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ABSTRACT BOOK
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Challenges of Interpreting NGS Liquid Biopsy (LB) Results in Advanced NSCLC: Are ESCAT and OncoKB Scales Reliable?

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Background: Plasma genotyping through next generation sequencing (NGS) is entering clinical practice in NSCLC. Several commercially available platforms can identify a wide variety of somatic aberrations. The correct interpretation of these results can be challenging and vendors include therapeutic suggestions to guide oncologists. Novel levels of evidence tools have been developed to rank genomic alterations in tissue, but not still used in LB.

Method: Advanced NSCLC patients underwent commercial 73-gene cfDNA NGS analysis. ESMO Scale for Clinical Actionability (ESCAT) and OncoKB were used to grade levels of evidence for categorize aberrations and compared with variant allele frequency (VAF), treatment decisions, and vendor suggestions.

Results: 77 samples from 73 advanced NSCLC patients at the time of diagnosis (49%) or during disease course (51%) were analyzed. Median turnaround time was 8 days (range 5-17), with no genotyping failures. cfDNA NGS analysis revealed 323 unique somatic alterations. According to ESCAT (IA-IV) and OncoKB (1-4), 87 and 88 genetic alterations were potentially actionable, respectively, and 26% received a matched targeted drug. Discrepancies between these two tools and vendor suggestions were reported in 4 cases (Fig. 1). We performed a subset analysis of 64 samples: Median VAF was 4.37% (range 0.16-43.05) and a VAF < 1% was reported in 16 samples; 45% of alterations of 64 samples: Median VAF was 4.37% (range 0.16-43.05) and a VAF < 1% was reported in 16 samples; 45% of alterations

Conclusion: The application of ESCAT and OncoKB is feasible in LB. Discrepancies between vendor therapeutic suggestions and evidence-based grading systems requests caution in the use of information outside the molecular tumor board. Driver mutations with low VAF are amenable to receive treatment. VAF could be included as complementary tool to grading systems to better understand the significance of aberrations.

Keywords: Liquid biopsy, NGS, precision medicine, NSCLC

Long-term Survival Outcomes with Nivolumab (NIVO) in Pts with Previously Treated Advanced Non-Small Cell Lung Cancer (NSCLC): Impact of Early Disease Control and Response


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Background: Historically, 5-y overall survival (OS) with chemotherapy for pts with metastatic lung cancer was ~5%; with the advent of immunotherapy, this has increased to ~15%. CheckMate (CM) 017, 057, 063, and 003 are NIVO studies with extensive follow-up in pts with previously treated advanced NSCLC. Using pooled data from these studies, we evaluated the long-term benefit (up to 4 y) of NIVO and impact of early response or disease control on subsequent long-term OS.

Method: Progression-free survival (PFS) and OS were estimated for pts with NSCLC across histologies treated with NIVO in pooled analyses of CM 017, 057, 063, and 003 (n=664), and for pts randomized to NIVO (n=427) or docetaxel (DOC; n=427) in pooled analyses of CM 017/057. Other analyses for CM 017/057 included estimation of OS in pts alive at 6 mo from time of response. For responders (CR/PR) from time of response.

Results: In pooled analyses of the 4 studies, 4-y OS rates for NIVO in all pts and those with PD-L1 ≥1% and <1% were 14%, 19%, and 11%, respectively. In CM 017/057, the 4-y OS rate in all pts randomized to NIVO (n=427) or docetaxel (DOC; n=427) in pooled analyses of CM 017/057. Other analyses for CM 017/057 included estimation of OS in pts alive at 6 mo from time of response with NIVO vs DOC; for pts with PD at 6 mo, 1-y OS rates were higher with NIVO vs DOC, while 2-4 y OS rates were similar (Table). For responders (CR/PR) in CM 017/057, 4-y OS rate from time of response with NIVO vs DOC was 54% vs 12%; median duration of response was 24 mo vs 6 mo, respectively. Overall, the NIVO discontinuation rate due to treatment-related adverse events (AEs) was 8.7%; most common treatment-related select AEs were skin reactions (incidence rate, 38.6 per 100 person-y).
Conclusion: These large pooled analyses show pts with CR/PR or SD with NIVO at 6 mo derived marked OS benefit; this long-term benefit was improved vs pts with DOC with the same response status at 6 mo. The NIVO safety profile was consistent with prior reports.

Keyword: non-small cell lung cancer, immunotherapy, nivolumab

O.03

Topic: Advanced NSCLC

KEYNOTE-189: OS Update and Progression After the Next Line of Therapy (PFS2) with Pembrolizumab + Chemotherapy for Metastatic Non-small NSCLC

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Background: Pembrolizumab plus chemotherapy (pemetrexed-platinum) significantly improved OS and PFS over chemotherapy alone as 1L therapy for metastatic nonsquamous NSCLC with manageable safety in the KEYNOTE-189 study (NCT02578680). Benefit was observed regardless of PD-L1 TPS and despite 54% of patients in the chemotherapy alone arm receiving subsequent immunotherapy.

Methods: Eligible patients were randomized 2:1 to pembrolizumab (n=410) or placebo (n=206) plus pemetrexed and carboplatin (n=410) or placebo (n=206) plus pemetrexed and carboplatin for 4 cycles followed by pembrolizumab or placebo for up to 35 cycles plus maintenance pemetrexed. Patients receiving placebo plus chemotherapy could crossover to receive pembrolizumab upon PD. Poststudy antitumor therapy and outcomes were collected. PFS2 was defined as time from randomization to PD per investigator after start of 2L therapy or death, whichever occurred first. There was no multiplicity adjustment, and all P values are nominal. Data cutoff was September 21, 2018.

Results: With 18.7-month median follow-up, pembrolizumab plus chemotherapy continued to provide longer OS (HR 0.56 [95% CI 0.45–0.70], P<0.00001; median 22.0 vs 10.7 months) and PFS (HR 0.48 [95% CI 0.40–0.58], P<0.00001). Benefit was seen in all PD-L1 TPS groups (Table). 2L+ therapy was received by 45% in the pembrolizumab plus chemotherapy arm and 59% (54% 2L+ immunotherapy) in the chemotherapy alone arm. PFS2 was longer for patients who received 1L pembrolizumab plus chemotherapy (HR 0.49 [95% CI 0.40–0.59], P<0.00001; median 17.0 vs 9.0 months), with no difference by TPS (Table).

Conclusion: Pembrolizumab plus chemotherapy continued to show substantial OS benefit in metastatic nonsquamous NSCLC, regardless of PD-L1 TPS and despite 54% of patients in the chemotherapy alone arm receiving subsequent immunotherapy. Median OS, PFS and PFS2 were approximately doubled with pembrolizumab plus chemotherapy. These data confirm that pembrolizumab should be given as part of 1L therapy to maximize outcomes in both PD-L1-expressing and PD-L1-non-expressing NSCLC.

Keywords: PD-L1, pembrolizumab, chemotherapy, NSCLC
and 7% Other. Respondents varied by specialty, including 45% Medical Oncologists, 12% Pulmonologists, 12% Thoracic Surgeons, 9% Pathologists, and 22% scientists or other. The frequency of MT was low overall and varied by region. Respondents from LA reported a higher frequency of patients who did not receive testing compared to other regions (74% vs 61% in requesting/treating track, p<0.0001; 88% vs 67% in tissue specimen acquisition, p=0.0017). The most frequent barrier to MT in every region was cost. The second largest barrier to MT in LA was access, similar to Europe/Other. 52% of respondents reported patients/physicians were unsure/not satisfied with the state of MT in their countries, with the highest dissatisfaction in LA (80%, p=0.0066). 82% of respondents who perform/interpret assays typically received results within 10 days, which occurred most frequently in LA (89%; p<0.0001). 23% reported >10% of cases were rejected due to inadequate samples, with 26% reporting this in LA (p=0.5590). However, across all regions, 47% stated there was no policy or strategy to improve the quality of the tissue samples in their countries. Among respondents who request/treat, 37% had difficulty in understanding MT reports, most of whom cited a need for more technical and scientific knowledge. However, LA and Europe respondents reported the least difficulty in understanding (p<0.0001). Overall, only 67% of respondents were aware of CAP/IASLC/AMP guidelines, 70% for LA (p=0.0041).

Conclusion: Adoption of MT in clinical practice for lung cancer is low in LA as well as across the globe, with cost and access being main barriers. Global and regional initiatives should be developed to address the barriers preventing MT in these regions.
**Invited Speakers**

**L1-1**

Thursday, October 17, 2019, 10:40 - 11:00

**IASLC Pre-Conference School of Thoracic Oncology**

**Oligometastatic Disease in Non-small Cell Lung Cancer. Single Center Experience Oncology Hospital XXI Century**

Y. Bautista, G. Cabada, G. Nuñez, M. Perez

1IMSS, Mexico/Mexico

**Objectives:** Radical treatment in oligometastatic disease in NSCLC has improved outcome in overall survival. We defined oligometastatic disease in patients with less than five synchronous metastases and 3 organs and mediastinal lymph node involvement is not counted as a metastatic site. We describe a single center experience of an academic hospital of oncology assessed by computed tomography for diagnosis, and radiotherapy as a radical treatment.

**Materials and Methods:** In this retrospective study we evaluate progression free survival using radiotherapy (stereotactic body radiotherapy and three-dimensional conformal radiotherapy) in patients with oligometastatic NSCLC with pathologically confirmed stage IV NSCLC with ≤5 synchronous metastases, and there were assessed by CT. All patients received four to six initial cycles of systemic treatment. We reviewed files from 2017 to 2019. During treatment of radiotherapy patients received pemetrexed as maintenance.

**Results:** Sixteen patients were included in the analysis. The mean age was 62.5 years (range: 48-78 years). At diagnosis, 31% of patients presented with CNS metastases. Following radiotherapy, 16 (68.75%) patients achieved a stable disease, while 4 (25%) had a partial response and 1 (6.25%) with complete response. The median PFS was 5.7 months (95% CI: 6.3-5.07).

**Conclusion:** Patients with oligometastatic NSCLC who undergo radiotherapy have a favorable response and progression free survival.

**Keywords:** Oligometastatic, Lung, Metastatic, Radiotherapy

**L1-2**

Efficacy of Pemetrexed maintenance in Patients of Metastatic Non-squamous Non-small Cell Lung Cancer. Single Center Experience. Academic Hospital IMSS XXI Century

Y. Bautista, G. Nuñez, G. Cabada, M. Perez

1IMSS, Mexico/Mexico

**Purpose:** Pemetrexed has been approved for maintenance therapy of advanced nonsquamous non-small-cell lung cancer (NSCLC). The purpose of this study was to describe real-world maintenance use of pemetrexed in Mexico City Oncology Hospital IMSS.

**Patients and Methods:** It was a retrospective study and where included files of patients with advanced nonsquamous NSCLC metastatic received carboplatin (area under the curve, 5), gemcitabine (1250 mg/m2) and pemetrexed (500 mg/m2) and carboplatin (area under the curve 5) for four cycles to six cycles. Patients without progression after four cycles to six cycles received pemetrexed (500 mg/m2) until progression. The primary point was response. SLP 16 patients have radiotherapy in oligometastatic disease concomitant with radiotherapy.

**Results:** We evaluated 35 files of patients with demographic/clinical factors: median age 60 years (45-78 years), gender (35% female and 62% male), about smoking status there were 65% positive, brain metastases (8.5%), median of cycles were 11.4 (5cycles -2 cycles) and follow-up of 24 months and median progression free survival of 8.2 months (95% CI: 8.8-7.5).

**Conclusion:** Pemetrexed is efficacious as maintenance therapy for advanced nonsquamous NSCLC and we had better progression free survival. However, it should be evaluated in a prospective study.

**Keywords:** Maintenance, Lung, Pemetrexed, Advanced

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**L1-3**

Thursday, October 17, 2019, 08:50 - 9:10

**IASLC Pre-Conference School of Pathology**

**Update of Staging, Challenges for Pathologists**

L. Dalurzo

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Clinical and pathological staging play a crucial role in predicting survivor and influencing treatment option in lung cancer patients. The last revision of AJCC and UICC 8th edition of lung cancer staging, was released in 2017 and has been effective internationally from 2018.

One of the most important changes in the 8th Staging Edition for pTNM are related with the size of the tumor (pT) and the application of 2015 WHO Lung Cancer Classification of adenocarcinoma. (1)

Several published studies demonstrated that the size of the tumor from 1 to 5 cm is very important in lung cancer, each centimeter increase in tumor diameter is associated with worsening survival. According to these studies, for (T) descriptors of 8th edition of TNM the new tumor-size groups were created: T1a, ≤1 cm; T1b, >1 to 2 cm; T1c, >2 to 3 cm; T2a, >3 to 4 cm; T2b, >4 to 5 cm; T3, >5 to 7 cm; and T4, >7 cm.

In 2011, new entities of adenocarcinoma as adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic predominant adenocarcinoma were defined and subsequently incorporated into the 2015 World Health Organization classification of lung cancer. To fit these entities into the T classification of the staging system, Tis and T1mi were introduced for adenocarcinoma in situ and minimally invasive adenocarcinoma, respectively.

In non-mucinous lung adenocarcinomas with a lepidic component, total gross tumor size should be recorded but only the invasive component is used as a descriptor of the T-categories. The lepidic component of the tumor as the amount of this growth, may potentially be difficult or could be underestimated grossly. To help to find and evaluate grossly these lesions we can carefully inlate the specimen with a mixture of optimal cutting temperature medium (OCT) before sectioning or we can make serial section followed by washing of the specimen before formalin fixation. To complete the evaluation of tumor size in non-mucinous lung adenocarcinomas with lepidic growth it is also important the microscopic reexamination of the specimen with a careful correlation with radiographic findings.

In microscopic evaluation, each adenocarcinoma subtype component of the tumor could be difficult to determine and the interpretation could be potentially different for different pathologists. There are interesting studies about intra observer and inter observer lung pathologists reproducibility of the classification of adenocarcinoma. (2) They represent the challenge that sometimes pathologists face with the application of 2015 adenocarcinoma classification, especially important when the subtype of the tumor evaluated impacts over the size of the invasive tumor and in consequence the pT for staging.

If the invasive and lepidic components are mixed in different areas and the size of the invasive component cannot be
measured in a single discrete focus, the pT can be estimated by multiplying the total size by the percentage of the invasive components: invasive size = % of invasive component x tumor diameter.

For separate tumor nodules (intrapulmonary metastasis), the classification recommended in the 7th edition has not changed: T3 for ipsilateral separate cancer nodules in the same lobe, T4 for ipsilateral separate cancer nodules in a different lobe, and M1a for a separate cancer nodule(s) in a contralateral lobe(s). The reported incidence of lung carcinoma patients presenting with multiple nodules ranges from 0.2% to 20%. Classification of multiple lung nodules as either multiple primary tumors or intrapulmonary metastases can be challenging. The 8th edition of the AJCC staging manual categorized multifocal lung cancer into four disease patterns. (I) two or more distinct and histologically different masses (considered unrelated and staged as individual cancers); (II) multiple ground-glass or part-solid nodules, histologically with lepidic growth pattern (considered separate tumors, T staged based on highest T stage lesion); (III) patchy areas of ground-glass and consolidations, histologically often invasive mucinous adenocarcinomas (considered single tumor with diffuse “pneumonic-type” involvement); and (IV) separate nodules with the same histologic features based on comprehensive histologic subtyping (considered intrapulmonary metastases). These patterns are based on clinical presentation (including radiologic impression and distribution of disease), histological assessment, and outcomes. Histologic and molecular features, in conjunction with clinical and radiological information, can all be tools to assist with staging of multiple nodules. Histologic features of adenocarcinomas are best characterized using histologic subtyping (percentage of lepidic, acinar, solid, papillary and micropapillary pattern) and comprehensive histologic assessment. Genomic alterations are commonly assessed using fluorescence in-situ hybridization and next generation sequencing (NGS). The AJCC considers exactly matching breakpoints by comparative genomic hybridization (CGH) as the only evidence for intrapulmonary metastases, and clearly different histologic types or subtypes as the only evidence for separate primary tumors. (3)

Involvement of the Pleura: When the visceral pleura is infiltrated by cancer, a pT1 cancer by size (3 cm or less) continues to be upstaged to pT2a. Erythema stains are of value in identifying pleural invasion in this setting. Beside there is no difference in staging between PL1 and PL2, this should be documented, tumor with neoplastic cells on the visceral pleural surface (PL2) have higher recurrence and worse prognosis.

The nodal stages have been able to consistently separate the patients into different prognostic group and remain unchanged from the earlier edition. The explorative analysis of pathologically-classified cases suggested that prognosis can be more accurately defined if combined with the number of stations in N1 and N2 location. Subdividing the N1 and N2 descriptors into involvement of single or multiple lymph node may help future studies on prognostication.

For metastatic disease (M descriptor) the new Mb category comprises patients with only one metastasis in one distant organ, whereas Mc implies multiple distant metastases in one or several organs.


Keywords: Staging, Pathology
there has not been a routine integration of exercise/cancer rehabilitation programs for patients in most parts of the world.

References

Keywords: Lung cancer rehab, Rehab

IASLC Pre-Conference School of Nursing
Symptom Management in Early Stage Lung Cancer
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The most common symptom leading to the diagnosis of lung cancer is cough, sometimes associated with wheezing or hemoptysis, from irritation due to a tumor located in or near the bronchus. Other early symptoms can include chest wall pain if the tumor is located peripherally, particularly if it is invading the pleura. Dyspnea is often a late symptom but can occur if the tumor is occluding the airway or causing volume loss. Anorexia with weight loss can occur in association with energy expenditure and fatigue from the effort of breathing, as well as the caloric demands of the tumor itself (usually late stage disease). Local effects of lung neoplasms include Horner syndrome (unilateral constricted pupil, drooping of the eyelid, and dry skin) if the tumor invades the sympathetic chain in the upper part of the chest, and superior vena cava syndrome if the tumor impedes venous return from the head, neck, and upper extremity. Pleural and pericardial effusions may cause dyspnea and chest pain syndromes. Metastatic disease may cause bone pain, and neurologic symptoms from brain involvement. Small cell lung cancer may produce hormones that are released independently from endocrine organs to cause what are classified as paraneoplastic syndromes, which can lead to Cushing's syndrome (high corticosteroid levels), SIADH (fluid retention and low sodium levels), and hypercalcemia.

Most early stage lung cancer produces few if any specific symptoms, and most of those, such as cough and/or dyspnea, are commonly associated with other diseases, so clinicians must be vigilant in inquiring about appropriate aspects of one's medical history (tobacco use, secondhand smoke, radon or asbestos exposure, etc.) and should have a degree of suspicion when a patient presents with vague symptoms. CT lung screening of appropriate asymptomatic individuals (>30 pack-years of tobacco use, age >55, less than 15 years since quitting) will identify an otherwise undiagnosed neoplasm in one out of 320 patients screened. This compares extremely favorably with other cancer screening. For example, almost 2000 asymptomatic women need to be screened with mammography to detect one patient with breast cancer.

IASLC Pre-Conference School of Nursing
Nutritional Support of the Lung Cancer Patient
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Lung cancer (LC) has the most lethal mortality rate between all the cancer types. In newly diagnosed LC patients the 5-year survival is estimated in 5-16%. Malnutrition is considered as a pivotal to decrease quality of life, prognosis and survival in LC. At the time of diagnosis, malnutrition can be observed in at least 45% of the patients and this proportion increase as the disease progression. LC patients present a considerable symptom burden and are at a high risk of involuntary weight loss. Anorexia, dysgeusia and cachexia are among the main factors that affect nutritional status. Over one half of the patients diagnosed with advanced LC experience anorexia (loss of appetite) and 35% of treatment naïve Non-small Cell Lung Cancer (NSCLC) patients reported dysgeusia (taste alteration), proportion increased until 56% in patients treated with chemotherapy and 66% in patients treated with radiotherapy. Anorexia and dysgeusia are directly related with lower energy and nutritional consumption and contribute to...
the development of cachexia. Cachexia is mainly characterized by the loss of muscle mass induced by cancer associated inflammatory response. Early assessment of nutritional status, including the determination of anorexia, dysgeusia and risk of cachexia in LC patients is imperative in order to timely treat them to improve prognosis. Nutritional support should be focused individualizing the nutritional risks confronting each patient, including mainly the energy balance of the diet, achieve energy needs, assess the need of nutritional supplements consumption or alternative ways of feeding.

There are recently available tools for an easy and fast assessment of nutritional risk in LC patients. The nutritional risk evaluation of LC patients should include the anorexia cachexia scale (ACS) section from the Functional Assessment of Anorexia–Cachexia Therapy (FAACT). ACS has been validated in LC patients identifying a cutoff value of ≤32 (sensitivity: 80.3% and specificity: 85%) for the determination of anorexia with the propose of consider a stimulant of appetite to achieve the energy requirements. Dysgeusia can be defined as a taste alteration and can be perceived as a distortion of taste (dysgeusia), absence of taste (ageusia), decreased detection sensitivity (hypogeusia), or increased sensitivity to any or all tastes (hypergeusia). But dysgeusia is closely related with quality of life because obstruct the pleasure of eat. So the identification of the magnitude of dysgeusia is the annoyance that represent for the LC patient. One of the most widely used tests is the taste and smell survey (TSS), which is a 16-item questionnaire that can help guide the taste alteration complain and give advice to improve the sense of taste making the eating process a more pleasant experience. Moreover, a cachexia grading system which takes into consideration body mass index (BMI) and weight loss to stratify patients into 5 risk categories (0 [pre-cachexia] - 4 [refractory cachexia]) was performed from a data set population of 8,160 heterogeneous cancer patients, with significant impact on survival according to the risk grade category.

After 8-weeks of treatment, patients who received Nabulbine increased their caloric-intake (342-kcal) compared to patients receiving placebo (p = 0.040). However, it was discontinued in Mexico. Another option considered to improve appetite is mirtazapina, available in Mexico and with preliminary reported improvement of appetite. Moreover, there is a current randomized clinical trial running in Instituto Nacional de Cancerología of Mexico comparing mirtazapina versus placebo in NSCLC-patients for the evaluation of improvement of appetite, energy-intake and quality-of-life. On the other hand, since dysgeusia is presented before treatment, nutritional advice should start at LC diagnosis to prevent or improve the taste disturbances. Preparing food with-reduced or absence altogether of condiments, choosing foods with a milder flavor, with a cold or warm temperature which could be more enjoyable to the patients. Additionally, LC patients classified with cachexia-grading system showed those with low-risk had a significantly longer survival compared with intermediate or high risk (Figure-1).

The highlights after the opportune nutritional risk evaluation of LC patients are concentrated in reach an optimums proportion of proteins, carbohydrate and lipids in the caloric intake including if is necessary oral nutritional supplements (ONS). Cancer patients consuming two ONS per day during 8 weeks after their first cycle of chemotherapy showed increment in body weight, fat-free mass, skeletal muscle mass, body cell mass, and fat mass compared to those without ONS. Once the cachexia is evident, a multitrargeted approach seems essential for its treatment, including combination of nutritional support, appetite stimulants drugs and a suitable program of pulmonary rehabilitation or physical exercisin. The food plan should be centralized in the complete symptoms burden and be promoting the enjoyment of eating. It is important to start as early as possible for avoid progression of cachexia stage even before weight loss can be presented. The continuous follow up of patients should be approximately every 3 weeks. The future of the multidisciplinary approach to the management of LC patients must therefore not overlook the important role of nutrition in the quality of life and clinical outcomes.

Keywords: Anorexia, Dysgeusia, Cachexia, Lung cancer

It has been shown that early involvement of palliative care improves outcomes for patients with advanced cancer as well as for their caregivers. Several trials, systematic reviews and meta-analyses have demonstrated benefits in quality of life, symptom control, mood, and satisfaction with care. However, palliative care services tend to be involved only in the last weeks of life. One possible reason for this reluctance to engage with palliative care is the stigma that is often associated with it, and the misunderstanding among healthcare workers and the public that palliative care is equivalent to end-of-life care. We conducted several studies investigating the opinions of oncologists, palliative care physicians, patients, caregivers and the public about palliative care in general and early palliative care in particular. Our overall aim was to investigate possible reasons for the lack of referral or late referral to palliative care in order to inform policy and practice in this regard.

We conducted a large qualitative study, in which we interviewed 71 patients with advanced cancer and their caregivers who had been randomized (or not) to receive early palliative care in a previous cluster randomized trial. A total of 48 patients (26 intervention, 22 control) and 23 caregivers (14 intervention, 9 control) completed interviews; we assessed their attitudes and perceptions about palliative care using a grounded theory methodology. We also conducted several surveys. The first was a national survey of oncologists (n=603, response rate 72%) regarding their referral practices to palliative care. We then conducted another survey, this time of palliative care physicians (n=531, response rate 71%) to assess their attitudes toward early palliative care and their readiness to provide this care. Both surveys were administered both online (by email) and by regular mail. Most recently, we conducted a large online survey of the Canadian public (n=1518) regarding their knowledge and attitudes related to palliative care. This last survey was distributed by MD Analytics, a healthcare research firm.

