The impact of PD-L1, TGF-β expression and tumor-infiltrating CD8+ T cells on clinical outcome of patients with advanced thymic epithelial tumors

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**Background:** Thymoma and thymic carcinoma are indolent and poorly responsive to chemotherapy. PD-1/PD-L1 inhibitors have shown remarkable clinical benefit in several cancers. However, many immunomodulatory molecules have been identified to affect the efficacy of immunotherapy. This study aimed to examine the expression of PD-L1, transforming growth factor-β (TGF-β), and CD8+ tumor-infiltrating lymphocytes (CD8+ TILs) in patients with advanced thymic epithelial tumors (TETs) and evaluated their prognostic roles.

**Methods:** Retrospective analysis was performed on 20 patients with stage IV thymic carcinoma and 13 patients with stage III/IV invasive thymoma. Tissue biopsies were obtained before the first-line chemotherapy. The expression level of PD-L1, TGF-β and CD8 were assessed using IHC. The high or low expression was separated by the median value of the IHC score. The outcomes including objective response rate (ORR), overall survival (OS) and progression-free survival (PFS) were then analyzed.

**Results:** The proportion of PD-L1 high was relatively higher in patients with advanced thymic carcinoma compared to patients with advanced invasive thymoma (65.0% vs 46.2%, p = 0.472). The proportion of TGF-β high in patients with thymic carcinoma was significantly higher than that in patients with invasive thymoma (65.0% vs 15.4%, p = 0.011). 5 of 7 patients in advanced thymic carcinoma with low PD-L1/TGF-β expression exhibited high level of CD8 staining. Among all patients, the median OS was 29.5 ms (95%CI: 20.8-39.0) with PD-L1 high versus 42.6 ms (95%CI: 38.0-98.3) (p = 0.186) with PD-L1 low. The median OS was 29.5 ms (95%CI: 18.6-40.4) with TGF-β high versus 62.9 ms (95%CI: 15.6-110.1) (p = 0.052) with TGF-β low. Among patients in advanced thymic carcinoma, the ORR was 30.0% with CD8 high versus 14.3% with CD8 low (p = 0.603), the median PFS was 13.3 ms with PD-L1 high versus 23.5 months (p = 0.043) with PD-L1 low. Furthermore, the ORR was 40.0% with TGF-β low versus 16.7% with TGF-β high (p = 0.538).
Conclusions: Our results showed the prognostic role of PD-L1, TGF-β and CD8+ TILs in patients with advanced TETs, and their potential for development of anti-PD-1/PD-L1 therapies.

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