Original Research

TISSUE BIOPSY AND PATHOLOGICAL DIAGNOSIS IN SCLC

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ABSTRACT

Lung cancer remains the most common cancer type and the leading cause of cancer mortality globally, and Small Cell Lung Cancer (SCLC) constitutes 13-15% of all such cases (Rudin et al., 2021). SCLC is an undifferentiated epithelial tumor ith neuroendocrine features that grows rapidly, metastasizes early, and has a poor prognosis. Although patients respond to chemotherapy at initial diagnoses, many patients relapse, and the five-year survival rate is below 7% (Keog et al., 2022). Being an aggressive form of cancer, there is a need to ensure that the illness is diagnosed early and accurately in order to provide corresponding treatment. An accurate pathological diagnosis is crucial for achieving an initial differentiation between SCLC and Non-Small Cell Lung Cancer (NSCLC) and determining the subsequent management. Chromogranin A, synaptophysin, and CD 56 are Immunohistochemistry (IHC) markers for recognizing SCLC with neuroendocrine features. However, these markers are not specific enough; thus, newer markers that include INSMA-associated protein 1 (INSM1) and Delta-like protein 3 (DLL3) are more specific for diagnosis and have the potential for targeted therapy. Despite restricted availability, tissue biopsy remains the most definitive method for SCLC diagnosis. However, other advanced tools such as EBUS-TBNA and CT-guided percutaneous needle biopsy are also used in today's practice. However, in more recent molecular categorization, SCLC has been further distinguished from NSCLC by other specific molecular markers that can be targeted for therapy. Immunohistochemistry, biopsies, and molecular markers can improve the identification of SCLC and assist with tailored therapy.

ROLE OF NOVEL IMMUNOHISTOCHEMICAL (IHC) MARKERS IN SCLC DIAGNOSIS

Traditional IHC Markers: Small cell lung cancer is a high-grade neuroendocrine carcinoma, the identification of which is based on IHC markers from NSCLC. Some well-established neuroendocrine biomarkers diagnosing SCLC include chromogranin A, synaptophysin, and Cluster of Differentiation 56 (CD56). Neuron-specific enolase is positive in 30% to 40% of SCLC patients, while chromogranin A is positive in 70% to 80% of SCLC patients; both are specific to neuroendocrine cancer (Rao et al., 2021). For example, synaptophysin, a vesicle-associated protein, is slightly more sensitive (80-90%) but less specific than chromogranin B due to its expression in select forms of NSCLC (Qu et al., 2022).

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CD56, a natural cell adhesion molecule (NCAM) combined with CD45, has an 85–95% sensitivity but lacks specificity because it is found in hematologic malignancies (Keogh et al., 2022). Although these markers have been essential in SCLC diagnosis, their drawbacks have prompted researchers to look for new IHC markers that offer enhanced specificity and diagnostic value.

Novel IHC Markers

Insulinoma-Associated Protein 1 (INSM1): Several neuroendocrine markers have been identified; however, INSM1 has been characterized to have a high sensitivity of between 95-98% and specificity of between 90-95% in diagnosing SCLC (Qu et al., 2022). In contrast to other conventional markers, INSM1 targets neuroendocrine tumor tissue only. It is more precise in cases wherein routine examinations reveal low sensitivity and specificity, such as chromogranin A and synaptophysin (Baine et al., 2022). Moreover, unlike other cytoplasmic antibodies like chromogranin A and synaptophysin, INSM1 immunolocalizes to the nucleus, aiding its interpretation (Raskova Kafkova et al., 2024). This is so because it is detectable in Limited-Stage Small Cell Lung Cancer (LL SCLC), and recent studies have established that INSM1 remains positive in

cases diagnosed with poorly differentiated SCLC (Raso et al., 2021).

Delta-Like Protein 3 (DLL3): DLL3, the transmembrane protein of the Notch receptor, is a novel marker somewhat selective for SCLC. On the other hand, DLL3 has been implicated in SCLC and is not detectable in normal lung tissue (Keogh et al., 2022). These studies have also reported upregulation of DLL3 in 80-90% of SCLC and immunostaining of membranous DLL3 in approximately seven out of 10 SCLC tumors (Rao et al., 2021). Therefore, DLL3 has been verified as a biomarker and target for ADC with antibody-drug conjugates (Baine et al., 2022).

Molecular Subtyping & Transcription Factors: More recent clinical investigations segregated SCLC into four molecular subtypes, which are based on the expression levels of four transcription factors, namely ASCL1, NEUROD1, POU2F3, and YAP1 (Qu et al., 2022). The SCLC-A subtype accounts for roughly 78% of cases and exhibits neuroendocrine features and chemosensitivity (Qu et al., 2022). SCLC-N is a subgroup that can be identified in about 6% of neuronal differentiation cases and has an unfavorable prognosis (Keogh et al., 2022). SCLC-P constitutes only 7% of cases, does not exhibit neuroendocrine features, and is chemoresistant (Baine et al., 2022). Last, the YAP1-dominant subtype, also known as SCLC-I, accounts for about 2.8% of patients presenting with an inflamed tumor microenvironment and is susceptible to immune therapy (Qu et al., 2022). Such classifications offer improved diagnostic outcomes and discern discriminant treatment for each regimen.

