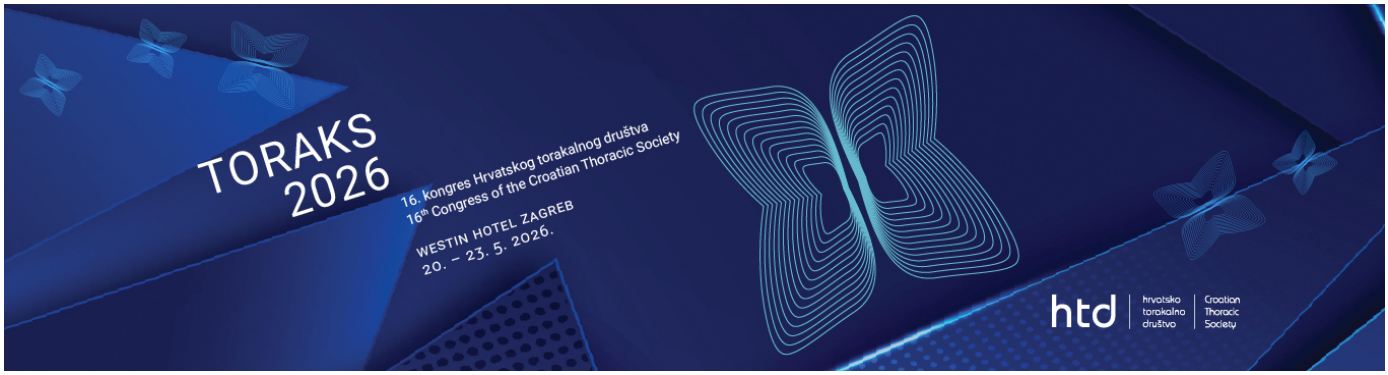


LUNG ADENOCARCINOMA WITH EGFR-RAD51 FUSION: A CASE DEMONSTRATING THE VALUE OF COMPREHENSIVE GENOMIC PROFILING

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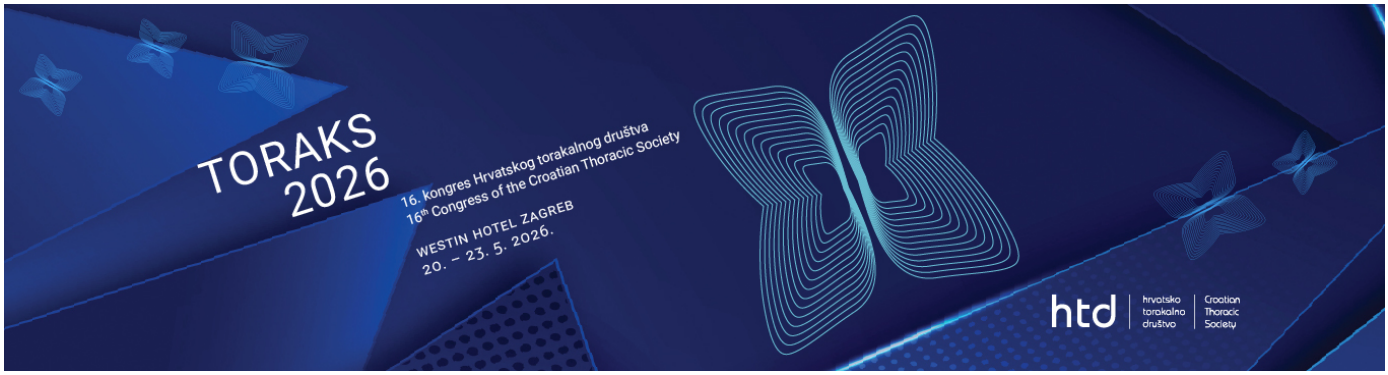
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Objective:

The aim of this case report is to demonstrate the importance of comprehensive genomic profiling in identifiying rare mutations that can expand therapeutic options in lung cancer treatment.