In the grounded theory study, participants in both trials arms associated palliative care with death, hopelessness, dependency and end-of-life comfort care. Participants stated that they feared and avoided palliative care, and that their perceptions often originated from interactions with health care professionals or from the media. During the trial, the impression of palliative care for intervention group participants changed to one of “ongoing care” that improved their “quality of living” but they still felt that the term palliative care carried a stigma. Intervention group participants emphasized the need for education by health care professionals on the meaning of palliative care; a vocal subgroup called for the renaming of palliative care, though they had no suggestion for a name.

In the survey of oncologists, 84% stated that they referred patients usually/always, but most referred late in the disease course. Forty-four percent agreed that patients had negative perceptions of palliative care. One third would refer earlier to palliative care if it was renamed supportive care. Predictors of earlier referral included satisfaction with palliative care service availability, acceptance of the palliative care service of patients on chemotherapy and completing a rotation in palliative care.

In the survey of palliative care physicians, more than 90% supported early palliative care referral, but only half had resources to deliver it, and only 20% received early referrals. Those with adequate resources were more likely to be family physicians (p=0.02) and to work on teams (p=0.03). Those receiving early referrals were less likely to agree that patients should stop chemotherapy before referral (p=0.009). Although...
60% agreed that patients perceive the term “palliative care” negatively, only 21% of palliative care specialists supported renaming the specialty.

In the survey of the Canadian public, 59% stated they did not know, prior to reading the World Health Organization (WHO) definition, that palliative care could be involved early in the course of illness, and 45% did not know palliative care could be provided together with other treatments aimed at prolonging life. Eighty-nine percent felt the WHO palliative care definition helped them to better understand what palliative care is, and 91% believed that Canadians should be made aware that palliative care can be included early in the course of a patient’s illness. Only 15% of participants thought that a change in name of palliative care would increase their willingness to engage with palliative care if they were diagnosed with a serious illness.

The stigma around palliative care is mainly due to the association of palliative care with end-of-life care and is perpetuated by late referral practices. Reasons for this late referral pattern may include factors at the level of the patient and family (e.g., lack of understanding of palliative care), the oncologist (e.g., lack of education in palliative care), and the palliative care team (e.g., lack of availability or prohibitive referral criteria). In order to reduce stigmatization of palliative care and to promote early access to palliative care for patients with cancer, several changes are suggested. Oncologists would benefit from palliative care training during their residency programs, which could promote integration with palliative care specialists and improve understanding of the relevance of palliative care early in the disease. Palliative care physicians would benefit from reviewing their referral criteria, and from collaboration with primary care teams to enable more timely provision of palliative care. Lastly, a coordinated effort needs to be made to educate the public about palliative care and its relevance early in the disease course. Although renaming of palliative care services could be considered on an individual basis, only a minority of oncologists, palliative care physicians and members of the public thought that renaming palliative care would be helpful.

**Keywords:** Palliative, Stigma, Referral, Cancer, Survey

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**I.8 Thursday, October 17, 2019, 11:45 - 12:00**

**IASLC Pre-Conference Advocacy Group Meeting**

**Re-thinking Access to Care**

M. Perez Vela

1Fundación Rebecca de Alba, A.C (FRA), Mexico City/Mexico

Lung cancer represents a burden to patients, families and governments around the world. In low income countries, it is a public health issue that needs public health policies to acknowledge and create quality access. In México, due to the complexity of the health system care access is linked to employment condition. Seguro Popular, a public health policy created in 2000 to give health coverage to informally employed patients includes in its Catastrophic Expense Catalogue only 7 types of cancer in adults excluding lung cancer. Other public health policies have limited access to quality and innovative treatments for many illnesses including lung cancer, besides, lung cancer patients are stigmatized and usually blamed for having brought the illness on themselves; Lung cancer in Mexico and other Latin American countries correlates to poverty, low educational and cultural level and the lack of public policies to create successful prevention and early detection programs. The importance of patient organizations is crucial in the construction of such policies.

FRA adapted a navigation model to meet the needs of cancer patients in Mexico based on the acknowledgement that every patient diagnosed with cancer has to deal with the same variables: losing health, losing their job, migration, to receive treatment, restructuration of the family system. Through a navigation model that systematically accompanies the patient and caregiver directly in the oncology medical center to process their clinical file, Schedule their treatment visits, understand the treatment scheme, supply them with information on how to navigate the health system and to get to know the support organizations available, empowers the patient and caregiver to comprehend the importance to complete treatment. Networking with other cancer organizations broadens the range of support to patients. Educational and information support groups are held periodically, monthly or every two weeks in different hospitals in order for patients and families to share their experiences dealing with cancer.

Patient navigation benefits cancer patients and their caregivers and families, it empowers and educates patients to better cope with the disease. Patient navigation accompanies the patient in their journey to complete treatment and in other cases to a better quality of life during the illness. Medical centers in Mexico do not consider patient navigation as an organic need to improve the service they offer to patients it is mostly done by organizations. Through patient navigation the organization gets to know and share the patient’s journey, the obstacles and barriers in the way to completing treatment, it is also a source of data that can help build better health care and access plans for the medical center but also for public policies.

Patient advocacy is core for any public policy Patient Navigation could be an important source of information to build it. Patient navigation should be organic to the health system in every country, foremost in low income countries. Lung cancer patients in Mexico are a particularly vulnerable group, patient navigation should be part of a public policy tending to improve their quality of life. Access is much more than been treated, it means been diagnosed at an early stage, been able to understand this diagnosis, been accompanied by someone who knows the system, been able to take informed decisions over the best treatment available and having a patient centered health system.

**Keywords:** Patient navigation, Access, Lung cancer

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**I.7 Thursday, October 17, 2019, 09:20 - 09:40**

**IASLC Pre-Conference Advocacy Group Meeting**

**Role of Patients in the Health System**

I. Zervino

1Fundacion Pacientes de Cancer de Pulmon, Beccar/Argentina

Health systems are designed for acute diseases and most pathologies are chronic. There are access barriers that do not depend only on financing.

Judicialization as a symptom of an unworkable system. Trends indicate that the situation will worsen if there are no structural changes.

Analysis of the experience of accompanying patients to navigate the health system.

It is necessary to explore the possible alternatives to involve patients in the public policy discussions in health.

The patient can play a significant role in the transformations necessary for the system.

**Keywords:** Patient, Health system, Public policies
C. Dresler1
1Action on Smoking or Health, USA, Montrose/United States

Tobacco use remains the leading cause of preventable death worldwide and is a significant risk factor for oncologic, cardiorespiratory, and pulmonary diseases. Evidence to date predicts that persistent tobacco use during therapy reduces the efficacy of disease treatment. (2014 US Surgeon General Report; Dresler, Lung Cancer 2003) To maximally improve outcomes from cancer therapeutic intervention, tobacco cessation in the persistent user should be uniformly provided as part of routine clinical care.

The 2014 US Surgeon General’s Report reported on a causal relationship between smoking and most cancers; continued tobacco use in cancer patients/survivors have higher all-cause and cancer-specific mortality, and people who continue to smoke have a higher risk of cancer recurrence, poorer response to treatment, and increased treatment toxicity. In addition, persistent smoking impacts weight, appetite, wound healing, pain control and second primaries.

Unfortunately, tobacco use is uncommonly captured in clinical oncology trials. If tobacco use is assessed, it is usually at the initiation of the study, and not assessed throughout the intervention. There has been the development of a validated survey (C-TUQ) for assessment of tobacco use in clinical trials. (Land S. 2016 Clinical Cancer Res) Also, in the paper by Gritz, et al., there is a survey that can be incorporated in the clinical assessment - outside of a clinical trials. (Gritz ER, 2005 Cancer Epidemiol Biomarkers Prev)

There is rarely an assessment of the impact of persistent tobacco use on the outcomes of the study. Although oncologists acknowledge the importance of tobacco use in cancer patients, they uncommonly intervene with their patients to assist in their tobacco cessation. (Warren GW, 2013 JOP; Warren GW, 2013 JTO) It is even difficult to identify the prevalence of smoking or other tobacco use in cancer patients or survivors.

Tobacco use rates are dropping in a few upper income countries, but even in patients with a diagnosis of lung cancer, there is still a substantial prevalence of smoking. In lower and middle income countries, where there is still a substantial prevalence of smoking, that prevalence in cancer patients is likely to be even higher. Although tobacco prevention and control are the best methods to prevent lung cancer - even with a diagnosis of cancer, it is important to assist patients to quit to maximize the treatment outcome.

Keywords: Smoking cessation in lung cancer
**Diagnostic Imaging Innovation**

**Initial Experience with EBUS TBNA for the Management of Lung Cancer in an Andean Latin American Country: Peru**

P. García-Mantilla1,2, S. Castro-Bernardini2

1Guillermo Almenara Hospital - Peruvian Social Health Insurance, Lima/Peru, 2SANNA San Borja Private Clinic, Lima/Peru

Endobronchial Ultrasound guided Transbronchial Needle Aspiration (EBUS-TBNA) is an established way for sampling mediastinal lymph nodes and parenchymal lesions located adjacent to the central airways to aid in diagnosis and staging of lung cancer. Real-time endobronchial ultrasound (EBUS) guidance is a particular method of fine needle aspiration biopsy, a minimally invasive diagnostic test used to obtain adequate samples of tissue with a high diagnostic yield.

In the developed world, EBUS has become the standard of care and has rapidly reached a pivotal role in the diagnosis and staging of lung cancer even with a potential high yield for molecular analysis. This safe technique is also a valuable and practical tool for re-staging of Non-Small Cell Lung Cancer.

Therefore, in the era of precision medicine for lung cancer treatment, developing countries in Latin America should already have access to this minimally invasive procedure that avoids unnecessary invasive methods and surgeries.

A total of 14 lesions were punctured, 13 were hilar and mediastinal lymphadenopathies and 01 was a right basal lung nodule. No complications were experienced. Six lesions were targeted in region 7, three in region 4R, three in region 4L, and one in region 11R. The size of the lesions ranged from 7 mm to 20 mm. EBUS-TBNA identified malignant cells in 11 lesions (10 adenopathies and 01 lung nodule) and benign cells in three adenopathies.

**Keywords:** Bronchoscopy, EBUS-TBNA, Lung cancer, Staging.

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**Diagnostic Imaging Innovation**

**Diagnosis in LATAM Region: Differences in Access to Technology**

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Inequality in service coverage and access to required assistance persist and is strongly determined by socioeconomic characteristics and geographical barriers. In Latin America (LATAM) and the Caribbean, over 30% of the population do not have access to health care for economic reasons, and 21% do not seek care because of geographical barriers. The latest available consensus shows that in 2010 there were about 42 million indigeneous people in LATAM, making up nearly 8 percent of the total population. Indigenous people face significant barriers to adequate healthcare due to linguistic differences between patients and healthcare professionals (1). Likewise, indigenous families who must travel long or costly distances to get medical attention experience apathy to search for health services. Furthermore, in urban areas, the population show high levels of dissatisfaction with their health care system, which may explain why a broad population of Latin Americans with sufficient income chose private services over universal public services.

In 2018, over 60% of newly diagnosed patients with lung cancer were located in low and medium-income countries as the ones in LATAM. Therefore two-thirds of the deaths attributed to lung cancer worldwide occur in these countries. In 2009 half of the economic resources destined for cancer were addressed only for pharmacotherapy. Compared to high-income countries, only 0.125% of the per capita income is intended for treatment acquisition (2, 3).

The challenges that face LATAM to make a diagnosis and give treatment are not always related with economic factors. There are other barriers such as a) lack in investment in research, b) limitations with the current established health care services where lung cancer is not considered a priority even though is the leading cause of cancer-related death worldwide, and c) limitations in drug supplies, and its affordability. Also, the low number of cancer specialists per head of population contributes to work overload and restricts them from participating in clinical cancer research (4). This situation is deleterious to the development of clinical trials, and national health authorities should ensure sufficient cancer specialists for the population volume. In this regard, we urge governments to design and implement better public policy and infrastructure for lung cancer prevention, screening, and treatment availability.

In the last decade, lung screening programs have been established in high-income countries. However, only two extensive studies have shown benefit in lung cancer timely detection within the high-risk population. These encourage the incorporation of early lung cancer detection campaigns (5).

The experience in low-income LATAM countries is limited to a Brazilian study in which they screened 800 patients with a high prevalence of granulomatous disease as in the rest of LATAM region. This research exposes LATAM ethnic differences and environmental exposures (wood-smoke exposure) that differs from high-income countries. Screening requires medical equipment and health care personal to obtain good results when detecting a vulnerable population. A Cost-effective lung screening program is subject to demographic characteristics and how the program is designed.

Inequalities in access to health services among and within LATAM countries prevails, which means that we need to ensure equity in both access and quality of services. We need new policies that allow better coverage of human and technological resources for lung cancer patients. Until now, there is insufficient evidence for screening and treatment programs for lung cancer done in LATAM despite being the most common cancer worldwide.

**References**

**Keywords:** Lung cancer diagnosis, LATAM cancer
Lung cancer is the leading cause of cancer death in the world; only 17% of stage I patients are inoperable at diagnosis; without treatment lost a 5-year survival of 6% and a half of 9 months. The locoregional therapies are an alternative with a curative intention for inoperable patients in stages I achieving focal cell death avoiding damage to healthy tissues.

There are multiple options which are the following: Thermal: Cryoablation, microwave ablation, radiofrequency ablation, FOCA; Nonthermal: irreversible alcohol and electroporation and finally SBRT.

Radiofrequency ablation: It is based on forming an alternating current circuit between the patient and the ablation machine: the electric current transmitted to the 14-17G needle travels through the tissue resistance by agitating the ions generating heat (60-100 °C necrosis coagulative and carbonization>110 °C), the residual energy is absorbed by a gel patch placed on the patient. Disadvantage: heat dissipation effect by cooling in vessels >3mm and bronchi of more than 2cm in diameter conditioning absence of ablation around the blood vessel.

Microwave ablation: Heat generation is based on the generation of electromagnetic fields that mobilize water to generating heat, its advantage is that the heat generated is homogeneous with temperatures around 150 °C without being affected by electrical conduction or dissipation of Heat however has a low availability, high cost and both microwave and radiofrequency ablation merit general anesthesia due to the pain generated by thermal ablation, especially the latter.

Cryoablation: Its effect is due to the expansion of the Argon at high pressure (Joule-Thompson effect) generating local cold from -20 °C there is a direct cellular damage due to rupture of the membrane by crystals following a period of defrosting of 10 minutes in which the endothelial damage allows the direct flow of vascular space to the extracellular space and through osmosis the interstitial water penetrates the permeable membrane destroying the cell, its advantage is the proper visualization of the ice ball, it does not need general anesthesia and generates immune response; Disadvantage is the low availability and the risk of bleeding.

Alcohol ablation: It is less and less used for its low effectiveness, its effect is due to the fact that it conditions coagulative necrosis and protein denaturation; Advantages: simplicity, low cost, safety- ablation of tumors difficult to treat with ARF due to proximity to vessels or bronchi, Disadvantages: high recurrence rate 49% in lesions >2 cm, multiple sessions (painful) and proximity to vessels or bronchi, Disadvantage: high recurrence rates 49% in lesions >2 cm, multiple sessions (painful), and proximity to vessels or bronchi, Disadvantages: high recurrence rate 49% in lesions >2 cm, multiple sessions (painful) and proximity to vessels or bronchi.

Irreversible electroporation: Its mechanism of action is due to electrical pulses of high voltage and low energy that creates irreversibility and toxic to the membrane by crystals following a period of defrosting of 10 minutes in which the endothelial damage allows the direct flow of vascular space to the extracellular space and through osmosis the interstitial water penetrates the permeable membrane destroying the cell, its advantage is the proper visualization of the ice ball, it does not need general anesthesia and generates immune response; Disadvantage is the low availability and the risk of bleeding.

Complications are minor in expert hands compared to that reported in most of the world literature: pneumothorax: 17-54%, 93% of the pulmonary mass resolve with Heimlich valve, 4% pulmonary hemorrhage, 4% self-limited hemoptysis 0.06% air embolem and seeding tumor 0.01-0.06%.

The immune-stimulating effect of ablative therapies is currently being studied; which is explained by the exposure of phagocytic tumor antigens by macrophages promoting the expression of (IL-1), IL-6, NF-κB and tumor necrosis factor-α (TNF-α).

Keywords: RFA, Interventional radiology, Lung cancer.

LALCA2019.IASLC.ORG
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Access to lung cancer (LC) diagnostic and treatment methods varies extensively around the globe. Latin America (LA, including Caribbean) is a large area comprising 30+ countries and 650+ million people. Incidence of lung cancer ranked third among the new cancer cases but first in death rate. In order to capture information regarding current practices and barriers to molecular testing (MT) in lung cancer, the IASLC conducted a survey among three tracks of health professionals. T1 included professionals performing, interpreting and reporting the molecular assays, T2 included professionals requesting the tests and treating LC patients, and T3 included professionals responsible for tissue/specimen procurement for LC MT. There is an IASLC committee working on the data analyses and on their behalf, I am presenting here some results from 254 participants from 17 LA countries, including 33 from T1 (15%), 169 from T2 (67%) and 52 from T3 (20%). These respondents represented respectively 8, 16 and 13 countries.

Based on the T1 data, the genes most commonly tested were EGFR, BRAF and KRAS for mutations, ALK and ROS1 for rearrangements and PDL1 for protein expression. Other genes less frequently tested were ERBB2 (HER2), RET and MET. In most labs (59%), single assays still prevailed, whereas 41% of labs multiplexed their assays. In most of the T1 respondents’ labs (74%) the fraction of cases rejected due to sample inadequacy was low, although in some labs these cases ranged between 10% and 30% of the workload. Two major factors influencing the failure to generate a result were insufficient amount of tumor cells in the specimen and poor tissue quality usually consequence of inadequate fixation. Enrichment for tumor cells through micro and macrodissection was often performed (85%). Twelve labs acknowledged offering MT on liquid biopsies. The average turnaround time (TAT) for providing results was listed as under 10 business days by most T1 respondents (89%). In most cases, the labs had costs reimbursed by pharmaceutical companies but patient direct payment, private health insurance system and government funds were also relevant financial resources. Most labs acknowledged conducting validation tests before implementation of new assays and regularly participating in proficiency testing efforts. Few T1 respondents (N=6) considered that LC patients/physicians in their countries were satisfied with the MT conditions, although N=10 respondents indicated that they were satisfied.

Based on the T2 data, we learned that 81% of respondents requested MT for all LC patients, while 17% requested only in special conditions, such as cases with adenocarcinoma histology or component, never-smoker, female, and young age. 30% of T2 respondents were not aware of the CAP/IASLC/AMP guidelines. Approximately 30% used labs in the same institution/city, 40% referred to a central lab in their country and 40% outsourced to a lab in another country. Tests more commonly ordered were EGFR and BRAF mutations, ALK and ROS1 rearrangements, and PDL1 expression. Less common, KRAS and HER2 mutations, MET amplification and exon 14 skipping, and RET rearrangement. Rebiopsy at disease progression was common when LC patient was on an EGFR TKI (85%), less common when other TKI was in use (52%). Overall, request for MT on liquid biopsy was common (74%). The MT was reported to fail to generate a conclusive result in <10%, 10 to 30%, or >30% of cases, respectively, by 58%, 31% and 11% of T2 respondents. The perception of TAT by T2 respondents was longer than the TAT declared by T1 respondents, 47% agreed to have received reports within 10 business days while 53% extended to >10 business days. About 23% of T2 respondents were not aware of test technical details but the knowledgeable ones have agreed with the T1 respondents in that single assays prevailed over multiplex assays. Most T2 respondents admitted to understand the MT report well (87%) but 13% recognized lack of scientific or technical knowledge or complained about poor quality of the report.

Among T3 respondents, only 38 worked actively in procurement of LC specimens for MT and only 76% of them conceded to know the ideal conditions for preservation of LC specimens for MT and have them available in their practice. 38% of T3 respondents had only a fair/poor degree of knowledge about how LC MT is performed but 72% have close pathologist assistance to evaluate tissue sufficiency and oversee tissue processing and handling after the procedure through detailed protocols, phone call or discussion in multidisciplinary meetings. Unfortunately, 29% of T3 respondents are not informed when a specimen they have procured fails to generate a result in the molecular lab.

Multidisciplinary meetings to discuss clinical cases at least once a month were common in the respondents’ institutions. These meetings are attended by physicians of different specialties such as pathologists, medical oncologists, thoracic surgeons, intervention radiologists, pulmonologists, hematologists, and by other health care professionals closely related to lung cancer care such as nurses, cancer scientists, biologists, biochemists, biotechnologists, biostatisticians, and bioinformaticians.

The perception of the T2 and T3 respondents regarding the fraction of LC patients who were molecularly tested differed when they compared the settings of their own clinic and of their country. Considering the 4 categories of LC patients tested as <25%, 25%–49%, 50%–74%, and 75%–100%, the T2 respondents estimated the frequencies of patients in their own clinic as 18%, 7%, 29% and 46%, and in their country as 39%, 35%, 22% and 4%, respectively. The T3 respondents estimated the frequencies of patients in their own clinic as 34%, 22%, 29% and 15%, and in their country as 66%, 22%, 10% and 2%, respectively. These differences strongly suggest that T2 and T3 respondents are not an unbiased representation of their peers in their countries.

Despite the limitation of the small sampling size, this study represents a significant effort in surveying the use of MT in LC in the LA region. These analyses identified strengths and weaknesses, and the detailed assessment will support regional initiatives to improve specific conditions and provide best therapeutic options to LC patients.

Special acknowledgments to Murry W. Wynes, Matthew P. Smeltzer, and Meghan B. Taylor for providing preliminary data.

Keywords: Biomarkers, Molecular diagnostic
for the patient, then to repeat or do multiple tissue biopsies to accomplish this goal and that becomes very cumbersome and difficult. In the specific case of lung cancer, biopsies are not easy because they can cause pneumothorax and lung cancer patients are not totally healthy most of them are smokers and they have already emphysema and/or COPD that increases the chances of complications if the biopsies don’t go well. However, there are still concerns about liquid biopsies how reliable are? and if they can totally replace tissue biopsies one day? Our own experience already published in more than 80 patients showed that tissue biopsies are not enough or don’t have any extra tissue in around 21% of the patients and all of these patients benefited of the liquid biopsy approach (NGS in cfDNA) however, there were cases that the liquid biopsy was unable to find the molecular aberration and the tissue did, then it’s for now safe to say that they are complementary. Another problem of the liquid biopsies is the cost specially for Latin America (LATAM), the NGS platforms are very expensive despite the fact that the prices have been decreasing in the last years but are still not affordable for the majority of the LATAM population; hence the options to do in LATAM hotspot testing, RT-PCR, FISH, exosomes and other technologies. However, there are challenges, we know for example that hotspot testing that is commonly used in LATAM due to its lower cost, it’s not very comprehensive and miss frequently mutations or genetic aberrations. RT-PCR is very sensitive and reliable but probably is a better test to find a specific genetic aberration than to do a panel analysis of several genetic aberrations at the same time unless we have the probes for all genes; and a similar problem we have with FISH: now we can use FISH to diagnose ALK, ROS1, NTRK1-3 and RET however that means that we will need to do at least 6 different FISH tests! Only to cover these genetic aberrations and we still have to test the patient for EGFR and other genes something that makes them more expensive than running NGS one time. Probably IHC is a good alternative for LATAM for now, we have good validation of IHC for ALK diagnosis and soon we hope to have one for ROS1; there are also several attempts to make NTRK 1-3 IHC better but probably with so many variants is a hard task and still will not cover other genetic aberrations like BRAF, KRAS and others. These are exiting times for LATAM very hard task and still will not cover other genetic aberrations.

**Keywords:** Lung cancer, Lobectomy, Segmentectomy

**Case Presentations and Review of New Developments in Surgery**

**Sublobar Resection for Lung Cancer**

**M. Block**

1Memorial Healthcare System · Department of Thoracic Surgery, Hollywood/United States

Small, less than 2 cm diameter lung cancers, present a challenge. Resection of just the nodule with a generous margin of normal lung is technically possible, but the only randomized trial to compare it to lobectomy demonstrated inferior survival. That trial is now 25 years old, and two important developments have led to renewed interest in the oncologic value of sublobar resection. First, increasing use of chest CT for early detection has led to the discovery of small lung cancers, many with biologically indolent behavior, for which a lobectomy seems extreme and possibly unnecessary. And second, developments in minimally invasive surgical techniques have led to increasing feasibility and decreasing morbidity of Sublobar resection, especially in patients with limited lung function. An important distinction to be made with Sublobar resection is the difference between a “wedge” resection and a Segmentectomy. A wedge is a simple excision by division of lung parenchyma around the tumor, without regard to anatomy. In contrast, a segmentectomy is an anatomic resection that mirrors a lobectomy in its attention to lymphatic and venous drainage, and parenchymal anatomic boundaries. Segmentectomy necessarily includes a hilar dissection with harvest of NI nodes. Thus segmentectomy should have better pathologic staging and improved oncologic outcomes, on par with lobectomy for small cancers. The renewed interest in Sublobar resection has led to a proliferation of retrospective and meta-analyses that suggest oncologic equivalence to lobectomy for small lung cancers. A prospective randomized trial is underway, but the results are not yet available. Current practice remains lobectomy when feasible, but segmentectomy should be a consideration for small cancers completely confined to an anatomic segment, especially for tumors with signs of indolent biology and in patients with limited lung function.

