PRESIDENTIAL SYMPOSIUM
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PS1: Phase 3 KEYNOTE-042 Study: Pembrolizumab vs Platinum-Based Chemotherapy as 1l Therapy for Advanced NSCLC with a PD-L1 TPS ≥1%

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Background: First-line (1L) therapy with pembrolizumab in patients with metastatic NSCLC without targetable aberrations and programmed death ligand 1 (PD-L1) tumor proportion score (TPS) ≥50% significantly improved the primary endpoint of PFS, and OS (secondary endpoint) compared to chemotherapy in the KEYNOTE-024 study. In KEYNOTE-042 (NCT02220894), we evaluated pembrolizumab vs chemotherapy at the lower PD-L1 TPS of ≥1%.
Method: Eligible patients were randomized 1:1 to ≤35 cycles of pembrolizumab 200 mg Q3W or investigator's choice of ≤6 cycles of paclitaxel + carboplatin or pemetrexed + carboplatin with optional pemetrexed maintenance (nonsquamous only). Randomization was stratified by region (east Asia vs non-east Asia), ECOG PS (0 vs 1), histology (squamous vs nonsquamous), and TPS (≥50% vs 1-49%). Primary endpoints were OS in patients with TPS ≥50%, ≥20%, and ≥1%. OS differences were assessed sequentially using the stratified log-rank test. Efficacy boundaries at the prespecified second interim analysis were one-sided $P = 0.0122$, 0.01198, and 0.01238, respectively.
Results: Overall, 1274 patients were randomized: 637 to each arm. 599 patients (47.0%) had TPS ≥50%, 818 (64.2%) had TPS ≥20%. After a median follow-up of 12.8-months, 13.7% were still on pembrolizumab and 4.9% were receiving pemetrexed maintenance. Pembrolizumab significantly improved OS in patients with TPS ≥50% (HR 0.69), TPS ≥20% (HR 0.77), and TPS ≥1% (HR 0.81) **(Table).** Grade 3-5 drug-related AEs were less frequent with pembrolizumab (17.8% vs 41.0%). The external DMC recommended continuing the trial to evaluate PFS (secondary endpoint).

Table: Overall Survival by PD–L1 TPS

	PD-L1 TPS					
	≥50%		≥20%		≥1%	
	Pembrolizumab n = 299	Chemotherapy n = 300	Pembrolizumab n = 413	Chemotherapy n = 405	Pembrolizumab n = 637	Chemotherapy n =
HR (95% CI); P-value	0.69 (0.56–0.85)		0.77 (0.64–0.92)		0.81 (0.71–0.9	
	P = 0.0003		P = 0.0020		P = 0.0018	
Median (95% CI), months	20.0 (15.4–24.9)	12.2 (10.4–14.2)	17.7 (15.3–22.1)	13.0 (11.6–15.3)	16.7 (13.9–19.7)	(11

Conclusion: KEYNOTE-042 is the first study with a primary endpoint of OS to demonstrate superiority of pembrolizumab over platinum-based chemotherapy in patients with previously untreated locally advanced or metastatic NSCLC without sensitizing *EGFR* or *ALK* abberations and a PD-L1 TPS ≥1%. These data confirm and potentially extend the role of pembrolizumab monotherapy as a standard 1L treatment for PD-L1-expressing locally advanced or metastatic NSCLC.

PS2: CheckMate 227: Nivolumab + Ipilimumab vs Chemotherapy as 1L Treatment for Advanced NSCLC With High Tumor Mutational Burden

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Background: CheckMate 227 (NCT02477826) is a large phase 3 study of first-line nivolumab-based regimens vs platinum-doublet chemotherapy in advanced non-small cell lung cancer (NSCLC). We report results from Part 1, including a preplanned co-primary endpoint evaluating progression-free survival (PFS) of nivolumab + ipilimumab vs chemotherapy in patients with high tumor mutational burden (TMB ≥10 mut/Mb), safety of nivolumab + low-dose ipilimumab, and patient-reported outcomes (PROs).
Method: Patients (N = 1739) with chemotherapy-naive, stage IV/recurrent NSCLC without known sensitizing *EGFR*/*ALK* alterations were randomized 1:1:1 to nivolumab (3 mg/kg Q2W) + ipilimumab (1 mg/kg Q6W), nivolumab monotherapy (240 mg Q2W), or chemotherapy for patients with ≥1% tumor programmed death-ligand 1 (PD-L1) expression and to nivolumab + ipilimumab, nivolumab (360 mg Q3W) + chemotherapy, or chemotherapy for patients with <1% tumor PD-L1 expression. Co-primary endpoints were overall survival for nivolumab + ipilimumab vs chemotherapy in patients with PD-L1–selected tumors and PFS (blinded independent central review) for nivolumab + ipilimumab vs chemotherapy in patients with high TMB ≥10 mut/Mb. TMB was determined from tumor tissue using the FoundationOne CDx™ assay. Safety analyses included time to onset and time to resolution of select treatment-related adverse events (select TRAEs; those with a potential immunologic cause) and corticosteroid use. PROs were assessed using the Lung Cancer Symptom Scale and EQ-5D instruments.
Results: Minimum follow-up was 11.2 months. PFS was significantly longer with nivolumab + ipilimumab vs chemotherapy in patients with high TMB ≥10 mut/Mb (HR = 0.58 [97.5% CI: 0.41, 0.81]; P = 0.0002); results were consistent across subgroups, including PD-L1 expression and tumor histology. Rates of TRAEs leading to discontinuation were 17% with nivolumab + ipilimumab and 9% with chemotherapy. Grade 3–4 TRAEs occurred in 31% and 36% of patients treated with nivolumab + ipilimumab and chemotherapy, respectively. Grade 3–4 select TRAEs by category with nivolumab + ipilimumab included hepatic (8%), endocrine (4%), and skin (4%), and were consistent with previous reports. Median time to onset of select TRAEs ranged from 2 to 15 weeks, and the majority resolved (median time: ≤10 weeks). PRO results will be reported in the final presentation.
Conclusion: First-line nivolumab + ipilimumab significantly prolonged PFS vs chemotherapy in patients with NSCLC and high TMB ≥10 mut/Mb regardless of PD-L1 expression. These results validate the role of TMB as a biomarker for the use of nivolumab + ipilimumab in first-line NSCLC. Safety of nivolumab + low-dose ipilimumab was manageable.

Keywords: tumor mutational burden, patient-reported outcomes, nivolumab, NSCLC

PS3: KEYNOTE-024 Update: Pembrolizumab vs Platinum-Based Chemotherapy for Advanced NSCLC with PD-L1 Tumor Proportion Score ≥50%

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Background: KEYNOTE-024 (NCT02142738) is a multicenter, international, phase 3, randomized, open-label trial of first-line pembrolizumab vs platinum-based chemotherapy for patients with advanced non–small-cell lung cancer (NSCLC; any histology) with PD-L1 tumor proportion score (TPS) ≥50% and without *EGFR/ALK* alterations. The primary analysis of KEYNOTE-024 showed significantly improved PFS (HR=0.50; *P*<0.001) and OS (HR=0.60; *P*=0.005) with fewer treatment-related AEs with pembrolizumab compared with chemotherapy after a median follow-up of 11.2 months. We report on updated results after a median follow-up of 25.2 months.
Method: Patients were randomized to pembrolizumab 200 mg every 3 weeks (35 cycles) or 4–6 cycles of investigator's choice of carboplatin/cisplatin + gemcitabine, carboplatin + paclitaxel, or carboplatin/cisplatin + pemetrexed with optional pemetrexed maintenance (for nonsquamous histology). Randomization was stratified by ECOG PS (0 vs 1), histology (squamous vs nonsquamous), and geographic region (East Asia vs non–East Asia). Treatment continued until disease progression per RECIST version 1.1, intolerable toxicity, or withdrawal of consent. Patients in the chemotherapy arm could cross over to receive pembrolizumab monotherapy upon disease progression. Response was assessed every 9 weeks per RECIST version 1.1 by blinded independent central review (stopped after the second interim analysis) and by investigator assessment. PFS was the primary endpoint; OS and safety were secondary endpoints.
Results: 305 patients were enrolled (pembrolizumab, n=154; chemotherapy, n=151). At data cutoff (July 10, 2017), 73 patients (47.4%) randomized to pembrolizumab and 96 patients (63.6%) randomized to chemotherapy had died. The hazard ratio (HR) for OS was 0.63 (95% confidence interval [CI], 0.47–0.86; nominal *P*=0.002). Median (95% CI) OS was 30.0 (18.3–not reached) months for pembrolizumab and 14.2 (9.8–19.0) months for chemotherapy. Estimated 12-month OS was 70.3% (95% CI, 62.3%–76.9%) for pembrolizumab and 54.8% (95% CI, 46.4%–62.4%) for chemotherapy. 82 patients allocated to the chemotherapy arm crossed over to receive pembrolizumab upon meeting eligibility criteria. Treatment-related AEs were less frequent with pembrolizumab than with chemotherapy (76.6% vs 90.0%, respectively) as were treatment-related grade 3–5 AEs (31.2% vs 53.3%).
Conclusion: With prolonged follow–up, first-line pembrolizumab monotherapy remains superior to platinum-based chemotherapy despite crossover from chemotherapy to an anti–PD-1 agent.

Keywords: pembrolizumab, non–small-cell lung cancer, overall survival, KEYNOTE-024

PS4: Clinical Outcomes in Hispanic Patients Treated with Checkpoint Inhibitors

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Background: All Immunotherapy studies done in non-small cell lung cancer (NSCLC) patients (pts) are so far in Non-Hispanic White (NHW) or Asian populations. There is little known about the outcomes in Hispanics (H). Hispanics in the US have a lower age-adjusted mortality in NSCLC and have a different gene expression profile than NHW with higher prevalence of EGFR mutations then it's important to know if H can have similar outcomes to the ones described for NHW.
Method: All Immunotherapy studies done in non-small cell lung cancer (NSCLC) patients (pts) are so far in Non-Hispanic White (NHW) or Asian populations. There is little known about the outcomes in Hispanics (H). Hispanics in the US have a lower age-adjusted mortality in NSCLC and have a different gene expression profile than NHW with higher prevalence of EGFR mutations then it's important to know if H can have similar outcomes to the ones described for NHW.
Results: The median age was 65 years (range: 37-88y); most of the pts were males: 116 (54%), 82% adenocarcinomas. The ORR was 16% and the DCR that shows the clinical benefit was 67%. ORR and DCR were similar in adenocarcinomas (20%/68%) and squamous cell carcinomas (17%/64%) respectively. PFS at 6 months (m) and 12m were 80% and 56% respectively. Median PFS 14.5m and median OS were 19m, respectively. When patients were analyzed by PD-L1 status the ORR was 24% if PD-L1 (+) vs 1% if PD-L1 (-). STK11 was only tested in 13 pts, from the 7/11 (+) patients 60% achieved SD vs and the 2/2 pts that were (-) had PR.
Conclusion: Hispanics might not have a benefit from immunotherapy to the extent that NHWs do, ORR for NSCLC pts treated with immunotherapy is 16% in Hispanics treated at 4 cancer centers compared to an expected 20% ORR for NHW as reported in the literature. We need a larger cohort and prospective studies to validate these findings in all genes.

Keywords: Disparities, NSCLC, Hispanics, immunotherapy

PS5: New Biomarkers to Follow Therapy Response in Plasma of NSCLC Patients

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Background: Immunotherapy (IMMUNO) has been successful in non-small cell lung cancer (NSCLC), however biomarkers are still in development. PD-L1 done by IHC in tissue has been the first one but blood based biomarkers present new opportunities. Circulating cell-free tumor RNA (cfRNA) can be now isolated and used to measure changes in the tumor burden and genome. We are correlating these changes in cfRNA, cfDNA, KRAS, ERCC1 and PD-L1 with clinical response to therapy (chemotherapy, IMMUNO or targeted therapy) in stage IV NSCLC pts.
Method: Blood was drawn from 35 pts under various treatments (TX) every 6-8 weeks, at the same time that CT scans were done. CfRNA was extracted from the resulting plasma and reverse transcribed with random hexamers to cDNA. Levels of cfRNA, KRAS, ERCC1 and PDl-1 were quantitated by RT-qPCR and correlated with pts clinical response (CR/PR/SD/PD), as determined by CT scans.
Results: 35 NSCLC pts were enrolled in a 2-year clinical study. 25 of 35 pts completed at least two cycles of TX and had CT scans done. 4/4 pts with partial response (PR) had no change (NC) or decrease (DEC) cfRNA; 6/8 pts with progressive disease (PD) showed INC levels of cfRNA, 9/13 pts with stable

disease (SD) showed either no NC or DEC cfRNA, corresponding to 76% concordance between cfRNA and clinical responses. PD-L1 expression measured in plasma cfRNA matched the tissue expression in 7/10 pts. In the one pt where PD-L1 was (-) in blood and (+) in tissue there was PD on IMMUNO. Among 8 pts treated with IMMUNO: 3/3 pts with PD showed INC PD-L1 cfRNA expression, 3/3 pts with SD had NC in negative PD-L1 status, and 2 pts with PR showed DEC PD-L1 cfRNA, corresponding to 100% correlation between PD-L1 expression levels and pt response. Ten pts harbored KRAS mutations in cfDNA. Of those with KRAS+ status by tissue-based testing, 83% matched with cfDNA results. Among KRAS+ pts, 80% (8/10) showed PD-L1 cfRNA expression in same blood draws with KRAS+ cfDNA, suggesting correlation between these cfDNA and cfRNA analyses. ERCC1 and response to platinum doublets correlated in 8/10 pts (80%).

Conclusion: There was concordance between tissue and blood-based testing in both DNA (KRAS mutations, 83%) and RNA (ERCC1 80% and PD-L1 expression, 70%). Significant association was observed between clinical response and changes in plasma cfRNA levels (76%). While on IMMUNO, plasma levels of PD-L1 expression could be used to monitor clinical responses.

PD.1.01: Health-Related Quality of Life with Pembrolizumab or Placebo + Pemetrexed + Platinum in Non-Squamous NSCLC: KEYNOTE-189

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Background: In the double-blind, phase 3 KEYNOTE-189 study (NCT02578680), pembrolizumab+pemetrexed/platinum significantly improved OS and PFS over placebo+pemetrexed/platinum as first-line therapy for nonsquamous NSCLC. Overall, the incidence and severity of AEs with pembrolizumab+pemetrexed/platinum was similar to those with placebo+pemetrexed/platinum. We report the prespecified patient-reported outcome (PRO) analyses from KEYNOTE-189.
Method: 616 patients were randomized to pembrolizumab 200 mg Q3W or placebo for 2 years; all patients received pemetrexed plus 4 cycles of carboplatin/cisplatin. EORTC QLQ-C30 and QLQ-LC13 were administered at cycles 1-5, then every 3 cycles during year 1, and every 4 cycles during years 2/3. Key PROs were change from baseline to weeks 12 and 21 in the QLQ-C30 global health status (GHS)/quality of life (QoL) score and time to deterioration in composite of cough/chest pain/dyspnea. PROs were analyzed in all treated patients who completed ≥1 PRO instrument (n = 602). *P* values are nominal and 2-sided.
Results: QLQ-C30 compliance was ~90% at baseline and week 12 in both arms and was ~76% with pembrolizumab and ~64% with placebo at week 21. Mean baseline scores were 61.98 and 60.56 in the pembrolizumab and placebo arms, respectively. At weeks 12 and 21, GHS/QoL scores were stable with pembrolizumab and decreased with placebo, with significantly greater decrement with placebo at week 21 (**Table**). The proportion of improved GHS/QoL was similar at week 12 (28.9% with pembrolizumab vs 26.5% with placebo) but was greater with pembrolizumab at week 21 (30.1% vs 22.5%). Median time to deterioration in composite of cough/chest pain/dyspnea was not reached (NR) with pembrolizumab (95% CI, 10.2 months-NR) vs 7.0 months (95% CI, 4.8-NR) with placebo (HR, 0.81; 95% CI, 0.60-1.09; *P*=0.161).

Table. Change from baseline in GHS/QoL scores.

| | Week 12 | | Week 21 | |
	Pembrolizumab Arm	Placebo Arm	Pembrolizumab Arm	Pl...
LS mean change from baseline (95% CI)	0.95 (−1.33 to 3.24)	−2.63 (−5.79 to 0.53)	1.25 (−1.15 to 3.64)	− (−7.70
Difference in LS means (95% CI)	3.58 (−0.05 to 7.22) P=0.053		5.27 (1.07 to 9.47 P=0.014	

LS, least squares.

Conclusion: In KEYNOTE-189, pembrolizumab+pemetrexed/platinum maintained or improved health-related QoL over placebo+pemetrexed/platinum. These data support use of pembrolizumab+pemetrexed/platinum as first-line therapy for metastatic nonsquamous NSCLC.

Keywords: pembrolizumab, non–small-cell lung cancer, health-related quality of life, KEYNOTE-189

PD1.02: Real-World Prevalence of PD-L1 Expression in Advanced Non–Small-Cell Lung Cancer: The Global, Multicenter EXPRESS Study

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Background: PD-L1 expression on tumor cells is associated with improved clinical benefit from immunotherapies targeting the PD-1 pathway. We conducted a global, multicenter, retrospective observational study to determine real-world prevalence of tumor PD-L1 expression in patients with advanced NSCLC.

Method: Patients ≥18 years with histologically confirmed stage IIIB/IV NSCLC and a tumor tissue block (≤5 years old) obtained before treatment at or after this stage were identified in 45 centers across 18 countries including 4 centers in Argentina and Colombia. PD-L1 tumor expression was evaluated at each institution using the PD-L1 IHC 22C3 pharmDx kit (Agilent, Santa Clara, CA, USA). The percentages of patients with PD-L1 tumor proportion score (TPS) ≥50%, TPS ≥1%, and TPS <1% were described overall and by relevant clinicopathologic characteristics.

Results: Of 2617 patients who met inclusion criteria, 2368 (90%) had PD-L1 data (of which 266 were from Argentina and Colombia sites); 530 (22%) were TPS ≥50%, 1232 (52%) were TPS ≥1%, and 1136 (48%) were TPS <1% (**Table**). The percentage of patients with PD-L1 TPS ≥50% and TPS ≥1%, respectively were: 22%/52% in Europe; 22%/53% in Asia Pacific; 21%/47% in the Americas, and 24%/55% in other countries. The prevalence of *EGFR* mutations (19%) and *ALK* alterations (3%) was consistent with prior reports in metastatic NSCLC. Among 1064 patients negative for both *EGFR* mutation and *ALK* alteration, the percentage of patients with PD-L1 TPS ≥50% and TPS ≥1%, respectively, were 27% and 53%.

Table: Prevalence of PD-L1 TPS

Characteristic, n (%)[a]	N	TPS ≥50%	TPS ≥1%
All patients	2368	530 (22)	1232 (52
Age, years			
≥75	450	105 (23)	224 (50)
<75	1917	425 (22)	1008 (53
Sex			
Female	899	189 (21)	471 (52)
Male	1468	340 (23)	760 (52)
Region			
Asia Pacific[b]	661	148 (22)	351 (53)
Europe[c]	831	181 (22)	428 (52)
The Americas[d]	363	77 (21)	172 (47)
Other[e]	513	124 (24)	281 (55)
Specimen type			
Surgical resection	610	127 (21)	327 (54)
Biopsy	1694	394 (23)	880 (52)
Specimen source			
Primary	1735	377 (22)	892 (51)
Metastases	565	133 (24)	297 (53)
Histology			
Squamous	500	114 (23)	286 (57)
Nonsquamous	1846	410 (22)	934 (51)
Smoking status			
Never	532	98 (18)	249 (47)
Former	642	154 (24)	349 (54)
Current	740	184 (25)	393 (53)
ALK translocation status			
Positive	74	15 (20)	48 (65)
Negative	1433	347 (24)	753 (53)
EGFR mutation status			
Positive	448	60 (13)	197 (44)
Negative	1260	319 (25)	673 (53)

[a]The number of patients with the specific characteristic (row total) is the denominator for per
[b]Includes Japan, Hong Kong, Korea, Singapore and Taiwan.
[c]Includes Denmark, France, Germany, Italy, Spain, Sweden, and The Netherlands.
[d]Includes Argentina, Canada, and Colombia.
[e]Includes Russia, Saudi Arabia, and Turkey.

Conclusion: This is the largest real-world study in advanced NSCLC to date evaluating PD-L1 tumor expression using the 22C3 pharmDx kit. Testing failure rate was low despite local evaluation of PD-L1 TPS across a large number of sites. Prevalence of PD-L1 TPS ≥50% and TPS ≥1% was similar across geographic regions and broadly consistent with central testing results from clinical trial screening populations.

Keywords: non–small-cell lung cancer, prevalence, EXPRESS, programmed death ligand 1

PD.1.03: Ensartinib in Anaplastic Lymphoma Kinase (ALK) Positive Non-Small Cell Lung Cancer (NSCLC) Patients: Updated Data

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Background: Ensartinib has demonstrated marked efficacy and safety in patients with advanced NSCLC who are ALK tyrosine kinase inhibitor (TKI) naïve and crizotinib resistant and has intracranial activity in the central nervous system (CNS). We report updated data.

Method: In this ongoing phase I/II study, patients (pts) with advanced ALK positive NSCLC and measurable disease were given ensartinib 225mg once daily (QD) on a continuous 28-day schedule (NCT01625234). Patients who were either ALK TKI-naïve or had received prior crizotinib and no other ALK TKI received ensartinib until disease progression (PD), unacceptable toxicity or investigator discretion. Patients with asymptomatic brain metastases were allowed to enroll. All pts were assessed for adverse events (AEs) using CTCAE version 4.03, and response was assessed locally every 8 weeks using RECIST 1.1.

Results: As of the June 01, 2018 data cutoff, 52 ALK evaluable pts (ALK+ NSCLC pts at ≥ 200mg QD with a post baseline response assessment) were assessed (26 male/26 female; median age of 54 (20-80) years; 56% with an ECOG PS of 1). The most common drug-related AEs included rash (54%), nausea (35%), pruritus (31%), vomiting (25%), and fatigue (24%). Most AEs were Grade (G) 1-2. The G3 treatment-related AEs were rash (14%), pruritus (6%), fatigue (3%), decreased appetite (2%), nausea (1%), vomiting (1%), edema (1%), and AST increase (1%). Overall, complete response (CR) or partial response (PR) was achieved in 37 pts, a response rate (RR) of 71%, and 12 pts had stable disease (SD), resulting in a disease control rate (DCR) of 94%. Of the 15 ALK TKI-naïve patients, responses were observed in 12 pts (RR 80%) and 1 had SD, resulting in a DCR of 87%. Interestingly, the 2 pts with PD were ALK FISH-positive via local testing, but negative when analyzed using NGS. In the 37 pts with prior crizotinib but no other ALK TKI, 25 pts responded (1 CR/24 PR) and 1 had SD, resulting in a DCR of 97%. Intracranial responses were observed in 3/3 ALK TKI-naïve pts with target brain lesions at baseline (including 1 CR) and 7/13 crizotinib resistant pts with target lesions at baseline (including 2 CR), resulting in an overall intracranial DCR of 100%.

