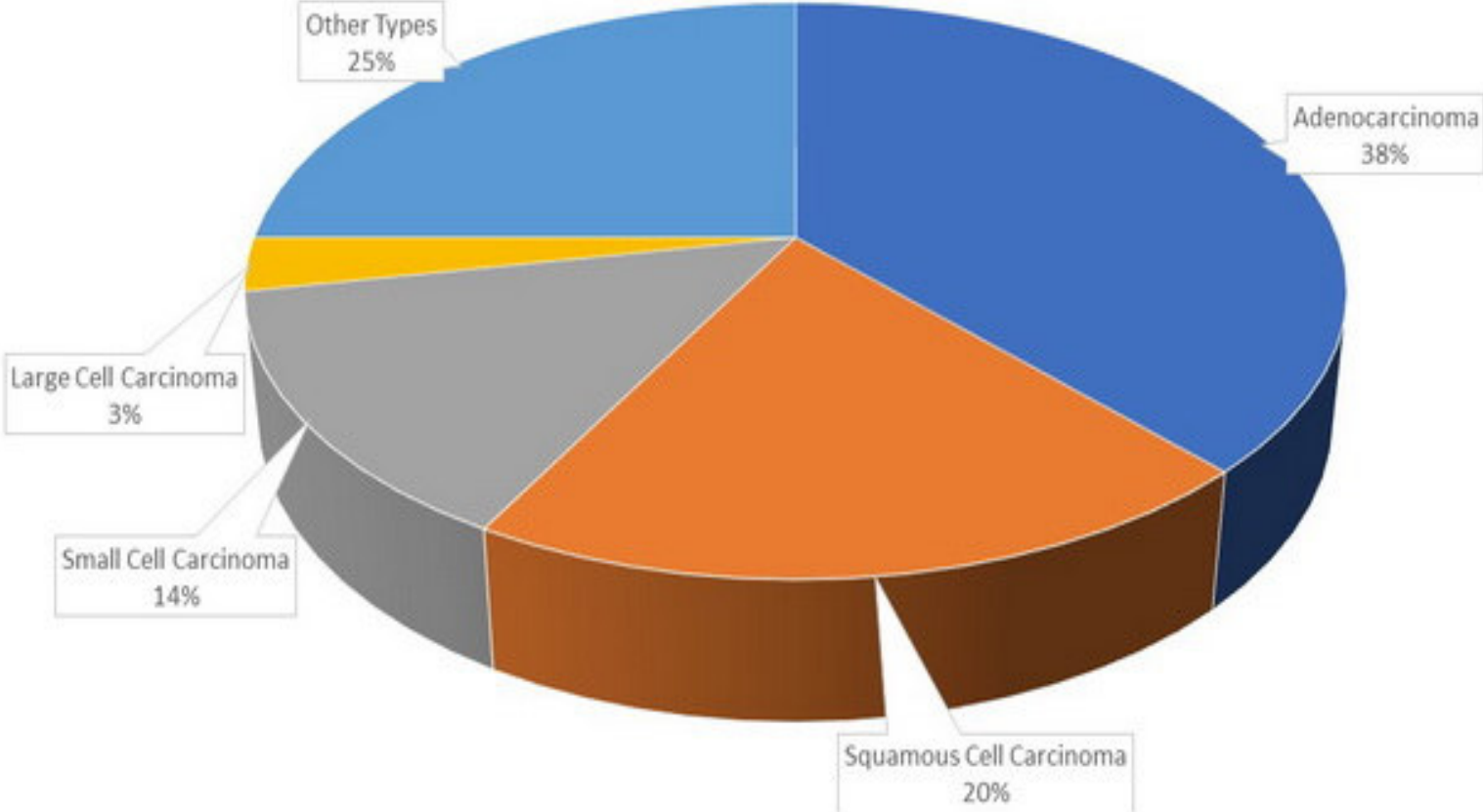# La diagnosi di neoplasia polmonare, il punto di vista dell'anatomo