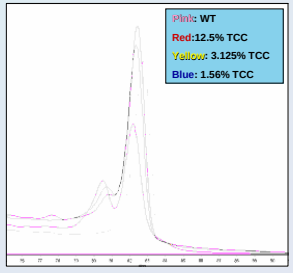


Figure 2: ex.19 delE746-A750

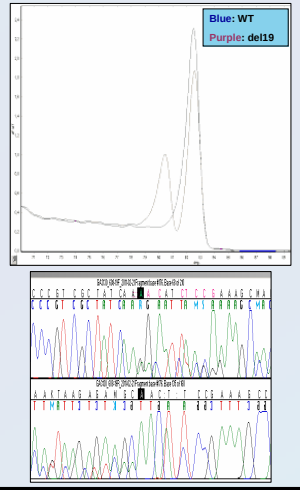
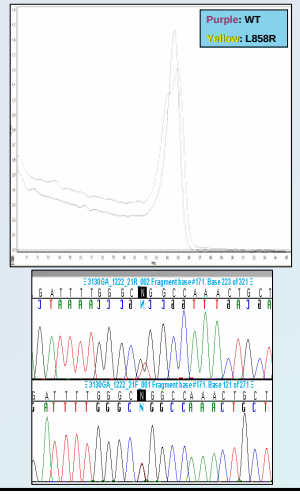


Figure 3: ex.21 L858R (T>G)



Results

The sensitivity of our HRM assays was found to be ≤1.5% (Fig.1).

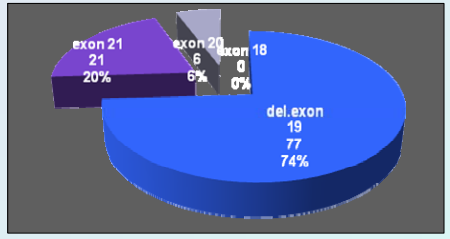
In the entire cohort (n=547) the frequency of activating mutations was 19% (104 mutations);

• 77 x exon 19 deletions (74%)
Spectrum: delE746-A750
delL747-A750insP
delL747-E749insP
delE746-T751
delT751-I759insN

• 21 x (exon 21) (20.2%)
Spectrum: L858R
L861Q

• 6 x exon 20 (5.8%) (Fig.4)
Spectrum: D770insDNP
D770insSVD
V769insASV
H773L
V774M

Figure 4: Mutation distribution among *EGFR* exons 18-21



Conclusions

Applying a very sensitive mutation detection technique in a large cohort of unselected Greek NSCLC patients in routine diagnostic practice, we obtained an overall mutation frequency of 19%. This mutation frequency is similar to that found by the SLADB and EURTAC studies in European populations.

References

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