**Keywords:** Lung cancer, Lobectomy, Segmentectomy

**Radiotherapy Innovations**

**Lung Cancer Oligometastatic: Radiosurgery**

**B. Amendola**

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Lung cancer represents the second most common malignancy in both men and women. It is estimated in 2019 that there will be 228,150 new cases in the U.S.A. with an estimated death of 174,510.

More than 40% of patients with lung cancer present with stage IV disease. However, there appears to be an oligometastatic disease state in select patients with lung cancer: controlled primary tumors, limited nodal burden, good performance status, and metachronous presentation. These patient and tumor attributes have consistently been demonstrated to predict for improved survival in patients with oligometastatic NSCLC.

This theory for cancer progression was described by Hellman and Weichselbaum in 1985, when they put forward the oligometastatic hypothesis. Their theory was based on a multistep progression of certain types of cancer, such as prostate, colorectal, and melanoma, suggesting different subcategories of metastatic disease. Early in the metastatic process, there could be limited progression when oligometastases may be treated aggressively and can be cured.

In this presentation, we will discuss the value of Radiosurgery in early and advanced lung cancer, and particularly the role in oligometastatic disease.

Review of the oligometastatic NSCLC literature, including 49 publications and 2,176 individual patients with NSCLC with five or fewer metastases in patients receiving locally ablative treatment to all sites of oligometastases showed significant control of disease. These locally ablative treatments consisted of surgical metastasectomy, percutaneous ablation, and stereotactic ablative body radiotherapy. Outcomes were variable with overall survival (OS) ranging from 6.2 to 52 months (median 19 months).

Significant predictors for OS included control of the primary tumor, N-stage, and disease-free interval ranging from 6 to 12 months. Since most of the patients were younger with good performance status and a controlled primary tumor, patient selection is of utmost importance.

Other factors for best overall survival were metachronous vs synchronous metastases, lower N-stage, and histology (adenocarcinoma vs squamous cell). Given the high 5-year OS and relatively low risk, the literature supports the aggressive management of oligometastatic lung cancer.

**Keywords:** Radiosurgery, Lung cancer, Oligometastases
Treatment paradigms for locally advanced non-small cell lung cancer (NSCLC) have not changed dramatically till recently. RTOG 0617 demonstrated that escalation of radiation dose was not associated with improved survival. It has shown, however, that with more modern radiation techniques, median survival at five years can reach 30%. As is the case with stage IV NSCLC, the use of immunotherapy has completely changed our strategies for treating stage III NSCLC patients. The PACIFIC study has now established the standard of care for locally advanced NSCLC patients, chemoradiation followed by adjuvant immunotherapy. This change in treatment paradigm may just be the tip of the iceberg. This presentation will provide an understanding of the foundations that have led us to a current standard of care for treatment of stage III NSCLC and will also provide a view of the many studies incorporating immunotherapy that have been initiated for this patient population. Finally, the presentation will offer speculation on the future directions of treatment strategies that may be employed to treat locally advanced NSCLC.

**Keywords:** Locally advanced NSCLC, Immunotherapy, Radiation Therapy (HR for PFS=0.49) (Camidge DR et al), but has never been compared to alectinib. Brigatinib was demonstrated to be clearly superior to crizotinib, both with regard to outcome as well as for CNS effect. A question is, however, whether brigatinib is equal or better than alectinib as first line therapy in ALK-positive patients.

The third generation ALK-inhibitors have been developed represented by lorlatinib. Ongoing randomized studies have to demonstrate the relative role of lorlatinib compared to other generation ALK-inhibitors.

The most important question on this stage is how to sequence the different generations ALK-inhibitors. At most places alectinib is adapted as first line therapy, but there is no clear consensus on what comes after alectinib when the patient is progressing. In the future guidance based on resistant mutation pattern might direct subsequent therapy, but mutation guided therapy for ALK-positive patients has still to be fully developed. The sequencing of different ALK-inhibitors are currently studied in the US national Cancer Institute launched ALK Masterprotocol.

**References:**

**Keywords:** Crizotinib, Ceritinib, Alectinib, Brigatinib, Lorlatinib

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**ALK Genomic Aberrations in NSCLC and Clinical Implications**

**F. R. Hirsch**

*University of Colorado Cancer Center, Aurora/United States*

Anaplastic Lymphoma Kinase (ALK) genomic aberrations in NSCLC was one of the first genomic aberrations, which was successfully targeted with specific drug, e.g. crizotinib, and led to rapid development of personalized therapy in NSCLC.

Crizotinib as single agent showed remarkable response (70-80%) in patients with advanced NSCLC, who had the EML-4/ALK-translocation, which occurs in 2-5% of the patients. The genomic abnormality was originally diagnosed by FISH using a defined criterion (split-apart FISH pattern in at least 15% of the cells). However, later the US FDA also approved ALK-IHC for diagnosis using the Ventana ALK-specific antibody, D5F3. Today, this genomic abnormality is mostly detected by NGS. Not only was crizotinib associated to high response rate, but also to long-term outcomes (Solomon BJ et al). However, most of the ALK-positive patients progressed, particularly in the brain. During the studies with crizotinib resistance mutations were seen

Second generation ALK-targeted therapies were developed, e. g. alectinib, ceritinib and brigatinib, primarily studied after progression of crizotinib. The new generation ALK-inhibitors showed significant better effect compared to standard chemotherapy and had particularly a good penetration and effect in the CNS. Alectinib was clinically compared to crizotinib as first line therapy in two large randomized studies (J-ALEX and ALEX), and both demonstrated significantly better outcome with alectinib (updated results from ALEX-study showed HR(DFS)= 0.43 with a median disease-free survival of 27.8 months versus 22.8 months for crizotinib), which was approved based on these studies for first line therapy in ALK-positive NSCLC ( Hida T et al, Shaw A et al).

Brigatinib was also developed as a second-generation agent and was compared to crizotinib in the ALTA-1 study as first line therapy (HR for PFS=0.49) (Camidge DR et al), but has never been represented by lorlatinib. Ongoing randomized studies have to demonstrate the relative role of lorlatinib compared to other generation ALK-inhibitors.

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**References:**

**Keywords:** Crizotinib, Ceritinib, Alectinib, Brigatinib, Lorlatinib
are yet approved. Retrospective studies showed that patients with MET mutations treated with MET TKIs had higher response rates and longer survival compared to those who received chemotherapy alone. Ongoing trials may lead to approval in the near future. A bispecific EGFR/MET monoclonal antibody (JNJ3723) is also in clinical trial.

RET fusions occur in about 2% of lung adenocarcinomas and like several other molecular drivers are more frequent in never smokers and younger patients. There are several fusion partners. Brain metastases seem to be more frequent in patients with any driver including RET fusions. Early trials with multi-targeted TKIs show activity but response rates were less than 50% and there was considerable toxicity. Newer agents including BLU-667 and LOXO 292 have been reported to have response rates of 55%-77%, have less toxicity and to produce responses in CNS metastases. It is likely that one or more of these might be approved in the next year. These advances highlight the need for NGS testing that includes these molecular changes in all adenocarcinoma and never and light smokers.

PARP inhibitors inhibit DNA repair caused by certain chemotherapies, radiation therapy and are more effective in patients with other underlying DNA repair deficits. Early phase trials of several PARP inhibitors including alaparib, velaparib, talazaparib, rucaparib, and iniparib have shown activity in both SCLC and NSCLC and in both stage III in combination with chemotherapies and in stage IV in combination with chemotherapy. These agents may be more effective in patients harboring SNF1-II overexpression. Trials of PARP inhibitors combined with checkpoint immunotherapy are also in progress. There are ongoing phase III trials in both SCLC and NSCLC in both stage III and stage IV.

In conclusion, the growing number of molecular drivers for which there are approved therapies is growing emphasizing the need for next generation sequencing studies in all lung cancer patients who have adenocarcinoma or who are never or light smokers. While many of these abnormalities occur in only 2% of patients the benefits of TKI therapy and the low cost of adding these to NGS tests make testing imperative. PARP inhibitors have the potential to improve outcomes with chemotherapy, radiotherapy and immunotherapy.

Keywords: MET, RET, BRAF, PARP
The function of AICDA supports the rationale for an NFκB-driven generation of T790M. It was demonstrated that, regardless of the use of gefitinib or osimertinib, NFκB, STAT3 and YAP1 were activated in EGFR-mutant cell lines, including the H1975 (that harbors T790M). The downstream effectors were inhibited when the EGFR TKI was combined with blockers of the STAT3 and Src pathway. Osimertinib showed a PFS of 10.1 months versus 4.4 with platinum-pemetrexed chemotherapy in EGFR-mutant patients with T790M.

Screening for EGFR mutations is of great usefulness in customizing therapy in LADCs. However, combinatory therapies with EGFR TKIs is warranted to avoid the mechanisms of drug resistance that occur following single EGFR TKIs. The activation of STAT3 occurred a few hours after treatment with EGFR TKIs. AKT pathway is commonly activated following treatment with first- or third-generation EGFR TKIs (Figure). In addition, co-expression of other receptor tyrosine kinases is commonly present with EGFR mutations. We demonstrated that AXL expression can be driven by the Src-yes-associated protein 1 (YAP1) activation, providing a glimpse for adequate combinatory approaches. Recent articles identify AXL as a mechanism of intrinsic and acquired resistance to osimertinib. YAP1 directly regulates the expression of PD-L1 in EGFR TKI-resistant LADCs. Another downstream central effector is the protein tyrosine phosphatase SHP2 (PTPN11). The urea cycle enzyme carbamoyl phosphate synthetase-1 (CP1) correlates with poor prognosis in EGFR-mutant LADCs (Figure).

The suppression of CPS1 potentiates the effects of EGFR inhibition and, therefore, opens an additional angle for optimizing therapy in EGFR-mutant LADCs that could most likely be extrapolated to other, oncogene driven LADCs. Among the transcriptional targets of YAP1 and its effector Forkhead box protein M1 (FOXM1), are the aurora kinases A and B (AURKA and AURKB) (Figure). Both AURKA and AURKB have been associated with resistance to EGFR TKIs. EGFR-mutant LADCs do not respond to immune checkpoint inhibitors.

**Keywords:** NFκB, T790M, STAT3, CPS1, LADCs

I.20 Saturday, October 19, 2019, 15:00 - 15:10

**Targeted Therapy**

**EGFR/ALK TKIs with Central Nervous System Penetration**

I. Gil-Bazo1

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Different studies have shown that the incidence of central nervous system (CNS) involvement among patients with non-small cell lung cancer at the time of diagnosis may vary from 20% to about 30% depending on the histological subtype and the molecular features of the tumor.

Moreover, up to 50% of the patients may eventually develop brain metastasis during the disease course. In some patients indeed, and especially in those with oncogene addicted tumors, CNS infiltration may be the only site of disease progression during systemic treatment. In addition, CNS involvement has been traditionally considered to confer a dismal prognosis to NSCLC patients at any time point of the disease.

Patients with untreated brain metastasis (BM) have traditionally been excluded from clinical trials due to concerns that the particular pharmacokinetics in the CNS could preclude the correct interpretation of the results. The exclusion of patients with active BM was supported by the fact that initial attempts to use systemic drugs against CNS involvement were discouraging.

However, in recent years, the development of new-generation highly penetrant tyrosine-kinase inhibitors (TKIs) targeting EGFR and ALK oncogenes, have shown that appropriately designed drugs are extremely active in the CNS. The results from the latest clinical trials using third generation EGFR TKIs or second generation ALK TKIs are challenging traditional dogmas that established first generation TKIs are not meaningfully active to prevent or even treat disease spread to CNS.

These findings have significantly changed clinical management of patients with NSCLC BM and warrant a review of the literature. In this presentation, we provide an overview of the recent results using EGFR or ALK TKIs to treat patients with CNS involvement, and how these results are challenging previous paradigms and current clinical practice including the role of brain irradiation in this new clinical setting.

**Keywords:** NSCLC, EGFR, ALK, TKI, CNS

I.21 Saturday, October 19, 2019, 14:10 - 14:20

**Immunotherapy**

**Checkpoint Inhibitor Combinations Among Themselves and with Chemotherapy**

C. Mathias1, H. Wakelee2

1NOB/Grupo Oncoclínicas, Salvador/Brazil; 2Stanford University, Stanford/USA

Single-agent anti-PD-1/PD-L1 agents have had tremendous success in the treatment of Non-Small Cell Lung Cancer (NSCLC), significantly improving overall survival (OS) in patients with advanced disease. With the success of single-agent checkpoint inhibitors (CI), interest has developed in combining CI with other therapeutics in order to improve outcomes. Biological rationales suggest potential additive or synergistic benefit for combining CI with other established therapies, including enhanced tumor antigen uptake and presentation for T-cell priming, reducing the activity of immunosuppressive cells, and potentially increasing PD-L1 expression on NSCLC tumor cells. Early clinical trial data on CI combinations showed promising activity, and rapidly emerging phase III data have led to the approval of some CI combinations for the first-line treatment of metastatic non-squamous (2) and squamous (3) NSCLC. The purpose of this review is to evaluate emerging phase III data on the efficacy and safety of CI combinations for first-line advanced NSCLC.

Phase III trials with published or presented evaluating CI combinations were evaluated.

Multiple trials have combined CI with chemotherapy as first line therapy. Regimens of Pembrolizumab-chemotherapy, atezolizumab-chemotherapy, and atezolizumab-bevacizumab-chemotherapy have shown significantly improved OS compared to chemotherapy alone.

1. Pembrolizumab: KEYNOTE-189 randomized PD-L1-unselected patients NSCLC 2:1 to pembrolizumab/pemetrexed/platinum-pembrolizumab/pemetrexed maintenance (Pembro-pem, n=410) or placebo/pemetrexed/platinum-pemetrexed maintenance (Pb-pem, n=206). See Table 1(2).

2. Atezolizumab: IMpower-132 trial randomized PD-L1-unselected patients with stage IV non-squamous EGFR-/ALK- NSCLC to atezolizumab/pemetrexed/platinum-atezolizumab/pemetrexed maintenance (Atez-pem, n=292) or pemetrexed/platinum/pemetrexed maintenance (pem, n=286). See Table 1(4).

3. Atezolizumab-Bevacizumab: IMpower-165 trial randomized PD-L1-unselected patients with stage IV non-squamous NSCLC to receive atezolizumab/carboplatin/paclitaxel-atezolizumab maintenance (Atez-CP, n=402), atezolizumab/bevacizumab/carboplatin/paclitaxel-atezolizumab/bevacizumab maintenance (Atez-Bev-CP, n=400), bevacizumab/carboplatin/paclitaxel- bevacizumab maintenance (Bev-CP, n=400). EGFR+/ ALK+ patients were eligible if they progressed on or were intolerant to one or more approved targeted therapies. At a median follow-
up of approximately 20 months, OS in the ITT EGFR−/ALK− population was significantly improved (median, 19.2 vs. 14.7 months; HR, 0.78; 95% CI, 0.64–0.96; p=.02). Although not yet mature, median OS was not significantly improved for Atez-CP versus Bev-CP (19.4 vs. 14.7 months; HR, 0.88; 95% CI, 0.72–1.08; p=.20) (5).

Two trials reported outcomes for squamous/NSCLC, with CI-chemotherapy showing improved OS compared with chemotherapy.

1. Pembrolizumab: KEYNOTE-407 study randomized PD-L1-unselected patients with stage IV squamous NSCLC to receive pembrolizumab/carboplatin/paclitaxel or nab-paclitaxel-pembrolizumab maintenance (Pembro-C(n)P, n=278) or placebo/carboplatin/paclitaxel or nab-paclitaxel-placebo maintenance [Pb-C(n)P, n=281]. See Table 2 (6).


The other combination regimens which have shown some success are the combination PD-(L)1 plus CTLA4 inhibition. The MYSTIC trial looked at Durvalumb plus tremelimumab versus durvalumab or chemotherapy alone, but was not an overall positive study. The CheckMate227 trial included nivolumab + ipilimumab as a first line option compared to chemotherapy and in patients with PD-L1 expression of at least 1%, the combination led to superior OS compared to chemotherapy alone or single-agent CI. Interestingly though, the combination of nivolumab plus chemotherapy was not superior to chemotherapy alone in patients without PD-L1 expression. Many other combination CI regimens are under investigation.

Results from phase III trials comparing CI combinations with previous standards of care have now been reported. First-line CI added to standard therapies improve overall survival for nonsquamous EGFR−/ ALK− and squamous advanced NSCLC.

New schedules and combinations involving CI are being studied in order to improve care and quality of care.

References:
4. Papadimitrakopoulou VA, Cobo M, Bordoni R et al. IMpower132: PFS and safety results with 1L atezolizumab + carboplatin/cisplatin + pemetrexed in stage IV non-squamous NSCLC; Abstract pres- ented at: World Conference on Lung Cancer 2018; September 23–26, 2018; Toronto, Canada; OA05.07

Keywords: Checkpoint inhibitor combinations

I.22
Saturday, October 19, 2019, 14:50 - 15:00

Immunotherapy

Small Cell Lung Cancer Immunotherapy

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Management of extensive small cell lung cancer has remained largely unchanged for the last two decades. Advances to the field have included consolidation radiation therapy to the chest and prophylactic cranial irradiation to patients responding to chemotherapy, albeit with minor / questionable impacts on outcomes.

Recently, immunotherapy has been approved by several regulatory agencies worldwide to be used in treatment-naive or previously treated patients with extensive small cell lung cancer, on the basis of phase 2 and phase 3 clinical studies. Immunotherapy options for this disease may include nivolumab, pembrolizumab, nivolumab/ipilimumab combination, platinum/etoposide/atezolizumab combination, and platinum/etoposide/durvalumab combination.

In the presentation, we will summarize results of the clinical trials that support use of the aforementioned immunotherapy-based strategies for extensive small cell lung cancers, including both efficacy and toxicity outcomes.

Keywords: Immunotherapy, Small-cell lung cancer

Keywords: Checkpoint inhibitor combinations
**Keywords:** Lung cancer, Metabolic parameters, Total cholesterol, Fasting blood glucose

**Background:** Variability of metabolic parameters, such as blood cholesterol, fasting blood glucose, blood pressure and body weight can affect outcomes in health. Previous studies have shown that components of metabolic syndrome can lead to increased risks for several types of cancers such as breast and colon cancer, but not many studies have shown such effects on lung cancer. This study aimed to investigate whether variability in metabolic parameters can lead to increased risk of lung cancer in the general population.

**Method:** Nationally representative data from the Korean National Health Insurance System was used, and a total of 8,011,209 who were not diagnosed with lung cancer and underwent over three health examinations from 2005 to 2012 were followed until the end of 2015. Variability was measured in fasting blood glucose, total cholesterol, systolic blood pressure and body weight by using the coefficient of variation, standard deviation, variability independent of the mean and average real variability, and variability was assessed by quartiles. Subjects were also classified according to number of high-variability components (for example, a score of 4 would indicate high variability in the 4 mentioned metabolic parameters). Cox proportional hazards models were used adjusting for age, sex, smoking, regular exercise, alcohol and income.

**Results:** There were 44,982 events of lung cancer occurrences. High variability in each metabolic parameter was associated with higher risks for lung cancer. For blood glucose, hazard ratios and 95% confidence intervals in the highest quartile was 1.07 (1.04-1.10); for systolic blood pressure, 1.08 (1.05-1.10); for body weight, 1.04 (1.01-1.07); and for total cholesterol, 1.11 (1.08-1.14). Furthermore, the risk of lung cancer increased significantly with higher risks for several types of cancers such as breast and colon cancer, but not many studies have shown such effects on lung cancer. This study aimed to investigate whether variability in metabolic parameters can lead to increased risk of lung cancer in the general population.

**Conclusion:** High variability in metabolic parameters, especially in total cholesterol levels, was shown to be an independent predictor of increased risk for lung cancer. Furthermore, increasing number of high-variability parameters was found to increase risk of lung cancer in a stepwise manner.

**Keywords:** Lung cancer, Metabolic parameters, Total cholesterol, Fasting blood glucose
**Topic: Prevention, Early Detection, Epidemiology and Tobacco Control**

**A Primer on Genetic Counseling on the Thoracic Oncology Unit. Family History of Lung Cancer in Two Independent Populations Tested for BRCA1 &amp;2 and EGFR.**

G. Pacheco-Cuellar, K. Campos-Gomez, J.J. Valdez-Andrade, S. Campos-Gomez

Thoracic Oncology Unit, Centro Oncologico Estatal ISEMYM, Toluca de Lerdo/Mexico

**Background:** Germline mutations explain a small percent of lung cancer (LC), previous reports have described mutations in genes involved in Homologous Recombination Repair pathway in LC patients (pts), notably BRCA2. Also, mutations in EGRF, like T790M at diagnosis, could be inherited. Genetic counseling (CG) is a process including education, genetic cancer risk evaluation, and guidance about Genetic Testing (GT). We started a GC pilot to identify candidates for GT.

**Method:** This is a retrospective work to identify family history (FH) of LC in: a) Hereditary Breast/Ovarian Cancer (HBOC) pts carrying BRCA pathogenic variants, and b) LC pts carrying T790M at diagnosis. Additionally, we searched for patterns of hereditary cancer syndromes in LC pts without T790M. We included: 42 HBOC pts tested from Nov2014-mars2019, and 88 LC pts tested for EGFR from mars2018-mars2019. 20 LC pts completed a GC session and 68 LC pts had a medical record available. We collected clinical, demographic and familial variables. Three generation pedigree was gathered through GC. Descriptive and non-parametric tests were used.

**Results:** Mean age of LC pts was 61.55y (SD 13.8), 49 (55.7%) were females and 38 (43.2%) were non-smokers. 3 (3.4%) pts had T790M (2 females/1 male), they were older than 60y; 1 pt had 1 relative with LC, the other 2 pts had more than 2 affected relatives but none with LC. 43 pts (50%) of LC pts without T790M, had no FH of any cancer, 12 pts (14.1%) reported more than 3 relatives with Cancer; notably, 3 pts had 6 affected relatives, and 1 pt reported 10 relatives. 8 pts reported 1 relative with LC, 2 pts reported 2 LC cases and 1 pt 3 LC cases. 13.6% met criteria for GT according to FH; we found overlapping of breast, pancreatic, prostate and ovarian cancer. No statistically differences were found between these groups. Among the BRCA population, 16 pts (38.1%) had a mutation in BRCA2. None of the BRCA1 pedigrees showed LC. Among the BRCA2 pts, 2 non-related cases of LC were reported. The C808B-2811del variation was present in both families.

**Conclusion:** We observed LC in BRCA2 families and in 1 pt with T790M. Our sample is small but we identified at least 15 LC pts who met criteria for GT. GC improves FH taking and can guide GT. Those pts could have benefits such as identify the genetic etiology, adjust surveillance, direct therapy, calculate transmission risk and even struggle with stigma.

**Keyword:** Genetic counseling, BRCA2, EGFR

PD1.04

**Topic: Early Stage NSCLC (Stage I - III)**

**Mid-term Outcomes of Uniportal Vats(U-VATS) for Early Lung Cancer**

K. Hirai1, J. Usuda2

1Department Of Thoracic Surgery, Nippon Medical School Chiba Hokusoh Hospital, Inzai/Japan, 2Department Of Thoracic Surgery, Nippon Medical School, Tokyo/Japan

**Background:** Minimally invasive surgery, U-VATS has rapidly spread in a part of countries. It has been reported that U-VATS contributed to shorten the hospital stay and decrease the postoperative wound pain in several journals. Based on my clinical experience for approximately six years, I hereby present the mid-term outcomes of U-VATS.

**Method:** U-VATS which is carried out via from 3.5 to 4.0-cm incision without using a rib spreader routinely has been applied to almost thoracic diseases in our hospital. We have experienced 162 patients with clinical stage I lung cancer undergoing U-VATS from 2012 Sept. to 2019 Jun. We hereby report mid-term clinical outcomes of U-VATS after surgery.

**Results:** The average of operation duration, blood loss, drainage duration and hospital stay after surgery were 162±42 min, 85.5±4 ml, 1.8±3 days and 6.4±5 days, respectively. The average of numeric rating scale on postoperative day 7 was 2.5±0.4. The average of tumor size and the number of dissected lymph nodes were 2.8±0.7 cm and 17.2±5.1. There was no severe complication after surgery. The conversion rate of two-port and thoracotomy was 4.9% and 2.5%. Postoperatively, pathological stage of all patients was divided into I:149/II:6/IIIA:7. Local recurrence related to lymph node (12%/2/162) was recognized in stage IIB and IIIC. There was no mortality rate within 30days after surgery. 5 year-disease-free survival rate and 5 year-overall survival rate was 84.1% and 80.5%, respectively.