Table 1: Comparison of IHC Markers

Marker	Sensitivity (%)	Specificity (%)	Clinical Utility	Reference
Chromogranin A	70–80	85	Conventional neuroendocrine marker	Rao et al., 2021
Synaptophysin	80–90	83	Moderate specificity	Raso et al., 2021
CD56	85–95	78	High sensitivity, low specificity	Baine et al., 2022
INSM1	95–98	90–95	Particular neuroendocrine marker	Qu et al., 2022
DLL3	80–90	92–98	Diagnostic and therapeutic target	Keogh et al., 2022

However, SCLC is difficult to diagnose using routine histology, and newer markers like INSM1 and DLL3 have enhanced the diagnosis of SCLC, mainly when arising in the background of NSCLC. Further studies should be conducted on refining these markers and identifying the optimum scoring scales to enhance the diagnosis and treatment outcomes (Penault-Llorca et al., 2022).

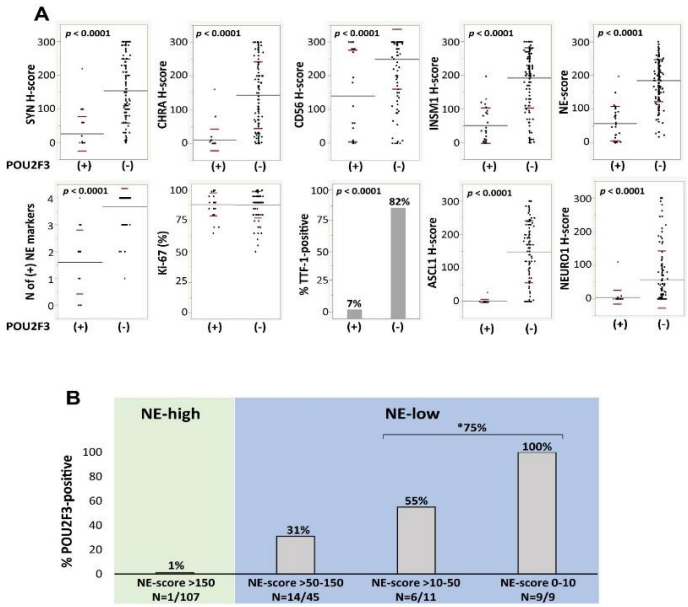

Figure 1. Immunohistochemical Characteristics of Sclc-P.

FIGs S2A–S2F: Dot plots showing the distribution of the indicated markers in POU2F3-positive (n = 30) and POU2F3-negative SCLC (n = 142 for all markers except for Ki-67 = 127 patients, TTF-1 = 122 patients). The mean and SD for each comparison are plotted using the gray line and the shaded red area, respectively. (B) Bar graph showing the breakdown of SCLC groups according to NE marker labeling by scoring NE-score (average H-score of conventional NE markers—synaptophysin, chromogranin A, CD56, INSM1) and percentage of POU2F3 positivity in all NE EL/N group 75%. CHRA, chromogranin A; NE, neuroendocrine; SYN, synaptophysin

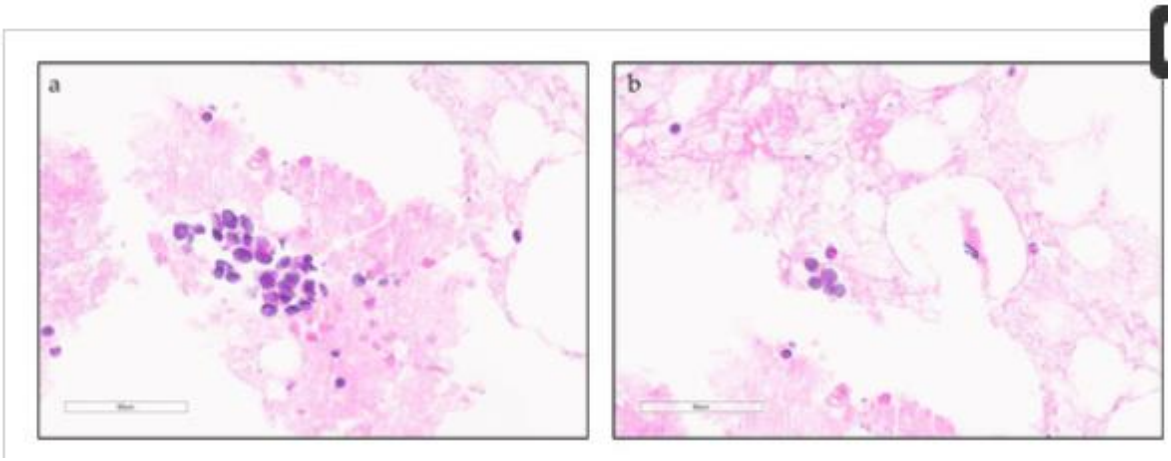

Figure 2. Histomorphological Features of Small Cell Lung Carcinoma (SCLC).

(a-b) Aspirates of SCLC; higher magnification x400. Small round to oval nuclei with inconspicuous nucleoli, low N/C ratio, and fine chromatin (arrow).