patologo, cosa dicono le linee guida, PDTA ASST Papa Giovanni XXIII
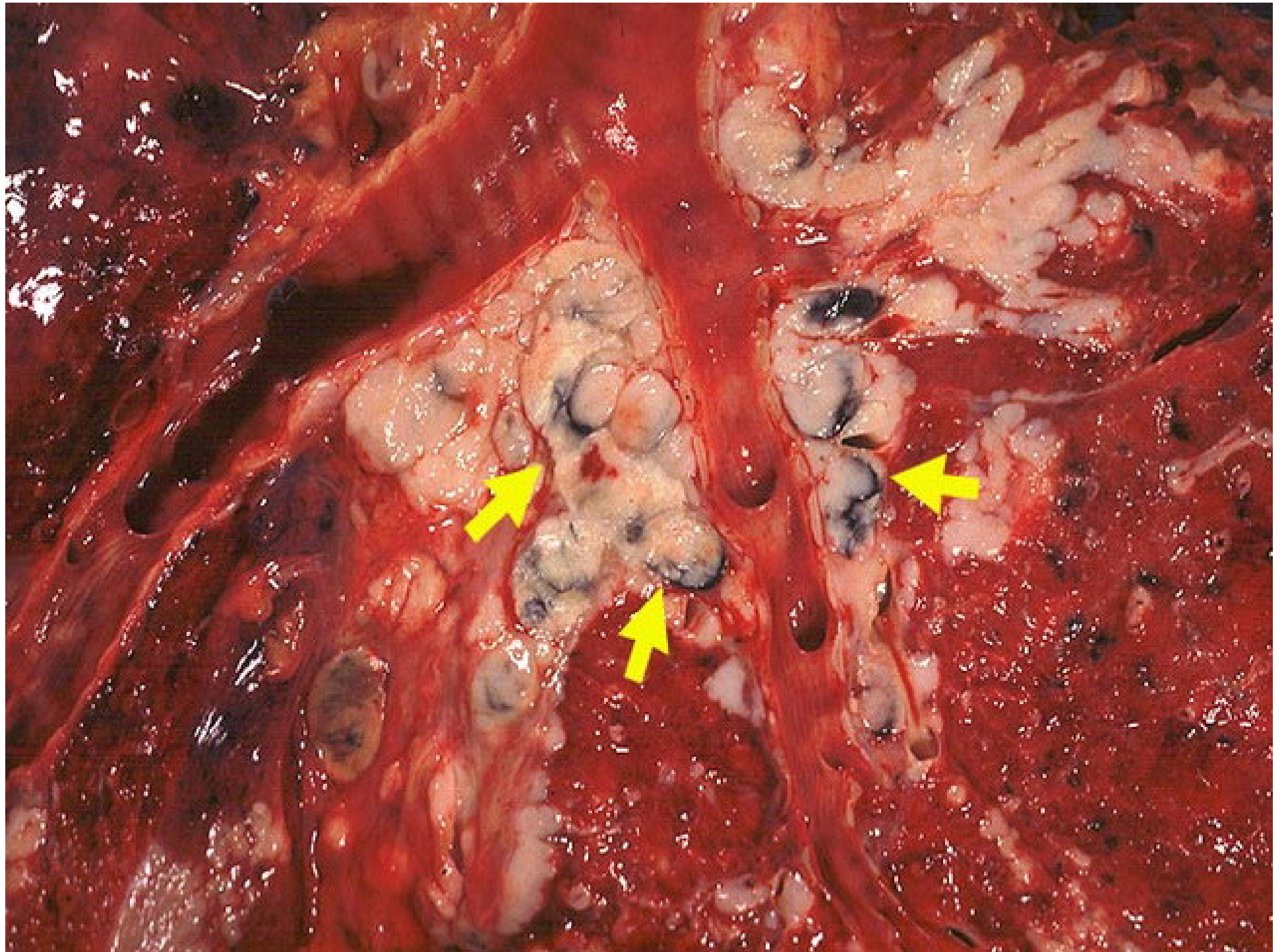