Conclusion: Ensartinib is well-tolerated and induces responses in both ALK TKI-naïve and crizotinib resistant ALK+ NSCLC pts, as well as patients with CNS lesions. Enrollment in this study and a global phase III study of ensartinib is ongoing.

Keywords: ALK, ensartinib, NSCLC, CNS

PD.1.04: A Comprehensive Description of the Molecular Epidemiology of Somatic Mutations in Actionable Genes in NSCLC Chilean Patients

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Background: Advances in precision medicine, which treats patients with therapies directed against the specific molecular alterations driving their cancers, have transformed oncology. This approach requires identification of the molecular alterations generating the cancer, the development of targeted therapies, and the validation of companion diagnostics assays to identify patient populations for clinical trials and eventual implementation. In developed countries from North America and Europe, the landscape of the actionable genomic alterations is well known. Thanks to global efforts, such as TCGA or ICGC, today it is possible to establish that a set oncogenic actionable driver mutations (including rearrangement and relevant mutation from KRAS, EGFR, ALK, ERBB2, BRAF, PIK3CA, MET, NRAS, MEK and AKT1) is found in about a 64% of lung adenocarcinomas patients. However, there is still very little information about the molecular epidemiology of lung cancer actionable genes in Latin American patients.
Method: The general aims of NIRVANA study (NCT03220230) are the validation of more sensitive and high-throughput technologies for the study of non-small cell lung cancer (NSCLC) genomics alterations, and the generation of a comprehensive, high quality, clinical, pathological, and genomics data of NSCLC in Chile, Brazil and Peru. So far, mutation prevalence of 52 genes (Oncomine Focus Assay, Thermo Fisher Scientific) were analyzed in 1253 NSCLC tumor samples from the NIRVANA Chilean patients. After the variant calling and quality filtering process, potential somatic mutations were annotated against COSMIC, dbSNP and ExAC to classify them as known or novel variants. SIFT and PolyPhen were used to assess the functional impact of the variants. Prevalence is reported within 95% CI of the gene and mutation type level (hotspot or gene fusions).
Results: The prevalence of genomic alterations in the 52 genes is similar to previous studies. For example, ALK fusions were present in 3.83% (CI 2.74% - 5.32%) of the tumors. Among the 973 DNA variants with a deleterious effect, 63% of them corresponded to novel variants that could be of clinical interest. Compared to the default variant calling process of known variants, this strategy increases by approximately 5-times the potential of finding new mutations for further analyses and new therapeutic opportunities.
Conclusion: This work constitutes one of the first approaches towards a comprehensive understanding of NSCLC genomic and actionable mutations in Chilean patients.

Keywords: Somatic mutations, NIRVANA, Precision Medicine, NSCLC

PD.1.05: Molecular Characterization of EGFR Somatic Mutations in Lung Adenocarcinoma Tumors from Chilean Patients

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Background: Lung cancer remains as the leading cause of cancer-related deaths worldwide, with non-small cell carcinoma (NSCLC) being the most frequent histology (85%). Therapies that target activating EGFR mutations are NSCLC first-line treatments that improve patient life expectancy and quality of life. However, despite the current availability of novel TKI drugs in Chile and other Latin-Americans countries, little is known about the molecular epidemiology of EGFR mutations in the region. In particular, Latin American patients are still largely under-represented in genomics databases or clinical trials for this

disease. We are presenting the results of a large NGS-based screening of the NSCLC EGFR mutations in Chilean patients. The study is aimed at describing the prevalence of specific somatic actionable mutations, within this population and correlated data with relevant clinical and tumor aspects such as gender, age, specific histology, smoking habits, progression stage and co-occurrence with KRAS mutations and other mutations.

Method: Non-small cell lung cancer FFPE samples from 821 subjects, part of the non-interventional clinical study NIRVANA (NCT03220230), were sequenced using Oncomine Focus Assay (Thermo Fisher Scientific), which covers the most frequent and actionable EGFR mutations through nine amplicons of ~100bp, spanning eight exons, to call variant at an expected mean coverage of 1000x. Variants called by the Ion Reporter Server were manually filtered by allele frequency >= 0.05 and at least 10 supporting reads, discarding synonymous substitutions and homozygous reference genotypes. Variants were annotated against COSMIC, dbSNP and ExAC databases to classify them in known or novel variants. Functional impact algorithms SIFT and PolyPhen were used. Clinical information was gathered on a GCP-compliant setup and monitored 100% on-site. Prevalence is reported within 95% CI, and associations with clinical characteristics are evaluated by Chi-Squared test or ANOVA, as appropriate ($p<0.05$).

Results: We found that 214 out of 821 subjects, or 26.06% (95% CI: 23.15% to 29.14%) of the studied population, harbor an EGFR mutation. Among known variants, exon 19 E746_A750 deletion (COSM13243) and exon 18 A698T (COSM41905) were the most abundant variations. Non-smokers and under 45 years old subjects were more likely to have a relevant EGFR mutation ($p<0.01$), in agreement with the literature. Gender did not correlate significantly as a predictor of EGFR mutations ($p>0.15$) in the cohort analyzed.

Conclusion: We expect these results shed light into the Chilean molecular epidemiology and supports initiatives to establish new diagnosis methods and treatment opportunities for Chilean cancer patients.

Keywords: Non-small-cell lung cancer, EGFR, NGS, NIRVANA

PD.1.06: EGFR Uncommon Mutations Frequency in a 1,688 NSCLC Patients Database in Brazil

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Background: EGFR mutation status is crucial to improving therapeutic results in advanced NSCLC, due to the development of highly effective EGFR-TKIs. Recent local data suggest that EGFR mutation frequency is lower in Brazil (22%-33%) than in Asia and higher than in North America and Europe. We intended to describe EGFR uncommon mutation frequency found in a large national-wide Brazilian population database.

Method: This retrospective analysis evaluated a database composed of samples collected between January and August 2017, from all Brazilian regions. Tumor tissue samples of patients with advanced NSCLC EGFR-TKI naïve were submitted, at discretion of attending physicians, for EGFR mutation testing. EGFR exons 18 to 21 were analyzed by cobas®, NGS, or other non-specified test.

Results: 1,688 tests were included. From all positive tests (n=429; 25.4%), exon 19 deletion was the most frequent (51.5%), followed by L858R (27.3%), and exon 20 insertion (8.4%). Uncommon mutations in each of these exons were found in a much lower frequency as shown in the Table 1, with the point

mutation S768I (2.10%) in exon 20 being the most common, followed by G719X (1.86%) in exon 18, and L861Q (1.63%) in exon 21. Smoking status data was not available and was not included in this analysis.
Table1 – Frequency of uncommon EGFR mutations.

Exon 18 n=15 (3.5%)	Exon 19 n=5 (1.1%)	Exon 20 n=18 (4.4%)	Exon 21 n=17 (3.9%)
G719X 8 (1.9%)	W731X 1 (0.2%)	S768I 9 (2.1%)	L861Q 7 (1.6%)
18 Del 3 (0.7%)	R748K 1 (0.2%)	H773Y 2 (0.5%)	L833F 2 (0,5%)
G696E 1 (0.2%)	A755T 1 (0.2%)	T783I 2 (0.5%)	G824D 1 (0.2%)
E709K 1 (0.2%)	E758K 1 (0.2%)	S768N 1 (0.2%)	M825I 1 (0.2%)
A722V 1 (0.2%)	D761N 1 (0.2%)	V769M 1 (0.2%)	R831H 1 (0.2%)
V726M 1 (0.2%)		H773L 1 (0.2%)	R832C 1 (0.2%)
		T790M 1 (0.2%)	A839T 1 (0.2%)
		G810D 1 (0.2%)	R841K 1 (0.2%)
		C818Y 1 (0.2%)	G873R 1 (0.2%)
			G874S 1 (0.2%)

Conclusion: Our findings show a considerable 12.8% rate of uncommon EGFR mutations in the presently studied patients. Its impact on response to EGFR-TKIs must be better addressed in real-world studies.

POSTER DISCUSSION SESSION PD.2
August 18, 2018 – 08:00 – 09:15

PD.2.01: Characterization of T790M According to Primary EGFR Mutation in Post EGFR-TKI Progression NSCLC in Brazil

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Background: The approval of Osimertinib in Brazil in 2016 for post EGFR-TKI progression T790M+ NSCLC treatment allowed offering to the patient the best available therapy, when, it is mandatory to identify the occurrence of T790M mutation before initiating the treatment. However, there is lack of data in Brazil from ct-DNA T790M detection in this patient set.
Method: We performed a retrospective analysis of a database of ctDNA samples collected between June 2016 and August 2017, from all Brazilian regions, positive for T790M and also primary EGFR mutation. Blood samples of patients with post EGFR-TKI progression were submitted, at the discretion of the attending physicians, for EGFR mutation testing. EGFR exons 18 to 21 were analyzed by cobas®. Prevalence of T790M mutation was not the objective of this analysis, since it considered only the positive T790M and primary mutation in ctDNA.
Results: 115 results were included in this analysis. 62.6% of the population was female; 94.8% of positive primary and T790M mutations were related do exon 19 deletion or L858R. There were no differences in frequency distribution between female and male population (Table 1). These frequencies were compatible with demographic data of AURA3 study. Still, more detailed testing using tissue and/or more sensitive methods are needed before a definitive conclusion. Table1 – Concomitant primary EGFR and T790M mutations in post EGFR-TKI progression in Brazil detected by cobas® test.

Detected Mutations	Female n (%)	Male n (%)	Total n (%)
T790m + Exon 18 Mutation	2 (2.8%)	2 (4.7%)	4 (3.5%)
T790m + Exon 19 Deletion	51 (70.8%)	28 (65.1%)	79 (68.7%)
T790m + L858R	18 (25.0%)	12 (27.9%)	30 (26.1%)
T790m + 2 Other Mutations	1 (1.4%)	1 (2.3%)	2 (1.7%)
Total	72	43	115

Conclusion: Our findings in Brazilian population demonstrated that there were no differences in frequency of T790M according to primary mutation between post EGFR-TKI progressive NSCLC female and male population detected by ctDNA cobas® test.

PD.2.02: Central Nervous System (CNS) Metastasis in Patients with T790M EGFRm Lung Cancer – Real World Data from a Brazilian Cohort

<u>C. Baldotto</u>[1], L. Araujo[2], P. De Marchi[3], G. Werutsky[4], G. Borges[5], C. Mathias[6], H. Freitas[7], A. Calabrich[8], C. Costa[9], F. Franke[10], E. Lima[11], Y. Neron[12], G. Schwartsmann[13], M. Custodio[14], C. Sansevero[15], G. Castro Jr[16]
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Background: Lung cancer is the most common cancer diagnosis and the leading cause of cancer-related death worldwide. CNS metastasis is usual in non-small-cell lung cancer (NSCLC), with an increased risk in EGFR-mutated tumors at the time of diagnosis as well as during disease course. Osimertinib is the standard of care for patients with metastatic *EGFR T790M* mutation–positive NSCLC following prior treatment with an EGFR-TKI, with demonstrated efficacy against CNS metastasis.
Method: ASTRIS is a phase IV, multinational, open-label trial of osimertinib for advanced T790M mutation NSCLC who received prior EGFR-TKI. Patients with CNS symptomatic disease were excluded. CNS metastasis screening were not mandatory in asymptomatic patients. Data presented here refer to the subset of Brazilian patients with CNS metastasis from the 14 participant sites.
Results: From August 2015 until March 2017, a total of 88 patients were included with a median age of 64 years (34-89), 66% female, and only 12.5% with PS2. Fifty-four patients (61%) had received prior therapy with erlotinib, forty-two (48%) with gefitinib, and 3 (3%) with afatinib. Only 46 patients (52%) had baseline brain scans. Magnetic resonance imaging (MRI) was performed in 81% and computed tomography (CT) in 19% of them. From this subgroup, a total of 25 patients (54%) had CNS metastasis; twenty-two (88%) with brain metastasis only, one (4%) with leptomeningeal disease only, and 2 (8%) with both presentation. Molecular testing was performed less often in tissue (40%), coming from metastatic site in 70% of cases. None of these biopsies came from CNS metastasis. Exon 19 deletions were the most common primary mutation in *EGFR*, present in 18 cases (72%), followed by L858R in 4 cases (16%), similar to non-CNS metastasis cohort. Of note, 2 cases (8%) harbored an exon 20 insertion. After a median follow-up of 9.3 months, 9 progression events (36% of patients) and 4 deaths (16%) were documented. Response evaluation was performed in 22 patients. The response rate was 59% (95%CI 36.4-79.3), compared to 58.2% (95%CI 46.6-69.2) in the total cohort of patients. At time of progression 33% had stable and 67% progressive CNS disease.
Conclusion: Real-world data may differ from controlled clinical trial, especially concerning patient selection. In this trial, results are consistent with previous reports of CNS response to osimertinib in patients with *T790M*-positive advanced NSCLC. However, very few patients were routinely screened for CNS metastasis, raising the question about the importance of a formal screening recommendation in this high-risk population.

PD.2.03: Autoantibody Test Helps Identify Malignant Pulmonary Nodules

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Background: Autoantibodies are produced by the immune system in response to aberrant tumor associated antigens and are detectable in the blood during the earliest stages of cancer development. *Early*CDT®-Lung is a blood test that measures a panel of seven autoantibodies specific for lung cancer-associated antigens and is being utilized by physicians to assess the risk of a pulmonary nodule being malignant. The test's high specificity and positive predictive value (PPV) complements the high sensitivity of computed tomography (CT). As a 'rule in' test, *Early*CDT-Lung helps identify which patients with a pulmonary nodule(s) are most likely to have a lung cancer.
Method: A cohort of nearly 2000 patients tested by *Early*CDT-Lung were followed up for clinical outcomes. Medical records were requested from physician offices and reviewed to determine clinical actions, nodule characteristics and any cancer diagnoses.
Results: *Early*CDT-Lung was found to complement CT and risk calculators (e.g., Swensen/Mayo nodule malignancy risk calculator), with a positive Moderate or High Level result increasing the pre-test malignancy risk of a nodule by ~2-fold (e.g., from 48% to 91%). For a nodule with a calculated pre-test risk that was intermediate (10-65%), a positive High Level result shifted the risk into High/Intervention risk (>65%), and a positive Moderate Level result added more than 25% to the pre-test risk of malignancy, shifting many intermediate risk nodules into the High/Intervention risk category. For those patients with a nodule detected prior to *Early*CDT-Lung who were diagnosed with a lung cancer within 12 months after having a positive *Early*CDT-Lung test, the average time to diagnosis was 45 days after the *Early*CDT-Lung test was reported. A positive *Early*CDT-Lung result was observed as early as 7 years before diagnosis of a stage 2 adenocarcinoma, which corroborates previous data showing autoantibodies are elevated very early in the development of a cancer.
Conclusion: As a 'rule in test,' *Early*CDT-Lung facilitates the reclassification of indeterminate pulmonary nodules in CT surveillance into a more appropriate category of management, thereby enabling faster diagnosis and earlier treatment.

Keywords: Lung cancer, early detection, blood test, nodule

PD.2.04: Effect of Nodal Skip Metastasis on Outcomes after Robotic-Assisted Pulmonary Lobectomy for Primary Lung Cancer

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Background: We analyzed both short- and long-term postoperative outcomes between patients with continuous nodal metastasis (NoSkip) compared to those with nodal skip-metastasis (Skip).
Method: We retrospectively analyzed patients who underwent robotic-assisted video-thoracoscopic (RAVT) pulmonary lobectomy by one surgeon between September 2010 and May 2017. Patients with final pathology reporting pulmonary metastasis or benign lesion were excluded. Inclusion criteria consisted of obligatory pathologic mediastinal nodal (pN2) classification. Patients were then stratified into two groups: Skip or NoSkip. Patients' demographics, perioperative outcomes, perioperative complications, and overall survival (OS) were compared.
Results: Of 423 total patients who underwent RAVT lobectomy, 390 patients had primary lung cancer (LC). While 319 patients with primary LC had pN0 or pN1 disease, 71 patients had pN2 disease, of which

18 (25.3%) were Skip and 53 (74.7%) were NoSkip. Mean age, gender distribution, and body habitus were similar between groups (p=0.617, p=0.194 and p=0.091, respectively). Patients with Skip had lower mean pre-operative forced expiratory volume in 1 second as percent of predicted (FEV1%; 79.5±3.5% vs. 89.7±2.8%), but this difference was not quite significant (p=0.053). Albeit not significant, patients in the NoSkip group had slightly more intraoperative complications (15.1% vs. 5.6%) and slightly more often required conversion to thoracotomy (15.1% vs. 5.6%) compared to the Skip group (p=0.293 and p=0.293, respectively). Incidence of postoperative complications were similar between groups (p>0.05). Patients in both groups had similar median estimated blood loss (EBL; 200 mL vs. 200 mL), operative time (214.5 min vs. 197 min), chest tube duration (4.5 d vs. 4 d), and hospital length of stay (LOS; 5 d vs. 5 d) (p=0.734, p=0.178 and p=0.973, respectively). Mean number of N1 lymph node (LN) stations reported and mean number of N1 LNs evaluated were similar between groups (1.9±0.1 vs. 1.7±0.1 [p=0.226] and 7.6±0.6 vs. 6.7±0.6 [p=0.441], respectively). Mean number of N2 LN stations reported and mean number of N2 LNs evaluated were also similar between groups (3.7±0.0 vs. 3.4±0.2 and 11.4±1.1 vs. 9.4±1.4, respectively). Patients with nodal skip metastasis (Skip group) had slightly less favorable 1-yr (50.7%±13.8% vs. 80.0%±6.4%) and 3-yr OS (42.2%± 13.9% vs. 57.1%±9.2%) (p=0.077).
Conclusion: Mean patient age, gender distribution, and body habitus did not differ between groups. Patients with Skip had reduced FEV1% pre-operatively, but the number of postoperative complications remained similar between groups. No significant differences were noted in EBL, operative times, chest tube duration, and hospital LOS. Skip is associated with worse OS compared to patients with NoSkip.

Keywords: nodal skip metastasis, outcomes, robotic-assisted lobectomy, primary lung cancer

PD.2.05: Circulating Tumor DNA Improves Genotypification and Detection of Targetable Alterations in Selected Lung Cancer Patients

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Background: Several studies have shown that NSCLC genomic background among Hispanics differs from other populations. The finding of low frequency genomic alterations in cfDNA to increase diagnostic accuracy in NSCLC could refine the treatment. We hypothesized that cfDNA can be an alternative or complement for detection of low frequency genomic targets. We aimed to understand the landscape of cfDNA-identified genomic drivers in a cohort of patients (pts) with NSCLC of Hispanic ancestry.
Method: We collected data from 51 Hispanic pts (Mexico and Colombia) with advanced NSCLC (Stage III/IV) who previously underwent tissue screening for ALK, EGFR, and ROS1. CfDNA was extracted from plasma and analyzed by a commercial NGS test (Guardant360â) which detects genomic alterations (alts) in up to 73 genes.
Results: Median age was 56 years (31-83). Most pts were female (64.7%) and never smokers (76.5%). 94% of cases (48/51) had cfDNA detectable alts with a mean number of 3.37 cfDNA alts per test (range, 1 -10). Of the 48 pts with cfDNA genomic alts, 23 (47.9%) had a known genomic driver (EGFR (27.4%), TP53 (13.7%), ALK (7.8%), KRAS (5.8%), and BRAF (3.9%)). Interestingly, cfDNA was able to detect some genomic alts previously undetected by tissue biopsy (either due to false negatives or to technical limitations such as insufficient or low-quality DNA). In the case of EGFR, 12 pts had EGFR alts through cfDNA which were previously undetected by tissue biopsy. Similarly, cfDNA detected 3 alterations in ALK which were previously undetected by tissue sample. Of 48 pts, 35.4% were switched to a targeted therapy as a result of alts detected through cfDNA, with adequate responses: disease control rate was 82.4% (partial response 47.2% and stable disease 35.2%) and progression free survival was 7.4 months (95%CI 2.6-28.1).

Conclusion: In a selected population of young Hispanics (especially never smokers and women) with NSCLC the use of comprehensive cfDNA analysis allowed a treatment change in 35% of the cases. Our data confirms the usefulness of Guardant360â as non-invasive panel to identify genomic alts in cfDNA.

Keywords: Liquid Biopsy, Genotypification

PD.2.06: Identifying Resistance to Checkpoint Inhibitors by Screening for PD-L1 and MHC I Expression on CTCs in NSCLC

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Background: PD-L1 expression on tumor predicts benefit to immune checkpoint inhibitors (ICI) in patients with advanced NSCLC. However, there are a significant number of patients whose tumor test positive for PD-L1 expression that do not derive benefit from ICI, suggesting the existence of intrinsic resistance mechanisms. PD-L1 blockade aims to trigger tumor cell recognition and lysis by CD8+ T cells, but this process requires concordant expression of MHC I by tumor cells. Recently, MHC I negativity was observed in 49% of patients with lung carcinoma, and correlated with a lack of CD8+ T cell infiltration, emphasizing the importance of screening for MHC I in combination with PD-L1.
Method: For the purposes of both screening and the detection of acquired resistance, we developed a minimally invasive diagnostic test using Circulating Tumor Cells (CTCs). CTCs were captured and stained on the ExtractMax system (Gilson, Inc.) with Exclusion-Based Sample Processing (ESP) technology (Salus Discovery, LLC). With automation, the ExtractMax simplifies complex multi-step procedures, reduces variability, and ensures gentle manipulation of rare cell targets for optimal yield and viability. invasive diagnostic test using Circulating Tumor Cells (CTCs). CTCs were captured and stained on the ExtractMax system (Gilson, Inc.) with Exclusion-Based Sample Processing (ESP) technology (Salus Discovery, LLC). With automation, the ExtractMax simplifies complex multi-step procedures, reduces variability, and ensures gentle manipulation of rare cell targets for optimal yield and viability.
Results: A range of PD-L1 and MHC I expression levels were detected on CTCs captured from a cohort of patients with NSCLC, with two patients showing no MHC 1 expression and all others with heterogeneous expression of MHC 1. PD-L1 expression was variable across all samples tested with subset of patients with PD-L1 positive CTCs but MHC I negative, suggesting intrinsic resistance to PD-L1 targeted therapies.
Conclusion: This data supports the feasibility of using an automated CTC processing system to detect and monitor PD-L1 and MHC I expression in patients with NSCLC. Ongoing efforts include expanding this patient cohort in larger clinical trials and transitioning this test into a clinical laboratory testing facility for regulatory approval and use as a clinically actionable diagnostic tool.