**Conclusion:** U-VATS was feasible and promising operative procedure. Further detailed study and multicenter study are necessary, however U-VATS is thought to be oncologically acceptable surgical treatment.

PD1.05

**Topic: Immunotherapy**

**Relevance of Antibiotic Use on Clinical Activity of Immune Checkpoint Inhibitors in Hispanic Patients with Advanced Non-small-cell Lung Cancer (CLICAP-ABs)**


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**Background:** The composition of gut microbiota affects antitumor immune responses, as well as preclinical and clinical outcomes following immune checkpoint inhibitors (ICI) in cancer. Antibiotics (ATB) alter gut microbiota diversity and composition leading to dysbiosis, which may influence the effectiveness of ICI.

**Method:** We examined patients with advanced non-small-cell lung cancer (NSCLC) treated with anti-programmed cell death ligand-1 mAb monotherapy alone or in combination in three different countries of Latin America. Those receiving ATB within 30 days of beginning ICI were compared with those who did not. Objective response, progression free survival (PFS) and overall survival (OS) were assessed.

**Results:** 18 of 140 (13%) NSCLC patients received ATB. The most commonly used ATB were b-lactam or quinolones for pneumonia or urinary tract infections. In NSCLC patients, ATB was associated with 4 cases of primary PD (28.6% versus 31.5%, P=0.818), non-significant decreased PFS (median 2.66 versus 1.94 months, HR 1.63, [95% CI 0.71-3.72], P=0.247) and significantly deleterious OS (median 12.42 versus 20.04 months,
Background: Stereotactic body radiation therapy (SBRT) can allow non-small cell lung cancer (NSCLC) patients (pts) to stay longer with the same therapy by eliminating oligometastatic progression (OMP) improving progression free survival (PFS) and overall survival (OS).

Method: One hundred pts with metastatic NSCLC undergoing chemotherapy (CHEMO), immunotherapy (IMMUNO) or target therapy (TARGET) that had OMP defined as less than four sites of metastasis and underwent SBRT were evaluated for PFS and OS. PFS1: Time between initiation of systemic therapy and development of OMP. PFS2: Time between OMP treated with SBRT and development of further PD requiring a change in systemic therapy. Pts received IMMUNO for second line and beyond. Robotic SBRT was delivered in 1-5 fractions on consecutive days or every other day. SBRT doses were determined based on the disease site and dose tolerance of the adjacent organs.

Results: Brain metastasis (BM) were seen in 45 pts and 55 pts had extracranial metastasis (EM). 34 pts were receiving CHEMO, 34 Target and 32 IMMUNO at the time of OMP. Main endpoints (m) are shown (Table). Pts with BM that received SBRT were able to continue the same therapy for a period of 6.5-9 extra months due to the control of BM. Pts with EM that have developed PD were able to continue the same therapy an 17-21 extra months due to the ablation of OMP by SBRT. Overall PFS was: 16.5m for BM and 34m for EM and the OS were: 31m and 53m respectively.

Conclusion:
- One hundred pts with metastatic NSCLC undergoing chemotheraphy, immunotherapy or target therapy that had oligometastatic progression (OMP) and underwent stereotactic body radiation therapy (SBRT) were evaluated for progression free survival (PFS) and overall survival (OS).
- Robotic SBRT was delivered in 1-5 fractions on consecutive days or every other day.
- SBRT doses were determined based on the disease site and dose tolerance of the adjacent organs.
- Brain metastasis (BM) were seen in 45 pts and 55 pts had extracranial metastasis (EM).
- 34 pts were receiving CHEMO, 34 Target and 32 IMMUNO at the time of OMP.
- Main endpoints (m) are shown (Table).
- Pts with BM that received SBRT were able to continue the same therapy for a period of 6.5-9 extra months due to the control of BM.
- Pts with EM that have developed PD were able to continue the same therapy an 17-21 extra months due to the ablation of OMP by SBRT.
- Overall PFS was: 16.5m for BM and 34m for EM and the OS were: 31m and 53m respectively.

Keywords: Antibiotics, Response rate, Immune checkpoint inhibitors
**PD2.02**

**Topic: Advanced NSCLC**

Pembrolizumab plus Pemetrexed-Platinum for Patients with Metastatic Nonsquamous NSCLC and Liver or Brain Metastases: Results from KEYNOTE-189

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**Patients With Liver Metastases**

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<th>Pembrolizumab-Platinum (n=410)</th>
<th>Placebo-Combination (n=206)</th>
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<td>Median OS (95% CI)</td>
<td>11.0 (9.9–12.1)</td>
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<td>HR (95% CI)</td>
<td>0.58 (0.45–0.75)</td>
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**Patients Without Liver Metastases**

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<td>Median OS (95% CI)</td>
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<tr>
<td>HR (95% CI)</td>
<td>0.59 (0.46–0.75)</td>
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**Patients With Brain Metastases**

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<th>Pembrolizumab-Platinum (n=73)</th>
<th>Placebo-Combination (n=35)</th>
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<tr>
<td>Median OS (95% CI)</td>
<td>11.0 (10.0–12.1)</td>
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<td>HR (95% CI)</td>
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**Patients Without Brain Metastases**

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<th>Pembrolizumab-Platinum (n=337)</th>
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<td>HR (95% CI)</td>
<td>0.59 (0.46–0.75)</td>
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*25 patients had both brain and liver metastases.

**Conclusion:** Pembrolizumab plus pemetrexed-platinum provided superior outcomes vs chemotherapy alone irrespective of liver or brain metastases in patients with untreated metastatic nonsquamous NSCLC. Benefit was observed in patients with brain or liver metastases, for whom prognosis is historically poor.

**Keyword:** PD-L1, Pembrolizumab, Chemotherapy, NSCLC

**PD2.03**

**Topic: Immunotherapy**

Exploration of Factors Relating to Immune Response in Patients Treated with Immune Checkpoint Inhibitors for Non-Small Cell Lung Cancer (NSCLC)


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Background: Although the introduction of immune checkpoint inhibitors (ICIs) has yielded substantial benefits in terms of survival in the treatment of Non-Small Cell Lung Cancer (NSCLC), the possibility of activation of dormant autoimmune diseases or onset of immune mediated toxicities is a reality. The objective of this study was to explore intrinsic immunological factors associated with poor outcomes.

Method: In a retrospective cohort study of 48 patients, without any prior medical history of autoimmunity, treated for advanced/metastatic NSCLC with ICIs, 73 patients with a history of autoimmunity (HLA-A*0201) were assessed. Determination of HLA-A*0201 as well as acute phase reactants and antiphospholipid antibodies was performed. Additionally, evaluation of survival in a time to event manner was conducted using the Kaplan Meier method and Cox regressions.

Results: Median follow-up was 27.3 months, of the included patients 26 were male (54%) with a median age of 62 years old and there were no individuals with and ECOG performance score >1. Median overall survival (OS) was reached at 22.47 months. When analyzing the presence of the HLA-A*0201 serotype, 6 patients tested positive (12.5%). Additionally, all presented with borderline or abnormal B2glycoprotein IgM and IgG, 2Bmicroglobulin and elevated C reactive protein. Four patients (66%) experienced reactive lymphadenopathy during treatment and all suffered some form of venous thromboembolism. When analyzing OS, this group of patients had a significantly worse outcome (6.35 vs 22.47 months, HR= 4.47, [95% CI 1.47 – 13.61], p<0.001) compared with their counterparts. Overall response rate for the whole was superior for the HLA-A*0201 positive patients achieving 41.4% and 33%, p<0.001, respectively.

Conclusion: The presence of the HLA-A*0201 could potentially predispose to a paradoxical and pathological activation of the immune system without offering any benefit in terms of tumor control. Larger studies evaluating these findings are warranted.

Keywords: B2glycoprotein, Autoimmune diseases, Antiphospholipid antibodies

PD2.04

Topic: Advanced NSCLC

Long Term Efficacy and Safety of Ensartinib in Pre-treated Anaplastic Lymphoma Kinase (ALK) Positive Non-small Cell Lung Cancer (NSCLC) Patients (eXalt2)

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Background: Ensartinib has shown efficacy in ALK+ NSCLC patients previously treated with crizotinib and/or next generation ALK inhibitors (ALKIs). This clinical benefit is associated with high intracranial (IC) activity in patients with brain metastases and a favorable safety profile. We report updated data in pre-treated NSCLC cohorts from the eXalt2 study.

Method: eXalt2 is an ongoing multicenter Phase II/II study. We report data on patients treated with ensartinib >200mg PO, once daily on a continuous 28-day schedule (NCT01625234). Patients received ensartinib until disease progression, unacceptable toxicity or investigator discretion. Patients with asymptomatic brain metastases were allowed to enroll. All patients were assessed for adverse events (AEs) using CTCAE version 4.03, and response to treatment was assessed locally every 8 weeks using RECIST 1.1.

Results: As of 20 May 2019, 73 pre-treated ALK+ NSCLC response evaluable patients were assessed (Table). The median progression free survival (PFS) was 91.9 months (m) (IQR, 5.8-11.7) and 2.8 m (IQR, 1.7-5.7) respectively in post-crizotinib (n=41) and post second generation ALKI (n=32) cohorts, with 12/32 (38%) having received >3 lines of ALK inhibitors. Overall response rate (ORR) was 59% (uORR 66%) in the post-crizotinib cohort resulting in a disease control rate (DCR) of 95%, and ORR in the post second generation ALKI cohort was 9% (uORR 16%) resulting in a DCR of 56%, IC responses were observed in both cohorts, with an IC ORR of 50% (8/16, including 2 complete responses) and IC DCR of 100%. Safety profile of these 73 patients is similar to previously reported safety data, with rash being the most common drug-related AE (56%, mostly grades 1-2).

<table>
<thead>
<tr>
<th>Table. Baseline Patient Demographics</th>
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<tbody>
<tr>
<td>N (%)</td>
</tr>
<tr>
<td>Median Age (Range)</td>
</tr>
<tr>
<td>Gender: Male / Female</td>
</tr>
<tr>
<td>Race: Caucasian Asian</td>
</tr>
<tr>
<td>Black/African American Unknown / Other</td>
</tr>
<tr>
<td>ECOG: 0 / 1</td>
</tr>
</tbody>
</table>

Prior ALK TKI Treatment: Crizotinib only 12/32 (38%) received >3 lines of ALK inhibitors. Overall response rate (ORR) was 59% (uORR 66%) in the post-crizotinib cohort resulting in a disease control rate (DCR) of 95%, and ORR in the post second generation ALKI cohort was 9% (uORR 16%) resulting in a DCR of 56%, IC responses were observed in both cohorts, with an IC ORR of 50% (8/16, including 2 complete responses) and IC DCR of 100%. Safety profile of these 73 patients is similar to previously reported safety data, with rash being the most common drug-related AE (56%, mostly grades 1-2).

Conclusion: Ensartinib is well tolerated and active in pre-treated ALK+ NSCLC patients with high DCR, remarkable intracranial efficacy and a favorable safety profile. Updated survival outcomes will be presented at the conference.

Keywords: ALK, NSCLC, Ensartinib, CNS

PD2.05

Topic: Advanced NSCLC

Overall Survival in Pts with EGFRm+ NSCLC Receiving Sequential Afatinib and Osimertinib: Updated Analysis of the Giotag Study


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Background: While the superiority of second- and third-generation EGFR tyrosine kinase inhibitors (TKIs) over first-generation agents has been clearly demonstrated, the optimal sequence of EGFR TKIs is less clear, especially as there is no established targeted therapy after osimertinib failure. In the observational GioTag study (NCT03370770), patients with EGFRm+ NSCLC were treated with sequential afatinib and osimertinib in a ‘real-world’ clinical setting, including patients with poor prognosis (ECOG PS ≥ 2; 15%; stable brain metastases: 10%). Encouraging time to treatment failure (TTF) was seen in the primary analysis (overall: 27.6 months; Del19-positive patients: 30.3 months; Asian patients: 46.7 months). In this analysis, we report OS and updated TTF.

Method: Data were retrospectively collected between Dec 2017 and June 2018 for 204 patients with EGFRm+ (Del19, LB58R) NSCLC who were T790M-positive after first-line afatinib and received subsequent osimertinib. TTF was the primary outcome; OS analysis was exploratory. Data were collected from electronic health records (EHRs; n=126) or medical charts (n=77). For logistical reasons, this interim analysis includes updated data (as at April 2019) from patients with available EHRs (all USA; n=94).

Results: After a median follow-up of 30.3 months, median OS was 41.3 months (90% CI: 36.8–46.3) in the overall dataset (n=203) and 45.7 months (90% CI: 45.3–51.5) in Del19-positive patients (n=146). At 2 years, OS was 80%; OS in Asian patients was immature. Updated median TTF was 281 months (90% CI: 26.8–30.3) in the overall dataset, and 30.6 months (90% CI: 27.6–32.0) in Del19-positive patients. Outcomes were not affected by afatinib starting dose. Median TTF with osimertinib was 15.6 months (90% CI: 13.1–18.1) in the overall dataset, and 16.4 months (90% CI: 14.9–17.9) in Del19-positive patients.

Conclusion: Encouraging OS and TTF were seen with sequential afatinib and osimertinib in patients with EGFR T790M-positive NSCLC, especially in Del19-positive patients, supporting the use of this regimen. Prior treatment with afatinib did not preclude prolonged TTF with second-line osimertinib (15.6 months overall; 16.4 months in Del19-positive patients). The final analysis, incorporating updated data from manual chart reviews and anticipated in early 2020, will provide further insights into the long-term OS of patients treated with sequential afatinib–osimertinib.

Keywords: Osimertinib, Sequential, NSCLC, Afatinib

PD2.06

Topic: Advanced NSCLC

EGFR Inhibitors + Bevacizumab Demonstrated Superior Efficacy Compared with EGFR Inhibitors Alone as First-line Treatment in Advanced NSCLC Patients with EGFR Mutations and BIM Deletion Polymorphisms

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Background: BIM activation is essential for EGFR-TKIs triggered apoptosis in EGFR-mutant Non-small-cell lung cancer (NSCLC). A 2903-bp germline deletion in intron 2 of the BIM gene results in generation of alternatively spliced isoforms that lack the crucial BH3 domain, impairing the apoptotic response to TKIs and conferring NSCLC cells intrinsic resistance to these medications. Patients with both alterations have poor clinical evolution. The current study aimed to investigate the clinical efficacy and tolerability of EGFR-TKIs plus bevacizumab (Bev) versus EGFR-TKIs alone as first-line treatment in advanced NSCLC patients with EGFR mutations and BIM deletions (BIMdel).

Method: A retrospective analysis was conducted. BIMdel was detected using polymerase chain reaction (PCR) analysis and direct sequencing of DNA from tumor and peripheral blood cells (PBcs). We also assessed BIM protein expression by immunohistochemistry and BIM mRNA levels by RT-PCR. Clinical characteristics, overall survival (OS), progression-free-survival (PFS), objective response rate (ORR) and treatment-related adverse events were compared in the EGFR-TKIs versus EGFR-TKIs plus Bev groups.

Results: 32 patients were included; 16 of them received EGFR-TKIs and 18 received EGFR-TKIs plus Bev. The addition of Bev resulted in a significantly higher ORR compared with TKIs alone (94% vs. 44%, p=0.0014). Median PFS was longer with the use of the combination compared with TKIs alone (11.1 vs. 7.77 months; p < 0.001). Median OS tended to be longer in the EGFR-TKIs plus Bev group than in TKIs alone (30.9 vs. 25.4 months; p = 0.06). EGFR-TKIs plus Bev was associated with more grade ≥3 hematological and thrombotic adverse events. The expression of BIM by immunohistochemistry did not influence PFS and OS, however when stratifying BIM mRNA levels by the median (≥2.2 vs. <2.1) allowed to find a prognostic trend in favor of those with higher BIM mRNA levels (32.2 vs. 25.2 months respectively; p = 0.058).

Conclusion: EGFR-TKIs plus Bev confered a significantly higher ORR and PFS in advanced NSCLC patients with EGFR mutation and BIMdel. Further prospective studies are needed to validate these findings.

Keywords: Bevacizumab, EGFR, BIM
**Poster Session 1**

**Friday, October 18, 2019**

**P1.01**

**Topic: Prevention, Early Detection, Epidemiology and Tobacco Control**

**EGFR Mutations in Lung Cancer in Northern Mexican Population**

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Hospital Universitario Dr. Jose Eleuterio Gonzalez, Monterrey, Nuevo Leon/Mexico

**Background:** Lung cancer is the most common cause of death from cancer worldwide, responsible for 1.59 million deaths. Multiple studies support the predictive value in treatment selection, EGFR mutations are also prognostic for survival benefit. EGFR gene exon 19 deletion and the exon 21 L858R substitution account for approximately 90% of all EGFR mutations. The aim of this study is evaluate the frequency of EGFR mutations in lung cancer in Northern Mexican population.

**Method:** DNA extraction is performed using a commercial extraction kit, the process is performed by real-time PCR on an automated platform in a closed circuit with a commercial panel. The DNA quantification quality control process is analyzed, validating with positive and negative controls, then analysis of the 29 known mutations of EGFR gene exons 18, 19, 20, 21. All the concepts were evaluated with descriptive statistics. IBM SPSS Statistics version 4 software was used, using Chi-squared test.

**Results:** This study includes 450 patients. The median age of the patients is 64 years (range 30-90). Activating mutations were found in the EGFR gene in 141 patients (31.33%). Of the patients with mutations found, 79 (56.02%) patients had exon 19 deletion (DelEx19) and 43 (30.49%) patients have L858R mutation (Ex21), which represent 86.52% of the total mutations found. EGFR mutations were more frequent in older patients (82.97% >51 years), than in the younger ones (14.18% <50 years). The age range with the highest number of EGFR mutations was 61-70 years (28.36%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>GENDER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women (%)</td>
</tr>
<tr>
<td>EGFR sensitizing mutation status Positive Negative</td>
<td>84 (59.57%) 137 (44.33%)</td>
</tr>
<tr>
<td>Specific mutation of EGFR</td>
<td>46 (58.22%)</td>
</tr>
<tr>
<td>exon 19 deletion</td>
<td>27 (53.17%)</td>
</tr>
<tr>
<td>Exon 21 L858R</td>
<td>17 (36.92%)</td>
</tr>
<tr>
<td>G719X L858R Insertion S768I T790M</td>
<td>13 (27.66%)</td>
</tr>
</tbody>
</table>

**Conclusion:** 31.33% of mutations were found in our cases. EGFR exon 19 deletions and the exon 21 L858R substitutions were more frequent compared to the other mutations. The frequency of mutations in EGFR coincides with the literature that mutations are more prevalent in women. A study published in 2011 evaluated the frequency of mutations in EGFR and KRAS in NSCLC in different ethnic groups and found that in Mexico the frequency of EGFR mutations was 31.2%.

**Keywords:** Non-small cell lung cancer, Mutation, EGFR, Mexico

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**P1.02**

**Topic: Prevention, Early Detection, Epidemiology and Tobacco Control**

**ALK Gene Rearrangement in Patients with Lung Cancer in Northern Mexican Population**

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Hospital Universitario Dr. Jose Eleuterio Gonzalez, Monterrey, Nuevo Leon/Mexico

**Background:** EGFR mutation and re-arrangement of the ALK gene are two of the molecular targets evaluated in all cases of patients with primary lung adenocarcinoma. ALK rearrangements are mutually exclusive with mutations in EGFR or KRAS. These mutations are helpful in choosing targeted therapy for the patient. The aim of this study is to evaluate the frequency of ALK gene rearrangement in patients with Lung cancer in Northern Mexico population and histological patterns.

**Method:** 450 patients with NSCLC were evaluated from 2006 to 2017. In all cases we perform immunohistochemistry with clone D5F3 in an automated platform. FISH rearrangement for ALK break apart were done a commercial kit. We follow the recommended criteria of IASLC for the evaluation of the FISH probes. Immunohistochemistry and FISH test were reviewed by 2 pathologists with experience and training in the evaluation of both test.

**Results:** This study includes 450 patients. The median age of the patients with ALK gene rearrangement was 53 years (range 37-82) and male to female ratio of 1.8. 65 (14.44%) were positive by immunohistochemistry in any intensity and percentage of neoplastic cells, and only 17 (3.77%) were positive or ALK rearrangement by FISH. All the cases which was negative for immunohistochemistry was negative by FISH.

**Conclusion:** We found ALK rearrangements in 17 cases (3.77%), this figure is similar in Hispanic resident in USA and Latin-American population, however reports in Mexican population are between 4 and 10.5 %. This difference will be due to different cohorts of patients, methodology types of FISH probes used for the detection of ALK rearrangements and ethnic differences.

**Keywords:** Mexico, Non-small cell lung cancer, ALK, Mutation

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**P1.03**

**Topic: Prevention, Early Detection, Epidemiology and Tobacco Control**

**Case Series of Double Mutations in Patients with Lung Adenocarcinoma**

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**Background:** The introduction of targeted therapies has increased the survival time in a subset of patients with NSCLC. The National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology recommend measuring the local EGFR gene mutations of NSCLC patients before treatment.
Sensitivity to EGFR TKIs in patients with double or multiple mutations is not well described. In the literature there are few reported cases of double mutations. We present a series of six cases of Lung Adenocarcinoma with double mutations found between 2006 and 2017 in a hospital in Northern Mexico.

Method: 450 patients with Lung cancer were evaluated from 2006 to 2017. DNA extraction is performed using a commercial extraction kit, the process is performed by real-time PCR on an automated platform in a closed circuit with a commercial panel. The DNA quantification quality control process is analyzed, validating with positive and negative controls, then analysis of the 29 known mutations of EGFR gene exons 18, 19, 20, 21.

Results: This study includes 450 patients, 141 (31.33%) patients had EGFR mutations, of which six (4.25%) had double exons EGFR mutations. Of the six cases with double mutations, male to female ratio was 11. The histological patterns reported in the double mutations were: 3 (50%) cases with acinar pattern, 2 (33.33%) with micropapillary pattern, and 1 (16.66%) solid pattern. The median age of the six patients is 54 years (range 38-78).

<table>
<thead>
<tr>
<th>First Mutation</th>
<th>Second Mutation</th>
<th>Histological pattern</th>
<th>Age of patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case #1</td>
<td>L858R</td>
<td>L861Q</td>
<td>Acinar</td>
</tr>
<tr>
<td>Case #2</td>
<td>L858R</td>
<td>Exon 19 deletion</td>
<td>Micropapillary</td>
</tr>
<tr>
<td>Case #3</td>
<td>Exon 19 deletion</td>
<td>L861Q</td>
<td>Micropapillary</td>
</tr>
<tr>
<td>Case #4</td>
<td>Exon 19 deletion</td>
<td>T790M</td>
<td>Solid</td>
</tr>
<tr>
<td>Case #5</td>
<td>Exon 19 deletion</td>
<td>L861Q</td>
<td>Acinar</td>
</tr>
<tr>
<td>Case #6</td>
<td>Exon 19 deletion</td>
<td>L858R</td>
<td>Acinar</td>
</tr>
</tbody>
</table>

Conclusion: EGFR co-mutation had a significantly lower mean progression-free survival than those with a single mutation (5.7 months vs. 12.3 months). The response rate to TKI was significantly worse in those with co-mutation compared to those without co-mutation (38% vs 89%). There are few studies evaluating all the characteristics of cases with double mutations, such as histological pattern and the mutations of EGFR gene exons. Further research on double mutations is suggested because of the impact on treatment and prognosis of the patient.

P1.04

Topic: Prevention, Early Detection, Epidemiology and Tobacco Control

Prevalence, Pattern and Factors Associated with Dual Tobacco Use in a Rural Community in South Eastern Nigeria

U. Ofonakara

Method: A cross-sectional descriptive study was carried out among 400 residents of Ukpo community selected using a two-stage sampling method. Data was collected using a pre-tested interviewer-administered questionnaire adapted from the Global Adult Tobacco Survey. Odd ratios and 95% confidence intervals were computed and P values of < 0.05 were considered statistically significant.

Results: The results showed that respondents were mostly male 300(61.2%) and aged between 20 and 70 years with a mean of 42.2 ± 15.4 years. Almost a quarter of the respondents, 101 (20.6%) were ever- dual tobacco users. Also, 210(42.9%) use only smokeless tobacco while only 110 (22.4%) use only smoked tobacco. Dry snuff (73.8% of smokeless tobacco forms) cigarettes 82.2% (of smoked tobacco forms) were the most common forms of tobacco used. The primary reasons for tobacco use were: to relieve stress (61.2%); to increase levels of alertness (56.4%); for personal pleasure (55.9%) and social acceptance (52.1%). Age (p<0.0001), male gender (p<0.0001) and lower educational attainment (p<0.0001) were associated with dual tobacco use. About half of the respondents (51%) were aware that dual tobacco is more dangerous to human health than mono use and only about (27.1%) were aware that tobacco use is associated with lung cancer and COPD. Many of the respondents agreed that tobacco is a way of promoting friendship (65%) and should be used within their community (73%).

