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The focus of the study performed by Casarrubios, M. et al. that the article “Tumor microenvironment gene expression profiles associated to complete pathological response and disease progression in resectable NSCLC patients treated with neoadjuvant chemoimmunotherapy” is neoadjuvant chemoimmunotherapy for non-small cell lung cancer (NSCLC) and the responses of different tumors. The goal of the researchers was to be able to identify biomarkers and mechanisms produced by tumors after NSCLC patients underwent surgery. These new responses would be a result of treatment with neoadjuvant chemoimmunotherapy. This research was being done an effort to gain more knowledge on disease recurrence.

Over the course of twelve months, the study was performed on 41 patients in total, who were at a resectable stage IIIA NSCLC treated with neoadjuvant chemoimmunotherapy. Researchers obtain 16 pre-treatment and 36 post-treatment tissue samples from these patients. Two categories, complete pathological response (CPR) and non-complete pathological response (non-CPR), were used to classify the tumors. The classification of the tumors was based upon the amount of viable tumor cells found in different regions of the tissue, specifically lymph nodes and the tumor bed, during surgery. To be classified in the CPR category, the samples must have had zero viable tumor cells in the analyzed regions. The samples of the tumor were analyzed using a panel targeting 395 genes related to the immunological processes that were used.

The results of this experiment revealed a few key findings, most of which highlight the vast differences between CPR tumors and non-CPR tumors. The impact from neoadjuvant chemoimmunotherapy is more significant to CPR tumors. This impact was also noticed in a reduction of tumor markers and IFNγ signaling after treatment. In comparison to non-CPR tumors, CPR tumors were also found to have shown a stronger pre-established immune infiltrate at baseline. This pre-established immune infiltrate was seemingly related to the CPR tumors having higher levels of specific immune-related genes and immune cell types. Additionally, it was found that non-CPR tumors had a higher expression of genes, along with an increased proportion of dendritic cells and neutrophils, that are related to relapse after surgery. Lastly, it was found that the post-treatment results were greatly influenced by mutations found in tumors and high pretreatment levels of PD-L1. These two factors lead to the downregulation of proliferation markers and type I interferon signaling molecules in surgery samples.

The findings of this study provide more knowledge on the potential mechanisms that are related to tumor response and disease relapse or recurrence. There is now a greater possibility that researchers and medical professionals can use this newfound knowledge to create personalized therapy approaches for immunotherapy-based regimens in the neoadjuvant treatment of NSCLC.

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References

Casarrubios, M. *et al.* Tumor microenvironment gene expression profiles associated to complete pathological response and disease progression in resectable NSCLC patients treated with neoadjuvant chemoimmunotherapy. *J Immunother Cancer* **10** (2022). https://doi.org/10.1136/jitc-2022-005320