Immunotherapy Treatment Landscape for Patients With Endometrial Cancer: Current Evidence and Future Opportunities

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Abstract: Endometrial cancer is the most common gynecologic cancer in the United States, with a rising incidence and mortality. Traditionally, systemic treatment has included combination platinum- and taxane-based chemotherapy. More recently, the identification of molecular subtypes has transformed the treatment paradigms for patients with endometrial cancer, especially in the immunotherapeutic arena. Given the recent advancements in immune oncology approaches, we review regimens approved by the US Food and Drug Administration as well as the interim results of ongoing phase 3 clinical trials.

Keywords
Anti-angiogenic therapy, checkpoint inhibitors, endometrial cancer, immunotherapy, PARP inhibitors

Introduction

Endometrial cancer is the most common gynecologic cancer in the United States. Although most patients with endometrial cancer have localized disease, with a 5-year relative survival rate of 94.9%, patients with distant disease have a 5-year relative survival rate of approximately 18.4%.[1] Given the rising incidence and mortality, with emerging data suggesting that endometrial cancer may overtake ovarian cancer as the most lethal gynecologic malignancy, there is a clear need to identify effective treatment options for patients with advanced-stage or metastatic disease.

Following a series of clinical trials examining radiation therapy as well as single and doublet chemotherapy regimens, the GOG-177 trial from the Gynecologic Oncology Group identified cisplatin, doxorubicin, and paclitaxel as an effective triplet combination. Despite improvements in progression-free survival (PFS) and overall survival (OS), this regimen was associated with significant treatment-related toxicity.[2] GOG-209 then demonstrated carboplatin and paclitaxel to be noninferior to cisplatin, doxorubicin, and paclitaxel,

Table 1. Current FDA-Approved Immunotherapies for Endometrial Cancer

Regimen	Mechanism of Action	Approved Indications	Date Approved
Pembrolizumab	PD-1 inhibitor	dMMR or MSI-H endometrial cancer that has progressed after first-line chemotherapy	May 2017
Dostarlimab	PD-1 inhibitor	dMMR or MSI-H advanced or recurrent endometrial cancer that has progressed after first-line chemotherapy	April 2021
Pembrolizumab + lenvatinib	PD-1 inhibitor + VEGF inhibitor	Non-dMMR and non-MSI-H advanced endometrial cancer that has progressed after first-line chemotherapy	July 2021

FDA, US Food and Drug Administration; dMMR, mismatch repair–deficient; MSI-H, microsatellite instability–high; PD-1, programmed death 1; VEGF, vascular endothelial growth factor.

with less toxicity, ushering in an era in which carboplatin and paclitaxel became the preferred chemotherapy regimen for patients with advanced-stage or recurrent endometrial cancer.[3] Importantly, however, GOG-209 required patients to be chemotherapy-naive, which calls into question the potential benefit of a combination platinum re-challenge in patients whose disease had progressed on prior systemic chemotherapy. This notion of reduced sensitivity to cytotoxic chemotherapy in the recurrent setting was demonstrated in KEYNOTE-775, in which the median PFS for patients randomized to chemotherapy of physician's choice was less than 4 months.[4]

Historically, the treatment of patients with endometrial cancer has been risk-stratified by clinical and pathologic criteria alone. We now understand the relevance of molecular signature in potentially informing treatment outcomes. With the publication of The Cancer Genome Atlas, 4 distinct subclassifications of endometrial cancer emerged: DNA polymerase epsilon, catalytic subunit (*POLE*)–mutated; microsatellite instability–high (MSI-H); copy number–low; and copy number–high. These discoveries are helping to catalyze the investigation of anticancer therapies in a molecularly informed manner and, it is hoped, enrich responses to newly identified therapeutics.