Conclusion: Efforts targeted at raising community awareness of the health effects of dual tobacco use are needed in rural communities where dual tobacco use is disproportionately high. Programs should be directed to males with lower educational attainment.

Keyword: Tobacco, Lung cancer

P1.05

Topic: Prevention, Early Detection, Epidemiology and Tobacco Control

Lung Cancer Patients – Major Causes of Hospitalization and Mortality

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Method: A retrospective analysis of patient’s clinical records admitted in the Pneumology ward of our hospital from May 2014 to May 2019 with LC diagnosis was performed. We characterized patients according to demographic characteristic, comorbidities, histology, clinical stage, causes of hospitalization and outcome.

Results: 246 patients (392 admissions) were analyzed. 72.4% were male. Mean age was 66.5 ± 10.2 years. 78.5% had active or past smoking habits. The most prevalent comorbidities were cardiovascular disease (48.8%) and chronic obstructive pulmonary disease (34.6%). Adenocarcinoma was the most frequent histology found (57.3%). 65.7% of patients had advanced stage disease at admission and 68.3% were under active therapeutics. The median length of hospitalization was 10 days (IQR 6-18). The major causes of hospitalization were respiratory infection (26.5%) and disease progression (18.4%). We found that empirical antibiotic therapy was used in 44.6% of admissions, only 11.2% of patients had positive bacteriological tests (most common bacteria identified were Klebsiella pneumoniae and Escherichia coli). 74 patients (30.1%) died. We found a strong statistically significant association between mortality and advance stage disease (p-value: 0.006) and disease progression as cause of hospitalization (p-value: 0.001). Hospitalization > 10 days was strongly associated with infectious intercurrence (p-value: 0.0001) and with mortality (p-value: 0.016).

Conclusion: Respiratory infection represents a major cause of admissions of LC patients in our ward. These patients have...
multiple causes for immunosuppression, therefore high suspicion and early intervention are needed to minimize the impact on patient's quality of life, length of hospitalization and associated mortality. Disease progression was the second cause, so in order to optimize end of life strategies and avoid potentially unnecessary admissions we reinforce the need of a palliative care with a multidisciplinary approach.

**Keyword:** Lung cancer, Hospitalization, Mortality, Palliative care

**P1.06**

**Topic:** Prevention, Early Detection, Epidemiology and Tobacco Control

**Determination of Exposure to Tobacco Smoke and the Percentage of Global DNA Methylation in Smokers and Patients with Lung Cancer**

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**Background:** Smoking is a disease caused by nicotine addiction and is the first cause of preventable death worldwide. In Mexico, according to the ENCODAT National Survey of Drug, Alcohol and Tobacco Consumption (2016-2017), the prevalence of consumption was 20.3% in the population aged 18 to 65 years. Smoking also is associated with cancer, the INCAN (National Institute of Cancerology) report that the 87% of cases of lung cancer and 82% of deaths due to lung disease are due to tobacco use.

**Method:** Therefore, the objective of this project was to quantify the degree of exposure to tobacco smoke (cotinine) and the percentage of global DNA methylation in non-smokers, smokers and patients with lung cancer, as possible factors associated with the development of lung cancer. We recruited 30 participants to evaluate these parameters in the groups of study, both methods were analyzed by ELISA.

**Results:** The results showed that cotinine values were in average averages of 1.24 ng / mL in non-smokers, 3.7 ng / mL in smokers and 0.4 ng/mL in lung cancer. Whereas the averages in the percentage of global DNA methylation were: 3.31%, 1.95% and 1.58%, respectively. Although there was no significant statistical difference between the groups, we observed similarity in the percentage of global DNA methylation with a value <1% in the 50% of patients with lung cancer and 22.2% of smokers.

**Conclusion:** The above suggests that these low of percent methylation values could be used as a possible predisposing factor for lung cancer.

**Keywords:** Cotinine, DNA methylation, Lung cancer

**P1.07**

**Topic:** Prevention, Early Detection, Epidemiology and Tobacco Control

**Habits in Tobacco Consumption of a Population of Queretaro**

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**Background:** According to ENCODAT in Mexico, 43,000 people die due to diseases attributed to smoking, an amount that represents 8.4% of the total deaths in the country. In addition, it represents a high economic cost for the Mexican health system. The tobacco epidemic has remained unchanged since 2009. The state of Queretaro has a population of 1.5 million people aged 12 to 65 years, of which 281 thousand are smokers of which 127 thousand smokes daily and 155 thousand smoke occasionally.

**Method:** Therefore, the objective of this project was describing the smoking habits of a group of active, passive and non-smoking smokers in the city of Queretaro. With the information of a form made to each participant, after the signing of their informed consent, the obtained data were analyzed to expose the results with the use of descriptive statistic.

**Results:** 165 people participated in the applied survey, with an age of 18 to 74 years. The prevalence of active smokers is higher in men than in women with 26.2% compared to 11.47% respectively, women have a higher prevalence in secondhand smoke and 34.32% of the population studied is free from the habit of smoking and second-hand smoke, the number of cigarettes per day on average was 5.3, the number of years on average of smoking was 13.1 years. 43.47% of active smokers do not perform any physical activity. In addition, no relationship was found between having a bad habit of smoking and poor diet. The main cancer observed in the family history was breast, then prostate and skin cancer.

**Conclusion:** It is important that in the city of Queretaro smoke-free places increase, that people have the education to ask if they are upset that they smoke in front of people who do not, and also that passive people can freely express that they do not like that habit, this would have the benefit of reducing secondhand smoke when it is not a decision of its own and increasing the percentage of the population not exposed. Lung cancer was not found among the main ones due to its frequency in the relatives of the study group, but it is known that of all the types it is the most deadly cancer and the main risk factor is the smoking that causes 85% of the cases.

**Keywords:** Querétaro, Prevalence, Tobacco consumption

**P1.08**

**Topic:** Prevention, Early Detection, Epidemiology and Tobacco Control

**A Retrospective Study of 230 Cases of Lung Disease - Talk about the Relationship Between Heavy Physical Labor and Lung Cancer**

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**Background:** In developing countries, there are still many patients with tuberculosis, chronic pneumonia, chronic bronchitis and silicosis and lung cancer. In China’s backward regions and rural areas, there are millions of patients who require long-term treatment and professional care for lung cancer. Most of the affected population are those who have been engaged in heavy physical labor for a long time. The age is between 38 and 55 years old, and it costs billions of dollars each year. How to find out the cause of the problem, how to solve this problem is urgently needed by us.

**Method:** This study conducted a retrospective study of 230 heavy-duty laborers hospitalized in the First Hospital of Lanzhou University from 2000 to 2018, including youth (18–30), middle-aged (31–50), and old (by age). >51) Three groups, divided into Non-small cell lung cancer, small cell lung cancer, special occupational lung cancer (painter and Asphalt road workers) by disease. Divided into three levels according to labor time and labor intensity: level 1 (labor time ≥8 hours, energy consumption ≥2000 calories / 24 hours), level 2 (labor time 8-12 hours, energy
consumption 2000-4000 calories / 24 hours), level 3 (Labor time > 12 hours, energy consumption > 4000 calories / 24 hours). To discuss the relationship between the patient’s illness time and labor time, the relationship between labor intensity and onset time, the relationship between sleep time and labor time distribution and disease, the relationship between disease type and hospitalization time and labor intensity and labor time were reviewed.

Results: The study found that age, labor time and labor intensity, as well as rest time are directly related to lung cancer. The older patients were equal to get the higher the incidence of lung cancer; the longer the physical labor time, the higher the incidence of lung cancer; the higher the physical labor intensity, the higher the incidence of lung cancer; the shorter the rest time, the higher the incidence of lung cancer; the longer the patient and the more labor intensive, the longer the hospital stay, and the slower the recovery and remission.

Conclusion: The correlation between heavy physical labor and lung disease may be related to the higher demand for cardiopulmonary function. A large amount of energy consumption will result in a decline in the function of the immune system, loss of nutrients, and decreased cell viability.

Insufficient sleep can also lead to immune system disorders and decreased organ function. The working environment, diet, and lifestyle habits of heavy physical labor can also affect the occurrence of lung diseases. How to pay attention to the health of heavy physical workers is the direction we need to work hard.

P1.08-A

Topic: Prevention, Early Detection, Epidemiology and Tobacco Control

Sherlock Lung Tracing Lung Cancer Mutational Processes in Never-smokers

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Background: Lung cancer in never-smokers represents 10-25% of lung cancers worldwide; ranks among the most common causes of cancer mortality; and has a distinct natural history, predominant histological subtype (adenocarcinoma), different profile of oncogenic mutations, and response to targeted therapy compared to lung cancer in smokers. There are few known environmental and genetic risk factors for lung cancer in never-smokers; however, a large fraction of cases cannot be explained. One promising approach to identify etiological factors involved in lung tumorigenesis in never-smokers is the study of “mutational signatures” that exogenous and endogenous processes leave on the tumor and surrounding tissue. This approach has identified 50+ mutational signatures in other cancer types, corresponding to several oncogenic processes.

Method: We are conducting an integrative genomic analysis of mutational signatures in tumors and surrounding non-tumor lung tissue from 2,000 never-smokers. Study subjects include a subset of “special exposure cases” exposed to high levels of known risk factors (n=500) and “general population cases” without known risk factors (n=1,500). Subjects are drawn from studies with lung tissue samples and high-quality epidemiological and clinical data. We are striving to include subjects from many geographical areas and ethnic groups to study the contribution of different germline and environmental factors. The tumor/normal genomics analysis are ongoing and include whole genome sequencing (WGS), RNA sequencing, and genome-wide methylation arrays. The integrated molecular landscape will be ordered along the evolutionary trajectory of the tumors to infer the cascade of events leading to tumor formation and progression. Data on the molecular and evolutionary landscape will be combined with data from histological examination of H&E slides from multiple tissue blocks per tumor and related to CT imaging to provide a more refined classification of lung cancers among never-smokers. Additional studies will include lineage phylogenetic analysis to infer the clonal evolution of lung tumors using multi-region tumor sampling; deep target sequencing of cancer driver genes and ultra-low pass WGS of cell-free circulating tumor DNA; tumor microenvironment analyses based on immunohistochemistry or fluorescence-based imaging and RNA sequencing; and analyses of large-scale electronic medical records.

Result: Preliminary results will be shown, highlighting the large differences in the molecular landscape of lung cancer in never-smokers from that of smokers.

Conclusion: This comprehensive study will improve our understanding of the etiology and progression of lung cancer in never-smokers and provide clues into prognosis and treatment.

Keywords: Lung cancer, Never-smokers, Mutational signatures, Whole genome sequencing

P1.09

Topic: SCLC, Mesothelioma, Thymoma

Heterogeneous versus Homogeneous Radiation Dose Calculations of Twice Daily Fractionation in Small Cell Lung Carcinoma

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Background: The standard radiotherapy treatment regimen for small-cell lung cancer was determined using homogeneous dose calculations, while modern trials use heterogeneity corrected treatment plans. We assessed differences in dose delivered using heterogeneous and homogeneous dose calculations in a cohort of patients treated for limited-stage small cell lung cancer (LS-SCLC).

Method: Retrospective analysis of 35 patients (3D-CRT, n=22; IMRT, n=13) with stage IIA-IIIB (American Joint Committee on Cancer 2010) treated with chemoradiotherapy from 2011-2017. Treatment plans were analyzed using superposition/convolution algorithms and dosimetric data was collected. Two plans were generated for each patient with one using the same unit density, and another plan with the same monitor units and applying a corrected/uncorrected plan sum. Variations in tumor dose >5% are considered clinically significant. A two-sided paired student t-tests was used to evaluate the dosimetric differences.

Results: Compared with homogeneous radiation dose calculations, heterogeneous plans resulted in a median dose difference in the PTV D95 of -3.0% (range -15.1% to 9.6%) with median dose differences of -0.1% (range -4.8% to 12.5%, p = 0.62) using 3D-CRT and -10.0% (range -15.9% to -5.3%, p < 0.01) using IMRT. The overall median dose differences found in the Lung V20 was -5.6% (range -17.3% to 5.4%); with median dose differences found of -4.2% (range -9.4 to 5.4, p < 0.01) using 3D-CRT and -8.9% (range -17.3 to -3.5, p < 0.01) using IMRT.

Conclusion: The incorporation of heterogeneity tissue correction results in an overall reduced dose delivered to the target...
Survival of Thymoma Is Extensive in Latin-American Patients: Results from over 10 Years of Experience (CLICaP-LATimus)


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Background: Thymomas are a group of rare neoplasm of the anterior mediastinum. Due to their low incidence, large cooperative studies are required to evaluate outcomes. The objective of this study is to present the results and experience in treatment of this pathology in Latin-America.

Method: A retrospective multicenter cohort study was conducted by The Latin-American Consortium for the Investigation of Lung Cancer (CLICaP). Patients with histologically proven thymomas between 1997 and 2018 were included in the analysis. Variables including clinical, pathological and therapeutic outcomes were registered in a centralized manner.

Results: A total of 105 patients were included. Median age at diagnosis was 54 years old (20-84), and with 60% (n = 63) of the included patients were female. Only 1% (n=7) of the patients had an ECOG performance score >1. Twenty-four patients (23%) had an ECOG performance score >1. Twenty-four patients (22.9%, 95% CI 14.5-31.9) presented with pulmonary or distant metastatic involvement with a median of 2 metastatic sites. Furthermore, 21.9% (95% CI 14.8-30.9) presented with pulmonary or distant metastatic involvement with a median of 2 metastatic sites. Twenty-four patients (22.9%, 95% CI 14.5-31.9) presented with pulmonary or distant metastatic involvement with a median of 2 metastatic sites.

Conclusion: Survival in patients with thymomas continues to be very favorable, especially in patients who receive adequate local control. The benefit of adjuvant treatment in this setting remains unclear.

Keywords: Local control, Adjuvant therapy, Survival
Predominant patterns of E-MPM were: 36.5% tubular/acinar, 33% solid, 12% trabecular, 11% papillary, 3% pleomorphic, 2% micropapillary, 2% adenoid cystic and one case was decidual. We highlight that 59% of the E-MPM presented a second pattern: papillary (16%), solid (15%), tubular (11%), trabecular (7.5%) and micropapillary (5%). Immunohistochemistry: There were no differences in Caletrinin expression between E-MPM and no E-MPM. The E-MPM had cytokeratin 5 expression in 91% of the cases and WT-1 in 90%; no E-MPM in 68% and 70% (p<0.001). Transitional morphological features were found in 12 surgical samples: 4 cases extensive and 8 cases focally (4 biphasic, 3 sarcomatoid and 1 epithelioid solid predominant). 3/4 extensive cases were ≥ 66 years old, 4/4 had necrosis and nuclear score II and III.

Conclusion: The findings show the intra-tumoral heterogeneity of MPM and that the variability of composite grading can be analyzed in routine cases. Standardizing immunohistochemical panels for MPM diagnosis is mandatory. Detailed histopathological diagnosis can help to select the appropriate treatment for each patient.

Keywords: Mesothelioma, Pathology

P1.2

Topic: SCLC, Mesothelioma, Thymoma

Real World Characterization and Treatment Patterns of Patients with Thymic Carcinoma: Lessons from a Latin American Collaborative Study (CLiCaP-LATImus)


Method:

Patients with Thymic Carcinoma were included. Background: Thymic carcinoma is a rare tumor that represents approximately 14% of all lung cancers, excluded from this epidemiological behavior; neuroendocrine tumors represent approximately 14% of all lung cancers, only one third of patients are diagnosed in a thorax confined disease; 24 patients (66%, [95%CI 62-92%]) as stage IVa and 7 (25%, [95%CI 12-51%]) as stage IVb (33%, [95%CI 7-37%]) with a median LDH level of 396.5 U/L (153-1529 U/L) and a median of 2 metastatic sites. 15 (41.9%, [95%CI 25-59%]) patients received preoperative chemotherapy consisting of chemotherapy (n=8, 42%) and chemoradiotherapy (n=5, 25%) and no E-MPM. The E-MPM had cytokeratin 5 expression in 91% of the cases and WT-1 in 90%; no E-MPM in 68% and 70% (p<0.001). Transitional morphological features were found in 12 surgical samples: 4 cases extensive and 8 cases focally (4 biphasic, 3 sarcomatoid and 1 epithelioid solid predominant). 3/4 extensive cases were ≥ 66 years old, 4/4 had necrosis and nuclear score II and III.

Conclusion: The findings show the intra-tumoral heterogeneity of MPM and that the variability of composite grading can be analyzed in routine cases. Standardizing immunohistochemical panels for MPM diagnosis is mandatory. Detailed histopathological diagnosis can help to select the appropriate treatment for each patient.

Keywords: Mesothelioma, Pathology

P1.12

Topic: SCLC, Mesothelioma, Thymoma

Advanced Small Cells Lung Cancer: 5 Year Experience at the National Oncology Institute of Panama, 2014-2018

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Background: Small Cell Lung Cancer (SCLC) is a very aggressive disease and it represents approximately 10%-15% of patients with Lung Cancer. Until recently with the promising activity of immunotherapy, there was no advance in treatment since the discovery of the role of platin-based/etoposide doublet chemotherapy in the 1980s but with frequent and rapid development of acquired resistance. In Panama, it is not a very common disease, but when it is found, the outlook for these patients with SCLC remains dismal as reported worldwide.

Method: We retrospectively reviewed the electronic medical records of patients diagnosed with SCLC between January 2014 and December 2018. The objectives were to describe the incidence, clinical characteristics, treatment and to determine the overall survival of our patients.

Results: There 36 patients diagnosed with SCLC during this period for an incidence of 8.0%. The mean age of diagnosis is 68 years (41 - 85) and 72,2% were males. EOCOG 0-1 was found in 50% of the patients. 87,9% of the patients were smokers with 66,7% being heavy smokers. The majority of cases were diagnosed with advanced disease with 83,3% in extensive stage disease. Brain metastasis was present in 35% of the cases and all received WBRT. 61,7% could receive first line chemotherapy: 51,7% with CDDP/Etoposide and 42,9% with Carboplatin/Etoposide, and 8,8% could receive second line chemotherapy with Irinotecan. The median overall survival was 6,7 months (95% CI 4.1 - 9.2).

Conclusion: Our findings shows a lower incidence but with similar clinical characteristics, treatment and overall survival as reported worldwide. This supports the aggressive nature of the disease and the need of new treatment strategies.

P1.14

Topic: SCLC, Mesothelioma, Thymoma

Morbidity, Mortality and Oncologic Outcomes in Bronchoplastic Procedures Performed in a Mexican Public Reference Hospital

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Background: Pulmonary cancer still represents the first cause of non-skin cancer related death worldwide, not being Mexico excluded from this epidemiological behavior; neuroendocrine tumors represent approximately 14% of all lung cancers, only one third of patients are diagnosed in a thorax confined
Stage: as a part of the multidisciplinary management of such pathology, surgery is, in early resectable disease (T1-T2, NO, MO), an adequate and standardized treatment option. Despite the benefit of oncological resection in these patients, a limiting factor result of the healthy lung tissue forfeited in classic oncological resections (lobectomy and pneumonectomy), thus, bronchoplastic procedures play an important role in selected patients by either sparing normal lung tissue and allowing resections in patients who otherwise would not tolerate a major resection without jeopardize oncologic results.

Method: We present a case series of 25 patients who underwent bronchoplastic procedures for neuroendocrine malignancy in a retrospective fashion over a 10-year period. We analyze the morbidity and mortality directly associated to the procedure as well as the oncologic results by disease free survival and overall survival.

Results: Morbidity presented in 20% of the patients: 30-day mortality in 0%; bronchopleural fistula in 16%, pneumonia in 12%, empyema in 8%, cardiac arrhythmias in 1%; 3-year survival was 47% and disease-free survival had a median of 23 months.

Conclusion: The oncological benefit of a bronchoplastic procedure is proved in selected patients with bronchial neuroendocrine tumors that fit anatomical requirements, the results may be equal to that of the mayor oncological resections and our surgical oncology department morbidity, mortality and oncologic outcomes match those mentioned in literature.

P1.16

Topic: SCLC, Mesothelioma, Thymoma

Awake Thoracoscopic Lung Cancer Biopsy

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Background: An adequate tissue biopsy in lung cancer permits the pathology to perform increasingly complex and quantitative biomarkers in the samples, that will allow the oncologist to see responses therapy over time according to the mutations that is the standard of care to lung cancer patients. The minimally invasive approach allows the patients to incorporate to his work with a lower hospital stay less pain and less damage to other tissues; and the awake protocol minimize the accompanying risk of traqueal intubation, the potential effects of general anesthetics, the risk of needed a longer intubation.

Method: All patients from high risk thoracic surgery consult with a limit spirometry, hipoxemia and hypercapnia, oxygen dependent secondary to chronic respiratory disease not related to recent neoplastic. It includes 34 (100%) plural biopsies of which 8 (23.5%) female, 26 (76.5%) male; lung biopsies were 6 (100%) of which 5 (83.3%) female male 1 (16.7%). Surgical approach include dexmedetomidine bolus 20 minutes prior to surgery, and continuous infusion oxygen delivery throw facial mask, transoperative psycotherapy and full cardiopulmonary monitoring, accompanying of hypnotic and ansiotics in short bolus, intercostal block in 3 spaces and spina erector patient partial lateral position, the unique porth was decided according to the target localization and the topographic relation at the CT. Looking for diminished damage to the oncologic tissues and preserved health surround structures and lung function. All patients tolerate the procedure, all with pleural dreinage, sufficient tissue to pathology and microbiology laboratory was achieved.

Results: All patients had a satisfactory histopathologic result including a relationship woman man for pleural pathologic disease 3:1, for lung disease 0.2. The pathologic diagnosis in pleural biopsies, 34 (100%), pleural fibrosis 6 (19.4%), paquipleuritis 17 (50%), mesothelial hyperplasia 2 (5.9%), mucinous adenocarcinoma 2 (5.9%), differentiated adenocarcinoma (20.6%) the pathologic diagnosis in lung biopsies 6 (100%), organized pneumonia 1 (16.7%), epidermoid cancer 2 (33.3%), lung abscess 1 (16.7%), adenocarcinoma 2 (33.3%) papilar 1 and mucinous 1. All of them had a short hospital stay average 2 days, no one needed mechanical ventilation, no transfusion, the average operating room time was 47 minutes, the average heart rate 84 beats per minute, oxygen saturation 87% and CO2 31.

Conclusion: The single porth approach with a localized target and the awake thoracic surgical procedure need a major surgical skills and expertise in thoracic anatomy, this approach is feasible and reproducible using specialized instruments, permit optimized surgical time room, avoid almost all the risk and adverse reaction of anesthesia in cancer patients, let the patient to start respiratory rehabilitation early, less damage, decrease the risk of needed an ICU entry, decrease damage to health tissue, permit a faster recovery, a faster inclusion in oncologic treatment and helps the patient to recover confidence to next steps in the oncologic process. A strict protocol in previously sick respiratory patients and a complete monitoring during surgery with psychologic support during the surgery and ansiolitic bolus permit a safe surgery with complete assessment.

Keyword: Awake surgery, Single porth, Thoracoscopic surgery, Lung cancer

P1.16-A

Surgical Therapy for Malignant Pleural Mesothelioma in Mexican Population

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Background: Malignant pleural mesothelioma (MPM) remains an aggressive thoracic malignancy associated with poor prognosis. There is no standard treatment regimen, and particularly, the impact of radical surgery remains controversial. The main goal of our retrospective single-centre study was to evaluate the surgical treatment at our division regarding their effect on the patient’s survival.

Method: We retrospectively reviewed data from 23 consecutive patients with histologically proven MPM, treated from 2012 to 2015 in National Institute of Respiratory Disease, Mexico City. The program was used: SPSS 20 SPSS Inc, Chicago, IL. Statistical tests were considered significant for P values <0.05

Results: There were 9 women (39%) and 14 men (61%) with a mean age of 57.6 years. Epitheloid subtype was found in 23 patients (100%). Extended pleurectomy/decortication was performed in 9 (39%) and extralveal pneumonectomy in 10 (43.4), in 4 (17.3) cases the procedure could not be completed. Clinical staging was: IIB in 6(26.1%) and III in 12 (52.2%).