Keywords: NSCLC, immunotherapy, PD-L1, CTCs

POSTER SESSION

PS01: Integrating Liquid Biopsy in Molecular Tumor Board Decision for Lung Cancer Patients

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Background: Molecular Tumor Boards (MTBs) for patient selection and assessment of treatment options were created for adequate precision medicine delivering. We evaluated the implementation of both the MTB of the region of Antwerp/Belgium and different next generation sequencing (NGS) panels – comprising panels performed on liquid biopsy specimens – in treatments selection. We present results concerning patients with lung cancer.

Method: Patients with lung cancer progressing to standard treatments who underwent NGS of tumor tissue, cell-free circulating tumor DNA (ctDNA) or both were included. The MTB expressed either a positive or negative opinion for the inclusion of the patient in a clinical trial, in an expanded access or as part of a compassionate use program. The alterations found were matched with OncoKB levels (MSKCC) of evidence for alteration-specific treatments.

Results: The MTB evaluated 38 lung cancer patients (NSCLC and SCLC) with at least one NGS panel available. Overall, the MTB proposed alteration-specific targeted therapy to 24 out of 38 patients (63.1%). In 13 patients (7 LUAD, 3 LUSC and 3 SCLC) with matched lbNGS and ttNGS, lbNGS and ttNGS detected, respectively, 26 and 10 point mutations: 2 mutations were detected only by the ttNGS, 18 only by the lbNGS and 8 by both of them. In this cohort the MTB could allocate 3 patients (23%) to a clinical trial even in the absence of a OncoKB recommendation level ≥ 3b.

Discussion: NGS panels were reported to improve patients outcomes [i] - [ii] - [iii]. This is not confirmed by the SHIVA trial[iv]. Previous studies reported only on the added value of use of an MTB without comparison to a commonly used standard of variant-classification such as OncoKb [v]-[vi]. To our knowledge, we are the first to compare MTB decisions with a set of evidence-based recommendations in patients with lung cancer, thus making it possible to measure the impact of MTB decisions as a change of treatment. The lbNGS appears to be more sensitive than ttNGS in patients with lung cancer.

[i] Pilot study using molecular profiling of patients' tumors to find potential targets and select treatments for their refractory cancers. Von Hoff DD JCO 2010

[ii] High-Throughput Genomics and Clinical Outcome in Hard-to-Treat Advanced Cancers: Results of the MOSCATO 01 Trial Christophe Massard CANCER DISCOVERY

[iii] Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial Dr Christophe Le Tourneau LANCET 2015

[iv] Randomized phase II trial comparing molecularly targeted therapy based on tumor molecular profiling versus conventional therapy in patients with refractory cancer: cross-over analysis from the SHIVA trial L. Belin M. Kamal ANNALS OF ONCOLOGY 2016

[v] Implementation and utilization of the molecular tumor board to guide precision medicine Shuko Harada ONCOTARGET 2017

[vi] Development of a Center for Personalized Cancer Care at a Regional Cancer Center Feasibility Trial of an Institutional Tumor Sequencing Advisory Board Brian R. Lane JOURNAL OF MOLECULAR DIAGNOSTIC 2015

Conclusion: Our MTB allows patients with refractory lung cancer to be included in clinical trials and improves the precision of clinical decisions compared to a standardized set of mutation-driven

recommendations.
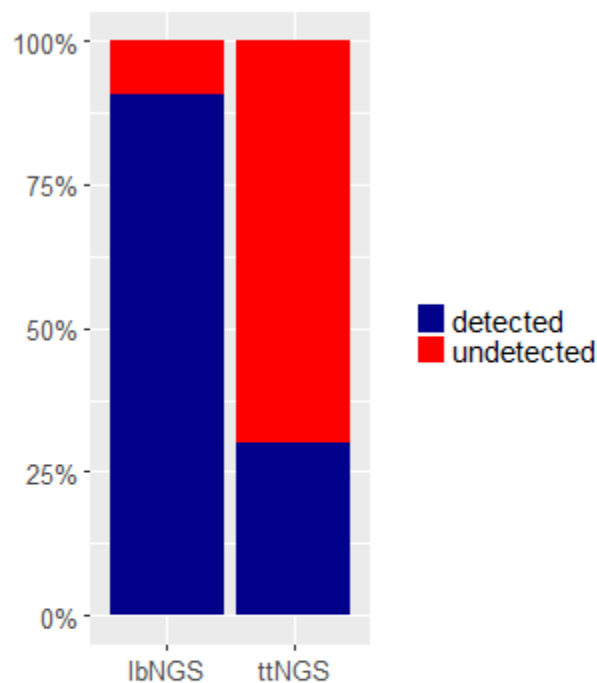
PS02: EGFR Amplification and Sensitizing Mutations Correlates with Survival from Erlotinib in Lung Adenocarcinoma Patients

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Background: Non-small cell lung cancer (NSCLS) is the most frequent cause of cancer-related mortality in the world. Tumor heterogeneity and *EGFR* mutation abundances are believed to be responsible for varied progression-free survival (PFS) in lung adenocarcinoma (ADC) patients receiving EGFR-TKI treatment. *EGFR* mutation abundance caused by *EGFR* amplification is associated with better response

rate and clinical outcomes in patients receiving EGFR-TKI therapy. The coexistence of the *EGFR* mutant allele and *EGFR* amplification can be determined by the *EGFR* copy number variation. The assessment of *EGFR* amplification status in *EGFR* mutant patients could predict the efficacy of EGFR-TKI treatment and correctly select the patients that would most benefit from this therapy.

Method: 72 lung ADC patients, who harbored *EGFR* activating mutations and received erlotinib as first line treatment, were examined for *EGFR* amplification by FISH. We analyzed the relationship between *EGFR* mutational status and copy number profile with clinical outcomes including response rate, overall-survival (OS), and PFS.

Results: Median age was 62-years (range: 20-87 years), 53 patients were females (73%), and 68 (94.5%) had common mutations. Twenty-two (30.6%) samples with *EGFR* activating mutations were identified as having *EGFR* amplification. *EGFR* amplification was more frequent in patients with exon 19 deletion (*p*=0.05) and in those with better performance status (*p*=0.01). Patients with *EGFR* gene amplification had a significantly longer PFS than those without [(28.5 months, 95%CI 22.3-34.6) vs. (11.0 months, 95%CI 8.23-16.7); *p*=0.002] as well as better OS [(*EGFR* amplified 37.8 months, 95%CI 30.9-44.7) vs. (*EGFR* non-amplified 27.1 months, 95%CI 12.8-41.3); *p*=0.009]. *EGFR* amplification significantly influenced the response to erlotinib (*p*=0.0001).

Conclusion: In the Hispanic population studied, *EGFR* amplification was present in one third of the patients with lung ADC harboring *EGFR* activating mutations. *EGFR* gene copy number detected by FISH, and sensitizing *EGFR* mutations are biomarkers associated with better OS, PFS, and response to EGFR-TKI therapy in patients with advanced NSCLC. *EGFR* copy number could serve as a predictive marker for the identification of patients with NSCLC who will most benefit from EGFR-TKI treatment.

Keywords: Lung adenocarcinoma, EGFR mutation, EGFR amplification, erlotinib

PS03: Histological Subtype of Lung Adenocarcinoma and Programmed Death Ligand 1 (PD-L1) Expression in Tumor Cells

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Background: Immunotherapies targeting the Programmed cell death-1 (PD-1)/programmed cell death-ligand 1 (PD-L1) axis have showed favorable results in non-small cell lung cancer (NSCLC) patients. However, there is controversy regarding the analysis of PD-L1 expression by immunohistochemistry, particularly the cut-off criteria: Pembrolizumab with the 22C3 assay with cut-off ranges of >1%, 1-49% and >50%; and Nivolumab with the 28-8 assay and ranges of <1%, 1-5%, 5 -10% and >10%. Furthermore, the association between the histological subtype of adenocarcinoma and PD-L1 expression remains unclear. In this work, we assessed the frequency of PD-L1 expression according to the histological subtype of adenocarcinoma.

Method: PD-L1 expression was evaluated using the PD-L1 IHC 22C3 pharmDx immunohistochemistry assay (Dako North America, Inc.). The histological subtype of adenocarcinoma was correlated with the frequency and intensity of PD-L1 expression, clinical variables, smoking history, *EGFR* and *ALK* status.

Results: Tissue samples from one hundred and eighty-two patients were analyzed, 106 patients (57%) were female, the median age was 61 years (range 31-86 years), 53.7% were never-smokers with no exposition to wood smoke or asbestos (62.3 and 91% respectively). Regarding the histological subtypes, 32.1% were acinar, 25.3% solid, 15.4% papillar, 3.1% lepidic, 1.9% micropapillar; 52% had a moderated tumor differentiation grade. Fifty-six patients (43%) had *EGFR* mutations and eigth patients (6.4%) had *ALK* rearrangements. Concerning to PD-L1 score, 42.9% of the patients were classified as negative (PD-L1<1%), 48.3% as lower (PD-L1 1 to 49%), and 8.8% as high (PD-L1>50%) expressors. A high PD-L1 tumor expression was associated solid histological subtype (**p<0.05**). Between patients

with *EGFR* mutation or *ALK* rearrangements, 49% and 71% were positive for PD-L1, respectively. Moreover, Exon 19 mutation was correlated with a high PD-L1 score. Tumor PD-L1 score was associated with a poor response to first line chemotherapy. Patients with negative PD-L1 expression had longer PFS to first line therapy (8.33 vs 4.97 months, **p=0.01**). Patients that received first line chemotherapy had a negative correlation between PFS and PD-L1 status (**p=0.002**). Nonetheless, no relationship was found among patients that received TKIs treatment.

Conclusion: Patients with adenocarcinoma tumors, solid histological subtype and poor differentiation grade can be more benefited with a PD-1 based immunotherapy. PD-L1 score can be a predictor factor for the response to first line chemotherapy.

Keywords: Programmed-death receptor ligand 1, NSCLC, Immunohistochemistry, immunotherapy

P04: Clinical and Pathological Characteristics of NSCLC and the Relationship with the Development of Brain Metastases

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Background: Non-small cell lung cancer (NSCLC) is one of the main causes of brain metastases. Most cases are diagnosed at an advanced stage, which elevates the risk for the detection of brain metastases. It is imperative to establish easily accessible criteria to determine clinical and pathological factors that could predispose to the development brain metastases, even before symptoms appear. Such a study has not yet been executed, and with increasing restrictions to basic diagnostic methods and follow-up strategies, clinical stratification becomes an alternative our clinicians can use in their daily practice.

Method: To recognize clinical and pathologic characteristics of patients with NSCLC and their relationship with the development of brain metastasis, we reviewed medical records at the Department of Medical Records at the Dr. Luis Razetti Oncology Institute, between 2008 and 2016, searching for patients with NSCLC describing their clinical and pathologic characteristics. The presence of brain metastasis was associated according to the other variables through the non-parametric analysis of Chi Squared ($X2$) and only the statistically significant results were reported. The level of statistical significance was of $P < 0,05$.

Results: Of 217 patients with NSCLC, 109 had brain metastases. 56.88% were male and the age averaged 59.49 ± 2.3 years, the age group between 45 and 65 years was significant (P=0,039). 72.47% of patients with brain metastases referred smoking habits. Adenocarcinoma was prevalent in 78.3%. Right mid-lobe primary, T3 and N2 disease at the time of diagnosis were significant (P= 0,0002). Nuclear grade 2 was more frequent (P=0,0000). Acinar pattern, presence of tumor emboli or lymphovascular invasion were more frequent in patients with brain metastases but not significant. Protein P63 was positive in 25.81% patients, especially in cases without brain metastases (P=0,00141). We recorded 9 EGFR mutations (8 in exon 19) and 7 had brain metastases (P = 0,0000). Also, 6 patients had ALK translocation detected, all with brain metastases (P=0,0248).

Conclusion: Male gender, age between 45 and 65 at the time of diagnosis, ECOG 2, moderately differentiated adenocarcinoma, located in the right middle lobe, sized T3, or N2 nodes, stage IV with M1B metastasis, absence of P63, and mutations of EGFR or translocations of ALK, were more associated with the detection of brain metastases in patients with NSCLC. Other characteristics, like acinar pattern, presence of tumor emboli or lymphovascular invasion, expression of CK7, TTF1, and Napsin-A, were not significant but were frequently present in patients with brain metastases.

Keyword: lung cancer, brain metastasis, clinical, pathological

P05: 30 Years' Experience of Endoscopic Operations on Trachea and Bronchi in Lung Cancer Palliative Treatment

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Background: Endoscopic operations on trachea and bronchi are palliative method of lung cancer common forms treatment. The use of this surgical interventions type in patients with the above pathology improves quality and extends the life span. We summarized the 30-year experience of performing endobronchial operations in patients with lung cancer.

Method: In the clinic, endoscopic operations on the trachea and bronchi in lung cancer were performed in 1,720 patients, of which 1384 were men and 336 women. Total number of operations 4781. All patients had complete or partial stenosis of bronchi and trachea. Radical surgery was impossible to perform due to the prevalence of the process, either because of the comorbidity presence. Basically, we used a rigorous Friedel bronchoscope - in 1255 patients, the remaining 465 patients used an Olympus fibrobronchoscope. Rigid bronchoscopy was performed using endotracheal anesthesia, interventions with the use of a fibroblochoscope were performed under local anesthesia. We used three methods of influencing the tumor: laser radiation (1259 patients), electrosurgical method (146 patients) and radiofrequency ablation (315 patients). As a source of laser radiation, we used YAG-Nd laser, with a wavelength of 1064 nm and a power of 40 W. Both contact and non-contact methods of influencing the tumor were used. Electrosurgical operations implemented by a contact method using a conventional surgical coagulator under local anesthesia using fibrobronchoscope. The radiofrequency ablation (RFA) method implies the use of an electron wave at a frequency of 500 kHz. As a power source was used Fotec 150 generator. Operative interventions were performed under local anesthesia with the use of fibrobronchoscopy method.

Results: In all 1720 patients we managed to achieve complete or partial trachea and bronchi recanalization. The best results were obtained in patients using the RFA method, complete recanalization was achieved in 85% of patients. The diathermocoagulation method showed significantly lower efficiency (complete patency was restored in 24% of patients) and in 28 patients of this group developed pulmonary hemorrhage, which could not be stopped in 8 patients. The use of the YAG-Nd laser made it possible to restore bronchial patency completely in 64% of patients.

Conclusion: 1. Endoscopic surgery for tumor stenosis of the respiratory tract are palliative, but their use can improve the quality of life and prolong the life of patients. 2. The RFA method for respiratory tract tumor stenoses recanalization is an effective, simple to implement and can be used in patients with severe comorbidities.

Keyword: endoscopic operations, lung cancer, palliative treatment

P06: Competing CNS or Systemic Progression Analysis for *EGFR* Mutation-Positive NSCLC Patients on Afatinib in LUX-Lung 3, 6, and 7

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Background: CNS metastases are known complications of advanced *EGFR* mutation-positive NSCLC, thus, LUX-Lung (LL) trials investigating afatinib allowed enrolment of patients with brain metastases (BM). LL3, 6 and 7 previously demonstrated activity of afatinib in patients with BM, with the magnitude of progression-free survival (PFS) improvement with afatinib vs chemotherapy or gefitinib in patients with BM being similar to that observed in patients without BM (HR 0.54, 0.47, and 0.76 in LL3, 6 and 7, respectively).[1,2] PFS was significantly improved with afatinib vs chemotherapy in a combined analysis of LL3 and 6 in patients with asymptomatic BM (HR 0.50, p=0.0297).[1] To investigate whether afatinib can prevent CNS progression or metastasis, competing risk analyses for the progression and metastasis pattern in the CNS or non-CNS region were carried out in patients with and without BM in LL3, 6 and 7.
Method: Competing risk analyses were performed in patients with stage IIIB/IV *EGFR* mutation-positive NSCLC who received afatinib 40 mg/day in LL3, 6 and 7. Analyses were performed separately for patients with baseline BM and without baseline BM. Risk of CNS progression vs non-CNS progression or death was calculated based on the cumulative frequency of the event of interest vs the competing risk event.
Results: In patients with baseline BM receiving afatinib in LL3 and 6 (n=48; median follow-up 10.3 months), the cumulative incidence of CNS progression was 39.9% lower than that of non-CNS progression (31.3% vs 52.1%). The cumulative incidence at 6 and 12 months for CNS progression was 15.5% and 24.5%, respectively. In patients without baseline BM receiving afatinib in LL3, 6 and 7 (n=485; median follow-up 13.0 months), risk of *de novo* CNS progression was very low (6.4%) compared with non-CNS progression (78.4%). Cumulative incidence at 6 and 12 months (CNS progression vs non-CNS progression) was 1.3% vs 17.2%, and 2.6% vs 41.2%, respectively.
Conclusion: Competing risk analyses using data from LL3, 6 and 7 add to the existing evidence that supports afatinib use in patients with *EGFR* mutation-positive NSCLC and CNS metastases. Taken together, these results show that afatinib delays the onset/progression of BM. 1. Schuler. J Thorac Oncol 2016;11:380–90 2. Park. Lancet Oncol 2016;17:577–89 **Clinical trial identification:** NCT00949650, NCT01121393, NCT01466660

Keywords: CNS metastases, EGFR, NSCLC, Afatinib

P07: Preliminary Orthogonal Analysis of EML4-ALK Gene Fusion Detection Methods in Chilean Patients with Lung Adenocarcinoma

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Background: Lung cancer is the leading cause of cancer death in women and men. ALK mutations show a prevalence of 5% or less among lung adenocarcinoma patients. Since ALK gene fusions are clinically actionable, it is important to know the mutation status for this gene to aid in treatment decisions for lung cancer patients. In Chile, Ventana ALK IHC is considered a gold standard methodology to identify ALK (+) patients for treatment. However, there is evidence showing that this method has some disadvantages; therefore, it's been suggested to consider additional diagnostic tests. This work reports the results of a preliminary orthogonal analysis using a next-generation sequencing based assay, Ventana ALK IHC, and qRT-PCR for the detection of ALK gene fusions in lung adenocarcinoma samples from Chilean patients under standard clinical settings.
Method: As part of the NIRVANA study (NCT03220230), 515 lung adenocarcinoma samples were analyzed by Ventana ALK IHC test (Roche Diagnostics) and Oncomine Focus Assay (OFA, Thermo

Fisher Scientific) NGS platform that includes the ALK gene fusion breakpoint assay. To estimate the analytical performance of Ventana ALK and OFA in an orthogonal analysis; a total of 50 samples (22 Ventana ALK and OFA negatives, 9 Ventana ALK+, 7 OFA+, and 12 Ventana ALK and OFA positives) were analyzed using a qPCR based EML4-ALK fusion gene detection kit (AmoyDx) as benchmark.
Results: The frequencies of ALK fusions detected were 3,76% and 3,69% by Ventana ALK and OFA respectively, with 57,1% of samples giving discordant results between Ventana ALK and OFA techniques. The orthogonal analysis revealed that both, Ventana ALK and OFA, have a sensitivity of 75% [CI95%:51 - 91]. However, OFA presents higher specificity than Ventana ALK (96% *vs.* 88%). This difference has a *post hoc* statistical power of 97%. While Ventana ALK test can detect only the aberrant ALK accumulation, by using NGS it was possible to establish that the most common ALK gene fusion was between exon 20 of ALK and 6 of EML4.
Conclusion: Considering this analysis a preliminary assessment, when OFA and Ventana ALK are compared using "real world" lung adenocarcinoma samples, OFA presents an advantage against Ventana ALK test in specificity. Also, NGS can detect multiple mutations at the same time using a small amount of sample. The use of this technique unlocks the possibility to identify patients that can be treated using targeted therapies.

Keywords: ALK, NGS, Orthogonal analysis, NSCLC

P08: Is Lung Cancer the First Cause of Cancer Death in Latin America?

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Background: Latin America is the name given to those countries of South, Central and North America that share cultures and languages of origin Spanish and Portuguese (also French for some by its Latin origin). We all know that lung cancer is the first cause of cancer mortality all over the world but is less known what it is happens in Latin- America. Our objective is to analyze the available cancer mortality data in the region in order to contribute to plan strategies for prevention, diagnosis and treatment.
Method: We analyzed the data corresponding to year 2012, available from Global Cancer Observatory, IARC, WHO (Http://gco.iarc.fr/today/home), for 20 Latino-American countries. We also reviewed statistics of the Ministries of Health and/or National Institutes of Cancer, but we exclude them because their heterogenity. We consider age-standarised rates per 100000 (ASR) to make fairer comparisons between groups with different age distributions. Analysis was performed by tumor site (excluding non-melanoma skin) and by country, and sex.
Results: Cancer mortality for the region is 94.9 for both sexes and lung cancer mortality is the third cause (12.0) behind prostate and breast cancer (16.6, 13.0). For men, cancer mortality rate is 108.4 and lung cancer is the first cause (16.7) followed closely by prostate cancer (16.6). For women cancer mortality is 84.7 and lung cancer is the third cause (8.1), mama and cervix are the first (13.0, 8.7). The lung cancer mortality in males by country showed that Uruguay, Cuba and Argentina present the higher mortality (47.1, 39.6, 30.9). It was the first cause cancer mortality in those countries and in Brazil and Paraguay also, and the second in Mexico, Dominican Republic and Venezuela. In women, lung cancer mortality is higher in Cuba, Venezuela, Argentina and Brazil (21.6, 10.5, 10.0, 9.5), but it is the principal cause of cancer mortality only in Cuba and the second one in Brazil. The analysis is limited by registry quality.
Conclusion: Latin America lung cancer mortality is heterogenous between countries. In men is the first cause in only 25 % of the countries analyzed, the second in 15 %. In women it is only first in one country and second in another. Better understanding the region could adapt screening and early detection plans and may improve patients access to diagnosis and treatment in a precise way and opportunity.

