



Abstracts

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Background & Objectives: Immunotherapy has transformed advanced non-small cell lung cancer (NSCLC) treatment, with PDL-1 expression as a key biomarker. Tumour microenvironment complexity suggests additional immune factors, such as CD8+ T-cell infiltration (TILs), may impact treatment efficacy. This study examines their relationship and prognostic significance.

Methods: A retrospective study analysed 50 NSCLC patients treated with immunotherapy (2016–2021, median follow-up: 43.5 months). CD8+ TILs were assessed using Donnen's classification. PDL-1 expression was determined by immunohistochemistry, and molecular profiling by next-generation sequencing (NGS). Associations with progression-free survival (PFS) and overall survival (OS) were evaluated.

Results: Higher stromal TIL density correlated with improved OS (median, $p = 0.04$), whereas intraepithelial TILs showed no survival impact. In a Cox regression model, both high stromal TILs and PDL-1 $\geq 50\%$ were significantly linked to lower mortality (HR stromal TILs: 0.46, $p = 0.037$; HR PDL-1 $\geq 50\%$: 0.49, $p = 0.046$). Molecular analysis identified EGFR, TP53, ROS1, BRAF, and KRAS mutations, though none correlated significantly with clinical response. These findings suggest that stromal TIL infiltration and PDL-1 expression serve as independent prognostic biomarkers in NSCLC patients receiving immunotherapy, highlighting their potential role in treatment stratification and outcome prediction. Further investigation of additional immune and molecular factors is warranted.

Conclusion: PDL-1 expression and stromal TIL infiltration are key prognostic markers in NSCLC patients treated with immunotherapy. Their combination identified distinct clinical outcome subgroups, supporting their relevance in personalized treatment. Despite frequent genetic mutations, no significant association with therapy response was found, underscoring the need for further research on tumour microenvironment interactions. These findings reinforce the importance of integrating immune biomarkers into clinical decision-making to optimize therapeutic strategies and improve patient outcomes in advanced NSCLC.

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Morphofunctional features of alveolar type II cells of offspring that developed in utero under maternal genitourinary system chronic inflammatory process conditions

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Background & Objectives: Maternal chronic inflammatory processes of the genitourinary system (GUS) often complicate the course of pregnancy and childbirth, negatively affecting the offspring health. The objective was to identify the morphofunctional features of alveolar type II cells of offspring that developed in utero under conditions of maternal chronic inflammatory process of the GUS caused by *Streptococcus pyogenes*.

Methods: An experiment was conducted on rats of the WAG population. Group 1 included 318 one-week-old, 204 one-month-old, and 214 two-month-old rats from mothers with physiological pregnancy. Group 2 included 257 one-week-old, 134 one-month-old, 121 two-month-old rats from mothers whose pregnancy occurred against the background of a chronic inflammatory process of the GUS caused by *Streptococcus pyogenes*. Fragments of the offspring lungs were the

study material. Microscope slides were stained with haematoxylin and eosin, sudan 3.

Results: During survey microscopy in group 2, compared to group 1, alveolar type II cells were characterized by focal dystrophic, necrotic and desquamative changes. In some visual fields, in areas of dystelektasis and atelectasis, alveolar type II cells were not detected or were found in the alveoli lumen. The relative number of such cells increased ($p < 0.05$) with age of the rats ((11.9 \pm 0.8) % in one-week-old rats, (20.5 \pm 0.3) % in one-month-old rats, (32.2 \pm 0.8) % in two-month-old rats). In group 2 compared to group 1, the sudanophilic layer on the alveolar cells surface, which was a surfactant, characterized by uneven thickness and were not detectable in some places.

Conclusion: Maternal chronic inflammatory process of the genitourinary system caused by *Streptococcus pyogenes* changes the morphofunctional state of the offspring alveolar type II cells. These changes increase with the animals' age and are manifested by focal dystrophic, necrotic and desquamative changes, which lead to a deficiency of surfactant as a result of its rapid destruction or insufficient production.

