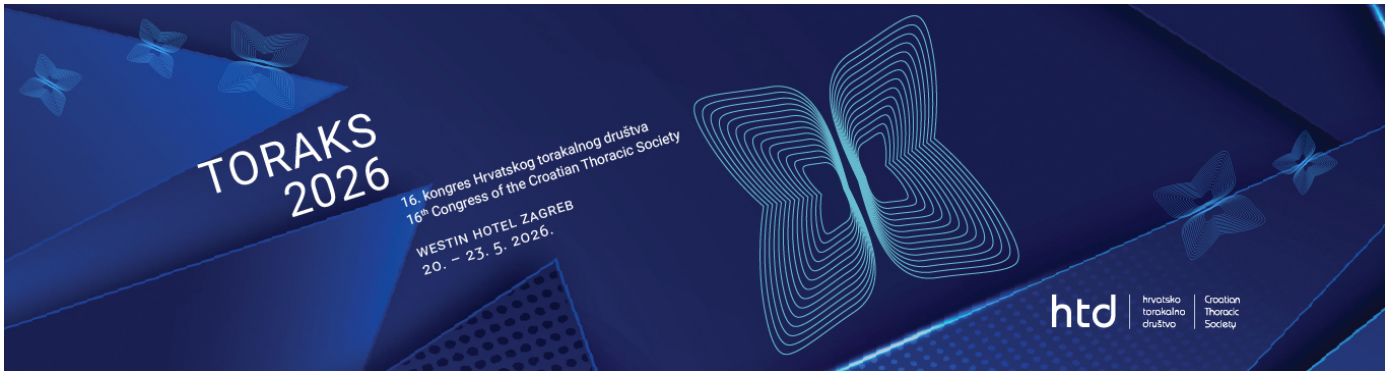

INTEGRATED CYTOLOGICAL AND HISTOLOGICAL APPROACH IN THE DIAGNOSTIC WORKUP OF LUNG CANCER

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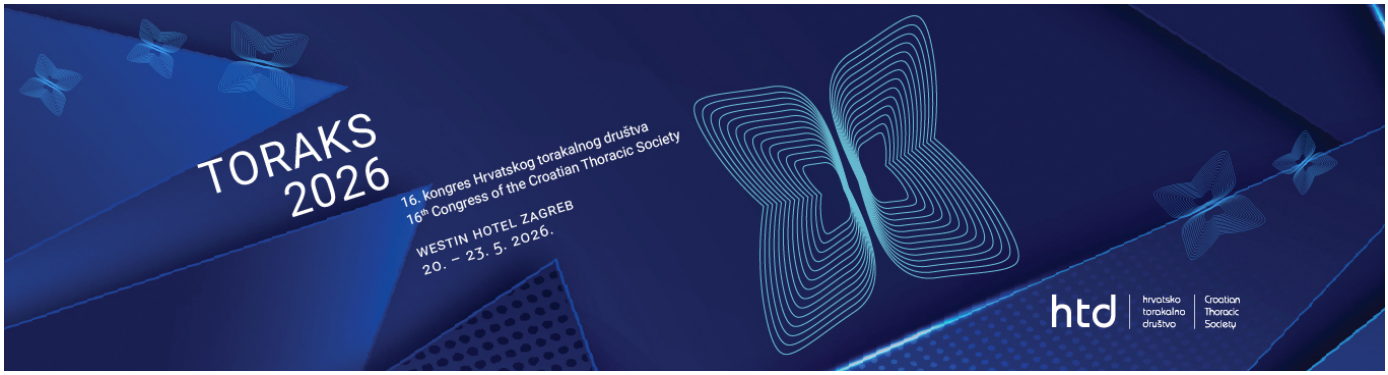
Objective:

To evaluate the diagnostic and predictive value of an integrated cytological and histological approach, emphasizing the role of cytological samples in cases with non-diagnostic histology.