Within the gynecologic oncology space, immunotherapy has emerged as an effective treatment strategy for certain patients, with arguably the most dramatic effect in patients with endometrial cancer. The endometrial tumor immune microenvironment is complex and dynamic. Tumor-infiltrating lymphocytes (TILs) have been observed in endometrial cancer, the association greater in cases with mismatch repair–deficient (dMMR) status.[5-8] However, the prognostic significance of TILs has been conflicting. Regulatory T cells (Tregs), which play a key role in immunosuppression and increased tolerance to tumor cells, have also been observed in patients with endometrial cancer.[9,10] Tregs secrete cytokines to signal an upregulation of M2 tumor-associated macrophages.[11] M2 tumor-associated macrophages are known to encourage tumor growth by promoting an immunosuppressive environment via programmed death ligand 1 (PD-L1) expression.[12] In an effort to capitalize on these potential immune vulnerabilities, clinical trialists have examined the potential therapeutic effect of immune checkpoint inhibitors. These successful efforts have resulted in multiple US Food and Administration (FDA)–approved immunotherapeutic options (Table 1). For patients with dMMR recurrent or progressive endometrial cancer, 2 FDA-approved second-line therapies are now available: pembrolizumab (Keytruda, Merck) and dostarlimab (Jemperli, GSK). For those with mismatch repair–proficient (pMMR) recurrent or progressive endometrial cancer, an FDA-approved second-line therapy with combination pembrolizumab and lenvatinib (Lenvima, Eisai) is available. Furthermore, multiple ongoing phase 3 trials are examining combinatorial strategies in patients with advanced-stage, recurrent, or metastatic endometrial cancer, suggesting a potentially promising future for the treatment of this disease (Table 2).

Current FDA-Approved Therapies

Initial strategies examining immune checkpoint inhibition in patients with endometrial cancer emerged following the efficacy signal in patients with dMMR colorectal carcinoma. In the KEYNOTE-158 study, patients with MSI-H or dMMR tumors were treated with single-agent pembrolizumab, an anti–programmed death 1 (PD-1) agent. Enrolled patients were treated for 2 years or until disease progression, unacceptable toxicity, or patient discontinuation. The subjects included 49 patients with endometrial cancer (21%), making it the most common noncolorectal cancer type. Those who had previously received 3 or more lines of treatment made up 33.5% of the cohort. Despite significant pretreatment, the overall response rate (ORR) was 57.1%, with complete responses reported in 8% of patients. Remarkably, the median duration of response (DOR) and median OS were not reached.[13] These dramatic findings, in a cohort of pretreated patients, helped lead to the FDA approval of

single-agent pembrolizumab for the treatment of patients with recurrent MSI-H or dMMR tumors, including endometrial cancer, in May 2017.[14] This was the first-ever disease site–agnostic drug approved by the FDA, ushering in a new paradigm of drug development.

In an analogous manner, the GARNET trial examined single-agent dostarlimab, an alternate anti–PD-1 agent, in dMMR endometrial cancer after first-line systemic treatment. In results presented as a late-breaking abstract at the Society of Gynecologic Oncology 2020 annual meeting, 71 patients with measurable disease and dMMR status demonstrated an ORR of 58%, with 13% of the patients having a complete response. The median DOR was not reached. The results of the GARNET trial informed the accelerated approval of dostarlimab in April 2021 for patients with dMMR advanced or recurrent endometrial cancer that had progressed after platinum-containing chemotherapy.[15,16] This approval was then expanded in August 2021 to all adult patients with dMMR recurrent or advanced solid tumors after progression on previous treatment.[17]

Unfortunately, the efficacy of single-agent immune checkpoint inhibitors in patients with pMMR endometrial cancer has been limited, ranging from 4% to 13%, and KEYNOTE-146/Study 111 was designed to develop effective treatment options for these patients. This was a single-arm phase 1b/2 clinical trial in which patients who had recurrent, metastatic endometrial cancer were treated with a combination of pembrolizumab at a dose of 200 mg given intravenously every 3 weeks and lenvatinib at a starting dose of 20 mg given orally daily. Analysis of the primary endpoint focused on the 108 participants who had been enrolled before July 1, 2018, and had previously received systemic therapy. Of the 108 patients, 11 had MSI-H tumors and 94 had microsatellite-stable tumors. The primary endpoint, which was ORR at 24 weeks for the entire cohort, was 38% (95% CI, 28.8-47.8%). Independently of microsatellite status, the median DOR was 21.2 months, the median PFS was 7.4 months, and the median OS was 16.7 months.[18] Given the magnitude of improvement in patients who did not have MSI-H or dMMR tumors, KEYNOTE-146/Study 111 led to accelerated FDA approval of the combination regimen of lenvatinib and pembrolizumab for the treatment of advanced endometrial cancer on September 17, 2019. The results of the confirmatory trial, KEYNOTE-775, ultimately led to full FDA approval of this regimen on July 21, 2021.[19]