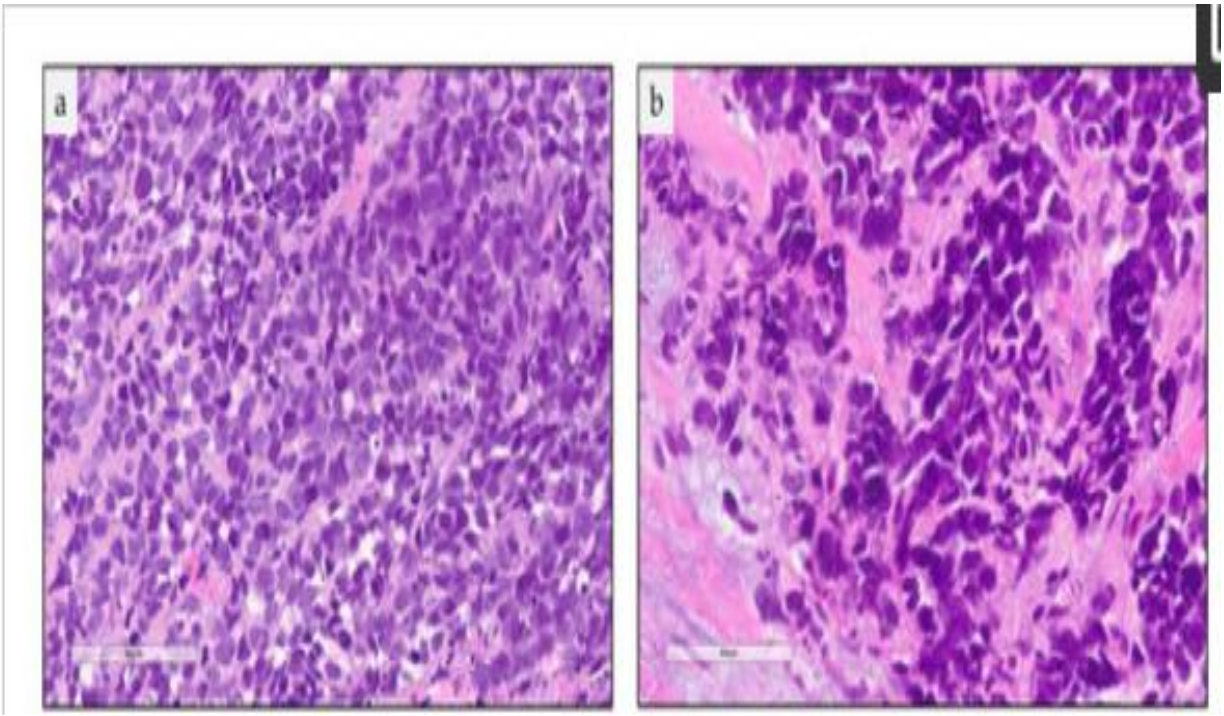

Figure 3. Small Cell Lung Carcinoma (SCLC) Cytological and Histological Characteristics.

A high-power field view of a formalin-fixed, paraffin-embedded tissue section stained with H&E is demonstrated in (a). sheets of small cells with scant cytoplasm and nuclear molding, and (b). Densely packed small nests of cells and intratumor necroses

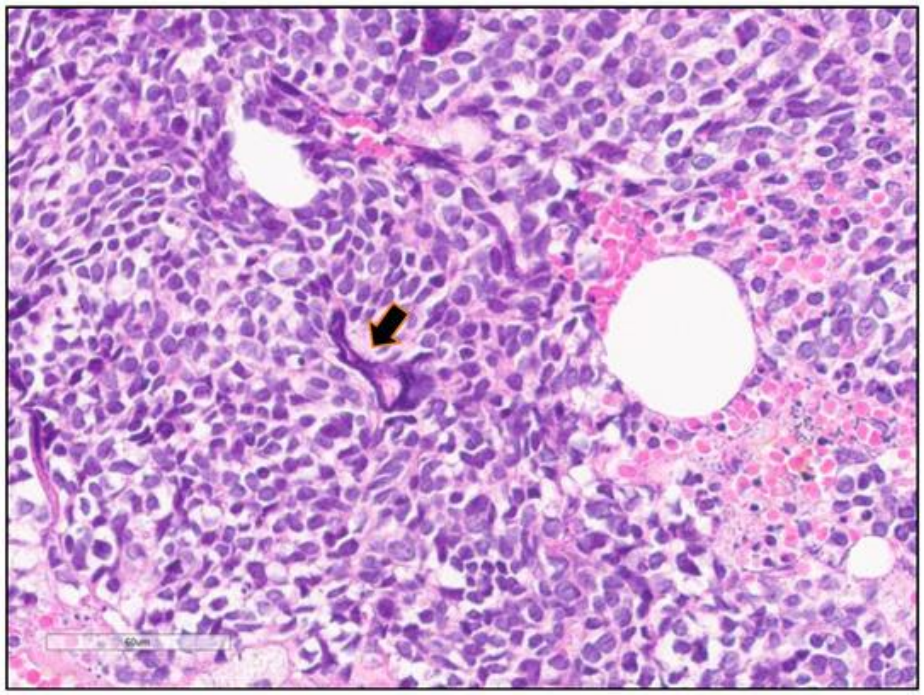

Figure 4: Azzopardi Phenomenon.