Methods:

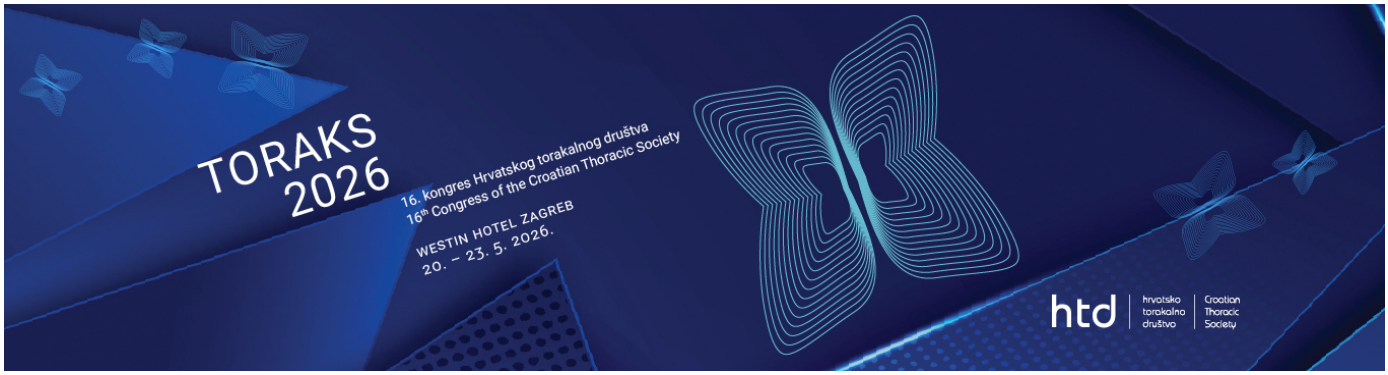
Non-small-cell lung cancer (NSCLC) is one of the most frequent cancer types and is responsible for the majority of cancer-related deaths worldwide.(Hendriks et al., 2024.)



Most common EGFR fusion is EGFR-RAD51 fusion, which contains EGFR domain fused with RAD51, a protein involved in DNA-damage response.(Konduri et al., 2016)

Result:

A 47-year old woman presented at our clinic with a three-month history of persistent dry, non-productive cough, accompanied by pain localized to the left side of the manubrium sterni. Imaging showed infiltration of left upper lobe involving left pleura with mediastinal lymphadenopathy and metastases to the femoral diaphysis and cranium. Bronchoscopy-obtained tissue showed lung adenocarcinoma. Molecular testing showed EGFR-negative, ALK-negative, PD-L1-negative disease. She received four cycles of pemetrexed/cisplatin and then transitioned to maintance therapy of thirteen cycles of pemetrexed. She developed disease progression and switched to 2nd line docetaxel for four cycles and then received four cycles of docetaxel-nintedanib combination. Progression of metastasis in the femur and thoracic spine prompted initiation of atezolizumab, given for seven cycles before switching to paclitaxel–carboplatin due to further disease progression. Around this time, molecular analysis showed an EGFR–RAD51 fusion, along with MYC amplification. A BAP1 rearrangement involving intron 9 was identified, as well as a PIK3C2G R1101H point mutation. Multidisciplinary board recommended initiation of erlotinib due to few case report series. She received 39 cycles of erlotinib before presenting with progressive neurological deterioration at the emergency department. An emergency intracranial ablation of the lesion was performed and she underwent brain and thoracic radiotherapy. Due to the progression of CNS metastasis, erlotinib was substituted with osimertinib. After 15 cycles of osimertinib, she underwent GammaKnife radiosurgery to treat the newly discovered brain metastasis. Imaging also showed metastatic lesions involving the T11 and T12 vertebrae which prompted adding pemetrexed and carboplatin to the treatment regimen. To treat the metastasis she underwent palliative spinal radiotherapy. To date, she remains on osimertinib in combination with



ongoing maintainance chemotherapy

Conclusion:

The discovery of a rare gene alteration expanded therapeutic options and had a positive impact on the treatment course and overall disease trajectory.