Frequency of complications was 12 (52.2%). 30-day mortality rate was 4.34%. Mean survival time for the collective was 25.4 months. Median survival of patients undergoing surgical resection with complete trimodal therapy was significantly longer than that of patients undergoing surgery only (36.1 versus 18.5 months; p < 0.05).
**Topic: Biology and Pathogenesis**

**How to Visualize Exosomes in NSCLC: “The New Guest Star in the Liquid Biopsy Movie”**

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**Background:** Exosomes are nano-vesicles secreted to the body fluids that act as cell-to-cell communicators, transferring genetic information. Studies on exosomes as liquid biopsy biomarkers in several tumours, including lung cancer, have become a hot topic in recent years. The discoveries regarding their composition and functionality have made them a major field of interest in cancer research. EVs, through the integrins expressed in the parental cells, are able to be internalized in a tissue-specific manner, being partially responsible of the progression of the tumour and the pre-metastatic niche formation among others. However, this specificity might lead also to new opportunities in the treatment of the tumour by using extracellular vesicles as devices for drug delivery. In order to further explore this topic, protocols and methods for exosome tracking are required. Our aim was to develop a reliable and standardized protocol for exosome isolation and visualization during internalization in non-small cell lung cancer (NSCLC) living cells.

**Method:** NSCLC cell cultured exosomes were isolated by three different methods, first consisting in single ultracentrifugation, second consisting in double ultracentrifugation, including exosome washing and the third using ExoEasy Maxi Kit based on membrane affinity spin columns. Exosomes were characterized with nanoparticle tracking analysis and scanning electron microscopy (SEM). Then, exosomes were stained with PKH67 and PKH26 dyes and observed in vivo by confocal microscopy.

**Results:** We observed that our double ultracentrifugation method resulted in the clear identification of exosomes in comparison with the single ultracentrifugation, that contained crystal precipitates that hinder exosome visualization. In contrast, exosomes isolated by ExoEasy could be clearly observed despite containing salt impurities. According to exosome staining, PKH67, compared to PKH26, provided a better visualization of lung cancer exosomes under confocal microscopy. In the in vivo experiment, we could observe how cells capture free exosomes by cytoskeleton filopodia elongation.

**Conclusion:** We showed, for the first time, the in vivo internalization of exosomes in NSCLC with our developed tracking protocol without ultracentrifugation, that can be very helpful for further studies to elucidate the mechanism of exosomes internalization by target cells in drug delivery studies.

**Keywords:** Exosomes, Liquid biopsy, NSCLC, Visualization

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**Update of the Analysis of the Status of Lymphocyte Infiltration in Patients with NSCLC**

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**Background:** Current evidence highlights the potential role of tumor-infiltrating lymphocytes (TILs) as a prognostic factor in many types of tumors. The TILs (CD4 and CD8) are being studied with different methods such as immunohistochemistry and optical microscopy. The main objective of our work is to identify TILs in patients with NSCLC, classified as present or absent, and its relation to progression free survival (PFS).

**Method:** Retrospective and analytical study of Instituto Oncologico de Córdoba, from 2004 to 2019. 187 patients with stage IIIIB and IV NSCLC were analyzed. TILs are descriptively classified as present or absent. Survival curve was calculated using the Kaplan-Meier method.

**Results:** 63% of patients had adenocarcinoma and 37% squamous cell carcinoma. 72% were men. 82% were smokers. 65% of patients with squamous histology and % 58 with adenocarcinoma, showed TILS. Patients with adenocarcinoma with TILS present had higher PFS 13.3 months, compared to patients with absent, 8.8 months. These differences were statistically significant (PFS: p=0.004). The patients with squamous cell carcinoma with TILS had 10.8 months PFS. Those who had infiltrated absent had a PFS of 5.6 months. These differences were also statistically significant (PFS: p = 0.001).

**Conclusion:** Our study shows that patients whose pathological samples presented inflammatory infiltrate had higher PFS. The presence of TILS could be used as an important prognostic factor in this patient population.
Molecular Characterization of Lung Cancer in Young Patients: A Single-center Study from Argentina

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Background: Lung cancer is infrequent in patients younger than 50 years. Several molecular alterations with clinical value have been described among these patients. Next-generation sequencing (NGS) is a robust diagnostic tool to assess this kind of genomic alterations, evaluating multiple mutations and fusions in the same assay, and reducing turnaround time compared to sequential single-gene testing. There is little data available about NGS molecular testing in lung cancer young patients in Latin America.

Method: A retrospective cohort study was conducted. Cases of patients younger than 50 years, with diagnosis of lung carcinoma in Hospital Italiano of Buenos Aires between 2014 and 2019 were included. Clinical data was collected from electronic clinical records.

DNA and RNA were extracted from formalin-fixed paraffin-embedded tissue. Mutations and fusions were assessed using Oncomine Focus Assay (Thermo Fisher) DNA and RNA panel in Ion PGM (Ion Torrent) sequencer.

Confidence Interval was calculated according to Wilson score interval method.

Results: A total of 13 patients were analyzed. 7 patients were female, 11 were non-smoker, and 8 were diagnosed at stage IV. Median age was 44 (range 26-49). According to WHO 2015 histological and immunohistochemical criteria, 12 cases were adenocarcinomas, whereas only 1 case was diagnosed as large-cell carcinoma. Regarding gene mutations or fusions, 2 cases were negative for those detected by the NGS panel. 7 cases showed 1, 3 cases showed 2, and 1 case showed 4 genomic alterations. The most prevalent mutated gene was EGFR (3 cases), followed by: PIK3CA and KRAS (2 cases each), JAK3, MTOR, AKT1, MET, ERBB2 (1 case each). Among fusions, 4 cases showed ALK and 1 case showed ROS1 fusions. 8 patients (61.54%; CI 95%: 35.52-82.29%) had targetable genomic alterations (according to drugs approved in Argentina), 4 of them (30.7%; IC 95% 12.68-57.63%) corresponded to ALK fusions.

Conclusion: In this patient cohort, we found that Oncomine Focus Assay NGS panel is a powerful tool, useful to detect clinically relevant genomic alterations, such as DNA mutations and gene fusions, taking less time than consecutive single-gene testing. Even though ours is not a large cohort study, the prevalence of targetable mutations is higher than the one present in cohorts including older lung cancer patients. Interestingly, the prevalence of ALK fusions is notably high. We conclude that performing NGS testing for clinically relevant genomic alterations in this age group of ALK fusions is notably high. We conclude that performing NGS including older lung cancer patients. Interestingly, the prevalence of targetable genomic alterations, such as DNA mutations and gene fusions, taking less time than consecutive single-gene testing.

Keywords: Mutations, Fusions, Young, NSCLC

S-allyl Cysteine Induces Cytotoxic Effects on Human NSCLC Cell Lines

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Background: Garlic and its sulfured compounds have been shown to modify the tumor microenvironment. Specifically, S-allyl cysteine (SAC), a hydrosoluble garlic-derived compound, suppresses tumor proliferation while induces apoptosis in a wide number of cancer types. However, its antiproliferative and potential mechanisms of action have been poorly explored in lung cancer.

Method: In this study we investigated the possible cytotoxic role elicited by the garlic-derived compound and well-known antioxidant molecule S-allyl cysteine, on different endpoints of toxicity in three different human cancer cell lines, A-549, HCC827, H1975, in order to provide enlightening and supporting information about the antitumor properties on this molecule. For this purpose, cell lines were cultured for 24, 48 and 72 hours in the presence of increasing concentrations of SAC.

Results: The incubation with SAC resulted in a dose- and time-dependent decrease in cell viability and augmented morphological changes in all cell lines. In addition, SAC increased the frequency of apoptotic/necrotic events and enhanced the oxidative damage to lipids.

Conclusion: These results demonstrate the cytotoxic properties inherent to SAC to reduce malignant growing and proliferation of lung tumor cells.

Keywords: Lung cancer cell lines, Cytotoxicity, Garlic-derived compound, S-allyl cysteine

Cryotherapy in the Treatment of Endobronchial Carcinoid, Is It a Valid Alternative Treatment to Surgery?

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Background: Each year in the UK around 2,900 patients are diagnosed with carcinoid, a rare, slow-growing tumour that originates in neuroendocrine cells, most commonly present in the gastrointestinal (60%) and respiratory (25–33%) tracts. Histopathologic diagnosis and classification require tissue biopsy whilst management depends on tumour’s anatomic site and size, extent, secretory profile, and general status of patient. Surgical resection remains the primary approach for most localized carcinoids; cryoextraction/cryoablation may be considered when surgery is not feasible or in preparation for surgery. We present a single centre experience in use of cryotherapy for management of carcinoid tumours.

Method: For this retrospective analysis, data were collected from prospectively populated patient databases, operative logbooks, and patients’ medical records. Between 2011-2019, a total of 26 patients diagnosed with carcinoid underwent a series of cryotherapy procedures, either alone or in combination with surgery, in our institution. Before deciding on their management strategy, patients had been appropriately discussed in our lung
POSTER SESSION 1

Service, Fundacion Valle del Lili, Cali/Colombia, 3Clinical Department Of Internal Medicine, Pulmonology Service, Department Of Pathology And Laboratory Medicine, Fundacion L. Fernandez-Trujillo1, E.I. Morales2, A. Castro3, L. Sua4

EBUS-TBNA: In a University Hospital in Latin America

P1.22

Carcinoid, Neuroendocrine tumours, Endobronchial tumours, Cryotherapy

Keywords:

Topic: Bronchoscopy

Endobronchial Ultrasound and Transbronchial Needle Aspiration EBUS-TBNA: In a University Hospital in Latin America

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Background: Endobronchial Ultrasound and Transbronchial Needle aspiration (EBUS-TBNA) nowadays it has a primordial role in the workup of malignant and nonmalignant pulmonary disease. It’s the most important advancement in pulmonary medicine in the last 20 years. EBUS-TBNA is a minimally invasive technique, well tolerated, cost efficient, for real time visualization of the airways with ultrasound and for sampling the mediastinum and hilum. Its indications: diagnosis, staging, restaging of lung cancer, evaluation of metastatic lesions and non-malignant diseases. It requires multidisciplinary evaluation with image analysis, general condition of the patient, risks and benefits, also close work with pathology, performing a Rapid On-Site Evaluation (ROSE) to improve the diagnostic performance. We describe the EBUS-TBNA in Fundacion Valle del Lili a University Hospital of Reference in Latin America.

Method: Prospective, descriptive study, period June/2015-June/2018. The indications were staging and restaging of lung tumors, diagnosis of lung or mediastinal masses, abnormal ganglia in CT or PET/CT equal or greater than 1cm. 108 patients were evaluated under general IV anesthesia, with a standardized protocol in the endoscopy room. The equipment used was Olympus® bronchoscope + US probe + 22G FNA.

Results: Average age of 63.5 +/- 12.9, women 53(49%), men 55(50,9%).

The quality of the sample was adequate in 105 (97.22%), positive in 103(100%).

Conclusion: EBUS-TBNA is the recommended technique for lung cancer mediastinal staging. Our results adjust to international results; it is safe, minimally invasive, in many cases an outpatient procedure and a good performance when accompanied with ROSE.

Keywords: Endobronchial ultrasound and transbronchial needle aspiration (EBUS-TBNA) , Rapid on-site evaluation (ROSE)

PI.23

Topic: Bronchoscopy

EBUS and Needle Aspiration in Diagnosis and Molecular Classification of Breast Cancer Progression Metastatic to Mediastinum

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Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) plays an important role in the evaluation of extrathoracic malignancy that compromises the mediastinum, modifies the prognosis and the sequence of treatments according to the results. In breast cancer there is metastasis to mediastinal lymph nodes during the progression of the disease, 30% of patients with limited disease receiving treatment recur with bone, lung, liver and lymphatic metastases. Breast cancer experiences alterations in the expression of estrogen hormone receptors (ER), progesterone receptors (PR) and in the amplification of human epidermal growth factor receptor 2 (HER2) during progression, by different adjuvant therapies, significantly affecting survival. Therefore, molecular re-characterization of tissue in relapses is vital for better therapeutic decisions and impact on survival. EBUS-TBNA is the procedure of choice in staging, re-staging and diagnosis of lung cancer; we present its usefulness in the diagnosis and molecular classification of breast cancer progression.

Method: Between January 2015 and June 2019, EBUS-TBNA was performed with rapid on-site evaluation (ROSE) in 12 patients with breast cancer and suspected progression. Procedures were ambulatory, under general anesthesia through laryngeal mask. 21G needle puncture was performed, cytology was elaborated in liquid base, material was obtained for cellblock, immunohistochemistry, digital analysis and fluorescent in situ hybridization (FISH) were performed.

Results: Average age 56.75 (SD: 10.6). Mediastinal stations studied: 7 subcarinal (8), E11L (2), E11R (2), malignancy was confirmed in the first pass in all cases with ROSE with Diff-Quik staining, material was collected for the rest of the studies. We performed: Papanicolaou (PAP), cellblock with Hematoxylin & Eosin (H & E), immunohistochemistry with GATA-3 (LSO-823), TTF-1 (SP-141), CK (A53-B / A2.26) to confirm mammary origin and ER (SP-1), PR (IE2), HER2 (4B5), Ki-67 (30-9) biomarkers with software approved by FDA (Virtuoso), which characterizes the molecular subtype of breast cancer. One case required FISH to evaluate HER2 oncogene. No patient required additional procedures such as mediastinoscopy to confirm the progression of their disease.

Conclusion: EBUS-TBNA is a minimally invasive, ambulatory, efficient and very useful procedure in the study of mediastinal, paratracheal or peribronchial lesions with suspicion of breast...
cancer progression. To be successful, must be well planned, with standardized and sequential analysis of the mediastinum. The feedback in the room with ROSE helps to optimize time, number of passes and stations studied avoiding second procedures.

**Keywords:** Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), Breast cancer, Rapid on-site evaluation (ROSE)

**P1.24**

**Topic: Bronchoscopy**

**Endobronchial Ultrasound plus Fine Needle Aspiration (EBUS-TBNA) in Lesions Simulating Pulmonary Neoplasm: Pulmonary Myospherulosis**

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**Background:** Myospherulosis, described in 1969 in African patients who, after receiving muscular injections of penicillin, developed inflammation at site with formation of cysts with intense infiltration of lymphocytes, histiocytes, plasma cells, giant cells, as foreign body reaction. Exogenous lipids react with patient’s erythrocytes; these are injured and perceived as foreign body by defense mechanisms, triggering severe inflammatory response. Degenerated erythrocytes are surrounded by a thin membrane, called “bag of marbles”, often confused with fungal infections or neoplastic lesions. This type of injury has not been described in lung. We present a case of pulmonary myospherulosis appearing after several thoracic surgical interventions and diagnosed with EBUS-TBNA.

**Method:** Case report. Review of the clinical history.

**Results:** Male, 63 years old, with dyslipidemia, consulted for 15 days of oppressive, severe thoracic pain with physical activity, irradiated to neck and upper limbs, which relieved at rest. Stress testing (+) with pain of maximum intensity. Referred to the emergency department, severe coronary disease was documented, arterial trunk and three vessels, percutaneous right coronary angioplasty was performed with good evolution and myocardial revascularization was planned. Pre-surgical evaluation revealed lung mass in lower left lobe (LLL), myocardial revascularization was first performed, the same day resection of LLL and lymph node dissection, histopathological diagnosis: pulmonary adenocarcinoma T2AN2M0 / EIIA. Received adjuvant chemotherapy / radiotherapy with good response. PET-SCAN / follow-up: Metabolically active posterior / basal left lesion, postsurgical/postradiotherapy expected changes. Lesion and lymph nodes studied with EBUS-TBNA, negative histopathological result for malignancy and expression profile compatible with myospherulosis.

**Conclusion:** Spherulosis is a rare entity, described around soft tissue, muscle, gynecological or otorhinolaryngological tumors, but not described in lung. In addition, the use of EBUS-TBNA is not described in the diagnostic approach, situation for which we describe this case.

**Keyword:** Endobronchial ultrasound plus fine needle aspiration (EBUS-TBNA)

**P1.25**

**Topic: Bronchoscopy**

**Rare Intimal Aortic Angiosarcoma Diagnosed via Endobronchial Ultrasound guided Transbronchial Fine Needle Aspiration (EBUS-TBNA): A Case Report**

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**Background:** Intimal sarcomas are very uncommon malignant tumors that develop in the main blood vessel, particularly in the pulmonary arteries and the aorta. In general, they denote a poor prognosis for the patient. The diagnosis is always challenging because of the anatomical difficulties to obtain a sample and because of the multiple possible differential diagnostics that can confuse and delay its identification. We present the case of a patient with an intimal angiosarcoma of the thoracic aorta diagnosed by an endobronchial ultrasound guided needle aspiration (EBUS-TBNA), a method that has not been reported in scientific literature before.

**Method:** Review of clinical history

**Results:** A 73-year-old man, with a previous history of smoking and chronic obstructive pulmonary disease, presented with abdominal discomfort, weight loss and dysphagia.
He had a normal abdominal ultrasound, colonoscopy and upper gastrointestinal endoscopy. An abdominal CT-scan was performed, reporting a mass intimately related to the esophagus with irregular extrinsic compression of this structure, heterogeneous enhancement and aortic infiltration. Chest CT showed a mass in the posterior mediastinum, with homogeneous density, expanding from T5 to T8, 78x53x76 mm in size, con extrinsic compression of the left main bronchus, anterior displacement of the esophagus without cleavage plane, surrounding and infiltrating the aorta, with an intra-luminal thrombus occupying 50% of the aortic lumen. PET-CT revealed a hypermetabolic aortic and mediastinal metastasis with metastasis to the suprarenal glands. An EBUS-TBNA was performed, real time samples were collected and submitted to ROSE (Rapid on Site Examination). Five samples were sent for liquid-based cytology and cell-block examination. The definitive diagnosis of the cell block reported a malignant neoplasm composed of pleomorphic large cells, abundant eosinophilic cytoplasm, anisokaryosis, dense chromatin, evident nucleolus and atypical mitosis (22 mitoses per high-power-field). The neoplasm was organized in a cohesive manner, with interposed mononuclear inflammatory cells and vast areas of tumor necrosis. Immunohistochemical analysis evidenced positive BCL-2, SMA and calponin. With Diff-Quick stain malignancy was confirmed in real time. It was classified as a high-grade mesenchymal sarcoma of the intima. Due to the extension of the lesion surgical management was not indicated. Chemotherapy with doxorubicin, ifosfamide and mesna was initiated with poor response and a bad tolerance to the treatment.

Conclusion: This is the first reported case of an intimal aortic sarcoma diagnosed with an EBUS-TBNA. It was the only suitable option to approach and obtain samples of the lesion, in this case with excellent diagnostic performance.

Keywords: Endobronchial ultrasound guided transbronchial fine needle aspiration, Angiosarcoma, Rapid on-site examination (ROSE)

P1.26

Topic: Nursing & Allied Health

Pharmaceutical Follow-up Program for Patients with Oral Drug Treatment in Non-small Cell Lung Cancer in a Heterogeneous Health Care System

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Background: Lung cancer has faced important changes in its history. With the improvement of main genetic mutations, the target-therapy have revolutionized that kind of tumour, made possible oral drugs administration procedures at anti-lung cancer treatment. In 2014, the National agency of health assistance in Brazil approved the compulsory coverage of oral drug. However, the delivered of these drugs are heterogeneus: at patient’s residence or by the patient’s health establishment. The purpose of this paper is to describe the follow-up lung cancer patient service model while making use of oral drugs in the household environment in a fragmented and heterogeneous health system.

Method: This article presents a multidisciplinary team’s expertise acting in an oral chemotherapy program, managed by pharmacists between April of 2016 and May of 2019. All patients had driver mutations at non-small lung cancer cells, were being treated at a private medical clinic and received oral drug through the health assistance.

Results: We developed a service program named the Oral Drug Project (Figure 1) in order to contribute to the better management of interdisciplinary team while handling the above mentioned patients. A total number of 79 persons where identified. 16% received the oral drug through the pharmacist at a health care facility (Group A) and 84% at home (Group B). Drug-food interactions: (Group A) 46% (Group B) 52%. Drug-drug interaction: (Group A) 67% (Group B) 61%. Suspend treatment due to non-manageable toxicity: (Group A) 1% (Group B) 1%; Presented 1st or 2nd degree of toxicity and prematurely managed: (Group A) 51% (Group B) 58%. No hospitalizations due to drug poisoning were registered. All toxicities were identified and there were no patient abandonment during treatment.

Keywords: Oral drug, Target therapy, Clinical pharmacist

P1.27

Topic: Nursing & Allied Health

Longitudinal Changes on Patient Reported Outcomes and Distress among Cancer Survivors Living in Regional and Rural Australia

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Background: This study investigates longitudinal patterns of physical functioning and psychological morbidity in cancer survivors residing in regional and rural communities in New South Wales, Australia.

Method: 119 patients who completed primary treatment for breast, colorectal, lung or prostate cancers self-completed the Distress Thermometer and the PROMIS-29 questionnaires at the end of treatment (T0), at three (T1) and six months (T2). Outcomes were modelled using generalized estimating equations. Associations between risk factors and physical functioning or psychological morbidity at T2 were assessed using multivariable logistic regression.

Results: Distress varied over time (p<0.001). Physical function (92%), sleep disturbance (70%), pain interference (60%) and satisfaction with role (54%) were the most commonly reported issues at T2. Approximately two fifths of survivors reported higher symptom severity for anxiety (41%), fatigue (44%) and depression (45%). At T2, depression was found to be associated with disadvantaged socio-economic index and living in regional/remote areas. Anxiety was associated with cancer type (colorectal) and advanced stage of cancer. Fatigue was associated with gender (male) and cancer type (colorectal and breast). While sleep disturbance was associated with treatment type (surgery).
**Clinical:** Persistent physical problems, in particular pain and sleep disturbance were important on-going issues to survivors. Continued monitoring of cancer survivors after cancer treatment is viewed as an essential aspect of strategic care planning. Health professionals may initiate earlier referrals and incorporate increased symptom management into clinical care to improve the wellbeing of survivors.

**Keyword:** Cancer, Survivorship, Breast, Colorectal, Lung, Morbidity

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**Poster Session 2**

Saturday, October 19, 2019

**P2.01**

**Topic: Early Stage NSCLC (Stage I - III)**

**Prognosis of Patients with Stage I Non-Small Cell Lung Cancer**

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**Background:** the prognosis of non-small cell lung cancer (NSCLC) largely depends on tumor stage, however despite early-stage presentation and is described as a constant relapsing risk after definitive R0 resection, when only about 60% of cases can be cured with surgery alone. Prognostic factors are still needed to stratify patients by relapsing risk to design more effective strategies including adjuvant chemotherapy. Our aim was to evaluate potential prognostic factors for patients with clinical stage I in a private cancer center. (Oncosalud – AUNA).

**Method:** We analyzed data of 28 cases with stage I NSCLC, treated at Oncosalud - AUNA from 2008 to 2014 (Lima – Peru). The clinical-pathological data were collected from digital medical records. Disease-free survival (DFS) and overall survival (OS) was determinate using Kaplan-Meier method and survival curves comparison were performed using log-rank or Breslow test. Cox model was used for multivariate analysis.

**Results:** The median age was 67 years (range 34–79), 75% were older than 60 and 57% of patients were women. Of all patients, 54% had an ECOG 0 scale and more than 70% were asymptomatic and were diagnosed incidentally. Extension of disease was T2 in 40% and the rest was T1. The most common histological type was adenocarcinoma (75%) and mainly moderately and well differentiated (78%). CYFRA 211 and CEA were elevated in 17% and 10% of cases, respectively. All patients had surgery with free surgical margins, negative lymph nodes, lymphovascular and perineural infiltration in 28 and 8%, respectively, and 25% had locally involved visceral pleura and 40% received adjuvant treatment with platinum-based chemotherapy. During the study period, 36% relapsed and 18% died, all relapses received platin-based chemotherapy. The median follow-up was 5 years (95%CI: 4.3–5.5), median survival was not reached, and 3-years and 5-years OS rates were 93 and 58%, respectively. The DFS rate at 3 and 5 years were 40% and 30%, respectively. From all clinical and pathological characteristics evaluated only the number of nodal resection (<6 or ≥6 nodes) was significantly associated with poor DFS with HR 7.5 (p=0.027). Other characteristics, as T stage, visceral pleura, vascular and perineural infiltration shown a slight trend to poor DFS but not statistically significant.

**Conclusion:** In our study, the main factor related to poor DFS was the resection of fewer than 6 nodes. Larger prospective studies are needed to evaluate the role of the number of nodes resected in stage I NSCLC as well as other pathological features.
Topic: Advanced NSCLC

Normalization of Carcinobembryonic Antigen Levels Are Associated with a Survival Improvement in Advanced Non-small Cell Lung Cancer Patients

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Background: Serum carcinoemobryonic antigen (CEA) levels are elevated in approximately 65% of the Non-small cell lung cancer (NSCLC) patients with adenocarcinoma histology. Although the relation between CEA serum levels and overall survival (OS) in early and advanced NSCLC stages is not completely understood. Previous reports from our group suggest that the decrease or increase in CEA serum levels is strongly associated with treatment response to platinum-based chemotherapy. However, determination of serum CEA is not included in standard guidelines, such as the National Comprehensive Cancer Network (NCNN). The aim of this study was to analyze the progression-free survival (PFS) and overall survival (OS) in NSCLC patients with elevated CEA levels at diagnosis and to determine its possible association with systemic treatment response.

