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 exogeneous 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
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 density corrections. The prescription was 45 Gy in 30 fractions of 1.5 Gy. Patients treated with multiple plans were evaluated using 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 compared with traditional planning. These differences are modest for 3D treatment plans but may be clinically relevant for the IMRT cohort (>5% deviation). Assessment of larger datasets may be warranted and consideration of twice-daily treatment regimens using higher dose per fraction may be worthy of future study. **Keywords:** Small Cell Lung Cancer, Radiation Dosimetry, Radiation Oncology, Heterogeneity Corrections

P1.10
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 = 38) of the included patients were female. Only 11% (n=7) of the patients had an ECOG performance score >1. Twenty-four patients (22.9%, 95%CI 14.8-30.9) presented with pulmonary or distant metastatic involvement with a median of 2 metastatic sites. Furthermore, 21.9 % of patients (n=23, 95%CI 13.9-29.8%) concurrently presented myasthenia gravis. Surgery was performed in 55 patients (52.3%, 95%CI 42.8 — 61.9%), comprising of 15 tumorectomies, 37 thymectomies and 5 biopsies achieving an R0 resection rate of 78% (95%CI 67.3-89.1%). Adjuvant treatment in the form of either chemotherapy, radiotherapy or both was offered to 3(5%), 7(12.7%) and 5(9%) patients, respectively. Disease progression was documented in 10 cases (9%, 95%CI3.9-15.1%) of which 6 (60%) were locoregional, 1 (10%) distant progression and 3 (30%) both locoregional and distant. Median overall survival (OS) was estimated at around 139.5 months (95%CI 86.1-NA). Cox regression indicated that OS was significantly improved by resection (139.5 vs 25.7 months, HR 4.17 [95%CI

12.6-17.8 months]). **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

P1.11
Multicenter Study of Histological Types Incidence and Pathological Features of Malignant Pleural Mesothelioma (MPM) in AR

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Background: The pathological diagnosis of MPM allows to identify different biological aggressiveness contributing to therapeutic decisions. OBJECTIVES: Analyze the morphological and immunohistochemical profile of a series of MPM and describe incidence of their histological types. Recognize the transitional pattern proposed as an aggressive clinical-pathological entity. **Method:** A retrospective and multicenter study was carried out by 8 Argentinian pathology laboratories. We review slides with MPM diagnosis (2009-2018) according the 2015 WHO criteria and iMig 2018 recommendations. We described: types, necrosis, nuclear atypia and mitosis/10HPF. The transitional pattern was considered extensive or focal. **Results:** Cases: 398. Men: 59%, female 41 %, median age: 66 (24-91). Samples: 78% surgical biopsies, 16.5% small biopsies; 2.5% from pleurectomies and 3% from pleuroneumonectomies. Histological types: 77% epithelioid (E-MPM), 12% biphasic, 10% sarcomatoid and 1% transitional. Patients ≥66 years had no E-MPM more than <66 (X^2: p<0.028).

Pathological features	EPITHELIOID (n=306)	NON-EPITHELIOID (n=92)	x^2
STROMA			
Desmoplasia	97	51	
Mixoid	38	3	p<0.001
Fibrotic	123	24	
NOS	47	14	
NECROSIS			
present	61	38	p<0.001
absent	245	54	
MITOSIS/10HPF			
0-1	193	29	p<0.001
2-4	81	48	
≥5	32	15	
NUCLEAR ATYPIA			
mild	91	8	p<0.001
moderate	166	59	
severe	49	25	
SCORE NUCLEAR			
Grade I	184	23	p<0.001
Grade II	98	61	
Grade III	24	8	

Predominant patterns of E-MPM were: 36.5% tubular/acinar, 33% solid, 12% trabecular, 11% papillary, 3% pleomorphic, 2% micropapillary, 2% adenomatoid and one case was deciduoid. 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 Calretinin 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

P1.12
Real World Characterization and Treatment Patterns of Patients with Thymic Carcinoma: Lessons from a Latin American Collaborative Study (CLICaP-LATimus)

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Background: Thymic carcinoma is a rare tumor that represents a clinical challenge, especially in resource limited settings. The objective of the present study was to characterize patients who presented this disease in Latin-America. **Method:** From 2014 until 2018, a multinational Latin-American cooperative retrospective cohort study was performed. Patients with histologically confirmed thymic carcinoma were included. Clinical, pathological and treatment variables were collected across 7 participating nations. **Results:** A total of 31 patients were included. Median age at diagnosis was 58 years old (34-69), 48% (n=15) of individuals were women with all but 2 patients (6.5%) achieving an ECOG performance score <2. All patients debuted with Stage IV disease; 24 patients (66%, [95%CI 62-92%]) as stage IVa and 7 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. 13 (41.9%, [95%CI 25-59%]) patients received preoperatory treatment consisting of chemotherapy (n=8, 42%) and chemoradiotherapy (n=5, 16%). Among these patients only 4 (12.9%) were subjected to surgery, two of which underwent a tumorectomy and 2 a thymectomy. 28 (90%, [95% CI 79.9-100%]) received palliative chemotherapy either with sunitinib (n=7, 25%) or cytotoxic agents. Median overall survival (OS) was reached at 20.2 months (95%CI 19-NA months). Patients who received preoperative treatment had a significantly prolonged OS (17.6 vs 26