Andrea Gianatti
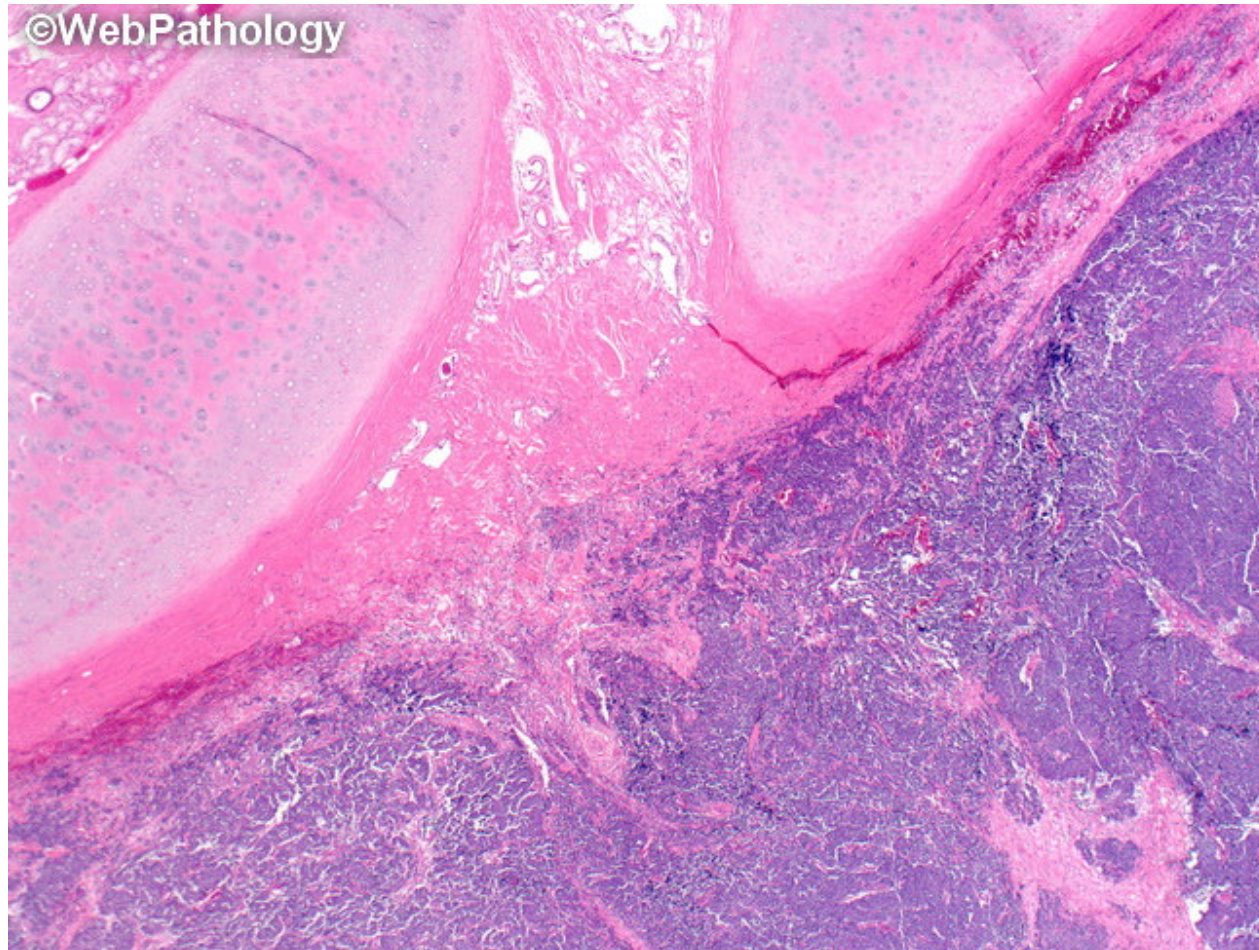
Anatomia Patologica ASST Papa Giovanni XXIII