Keywords: epidemiology, Latin American lung cancer mortality

P09: Comparison of Liquid Biopsy and Histopathologic Results with Clinical Outcomes in Non-Small Cell Lung Cancer Patients

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Background: Mutations in tumor DNA identify patients who may benefit from targeted therapy. Genetic or proteomic profiles may identify treatments that may be futile in these cancer patients. When tumor biopsies are unavailable or insufficient, liquid biopsy of peripheral blood circulating tumor DNA (ctDNA) and protein may easily and noninvasively capture data that represent the entire tumor burden of each cancer patient. We investigated whether liquid biopsy can correlate histopathologic factors, treatment, or outcomes with ctDNA mutations and proteomic signatures.
Method: We retrospectively analyzed data from non-small cell lung cancer (NSCLC) patients who underwent liquid biopsy analysis of ctDNA and proteins in peripheral blood between August 2016 to February 2018. Liquid biopsy ctDNA analysis detected targetable mutations, and proteomic analysis grouped patients as Good or Poor status. Patients with targetable mutations were excluded. Liquid biopsy results were correlated with tumor histopathology, differentiation grade, tumor(T) status, nodal(N) status, metastasis(M) status, pathologic stage, and treatment. Student's t-test, Kruskal-Wallis test, or Chi-square test compared factors between groups, and Kaplan-Meier curves compared survival. Statistical differences were significant at $p \le 0.05$.
Results: From 387 total patients analyzed, 111 (28.7%) mutation-positive patients were excluded. Of 276 (71.3%) mutation-negative patients, 240 (87.0%) had proteomic-Good status, and 36 (13.0%) had proteomic-Poor status. Mean age (68.4y vs. 66.1y; p=0.295) and mean primary tumor size were similar (0.215) between Good and Poor groups. Histology (i.e. adenocarcinoma, squamous cell carcinoma, neuroendocrine carcinoma, etc.) were similar between Good and Poor groups (p=0.209). Differentiation grade, N status, and M status differed between Good and Poor groups, with the Poor group having proportionately more poorly-differentiated (G3) tumors (p=0.019), mediastinal N2 and N3 involvement (p<0.01), and more M1 status (p<0.01). Treatment differed between Good and Poor groups, with the Good group more often had surgery or radiation alone, while the Poor group more often had systemic therapy (p=0.001). In Kaplan-Meier analysis, the Good group had 1-yr overall survival (OS) of 87.6% compared to a 1-yr OS of 63.3% for the Poor group (p<0.01).
Conclusion: Using a commercially-available peripheral blood liquid biopsy kit, mutation-negative NSCLC patients were identified by ctDNA analysis and as Good or Poor status by proteomic analysis. While age, tumor size, or T status did not correlate with Good versus Poor status, the Poor group had more poorly-differentiated tumors, more mediastinal N2 and N3 involvement, and more distant metastases, required systemic therapy more often, and had worse 1-yr OS than proteomic-Good patients.

Keywords: outcomes, Non-small cell lung cancer, Liquid Biopsy, histopathology

P10: Impact on PFS from Lack of Access to EGFR Inhibitors in Non-Small Cell Lung Cancer in the Brazilian Public Health Care System

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Background: Despite targeted therapies impacted on progression-free survival in EGFR positive metastatic non-small cell lung carcinoma (NSCLC) these agents are not available in brazilian public health care system (SUS). Polychemotherapy based on platinum still being used in this situation in contrast with international guidelines. This analysis aims to estimate the impact of the lack of access to anti-EGFR therapies on the PFS of these patients.
Method: The annual number of patients diagnosed with lung cancer was based on epidemiologic data of Cancer National Institute (INCA). Patients who have access to private health insurances were excluded. Only adenocarcinoma histology was considered. The INCA database, a cohort (Wong, 2016) and four clinical trials: EURTAC, LUX-Lung 3, LUX-Lung 7 and FLAURA were used to estimate stage distribution at diagnosis, recurrence rates and progression free survival in 2 years. The population without mutation in EGFR also was excluded.
Results: INCA estimates 28,220 new cases of lung cancer per year in Brazil. Of these, 76.3% are supposed to treated in SUS, totalizing 21,532, upon which 3,790 (40%) have adenocarcinoma histology. Of these, 3,790 (44%) have metastasis at diagnosis, and 3,703 (43%), 603 (7%), 517 (6%) are diagnosed in stages III, II and I, respectively. A recurrences rate of 53.79% in stage III (1,992), 46.49% in II (280) and 26.06% in I (135) in 5 years from diagnosis. Of these, 28% have mutation in EGFR. The outcome of our study was that, if they were treated with polychemotherapy, only 71 would be free of progression after 24 months. In contrast, with the use of inibitors of tyrosine kinase anti-EGFR, the expectation was 312 patients free from disease for Erlotinib, 377 for Gefitinib, 388 for Afatinib and 720 for Osimertinib.
Conclusion: The monthly drug costs, in Brazil, were, approximately, R$ 4,000 for Gefitinib, R$ 5,000 for Afatinib, R$ 8,000 for Erlotinib and R$ 32,000 for Osimertinib. With this, a cost-effectiveness study, presented by Gilberto De Lima Lopes Jr. in ASCO this year, showed that Osimertinib, although its high PFS, was not cost-effective in our country. Larger discounts, pharmaceutics support and more clinical trials are necessary to improve access to Osimertinib. In contrast, the incorporation of Gefitinib, Afatinib and Erlotinib in the public health care system should influence in PFS. Despite this, our study showed that, in two years, should avoid the progression of disease in 378 patients.

Keywords: Non-small cell lung cancer, Brazilian Public Health Care System, EGFR Inhibitors, Lung cancer

P11: Afatinib in Patients with *EGFR* Mutation-Positive (*EGFR*m+) NSCLC Harboring Uncommon Mutations: Overview of Clinical Data

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Background: Approximately 10–12% of patients with *EGFR*m+ NSCLC have tumors harboring uncommon *EGFR* mutations; however, there is a paucity of clinical data on the sensitivity of these tumors to EGFR tyrosine kinase inhibitors (TKIs). The clinical activity of afatinib, an irreversible ErbB family blocker, has been assessed in patients with NSCLC harboring certain uncommon *EGFR* mutations.
Method: Here, we review the key clinical data available for afatinib in *EGFR*m+ NSCLC harboring

uncommon *EGFR* mutations.

Results: Post-hoc analysis of the Phase II LUX-Lung 2, and Phase III randomized LUX-Lung 3, and 6, trials[1] identified 75 afatinib-treated pts with NSCLC harboring uncommon *EGFR* mutations not previously treated with a TKI. The objective response rate (ORR) against G719X (n=18), L861Q (n=16) and S768I (n=8) single/compound mutations was 78%, 56% and 100%, respectively. Response rate was lower in patients with exon 20 insertions (n=23; 9%) or de novo T790M (n=14; 14%). In 38 patients with uncommon mutations/duplications in exons 18–21, progression-free survival (PFS) was 10.7 months (95% CI: 5.6–14.7) and overall survival was 19.4 months (95% CI: 16.4–26.9). The clinical activity of afatinib against uncommon mutations is substantiated by observations outside of the clinical trial setting. In a Phase IIIb single-arm open-label study of afatinib, 55 of 479 TKI-naïve patients had NSCLC harboring uncommon mutations.[2] Among 35 pts with NSCLC harboring point mutations/duplications in exon 18–21, median PFS was 9.5 months (95% CI: 5.7–not evaluable [NE]) and time to symptomatic progression was NE (95% CI: 8.2–NE).[2] In an analysis of 165 patients with *EGFR*m+ NSCLC treated with first-line afatinib in real-world practice in South Korea, median PFS in those with uncommon mutations excluding T790M (n=10) was not reached with a median follow-up of 17.7 months (95% CI: 16.2–18.9).[3]

Conclusion: Afatinib has clinical activity in patients with NSCLC harboring uncommon *EGFR* mutations, including G719X, L861Q and S768I. These data could help inform clinical decisions in this patient population. 1. Yang. Lancet Oncol 2015;16:830-838 2. Marten. ELCC 2018 #158P 3. Kim. WCLC 2017 P3.01–023

Keywords: EGFR mutation, NSCLC, Afatinib, Uncommon

P12: Lung Tumor Histology as a Prognostic Factor for Short- and Long-Term Postoperative Outcomes

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Background: Based on the 2015 World Health Organization (WHO) Classification of Lung Tumors, we investigated whether lung tumor histology serves as a clinical factor that predicts short-term and long-term perioperative outcomes.

Method: We retrospectively analyzed patients who underwent robotic-assisted video-thoracoscopic lobectomy by one surgeon over 81 months. Patients were grouped by tumor histology based on final pathology report. Patients' demographics, smoking history, lobar tumor location, extent of resection, intraoperative outcomes, perioperative complications, and hospital length of stay (LOS) were compared.

Results: Among 420 study patients, the most common tumor type was adenocarcinoma (AD, 59.8%), followed by squamous cell carcinoma (SQ, 19.3%) and neuroendocrine carcinoma (NEC, 11.7%). Final histology for the remainder of the study cohort consisted of adenosquamous carcinoma (AdSq, 2.1%) and pulmonary metastasis (PM, 7.1%). All patients with AdSq histology had a positive smoking history, while those with NEC histology had the lowest smoking history rate (100% vs 71.4%; p<0.001). Patients with AdSq histology were both older and had larger tumors at time of resection (p<0.001 and p=0.003, respectively). Patients with AdSq histology required more extensive resections (p<0.004) and experienced greater estimated blood loss (EBL; p=0.005) and longer operative times (p=0.018) than the other three groups. While SQ or PM patients had slightly more postoperative complications, this difference was not significant (p=0.990). Patients with AdSq and PM histology had significantly worse 3-year overall survival (3-yr OS) (20.0% and 52.4%, respectively) compared to 76.2% and 73.9% for AD and NEC patients, respectively (p≤0.001).

Conclusion: Patients with AdSq histology were older and had larger tumors, which put them at risk of intraoperative difficulties, with more extensive resections, longer operative times, and greater EBL.

Having AdSq histology did not affect the short-term postoperative course, but AdSq histology resulted in worse 3-yr OS.

Keywords: lung, tumor histology, prognostic factor, postoperative outcomes

P13: Impact of ErbB Mutations on Clinical Outcomes in Afatinib- or Erlotinib-Treated Patients with SCC of the Lung

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Background: In LUX-Lung 8 (LL8), second-line afatinib (an irreversible ErbB family blocker) significantly improved OS (median 7.9 versus 6.8 months; HR [95% CI]: 0.81 [0.69–0.95]; p=0.0077), and PFS (2.6 versus 1.9 months; 0.81 [0.69–0.96]; p=0.0103) versus erlotinib in lung SCC (N=795). Comprehensive genetic analysis in LL8 patients assessed whether afatinib efficacy varied according to genetic aberrations in cancer-related genes, including ErbB family mutations.

Method: Tumor genetic analysis (TGA) was performed using Foundation Medicine FoundationOne™ next-generation sequencing (NGS). The cohort was enriched for patients with PFS >2 months, reflecting a range of responsiveness to EGFR-TKIs. EGFR expression was assessed by immunohistochemistry (IHC) in a largely separate cohort. Cox regression analysis correlated PFS/OS with genetic mutations (individual/grouped) and EGFR expression.

Results: Of 440 patients selected for TGA (PFS >2 months: n=320; ≤2 months: n=120), samples from 245 were eligible (afatinib: n=132; erlotinib: n=113). In the selected TGA population, PFS/OS outcomes were improved in the afatinib versus erlotinib arm. Baseline characteristics were similar in TGA and IHC cohorts and LL8 overall. In the TGA subset, 53 patients (21.6%) had ≥1 ErbB family mutation (EGFR: 6.5%; HER2: 4.9%; HER3: 6.1%; HER4: 5.7%). Beyond the benefit seen for afatinib in the overall population, in afatinib-treated patients PFS/OS were longer when ErbB mutations were present (PFS: 4.9 versus 3.0 months; OS: 10.6 versus 8.1 months). Conversely, survival outcomes in erlotinib-treated patients were similar with/without ErbB mutations. Presence of HER2 mutations predicted favorable PFS/OS with afatinib versus erlotinib. The Table shows outcomes in patients with/without ErbB family mutations, and by EGFR expression levels (afatinib: n=157; erlotinib: n=188).

| Subgroup | n | Afatinib vs erlotinib |
| | | PFS |
		HR (95% CI)
ErbB mutation-positive ErbB mutation-negative	53 192	0.56 (0.29–1.08) 0.70 (0.50–0.97)
EGFR mutation-positive EGFR mutation-negative	16 229	0.64 (0.17–2.44) 0.67 (0.50–0.91)

HER2 mutation-positive HER2 mutation-negative	12 233	0.06 (0.01–0.59)	0.72 (0.54–0.97)
HER3 mutation-positive HER3 mutation-negative	15 230	0.52 (0.16–1.72)	0.69 (0.51–0.94)
HER4 mutation-positive HER4 mutation-negative	14 231	0.21 (0.02–1.94)	0.67 (0.50–0.91)
EGFR IHC positive EGFR IHC negative	292 53	0.74 (0.56–0.97)	0.76 (0.41–1.40)
EGFR amplification present EGFR amplification absent	17 228	0.72 (0.18–2.90)	0.68 (0.50–0.92)
HER2 amplification present HER2 amplification absent	9 236	0.94 (0.20–4.38)	0.68 (0.50–0.91)

Conclusion: **These data are provocative and suggest that NGS may enable identification of lung SCC** patients who would derive additional clinical benefit from afatinib. Differential outcomes with respect to ErbB mutations for afatinib and erlotinib are hypothesized to reflect afatinib's broader mechanism of action. Clinical trial identification: NCT01523587

Keywords: lung SCC, Afatinib, erlotinib, ErbB mutations

P14: Detection of EGFR/T790M Mutation in Advanced NSCLC Post TKI Treatment: First Experience of Liquid Biopsy in Argentina

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Background: Genetic alterations in the tyrosine kinase domain of EGFR are key oncogenic events in non-small cell lung adenocarcinoma (NSCLC). In Argentina, 15% of NSCLC patients presents *EGFR* mutations which direct therapy with *EGFR* tyrosine kinase inhibitors (TKI) at the moment of diagnosis. Nearly 50% of patients progressing to TKI have T790M resistance mutations of EGFR exon 20. This mutation is detected either in formalin fixed paraffin-embedded (FFPE) tumor tissue and cell free tumor DNA (ctDNA) in plasma (liquid biopsy). This work describes the findings in T790M evaluation in TKI progressed patients either in FFPE tumor tissue or cell free tumor DNA (ctDNA) in the first experience of liquid biopsy application for targeted therapy in Argentina.
Method: NSCLC samples in either FFPE tumor tissue or ctDNA were processed from March 2017 to March 2018, from *EGFR* mutated patients who have radiological evidence of progression to TKI treatment. Samples were evaluated for T790M resistance mutation as requested by Oncologists or Pathologists all over the country. Due to clinical sensitivity and in case of negative results, physicians could request a retest in a newly fresh FFPE or ctDNA sample. T790M mutation was evaluated by digital droplet PCR (ddPCR) methodology (BIORAD QX 200 ™) in the ctDNA samples and by Real Time PCR (EntroGenRT52) for FFPE tumor tissue samples.
Results: NSCLC samples in either FFPE tumor tissue or ctDNA were processed from March 2017 to March 2018, from *EGFR* mutated patients who have radiological evidence of progression to TKI treatment. Samples were evaluated for T790M resistance mutation as requested by Oncologists or Pathologists all over the country. Due to clinical sensitivity and in case of negative results, physicians could request a retest in a newly fresh FFPE or ctDNA sample. T790M mutation was evaluated by digital droplet PCR (ddPCR) methodology (BIORAD QX 200 ™) in the ctDNA samples and by Real Time PCR (EntroGenRT52) for FFPE tumor tissue samples.
Conclusion: In TKI progressed EGFRm+ advanced NSCLC patients, T790M resistance mutation

in *EGFR* was found in 42% by ctDNA from plasma and 19% by FFPE tumor tissue. In the retesting scheme, the enriched population was positive in 30% when retesting was by FFPE tumor tissue and in 43% by ctDNA showing the importance of retesting algorithm for the correct identification of patients. The detection of T790M is of radical importance with the advent of new targeted therapies towards this oncogenic driver.

Keywords: Advanced NSCLC, EGFR/T790M, Liquid Biopsy, Digital droplet PCR

P15: Prevalence of EML4- ALK Fusion Gene in Adenocarcinoma Lung Patients by Using Immuno Histo Chemistry

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Background: An oral ATP- competitive TKI of ALK and c- MET, Crizotinib has shown impressive clinical activity in advanced non-small cell lung cancers especially in the tumors harbouring ALK rearrangements. With FISH as the mainstay for detection of ALK rearrangements, the ALK Break Apart FISH Probe Kit (Abbott Molecular, Des Plaines, IL) has become an FDA-approved companion diagnostic for targeted therapy with the ALK inhibitor crizotinib in lung cancers. The objective of this molecular epidemiological study is to estimate the prevalence of EML4-ALK fusion gene using IHC as a cost effective alternative to FISH for Indian patients with adenocarcinoma lung.
Method: Patients with NSCLC, adenocarcinoma histology, whose tumours had been tested for EML4-ALK fusion gene using IHC were considered for this study. Permission was obtained from the Ethics committee before the start of the study. Clinical characteristics and treatment details were collected from the patient's medical records. IHC analysis was performed using a Ventana automated immunostainer (Ventana Medical Systems, Illkirch Graffenstaden, France). Detection was performed using a multimer-technology system with the UltraView Universal DAB detection kit.
Results: A total of 204 NSCLC adenocarcinoma patients were included in the study. There were 126 (61.7%) men and 78 (38.23%) women with a median age of 57 years. Of the 204 patients, 47 (23.03%) were non-smokers and 175 (85.78%) had stage-IV disease at the time of initial diagnosis. 48 (23.52%) blocks were positive for EGFR mutations whereas 156 (76.47%) were EGFR wild type. EML4-ALK fusion gene was present in 27 (13.23%) patients whereas 177 (86.76%) tumors were EML4-ALK negative. 25 out of the 27 patients with ALK positivity received Crizotinib therapy.
Conclusion: The incidence of EML4-ALK gene fusions (13.23%) in this Indian population is four fold high than the previous reported incidences and supports the claim of several recent studies that a relatively new ALK clone, 5A4 and D5F3 from cell signaling technology (Ventana) can accurately identify ALK rearranged lung ACA as compared to FISH. The inclusion of IHC for the detection of EML4-ALK gene fusions as a low cost alternative seems warranted.

Keyword: EML4- ALK Immuno histo chemistry.

P16: Experience with First Line Crizotinib in ALK Positive Lung Cancer Patients, Instituto Oncologico Nacional – Panama

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Background: ALK rearrangement is present 4% - 6% of all patients with NSCLC. Patient with this disease are treated with ALK inhibitors. Crizotinib was the first ALK TKI approved in the first line setting, after showing superiority over chemotherapy

Method: We retrospectively reviewed the medical records of patients with ALK positive lung cancer from February 2014 to May 2018. The objective was to describe the incidence, clinical and pathological characteristic, and to determine the progression free survival in the patients that received first-line crizotinib

Results: There were 406 patients diagnosed with lung cancer and 26 of the cases were ALK positive, representing 6,4%. The mean age of diagnosis is 64 years (37 – 85) and 53,1% of patients were females. 92,4% of the patients had PS between 0 – 2. 43,2% of the patients were smokers. All patients were diagnosed with at least locally advanced disease and 73,1% had stage IV disease. At baseline, 2 patients had SNC metastasis (10,3%). 20 patients received first line therapy with crizotinib.

N at risk 20   14   8   5   2   1   0
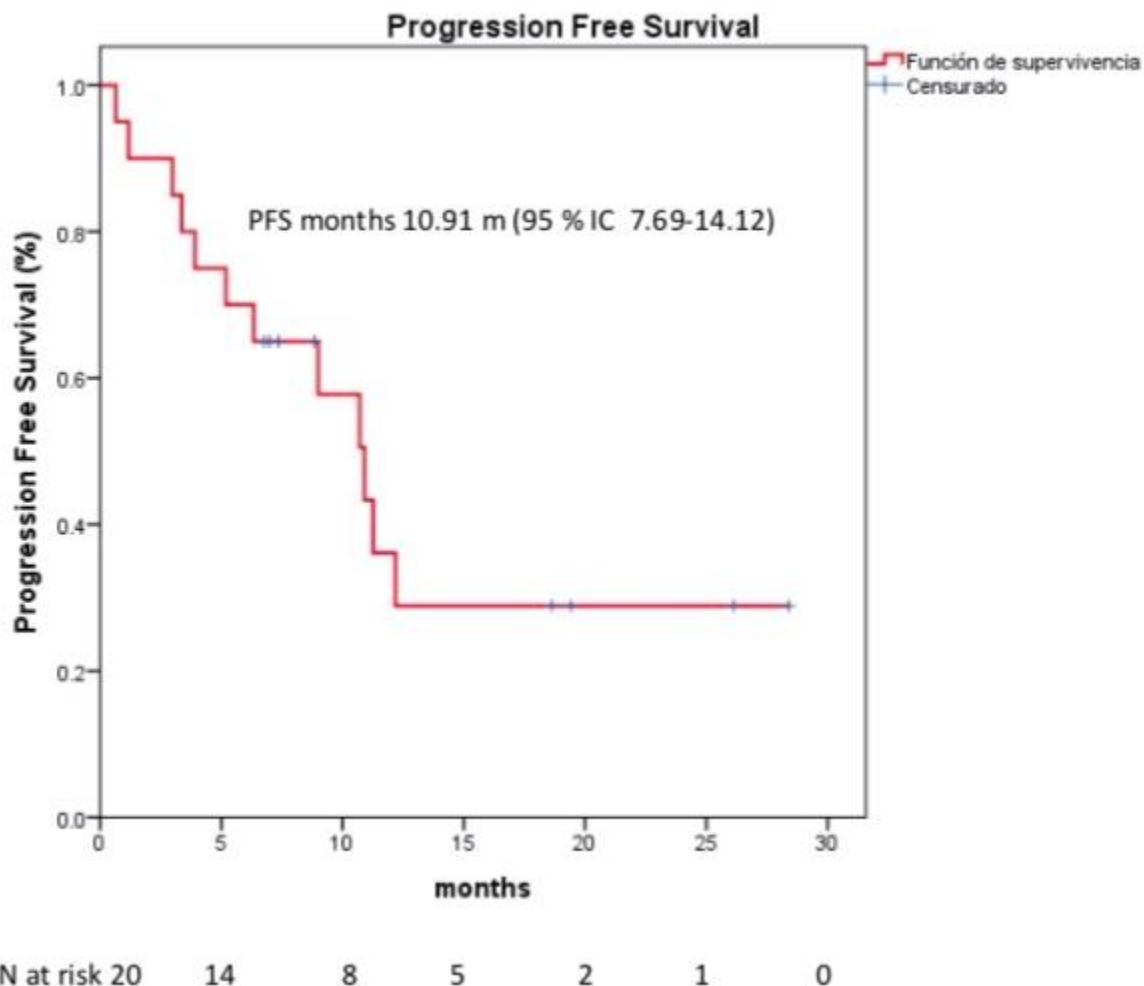
Conclusion: The median progression free survival 10.9 months (95% IC 7.69 – 14.12). with first line crizotinib at our institution is similar to pivotals trials.

