**CHECKPOINT INHIBITORS ARE BEING EVALUATED FOR THE TREATMENT OF GYNECOLOGIC CANCERS**

**Checkpoints Inhibitors Block Binding of T-Cell Inhibitory Receptors to Their Ligands**

Blocking this interaction promotes T-cell killing of tumor cells.

**Tumors With an Immunogenic or Inflamed Phenotype Are Often Responsive to Checkpoint Inhibitors**

<table>
<thead>
<tr>
<th>Immunogenic/Inflamed Tumors</th>
<th>Non-Immunogenic Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dense infiltration with T cells</td>
<td>• Sparse infiltration by T cells</td>
</tr>
<tr>
<td>• Cytotoxic cytokines</td>
<td>• Immunosuppressive cells or cytokines</td>
</tr>
<tr>
<td>• High PD-L1 expression</td>
<td>• Low or no PD-L1 expression</td>
</tr>
<tr>
<td>• High mutational burden</td>
<td></td>
</tr>
<tr>
<td>• Genomic instability</td>
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</tbody>
</table>

**Many Gynecologic Cancers Have Immunogenic Features**

Many endometrial cancers are highly mutated and have dense T-cell infiltration and high PD-L1 expression.

HPV-associated cervical cancers have dysfunctional PD-1/PD-L1 activity and often express PD-L1.

Ovarian cancer prognosis is linked to immune response and T-cell infiltration.

**Numerous Clinical Trials Are Evaluating Checkpoint Inhibitors for Treatment of Gynecologic Cancers**

- **Checkpoint inhibitors** are being evaluated as monotherapies and in combinations.
- **Combination strategies** include:
  - Checkpoint inhibitor + Immunotherapy
  - Checkpoint inhibitor + PARPi
  - Checkpoint inhibitor + TKI
  - Checkpoint inhibitor + Anti-angiogenic + Chemotherapy

**Checkpoint Inhibitors Are Associated With a Well-Characterized Pattern of Inflammatory Side Effects**

**irAEs**
- Are most common in the GI tract, endocrine glands, skin, and liver
- May have a delayed onset and longer duration than chemotherapy-related AEs

**Checkpoint Inhibitor Therapy Is FDA-Approved for Some Gynecologic Cancers**

Pembrolizumab is indicated for patients with:
- Previously treated, PD-L1-positive, recurrent or metastatic cervical cancer
- Previously treated, MSI-H/dMMR, unresectable or metastatic solid tumors

**Checkpoints**
- Dysfunctional immune checkpoints have been implicated in the pathogenesis of some gynecologic cancers
- Inflamed tumors with immunogenic features often respond to treatment with checkpoint inhibitors
- Combing checkpoint inhibitors with other therapies may increase efficacy and broaden the spectrum of patients who respond to therapy

**For additional content on this topic, please visit [www.GemstoneOncology.com](http://www.GemstoneOncology.com)**