Bergamo, 7 giugno 2019

Lung Cancer : Histologic Types

Other Types
25%

Adenocarcinoma
38%

Large Cell Carcinoma
3%

Small Cell Carcinoma
14%

Squamous Cell Carcinoma
20%

Small cell carcinoma

Supplement | 02 January 2019
USCAP Long Course 2018:
The limited sample -- doing more with less

- In this era of minimally-invasive procedures for diagnosis, prognosis and treatment decisions, pathologists are asked to make more specific diagnoses from smaller samples.

- Publication of this supplement is sponsored by United States & Canadian Academy of Pathology (USCAP).
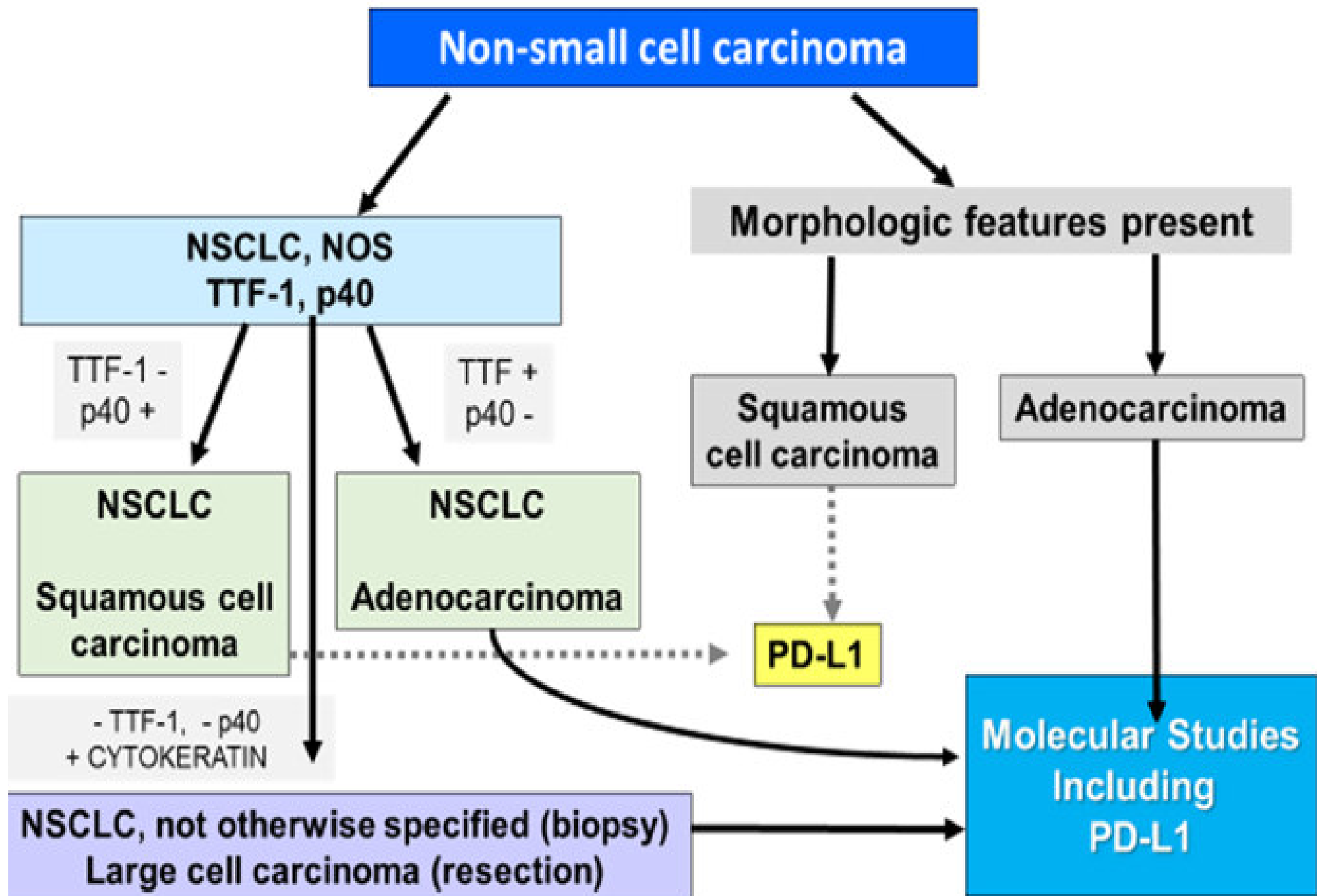
The diagnosis of non-small cell lung cancer in the molecular era.

J Brainard, C Farver

Determining Tumor Type in Small Biopsy Specimens

Normal lung tissue

Endoscopic Transbronchial biopsy
    EBUS-TBNA
    TBNA

Transthoracic biopsy
    CT-guided
    Ultrasound-guided

Tumor

Squamous cell carcinoma

Adenocarcinoma

Small biopsy specimens

ADC

SqCC

No clear subtype on H&E

Adequate for molecular testing?