Keywords: ALK rearrangemen, Crizotinib

P17: Neutrophil to Lymphocyte Ratio as an Inexpensive Prognostic Marker in Metastatic Non-Small Cell Lung Cancer

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Background: The neutrophil to lymphocyte ratio (NLR) has been used as systemic inflammation marker and related to worse prognosis in both, neoplastic and non-neoplastic diseases. Several studies in surgically treated lung cancer patients have shown the correlation between NLR and survival using 5 as the cut-off. However, its value in metastatic disease has been little investigated. The aim of this study was to explore the correlation between NLR (cut-off of 5) and overall survival and its value as a prognostic biomarker in patients with metastatic non-small cell lung cancer (NSCLC).

Method: The clinical chart of consecutive metastatic NSCLC patients treated in Edgardo Rebagliati Martins National Hospital, Lima-Perú, between July 2014 and December 2015, were retrospectively evaluated. Epidemiological, disease and extension data were collected, as well as white cell differential before either, definitive treatment or best supportive care. Survival analysis was performed using log-rank test, Kaplan-Meier method and Cox regression analysis using NLR cut-off point of 5 as previously reported. R language was used for statistical analysis.

Results: Ninety clinical charts of advanced NSCLC patients were evaluated, of which 36 cases were considered for final analysis. The mean age was 69 years (SD 11.9). Twenty-three patients were female (63.9%), 28 were non-smokers (77.8%) and 32 had adenocarcinoma (88.9%), median NLR was 3.4. The median overall survival (OS) was 7.95 months. Median OS for patients with NLR ^{3} 5 was 3.97 months vs. 12.07 months for NLR < 5 (p = 0.0041). Cox analysis for NLR < 5 was performed, adjusting with variables such as age (HR: 0.27, p = 0.008), gender (HR: 0.30, p = 0.012) and systemic treatment (HR: 0.34, p = 0.038). Finally, we performed multivariate analysis adjusting for all variables that potentially can influence in mortality such as age, gender, systemic treatment and metastatic sites and we found HR 0.27 for NLR < 5 (95%CI 0.09 - 0.84, p = 0.024).

Conclusion: NLR < 5 was statistically associated with better overall survival. Multivariate analysis adjusted by age, gender, systemic treatment and metastatic compromise, was able to predict better overall survival, with a hazard ratio of 0.27 for NLR < 5. The retrospective design and limitations of our study only allow us to generate the hypothesis that NLR < 5 could be an easy and inexpensive marker of better survival in metastatic lung cancer patients and support design of larger and prospective trials.

Keywords: Neutrophil to lymphocyte ratio, Advanced lung cancer, Prognostic marker

P18: Targeting Lung Cancer Initiating Cells by Aptamers

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Background: Lung cancer is the most common cause of cancer death worldwide, as detection of the disease only occurs in advanced stages. The heterogeneity of lung tumor cells suggests that these may originate from multipotent cells. Several studies suggest that tumor-iniating cells (cancer stem cells, CSCs) may be the cause of tumor growth, metastasis and resistance to conventional therapies leading to tumor recurrence. The lack of specific markers for CSC detection hinders the use of these cells in determining disease prognosis in clinical practice. Thus, the objective of this project is the development of DNA aptamers for selective identification of the molecular signature of lung CSC.

Method: Using A549 human lung cancer cells as target to perform the isolation of DNA aptamers from a random library through the cell-SELEX (Systematic Evolution of Ligands by EXponential enrichment) it

was possible to isolate stem-like cells by cell sorting using fluorescence-tagged aptamer. To eliminate DNA aptamers binding to common epitopes between different cell types, blood cells were used as target in subtractive-SELEX. To analyze the affinity and specificity of selected aptamers, we used conventional analytical technologies (cytometry, microscopic analysis).

Results: After seven cycles of cell-SELEX we obtained a pool of aptamers able to identify $CD90^+$ lung cancer cells. CD has been described as a marker for cancer stem cells. The aptamers were divided into families based on homology between sequences. Eight aptamers were identified, whose affinity and specificity are currently being analyzed. The results of *in vitro* tumorigenesis assays suggest that aptamer-positive cells increase their capacity for invasion and migration.

Conclusion: Our results indicate that the selected aptamers, identify a population of tumor cells with enhanced tumorigenic potential. Financial support: FAPESP; CNPq (Brazil)

Keywords: Molecular signature of membrane, Cancer initiating cells, Aptamers, Tumorigenesis

P19: Analysis of the Status of Lymphocyte Infiltration in Patients Diagnosed with Non-Small Cell Lung Cancer

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Background: The present evidence refers to the potential role of tumor infiltrating lymphocytes (TIL) in determining the survival of non-small cell lung cancer (NSCLC). TILs are generally determined using semi-quantitative subjective methods. While several studies have researched the prognosis of different subtypes of TIL, the data are limited to the co-expression of TIL subpopulations and their clinical relevance. Primary objective: to identify subgroups of patients with NSCLC, according to the status of lymphocyte infiltration in the tissue sample, classified as mild, moderate, severe or absent, and research its relationship to progression-free survival (PFS) and overall survival (OS).

Method: The medical records of 480 patients with non-small cell lung cancer stages IIIB and IV were analysed. 166 patients out of 480 met the selection criteria. The tumor-associated lymphoid infiltrates were descriptively classified as mild, moderate, severe or absent, based on morphological observation only. The relationship with the clinicopathological variables were assessed by Chi-square analysis, and the association with overall survival was performed using the Cox proportional hazards analysis model. The Kaplan-Meier method was used to compare survival curves.

Results: 56% of patients had been diagnosed with adenocarcinoma, 39% with squamous cell carcinoma, and only 5% had undifferentiated carcinoma histology. 70% of patients were male, and 82% of the patients were smokers. Regarding PFS in all patients, those with an intense lymphocyte infiltrate had higher PFS (9.66 months) compared to moderate (6.22 months) and minor (5.66 months). Also the OS of all patients was higher in those who presented severe lymphocyte infiltrate (17.44 months), followed by those with infiltration moderate (10.08 months) and patients with lower OS were patients with mild infiltrate (9.17 months). As adenocarcinoma patients, those with an intense lymphocyte infiltrate had higher OS and PFS; 15.28 and 9.25 months, respectively. Compared to patients with moderate infiltrate, 10.07 and 6.25 months, patients with mild infiltrate, 8.25 and 5.55 months. Only OS different values were statistically significant (p = 0.019).

Conclusion: Patients whose pathology reports showed an intense inflammatory infiltrate increased pfs and had higher OS. These differences were statistically significant only for OS in patients with adenocarcinoma (p = 0.019). We observed that those with a greater number of lymphocytes in the tumor tissue samples showed a higher OS. However, we are performing prospective studies prospective with a larger number of patients to draw conclusions with greater statistical significances.

Keywords: non-small cell lung cancer (NSCLC), TIL, Lung cancer, lymphoid infiltrates

P20: Molecular Characterization of Non-Small Cell Lung Cancer (NSCLC) Patients by Next Generation Sequencing: Preliminary Data

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Background: Profiling of targetable oncogenic drivers has significantly improved outcomes in patients with non-small cell lung cancer (NSCLC). About 40% of individuals with metastatic lung adenocarcinomas may benefit from personalized treatment with kinase inhibitors. There is limited data of the distribution of oncogenic drivers other than ALK and EGFR in our region. In this study we performed next generation sequence (NGS) to study the distribution of molecular alterations in patients with advanced lung cancer. Herein we present preliminary data of a single center experience.
Method: A prospective, single-center, observational study was conducted. We included 125 patients > 18 years old with NSCLC from 06/2015 to 06/2018. NGS was performed with DNA/RNA from formalin-fixed, paraffin-embedded (FFPE) tumour tissue with OncomineTM Focus Assay (Ion 520 Chip), sequenced in Ion S5 Next Generation Sequencing Systems, analysed with Ion ReporterTM Software 5.2.1 and informed with Ion TorrentTM OncomineTM Knowledgebase Reporter. Results were compared with those from standard pathology and molecular biology techniques, when available, like immunohistochemistry (IHQ) and FISH for ROS1 and ALK and PCR and sequencing for EGFR. We report partial results from the first 51 patients included.
Results: Median (IQR) age was 65 years (59-74), n=28 were men (55%), smoker/former-smoker/non-smoker n=11 (21.6%)/ n=31 (60.8%)/ n=9 (17.6%), Stage IIIa n=7 (13.7%), IIIb n=6 (11.8%), IV n=38 (74.5%). Adenocarcinoma histology n=43 (84.3%). Assay performance was 100% for DNA analysis and 60.8% for the study of fusions and CNV from RNA. Distribution of molecular alterations: KRAS n=18 (35%), EGFR n=8 (17.6%) BRAF n=2 (4%), METex14 skipping n=2 (4%), HER2 n=1 (2%), ALK rearrangements n=5 (10%) y ROS1 rearrangements n=2 (4%). Co-mutations: EGFR+BRAF n=1, ALK+KRAS n=1, KRAS+AKT n=1.
Conclusion: NGS allows to optimize the molecular profiling of tumors from patients with lung cancer in our population. It can simultaneously identify mutations, rearrangements and alternative splicing events in key oncogenic drivers that can select patients to treatment with kinase inhibitors, currently available in the daily practice and in clinical development.

Keywords: Next Generation Sequencing, Non-small cell lung cancer, Molecular profiling, Targetable oncogenic drivers

P21: Outcomes of Lung Cancer Surgical Patients in a District Hospital

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Background: Lung cancer is the leading cause of cancer-related mortality worldwide and its incidence continues to rise. Overall survival remains low, hence the importance of accurate staging and approach. When indicated, surgical resection remains the gold standard. Our aim was to compare outcomes in surgical patients of a district hospital with those described in the literature.

Method: Data was collected retrospectively from March 2012 to December 2017 and analysed using MS Excel. All patients were evaluated in a multidisciplinary board. Patients operated for diagnostic purpose were excluded.

Results: Out of 488 patients diagnosed with lung cancer, 101 surgeries were performed, regarding 88 patients. Mean age was 63,5 (±9,4) and 68% were male. Smoking habits were present in 77% of patients, COPD and enphysema in 19%, diabetes mellitus in 14% and previous lung cancer in 1 patient. Adenocarcinoma (71%) was the most frequent tumour. Concerning pathological stage, 54% of patients were stage IA or IB. 23% were operated after neoadjuvant treatment. 71% of patients were submitted to lobectomy with systematic lymph node dissection and 14% to wedge resection. 41% of cases were approached using VATS techniques. Adjuvant chemotherapy, radiotherapy and chemotherapy plus radiotherapy were indicated in 34%, 4% and 9% of cases, respectively. Perioperative mortality was 0,9% (1 case) and 10,9% had complications, pneumonia being the most frequent. Mean follow-up time was 31 months (±16). Overall survival at 24 months was 79,2%.

Conclusion: These outcomes are comparable with those reported in the literature, which demonstrates the importance of a dedicated multidisciplinary team in replicating international results.

Keywords: surgery, early-stage, overall survival

P22: ASTRIS a RWT with Osimertinib in NSCLC EGFR T790M Mutated: Disease Characteristics from Patients Included in Argentina

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Background: We present demographic and disease characteristics for the first interim analysis of ASTRIS study in Argentina.

Method: ASTRIS is a Phase III open-label, single-arm, multi-national, real world treatment (RWT) study assessing the efficacy and safety of osimertinib in patients with advanced T790M mutation positive non-small cell lung cancer (NSCLC), who have previously received an EGFR-TKI. Key inclusion criteria are adults with locally advanced or metastatic NSCLC having a confirmed T790M mutation who received a prior EGFR-TKI and have WHO performance status 0 − 2. T790M status must be confirmed by an appropriately validated test. Patients with asymptomatic CNS (central nervous system) metastases are allowed. Patients receive Osimertinib 80 mg once daily for as long as the patient continues to receive clinical benefit, as judged by the investigator.

Results: Argentina enrolled 29 patients from three centers. At data cut-off (20 Oct 2017) 25 patients (78,1%) were still ongoing, 4 patients had died. Median follow up 3,3 months (0-8). The mean age was 59.6 years (35-91); 72,4% (21) were less than 65 years old; 82,8% females; 96,6% caucasian; ECOG 0-1 65,5%, ECOG 2 20,7%. Stage IV 89,7%. Previous cancer therapies included gefitinib 37,9%, erlotinib 31% and afatinib 37,9%. 48,3% of the patients had received previous chemotherapy, 6,9% previous immunotherapy and 31% previous radiotherapy. Only patients with T790M positive were enrolled in this study, 27,6% (8) had tissue biopsy at progression; 65,5% (19) were diagnosed by plasma sample[FT1] [BP2] , 3,4% (1) by cytology and 3,4% (1) after bone marrow biopsy. The origin of the biopsy tissue was primary tumor in 87,5% and metastasis in 12,5%. T790M mutation was found in all the patients. T790M alone in 72,4% (21) and in combination with other EGFR mutations in 27,6% (8)[FT3] . The other EGFR mutations were exon 19 deletion 20,7%; exon 20 insertion 6,9% and L858R 6,9%. Testing methods: Roche Cobas 1; Qiagen Therascreen 16; Entrogen EGFR kit 3, sanger sequencing 1, ddPCR 7, unknown 1.

Conclusion: We present real word evidence data of demographics and diagnostic patterns of patients beyond progression. Efficacy data is still immature and will be presented in subsequent interim analysis.

P23: Stage IIIb NSCLC and Curative Intention Treatment: Difficulties and Disparities in Brazil

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Background: Lung cancer is the second most incident among men and the fourth among women in Brazil. Data on how it is diagnosed and staged are relatively scarce in Brazil. According Brazilian data published in the last 15 years, NSCLC is the most frequent histological subgroup (≥80%), being diagnosed, unfortunately, in advanced stage (71% to 94% in stage III and IV). Besides, Brazilian health care system is divided into private and public coverage (27% and 73%, respectively), and there are significant discrepancies in health care resources availability, which may impact on patients' outcome. This study aims to characterize treatment patterns among stage IIIb NSCLC Brazilian patients and their outcomes.
Method: In this retrospective cohort study, newly diagnosed (between January and December 2014) advanced NSCLC patients were consecutively included. Data were collected from medical records of 10 Brazilian cancer institutions and recorded in electronic clinical report form. Demographic data, medical history, tumor staging, pathological characteristics, treatments and outcomes were collected and analyzed. For each patient, maximum follow-up was 36 months.
Results: 391 patients from 8 different Brazilian states were enrolled, 69 (17.6%) had stage IIIb disease and were the focus of this analysis. 48 were men (69.6%), median age was 64 years, 85.5% have been treated in public and 14.5% in private health system; 82.6% were former or current smokers. The most frequent histological subtypes were squamous cell carcinoma (SqCC) with 32 cases (46.4%) and adenocarcinoma (ADC) with 30 (43.5%). Among smokers, 45.6% had ADC and 43.9% SqCC. At diagnosis, WHO-PS 0, 1, 2, 3, and unknown status were 5.8%, 40.6%, 21.7%, 15.9%, and 15.9%, respectively. Initial treatment according to health systems is described in Table 1. Median overall survival observed in overall group was 9.4 months (CI95% 6.6-12.1). Table1 – Initial NSCLC stage IIIb treatment in Brazil according to health system insurance.

Treatment	Public Health System n=59 (86.0%)	Private Health System n=10 (14.0%)	Total n=69 (100%)
Concurrent Chemoradiation	20 (33.9%)	1 (10%)	21 (30.4%)
Sequential Chemoradiation	4 (6.8%)	2 (20%)	6 (8.7%)
Concurrent or Sequential Chemoradiation	24 (40.7%)	3 (30%)	27 (39.1%)
Radiotherapy only	17 (28.8%)	3 (30%)	20 (29.0%)
Chemotherapy	10 (16.9%)	4 (40%)	14 (20.3%)

only			
Surgery only	3 (5.1%)	0 (0%)	3 (4.4%)
No described treatment	5 (8.5%)	0 (0%)	5 (7.2%)

Conclusion: Our findings in stage IIIb NSCLC Brazilian population demonstrated that only 39.1% of patients was treated with curative intention chemoradiation therapy and treatment strategies may differ according to the health care system.

Keyword: Stage IIIb NSCLC; Health System; Chemoradiation

P24: Access to Oncological Care in Patients with Lung Cancer Treated in Public and Private Hospitals in Buenos Aires, Argentina

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Background: Timely access of patients to cancer care is a major factor influencing treatment initiation. There is limited data on waiting times to lung cancer diagnosis and treatments in Latin-America. In Argentina, oncological care is provided mainly in public and private hospitals. In this study, we describe and compare the time elapsed from the first consultation to the diagnosis and treatment of patients with non-small cell lung cancer (NSCLC) treated with chemotherapy at public and private academic hospitals in Buenos Aires. We also describe and correlate social, economic and educational factors that could have an effect on the time to treatment as a surrogate of patient's access.
Method: Multicenter, retrospective cohort study. Patients >18 years old with diagnosis of NSCLC treated with chemotherapy were included. Clinical and epidemiological data were collected. Kaplan-Meier method was used to study time intervals from first consultation to diagnosis and treatment; and the log rank test for comparisons between public and private hospitals. We performed multivariate analysis (Cox Regression Models) to study the correlation between social, economic and educational factors and the time to therapy.
Results: Between 06/2016 and 09/2017, 100 patients with NSCLC were included, 41 in Public Hospitals (PuH) and 59 in Private Hospitals (PrH). Median age (IQR) was 65 years (58-71), male individuals (PuH/PrH): 63.4%/59.3%. There were no significant differences in smoking habits between groups. Stage (I/II/III/IV/Relapse), PuH: 2.4%/7.3%/17.1%/70.7%/2.5%; PrH: 0%/10.2%/ 30.5%/57.6%/1.7%. Chemotherapy treatment for metastatic disease (PuH/PrH): 73.2%/55.9%, adjuvant chemotherapy (PuH/PrH): 9.8%/11.9%, chemoradiation therapy (PuH/PrH): 12.2%/32.2%. Adenocarcinoma histology (PuH/PrH/): 61%/83%, squamous cell carcinoma (PuH/PrH): 31.7%/13.6%. Median (IQR) time interval between the first consultation and diagnosis was 86 days (69-116) in PuH and 48 days (33-61) in PrH (p=0.0014). Globally, median (IQR) time elapsed between diagnosis and treatment with chemotherapy was 71 (60-83) days in PuH and 31 (24-39) days in PrH (p=0.0002). For patients with metastatic disease, median (IQR) time from diagnosis to treatment was 63 days (45 - 83) in PuH compared to 33 days (26 -

44) in PrH (p= 0,005). For patients treated with neoadjuvant, adjuvant chemotherapy or chemoradiation therapy, median (IQR) time to treatment was 83 (64-99) days in PuH and 22 (14-37) days in PrH (p<0.0091). In multivariate analysis, only treatment at private hospitals was associated with lower time intervals to treatment.
Conclusion: Our findings show that there are inequalities in the access of patients to lung cancer diagnosis and treatment between the private and public hospitals in Buenos Aires, Argentina.

P25: Preliminary Experience With the Use of Osimertinib in Chilean Patients

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Background: The current standard of care for patients with advanced non–small-cell lung cancer (NSCLC) harboring epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI)–sensitizing mutations is treatment with a EGFR-TKI. The frequency of these mutations varies from approximately 10% of lung adenocarcinoma in North American and European populations to 50% in Asian population. In Latin America the frequency varies between 14 and 51%. Approximately 50% of EGFR TKI resistance is due to a second site mutation, the T790M mutation occurring within exón 20. Osimertinib is an oral, third-generation, irreversible EGFR-TKI that selectively inhibits both EGFR-TKI–sensitizing and EGFR T790M resistance mutations, with lower activity against wild-type EGFR.
Method: To describe the first natural history protocol regarding the use of Osimertinib in Chilean patients with the diagnosis of lung cancer with the EGFR mutation and progression to tyrosine kinase inhibitors with detectable T790 mutation. We also included patients with de novo T790 mutation. We evaluated demographic data, diagnostic method of resistance, sites of progression, toxicities and treatment efficacy
Results: We analyzed 28 patients in the period of June 2016 and April 2018.
Median age was 65 years old, female sex corresponded to 36%; PS 0,1 96%, 7% of patients were de novo T790 mutations, 93% patients had a history of EGFR-TKI therapy, gefitinib in 3 patients, erlotinib in 15 pts, and afatinib in 8 pts. Upon the initial evaluation 86% patients were diagnosed with stage IV NSCLC Central nervous system (CNS) lesions were observed in 6 patients (21%). T790M was confirmed by histologic evaluation in 16 patients and by Liquid biopsy in 12 patients. The response rate, disease control rate progression free and overall survival will be presented in a later publication.
Conclusion: In our very early experience with the use of osimertinib, we report a relatively similar patient characteristics compared with the registration studies of Osimertinib. At the moment adhesion and tolerance profile compares favorable with older generation TKI inhibitors.

Keywords: osimertinib, EGFR, ADVANCED DISEASE

P26: Lung Cancer in Adolescent & Young Adults: Single Center Experience from Eastern India

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Background: Lung cancer is the most common cancer and cancer related death amongst male in India. There is paucity of data about AYA lung cancer epidemiology and treatment outcome in India. Here, we have analyzed demography, molecular features and treatment outcome in AYA lung cancer patients

treated at our center.

