

Examining the immune tumor microenvironment of Endometrial Cancer patients treated with Pembrolizumab plus Lenvatinib

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Topic: Endometrial

Objectives

Our aim is to examine the immune microenvironment of endometrial cancer (EMCA) patients treated with pembrolizumab plus lenvatinib (P+L) that could contribute to increased time on treatment. This may help inform patient selection and identify new therapeutic targets among aggressive endometrial cancer subtypes.

Methods

229 endometrial cancer patients were analyzed using Next-Gen sequencing of the DNA (NextSeq, 592 genes or NovaSeq, WES) and RNA (NovaSeq, WTS) (Caris Life Sciences, Phoenix, AZ). Time on treatment (TOT) was obtained from insurance claims and Kaplan-Meier estimates were calculated for molecularly defined patient cohorts as the time of first to last treatment of P+L. Responders (R) and non-responders (NR) were defined by treatment for > or < 6 months, respectively. Relative abundance of immune-cell infiltrates was calculated by Quantiseq. T-cell inflamed score was calculated from a 160 gene expression signature, and the interferon (IFN) score was calculated from an 18-gene signature. Statistical significance was calculated using Mann-Whitney U test.

Results

The median TOT of P+L was 4.97 months for all EMCA patients treated with P+L (n=229). The mTOT for endometrioid EMCA patients (n=93) was 5.96 months compared to 3.49 mToT for serous EMCA (n=76) (HR: 0.543, 95% CI (0.395-0.746), p-value < 0.001). Overall, all EMCA responders had higher median HLA class 2 gene expression (HLA-DQB2, 2.31-fold; HLA-DPB1, 1.42-fold; HLA-DQA1, 1.66-fold; HLA-DRB1, 1.40-fold; HLA-DPA1, 1.33-fold) and CD8+ T-cells (0.42% vs 0.06%) (p< 0.05). Of endometrioid EMCA patients, responders had increased median HLA class 2 gene expression (HLA-DPB1, 2.059-fold; HLA-DQA1, 2.580-fold; HLA-DRB1, 1.568-fold; HLA-DPA1, 1.765-fold) (all p< 0.05), but no significant differences in immune cell infiltrates or immune signatures. In serous EMCA, responders also had higher median HLA class 2 gene expression (HLA-DQB2, 4.30-fold; HLA-DPB1, 1.60-fold; HLA-DOB, 2.10-fold), CD8+ T cells, (1.41% vs 0.16%), IFN score (-0.0383 vs -0.265) and T-cell inflamed score (48 vs -67) (all p< 0.05).

Conclusions

Components of cytotoxic T-cell response in the TME including elevated IFN-γ and T-cell inflamed scores in conjunction with high expression of HLA class II was associated with longer time on treatment with P+L among serous endometrial cancers.