Ancillary panel for subclassification

Markers For ADC	Markers For SqCC	Markers For small cell lung carcinoma
	CK 5/6	CD56
TTF	P63	Synaptophysin
Napsin A	P40	Chromogranin
		Ki67

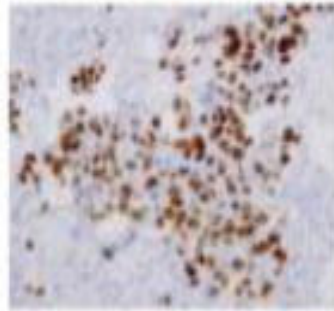**Molecular characteristics of the tumor**
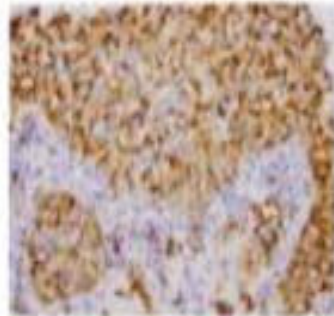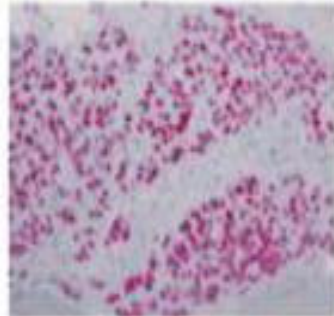
TTF-1
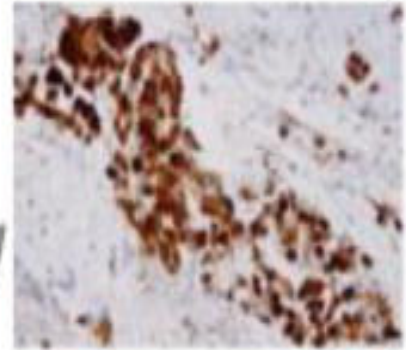(nuclear staining)

Napsin A
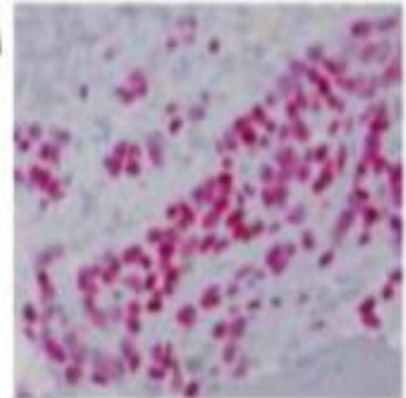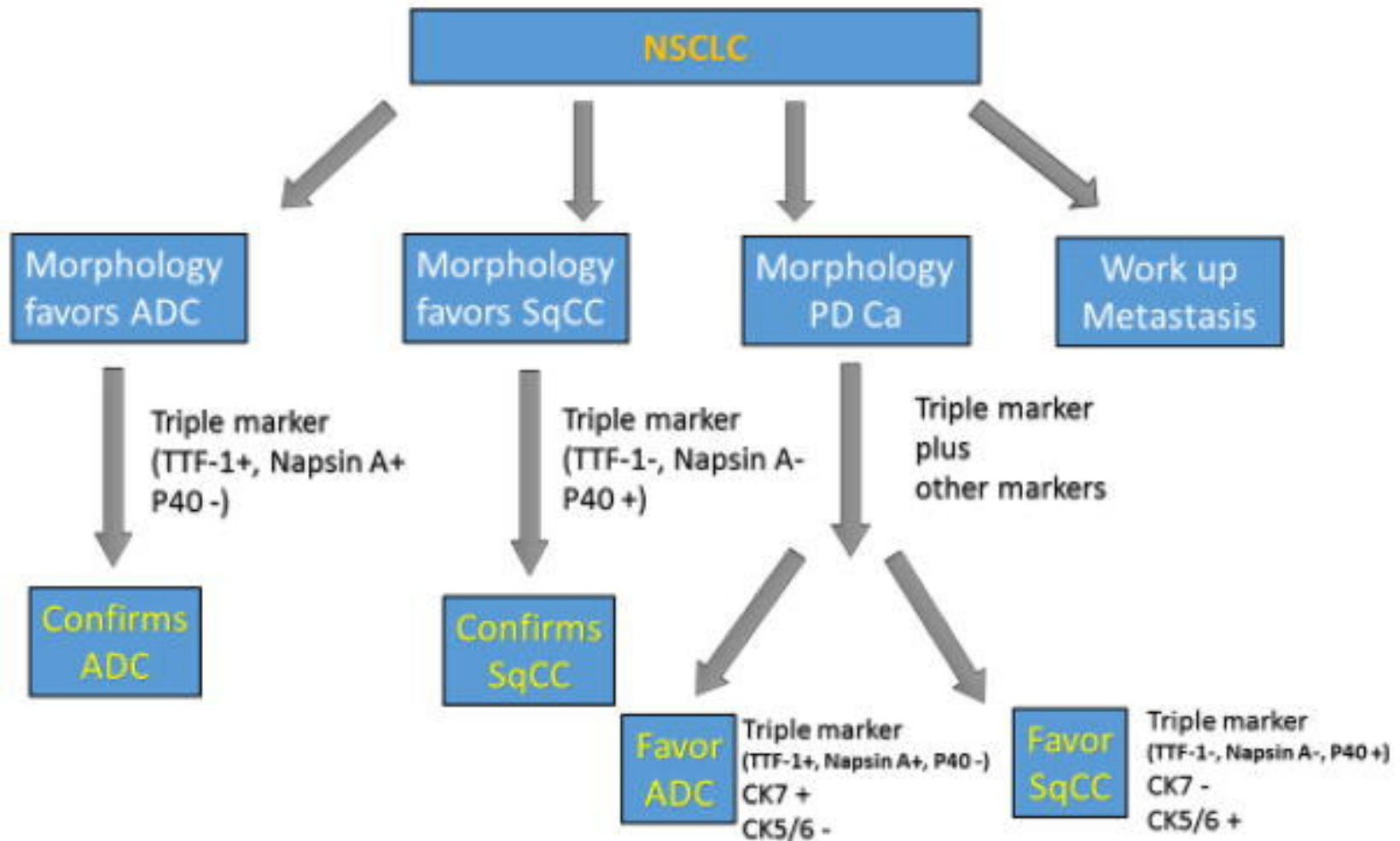(cytoplasmic staining)