Method: This is a single institutional review of patients aged 10 to 35 years treated between Oct'13 and Feb'18 with diagnosis of Lung cancer. Those with diagnosis of squamous cell carcinoma (SCC) and adenocarcinoma were analyzed for demographic feature, clinico-pathological characteristics whereas treatment outcome and survival analysis was done in patients with advanced disease who received treatment

Results: Total 48 patients were registered with median age of 30 years (range: 10-35). Histology was – neuroendocrine tumor in 6 (13%), mucoepidermoid carcinoma in 3 (6%), SCC in 4 (8%) and adenocarcinoma in 35 (73%) patients. Baseline features are outlined in Table 1. Thirty-two (82%) patients had metastasis on diagnosis and 40% (n=10) patients had ALK-rearranged adenocarcinoma. After median follow-up of 9.6 months (range: 1.1-56.2), median progression-free survival (PFS) was 14.4 months (95 CI: 6.2-35) and median overall survival (OS) was 31.6 months (95 CI: 8.2 – not reached). Median PFS was 8.7 months & 35.5 months whereas median OS was 17.9 months & 56.2 months in patients treated with chemotherapy (n=16) and with tyrosine kinase-inhibitor (n=11), respectively. Median PFS was 35.5, 14.4 & 6.2 months whereas median OS was 56.2, not reached & 8.9 months in patients treated with EGFR mutation (n=5), ALK-rearrangement (n=9) and molecular negative (n=11) tumors, respectively. Table 1: Baseline characteristics and treatment details (n=39).

Characteristics
Age (years)
Sex Male Female
Smoking status (n=37) Never smoker Current smoker
Symptom duration (months)
Symptom Hemoptysis Weight loss
Eastern Cooperative Oncology Group performance status PS 1 PS 2 PS 3
TNM Stage 2 3 4
Upfront treatment type, localized disease (n=6) Chemoradiation Surgery + adjuvant chemotherapy
Metastatic disease (n=32)
No or involved organ metastasis Single Two Three Four Five
Site of metastasis Lung/pleura Bone Brain Liver
Treatment taken Yes No
Molecular profile (n=25) EGFR mutation ALK rearranged ROS1 rearranged
Upfront treatment type (n=27) Chemotherapy Chemotherapy f/b Tyrosine kinase inhibitors Crizotinib Gefitinib
Treatment response (n=24) Partial response Stable disease Progressive disease
2nd line treatment (n=08) Chemotherapy Tyrosine kinase inhibitors

Conclusion: Adenocarcinoma was the predominant histology and ALK-rearrangement was very high (40%) in our AYA lung cancer cohort, and majority (82%) had advanced disease on diagnosis. Outcome was excellent with molecular targeted therapy.

Keyword: AYA, Lung cancer, India, overall survival

P27: Prognostic Value of Lymph Node Ratio N2 Non-Small Cell Lung Cancer Fulfilling NCCN Resection Criteria

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Background: The aim of the study was to evaluate the prognostic value of lymph node ratio in N2 non-small cell lung cancer fulfilling NCCN resection criteria.

Method: 203 cases of pathological N2 non-small cell lung cancer patients were enrolled who received radical resection fulfilling NCCN resection criteria at the department of Thoracic Surgery Ⅱ, Peking University Cancer Hospital from January 2006 to December 2014. The univariate analysis between clinicopathological variables and prognosis used log-rank. Cox regression was conducted to identify the independent prognosis factors for N2 non-small cell lung cancer.

Results: The 5 year over survival was 44.8%. Age, gender, pathology, T stage, viscerl pleural invasion and single N2 metastasis were not correlated with the prognosis. Tumor size (P=0.030), skip N2 metastasis (P=0.009), single station N2 metastasis (P=0.01) and lymph node ratio (P<0.001) significantly impacted N2 non-small cell lung cancer prognosis. Cox regression analysis confirmed that tumor size (P=0.017) and lymph node ratio (P=0.010) were the independent prognosis factors. The 5 year over survival was 70.1% for the low risk group with tumor size less than 3cm and lymph node ratio less than 0.19. However, the 5 year over survival of high risk group with tumor size more than 3cm and lymph node ratio more than 0.19 was 24.5%, which was significantly different with the low risk group(P<0.001).

Conclusion: Lymph node ratio and tumor size were the independent prognosis factors for N2 non-small cell lung cancer fulfilling NCCN resection criteria, the risking groups based on lymph node ratio and tumor size can be better to predict the prognosis of N2 non-small cell lung cancer.

Keywords: Lymph node ratio, Prognosis, NCCN resection criteria, N2 non-small cell lung cancer

P28: 75 Mg of Erlotinib in Latin American Patients with Metastatic Non-Small Cell Lung Cancer - Long Term Analysis

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Background: The recommended dose for erlotinib of 150 mg was developed based on the maximum tolerated dose (MTD); meanwhile the suggested dose for gefitinib is only one third of its MTD. Studies suggest that the optimal biologic dose of erlotinib should be lower and dependent of the body mass index. Hereby we present results and toxicity with 75 mg/day dose in Chilean patients.

Method: We performed a retrospective review of patients with histologically proven (+) EGFR (+) mutation mNSCLC treated with 75mg/day erlotinib as starting dose at Centro Internacional de Estudios Clinicos Bradford Hill, Santiago, Chile. Clinical information, including toxicity grade 1-4, drug discontinuation, clinical evolution and radiological evaluation and overall survival were revised.

Results: Patients received 75mg/day of erlotinib as starting dose. Sixteen (89%) patients were treated in first and two (11%) in second line treatment. Mean age was 62 years (range 36-89 years) and 50% patients were female. 16% patients had brain metastases at first diagnosis. 2 patients were tested for T790 mutation positive. 38% of patients had smoking history. All patients had mutation positive EGFR, 12 (66 %) had Del19 and 6 (34%) exon 21 mutation. Median progression free survival was 18 and overall survival 23 months. The main grade 1-2 toxicities were rash (33%) and diarrhea (25%). No grade 3-4 toxicity and no cases of drug discontinuation were reported.

Conclusion: In South American population with mutated mNSCLC, a dose of 75mg/day of erlotinib was well tolerated. This dose resulted in comparable benefits in PFS and OS when compared to those reported in the literature with the standard dose. Genetic polymorphism in metabolic enzymes and lower body mass index could explain the same efficacy at lower dose. More studies are needed to explore the use of adjusted doses of biological agents in different ethnic backgrounds.

P29: Fast Response to Osimertinib in Patients with EGFR Mutated NSCLC with Brain Metastasis and Carcinomatous Meningitis

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Background: Approximately 25% of the patients with lung adenocarcinoma stage IV with EGFR mutation show CNS compromise when diagnosed. Osimertinib is a third generation TKI (tyrocinkinasa inhibitor) active against sensitivity and resistant mutations of EGFR (Del Ex19/L858R) & (T790M) with high penetration into the CNS. Here we show two cases of lung adenocarcinoma patients with CNS compromise who received first line osimertinib treatment. Case 1: 42 year old, non smoker female with lung adenocarcinoma who underwent surgical resection in 2007. In 2017 developed endocraneal hypertension syndrome and craneal VI left par palsy. CSF: high spinal fluid protein concentration with normal glucose level, non celular (x 3) CT: solid nodule in the lower left lobe LII (36 mm) and ground glass multiple opacities. BRAIN MRI: hyperintensity of signal in FLAIR in the interior side of the encephalic trunk, enhanced with gadolinium. Lung biopsy: Moderately differentiated adenocarcinoma (T2aNxM1b), with EGFR exon 19 deletion. Suspected carcinomatous meningitis. Initial treatment: Erlotinib 150 mg Qd, switching to osimertinib 80 mg Qd due to symptom progression. She showed a fast response within 5 days with resolution of neurological symptoms and partial response to lung lesions 90 days after initiation of treatment. Case 2: 47 year old female, mild smoker (7 pack/y). Pericardic tamponade at diagnosis. PET/CT: bone hyperuptake, multiple ganglionar and ground glass opacities mostly in the upper right lobe. Brain MRI: with cortical and subcortical, brain and cerebellum sub centimetric multiple lesions. Supraclavicular lymph node biopsy: Poorly differentiated adenocarcinoma (TXN3M1c). with EGFR L861Q mutation. It also was detected with in serum and pericardial fluid (Cobas EGFR Mutation test V2). She start Osimertinib 80 mg qd, CT control showed a decrease of the ground glass opacities and partial response in the CNS.
Method: not applicable
Results: Not applicable
Conclusion: Conclusions: Both cases showed fast intracraneal responses to Osimertinib for the classic and the less frequent mutation (Del 19 & L861Q) supporting its use in first line treatment in this patient.

Keywords: EGFR mutated, NSCLS, osimertinib, Brain metastasis

P30: Analysis of Toxicities in Patients with Lung Cancer Compared Other Tumors in Inmune Therapy in Our Institution

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Background: In this study, we analyzed and compared the various toxicities presented by patients who performed immune therapy with diagnosis of lung cancer (LC) against other tumors in advanced stages,

basedontheknowledgeofthegreaternumberofcomorbiditiesthatpatientswith PC have in relationship to other tumors. The comorbidities associated with LC are the set of alterations and disorders that may be associated, for one reason or another, with this disease. The most prevalent comorbidities are severe smoking, hypertension, diabetes and is chemic heart disease, followed by COPD, asthma and anemia. Regarding immune therapy, we can say that it is a type of treatment designed to stimulate the body's natural defenses in order to fight cancer. **PRIMARY OBJECTIVE** To compare the most frequent toxicities in patients diagnosed with lung cancer vs other types of tumors (kidney cancer, melanoma, gastric cancer, and mesothelioma) in stage IV, in treatment with immune therapy.

Method: A retrospective observational descriptive study, 58 medical charts of patients of the Instituto Oncologico de Cordoba were analyzed. All patients received immune therapy. Two groups were selected; the first one was diagnosed with lung cancer and in the second group other types of tumors, both with stage IV pathologies. The entire study population was evaluated for PDL-1 before starting treatment, by IHC.

Results: We included 58 patients, 33 patients (57%) had lung cancer and 25 (43%) had other types of tumors. When analyzing the toxicities of both groups it was observed that, the patients with lung cancer showed: Asthenia 20 patients (44%), Skin Rash 8 patients (18%), Diarrhea 3 patients (7%), hypothyroidism 2 patients (5 %), liver toxicity 6 patients (13%) and hematological toxicity 6 patients (13%). In the second group patients exhibited: Asthenia 17 patients (61%), Skin Rash 4 patients (14%), Diarrhea 2 patients (7%), hypothyroidism 2 patients (7%) and hematological toxicity 3 patients (11%).

Conclusion: In this work, we can observe that in both groups there were expected toxicities. The most frequent one was asthenia, but the group with lung cancer showed greater hepatic and hematological toxicity with a significant difference compared to other tumors.

Keywords: immune therapy, toxicities, lung cancer compared other tumors, Lung cancer

P31: Genetic Profile in NSLC Biopsy Samples - A Multicenter Local Study

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Background: Substantial progress has been made in the characterization of the molecular abnormalities in NSCLC tumors such as activations of oncogenes by mutations, translocations and amplifications, which are being used as molecular targets and predictive biomarkers. The aim of present work was to determine the frequency of molecular alterations in EGFR and gene fusion ALK and to assess associations with age, gender and tobacco habits in our Caucasian and Hispanic to decide the adequate treatment.

Method: 115 small biopsies and resection specimens of patients (pts) with NSCLC Adenocarcinoma (AC) were studied during the period 2014 - 2017. Histopathology type, Immunohistochemistry (IHC) characteristics as well as molecular profile were analyzed. EGFR mutation was studied by therascreen kit, PCR, in order to detect genetic alterations in exons 18, 19, 20 and 21. (Fig. 1) ALK translocations were analyzed by FISH (Vysis- Break Apart, Abbott) and IHC (clon D5F3, ventana, Roche). (Fig. 2). Molecular profiles were correlated with different clinical variables (age, gender, and tobacco habits).

Results: 83% of subjects had smoking habit and this pattern was even significantly associated with gender (70% and 92% for women and men respectively, p=0.003). 76% the subjects were older than 56 years, having similar distributions between sexes (p=0.183): mean (standard deviation) equal to 60.8(1.37) years old for women and 63.4(1.1), for men. 26 pts (23 %), 11 men and 15 women expressed EGFR alterations which were associated with gender (p=0.020, Fig. 4). Women had more chance of having positive alterations of the gene (OR 2.82, 95CI:1.15-6.91). Figure 5 shows how women have more greater predicted probabilities for positive EGFR than men, adjusting by smoking status. Age and

smoking habit of patients did not show significant effects (p=0.61, and p=0.105, respectively). Figure 6 illustrates the age distributions by EGFR and ALK categories. We identified 3 pts (3%) with fusion gene EML4-ALK which were not related to sex (p=0.305), age (p=0.859) and smoking habit (p=0.631). Even though this analysis was performed stratifying by sex, the associations between AKL and covariates were not significant.

Conclusion: These results showed a comparable frequency in EGFR mutations and ALK gene fusion translocation to the data published in western population. These data allow an adequate diagnosis and appropriate therapy.

Keyword: lungcancer

NOTE: Figures are missing for this abstract. We have reached out to the submitter.

P32: Identification of EGFR Mutational Profile in Lung Cancer Moroccan Patients Using ARMS Technology

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Background: Despite recent progress in diagnostic and oncology therapy, lung cancer constitutes the leading cause of cancer-associated mortality worldwide, with approximately 85% of lung cancer cases being non-small cell lung cancer (NSCLC) histological type. The study of epidermal growth factor receptor (EGFR) gene mutational profile in non-small cell lung cancer patients has a special clinical significance in the selection of patients for tyrosine-kinase inhibitor therapy. The aim of this study was to identify the frequency and spectrum of EGFR mutations in a cohort of Moroccan patients with lung cancer using the ADx-ARMS technology.

Method: We performed a retrospective study by processing 164 cases of NSCLC patients recruited between March 2015 and March 2018. Using the DNA extracted from the formalin-fixed paraffin-embedded FFPE tissue, we attempted to identify somatic mutations in exons 18 to 21 of the tyrosine-kinase "TK" domain of EGFR gene. We evaluated EGFR mutations using High Resolution Melt (HRM) polymerase chain reaction (PCR) and real time PCR "ADx-ARMS technology" for results confirmation.

Results: Among the positive mutant cases, the resulting mutations were as follows: 70% of patients have a deletion in exon 19, 10% in exon 21(L858R), 10% in exon 20 (6.7% T790M and 3.3% S768L) and 10% in exon 18 (G719A/C). The EGFR mutations were more frequent among males compared to females (51,7% and 48,3% respectively), all of the positive patients with EGFR mutations were adenocarcinoma (ADK) and 37,9%% of them were smokers.

Conclusion: The presented method can be implemented at the laboratories to identify the most frequent EGFR mutations that are important for targeted therapy of advanced lung cancer patients.

Keywords: EGFR mutations, Moroccan cohort, ADx-ARMS technology, Lung cancer

P33: The Retrospective Analysis of Apatinib as Maintenance Therapy in Extensive-Stage Small Cell Lung Cancer

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Background: Small cell lung cancer (SCLC) accounts for about 10%-15% of the total number of lung cancer and with a poor outcome. Especially in extensive-stage (ED) small cell Lung Cancer, the 5-year survival rate is less than 5%. To improve the survival outcome, a number of therapeutic approaches have been tried, such as dose dense chemotherapy, high-dose chemotherapy, maintenance therapy and consolidation chemotherapy. However, the results was of no proven benefit. Patients with a lower pretreatment circulating VEGF levels were more likely to respond to chemotherapy compared to those with higher levels of VEGF. The results from these studies suggest that VEGF may be linked to overall poor outcome in SCLC. Therefore, inhibition of VEGF represents a rational therapeutic strategy for evaluation in SCLC. Apatinib is a tyrosine kinase inhibitor that selectively inhibits the vascular endothelial growth factor receptor-2 (VEGFR2). Although there have been few studies of small cell Lung Cancer treated with apatinib so far, a retrospective study showed that apatinib exhibits modest activity and acceptable toxicity for the heavily pretreated patients with extensive-stage SCLC. The disease control rate was 81.8%. However, is there a benefit in survival of apatinib as maintenance therapy in extensive-stage SCLC is unclear. Therefore, the aim of this study was to analyze the efficacy and safety of apatinib as maintenance therapy in extensive-stage SCLC.
Method: Retrospective analysis of 23 cases extensive-stage SCLC that admitted to The Affiliated Cancer Hospital of Zhengzhou University from January 2015 to December 2017. The patients without progression after induction chemotherapy, received apatinib 250mg per day until disease progression or unacceptable toxicity occurs. We analyzed the median progression-free survival (PFS), median Overall survival (OS) and safety.
Results: Of 23 enrolled patients,1 was lost to follow-up. The median PFS from the time of maintenance therapy was 4.1 months (95%CI,3.63 to 4.57 months). The median PFS from the time of induction chemotherapy was 8.3 months (95%CI,7.20 to 9.40 months). The median OS from the time of maintenance therapy was 12.5 months (95%CI,5.51 to 19.49 months). The median OS from the time of induction chemotherapy was 17.0 months (95%CI,9.86 to 24.14 months). The most frequent treatment-related adverse events were hand-foot syndrome (43.5%, 10/23), secondary hypertension (30.4%, 7/23). Fatigue, proteinuria, nausea, oral mucositis were 17.4%, 13.0%, 13.0%, 8.7%, respectively. Hematologic toxicity includes thrombocytopenia (30.4%), leucopenia (26.1%), and anemia (17.4%). Main grade 3 or 4 toxicities were hand-foot syndrome (8.7%, 2/23), and hypertension (4.3%, 1/23).
Conclusion: Maintenance apatinib was safe and achieved encouraging PFS and OS in extensive-stage SCLC.

Keywords: small cell lung cancer, apatinib, maintenance therapy, extensive-stage

P34: Identification of the Genetic Determinants of Susceptibility to Lung Cancer in a Moroccan Cohort

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Background: Lung cancer is the most common cause of death from cancer worldwide, estimated to be responsible 1.59 million deaths, representing 19.4% of all cancer types. Representing 80–85% of all cases non-small cell lung cancer (NSCLC) is the most predominant type of lung cancer. Lung cancer has been recognized as a complex multifactorial disease resulting from the interactions between various genetic and environmental factors. Identification of genes involved in the occurrence and development of lung cancer could contribute to further understanding of the underlying mechanisms, and even a very

important additional appropriate prevention strategies and targeted treatments for reducing lung cancer burden. Many studies have suggested that key cytokines in inflammation pathways may exert important roles in the etiology of lung cancer. The aim of this study was to investigate whether common variants in inflammatory and immune response genes influence lung cancer risk in Moroccan patients.

Method: Using a candidate gene approach, 6 single nucleotide polymorphisms (SNPs) in 4 genes were assessed in 117controls and 117 lung cancer patients. Genotyping was performed with the TaqMan® allelic discrimination technology. The results were analysed using SPSS 24.0 software.

Results: Among the 5 studied genes, we found a significant association for the MIF (rs755622) (OR=1.63; 95% confidence interval 1.04-2.56; p =0.03), IL-6 (rs2069840) (OR=1.63; 95% confidence interval 1.08-2.47; p =0.01) and STAT3. No significant association was observed for the remaining SNPs in the following genes: IL17A rs7747909, IL-6R_rs2228145, IL6ST_rs2228044.

Conclusion: The results founded suggest the important role of genetically determined high inflammatory response in the pathogenesis of lung cancer in the Moroccan population

Keywords: Lung cancer, Inflammatory system, Cytokines, polymorphisms

P35: Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) in Patients (P) Older Than 70

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Background: More than 50% of advanced NSCLC patients are older than 65 years old (y), with a median age at diagnosis of 68 y. This group of patients have been usually underrepresented in clinical trials. The aim of our study is to compare whether clinical characteristics, toxicity, response rate, overall survival (OS), and progression free survival (PFS) are different in p > 70y vs. < 70y, treated with platinum based chemotherapy.

Method: We reviewed the database of the Instituto Oncologico Córdoba, Argentina (IONC). Survival curves were made up by Kaplan-Maier method and compared using the log-rank test.

Results: Out of 198 p; 103 p (52 %) < 70y, and 95 p (48 %) > 70y We found significant differences in OS (9.4 vs. 7.5 months, p=0.003) and PFS (6.4 vs. 5.1 months, p=0.002) Significant differences in OS were also found between the two groups regarding anemia, Performance status (PS) and response rate with no difference on sex and histology.

Conclusion: Significant differences in OS and PFS were evident between both groups. We observed increased toxicity in p > 70y, but without greater treatment-related mortality. OS and PFS were superior in patients treated with platinum-based doublets when compared to monotherapy (according to historical records); therefore we should choose the former in elderly patients.

Age cohort	<70y(%)	>70y(%)	p
toxicity *(95% CI)* Neutropenia Anemia Thrombocytopenia Neurotoxicity Nauseas	3 26 38 31 30	9 70 39 57 51	NS 0.00001 NS 0.0003 0.0004

Outcome			
PFS (m)	6.4 9.4	5.1 7.5	0.002
OS (m)			0.003

Keywords: Treatment of advanced, Lung cancer, non-small cell lung cancer (NSCLC), older than 70

P36: Diagnostic Accuracy and Complication Rate of CT-Guided Core Biopsies of Lung Lesions in a Thoracic Oncology Unit in Mexico

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Background: Core biopsies are valuable in obtaining sufficient tissue to ensure diagnosis of diseases in the thorax. The main complications are pneumothorax or intrathoracic bleeding. Studies have shown that this technique is suitable for obtaining tissue samples of sufficient quantity and quality from which correct histological diagnosis can be made as well as allowing for molecular analysis of biomarkers.
Method: The objective of the study was to evaluate the complication rate and the diagnostic yield in computer tomography (CT)-guided core biopsies performed as standard procedure in a Thoracic Oncology Unit in Mexico. Medical journals, pathology reports and CT scans were reviewed in 164 consecutive cases, where a transthoracic core biopsy was performed between January 2013 and December 2017. A experienced radiologists member of the Thoracic Oncology Unit performed the biopsies. Of these total biopsies, 78 (47.5%) were for primary lung cancer, 91 % taken of lung lesions and 8.97% (7) of pleural lesions.
Results: From January 2013 to December 2017, 78 patients (52.56 % male; median age 59.86 years [range: 26-88 years]) were enrolled. All patients underwent a chest X-ray 4 hours post-biopsy and pneumothorax was seen in 8/78 (10.25%) patients even though only 1 patient (1.28%) need a chest tube insertion. Small intraparenchymal hemorrhages and hemoptysis were observed with subjective difficulty in only one case. None of patients need transfusions nor further treatment.
Conclusion: A transthoracic core biopsy ensures diagnosis with a low complication rate and is suitable as an outpatient procedure. A CT-guided core biopsy is safe and applicable in our hospital in a Thoracic Oncology Unit allowing molecular analysis of biomarkers and personalized treatment.