These images at higher magnification depict Small cell lung carcinoma (SCLC) with basophilic nuclear debris encrustation of the blood vessel wall marked with an arrow.

SENSITIVITY AND SPECIFICITY COMPARISON OF IMAGE-GUIDED BIOPSY TECHNIQUES

Surgical biopsy is a crucial step in managing SCLC because it helps confirm the histological type of the malignancy and the molecular subtyping. Current biopsy techniques include Endobronchial ultrasound-guided transbronchial needle aspiration(EBUS-TBNA), Computed tomography-guided percutaneous needle biopsy, and conventional bronchoscopy(Lahiri et al., 2023). The technique used can vary depending on the tumor's location and size, the patient's condition, and the surgeon's experience since the characteristics of the obtained material (specificity and sensitivity) and the rate of complications may differ in each case.

Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA): EBUS-TBNA is less invasive than mediastinoscopy and permits the sampling of mediastinal and hilar lymph nodes under ultrasound guidance. They are handy for peripheral lung masses and lymph nodes where other biopsy techniques would be more injurious (Kiani et al., 2024). The sensitivity and specificity of EBUS-TBNA is 89-94% for the diagnosis and staging of lung cancer and for confirmation of histological subtype of SCLC (Park et al., 2024). Further, relatively few complications have been reported for EBUS-TBNA, including pneumothorax under 2% and hemoptysis in about 2.6% of the patients (Park et al., 2024). Additionally, the combination with ROSE increases the diagnostic yield since it assesses sample adequacy during the procedure and reduces the need for additional biopsies (Graham et al., 2024).

CT-Guided Percutaneous Needle Biopsy: Computed tomography (CT)-guided percutaneous needle biopsy is one of the most precise approaches to diagnosing peripheral lung masses. It affords direct tissue access under imaging guidance, thus enabling accurate sampling. Meta-analysis has revealed that CT-guided biopsy has a sensitivity of 90 – 97% and a specificity of nearly 100%, making it one of the most accurate biopsy techniques (Baratella et al., 2022). However, this method is accompanied by the risk of complications, in particular pneumothorax, which is present in up to 45% of cases, and pulmonary hemorrhage, which is frequent in 4-27% of patients (Constantinescu et al., 2024). However, CT-guided biopsy is still considered the gold standard for peripheral lung lesions, mainly when bronchoscopy methods cannot be used. These risks can be presumed by implementing early measures, including reducing needle passes and ensuring the patient is in the correct position (Saggiante et al., 2024).

Conventional Bronchoscopy: Bronchoscopy as a conventional modality has been one of the most common approaches to assessing centrally located lung malignancies. However, diagnostic accuracy is relatively low compared to EBUS-TBNA and CT-guided biopsy. Its sensitivity ranges from 60% to 70%, with a specificity of 85-90%; therefore, it is

less reliable for diagnosing small or peripheral lung masses (Liu et al., 2022). Newer techniques like robotic-assisted bronchoscopy have also provided high diagnostic yields, especially for small pulmonary nodules. A study by Hammad Altaq et al. (2023) showed the diagnostic yield of robotic-assisted bronchoscopy to be 88.1 % and zero incidences of pneumothorax or excessive bleeding; therefore, robotic-assisted bronchoscopy can be considered an alternative to biopsy.

Table 2: Comparison of Biopsy Methods

Biopsy Method	Sensitivity (%)	Specificity (%)	Complication Rate (%)	Reference
EBUS-TBNA	89–94	91–98	<2 (pneumothorax), 2.6 (hemoptysis)	Kiani et al., 2024; Park et al., 2024
CT-Guided Biopsy	90–97	~100	12–45 (pneumothorax), 4–27 (hemorrhage)	Baratella et al., 2022; Constantinescu et al., 2024
Conventional Bronchoscopy	60–70	85–90	Minimal	Liu et al., 2022