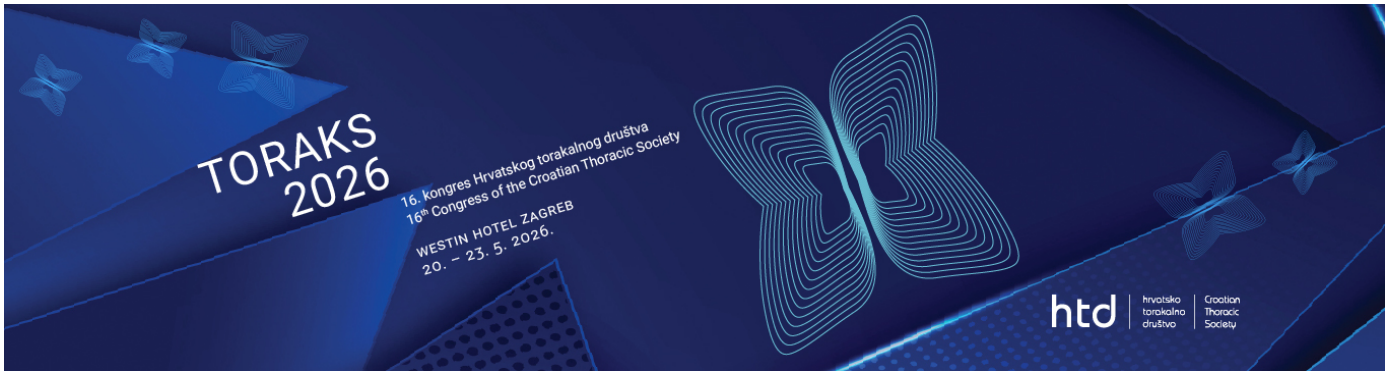
Methods:

A retrospective analysis included 485 reports of cytological bronchial biopsy imprints and additional cytological samples (bronchial aspirations, brushings, and transtracheal and/or transbronchial fine-needle aspirations), together with corresponding parallel formalin-fixed paraffin-embedded (FFPE) bronchial biopsies, processed at the Department of Pathology and Cytology, University Hospital Centre Zagreb, in 2024. Reports of diagnostic and predictive immunocytochemistry (ICC) and/or immunohistochemistry (IHC), EGFR mutation testing, and gene fusion analyses were also included. According to the internal algorithm, diagnostic and predictive ICC on cytological samples was performed in cases of negative or inadequate parallel FFPE bronchial biopsies. EGFR mutation testing was routinely performed on cytological samples regardless of parallel FFPE bronchial biopsy results.

Result:

In addition to biopsy imprints, other types of cytological samples were obtained in 383 (78.9%) cases. A cytological diagnosis of lung cancer, including tumors of non-pulmonary origin, was established in 345 (71.1%) patients, based on a combination of 329 (67.8%) malignant imprints and 240 (49.5%) malignant additional cytological samples. A histological diagnosis of lung cancer was achieved in 297 (61.2%) patients. Among 131 negative or inadequate FFPE bronchial biopsies, 64 (48.9%) cases showed complementary malignant cytology (28; 21.4% biopsy imprints and 36; 27.5% additional cytological samples).

Diagnostic ICC for tumor subtyping was required in 36 (10.4%) cases. In 10 (27.8%) cases, ICC relied exclusively on additional cytological samples. Among all malignant cases, predictive ICC for non-small cell lung cancer (NSCLC), including ALK and ROS1 rearrangements and PD-L1 expression, was performed on 67 (19.4%) cytological samples, primarily biopsy imprints. Diagnostic IHC was performed on all malignant FFPE bronchial biopsies, while predictive IHC



was applied in 168 (56.6%) cases. In seven cases, combined cytological and histological samples were necessary to complete predictive biomarker testing due to limited cellularity.

EGFR mutation analysis for NSCLC was performed in 136 (39.4%) cases using cytological samples (78; 22.6% biopsy imprints and 58; 16.8% additional cytological samples) and in 43 (14.5%) cases using FFPE bronchial biopsies. Gene fusion testing for NSCLC was conducted in 64 (18.6%) cases during the initial implementation phase, predominantly on FFPE bronchial biopsies, with a smaller proportion of cytological samples.

Conclusion:

An integrated cytological and histological approach is essential for the accurate diagnosis and comprehensive assessment of predictive biomarkers in non-small cell lung cancer.