Keywords: CT-guided core biopsies, Lung cancer, Diagnostic

P37: Induction of DNA Double Strand Breaks in Human Primary Lung Cells

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Background: DNA double strand breaks (DSB) are the most detrimental effects on cells by which ionizing radiation (IR) causes cancer. The frequency of DSB induced decreases with time, indicative of DSB repair. One of the earliest responses to DSB damage is the recruitment of the repair protein, 53BP1, to DSB sites. Fluorescent-tagged antibodies specific for 53BP1 can therefore be exploited to detect DSB lesions as discrete 'fluorescent foci'. This project aimed to assess the frequency of induction and kinetics of DNA DSB repair in cells exposed to IR.

Method: Primary human bronchial epithelial cells were cultured, irradiated and fixed at different time-points. Radiation induced DNA DSB were identified by immunofluorescence technique using 53BP1 as a marker protein. Images were captured and analysed by fluorescence microscope and axiovision software.

Results: After exposure to 2Gy radiation, the highest number of foci was visible within 10min (6.613foci/nucleus). The score at 10min in unirradiated and IR cells were significantly different (P=0.00001). After then the trend declined. Average number of 53BP1 foci decreased up to 6hr (2.83 foci/nucleus at 6hr). The score at 10min was statistically different from that of 6hr (P=0.0008). Data stayed the same from 6hr to 16hr (P at 6hr=0.552, at 8hr=0.615 and at 16hr=0.768). After 16hr the foci reduced up to 24hr where it returned to nearly baseline but significant variation remained from that of unirradiated cells at 24hr-point (P=0.001). In case of unirradiated cells, difference was not observed over the whole duration (P>0.05). Initially, after irradiation, a wide variation existed among the proportion of small, medium and large foci which was, however, getting closer with time, and by 24hr it appeared like a cluster of proportion where all fractions of foci remained the same.

Conclusion: In unirradiated cells, an average of 1 DSB was seen in each nucleus for a 24hr duration whereas radiation of a dose of 2Gy produced as many as 6 DSB within 10min. DSB were quickly repaired for the first 6hr, and more than half of DSB got repaired within this period. Few DNA lesions persisted even after 24hr. Changes in the proportional size distribution of foci may be indicative of migration and clustering of radiation-induced foci representing slow DSB repair, leading to chance of chromosomal rearrangement, and subsequently increase the risk of cancer cell formation. If this hypothesis is valid and we can locate these clustering time-points specifically, specific time-points of transforming cancer cells after irradiation may be identified.

Keywords: Lung cancer, DNA double strand breaks, Ionizing radiation, DSB

P38: Incidence and Survival of Lung Cancer at Oncosalud - AUNA: A Dynamic Cohort Study

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Background: Lung cancer is the most common cancer and remains the main death cause worldwide. The aim of study was to determinate the incidence and survival rate of lung cancer in a population of affiliates in a private institution (ONCOSALUD-AUNA).

Method: In a dynamic cohort, the incidence of lung cancer was evaluated in a population of affiliates to ONCOSALUD - AUNA between 2008 - 2013 (n=1'096,140). Overall survival (OS) was evaluated in patients treated in ONCOSALUD – AUNA between 2000-2005 (n = 114). The incidence rate was calculated based on new cases/persons-year of observation. The incidence rate standardized by age was calculated having the structure of the world standard population. OS was estimated using the Kaplan-Meier method and comparisons of survival curves were performed using the Log-rank or Breslow test.

Results: The median age at affiliation was 33 years (range: <1, 98), 18.9% were under 15 years old, 5.6% were older than 64, and 55.7% were women. A total of 2,611,438.3 persons-year of observation was calculated and 394 affiliates (193 and 201 in women and men, respectively) were diagnosed with lung cancer. The median age at diagnosis was 70 years (range: 35, 98). The standardized incidence rate by age was 7.9 per 100,000 persons-year (6.5 and 10.0 in women and men per 100,000 persons-year, respectively), and 74 years cumulative risk was 1.0% (0.9 and 1.3% in women and men, respectively).

For survival assessment, the median age at diagnosis was 69 years, 37.9% were women and 76.3% had advanced disease (CS III: 18.2% and CS IV: 58.1%). With a 10.6-year follow-up, the median survival was 0.62 years (CI95%: 0.46, 0.78). The OS rate at 5 and 10 years were 16.4% and 12.9%, no significant differences in relation to sex (p = 0.118), age (<60 vs. >60 years: p = 0.300) were observed, and it shows significant difference according clinical stage (CS I-II vs. III–IV: p < 0.001).

Conclusion: The incidence rate of lung cancer in our population is slightly lower than reported by the IARC for the Peruvian population. The survival rate at 5 and 10 years is similar to reported by other series.

P39: Predictive Factors of Brain Metastases Development in Non-Small Cells Lung Cancer (NSCLC)

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Background: Brain metastases are present in 10 to 30 % of NSCLC patients sometime during the disease. The aim of our research is to identify the clinical pathological characteristics in patients with stage IIIB-IV related to the development of brain metastases.

Method: 590 patients diagnosed with NSCLC stage IIIB-IV at our institution were included. Of these, 496 showed an advanced stage. The variables included in the analysis of patients with and without brain metastases were: gender, age, histology, smoking status and ECOG. The multivariate logistic regression model was used to identify factors related to brain metastases.

Results: The development of brain metastasis was proportionally higher in women compared to men (77.7% vs 22.2%). Over 80% of patients presented ECOG of 0-1. Regarding histology, 60.32% were adenocarcinomas; 30% squamous, and 9.5% undifferentiated. 65% of patients were under 65 years old. 66.6% of patients were former smokers. Patients under 65 years old are at increased risk of developing brain metastases than older patients (HR=0,5-IC95%= 0,6-1,16- p=0,045). Adenocarcinoma histology is associated with an increased number of brain metastases development (OR = 2.42 - 95% CI = 1.84 to 3.00 - p= 0.003).

Conclusion: In this trial was observed that patients younger than 65 years and etiology of adenocarcinoma have a higher risk of developing brain metastases. Regarding gender, we observe an increased risk in men, however, the differences were not statistically significant.

Keywords: brain metastases, Predictive factors, Predictive factors of brain metastases, Non-Small Cells Lung Cancer (NSCLC)

P40: Analysis of Family Clustering in Lung Cancer (LC): Genetic Cancer Risk Assessment (GRCA) into the Thoracic Oncology Unit

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Background: Inherited susceptibility for lung cancer (LC) has been described, a recent paper showed that 2.5% of LC patients (pts) carried a pathogenic germline variation in genes such ATM, TP53, BRCA2, EGFR, and PARK2. Some of those genes cause well recognized syndromes. Thus, GRCA for LC could help to identify a genetic predisposition syndrome, guide genetic testing, offering specific treatments and genetic counseling.

Method: This is a retrospective and descriptive study. We performed a review of 66 medical records of LC pts diagnosed between 2011 and 2016. We collected age at diagnosis, smoking, previous cancer diagnosis, and family history (FH) for cancer: number of affected family members and sort of cancer. Genetic evaluation and testing was not available at time of first evaluation, but we tried to identify genetic syndromes according to the clustering pattern and NCCN criteria.

Results: Mean age was 62.5 years (range 26-88y); 30 pts (45.5%) had FH with 46 affected relatives: 21 pts had at least one first degree affected member, only 2 pts had more than 3 affected members. Among the tumors, Breast cancer (BrCa) was found in 12 family members; one pt had a previous BrCa diagnosis at 33y; LC was found in 1 relative; 4 cases of colon cancer were described; 1 case was found for prostate and melanoma respectively. Other tumors were described, but they are not frequently associated to other genetic syndromes. We found no statistical differences on smoking between pts with or without FH. Pts with FH tended to be younger (p=0.026). Based on the family assessment, 8 (10.6%) cases met NCCN criteria for genetic counseling and testing for BRCA and Homologous Recombination (HR) pathway genes.

Conclusion: Unfortunately, age of diagnosis for family members was available in 8 out 46 cases, data available were taken from the first clinical assessment which limits this analysis. Even if the expected number of pts with inherited susceptibility to LC is low, a proper GRCA could improve the diagnosis of genetic syndromes. This could bring advantages, such as offering PARP inhibitors for Pts carrying mutations in HR pathway genes, cascade screening and set up prevention measures adapted for each gene risks. Finally, more extended genetic analysis could be offered based on clinical features of index cases. At our knowledge, GRCA clinics for LC is not frequent in Mexico, these results underline the importance of setting up this clinic at our center.

Keywords: inherited susceptibility, BRCA, Genetic cancer risk assessment, PARP

P41: Characterization and Management of Elderly and Very Elderly Patients with Non-Small Cell Lung Cancer

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Background: Despite non–small cell lung cancer (NSCLC) high prevalence and increasing incidence, evidence specific to the elderly and very elderly is sparse. **Objective:** To retrospectively compare characterization and approach of NSCLC patients (pts) aged 70-79 and ≥ 80 years.

Method: We performed a retrospective analysis of 297 adult NSCLC pts who registered and initiated NSCLC management in our Pulmonology Oncology Unit from January 2013 to December 2016 corresponding to 38.2% of all NSCLC patients (n=778). Demographic data and lung cancer management were analyzed.

Results: Pts were categorized as elderly (n=211, 71.0%) and very elderly (n=86, 29.0%). Very elderly pts had worse ECOG PS (p=0.03), higher Charlson-age comorbidity index (p<0.001) and the majority had stage IV cancer (66.3%, p=0.04). First management option in very elderly pts was chemotherapy (CTX) (30.2%, p=0.37) and in elderly pts was multimodal therapy (30.3%, p=<0.001). First-line targeted (EGFR or ALK-positive) and support therapy were more common in the very elderly (23.6%, p=0.001; 17.4% p=0.002, respectively). Curative radiation or surgery rates did not differ between groups. Reasons for premature first-line CTX stop, toxicity and hospitalization did not differ. Death rate (69.7% *vs.* 63.5% for

very elderly and elderly, respectively) and mean survival since diagnosis (11.5 months *vs.* 11.6 months for very elderly and elderly, respectively) did not differ.

Conclusion: There was significant differences in pts characteristics having the very elderly more multimorbidity and advanced state of disease. First management options were significantly different in respect to multimodal, targeted and support therapy.

Keywords: Non-small cell lung cancer, Elderly, Approach

P42: LPCAT1 Up-Regulation Promotes Brain Metastasis of Human NSCLC by Up-Regulating pi3k/Akt/ Myc Pathway

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Background: This study aimed to explore the effect of lysophosphatidylcholine acyltransferase 1(LPCAT1), a cytosolic enzyme, on lung cancer and brain metastasis (BM) of lung cancer both *in vivo* and *in vitro*.

Method: Small hairpin RNA (shRNA) specific for LPCAT1 was used to knockdown the expression of LPCAT1 both in HCC827 and PC-9 non-small cell lung cancer (NSCLC) cell lines. CCK-8, transwell migration and invasion assays in vitro was used to examine the effect of LPCAT1 on cell proliferation, migration and invasion. GSEA analysis was performed to characterize signaling pathways associated with LPCAT1. Western blotting and RT-PCR were used to detect the expression of LPCAT1 and PI3K/AKT/MYC signal pathway. Immunohistochemical (IHC) and RNA-Seq analysis were used to detect the expression of LPCAT1 in situ tissues of lung cancer patients with or without BM and normal human lung tissues. Xenograft model were used to examine the effect of LPCAT1 on cell proliferation. The data about clinical stages of LUAD patients was obtained from, an online database, Oncomine.

Results: LPCAT1 was up-regulated in NSCLC tissues and cell lines and it's essential for the proliferation, migration and invasion of NSCLC *in vitro*. LPCAT1 amplification status was correlated with MYC-activated geneset by GSEA analysis. What's more, down regulating of LPCAT1 attenuates the PI3K/AKT signaling pathway in part by targeting MYC. The expression of LPCAT1 in human lung tissues was highest in lung tumor tissues from lung cancer patients with BM, followed in tissues from lung cancer patients without B and the lowest in normal human lung tissues. LPCAT1 promoted tumorigenesis in vivo and was associated with poor clinical outcomes.
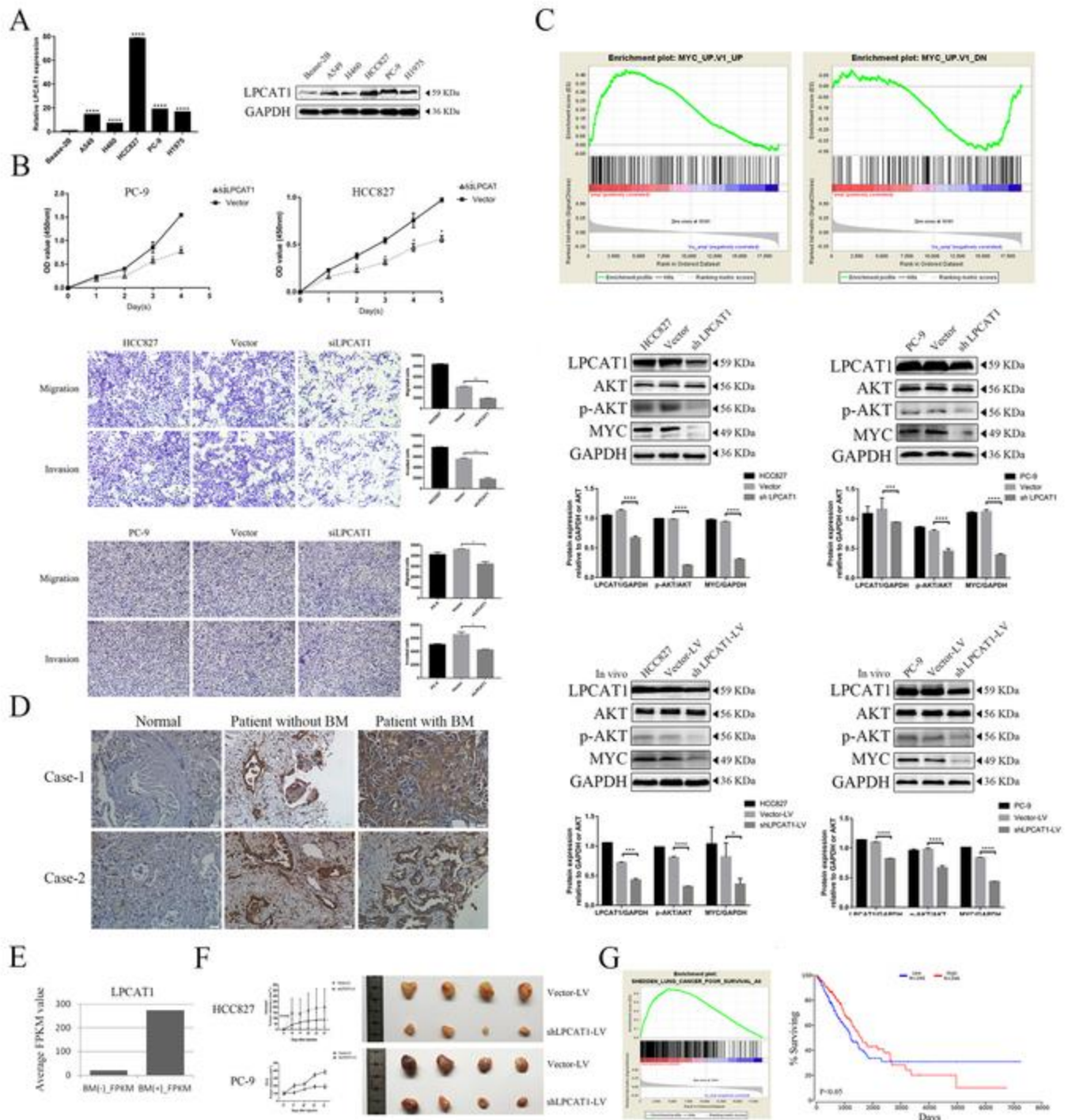
Conclusion: LPCAT1 promoted NSCLC proliferation, metastasis and tumorigenesis in vitro and in vivo, More importantly we uncovered that this effect of LPCAT1 was partially via the PI3K/AKT/MYC pathway.

Keywords: NSCLC, Brain metastasis, LPCAT1, proliferation

P43: Relationship Between the Expression of pdl1and the Tumor Infiltrating Lymphocytes in Patients with Advanced Lung Cancer

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Background: Several studies show that those patients with a PD-L1 expression have greater benefits in the response rate, PFS and OS. In our institution, in 2014, we conducted a study in which it was possible to show that the presence of infiltrating lymphocytes of the tumor is associated with a longer PFS and OS. In another study, we showed that the presence of lymphocyte infiltration, in patients with breast cancer had higher survival; that is why in this study we want to analyze the relationship between the expression of the PD-L1 and the tils. **OBJECTIVE** The objective of this study is to analyze the relationship between the expression of PD-L1 and the intratumoral and stromal TILS in patients with advanced lung cancer and the overall survival of these patients
Method: Retrospective and analytical study in which patients with advance NSCLC from Instituto Oncológico de Córdoba were studied. The tumor samples have been analyzed. Immunohistochemistry will be the procedure used to evaluate the expression of PD-L1 and intratumoral and stromal lymphocytes. The survival analysis will be evaluated by the Kaplan-Meier method and by the log-rank test.
Results: We analyzed 46 patients, 34 men and 12 women. Out of those patients studied, 26 pts. (56%) had TILSi in their tumor samples, 20 pts. (43.47%) absence of TILS i. Regarding TILSs, 34 pts (73%) showed infiltrate in the sample and 12 pts. (26%) did not present TILSs. Out of those 46 samples analyzed, 22 pts. (48%) showed expression of PD-L1, and 4 pts. (52 %) did not express PD-L1. Patients who presented TILSi had a median OS of 11.4 m vs 8.7 m in those without TILSi, these differences were statistically significant and were related to the expression of PD-L1 p: (0.01 vs 0.4) respectively. Those that evidenced TILs vs absence of TILs. the OS was 11.7 m vs 7.5 m; these differences were significant and were also related to the expression of PD-L1 (0.03 vs 0.1) respectively.
Conclusion: We were able to conclude that those patients with NSCLC who had TILi and TILSs, and who also had expression of PD-L1 in their tumor samples, had higher OS than those patients who did not have TILS or expression of PD-L1. This was statistically significant

Keywords: PD L1, Infiltrating Lymphocytes, Lung cancer, PD-L1 and the intratumoral and stromal TILS

P44: Solitary Pulmonary Nodule: Primary or Metastatic Neoplastic Lesion?

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Background: A solitary pulmonary nodule (SPN) is a common and increasing clinical problem. Differential diagnosis is broad and often challenging, mainly in patients with previous cancer. Aim: Analyze patients with SPN and previous cancer and compare metastatic and primary lung cancer (PLC) lesions.
Method: Patients with SPN on computerised tomography scan and history of cancer (except basal cell

carcinoma) who underwent surgical resections between January 2015 and December 2017 at Hospital da Luz–Lisboa were included. All cases were evaluated at a multidisciplinary lung cancer tumour board team meeting. We analyzed histology, demographic and radiological features. p-values ≤0.05 were considered significant.

Results: There were included 29 patients with history of cancer: 12 colorectal, 8 breast, 4 genitourinary, 4 lung and 1 sarcoma. PLC was diagnosed in 15 (51.7%), metastasis in 11(37.9%)- 8 colorectal, 1 genitorectal, 1 atypical lung carcinoid and 1 sarcoma - and benign lesions in 3. Surgery was the diagnosis procedure in 24(82.8%)–17 with frozen section. There were no significant differences between primary and metastatic neoplastic lesions in gender, age and smoking history (p>0.05). All subsolid nodules (n=5) were PLC. In solid neoplastic SPN, 10 PLC and 11 metastasis, there was no difference in diameters. Irregular edge was associated with PLC lesions (p=0.008) and smooth margin with metastasis (p=0.001). Lobulated margins did not seem differentiate neoplastic lesions (p=1.0).

Conclusion: PLC is an important diagnosis in the differential diagnosis of NPS, including in patients with a history of cancer. Radiological features can help to discern primary to metastatic SPN in this group.

Keywords: Solitary pulmonary nodule, Lung cancer, Pulmonary metastatic lesion

P45: Prognosis of Elderly Patients with Metastatic Lung Cancer in Oncosalud-AUNA

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Background: Lung cancer is the one of the most common cancer in the elderly, advanced disease among older people has still worse outcomes and represents a challenge for the management. The aim of study was to evaluate the prognosis of elderly patients with metastatic lung cancer in a population of affiliates to a private institution (ONCOSALUD-AUNA).

Method: In a retrospective study, we reviewed prognostic factors of patients diagnosed of metastatic lung cancer older than 60 years whom received treatment in our institution (ONCOSALUD-AUNA) between 2011-2014. Clinical characteristics, treatment and survival were evaluated from electronic medical records. Overall survival (OS) was estimated using the Kaplan-Meier method and comparisons of survival curves were performed using the Log-rank or Breslow test. Multivariate analysis was performed using Cox model.

Results: In the study period, 92 cases older than 60 years were diagnosed. Median Age was 70 years (range: 61, 86), 44% were women, 35% had 2-4 ECOG scale, 58.6% had primary tumor in the right lung and the most common site of metastasis were brain, bone, pleura and liver. 65% were adenocarcinoma and 40% poorly differentiated. About 20% of cases did not received any treatment. The chemotherapy regimen was based on carboplatin and cisplatin, 82% received more than 3 cycles of chemotherapy and overall response rate was 44%. In 5 years median follow-up, 81% died, median survival was 0.9 years (CI95%: 0.6, 1.2), 2- and 5-years survival were 24 and 13%, respectively. OS showed differences according to ECOG (0-1 vs. 2-4, p=0.008), primary site (right vs left, p = 0.060), histology (adenocarcinoma vs non-adenocarcinoma, p = 0.090), CYFRA 21.2 (<3.3 vs. >3.3, p = 0.017), neutrophil-to-lymphocyte ratio (NLR) (3.6 vs. 3.6, p = 0.001). In a Cox model, CYFRA 21.2 > 3.3 (HR: 2.2, p=0.036), NLR > 3.6 (HR:2.8, p=0.001) and histology (non-adenocarcinoma, HR:2.7, p=0.01) were associated to worse survival outcomes.

Conclusion: Lung cancer among elderly still has the worse prognosis, however patients with 0-1 ECOG scale, adenocarcinoma, CYFRA 21.2 < 3.3 and NLR < 3.6 were associated to better survival outcomes.