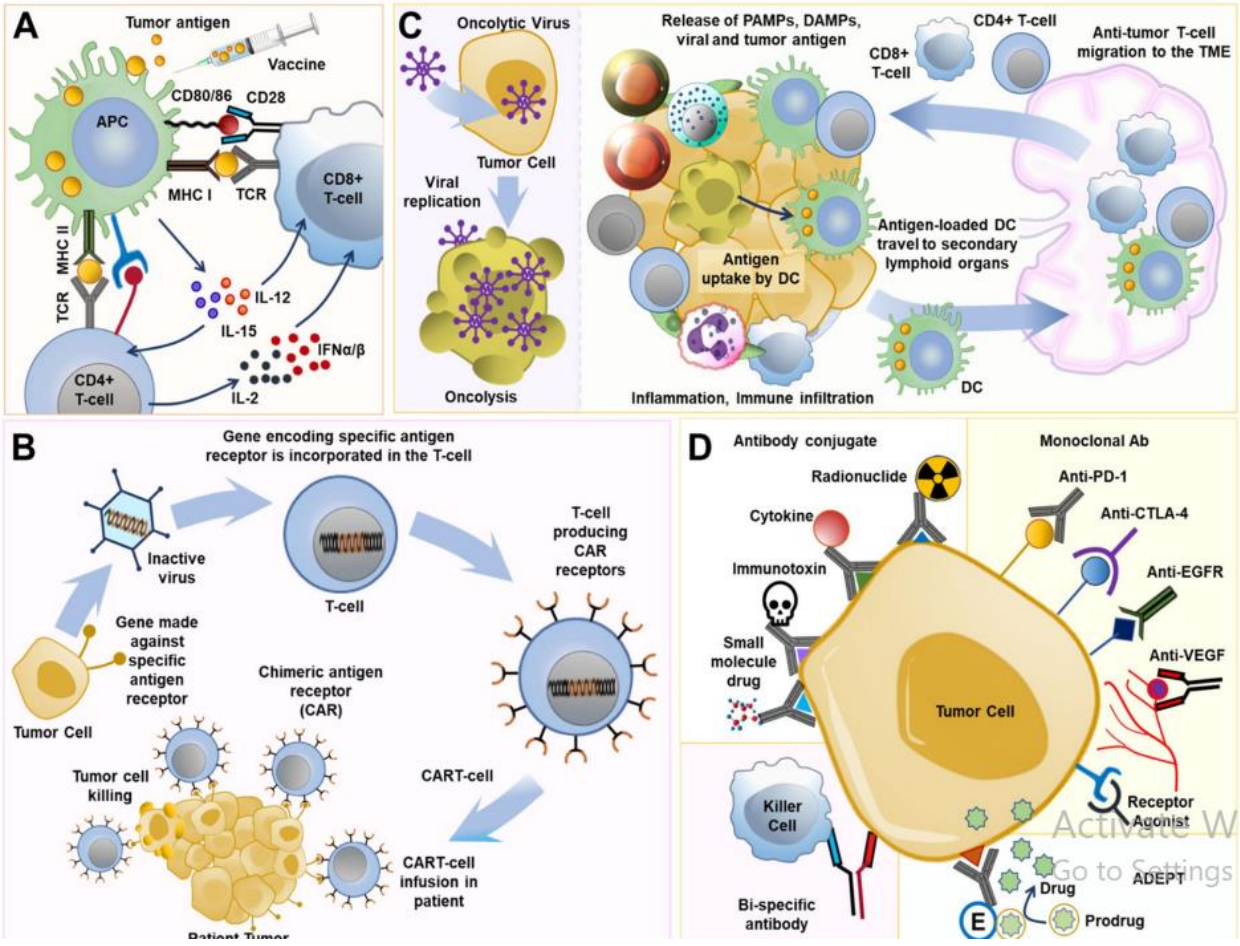

Fig. 5 Different Aspects of Lung Cancer Immunotherapy.

Q: What health issue do you believe can be solved through nanotechnology? A: Lung cancer immunotherapy by utilizing a tumor-specific vaccine against cancer. B: Donor or patient T cells are first harvested asexually ex vivo, after which Chimeric Antigen Receptor (CAR) receptors are transduced before growing them in large numbers in the laboratory to treat cancer. The CAR T-cells are then infused back into the patient, attacking the tumor. C: Oncolytic virus and lung cancer cell oncolysis. D: Monoclonal antibodies (mAbs) might help treat lung cancer since they can attack a specific segment of the cancer cell.

MOLECULAR DIFFERENTIATION BETWEEN SCLC AND NSCLC

SCLC and NSCLC are two subtypes of lung cancer that differ in molecular profiles, disease presentation and progression, and therapeutic management strategies. SCLC is rapidly growing, rapidly metastasizing, and has fewer treatment options. At the same time, NSCLC, which is the most frequent form of lung cancer and accounts for 85% of cases, progresses more slowly and has more therapeutic applications (Liang et al., 2022). There are two main subtypes of ovarian cancer: the serous and the non-serous, which have been shown to have distinct molecular profiles that affect the diagnostic approach and treatment plans.

Key Genetic & Molecular Markers Distinguishing SCLC from NSCLC: SCLC is characterized by the inactivation of two tumor suppressor genes, TP53 and RB1, with a more than 90% frequency. These contribute to the increased proliferation and elevated mutational load in SCLC (Rudin et al., 2021). Specifically, TP53 alterations are detected in ~50% of NSCLC, while RB1 alterations are rare in NSCLC, which points to a primary molecular difference between them (Metovic et al., 2021). Another striking difference is that Myelocytomatosis oncogene (MYC) amplifications in SCLC contribute to tumor growth and resistance to treatment. MYC amplification is found in around 20% of SCLC cases and is accompanied by more aggressive clinicopathological characteristics and poor prognosis rates (Simbolo et al., 2022). MYC amplifications are less prevalent in NSCLC and are more commonly linked to squamous rather than adenocarcinomas (Ding et al., 2022). Most SCLC patients had the primary tumor arising from oncogenic alterations such as Kirsten rat sarcoma viral oncogene homolog (KRAS), Epidermal Growth Factor Receptor (EGFR), or Anaplastic Lymphoma Kinase (ALK), which are seldom seen in SCLC. KRAS is mutated in about 30% of NSCLCs, mainly in adenocarcinomas; these mutations affect n in SCLC, and the presence or absence of KRAS mutation can help to distinguish between the two subtypes.