Method: We performed a retrospective analysis of patients with advanced NSCLC with an elevated serum level baseline of CEA (>20 pg/ml) that received treatment according to international guidelines. The serum CEA levels were measured every two cycles of platinum-based chemotherapy or a tyrosine kinase inhibitor (TKI) treatment. The change in serum CEA levels in response to treatment, OS and PFS were evaluated.

Results: Between March 2004 and February 2018, 748 patients with a diagnosis of advanced NSCLC and CEA levels >20 ng/mL were included in the analysis. The median age was 60.2 years old, 631 patients (84.4%) had adenocarcinoma histology. From 338 patients evaluated for EGFR mutations, 139 (31.3%) harboured an EGFR mutation. The median OS was 23.3 months (95% CI 19.4-26.9) in patients who completely normalized CEA with a diagnosis of advanced NSCLC who did not achieve CEA normalization, with an HR 0.48 95% CI (0.35 –0.67) p <0.0001. The median OS was 15.5 months (95% CI 13.4-17.6) in patients who showed a decrease in CEA levels vs 8.8 months (95% CI 7.5-10.1) in those who did not. Reduction in CEA levels was associated with better OS, either in patients treated with TKI or platinum-based chemotherapy.

Conclusion: Although previous studies have suggested a possible relation between CEA levels and clinical outcome, its utility in the clinic has been controversial. In this study, we demonstrate normalization of serum CEA levels is related to longer OS rates and could be useful as an indirect biomarker for treatment response evaluation. Hence, we suggest its determination for the standard follow-up of advanced NSCLC patients under TKI or platinum-based chemotherapy treatment.

P2.04

Topic: Advanced NSCLC

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


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Background: Several studies have shown that NSCLC genomic background among Hispanics differs from other populations, therefore genotyping tumors in order to assess their molecular profile is adamantly needed in the current era of targeted therapy. Panel-detected oncodriver mutations can drive therapeutic approaches, and can help classify the information in order to propose strong evidence-based interventions in treatment guidelines. In this study we sought to understand the landscape of genomic drivers in a cohort of patients with lung adenocarcinoma of Hispanic ancestry.

Method: Tumor samples were collected from 48 patients with lung adenocarcinoma from March 2017 until March 2019. Samples were submitted for testing to Foundation Medicine and hybrid capture NGS was performed.

Results: A total of 282 samples were sent for evaluation, among which 48 (17%) with lung adenocarcinoma were tested by FoundationOne (FO) in tumor tissue. Among the patients included, 54.2% were men and 79.2% were >50 years of age. Most patients had a previous negative report for EGFR and ALK (in tumor tissue). Results for tumor mutation burden (TMB) were obtained from 48 (100%) samples. Median TMB was 4 mutations/Megabase (m/Mb). High TMB (>10 m/Mb) was identified in 9 (18.8%) samples. The most frequently detected alterations were in P53, KRAS and EGFR genes (Figure 1). In terms of the level of evidence for therapeutic actionability, level-1 was 33.5 %, level-2 was 12.5%, level-3 14.6% and level-4 37.5% (Figure 2).

Conclusion: With the genomic landscape of lung adenocarcinomas in Hispanic patients, we could identify potential actionable mutations and evaluate the level of evidence for the treatment of each patient. This analysis can provide strong evidence for therapeutic actionability for targeted therapies. The results will be used to propose strong evidence-based interventions in the clinical practice of Hispanic patients with lung adenocarcinoma.
Conclusion: Despite an initial assessment of actionable alterations (EGFR and ALK), through a NGS-approach we were able to detect a high amount of genomic alterations linked to a high-level of evidence for therapeutic actionability (33.5%), possibly due to higher sensitivity and a higher number of genes tested in the panel, increasing therapeutic options in this molecular-driven era. This research work was conducted with the support of Roche Foundation Medicine.

Keywords: Foundation one, Adenocarcinoma, NGS

P2.06

Topic: Advanced NSCLC

Lung Cancer Driver Mutations and PD-L1 Expression in US Latino Patients with Advanced Lung Cancer

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Background: Lung cancer incidence rates in US Hispanics/Latinos (H/L) tend to be higher than those reported for most Latin American countries while mortality rates tend to be lower for H/L compared to non-Hispanic whites (NHW). Incidence and outcome disparities are probably multifactorial, however an underlying genetic basis is likely. Our aim was to report frequencies of driver mutations and PD-L1 expression in H/L in Miami in an attempt to improve therapeutic strategies that may benefit this population.

Method: Retrospective analysis on H/L pts with advanced NSCLC who received chemotherapy, immunotherapy (IO), chemotherapy combined with immunotherapy (chemoIO), and/or targeted treatment (TT) at Sylvester Comprehensive Cancer Center (SCCC) in Miami-FL. EMR was reviewed to obtain pertinent clinical information. Genomic results were obtained from Guardant 360 and Foundation One testing in blood and in tissue, respectively.

Results: 131 H/L charts were reviewed. 44% were males and 81% were adenocarcinomas. 29% were never smokers, 57% were current or former smokers (38% with ≥ 30 pack year history), and 14% had unknown smoking status. 120 pts were tested for PD-L1: 91% were positive (with 71% having TPS ≥ 50%) and 8% were negative (TPS 0%). 28% received IO, 5% as first line. 14% received chemoIO, 10% as first line. 24% received TT, 13% as first line. Frequencies of the main driver mutations are presented on the table below. Other mutations were MET (12.5%), BRAF (9.56%), PI3K (8.09%), STK11 (5.15%), PTEN (1.47%), and ROS1 (0.74%).

<table>
<thead>
<tr>
<th>Mutation</th>
<th>H/L from SCCC (N=131)</th>
<th>Hispanics from Latin American Countries</th>
<th>Other populations (as reported in the literature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>25.74%</td>
<td>32.5%</td>
<td>NHW=10%, East Asian=30%</td>
</tr>
<tr>
<td>K RAS</td>
<td>14.71%</td>
<td>16.6%</td>
<td>NHW=15-25%</td>
</tr>
<tr>
<td>ALK</td>
<td>4.41%</td>
<td>4.2-10.5%</td>
<td>NHW=1-3%, Asian=2.3-6.7%</td>
</tr>
</tbody>
</table>

Conclusion: US H/L present a higher frequency of driver mutations than NHW as well as a high rate of PD-L1 overexpression, yet only a minority receives TT or IO as upfront therapy. Identifying persisting challenges in providing US H/L with the most appropriate treatment at the most beneficial time remains a crucial step towards achieving the goal of precision medicine in thoracic oncology.

Keywords: Mutations, Hispanics, Precision medicine
P2.07
Topic: Advanced NSCLC
Prevalence of Hypovitaminosis D in Patients with Advanced Adenocarcinoma of Smokers and Non-smokers

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Background: In lung cancer (LC) most patients are diagnosed in advanced stages of the disease, symptomatic and eligible for systemic treatment. And adequate levels of vitamin D (VD) in this population can contribute to symptom control such as pain, decreased cytotoxic effects of chemotherapy and improve immunity and muscle function. The objective of this research was to verify the nutritional status of the VD in patients in homogenous samples with advanced adenocarcinoma of smokers and non - smokers and to relate to the habits of previous solar exposition to the disease.

Method: This was a prospective observational study, approved by an Ethics Committee, carried out with data from ambulatory patients with lung adenocarcinoma with clinical stage IV, in a specialized center for chest tumors in Rio de Janeiro, of both sexes, of the same age or greater than 20 years and Performance Status (PS) <2 seconds ECOG. The data were collected at the time of diagnosis from September 2017 to March 2019. The VD assessment was quantified by 25 (OH) D by high performance liquid chromatography (HPLC) and the cut points adopted for groups was <30ng / mL. A validated solar exposure questionnaire to complement VD status assessment was included. The sample was divided into smokers and non-smokers according to criteria adopted by the World Health Organization (WHO). The Mann Whitney test was used to compare the numerical variables between the smoking and non-smoking categories.

Results: Of the 73 patients included in the study, 54.8% were non-smokers, 50.7% were female, and 75.5% were elderly. The median VD concentration was 25.3ng / dl (17.6-32.1) and 27.2ng / dl (19-32.2) for non-smokers and 23ng / dl (16.2-32.9 ) for smokers. 65.8% of the sample had a VD deficiency according to criteria for risk groups, although we did not find differences between smokers and non-smokers (p=0.18). The median time of sun exposure was 15.7min / day and 13.83min / day for non-smokers and smokers respectively and there were no differences among them (p = 0.85).

Conclusion: We observed a higher proportion of individuals with VD deficiency in advanced stage lung adenocarcinoma in a sample of elderly individuals, with a history of low solar exposure prior to diagnosis in a country that presents adequate latitude for sun exposure throughout the year.

Keyword: Lung adenocarcinoma, Nutritional status, 25 hydroxyvitamin D, Smoking

P2.08
Topic: Advanced NSCLC
Osimertinib for Metastatic, EGFR Mutated Non-small Cell Lung Cancer. Real World Evidence at National Oncology Institute, Panama

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Background: In the Flaura Trial, Osimertinib resulted in a superior progression free survival (PFS) as shown in clinical trials in real-world population. The main toxicities reported were three: diarrhea, rash and paronychia, but most of it (8%) were of first grade.

Method: We did a retrospective, descriptive review of EGFR mutated metastatic NSCLC patients treated with Osimertinib, in our institution from July 2018 to June 2019. We did a preliminary descriptive analysis of the patients using SPSS – 24 for the analysis.

Results: A total of 45 patients received Osimertinib in the evaluated period, 32 (75%) as first line therapy and 13 (28.9%) as second line therapy. The mean age was 65.2 (51.3-79.1) years, 34 patients (75.6%) were female, 77.8% non - smokers and 91.1% had a good performance (ECOG 0-2). The most common mutation detected was in the exon 19 (60%) and, with a median follow up of 75 months, just 4 (22.5%) patients treated in a first line setting, and 3 (23%) of the second line setting, has progressed. the response rate was 50%, with a disease control rate of 80.4%. This finding was independent of therapeutic line, and smoking status. Of the 10 patients with SNC disease, 6 had partial response. The main toxicities reported were three: diarrhea, rash and paronychia, but most of it (8%) were of first grade.

Conclusion: Our results support that the use of osimertinib as first line therapy is feasible in developing countries, with similar outcomes with the reported in the pivotal trials and good tolerability.

P2.09
Topic: Advanced NSCLC
Access and Outcomes of TKI EGFR in Lung Cancer Treatment from Uruguayan Population

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Background: Lung cancer represents a serious global health problem. Our country is not alien to this reality, being the most common cause of cancer deaths and representing 1400 newly diagnoses/year. The role of Tyrosine Kinase Inhibitors (TKI) of the epidermal growth factor receptor (EGFR) for the treatment of advanced non small lung cancer (NSCLC) is well known. In Uruguay EGFR mutations have an overall prevalence of 18%, the access to TKI-EGFR, erlotinib or gefitinib, is covered by the Fondo Nacional de Recursos (FNR). The FNR, is a non-state public person which provides financial coverage for highly specialized medicine procedures and high-priced medicines for the Uruguayan population. The requirements for the coverage are based on clinical trials inclusion/exclusion criterial.

Method: We use the FNR registry that collects observational data from patients receiving treatment under its coverage. Adults patients with advanced EGFRMut+ NSCLC, who had received TKI EGFR treatment between November 2011 and December 2017 were included. Demographic, clinical characteristics were analyzed, overall survival (OS) and progression free survival (PFS) were the outcomes evaluated. The study was approved by a local ethical committee.

Results: 130 treatment requests were made. The median age at diagnosis was 63 years, being 61.5% of female patients and 38.5% male. 87% were non-smokers. The most frequent mutation reported was the exon 19 deletion (63.8%), followed by the exon 21 mutation (30%), others represented 4.3%. PFS for the global population was 12.9 months (95% CI: 10.4-15.3) and the OS was 19.7 months (95% CI: 16.8-22.5).

Conclusion: Our results support that the use of the evidence-based approach constitutes an important element for the formulation of sustainable public policies, this cohort reported similar OS and PFS as shown in clinical trials in real-world population. The main
Respiratory Diseases, MEXICO/Mexico, had clinical indication and enough histologic material to perform a functional diagnosis. Out of the 113 patients diagnosed with stage IV or stage 11B non-small cell lung cancer (NSCLC) and with ALK rearrangement, 3.3% presented with stage IV disease and 3.3% presented with stage 11B disease.

**Background:** Lung cancer is the leading cause of cancer death. The treatment of lung cancer is currently based in the consideration of genetic tests and targeted therapy based on genomic alteration is now the standard of care in patients with advanced pulmonary adenocarcinoma. The new generation sequencing (NGS) allows to identify the presence or absence of mutations, it is approved as a diagnostic method to identify such alterations in patients with non-small cell lung cancer (NSCLC) and confers sensitivity to ALK inhibitors. This study was conducted at the National Institute of Respiratory Diseases with the aim of describing the clinical and tomographic characteristics of patients with ALK rearrangement taking into account the biological behavior of this type of lung cancer is different.

**Method:** Retrospective observational study of patients with lung cancer from January 2013 to June 2018. Review of clinical and radiological records, with registration of sociodemographic variables, clinical, molecular profile and immunohistochemical staining (IHC) for ALK. Results expressed through measures of central tendency.

**Results:** A cohort was analyzed from 2013 to 2018 with a total of 751 patients diagnosed with lung cancer. The CPCNP was the most frequent with 93.74% (n = 704). The adenocarcinoma was found in 86% (n = 606). ALK rearrangement was reported in 3.3% (n = 20). The majority were 65% female, the average age was 58 ± 2.4 years, smoking 40% (n = 8). Of the patients who never smoked, 92% (n = 11) reported exposure to biomass. In 25% (n = 5) functional diagnosis was the low number of treatments requested for coverage, and only 130 treatments in 6 years when it was expected 130 EGFRm+ NSCLC new diagnoses per year. Meantime other countries struggle against access, in Uruguay having that resolved, we have to improve EGFR mutation testing in NSCLC in daily oncology practice to offer the best treatment to our patients.

**Keywords:** Lung cancer, Uruguay, ITK, Real word outcomes

P2.10

**Topic:** Advanced NSCLC

**Mutational EGFR Profile in Mexican Patients with Pulmonary Adenocarcinoma Measured by New Generation Sequencing (NGS)**

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**Background:** Lung cancer is the leading cause of cancer death. The treatment of lung cancer is currently based in the consideration of genetic tests and targeted therapy based on genomic alteration is now the standard of care in patients with advanced pulmonary adenocarcinoma. The new generation sequencing (NGS) allows to identify the presence or absence of mutations, it is approved as a diagnostic method to identify such alterations in patients with non-small cell lung cancer (NSCLC) and confers sensitivity to ALK inhibitors. This study was conducted at the National Institute of Respiratory Diseases with the aim of describing the clinical and tomographic characteristics of patients with ALK rearrangement taking into account the biological behavior of this type of lung cancer is different.

**Method:** Descriptive, prospective and cross-sectional study. We studied 68 samples of tumor tissue with a diagnosis of pulmonary adenocarcinoma in the period July-October 2018, analyzed by NGS for the determination of mutations in molecular drivers.

**Results:** Altered EGFR was found in 29.4% of the samples, of which 65% were in women and 35% in men. The most frequently identified mutation descending; Leu858Arg in exon 21 (60%), exon 20 (20%), exon 19 (15%) and exon 18 (5%). Mutation of resistance to tyrosine kinase inhibitor (T790M) was identified in 0.5%. We also analyzed whether patients who presented mutations in EGFR had a smoking risk factor found only in 5% of cases. 60% of patients with EGFR mutation had a history of exposure to biomass smoke.

**Conclusion:** The NGS is an alternative to identify genetic alterations in EGFR in NSCLC.

**P2.11**

**Topic:** Advanced NSCLC

**Three Years of Experience with ALK-positive Patients**

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**Background:** The new tyrosine kinase inhibitors approved for the therapy of non-small cell lung cancer (NSCLC) caused by ALK rearrangement, have been showing an improvement on overall survival, disease progression and toxicity.

**Method:** We performed a retrospective analysis of all the patients with NSCLC and ALK rearrangement that received crizotinib, ceritinib and alectinib as first-line or second-line therapy in our health care unit, by investigating its toxicity and the disease progression.

**Results:** Out of the 113 patients diagnosed with stage IV or stage 11B lung adenocarcinoma, 17 were ALK positive (from those who had clinical indication and enough histologic material to perform the test). In this population, the mean age was 60.76 years-old and 76.47% (n = 15) were females. Sixteen patients (94.12%) were non-smokers and one (5.88%) was a smoker. By the time of the diagnosis, 94.12% (n = 16) presented with stage IV disease (one of them had brain metastasis and was treated with holocranial radiotherapy) and 5.88% (n = 1) presents with stage 11B disease.

**Conclusion:** The experience in our health care unit is similar to the data from other studies, showing high response rates, high overall survival and low toxicity associated to these drugs.
of COPD was documented. The most frequent tomographic patterns were: mass in 70% (n = 14), pleural thickening with pleural effusion in 20% (n = 4) and micronodular pattern in 10% (n = 2).

**Conclusion:** A clinical phenotype and behavior different to the rest of patients with NSCLC is demonstrated in ALK positive patients.

**Method:**

**Results:** EGFR mutation was documented in 85 cases, of which around 40% of the mutations and around 20% in the Caucasians. EGFR mutations are diverse. Approximately 85%-90% of EGFR mutations occurred in exon 19 deletions and exon 20 point mutations L858R. Among Latinos, EGFR mutations were found in 23.3%. The highest frequency was observed in Latinos from Peru (37%) followed by the United States (23%) and Mexico (18%).

**Background:** Lung cancer is one of the neoplasms with the highest mortality around the world, being adenocarcinoma the most common subtype. EGFR is a common mutation present in adenocarcinoma, mainly in young women and nonsmokers. In Asians has a significantly higher frequency of about 40% of the mutations and around 20% in the Caucasians. EGFR mutations are diverse. Approximately 85%-90% of EGFR mutations occurred in exon 19 deletions and exon 20 point mutations L858R. Among Latinos, EGFR mutations were found in 23.3%. The highest frequency was observed in Latinos from Peru (37%) followed by the United States (23%) and Mexico (18%).

**Conclusion:** The behavior of EGFR mutations in Costa Rica is similar to that already studied in the rest of the Latin American population.

**Keyword:** EGFR, Uncommon mutations, Adenocarcinoma

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<table>
<thead>
<tr>
<th>CLINICAL CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CASE NUMBER, AGE, GENDER, DIAGNOSIS DATE</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>180 FEMALE 2016 NON SMOKER</td>
</tr>
<tr>
<td>2 34 MALE 2018 NON SMOKER</td>
</tr>
<tr>
<td>3 40 FEMALE 2018 NON SMOKER</td>
</tr>
<tr>
<td>4 53 MALE 2018 NON SMOKER</td>
</tr>
<tr>
<td>5 73 FEMALE 2018 NON SMOKER</td>
</tr>
</tbody>
</table>

**Conclusion:** A clinical phenotype and behavior different from the rest of patients with NSCLC in patients with positive ALK rearrangement is demonstrated. Alectinib is associated with disease control with minimal well tolerated adverse effects.

**Keyword:** Lung cancer, Prognosis, ALK, Alectinib

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**Topic:** Advanced NSCLC

**Response Profile of Non-small Cells Lung Cancer with ALK Positive Treated with Alectinib**

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**Background:** The diagnosis and treatment of lung cancer is currently governed by the selection of patients based on oncogenic alterations that allow specific therapies to be offered. The gene (ALK) is present in 3 to 7% of patients with non-small cell lung cancer (NSCLC) and confers sensitivity to ALK inhibitors with better response rates and PFS than with chemotherapy.

**Method:** We performed a descriptive review of the response profile in patients with NSCLC with positive ALK mutation and who received treatment with alectinib. Tomography patterns were described, as well as the response achieved with the treatment.

**Results:** We found 5 cases of patients with a diagnosis of NSCLC with ALK positive mutation who received treatment with Alectinib. It was found that all patients reached, until the time of the last evaluation, a partial response based on RECIST 1.1 criteria. The adverse effects presented were explained by the use of TKI.

**Keyword:** Lung cancer, Prognosis, ALK, Alectinib

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**Topic:** Advanced NSCLC

**Progression under Osimertinib, What Now?**

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**Background:** Patients with epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC) generally respond well to treatment with EGFR-targeted tyrosine kinase inhibitors (TKIs) but acquired resistance to therapy is inevitable, reflecting tumor evolution. Positive clinical activity and favorable toxicity profile has led to the use of
osimertinib mesylate to treat EGFR-mutant NSCLC with TKI resistance mediated by the EGFR T790M mutation.

Method: This is a retrospective, multicenter study of 465 patients from Argentina, Uruguay, Chile and Colombia diagnosed during 2017. Of these, 432 were newly diagnosed, treatment naïve advanced or metastatic NSCLC (Cohort 1) and 31 were EGFR-mutant patients who had progressed after a first- or second-generation EGFR-TKI (Cohort 2).

Results: For newly diagnosed patients, 77.9% of the private sector underwent molecular diagnosis but only 53.9% of the public sector had access to the testing. EGFR mutation was found in 15.05% of the population (60/432) and in 16.25% of the patients who received target therapy only after a first line of chemotherapy. 20.4% of the patients had CNS metastasis at diagnosis and almost 75% received any CNS related treatment (35% radiotherapy; 15% surgery). For cohort 2, the main site of progression was seen within the thorax (59.3%) while the second site of progression was CNS (21.8%) followed by the bone (18.7%). Of the 32 patients, only 24 (75%) underwent biopsy after progression. Reasons for not performing a biopsy included poor PS and physician decision.

Conclusion: In real word, for Latin American patients, access to molecular testing is still challenging, especially in public health systems. Turnaround times and test availability may interfere with the choice of first line treatment for the patients. Progression within the thorax and in CNS were the two more frequent sites of relapse. After progression to a first line target therapy, only 75% had access to a rebiopsy and of these 46.6% received a third generation TKI. These data should encourage physicians to give most effective therapy in 1st line for patients with EGFR mt+ tumors.

P2.15-B

Topic: Advanced NSCLC

Update of Mutation Status and PDL1 Expression in Lung Cancer. A Multicenter Local Study

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Background: Advances have been made in the understanding of the biology of NSCLC in relation to the characterization of molecular features such as activations of oncogenes by mutations, translocations and amplifications, and check point expressions which are being used as predictive biomarkers.

Method: We determined the molecular alterations in EGFR, gene fusion ALK, and PDL-1 in our Caucasian and Hispanic populations. 171 small samples and resection specimens of patients with NSCLC in different institutions of Cordoba were studied during a period (2014 - 2019). In addition to Histopathology Type, we analyzed immunohistochemistry (IHC) characteristics, molecular profiles, and several clinical variables were studied.

Different tests were used to detect alterations of EGFR and fusion gene EML4-ALK expression, with the aim to identify our own profile. EGFR mutation was studied by therascreen kit, PCR, in order to detect genetic alterations in exons 18, 19, 20 and 21. ALK translocations were analyzed by FISH (Vysis- Break Apart, Abbott) and IHC (clon DSF3, ventana, Roche). With used to determine checkpoint expression by Platform Dako/Autostainer Link 48, Kit PD-L1 IHC 22C3 pharm Dx. We correlated the molecular profile and PDL-1 expression with different clinical variables (age, gender, and tobacco habits). Qualitative variables were compared using chi-squared test or Fisher’s test and quantitative variables were compared using the T-test.

Results: 171 samples were tested for EGFR expression and ALK alterations 63.2% of subjects were men and 88.9% were smokers.

P2.15-B

Topic: Advanced NSCLC

Panorama Retro: Real World Evaluation of Molecular Testing and Treatment Patterns for EGFR Mutations in Patients with Advanced or Metastatic NSCLC (D133PR00143)

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Background: Stage IV NSCLC is a challenging disease because treatment is driven by molecular and biomarker testing. Management of these patients is well established, but real world data might not always reflect the guidelines especially in emerging countries where the lack of accurate information is a constant.

Conclusion: Management of these patients is well established, but real word treatment is driven by molecular and biomarker testing.
Novel KRASG12C Inhibitor, in Non-small Cell Lung Cancer

**Table 1. Characteristics of the 171 cases of lung adenocarcinoma according gender.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male</th>
<th>Female</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, ±SD), years</td>
<td>64.7 (8.9)</td>
<td>61.8 (8.2)</td>
<td>0.032</td>
</tr>
<tr>
<td>Smoking</td>
<td>101 (93.5)</td>
<td>51 (81.0)</td>
<td>0.012</td>
</tr>
<tr>
<td>EGFR expression</td>
<td>12 (11.1)</td>
<td>19 (30.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>ALK alterations</td>
<td>1 (0.9)</td>
<td>2 (3.2)</td>
<td>0.555*</td>
</tr>
</tbody>
</table>

**Table 3. Characteristics of the 39 cases of lung adenocarcinoma which PDL-1 was tested.**

<table>
<thead>
<tr>
<th>PDL-1 total, n=39</th>
<th>PDL-1+, n=16 (41%)</th>
<th>PDL-1-, n=23 (59%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, n (%)</td>
<td>23 (59.0)</td>
<td>11 (68.8)</td>
<td>12 (52.2)</td>
</tr>
<tr>
<td>Age (year), mean (±SD)</td>
<td>65.72 (7.27)</td>
<td>62.12 (7.35)</td>
<td>65.43 (8.71)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>39 (100)</td>
<td>16 (100)</td>
<td>23 (100)</td>
</tr>
<tr>
<td>EGFR expression, n (%)</td>
<td>3 (7.7)</td>
<td>1 (6.2)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>ALK alterations, n (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: Qualitative variables were compared using chi-squared test or Fisher's test (*) and quantitative variables were compared using the T-test.

