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Autoantibodies production as an adverse effects indicator of lung cancer immunotherapy

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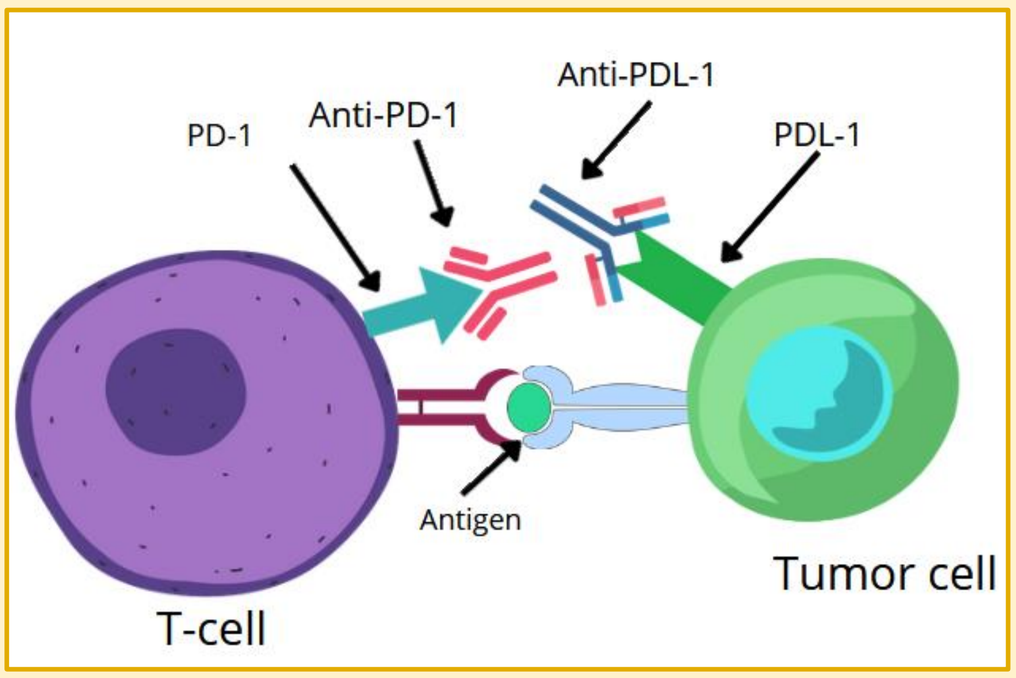
Introduction

Immunotherapy is an innovative method of cancer treatment. Unlike traditional chemotherapy, which is centered on elimination of cancer cells directly, immunotherapy activates the immune response of the patient organism against tumor. As a result, immunotherapy does not disrupt the proliferation of healthy cells, leading to lower toxicity.

However, adverse effects of immunotherapy can occur due to excessive immune stimulation, resulting in non-specific inhibition of tolerance towards both, cancer cells and normal host cells. This mechanism can potentially lead to organ toxicity and the induction of autoimmune diseases.

Immunological pathway



Immune checkpoint inhibitors

PD-1 inhibitors
- niwolumab
- pembrolizumab
- cemiplimab

PDL-1 inhibitors
- atezolizumab
- durwalumab

PD-1 is a cel membrane receptor of lymphocytes and macrophages. The ligand (PDL-1) for this receptor is present on various body cells. Binding of the ligand and receptor constitutes a non-threat signal for the immunological system. The expression of PDL-1 on cancer cells membranes mimics healthy cells leading to patological tolerance for cancer cells. Immune checkpoint inhibitors are antibodies directed against the PD-1 receptor or its ligand. This blockade unlocks the response against tumor cells.

Research schedule

treatment initiation → 3 weeks → 3 months → 6 months → long-term observation

Enrolled patients: IV stage or III stage lung cancer with no option of radical treatment lung cancer

Each visit: medical interview, physical examination, adverse effect assessment, blood sample collection for ANA, ANCA, onconeuronal antibodies, RF, anty-CCP, then long term observation in terms of progression free survival, overall survival

Research hypothesis:
- Immunotherapy can trigger autoimmune disease in predisposed individuals
- Presence of autoantibodies may predict the occurrence of adverse effects; higher levels of antibodies may correlate with more severe adverse effects
- Long-term treatment outcomes are better in patients who experience adverse effects or develop autoantibodies

Results

So far, 15 patients have been enrolled in the study. Following the first cycle of treatment, one patient, who received dual immunotherapy combined with chemotherapy, had significant increase in various ANA antibodies. No adverse effects have occurred in enrolled patients yet.

Antibody	nRNP/ Sm	SM	Scl-70	DFS-70	Anty-nucleosome	Anty-histone	Pm-scl
Before	-	-	+	-	-	-	-
after 3 weeks	+	+	++	++	++	++	+