P40
(nuclear staining)

Combine three markers into a single marker (Triple marker)

Lung adenocarcinoma

Lung squamous cell carcinoma

Bironzo P, Di Maio M. A review of guidelines for lung cancer. J Thorac Dis 2018;10(Suppl 13):S1556-S1563.

- …We reviewed the recommendations about the use of these immune checkpoint inhibitors in clinical practice guidelines issued by three scientific societies [European Society of Medical Oncology (**ESMO**); American Society of Clinical Oncology (**ASCO**); Italian Association of Medical Oncology (**AIOM**)] and one not-for-profit U.S. alliance [National Comprehensive Cancer Network (**NCCN**)]

- … Clinical practice guidelines are useful tools that assist clinicians treating lung cancer patients with immune checkpoint inhibitors. Their use would improve homogeneity and appropriateness, even in this rapidly evolving field.

Current WHO guidelines and the critical role of immunohistochemical markers in the subclassification of non-small cell lung carcinoma (NSCLC): Moving from targeted therapy to immunotherapy.

Lais Osmani, Frederic Askin, Edward Gabrielson and Qing Kay Li

Recent large scale genomic studies from the Clinical Lung Cancer Genome Project have identified different driver gene mutations in the subtypes of non-small cell lung carcinoma (NSCLC).

These findings not only lead to remarkable progress in targeted therapies for lung cancer patients, but also provide fundamental knowledge for the subclassification of NSCLC.

More recently, the advancement and clinical application of immunotherapy have reinforced the need for the accurate subclassification of NSCLC.

In 2015, the World Health Organization (WHO) and the International Association for the Study of Lung Cancer (IASLC) updated their guidelines for the subclassification of lung cancers.

GUIDELINES «for Pathologist»

- The subclassification of NSCLC.
- The critical role of molecular characterization of tumors for targeted therapy.
- The unique terminology for subclassifying NSCLC using small biopsy specimens.
- The utility of IHC biomarkers in the accurate diagnosis and subclassification of lung cancer.

TEST

L'uso dell' immunoistochimica permette una migliore definizione diagnostica del carcinoma del polmone; quale delle seguenti affermazioni è corretta?

- 1. E' una metodica ancillare di difficile applicazione nella diagnostica routinaria.

- 2. E' controindicata nella classificazione del carcinoma non a piccole cellule del polmone.

- 3. E' utile solo nella classificazione del carcinoma a piccole cellule.

- 4. Nessuna delle precedenti.

