Investigation of PD-L1 expression on circulating immune cells in the peripheral blood of patients with small cell-lung cancer (SCLC) receiving first-line treatment

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ABSTRACT

Background: PD-L1 expression has been reported on tumor-infiltrating immune cells in SCLC tissue, however its prognostic role is not clear as yet. We herein assessed the incidence and clinical value of PD-L1 expression on immune cells circulating in the peripheral blood (PB) of SCLC patients receiving first-line treatment. **Methods**: PB was obtained from 34 SCLC patients (limited-stage: n=7; extensive-stage: n=27) at baseline and at the end of first-line treatment, consisting of chemotherapy alone (n=18) or in combination with atezolizumab (n=16). Peripheral blood mononuclear cell (PBMC) cytospins were immunofluorescently stained for dapi/PD-L1 (Clone: E1L3N) and PD-L1 expression was quantified on 1.000 randomly selected intact PBMCs/per sample via the Ariol microscopy system. **Results**: PD-L1^{positive} PBMCs were identified in 70.6% and 73.5% of patients at baseline and post treatment, respectively, while PD-L1^{high} PBMCs in 17.6% and 26.5%, respectively. In 23.5% of patients, PD-L1^{high} PBMCs were detected in the post-treatment sample only (in 31.3% and 16.7% of patients treated with chemoimmunotherapy as compared to chemotherapy alone, respectively; p=0.429). The detection of PD-L1^{high} PBMCs in the post-treatment sample only was associated with disease progression in the brain (in 38.5% versus 0% of patients with and without brain progression, respectively; p=0.009). Kaplan Meier analysis showed that patients harboring PD-L1^{high} PBMCs post-treatment only, had numerically reduced progression free survival (median PFS: 5.3 versus 6.7 months; p=0.089) and overall survival (median OS: 8.4 versus 15.8 months; p=0.152). In addition, patients treated with chemoimmunotherapy and post-treatment only PD-L1^{high} PBMCs, had significantly shorter OS (8.4 versus 15.7 months; p=0.007). **Conclusions**: PD-L1 is frequently expressed on PBMCs of SCLC patients receiving first-line treatment. The detection of PD-L1^{high} PBMCs post-treatment might be associated with disease progression in the brain and worse survival measures. To further delineate its role, PD-L1 expression on PBMCs is currently being investigated in a larger SCLC patient cohort.

CONCLUSIONS

- **The induction of PD-L1 expression on PBMCs post-treatment might be associated with disease progression in the brain and unfavorable patient outcomes**
- **The role of PD-L1 expression in the peripheral immune compartment merits further investigation in SCLC**

REFERENCES

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INTRODUCTION

Programmed death-ligand 1 (PD-L1) holds a key role in tumor immune evasion (1). Recent incorporation of anti-PD-L1 immunotherapy in addition to platinum-based chemotherapy has brought moderate benefit to patients with SCLC. The prognostic and/or predictive role PD-L1 expression on tumor-infiltrated immune cells in SCLC tissue is not clear as yet (2,3). The role of PD-L1 expression in the peripheral blood of SCLC patients is largely unexplored.

AIM OF THE STUDY

To investigate the incidence and clinical relevance of PD-L1 expression on immune cells circulating in the peripheral blood of SCLC patients receiving first-line treatment

PATIENTS AND METHODS

- The study included 34 SCLC patients (limited-stage: n=7; extensive-stage: n=27), receiving first-line treatment (chemotherapy: n=18; chemotherapy/atezolizumab: n=16).
- Peripheral blood (10ml) was obtained at baseline and at the end of first-line treatment, and peripheral blood mononuclear cell (PBMC) cytospins were immunofluorescently stained for PD-L1 (E1L3N)
- PD-L1 expression was quantified on 1000 randomly selected intact PBMCs/per sample using the Ariol microscopy system.

RESULTS

Monitoring of PD-L1 expression on PBMCs during first-line treatment

- PD-L1^{high} PBMCs (Figure 1A) are identified in **17.6**% and **26.5%** of patients at baseline and at the end of treatment, respectively.
- The percentage of PD-L1^{high} PBMCs per patient is numerically higher at the end of treatment as compared to baseline (mean%±SEM: **7.8**±3.2 vs **3.6**±2.2, respectively (Figure 1B).
- In 23.5% of patients, PD-L1^{high} PBMCs are detected in the post-treatment sample only; this observation is more frequent in the chemoimmunotherapy group as compared to the chemotherapy group (**31.2% vs 16.7%** of patients).

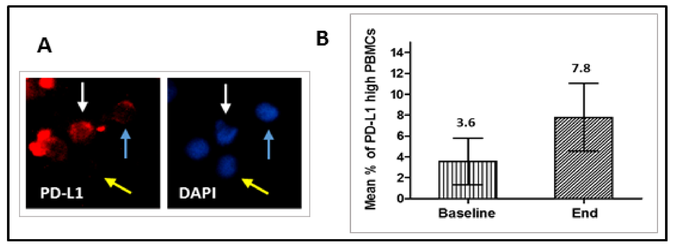

Figure 1: Monitoring of PD-L1 expression on PBMCs of SCLC patients during treatment. **A**) Representative image of PBMCs with distinct PD-L1 expression levels: high (white), low (blue) and negative (yellow), Ariol system x400. **B**) Percentage of PD-L1^{high} PBMCs per patient pre and post-treatment (Bars: mean±SEM)

Clinical relevance of PD-L1 expression on PBMCs

- The detection of PD-L1^{high} PBMCs post-treatment only is associated with disease progression in the brain (in **38.5% versus 0%** of patients with and without brain progression, respectively; p=0.009).
- A significantly shorter OS is recorded for patients treated with chemoimmunotherapy and post-treatment only PD-L1^{high} PBMCs (median OS: 8.4 versus 15.7 months; p=0.007) (Figure 2).

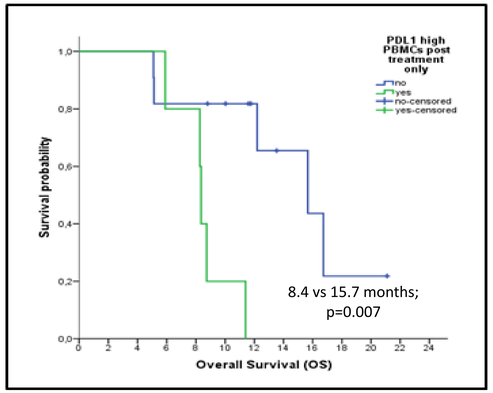

Figure 2: Kaplan Meier curve for OS of SCLC patients treated with chemoimmunotherapy, based on the detection of PD-L1^{high} PBMCs post-treatment only (no of patients: n=16).

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