Immunotherapy and Cytotoxic Chemotherapy

The combination of immunotherapy and cytotoxic chemotherapy has been under active investigation in many solid tumors, with perhaps the greatest success to date in the lung cancer arena. Targeting highly proliferating cells, cytotoxic chemotherapy (such as with platinum agents) causes DNA damage, which is hypothesized to prime the response to immunotherapy by creating neoantigens for immune identification.[20] Ultimately, the intent with combination strategies in which chemotherapy is used is to help convert less immune-responsive tumors into more immunogenic lesions. After the immunosuppressive PD-1/PD-L1 interaction is inhibited, the immune system is ignited to respond to these neoantigens, potentiating the anticancer response. In mouse models, platinum agents increased the antitumor activity of immune cells through reduced expression of PD-L2 in dendritic cells.[21] In the gynecologic cancer space, the combination of chemotherapy and immunotherapy (with or without the anti-angiogenic agent bevacizumab) resulted in a significant improvement in OS among patients with cervical cancer. In subset analysis, this efficacy benefit appeared to be limited to those cervical cancers that were PD-L1–positive as defined by a combined positive score.[22] Multiple ongoing phase 3 trials in the endometrial cancer space are examining the addition of immunotherapy to cytotoxic chemotherapy.

NRG-GY018 from NRG Oncology is designed to compare carboplatin/paclitaxel with or without pembrolizumab followed by maintenance with either pembrolizumab or placebo (NCT03914612). Participants must either be chemotherapy-naive or have had a chemotherapy-free interval of at least 12 months after prior adjuvant therapy. Importantly, this trial is designed with 2 separate patient cohorts (pMMR and dMMR), in light of the potential variability of efficacy according to biomarker status. The primary outcome of the study is investigator-assessed PFS. Secondary outcomes include OS, DOR, incidence of adverse events, objective tumor response, quality of life, incidence of self-reported neurotoxicity associated with pembrolizumab treatment, concordance between institutional MMR immunohistochemistry testing and centralized MMR immunohistochemistry, effect of pembrolizumab on PFS and OS by PD-L1 immunohistochemistry, and association between PD-L1 and MMR status.[23]

RUBY, an alternate prospective phase 3 clinical trial, evolved to have 2 parts (NCT03981796). Part 1 is designed to evaluate the addition of dostarlimab to carboplatin/paclitaxel followed by dostarlimab maintenance. Participants are required to be chemotherapy-naive or to have had a chemotherapy-free interval of at least 6 months after prior adjuvant chemotherapy. The primary outcome measure is PFS as assessed by the treating investigators. The secondary outcome measures include OS, ORR, DOR, disease control rate, and results of a quality-of-life evaluation.[24] RUBY part 2 is designed to determine the potential therapeutic

benefits of adding niraparib (Zejula, GSK), a poly(ADP-ribose) polymerase (PARP) inhibitor, in the maintenance setting, which we discuss later in this article.

DUO-E is enrolling patients with advanced-stage or recurrent endometrial cancer and randomizing them to platinum-based chemotherapy with or without the anti–PD-L1 agent durvalumab (Imfinzi, AstraZeneca), followed by placebo plus durvalumab or a combination of durvalumab and the PARP inhibitor olaparib (Lynparza, AstraZeneca; NCT04269200). Participants must be chemotherapy-naive or have had a chemotherapy-free interval of at least 12 months after prior adjuvant therapy. The primary outcome is PFS per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) by investigators. Secondary outcomes include OS, second progression, ORR, DOR, time to first and second subsequent therapy, time to discontinuation or death, pharmacokinetics, and safety.[25]

AtTEnd/MANGO is a European trial that is enrolling patients with advanced-stage or recurrent chemotherapy-naive endometrial cancer and randomizing them to carboplatin/paclitaxel with either the anti–PD-L1 agent atezolizumab (Tecentriq, Genentech) or placebo (NCT03603184). The primary outcomes of the study are OS and radiographic PFS. Secondary outcomes include ORR, DOR, safety, quality of life, and adherence.[26]

As clearly outlined above, the strong similarities in these prospective phase 3 clinical trials reflect the excitement around chemotherapy and immunotherapy combinations in the endometrial cancer space.

