O22 | Impact of anti-PD-1 Treatment on DSA Generation in Cancer Patients

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Here, we describe the generation of Donor-Specific Antibodies (DSA) in patients with non-small cell lung cancer treated with the cancer vaccine PDC*lung01 in combination or not with anti-PD-1 (NCT03970746). PDC*lung01 product, based on an irradiated plasmacytoid dendritic cell line (PDC*line) loaded with 7 HLA-A*02:01-r estricted tumour peptides, was injected intravenously and subcutaneously (140 million cells) on 6 occasions one week apart in stage II/IIIA (Cohort A ($n=10$), monotherapy) or stage IV (Cohort B ($n=42$); in combination with pembrolizumab) patients. Pembrolizumab (200mg) was administered IV every three weeks until progression or up to 2 years. PDC*line cells express HLA-A*02:01, B*07:02, B*44:02, DRB1*01:03, DRB1*08:01; DPB1*04:02, DPB1*05:01. DSA generation (MFI > 1,000, LIFECODES® Single Antigen) was depending on patients' genotype at haplotype and eplet levels and was observed in 100% and 60% of cohorts A and B, respectively. These antibodies appeared in 60% of patients after the 6th injection, reaching the maximum level 1 month later and gradually decreasing over 2 years, with no major difference between the 2 cohorts. Anti-HLA Ab with an MFI equal to or greater than 20,000 were observed both against class II (mainly DRB1*01:03 & DRB1*08:01) and class I (both B*07:02 & B*44:02). The MFI intensity was dependent on patients and HLA molecules, with anti-class II molecules appearing first. Using the lymphocytotoxicity assay, HLA IgG and IgM anti-class I or class II molecules showed similar functional activity against control B cells regardless of cohort. In addition, we showed that PDC*line cells were resistant to complement-dependent killing mediated by the patient's anti-HLA Ab independently of the cohorts, due to a high expression of membrane-bound complement-regulatory proteins. Taken together, these results show that anti-PD-1 treatment does not appear to alter the specificities and dynamics of DSA induced by a cancer cell vaccine in lung cancer patients.