**Conclusion:** Our results showed a comparable frequency in EGFR mutations and gene fusion ALK in relation to the data published in western population. Molecular analysis of NSCLC, adenocarcinoma (AC) EGFR, ALK, and tumor proportion score in PDL-1 expression is the standard of diagnosis. These results allowed providing the most adequate therapy for patients.

**Method:** This is a phase 1, first-in-human, multicenter study of AMG 510 in patients with locally advanced or metastatic KRASG12C mutant solid tumors, including NSCLC. The primary endpoint is safety; key secondary endpoints include objective response rate, assessed every 6 weeks, duration of response, progression-free survival, and PK. Key inclusion criteria: KRASG12C mutation identified through DNA sequencing; measurable or evaluable disease; progression on standard therapy; and ECOG PS ≤ 2. Patients with active (untreated) brain metastases and myocardial infarction within 6 months of study initiation were excluded. Once maximum tolerated dose is identified during dose escalation, additional patients will be enrolled in the dose expansion part. AMG 510 is given orally once daily until disease progression, intolerance, or consent withdrawal.

**Results:** Of 4 April 2019, 13 patients (8 females; median age: 63 years [range: 53–77]) with NSCLC were enrolled into 4 dose escalation cohorts. Median number of prior lines of therapy was 3 (range: 1–5). Median duration of treatment was 59 days (range: 9–192). No dose-limiting toxicities were identified. The most frequently reported adverse events (AEs) were decreased appetite and diarrhea, observed in 4 and 3 patients, respectively. Six patients reported 10 treatment-related adverse events (TRAEs) (6 grade 1; 2 grade 2; 2 grade 3). Two grade 3 TRAEs were anemia in a patient with baseline grade 2 anemia and diarrhea that lasted 2 days in another patient. 10 patients were evaluable for tumor response: 5 patients had a partial response (2 of which were confirmed), 4 had stable disease, and 1 had progressive disease (PD). Of all 13 patients enrolled, 11 remained on study, and 2 discontinued due to PD.

**Conclusion:** AMG 510 is well tolerated at all 4 dose levels and showed antitumor activity in patients with advanced KRASG12C mutant NSCLC. Enrolment is ongoing (ClinicalTrials.gov identifier: NCT03600883).

**P2.16**

**Topic: Pathology**

**PD-L1 Expression in a Population with Non-Small Cell Lung Cancer in a Reference Healthcare Center in Latin-America**

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**Background:** Non-small cell lung cancer (NSCLC) is the most common type among malignancies of the lung, and among its histological subtypes, different mutations and protein expressions have been of object of study for the past years. Epidermal growth factor receptor (EGFR) mutations and EML4-ALK fusion as driver mutations have been reported to upregulate programmed death-ligand 1 (PD-L1) expression. Despite therapeutic significance of these associations has not been yet completely elucidated, studying the prevalence and correlation of these features becomes more important with time.

**Method:** Clinical and mutational features were described in 114 patients diagnosed with NSCLC between 2013 and 2016 at a reference health care center in Colombia. Among the patients in whom PD-L1 expression was tested, we reported its prevalence and distribution in patients positive for EGFR and ALK.

**Results:** The mean age was 65±12 years. 72.8% (n=83) were female. 72.3% (n=83) were smokers. EGFR mutations were found in 27% (n=30) of patients; of these, 80.7% (n=24) were exon 19 deletion and 19.3% (n=6) were L858R. The prevalence of ALK alteration was 3.2% (n=4). No association was found between gender and PD-L1 expression.

**Conclusion:** Gender and PD-L1 expression was not associated.
and being a non-smoker was associated with a lower expression of the protein.

Conclusion: The prevalence of EGFR mutations was similar to that reported worldwide, and fusions in the EML4-ALK gene were higher than expected, as well as PD-L1 expression. Smoking has already been reported to be associated with a higher expression of PD-L1, as found in this study. More studies must be done regarding expression of the protein in patients with driver mutations to establish reliable associations and elucidate the clinical significance of blocking PD-1/PD-L1 in EGFR and ALK-mutant NSCLC treated with TKIs.

**Keywords:** Non-small cell lung cancer, PD-L1

**P2.17**

**Topic:** Pathology

**Interssegmental Plane Identification with Single Lung Ventilation in PSN Resection**

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**Background:** Taking in account that primary lung cancer is the leading cancer mortality worldwide with approximately 428900 deaths per year, and its several distinct histologic types it makes these disease a challenge in diagnostic and treatment. Also with the imaging tool that plays an important role in diagnosis and stadification in a chest X ray only when the nodule size is 40mm the diagnosis will be in a 100%. The follow up will be with thin solid sub solid aspect at CT and its change or if presents a grow in diameter over 34%.

**Results:**

- 208 patients were included, 83 female (40%) 125 male (60%) age average 62 years old accept and sign informed consent for surgery.
- 47% this put the balance between curability and unnecessary surgery and localization of the PSN will help to avoid unnecesary and being a non-smoker was associated with a lower expression of the protein.

**Conclusion:** The correct identification of the segmental plane for a surgery and localization of the PSN will help to avoid unnecessary resection and maintain the lung function; the labeling and the mapping with indocyanine green or blue metilien sometimes in developing countries is not possible and the correct lung isolation in some patients is a challenge for the anesthesiology, these factors are related to the economy and the infraestructure of each hospital.

**P2.18**

**Topic:** Pathology

**Sternal Cavernous Hemangioma and Anterior Thoracic Wall Reconstruction: Case Report**

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**Background:** The sternum is considered an unusual site of tumors, with an overall incidence of 15% of all thoracic wall tumors. Primary sternal tumors are even rarer and are more malignant. Benign lesions are of varied nature, among these hemangiomas, which usually occur in soft tissues and when they appear in bone, they usually present in the skull and vertebrae. We present the case of a young male who debuted with a painful sternal mass that was evaluated and resected, confirming a cavernous hemangioma.

**Method:** Case description. Review of the clinical history.

**Results:** Male, 39 years old, with no relevant personal history, with sternal pain, not irradiated, of 2 years of evolution that had worsened in the last months and emergence of a palpable mass at that level. Physical examination: bulging of the sternum in its upper portion without inflammatory changes, without collateral circulation, no murmurs and no lymph node enlargement.

Thoracic CT: expansive lytic lesion of the sternum involving the manubrium and extending to the third costo-sternal joint, without intrathoracic involvement with a cleavage plane with mediastinal vascular structures. Resection of the sternum and reconstruction with prosthetic material, pectoral and fasciocutaneous muscle flaps was performed. Intraoperative findings: Large tumor of the sternal manubrium without involvement of the clavicles or the first ribs. He presented satisfactory clinical evolution during the postoperative period. Histopathological study: Neoplasm composed of irregular vascular dilatations containing abundant erythrocytes, without cytological atypia or mitosis.

**Conclusion:** Hemangiomias of the sternum can cause defects in the bone cortex with an expansive growth. It is very difficult to differentiate its benign nature from malignant lesions. They are considered malignant until proven otherwise; treatment is proposed with radical surgery to achieve healing, with reconstruction to improve the quality of life, as in our case.
Fundacion Valle del Lili, Cali/Colombia, 4Department Of Health Sciences, Universidad Icesi, Cali/Colombia,

chemotherapy; a multifocal papillary thyroid carcinoma, stage T3N0M0 with negative hormone radical lymphadenectomy; an apocrine ductal carcinoma in with a distal pancreaticoduodenectomy, splenectomy and vascular and perineural compromise, stage T2N0M0, managed adenocarcinoma of the head of the pancreas with extensive adenocarcinomas including a well-differentiated ductal mellitus II and hypothyroidism presents with multiple primary results:

A 76 year old female with previous history of diabetes review of clinical history method:

adenocarcinomas who develops pulmonary nodules, requiring further evaluation. Here, the available genetic tests were inconclusive and the case illustrated. Hereditary cancer syndromes such as Lynch syndrome, Von Hippel-Lindau syndrome, Li-Fraumeni syndrome and multiple endocrine neoplasias must be studied in this patient. Here, the available genetic tests were inconclusive and the case requires further evaluation.

Keywords: Pulmonary metastasis, Multiple primary adenocarcinomas

P2.19

Topic: Pathology

Pulmonary Metastasis in a Patient with Multiple Primary Adenocarcinomas: A Case Report

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Background: Cancer diagnosis increases with age, which is also a risk factor for the development of multiple malignant neoplasms. Patients with a primary tumor are at an 8.5% risk of developing secondary tumors. The incidence of primary neoplasms varies between 2.4% and 8%; 26% of the secondary presentations are synchronous and 74% are metachronous. We describe the case of a patient with multiple primary adenocarcinomas who develops pulmonary nodules, requiring further evaluation.

Method: Review of clinical history

Results: A 76 year old female with previous history of diabetes mellitus II and hypothyroidism presents with multiple primary adenocarcinomas including a well-differentiated ductal adenocarcinoma of the head of the pancreas with extensive vascular and perineural compromise, stage T2N0M0, managed with a distal pancreatectoduodenectomy, splenectomy and radical lymphadenectomy; an apocrine ductal carcinoma in situ of the breast, stage T3N0M0 with negative hormone receptors, managed with a mastectomy and neoadjuvant chemotherapy; a multifocal papillary thyroid carcinoma, stage T1ANOM0, compromising the left vocal cord, managed with total thyroidectomy, radioactive iodine therapy and lymphadenectomy; and a gastrointestinal stromal spindle cell lesion, without necrosis but positive CD117, CD34, actin and desmin. A multi-gene panel test is performed for hereditary cancer syndromes (MyRISK) with complete sequencing and MLPA for BRCA1, BRCA2 with a negative result; and later MLPA and sequencing for APC, ATM, BARD1, BMPR1A, BRIP1, BRIPI, CDH1, CDK4, CDKN2A, CHECK2, EPCAM, MLH1, MSH2, MSH6, MUTH1, NBN, PALB2, PMS2, PTER, RAD51C, RAD51D, SMAD4, STK11 and TP53 showing variants of uncertain significance and MLH1 polymorphism. Due to the positivity of serum cancer antigen 19-9, a PET-CT scan is performed identifying hypermetabolic nodules in the lungula and the left lower lobe. The patient is taken to lobectomy and wedge resection; pathology report is notable for a metastatic adenocarcinoma originated in the pancreas. NAB-Paclitaxel is initiated with complete remission.

Conclusion: In this case the patient had breast, pancreatic, thyroid and gastrointestinal adenocarcinomas, with metastatic lesions in the lung of pancreatic origin. In the literature similar reports have not been described; however hormone associated carcinomas such as simultaneous ovarian, breast, uterine and thyroid malignancies have been reported before. Cases of primary lung adenocarcinoma associated with colorectal(22%), breast(18.4%), and gastric(14.4%) neoplasms have also been illustrated. Hereditary cancer syndromes such as Lynch syndrome, Von Hippel-Lindau syndrome, Li-Fraumeni syndrome and multiple endocrine neoplasias must be studied in this patient. Here, the available genetic tests were inconclusive and the case requires further evaluation.

Keywords: Sternal Cavernous Hemangioma, Thoracic surgery, Thoracic Wall Reconstruction

P2.21

Topic: Immunotherapy

Clinical Responses and Survival in Hispanic Patients vs Non-Hispanic White Patients with Non-Small Cell Lung Cancer Treated with Immunotherapy

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Background: Hispanics in the US have a lower age-adjusted mortality in NSCLC and may have a different gene expression profile than NHWs. Additional data is thus needed to validate outcomes in Hispanic patients with NSCLC treated with ICIs. Our aim was to compare clinical outcomes between Hispanic and NHW patients with advanced NSCLC treated with ICIs at 5 large institutions in the US and Latin America.

Method: Retrospective clinical review on 436 Hispanic pts with advanced NSCLC that had failed at least one prior line of chemotherapy or were treated with single-agent immunotherapy as first line. Pts with actionable genetic aberrations (EGFR, ALK, and ROS-1) were excluded. Primary endpoints assessed were OS, PFS, and ORR (CR+PR) while secondary endpoint was DCR (ORR+SD).

Results: Patient characteristics are summarized in table 1. Primary endpoint results are summarized in table 2. There were no statistical significant differences seen in the secondary endpoint (DCR) among Hispanics and NHW pts.

Keywords: Pulmonary metastasis, Multiple primary adenocarcinomas
Table 1

<table>
<thead>
<tr>
<th></th>
<th>Hispanics (n=256)</th>
<th>NHW (n=180)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>65</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Males (%)</td>
<td>52</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Line of treatment First line</td>
<td>57 198 1</td>
<td>45 133 2</td>
<td></td>
</tr>
<tr>
<td>Second line Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histology Adenocarcinoma</td>
<td>191 46 19</td>
<td>121 48 11</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Hispanics (n=256)</th>
<th>NHW (n=180)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR First Line</td>
<td>35%</td>
<td>30%</td>
<td>0.6590</td>
</tr>
<tr>
<td>ORR Second Line</td>
<td>18%</td>
<td>19%</td>
<td>0.5236</td>
</tr>
<tr>
<td>ORR Adeno</td>
<td>22%</td>
<td>24%</td>
<td>0.6714</td>
</tr>
<tr>
<td>ORR SQCC</td>
<td>24%</td>
<td>23%</td>
<td>1.0000</td>
</tr>
<tr>
<td>ORR PDL1 (+)</td>
<td>29%</td>
<td>32%</td>
<td>0.4839</td>
</tr>
<tr>
<td>ORR PDL1 (-)</td>
<td>5%</td>
<td>17%</td>
<td>0.3040</td>
</tr>
<tr>
<td>Median PFS os</td>
<td>4m</td>
<td>4m</td>
<td>0.7509</td>
</tr>
<tr>
<td>Median OS</td>
<td>22m</td>
<td>22m</td>
<td>0.2004</td>
</tr>
</tbody>
</table>

Conclusion: No significant differences were found in the clinical outcomes between Hispanic and NHW patients despite expected genomic differences. As expected, higher response rates were seen in first line therapy and patients with PD-L1 (+) status. These findings validate efforts in making immunotherapy more available to Hispanic patients worldwide.

Keywords: Immunotherapy, Hispanics

P2.22

Topic: Immunotherapy

Immunotherapy-related Thrombosis: Considerations and Associated Factors in Non-small Cell Lung Cancer (NSCLC) Patients

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Background: Widespread use of immune checkpoint inhibitors (ICIs) for the treatment of lung cancer has exposed a large number of patients to these medications, increasing the incidence of rare adverse reactions such as thromboses. The present study elaborates on factors related to the occurrence of these events.

Method: In a retrospective cohort study, a total of 48 patients, 24 who experienced thrombosis and 24 matched controls who underwent evaluation after initiation of ICIs therapy for advanced/metastatic NSCLC, were included. Clinical and pathological as well as serum inflammatory and coagulation markers were evaluated.

Results: Among the 48 patients, 46% (n=26) were female, median age was 62 years old and all patients had an ECOG performance score of < 2. The median overall survival reached by the cohort was 22.47 months. Among patients who developed thrombosis there were 8 cases of deep venous thrombosis (DVT) (33%), 13 pulmonary embolisms in addition to DVT (62.5%) and 1 case of brain venous sinus thrombosis (4.2%). Apart from expected thrombosis markers such as D dimer, differences in inflammatory and immune related markers between patients who experienced thrombosis and those who did not, were observed. Abnormal values were found in the thrombosis group for B2glycoprotein 1 (35% vs 0%, OR= 4.08, [95%CI 1.65 - 12.1], p = 0.005), B2glycoprotein 1 IgG (29.2% vs 0%, OR= 4.64, [95%CI 1.73 - 16.9], p = 0.007), C Reactive protein (83.3% vs 12.5%, OR= 35, [95%CI 7.9 - 213], p < 0.001), B2microglobulin (62.5% vs 8.3%, OR= 14, [95%CI 3.1-103.7], p = 0.002), Prothrombin time (41.7% vs 4.2%, OR = 2.4, [95%CI 1.64 - 3.68], p = 0.001) and C Coagulation protein (50% vs 16.6%, OR =1.79, [95%CI 1.53 - 2.91], p < 0.001).

Conclusion: Abnormalities in antiphospholipid antibodies, C reactive protein, B2microglobulin and coagulation in patients who suffered thrombosis during ICI treatment suggest that this phenomenon could be the result of immune and autoimmune induced intravascular dysfunction.

Keywords: Immunotherapy, Thrombosis

P2.23

Topic: Immunotherapy

Characterization of Hispanic Patients Who Experienced Hyperprogression During Treatment for Advanced NSCLC with Immunotherapy

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Background: To characterize and identify factors associated with the presentation of hyperprogression after initiation of immunotherapy in patients with advanced non-small cell lung cancer (NSCLC).

Keywords: Immunotherapy, Thrombosis
Method: A multicenter international retrospective study on 110 patients was conducted. Clinical variables as well as routine blood studies were recorded before initiation of treatment. Regression analysis was used to find associations. A random forest tree analysis (RFTA) based on continuous and discrete variables was used to stratify patients based on occurrence of hyperprogression.

Results: Median age was 64 years (Range 34-90) and 59.8% were male patients. ECOG performance status was ≥1 on 86% of patients. Median overall survival was 12.7 months (95% CI 9.67-14 months) and progression-free survival of 4.27 months (95% CI 3.97-5.0). 44 hyperprogressors were documented (19.8%, [95%CI 14.5-25.1%]). Median time to progression was approximately 5 weeks after initiation of treatment. Factors associated included albumin and hemoglobin levels (p = 0.046 and 0.037 respectively), presence of CNS (p = 0.0009) and bone metastasis (p = 0.004) and weight loss (p= 0.004). RFTA revealed that a leucocyte count over 5,500 cells/dl was present in all hyperprogressors.

Conclusion: Hyperprogression is a phenomenon after initiation of immunotherapy which is associated with clinical and paraclinical variables. These associations could be used to withhold certain agents and prevent its occurrence in NSCLC treatment.

Keywords: Albumin, Leucocyte count, Hyperprogression

P2.24

Topic: Immunotherapy

Lung Immune Prognostic Index in Patients with Non-small Cell Lung Cancer Treated with Either Chemo or Immunotherapy

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Background: The Lung Immune Prognostic Index (LIPI) is calculated prior to the initiation of treatment in patients with advanced Non-Small-Cell Lung Cancer (NSCLC). It is currently useful to stratify patients into groups that can receive a significant beneficial outcome following immune checkpoint inhibitor (ICI) therapy. The LIPI score combines the pretreatment-derived neutrophil-to-lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH) levels. LIPI index divides groups into a “good candidate group”, with dNLR < 3 and normal LDH; an “intermediate candidate group”, with dNLR > 3 or LDH > upper limit of normal (ULN); and a “poor candidate group”, with dNLR > 3 and LDH > ULN.

Method: In this prospective study, we decided to evaluate the prognostic value of LIPI score in pre-treated patients with advanced NSCLC treated with ICI. We included patients treated with either Pembrolizumab or Pembrolizumab plus Docetaxel, between June 2016 to May 2019 in the National Institute of Cancer, in Mexico City. LIPI index was calculated for all subjects before treatment.

Results: We included 66 patients for analysis. Median age at diagnosis was 59 years (32-83). Predominant histology was adenocarcinoma (90%), 19 (28.8%) had EGFR mutations, 27 (40.9%) were male, 56 (54.5%) were current or former smokers and 76 (97%) had a performance status of 1 or less. Among 33 patients (50%) with PD-L1 data, 15 (45.4%) had PD-L1 at least 1% and 18 patients (54.5%) had negative results. All patients were treated with pembrolizumab, 40 patients (60.6%) as second line and 26 patients (39.4%) as the third line. The median number of cycles was 7 (1-39). Median PFS and OS were 5.1 (95% CI, 4.1-6.9) and 14.9 (95% CI, 9.6-NR) months, respectively. After calculating LIPI score, 48.4% were LIPI 0 (good prognosis), 31.8% LIPI 1 (intermediate prognosis), and 18.8% LIPI 2 (poor prognosis). Median OS for good, intermediate, and poor LIPI was NR (95% CI, 14.9- NR), 9.6 months (95% CI, 7.5-NR) and 5.9 months (95% CI, 2.6-16.9), respectively (p=0.001).

Conclusion: Our data are consistent with prior reports in patients with NSCLC treated with PD-1 inhibitors in second or later lines of treatment and strongly suggest LIPI index can be a useful tool to identify patients which are likely to benefit from treatment with ICI.

Keywords: LIPI, Immunotherapy, Non-small-cell lung cancer, Benefit

P2.25

Topic: Immunotherapy

Immunotherapy at Any Line of Treatment Improves Survival in Hispanic Patients with Advanced Metastatic Non-small Cell Lung Cancer (NSCLC) Compared with Chemotherapy (Quijote-CLiCaP)

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Background: A significant proportion of NSCLC patients present without targetable alterations, in such case immune checkpoint inhibitors (ICIs) have become the choice of therapy. Nonetheless, the Hispanic population is commonly underrepresented in the studies pertaining to these drugs. In this study we sought to compare survival outcomes of patients with advanced or metastatic NSCLC who received immunotherapy at first, second or beyond versus matched patients receiving standard chemotherapy.

Method: A retrospective multicenter international cohort study of 296 patients with unresectable/ metastatic NSCLC treated with immunotherapy either as first, second, third or fourth line was conducted. A matched comparison with a historical cohort of first line chemotherapy was conducted.

Results: Median age was 64 years (Range 34-90) and 40.2% were female patients. 91.2% of patients had an ECOG performance score ≤1. Immunotherapy as first line was given to 39 patients (13.7%), second line to 140 (48.8%), and as third line and beyond to 108 (37.6%). Median overall survival was 19.9 months (95% CI 14.5-22.7 months) and progression-free survival was 3.73 months (95% CI 2.8-4.2). Factors associated with increased survival included treatment as first-line (p < 0.001), type of response (p < 0.001) and PD-L1 status (p = 0.0039). Compared with the historical cohort, immunotherapy proved to be superior in terms of OS (p = 0.05) but not PFS (p = 0.2).
Conclusion: Patients who receive immune checkpoint inhibitors as part of their treatment for NSCLC have better OS compared with matched patients treated with standard chemotherapy, regardless of treatment line.

Keywords: Immunotherapy, Survival, PD-L1

P2.26

Topic: Immunotherapy

Budget Impact Analysis of Immunotherapy as Second-line Treatment of NSCLC at Mexico’s National Institute of Cancer

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Background: The highest mortality due to cancer worldwide corresponds to lung cancer (LC). Nowadays, novel therapeutic strategies such as Immune Checkpoint Inhibitors (ICI), have dramatically improved overall survival (OS), progression-free survival (PFS), and quality of life as the first or second line of treatment in patients with NSCLC. The objective of this study is to estimate the budget impact of immunotherapy as a second-line treatment for advanced NSCLC.

Method: A retrospective, descriptive analysis on resource use and a direct medical cost analysis was performed to assess the budget impact of 60 patients treated with immunotherapy as second-line treatment of NSCLC conducted at the National Institute of Cancerology (INCAN) in Mexico during 2016-2018. Resource utilisation data were collected by means of medical records. The costs associated with the total costs of treatment were estimated as a mean value with confidence intervals of 95% confidence by costing the elements of the treatment of the disease and adverse events, as well the frequency of consultations, hospital stays, and monitoring obtained in the records. Costs are presented in US dollars.

Results: The total mean monthly treatment cost was $1,649 (95% confidence interval [CI] = $1,484–$1,814), of which 93.8% represented immunotherapy costs, 5.4% drug application and monitoring, 0.8% adverse events treatment. We identified 30 potential patients per year candidates to receive immunotherapy as the second line. From which the expected costs of treatment will be $49,476 [CI] = $44,528–$57,392, of which $41,766 are immunotherapy costs, application and monitoring represent $2,400 and the rest for adverse events.

Conclusion: The therapeutic approach for the second-line treatment of patients with advanced NSCLC without actionable mutations has been revolutionized by the approval of new more efficacious drugs like pembrolizumab. Healthcare costs during immunotherapy treatment with pembrolizumab were largely attributed to anti-cancer therapy and less for adverse events. Pembrolizumab as second-line treatment of patients with advanced non-small-cell lung cancer, prolong overall survival, leading to fewer adverse events than chemotherapy.

Keywords: Pharmacoeconomy, Immunotherapy, Costs, Pembrolizumab
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