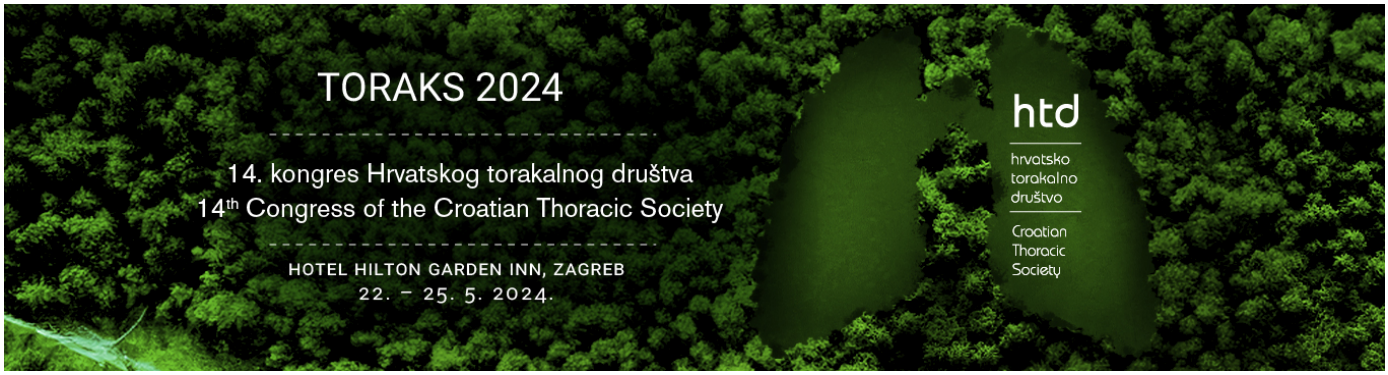

CYTOMEGALOVIRUS INFECTION IN CYTOLOGICAL SMEARS AND IMMUNE RESPONSE IN PERIPHERAL BLOOD OF LUNG ADENOCARCINOMA PATIENTS ACCORDING TO EGFR MUTATION STATUS

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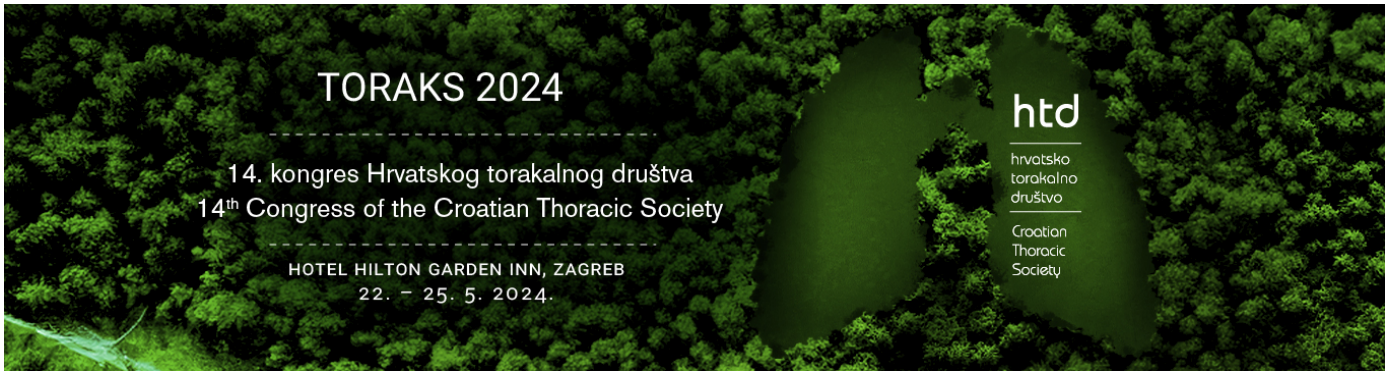

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Objective:

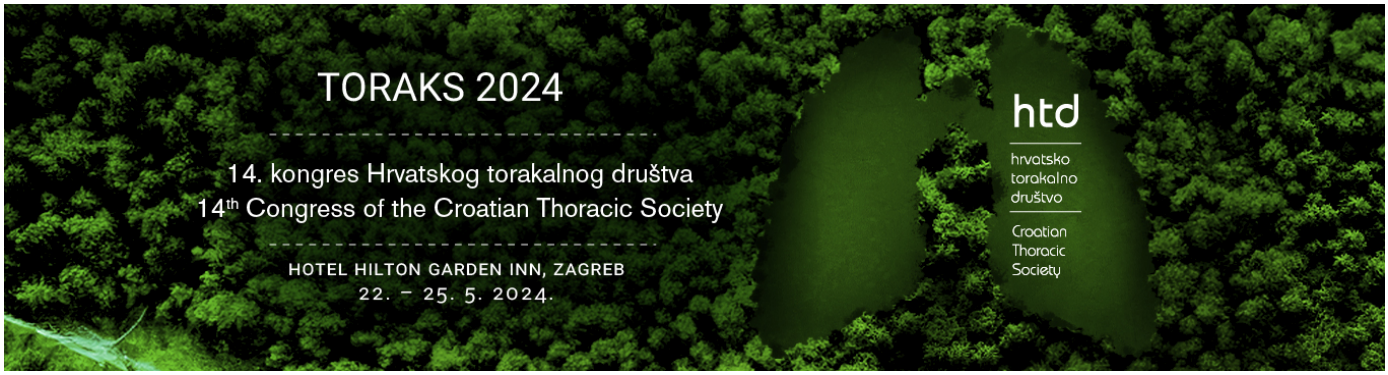
Cytomegalovirus (HCMV) is associated with different types of carcinomas. The study aimed to determine whether there is an association between HCMV infection in tumor cells and the immune response to HCMV antigens in the peripheral blood of patients with EGFR-positive and EGFR-negative lung adenocarcinoma.

Methods:

This prospective study included DNA isolates from 102 May-Grünwald-Giemsa stained cytological smears of lung adenocarcinoma routinely prepared at the Division of Pulmonary Cytology, Department of Pathology and Cytology, at the University Hospital Center Zagreb. The HCMV infection in lung adenocarcinoma cells was analyzed by PCR, amplifying the viral major immediate early gene (*MIE*) and the glycoprotein B (*gB*) regions. The immune response to HCMV antigens was analyzed in peripheral blood obtained from 80 lung adenocarcinoma patients, using the QuantiferonCMV ELISA test. The results were statistically analyzed using a chi-square test with a significant value set at $p<0.05$.

Result:

The HCMV infection in lung adenocarcinoma cells was analyzed in 51 EGFR-positive and 51 EGFR-negative patients. The HCMV *MIE* gene was detected in eight (15.7%) EGFR-positive samples and one EGFR-negative sample from lung adenocarcinoma patients. The HCMV *gB*



gene was detected in four (7.8%) EGFR-negative samples while not in EGFR-positive samples.

The immune response to HCMV antigens was analyzed in the peripheral blood of 29 EGFR-positive and 51 EGFR-negative lung adenocarcinoma patients. The results showed that 18 (62.1%) EGFR-positive and 26 (50.9%) EGFR-negative patients had an immune response to HCMV. Together immune response to HCMV and HCMV *MIE* gene were detected in samples from two EGFR-positive and one EGFR-negative patient. Immune response to HCMV in combination with the HCMV *gB* gene in tumor cells was detected in three samples from EGFR-negative patients. The HCMV *gB* gene was also detected in one EGFR-negative sample without immune response to HCMV antigens in peripheral blood.

Conclusion:

Although HCMV *MIE* and *gB* genes were detected in lung adenocarcinoma smears there was no significant association between HCMV infection in tumor cells and the immune response to HCMV antigens in the peripheral blood of EGFR-positive and EGFR-negative patients. A negative immune response to HCMV antigens in peripheral blood does not exclude viral infection in lung adenocarcinoma cells.