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ABSTRACT SESSION 1: Immunotherapy, Gene Therapy & NK cells - TUESDAY 21 MAY 2024

Chairpersons: Britta Eiz-Vesper, Roberto Crocchiolo

Humoral response in lung cancer patients treated with a plasmacytoid dendritic allogeneic cell line-based cancer vaccine

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We are conducting a Phase I/II clinical trial with PDC*lung01 product based on an irradiated plasmacytoid dendritic cell line loaded with 7 HLA-A*02:01-restricted tumor peptides for treatment of HLA-A*02:01+ lung cancer patients in combination of not with anti-PD1 (NCT03970746). PDC*lung01 is injected intravenously and subcutaneously for 6 times at two dose levels, 14 million, or 140 million cells in stage II/IIIA (cohort A1 & A2, monotherapy) or stage IV (cohort B1 & B2; in combination with pembrolizumab) patients. PDC*line cells express HLA-A*02:01, B*07:02, B*44:02, DRB*01:03, DRB*08:01, DPB*04:02, DPB*05:01. We describe here, the dynamic and functionality of anti-HLA antibodies (Ab) against PDC*line that develop over time in cohort A1 (n=1) and A2 (n=11). One patient in A1 and all patients in A2 cohort developed anti-HLA Ab against HLA-B7 (n=6), -B44 (n=4), -DR103 (n=10), -DR801 (n=12), with MFI>1,000, starting before the last vaccine injection and reaching a peak (>20,000) one month after the last injection. The MFI intensity was depending on patients and HLA molecules, anti-class II molecules appearing first. Interestingly, no clinical side effect was associated to the presence of anti-HLA Ab. We demonstrated that anti-HLA Ab bind very well to PDC*line. Using an antibody-mediated complement-dependent cytotoxicity (CDC) assay in flow cytometry using healthy donor's or patient's sera, we have shown that PDC*line cells were resistant to the complement dependent killing mediated by patient's anti-HLA Ab despite the functionality of the patient's complement system. Interestingly, we have shown that PDC*line cells express high level of membrane-bound complement regulatory proteins (mCRPs: CD46, CD55, and CD59) render them resistant to Ab-mediated CDC as shown by experiments using blocking Ab. Altogether, these results show the innocuity and the absence of deleterious effect of anti-HLA Ab on PDC*line cells used as a cancer vaccine platform.