The Role of Next-Generation Sequencing (NGS) in SCLC Dsignaling Paths and Result in Tumor Development (Harada Et Al., 2023). Conversely, KRAS Mutations are Less Commoiagnosis: These changes in lung cancer can now be described more accurately thanks to emerging NGS methods. In the case of SCLC, NGS has shown that TP53 is commonly mutated, as is RB1, which are various therapeutic targets, for example, NOTCH, involved in differentiation and immune escape (Megyesfalvi et al., 2023). In NSCLC, for example, NGS has facilitated the identification of biomarkers such as EGFR, ALK, and ROS1 that are essential for TKI therapy (Harada et al., 2023). Furthermore, the advances in using buccal swabs and ctDNA liquid biopsy approaches have similarly improved the diagnosis and monitoring of NSCLC mutations (Padinharayil et al., 2023).

Impact of Molecular Differentiation on Targeted Therapy Development: SCLC also differs from NSCLC in its pathologic features, and these differences also apply to intervention sites. These results suggest that targeted drugs like EGFR inhibitors (samosa oamingosinib), ALK inhibitors (alectinib), and immunomodulatory drugs, particularly immunostimulant agents, could be helpful in NSCLC patients (Harada et al., 2023).

Impact of Molecular Differentiation on Targeted Therapy Development: These differences define SCLC and NSCLC at a molecular level and guide the treatment plan. For example, NSCLC cooperated in targeted therapies with osimertinib in EGFR and alectinib in ALK, Immune checkpoint inhibitors (Harada et al., 2023). SCLC is missing actionable mutations compared to NSCLC, limiting the available treatment options. Nonetheless, chemotherapy has continuously been the go-to treatment method, with initial platinum-etoposide combinations yielding reliable results, but later, cancer tends to become resistant (Rudin et al., 2021). New molecular targeted agents and recent immune checkpoint inhibitors, atezolizumab and durvalumab, have been authorized for extensive-stage SCLC treatment, creating a significant step forward in immunotherapy (Ding et al., 2022). The targeted molecular markers discovered, most notably DLL3, an SCLC-specific cell surface protein, have given hope for treatment planning (Guan et al., 2022). Rovalpituzumab tesirine, a DLL3-targeting ADC, has demonstrated promising activity but had safety issues in early trials (Simbolo et al., 2022). Future studies targeting molecularly well-defined SCLC subtypes could unlock more individualized approaches to management.

Table 3: Comparison of Molecular Markers in SCLC vs. NSCLC

Molecular Marker	SCLC	NSCLC	Reference
TP53 Mutation	>90%	~50%	Rudin et al., 2021
RB1 Mutation	>90%	Rare	Metovic et al., 2021
MYC Amplification	~20%	Less frequent	Simbolo et al., 2022
KRAS Mutation	Rare	~30% (adenocarcinoma)	Harada et al., 2023
EGFR Mutation	Absent	~15% (adenocarcinoma)	Padinharayil et al., 2023

ALK Rearrangement	Absent	~5%	Liang et al., 2022
DLL3 Expression	Present (~80%)	Absent	Ding et al., 2022
High Tumor Mutation Burden	Yes	Variable	Megyesfalvi et al., 2023

The genetic difference between SCLC and NSCLC proves the effectiveness of creating an accurate classification for the appropriate line of treatment. While NSCLC has made progress with multiple target therapies for precision medicine, SCLC still largely relies on conventional chemotherapy and immunotherapy due to the difference in genetic background (Senet al., 2024). With time, the discovery of a large number of targets in SCLC may lead to improved therapeutic options and better prospects for patients with this relentlessly invasive cancer.