Inamura K (2017) Lung Cancer: Understanding Its Molecular Pathology and the 2015 WHO Classification. *Front. Oncol.* 7:193.

- Close associations exist between histology/morphology and genetic profiles.
- **Driver Genetic Alterations and Histology of Lung Adenocarcinoma**

- *EGFR* mutation is one of the most common driver mutations in lung adenocarcinoma, and *EGFR*-mutated adenocarcinoma is characterized by East-Asian ethnicity, female gender, and non/light-smoking history . Pathologically, *EGFR*-mutated lung adenocarcinomas typically show nuclear TTF-1 (NKX2-1) immunostaining and a hobnail cell type. Adenocarcinomas with a micropapillary pattern have a higher frequency of *EGFR* mutations than adenocarcinomas without this pattern.

- *ALK*-rearranged adenocarcinoma comprises 4–5% of adenocarcinomas. *ROS1*- and *RET*-rearranged adenocarcinoma each comprises approximately 1%. *ALK*-rearranged adenocarcinoma is characterized by a TTF-1 cell lineage, an acinar structure with mucin/signet-ring cell pattern, non-/light-smoking history, and young onset . *ROS1*- and *RET*-rearranged adenocarcinomas have a similar histology to *ALK*-rearranged adenocarcinoma, such as mucinous cribriform pattern or solid signet-ring cell pattern .

TEST

Esiste una correlazione tra la classificazione morfologica ed il profilo molecolare del carcinoma del polmone?

- 1. Nessuna correlazione.

- 2. Esistono correlazioni sopratutto in particolari istotipi di adenocarcinoma.

- 3. Esiste correlazione unicamente per il carcinoma a cellule squamose.

- 4. Esiste una debole correlazione con il carcinoma a piccole cellule.

Quali linee guida per patologo?

- Non esistono indicazioni stringenti nella diagnostica anatomo-patologica.
- Variabilità estrema nella fase preanalitica della processazione dei prelievi.
- Autonomia organizzativa del flusso di lavoro all'interno dei laboratori di anatomia patologica.
- Assenza di precise indicazioni in termini di piattaforme diagnostiche.
- Cosa facciamo a Bergamo?

The CAP Cancer Reporting Protocols provide guidelines for collecting the essential data elements for complete reporting of malignant tumors and optimal patient care.

- Template for Reporting Results of Biomarker Testing of Specimens From Patients With Non-Small Cell Carcinoma of the Lung.

- Protocol for the Examination of Specimens From Patients With Primary Non-Small Cell Carcinoma, Small Cell Carcinoma, or Carcinoid Tumor of the Lung.

Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors.

Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology

Upcoming CAP Guidelines
Collection and Handling of Thoracic Small Biopsy and Cytology Specimens for Ancillary Studies

- With the advances in minimally invasive sampling techniques, laboratories can perform multiple ancillary studies on small biopsy and cytology specimens to help in the diagnosis and management of pulmonary pathology. To provide treating physicians with valuable diagnostic, predictive, and prognostic information from small biopsy and cytology specimens, it is critical to establish **evidence-based recommendations for the appropriate collection, handling, and triage for relevant ancillary tests**.

PDTA patologico a Bergamo?

- Gestione delle richieste di biomarcatori da parte dei patologi.

- Ottima, ma migliorabile interazione multidisciplinare per definire il quadro clinico dei pazienti.

- Adeguamento continuo di PDTA rispetto all'introduzione di nuovi farmaci.

- Necessità di coperture finanziarie per test di ricerca di biomarcatori.

TO ROSE OR NOT TO ROSE?

Bibliografia

- **Current WHO Guidelines and the Critical Role of Immunohistochemical Markers in the Subclassification of Non-Small Cell Lung Carcinoma (NSCLC). Moving from Targeted Therapy to Immunotherapy**

  Lais Osmani, MD, Frederic Askin, MD, Edward Gabrielson, MD, and Qing Kay Li, MD, PhD.

- **The diagnosis of non-small cell lung cancer in the molecular era.**

  Jennifer Brainard, Carol Farver

  United States & Canadian Academy of Pathology 2019

- **Non small cell lung carcinoma: diagnostic difficulties in small biopsies and cytological specimens**

  Lukas Bubendorf, Sylvie Lantuejoul, Adrianus J. de Langen and

  Erik Thunnissen.

  Number 2 in the Series "Pathology for the clinician"