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Short Communication

New Biomarkers in Oncology in the COVID-19 Era

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Cancer is one of the most frequently diagnosed diseases with increasing incidence worldwide. The treatment of cancer requires a multidisciplinary methodology due to the complexity of the disease, the therapeutic possibilities of personalized medicine and the peculiarities of carcinogenesis, which is essential for the selection of an appropriate therapy [1]. Extensive evidence has been published on the molecular background of cancer development and progression, which can help tailor therapy to individual patients and improve their survival prognosis. Drug-specific therapeutic methodologies for cancer have contributed to substantial enhancements in overall survival and general quality of life for patients. However, there remains a pronounced need to expand personalization of treatments based on genetic and epigenetic tumor profiles in order to maximize quality and efficiency while limiting cytotoxicity of the oncological treatment. Early detection, accurate diagnosis, and treatment monitoring of cancer with specific markers and targeted molecular testing can be of great benefit to cancer patients [2].

Currently, only a limited number of blood biomarkers are available in clinical practice. Therefore, scientific efforts are being made to find new reliable specific biomarkers for patient profiling that have both prognostic and predictive value while being economically acceptable and easy to determine. Here, "liquid" markers are a promising alternative to tissue markers [3]. While mechanisms for analyzing circulating tumor DNA have proven to be inaccurate, detection and analysis of circulating tumor cells and protein analysis of exosomes are more promising options, especially when combined with tissue analysis by pathologists. In the search for new biomarkers that could replace the old ones, a promising noninvasive technique called "liquid biopsy" has been developed for various body fluids (blood, saliva, and urine). Liquid biopsy from peripheral blood is used for diagnostic screening as well as to determine response to therapy and to evaluate disease progression as presented in our recent review [4]. Peripheral blood may contain CTC, ctDNA, and vesicular structures containing proteins and RNA molecules (exosomes) that can be released into the circulation by numerous cells, including tumor cells. This could help determine the molecular profile of the disease, the extent of affected tissue, and the response to therapy in a noninvasive manner. Future molecular profiling, ideally assessed and monitored by liquid biopsy, could further personalize decision making in adjuvant treatment of cancer patients [5]. Nonetheless, liquid biopsy results need to be combined and estimated with tissue pathology findings before final validation of the suggested tactic. The existing scenery presents additional challenges in the implementation of liquid biopsy in clinical practice [6].

Research conducted in recent years has increased knowledge of the role of the immune system in tumor development and progression. Although cytotoxic chemotherapy has long been the backbone of systemic treatment of cancer, it has given way to the

precision of targeted therapy and the power of immunotherapy. Immunotherapy with immune checkpoint inhibitors (ICI) represents one of the most important breakthroughs in the treatment of solid tumors and has shown promising results in numerous clinical trials. Immune checkpoint inhibitors, particularly inhibitors of the PD -1 axis, have changed the therapeutic landscape of cancer treatment. In addition to PD-L1 mutation and tumor mutation burden (TMB) biomarkers, an important segment in immuno-oncology, continue to be the subject of intense scientific research. However, due to the heterogeneity of PD -L1 mutations and TMBs and their mismatch in scoring systems, they are not suitable as predictive markers in immuno-oncology [7]. The prognostic and predictive value of several inflammation-related markers, such as neutrophil-to-lymphocyte ratio (NLR) and derived neutrophil-to-lymphocyte ratio (dNLR), has been shown to play an important role in cancer cell destruction. The lung immune prognostic index (LIPI), which integrates pretreatment baseline dNLR and LDH levels-two readily available risk factors for poor prognosis in clinical practice is an understudied prognostic and predictive biomarker in lung cancer research [8].

The emerging pandemic caused by COVID-19 poses a significant threat to lung cancer patients because of the specificity of the respiratory infection it causes. Respiratory disease, immune responses, lymphopenia, and cytokine cascades caused by this virus play a fundamental role in the development and severity of symptoms. The PD-1/PD-L1 pathway has been shown to provide an escape mechanism for certain pathogens, and the use of anti-PD-L1 may increase the clearance of some viruses. Based on the positive effect of ICI on the reactivation of T lymphocytes against cancer cells as well as cells infected with the virus, it can be considered that the use of ICI during this pandemic is unlikely to pose a risk to cancer patients and can be suggested for the therapy of cancer patients infected with COVID-19 [9]. Our recently published research shows that infection with COVID -19 did not affect the survival of patients treated with ICI, but that these patients had better overall and progression-free survival and disease control rates. However, this may be attributed to more dedicated medical care and hospitalization of patients with COVID -19 infection [10]. Although significant improvements in survival have been achieved in recent years through earlier detection, improved surgical and radiation techniques, and a dramatic paradigm shift in systemic therapy, new biomarkers are critical in cancer research to predict and improve therapeutic outcome. To our knowledge, our study was the first to investigate LIPI in patients treated with a combination of ICI and chemotherapy and in patients receiving the above therapy who had recovered from COVID-19 infection. Analysis of the results obtained showed that LIPI was not associated with outcomes in patients treated with chemotherapy (predictive factor), raising the hypothesis that LIPI is a predictive factor in patients treated with ICI. The understudied and uncertain predictive power and clinical relevance of LIPI as a biomarker in patients with lung cancer was confirmed. These results may provide new insights in determining treatment options depending on the clinical status of the patient by using LIPI values as a noninvasive, readily available, and economically acceptable predictive biomarker in lung oncology [10].

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