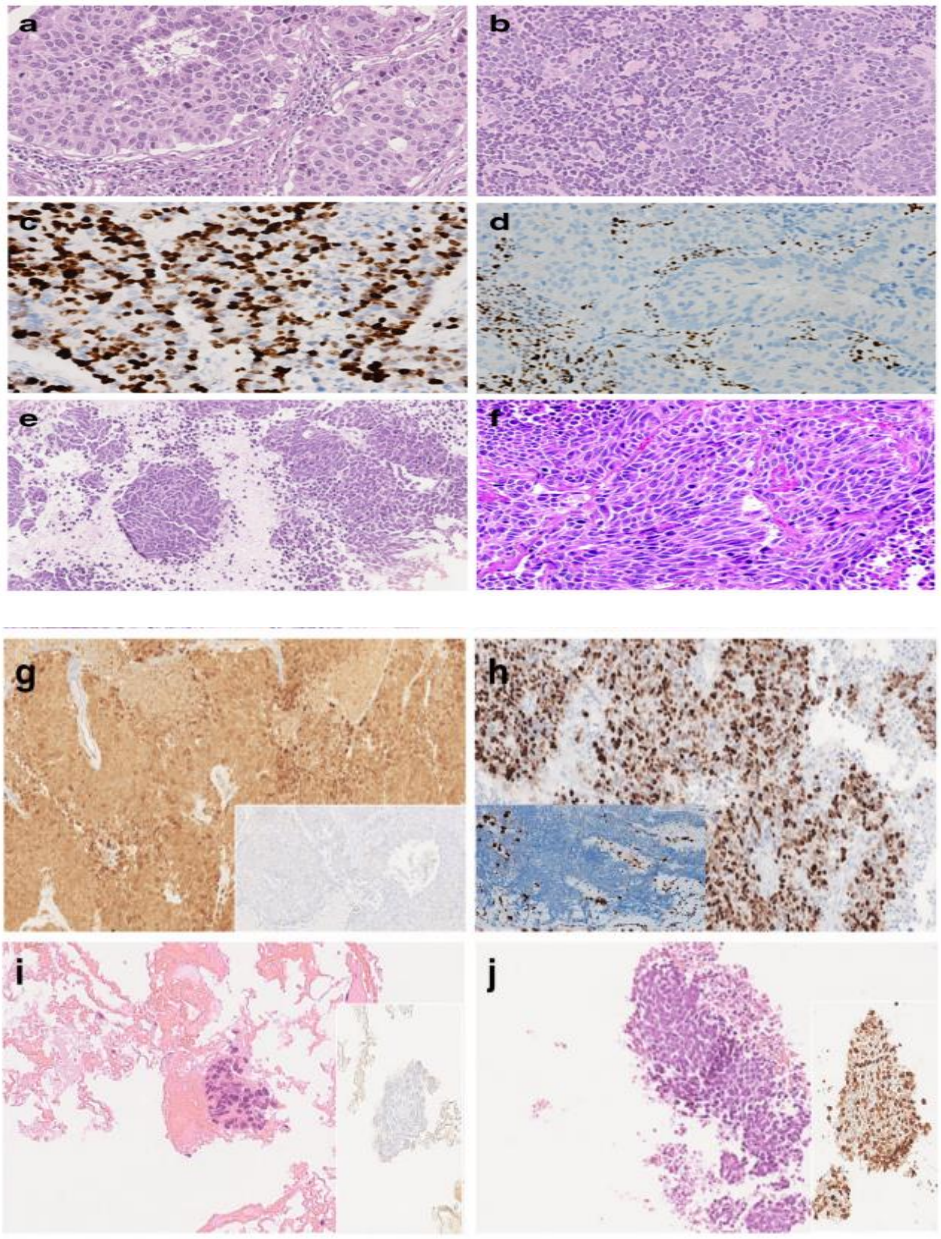

Fig. 3 Histomorphologic and Immunohistochemical Features of Lung Neuroendocrine Carcinomas.

LCNEC presents organoid aggregates with peripheral palisading and many mitoses (a), whereas it may also exhibit an SCLC-like appearance (b). LCNEC tends to be positive for INSM1 (c) but lacks retinoblastoma nuclear staining (d). SCLC exhibits small cells with prominence of nuclear molding, inconspicuous nucleoli, and a high degree of necrosis (e), but cohesiveness or spindling of neoplastic cells could also be present (f). Synaptophysin immunostaining remains in this case

(g), as well as INSM1 labeling (h), while CHGA is primarily negative (g, inset), like retinoblastoma, which does not stain (h, inset). Borderline cases between carcinoids (i) and SCLC (j) may prove challenging on morphological grounds in cytology samples, but Ki-67 stain permits their differentiation with certainty: carcinoids (i) exhibit low Ki-67 (inset) while SCLC displays high Ki-67.

DISCUSSION

Immunohistochemistry (IHC) stains are used in diagnosing and staging lung cancer to determine the appropriate treatment. Despite being moderately useful clinically, markers such as chromogranin A, synaptophysin, and CD56 remain relatively insensitive and may be non-contributory (Raso et al., 2021). These antigens have helped improve diagnosis; according to the literature, INSMA has a sensitivity of 98% and a specificity of 95% in SCLC (Qu et al., 2022). Thus, these results have implications for the role of IHC markers in diagnosing SCLC and identifying patients primed for novel targeted therapies. Different types of biopsy methods are used in diagnosing SCLC, each with advantages and disadvantages. Regarding mediastinal lymph node sampling, EBUS-TBNA is very successful, with a sensitivity range of 89-94% and specificity of up to 98% (Park et al., 2024). This procedure is relatively less invasive with a significantly minimized complication rate, which makes it ideal for midline masses.

On the other hand, CT-guided percutaneous needle biopsy remains a gold standard approach for peripheral lung masses, of which the sensitivity ranges above 90% coupled with nearly 100% specificity (Baratella et al., 2022). However, pneumothorax may complicate CT-guided biopsy in as many as 45% of patients (Constantinescu et al., 2024). However, conventional bronchoscopy, although more commonly applied, has a lower diagnostic sensitivity, especially in peripheral lesions, and is therefore less helpful (Liu et al., 2022). Robotic bronchoscopy has shown potential in recent years, and several studies have indicated better diagnostic yields and safety than conventional bronchoscopy. The biopsy technique must, therefore, be guided by tumor location, the patient's general state of health, and requirements for molecular characterization (Xiang et al., 2024). Molecular testing is transforming the diagnosis and ongoing management of lung cancer. In the future, recent research advances for SCLC include NGS, which has characterized genetic differences between SCLC and NSCLC that could point to future therapeutic targets (Megyesfalvi et al., 2023). Based on their research, Rudin et al. identified that SCLC molecular traits include near-unanimous inactivation of TP53 and RB1 and frequent MYC amplifications.

