

For decades, basic research and clinical trials have aimed to establish a meaningful cancer immunotherapy. An unprecedented number of medicinal products for cancer immunotherapy are currently being authorised. For this success, the selection of the right molecular targets for immunotherapy has been crucial. Monoclonal antibodies targeting cell surface receptors for growth factors were successfully introduced in clinical routine for the treatment of common solid tumours more than 10 years ago. Since then, however, the focus of cancer immunotherapy has shifted. More recently, many authorized medicines targeting growth factors receptors in solid tumours are no longer based on antibodies, but on small molecule protein kinase inhibitors. Currently, medicines with recent European marketing authorizations for the immunotherapy of cancer come from three major categories: (1) monoclonal antibodies targeting blood cell surface antigens; (2) CAR-T cells for the therapy of haematological neoplasia; and, with broader use including solid tumours, (3) checkpoint inhibitors. For the successful use of many of these medicines, the appropriate companion diagnostics (CDx) are required. Therefore, precision medicine also means selecting precisely the patients who will profit from a specific treatment (using, for example, a CDx). But, how can an informed choice be made with regards to CDx? We will give an overview on the cancer immunotherapies that depend on CDx and outline what to look for when choosing a suitable CDx.

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P05 Reverse translation

P05.01 PLATELETS ROLE IN IMMUNOTHERAPY RESPONSE IN NON-SMALL CELL LUNG CANCER

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Background Immunotherapy has revolutionized the therapeutic landscape of non-small cell lung cancer (NSCLC). In particular, therapy based on immune checkpoint inhibitors (ICIs), such as monoclonal antibodies (mAbs) targeting programmed cell death protein 1 (PD-1) pathway, has changed the survival rate of NSCLC patients. However, a subset of patients is responsive to ICIs and another subset develops acquired resistance to ICIs. In the past few decades, increasing studies have highlighted that high platelets (PLTs) count is associated with poor prognosis of NSCLC patients. Therefore, the aim of this research was to investigate the contribution of PLTs in response to immunotherapy.

Materials and Methods Blood samples from advanced (non-resectable, stage IV) NSCLC patients treated with Atezolizumab were collected at the baseline (T0, prior to the first cycle) and at disease progression (PD). PLTs were isolated by PLT-rich plasma by centrifugation. PD-L1 and Fc gamma receptors (FcγR) PLTs expression were analyzed, and the release of activated PLTs-associated mediators were measured.

Results We found that PLTs count was higher in NSCLC patients at stage IV than earlier stages. These PLTs showed higher levels of PD-L1 than early stages. Moreover, although

not in a statistical manner, ICI-non responder NSCLC patients had slightly higher levels of PD-L1. No differences were found in terms of FcγRIII (CD64), FcγRII (CD32) and FcγRI (CD16) expression on isolated PLTs either at baseline or after treatment. In order to better understand whether drug treatment with atezolizumab could alter PLTs activity, the isolated cells were treated in vitro with the mAb (1 μg/mL) to evaluate the release of mediators associated with PLTs activation. We found that differently than healthy PLTs, the stimulation of PLTs derived by NSCLC non-treated patients with Atezolizumab for 30 minutes induced the release of platelet factor 4 (CXCL4). Similarly, the challenge with Atezolizumab was able to trigger the release of TGF-β from NSCLC-derived PLTs after 5 hours of treatment; nevertheless, we observed that PLTs collected from patients who did not respond to treatment (PD) secreted higher amount of TGF-β at earlier time point (1 hour after Atezolizumab addition).

Conclusions Currently simple and robust biomarkers to predict therapy responses towards ICIs are still missing. Our data suggest that the PLTs expression of PD-L1 at PD may reflect the reduced drug efficacy due to the interaction and binding of mAbs (such as Atezolizumab) to the surface PD-L1 by limiting the drug which is not able to exhibit its pharmacological activity on tumor tissues or innate tumor-infiltrated immune cells.

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P06 Cell therapy in solid tumors

P06.01 ROR1-CAR T-CELLS AS NOVEL TREATMENT STRATEGY FOR ANAPLASTIC THYROID CARCINOMA

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Background Anaplastic thyroid carcinoma (ATC) and poorly differentiated thyroid carcinoma (PDTC) are rare thyroid malignancies with an extremely poor prognosis. Current therapies include operation, radiochemotherapy and kinase inhibitors, but finally most patients relapse and require further treatments. Thus, new therapeutic strategies are needed. CAR-T (chimeric antigen receptor) therapy is a modern approach to manipulate and target the patient's own T cells against a specific marker on tumor cells. The Receptor Tyrosine Kinase Like Orphan Receptor 1 (ROR1) is an essential transmembrane receptor during embryonic development and is associated with the non-canonical Wnt signaling pathway. ROR1 is barely expressed in adult healthy tissue, but can be re-upregulated on specific tumor cell types. In this study we investigated ROR1 as a potential target for CAR T-cell therapies in thyroid carcinoma.

Materials and Methods Initially, the expression of the ROR1 receptor was determined in primary ATC/PDTC and compared to non-malignant thyroid tissue. ROR1 mRNA expression on ATC cell lines was correlated with ROR1 surface expression