CHECKPOINT INHIBITORS ARE BEING EVALUATED FOR THE TREATMENT OF GYNECOLOGIC CANCERS

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

Blocking this interaction promotes T-cell killing of tumor cells

Anti–PD-1 or anti–PD-L1 mAbs

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

Immunogenic/Inflamed Tumors

- Dense infiltration with T cells
- Cytotoxic cytokines
- High PD-L1 expression
- High mutational burden
- Genomic instability

Non-Immunogenic Tumors

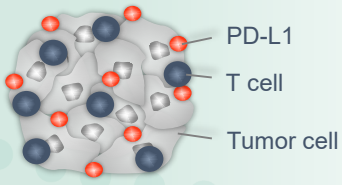
- Sparse infiltration by T cells
- Immunosuppressive cells or cytokines
- Low or no PD-L1 expression

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**



These features may render gynecologic tumors sensitive to checkpoint inhibitors

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

irAEs may have a **delayed onset** and **longer duration** than chemotherapy-related AEs

Detailed, organ-specific strategies for managing irAEs are available

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

Checkpoint inhibitors are being evaluated as monotherapies and in combinations

Combination strategies

Triple combinations

Checkpoint inhibitor

+ Immunotherapy
+ PARPi
+ TKI
+ Anti-angiogenic
+ Chemotherapy

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**

Dysfunctional immune checkpoints have been implicated in the pathogenesis of some gynecologic cancers

Checkpoint inhibitors block binding of T-cell inhibitory receptors and their ligands to activate T-cell killing of tumor cells

Inflamed tumors with immunogenic features often respond to treatment with checkpoint inhibitors

Combining checkpoint inhibitors with other therapies may increase efficacy and broaden the spectrum of patients who respond to therapy

Strategies for identifying and managing irAEs associated with checkpoint inhibitors are well-established

For additional content on this topic, please visit www.GemstoneOncology.com

AE, adverse event; dMMR, deficient mismatch repair; GI, gastrointestinal; irAE, immune-related adverse event; mAb, monoclonal antibody; MSI-H, high microsatellite instability; PARPi, poly ADP ribose polymerase inhibitor; PD-1, programmed cell death 1; PD-L1, programmed death ligand 1; TKI, tyrosine kinase inhibitor.

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