In contrast to SCLC, NSCLC is associated with mutations in the EGFR, KRAS, and ALK genes, allowing targeted treatment (Harada et al., 2023). Whereas NSCLC has seen improvement with tyrosine kinase and immune checkpoint inhibitors, SCLC lacks molecular targets. However, biomarker-driven therapies such as DLL3 targeted and immunotherapy are starting to turn this around (Simbolo et al., 2022). Circulating tumor DNA (ctDNA) continues to refine molecular diagnostics through noninvasive mutation detection using liquid biopsy techniques, especially in NSCLC (Padinharayil et al., 2023). However, several issues are still associated with the standardization of IHC and biopsy procedures across various facilities. Transcriptional variation in sample preparation, choice of antibodies, and evaluation of staining patterns may contribute to diagnostic errors (Metovic et al., 2021). Consequently, the variability of the biopsy and tissue fixation procedure may inflate variability in molecular tests, implying that standardization is crucial (Restrepo et al., 2023). These disparities can be mitigated if healthcare executives apply artificial intelligence, particularly in pathology and radiology, which can reduce inter-observer variations and improve diagnostic accuracy (Ding et al., 2022). In addition, cooperation between research institutions and clinical centers is crucial to optimize biomarkers and improve the availability of advanced molecular diagnostics (Jachowski et al., 2023). Future approaches will involve IHC, biopsy techniques, and molecular profiling to improve therapy personalization in SCLC (Cannone et al., 2023). Further understanding of molecular subtypes and novel biomarkers will likely refine specific therapeutics and enhance patient prognosis. Contemporary precision medicine utilizes pathology, radiology, and genomics to reduce variability in the diagnosis and treatment of lung cancer.

FACTORS/CRITICS CONTRIBUTING TO VARYING CONCLUSIONS IN STUDIES

Inconsistencies seen in the diagnosis of SCLC and its molecular differentiation can be attributed to variations in sample size, study type, and patients under study. One of the main problems is the discrepancy in the claimed level of sensitivity and specificity of IHC markers. Despite receiving higher diagnostic performance with INSM1 and DLL3, disparities in staining techniques, antibody specificity, and the criteria for interpreting results have led to inconsistencies among different laboratories (Qu et al., 2022). Some studies may overestimate the sensitivity due to sample bias, and others may underestimate the specificity due to cross-reactivity with other tumors but not SCLC (Baine et al., 2022). The success rates of biopsy techniques also vary with different study reports. EBUS-TBNA and CT-guided biopsies are

commonly employed, yet their results depend on the location of the lesion, operators' experience, and real-time imaging technologies (Park et al., 2024). Some sources indicate increased sensitivity with robotic bronchoscopy, while some believe the CT-guided biopsy is still superior for peripheral masses (Hammad Altaq et al., 2023). These variations also demonstrate the impact of institutional resources and technical variables on the overall study performance. Similarly, molecular testing raises additional concerns about repeatability. Some of these alterations, such as TP53 and RB1, are most frequently mutated in SCLC, while other, may not be equally spread due to the disparity in the available sequencing data or patients cohorts (Rudin et al., 2021; Simbolo et al., 2022). Some employed whole-exome or whole-genome sequencing or both while others used targeted gene panel sequencing, which affected mutation yield (Megyesfalvi et al., 2023). This is why simple and fundamental aspects relevant to standardization, for example, immunohistochemical protocols, biopsy selection criteria, or molecular testing have to be considered in order to enhance the replicability of research findings. These discrepancies should be minimized in the subsequent studies to improve the reliability of the diagnostic markers and targets in SCLC by multi-institutional cooperative study with unified methods.

CONCLUSION

This study suggests that IHC markers, biopsy techniques, and molecular testing should be integrated into diagnosing and managing SCLC. Conventional antigens used for IHC include neuroendocrine markers; newer markers such as INSM-1 and DLL3 have been identified and could be therapeutic. These advances have the potential to pave the way for finding new biomarkers that can differentiate SCLC from other subtypes of lung cancer and improve biomarker-based therapies. Using tissue sampling helps to have enough tissue for tissue diagnosis and molecular analysis. EBUS-TBNA is recommended for centrally located tumors, while CT-guided percutaneous biopsy is preferable for peripheral tumors. The development of robotic-assisted bronchoscopy and the adoption of ROS can further improve diagnostic yield and reduce the number of interventions logged. Immunohistochemical and molecular analyses have significantly contributed to diagnosing and treating SCLC. Several gene alterations have been discovered, leading to developing DLL3-targeted therapies and immunotherapy for Lung Cancer patients. The near future of SCLC treatment is headed toward molecular subtyping and subsequent target-based treatment paradigms. Hence, better diagnostics and therapeutic measures are needed, so turning to IHC, biopsy methods, and molecular examination may be necessary. Regarding the Precision Medicine context, the predisposition to provide increasingly targeted treatment based on tumor features should undoubtedly enhance patient outcomes and redefine the care approach to SCLC.

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