

# Artificial intelligence-based spatial analysis of tertiary lymphoid structures (TLSs) and the efficacy of immunotherapy for endometrial cancer

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## **Abstract**

Tertiary lymphoid structures (TLSs) are known to be a marker of peripheral inflammation in several cancer types, there is no evidence of clinical benefit of immune checkpoint inhibitor (ICI) and special interplay pattern of TLS in endometrial cancer.

We developed an artificial intelligence (AI)-based TLSs detection program using transfer learning DeepLabV3 and performed spatial analyses of TLSs in 958 tiles from tumor samples of 258 endometrial cancer patients. And we applied this AI-based program to evaluate the relationship between spatial distribution of TLSs and survival rate or antitumor effect of immune checkpoint inhibitors for endometrial cancer patients.

A deep learning-based program that automatically recognized TLS in tumor samples showed high accuracy agreement rate (92%) for evaluation data. In 104 patients with endometrial cancer, TLSs were detected in 78% of patients, and the patients with TLSs far from tumor burden (extra-TLSs) showed more favorable progression free survival than the patients TLSs near from tumor burden (peri-TLSs) ( $p < 0.01$ ). Besides, among 12 endometrial cancer patients treated with anti-PD-1 antibody, clinical response rate of patients were 80% versus 14%.

Spatial distribution of TLSs may be closely related to patients' survival, and extra-TLSs may represent local immune status in tumor microenvironment of endometrial cancer.