P46: Experience in the Treatment of 13 Cases of Pulmonary Lymphangitic Carcinomatosis with Apatinib

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Background: Pulmonary lymphangitic carcinomatosis is a disease in which advanced malignant tumors spreads diffuse throughout the lungs along lymphatic vessels. The previous treatment methods of PLC have no special curative effect except standard chemotherapy and symptomatic support. This paper retrospectively analyzed 13 patients with advanced lung cancer of PLC treated by apatinib in our hospital in 2017, whose clinical symptoms and therapeutic effects are as follows:
Method: To summarize and analyze 13 cases of pulmonary lymphangitic carcinomatosis of my department , and evaluate the therapeutic effect of apatinib on pulmonary lymphangitic carcinomatosis, for the effective treatment of pulmonary lymphangitic carcinomatosis. 13 cases of pulmonary lymphangitic carcinomatosis treated by our department from June 2017 to June 2018 were retrospectively analyzed, all patients were treated with apatinib orally at a daily dose of 425 mg for 6 consecutive weeks. Its therapeutic effect was summarized and analyzed , and the progression-free survival period (PFS) and overall survival rate (OS) were followed up. CT imaging findings before and after the treatment was the main index, supplemented by tumor markers (CEA, CA - 125, CYFRA21-1), analysis of blood gas, the change of clinical symptom index, etc for the analysis of adverse drug reactions.
Results: The efficacy of 13 patients with pulmonary lymphangitic carcinomatosis was evaluated. Classification of the therapeutic effect included 6 patients (46.1%) of partially relieved (PR),3 patients (23.0%) of stable disease (SD),4 patients (30.7%) of progressive disease (PD). Objective response rate (CR+PR) was 46.1%.Disease control rate DCR(CR+PR+SD) was 69.2%. Progression-free survival (PFS) was 5.2 months. Overall survival OS was 10.2 months. The CT imaging features of part patients before and after treatment improved markedly, the differences of tumor markers CEA, ca-125, cyfra21-1 and blood gas analysis were statistically significant ($P<0.05$), Pleural effusion, dyspnea and other clinical symptoms have different degrees of relief. Adverse events were mainly high blood pressure (3/13), rash (4/13), hand-foot syndrome (6/13), mild proteinuria (2/13), and All are tolerable.
Conclusion: Pulmonary lymphangitic carcinomatosis is a disease of lymphatic spread in the advanced malignant tumors, Apatinib not only has good curative effect, but also brings obvious survival benefits, and the incidence of adverse reactions is low and the patient is well tolerated. Apatinib has become the main treatment of PLC compared to the traditional treatment.

Keywords: apatinib, Diagnosis, Therapy, pulmonary lymphangitic carcinomatosis

P49: Lung Adenocarcinoma with Double Heterozygote EGFR mutation and Combined Resistance: ALK Translocation and EGFR T790M

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Background: About 14% of patients with metastatic lung adenocarcinomas in our population have tumors harboring EGFR mutations or deletions. Herein we report the case of a patient with lung adenocarcinoma with a double deletion of EGFR who had a partial response for 6 months treated with afatinib and, upon progression, an EGFR T790M mutation and an ALK translocation were detected.
Method: "Not Applicable"
Results: Case Report: A 32-year-old male, non-smoker, presents with abdominal pain, cough and fatigue. Abdominal ultrasound showed a large left adrenal lesion and the chest X-Rays, a consolidation in the right inferior lobe. PET-CT with 18FDG scan was performed evidencing a 7.2 cm tumor in the right

lower lobe with high affinity for FG, as well as mediastinal and retroperitoneal enlarged lymph nodes, right adrenal mass, left acetabular and posterior costal lesion. A diagnostic transbronchial tumor-biopsy showed an undifferentiated carcinoma TTF1 + (T3N3M1c). EGFR status, assessed by PCR and sequencing, showed an exon 19 deletion (delE746_A750) with no ALK (clon D5F3) nor ROS1 (clon D4D6) translocations by immunohistochemistry (IHC). Next generation sequencing (NGS) with the Oncomine TM Focus Assay panel (Ion 520 Chip) revealed a double deletion in EGFR (p.delE746_A750 and p.delL747_T751insQ) in separate reads. The patient started treatment with afatinib and achieved a partial response at 3 months. After 6 months he experienced progressive lung abnormalities (metastasis???) and brain and cerebellar metastasis consistent with disease progression. Afatinib was stopped and both CNS lesions were resected. Standard ALK, ROS1 and EGFR determinations were repeated on brain tissue. An ALK translocation was identified by IHC and confirmed by FISH as well as the EGFR exon 19 deletion p.delE746_A750, without T790M mutation. The pre-treatment lung biopsy was reviewed and was negative for ALK translocation. EGFR testing in circulating tumor DNA was positive for the T790M secondary resistance mutation. Patient had rapid retroperitoneal progression with ascites, bleeding and abdominal pain requiring surgical intervention. Crizotinib was started without response and the patient died.

Conclusion: Here we report a case of a patient achieving a partial response with afatinib in a tumor with two EGFR deletions and the co-occurrence of secondary EGFR T790M mutation and ALK translocation as mechanism of resistance. In addition, the lack of detection of the EGFR deletion p.delL747_T751insQ, suggests a complex subclonal evolution secondary to tumor heterogeneity.

Keywords: Non-small cell lung cancer, Next Generation Sequencing, Targetable oncogenic drivers, Resistance mutation

P50: A Case of a Patient Harboring an EGFR -T790M Mutation Positive in Squamous Cell Lung Cancer

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Background: Actually, the treatment of lung cancer who express driver mutations consist in block this target, the majority of this patients has an adenocarcinoma histology only few of them has the squamous type.

Method: We describe a case report of a 58-year-old female, non smoker, with a persistent cough of 2 months of evolution. On May 2016, the CT scan reported lesion of 72x56mm in right segment 6, infiltration of hilum, pulmonary artery and mediastinal adenopathies. No extrathoracic disease. Biopsy: squamous cell carcinoma. Since the lesion was considered unresectable, she initiates concurrent ChT-RT (cisplatin / gemzar). After the 4th application, local progression was evidenced. Mutation studies, showed EGFRm Exon 19. She starts treatment with Afatinib (40mg / d) but, after 2 weeks, presented G3 gastrointestinal toxicity, so a dose-adjustment to 30mg / d was performed, G2 dermal toxicity also was reported. By December 2016, due to the response obtained, a medial and inferior lobectomy was performed. Pathological report (PR): middle lobe: pneumonitis. Lower lobe: squamous carcinoma. T: 3.5cm, G1, LVI (+), parenchymal margin (+). A PET / CT scan 4 weeks after the surgery, demonstrating right parahilar hypermetabolic lesion, pleural nodules and subcarinal adenopathy. The systemic treatment was restart in January 2017 with erlotinib 150mg /d. A PET / CT control 2 months later just showed slight metabolism in subcarinal adenopathy. She remains asymptomatic until October 2017, when presented aphasia and behavioral alterations. MRI: single left cortico-subcortical lesion of 2.2 x 2 cm with edema and subfalcial herniation. An hypo-fractionated radiotherapy scheme with corticoids was programmed but with minimal benefit. Six weeks after having completed RT (December 2017), greater neurological involvement is evidenced associated with weakness in lower limbs. MRI: lesion of 17.6 x17.3mm with contrast hyper-uptake and edema. CT thorax: no evidence of disease. Considering these findings and

clinical deterioration a cerebral metastasectomy was performed. PR: squamous cell carcinoma. EGFRm deletion 19 (+) T790M (+).

Results: Due to the post-surgery clinical deterioration, the patient did not receive systemic treatment until March 2018, CT scan: multiple subcarinal adenopathies, contralateral pulmonary nodules and a 6mm nodule in the right lobe of the cerebellum. Patient is currently under treatment with osimertinib, with clinical neurological recovery and no respiratory symptoms.

Conclusion: The use of TKI in SQCLC has a benefit in this patient, but the magnitude of this could be lower than adenocarcinoma according with a few series. However, this does not seem to be the case.

Keywords: T790M, Squamous Cell Lung Cancer, EGFR mutation
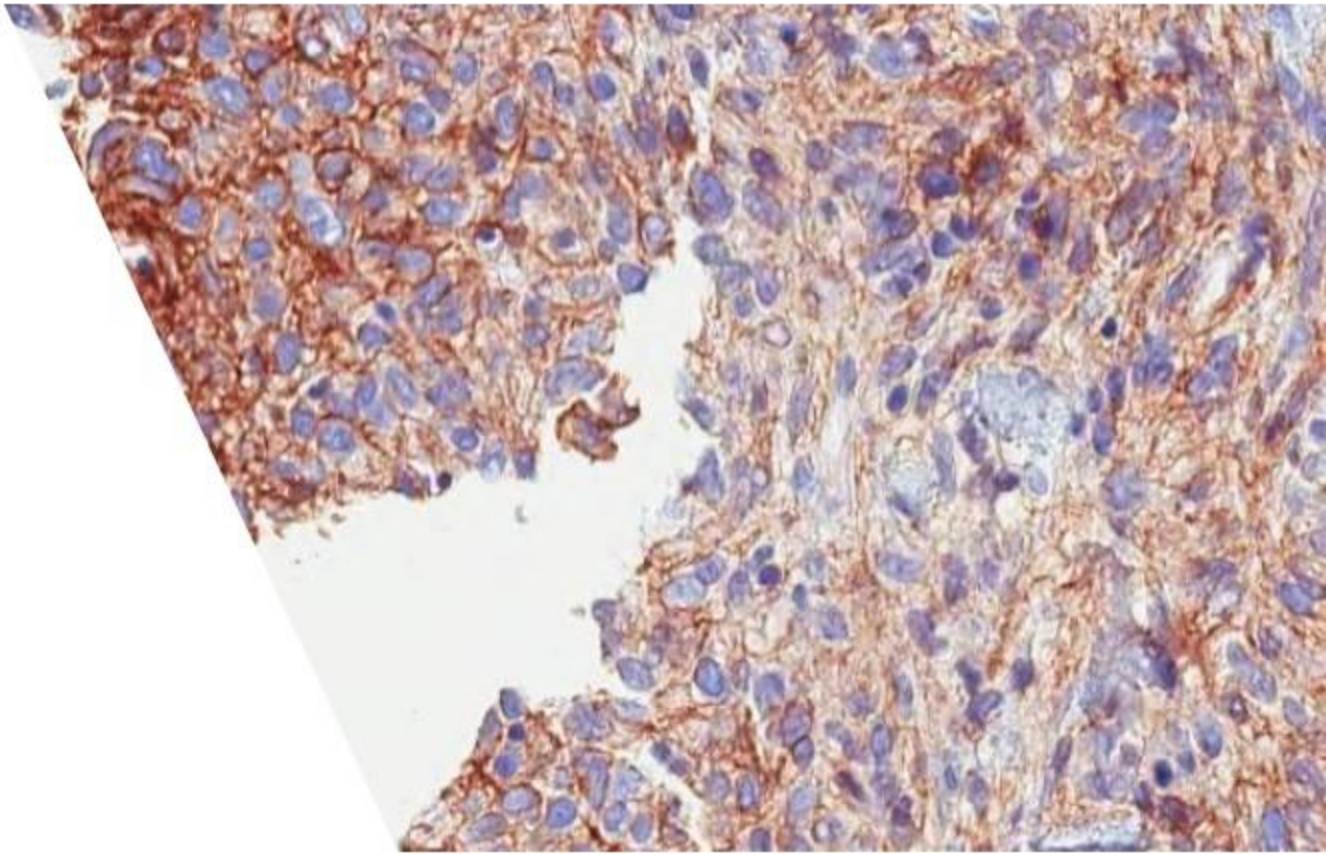
P51: Localized Pleural Solitary Fibrous Tumor

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Background: Solitary fibrous tumor described in 1931 comprises an spectrum of rarely metastasing fibroblastic mesenchymal neoplasms, that can occur anywhere with predilection for body cavity sites, comprising 5% of tumors in the pleura with noenvironmental or inherited risk factors.

Method: Female of 56 years old with pain in neck and arms during 1 year associated to swelling of hands does a Magnetic resonance showing herniated disc in C5-C6. In a preoperatory Thorax X Ray a right pulmonary mass is seen, confirmed by Computed Tomography that it was in contact with the thoracic wall, an initial biopsy didn´t showed malignancy, but the second biopsy reports Solitary fibrous tumor. The mass was resected with pathologic report of a 5.9 cms Classic Solitary fibrous tumor with negative margins (immunohistochemistry positive for CD99, CD34, BCL-2), the patient didn´t required adjuvant treatment and is on surveillance with no evidence of disease at 9 months.

Inmunohistochemistry positive for CD 99

Rib and pleural tumor: portion o
ovoid tumor attached to th

Results: not applicable

Conclusion: Solitary fibrous tumor is suspected based on imaging and unspecific symptoms requiring histologic confirmation. Treatment for localized disease is surgery with negative margins because of its indolent behavior (10-25% recurrence, survival 73-100% at 10 years) and lack of effective adjuvant treatment

Keywords: Solitary, fibrous, tumor

P52: Visual Disorder as a Main Clinical Presentation of Thymic Carcinoma: Case Report

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Background: Thymic tumors are rare neoplasms that arise in the anterior mediastinum, with a low incidence of approximately 1.3/1,000,000 people. According to the World Health Organization (WHO) classification in 2004, we can identify two histopathological types: thymoma and thymic carcinomas. Thymic carcinomas are aggressive tumors, not typically associated with paraneoplastic autoimmune disorders in contrast with thymomas. The first symptoms usually are related to respiratory issues. To our knowledge, this is the first case of a thymic carcinoma with acute amaurosis as a main clinical manifestation.
Method: Section not applicable.
Results: A 51-year-old male patient with no previous medical report, presented with acute amaurosis of the right eye. The patient was evaluated by an ophthalmologist and diagnosed with thrombosis of the central vein of the retina and start anticoagulation treatment. Nuclear magnetic resonance of brain and orbits were normals. Few weeks later, because of dorsal pain and persistent cough, a chest X-ray was perfomed showing a mediastinal mass. A chest-CT revealed a mass at the level of the right anterior mediastinum of 11.5 x 8 x 13 cm with areas of necrosis in its interior associated with mediastinal adenopathies. The histological examination was compatible with round cell neoplasia. Immunohistochemical examination report: Pankeratin (+), p63 (+), CD5 (+), Synaptophysin (+), Chromogranin (+), PAX8 (+), CD117 (+) compatible with thymic carcinoma with neuroendocrine differentiation. There was no metastasis to other organs in detailed examinations. The tumor was considered unresectable by the surgeons and platinum based chemotherapy was initiated. After 6 cycles of chemotherapy, the best response achieved was stable disease. He continues with anticoagulation treatment, but only partial vision was recovered.
Conclusion: Our case demonstrates that thymic carcinomas not only presented with respiratory problems, although we considered this is an unusual presentation, we encourage to look for a cause when we face uncommon symptoms. Treatment options are limited for thymic carcinoma. For people with advanced-stage, complete surgical resection is not possible, and the only treatment option is palliative chemotherapy even though the ideal approach remains unknown.

Keywords: Thymic carcinomas, Amaurosis, visual disorder

P53: Cryptococom as a Differential Diagnosis of Pulmonary Metastase in a Patient with Challenging Adenocarcinoma: Case Report

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Background: Pulmonary cryptococcosis is a potentially serious fungal disease that may have several clinical presentations. Radiologically, it can be found as single or multiple nodules, thus being able to mimic primary neoplasms of lung or metastasis. It usually presents asymptomatically and is detected by incidental radiological findings.
Method: Retrospective case report based on medical record analysis, surgical pathology result and immunohistochemical evaluation.
Results: The present report describes the case of a female patient, 42 years old, who presented with

rectum adenocarcinoma for 2 years, who had already undergone chemotherapy and radiotherapy, and was considered to have eradicated disease. During control examinations, the presence of pulmonary nodule in the basal segment of the right lower lobe, in the upper left apical segment and in the posterior apex of the left upper lobe, with characteristics of pulmonary metastases, was evidenced in Thoracic Computed Tomography (CT). She was then admitted to the Thoracic Surgery Service of the Oswaldo Cruz University Hospital (HUOC-Recife), and atypical segmentectomy was performed to remove right nodulation. The anatomopathological result of the surgical resection showed cryptococoma, being indicated, together with the Service's pulmonology, the accomplishment of systemic treatment for cryptococcosis, in addition to a new surgical approach for the removal of contralateral cryptococoma. **Conclusion:** Thus, the differential diagnosis of infectious diseases, even with any scenario conducive to neoplasia, is essential. The benefit of doubt in such cases may not only change prognosis but also add disease-free survival. In this new context, therefore, it is urgent to create a specific treatment standard, either with systemic therapy or alone.

Keywords: Lung nodule, metastasis, Differential diagnosis, Cryptococcosis

P54: Case of Complex Tracheal Stenosis in Second Trimester Pregnant Woman: Idiopathic or Sequel of Endotracheal Tuberculosis?

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Background: Trachea is essential for ventilation and lesions that cause its stenosis impair this function. There are several causes of this injury and, although the most common benign cause is prolonged orotracheal intubation, diseases such as Tracheal Tuberculosis can progress with tracheal stenosis. The prevalence of tuberculosis-induced tracheobronchial stenosis is estimated at 10% to 40% and its diagnosis is suggested in the presence of a compatible clinic, confirmed by histopathological examination (obtained by bronchoscopy) or by positive culture of bacilli in the microbiological examination. The culture obtained by examination of sputum is less sensitive, generating false negative results, as in the described report.
Method: Retrospective case report based on chart analysis and bronchoscopic evaluation
Results: Female patient, 23 years old, in the 21st week of pregnancy with dyspnea and stridor for 2 years. She presents past Pulmonary Tuberculosis treatment with COXCIP scheme (Rifampicin, Isoniazid, Pyrazinamide, Etambutol) for 6 months. After end of treatment, she underwent three sputum smear microscopies, with negative results. A chest CT scan showed significant reduction of the tracheal lumen in the area next to the plane of the sternal furcula, extending to thoracic follow-up, becoming quite critical in the supracarinal region, until extension to the left bronchus-source. Bronchoscopy ratifies CT findings, evidencing edema and mucosal leukoplakia, with marked narrowing of the ostium of left bronchus-source. The treatment for Wegener's granulomatosis has started with Cyclophosphamide and Prednisone. New chest CT, after 10 months, evidences absence of regression of the stenosis. As the patient became pregnant during the investigation, she was referred to the High Risk Maternity, with replacement of Cyclophosphamide by Azathioprine, and association with inhaled corticoid. As the patient did not present a therapeutic response, she sought the Thoracic Surgery of the Hospital Universitário Oswaldo Cruz (HUOC-Recife) after episode of dyspnoea, cough and lymphocyte. Treatment for Tracheal Tuberculosis with COXCIP scheme was initiated again due to epidemiology, pathological antecedent and patient's condition.
Conclusion: In pregnancy, tracheal stenosis can arise and significantly affect maternal and fetal oxygenation and ventilation. It is necessary to perform its treatment according to clinical presentation, degree of stenosis, gestational phase and maternal-fetal safety. Despite the efficacy of the drug for tuberculosis, tracheal stenosis is unavoidable in these settings, but the therapeutic regimen triggers

improvement of the respiratory pattern and reduction of symptoms. In the case reported, it was decided to start the empirical treatment for tuberculosis, obtaining a good clinical result, enabling termination of pregnancy.

Keywords: TRACHEAL STENOSIS, bronchoscopy, pregnancy, tuberculosis

P55: Digestive Metastasis from Primary Lung Adenocarcinoma: Case Report

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Background: Lung cancer is a major cause of cancer-related death worldwide. Gastrointestinal (GI) tract involvement in lung cancer is uncommon but well-documented
Method: We report an clinical case from the oncology department of the military hospital of Tunis about digestive metastases of a primary pulmonary adenocarcinoma while underlining the interest of cytoplasmic staining of carcinomatous cells with anti-cytokeratin 7, anti-cytokeratin 20 and anti-TTF1 antibodies (thyroid transcription factor -1).
Results: A 64-year-old male active smoker at 40 year pack presented in the military hospital of Tunis with melena. PS was1. In June 2016, appearance of low digestive bleeding. Oeso-gastroduodenal fibroscopy was performed showing a range of gastric ulceration. The biopsies concluded in a well-differentiated adenocarcinoma whose immunohistochemical study revealed the presence of anti-CK7 and anti-TTF1 antibodies and the absence of anti-CK_{20} and HER 2 antibodies. Colonoscopy revealed a suspicious polyp. Biopsies of this polyp confirmed the diagnosis of well-differentiated adenocarcinoma whose immunohistochemical study revealed positive labeling of carcinomatous cells with anti-ck7, anti-ck20 and anti-TTF1 antibodies. Primary duodenal adenocarcinoma or metastasis of lung carcinoma could be considered, but in view of this immunohistochemical profile, the pulmonary origin was the most likely. Hence the diagnosis of metastatic pulmonary adenocarcinoma was mentioned. A subsequent chest/abdominal CT scan was performed showing 2 lesions in the lower right lung lobe with multiple secondary lesions, peritoneal carcinomatosis associated with centimetric celiac and retroperitoneal lymphadenopathies. However, cerebral CT scan was without abnormalities. Following the diagnosis, the patient received chemotherapy with cisplatin and pemetrexed protocol. The evolution was marked by the increase of the digestive symptomatology after 4 cycles of chemotherapy justifying the realization of an early reassessment. The thoraco-abdominopelvic CT showed firstly a regression of the lesion in the right lower pulmonary lobe and, on the other hand, a marked increase in intrahepatic secondary lesions without any change in the appearance of retro-peritoneal and left latero-aortic lymphadenopathy. IBecause of the discordant response, we discussed the concomitant existence of two different cancers. Bronchial fibroscopy was then performed showing no macroscopic abnormalities. The biopsy confirmed the diagnosis of an adenocarcinoma weakly expressing anti-TTF1 antibody compatible with bronchopulmonary localization. The biomolecular study of the EGFR mutation (Epidermal growth factor receptor) or ALK rearrangement was negative. Hepatic biopsy found an adenocarcinoma expressing only anti-CK7 and anti-TTF1 antibodies while anti-CK20 antibodies were negative.
Conclusion: The presence of GI metastasis in lung cancer is associated with poor prognosis. The TTF-1, CK7 and CK20 staining is important for the diagnosis.

Keyword: Lung adenocarcinoma, GI metastasis, digestive bleeding