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Clinical and pathological characteristics of multiple primary malignancies in patients diagnosed with lung carcinoma: a single-centre retrospective analysis

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Background & Objectives: Multiple primary malignancies (MPMs) represent a significant clinical challenge due to their complexity in diagnosis, treatment, and follow-up. While MPMs involving breast, gynaecologic, and gastrointestinal cancers are well-documented, data regarding those associated with lung carcinoma remain limited. This study aimed to retrospectively evaluate the clinical, pathological, demographic, and prognostic features of patients diagnosed with primary lung carcinoma with additional primary malignancies.

Methods: This retrospective study included 76 patients diagnosed with MPMs between 2005–2023 at a single centre, all with a primary lung carcinoma diagnosis. Data collected included demographic characteristics, tumour locations, histopathological types, treatment modalities, comorbid conditions, prognostic indicators, and survival outcomes.

Results: Of the patients, 76.3% were male (male-to-female ratio: 3.22), with a mean age of 66.39 years (range: 33–86). Smoking history was present in 57.9% of patients. Common comorbidities included chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and cardiovascular disease. The most frequent histological types were adenocarcinoma (55.3%) and squamous cell carcinoma (26.5%). Secondary primary malignancies commonly affected the bladder, larynx, breast, prostate, colon, and other sites. Twelve patients developed a third primary cancer. Synchronous tumours were observed in 26.3% of cases, with significantly shorter intervals between malignancy diagnoses ($p < 0.001$). The mean interval between the first and second malignancy was 45.46 months, and between the second and third was 42.9 months. Kaplan-Meier analysis revealed a mean overall survival of 164 months. Though patients with synchronous tumours had shorter survival, the difference was not statistically significant ($p = 0.191$).

Conclusion: MPMs in patients with lung carcinoma are clinically complex and limited in the literature. Recognition of associated malignancies is crucial for effective clinical management, emphasizing the importance of risk factors such as smoking and chronic diseases. Early detection, a comprehensive multidisciplinary approach, and vigilant long-term surveillance are essential for optimizing outcomes in patients with multiple malignancies including primary lung carcinoma.

Background & Objectives: The L252P (formerly L265P) mutation in the *MYD88* gene is a characteristic alteration of lymphoplasmacytic lymphoma (LPL), making its detection essential for differential diagnosis with other lymphomas. This mutation is frequently analysed in formalin-fixed paraffin-embedded (FFPE) biopsies including bone marrow samples, often with a low percentage of neoplastic cells or with degraded DNA. Therefore, it is crucial to have a highly sensitive method. In our laboratory, pyrosequencing is routinely used to detect this mutation, with a limit of detection (LOD) of 3.5%. To increase sensitivity, droplet digital PCR (ddPCR) was set up, and its sensitivity was compared to pyrosequencing by analysing cases with prior wild-type (WT) results.

Methods: The L252P *MYD88* mutation was detected by ddPCR (Bio-Rad) in 21 FFPE samples with *MYD88* mutations previously characterized by pyrosequencing. Additionally, 16 normal tissue samples were analysed to establish the cut-off for the technique. A total of 17 samples with lymphoproliferative processes requiring a differential diagnosis of plasmacytic lymphoma and WT by pyrosequencing were also analysed. Furthermore, the sensitivity (LOD) of

ddPCR was established in the wt cases taking in account that this value is experiment and sample dependent. Variant allele frequency (VAF) was also evaluated in the mutated cases.

Results: The L265P mutation was confirmed by ddPCR in all 21 *MYD88* mutated cases detected by pyrosequencing once the ddPCR cut-off was established using normal tissues. Additionally, *MYD88* mutation was detected by ddPCR in 5 of the 17 wt cases by pyrosequencing, with VAFs ranging from 0.4% to 3.11%. Negative results were confirmed with an sensitivity ranging from 0.09% to 0.89%.

Conclusion: The results of this study confirm that ddPCR offers greater sensitivity than pyrosequencing for detecting the L252P *MYD88* mutation, making it a highly valuable tool in the diagnosis of LPL, particularly in cases with low neoplastic cell representation and degraded genetic material.

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