Background: Therapy surveillance is a corner stone in advanced lung cancer clinical management. Due to the ease of sampling, analysis of tumor derived circulating DNA in plasma for treatment monitoring and decision making is desirable. Patients with tumors harboring a sensitizing *EGFR* mutation benefit from targeted therapy using tyrosine kinase inhibitors (TKIs). Unfortunately, the majority of patients develop resistance towards the initially administered TKI either through intrinsic mechanisms of *EGFR* or mutations of additional genes such as amplification of *MET*. Osimertinib can be administered at disease progression due to the resistance mutation T790M in *EGFR*. In this study we used liquid biopsy at progression after TKI treatment to assess mutational status of sensitizing and T790M mutations. In some cases, a tumor biopsy was analyzed in parallel as part of clinical management. **Method:** Six 10 ml Streck Cell free BCT® tubes were collected and plasma was isolated. Cell free circulating DNA was purified and used in an ultra-sensitive ddPCR assay IBSAFE (George et al, manuscript in preparation). Both the sensitizing *EGFR* mutation and T790M was analyzed. In some cases, a solid biopsy was analyzed in the clinic in parallel to our plasma analysis. Patient outcome data will be collected from patient files. **Result:** Eighteen of 25 patients tested positive in plasma for the previously known sensitizing *EGFR* mutation (72%). Twelve of 25 tested positive in plasma for T790M mutation (48%). Among plasma samples positive for the sensitizing mutation, 67% were also positive for T790M. The minor allele frequency (MAF) fraction of T790M in comparison to the sensitizing mutation varied extensively from 0.01% to 90% and also the MAF compared to total DNA varied (0.005% to 23%). Updated clinical follow up data will be presented. **Conclusion:** For a subset of patients were a tumor biopsy is not feasible, a liquid biopsy could provide information about the mutational status. As the MAF vary considerably and can be very low, a highly sensitive assay such as the IBSAFE ddPCR assay, capable of confirming a mutation at a MAF as low as 0.005% is advantageous. Further, a large plasma input volume may aid in identifying patients positive for mutations at a low MAF. Updated clinical follow up data will be discussed. **Keywords:** plasma, EGFR, ddPCR

EP1.14-17

Acquired T790M Mutation in Patients Failing Treatment with First or Second-Generation EGFR-Tyrosine Kinase Inhibitors

C.K. Liam,[1] C.S. Chai,[2] M.E. Poh,[1] D.B.L. Ong,[3] P.L. Cheah,[3] Y.K. Pang,[4] G.F. Ho,[5] A. Alip[5] *[1]Department of Medicine, Faculty of Medicine, University of Malaya, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur/MY, [2]Department of Medicine, Faculty of Medicine and Health Science, University Malaysia Sarawak, Kota Samarahan/MY, [3]Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur/MY, [4]Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur/MY, [5]Department of Clinical Oncology, Faculty of Medicine, University of Malaya, Kuala Lumpur/MY*

Background: The majority of patients with epidermal growth factor receptor *(EGFR)*-mutant advanced non-small cell lung cancer (NSCLC) develop resistance to first- or second-generation *EGFR*-tyrosine kinase inhibitor (TKI) after a median treatment period of 12 months. This study aimed to determine the prevalence and predictors of acquired *T790M* mutation as a resistance mechanism among these patients. **Method:** This was a retrospective study of patients with sensitising *EGFR*-mutant advanced NSCLC who experienced disease progression (PD) while on first- or second-generation *EGFR*-TKI treatment and underwent investigations to determine the resistance mechanisms in University of Malaya Medical Centre from 1st January 2015 to 31st December 2017. **Result:** Of 87 patients, acquired *T790M* mutation was detected in 55 (63.2%) patients at PD. *T790M* mutation was significantly more frequent in patients who achieved partial response (PR) as

the best response (p = 0.008) or had new lung metastasis (p = 0.048); and significantly less frequent in patients who developed new symptomatic brain metastases (p = 0.021). Patients with *exon 19* deletion were more likely to acquire *T790M* mutation compared to those with *exon 21 L858R* point mutation (p = 0.077). In multivariate analysis, PR with *EGFR*-TKI treatment was a significant independent predictor of acquired *T790M* mutation (p = 0.021) while having new symptomatic brain metastases (p = 0.034) or new lymph node metastases (p = 0.038) were significant independent predictors against acquired *T790M* mutation. **Conclusion:** Acquired *T790M* mutation was a common resistance mechanism leading to first- or second-generation *EGFR*-TKI treatment failure. Patients with tumours harbouring *exon 19* deletion mutation were more likely to acquire *T790M* mutation. A best tumour response of PR to *EGFR*-TKI treatment was an independent predictor of acquiring this resistance. This information is helpful to clinicians in the early prognostication and management planning for patients with *EGFR*-mutant NSCLC. **Keywords:** EGFR-TKI, T790M mutation, Acquired resistance

---

EP1.14-18

NGS-Molecular Characterization of Lung Adenocarcinomas from Hispanic Patients: Level of Evidence for Therapeutic Actionability

O.G. Arrieta,[1] R. Gerson,[2] C. Blanco,[2] J. Alexander Meza,[3] A. Silva,[4] S. Rivera Rivera,[4] C. Zuloaga Fernández,[5] M. Lazaro,[6] E. Kazakova,[7] A. Villa[8] *[1]Instituto Nacional de Cancerologia, Mexico City/MX, [2]Abc Medical Center, Mexico City/MX, [3]Unidad de Cancerología, Guadalajara/MX, [4]Hospital de Oncología Cmn Siglo Xxi, Instituto Mexicano Del Seguro Social (Imss), Mexico City/MX, [5]Anker Oncología Global, Mexico City/MX, [6]Hospital General de Mexico, Mexico City/MX, [7]Roche, Mexico City/MX, [8]Universidad Nacional Autónoma de México, Mexico City/MX*

Background: Several studies have shown that NSCLC genomic background among Hispanics differs from other populations, therefore genotyping tumors in order to assess their molecular profile is adamantly needed in the current era of targeted therapy. Panel-detected oncodriver mutations can drive therapeutic approaches, and can help classify the information in order to propose strong evidence-based interventions in treatment guidelines. In this study we sought to understand the landscape of genomic drivers in a cohort of patients with lung adenocarcinoma of Hispanic ancestry. **Method:** Tumor samples were collected from 48 patients with lung adenocarcinoma from march 2017 until march 2019. Samples were submitted for testing to Foundation Medicine and hybrid capture NGS was performed.

Figura 1