Combining Immunotherapy and Anti-angiogenic Therapy

Angiogenesis is necessary to support tumor growth and has been an area of treatment investigation in gynecologic cancers for many decades. Vascular endothelial growth factor (VEGF) plays a critical role in neovascularization and is also thought to suppress T-cell activation, promoting an immunosuppressive environment.[27-29]

Bevacizumab is an anti-angiogenic monoclonal antibody that binds to free circulating VEGF, preventing it from binding to its receptors.[30] GOG 229-E was a single-arm phase 2 study that explored the use of bevacizumab in advanced and recurrent endometrial cancer. The results demonstrated an ORR of 13.5%, with a surprising 6-month PFS rate of 40%.[31] In the MITO END-2 trial, bevacizumab was combined with cytotoxic chemotherapy in patients who had advanced or recurrent endometrial cancer. Although it was not statistically significant, a trend toward improvement in PFS, ORR, and OS was noted with the addition of bevacizumab to cytotoxic chemotherapy.[32]

GOG-86P was a phase 2 study that explored anti-angiogenic therapy in combination with cytotoxic chemotherapy in advanced and recurrent, chemotherapy-naive endometrial cancer. The study had 3 arms: carboplatin and paclitaxel plus bevacizumab, carboplatin and paclitaxel plus temsirolimus, and carboplatin plus ixabepilone (Ixempra, R-Pharm US) plus bevacizumab. All 3 regimens were compared with historical response rates based on the carboplatin/paclitaxel arm of GOG-209. The bevacizumab arm of the study had an ORR of 59.5% and a complete response rate of 24.7%. PFS with the addition of bevacizumab did not significantly differ from that of the carboplatin/paclitaxel group. However, in a post hoc cross-trial comparison with the carboplatin/paclitaxel arm of GOG-209, the addition of bevacizumab demonstrated a significant improvement in OS, 34 months, in comparison with 22.7 months for carboplatin/paclitaxel ($P<.039$).[33]

Lenvatinib is an oral multikinase inhibitor that targets VEGF receptors 1 to 3, fibroblast growth factor receptors 1 to 4, platelet-derived growth factor receptor alpha, RET, and KIT. The rationale for combining an anti-angiogenic multikinase inhibitor with immune checkpoint inhibition emerged after preclinical mouse xenograft models suggested more potent antitumor activity with the combination than with either agent alone. Furthermore, in the melanoma and renal cell cancer arenas, studies examining the combination of the anti–cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) agent ipilimumab (Yervoy, Bristol Myers Squibb) and bevacizumab in patients with metastatic melanoma reported that during treatment, biopsy specimens demonstrated increased CD8+ and macrophage cell infiltration in tumor beds. Additionally, extensive morphologic changes were identified in CD31+ endothelial cells, and widespread immune cell infiltration with the combination regimen.[34] Furthermore, Wallin and colleagues, in a cohort of 10 subjects with metastatic renal cell carcinoma treated on GP28328, detailed how the combination of atezolizumab and bevacizumab resulted in increased intratumoral CD8+ T cells, with a related increase in intratumoral major histocompatibility I expression, natural killer cells, helper T cells, T-effector markers, and chemokines such as CX3Cl1, also known as fractalkine.[35] These synergistic effects were hypothesized to stem from the pro-inflammatory effect of VEGF blockade, as well as hypoxia in the tumor microenvironment. Aside from their direct anti-angiogenic effects, these agents may result in more robust antitumor immunity by inhibiting VEGF-related Treg function while promoting immune cell trafficking and T-cell priming/activation.

As previously reviewed, the results of the phase 1b/2 KEYNOTE-146 study led to the design and development of the phase 3 KEYNOTE-775 study, which compared the combination of lenvatinib and pembrolizumab with

Table 2. Current Phase 3 Clinical Trials of Endometrial Cancer Treatments That Include Immunotherapy

Study Name	Included Participants	Arms	Anticipated Accrual, N	Endpoint	Current Status
Frontline setting					
LEAP-001 (NCT03884101)[36]	Stage III-IV or recurrent endometrial cancer with no prior systemic treatment	Pembrolizumab/lenvatinib Carboplatin/paclitaxel	875	BICR-assessed PFS and OS	Active, not recruiting
NSGO-RUBY/ GOG-3031 (NCT03981796)[24]	Stage III-IV or recurrent endometrial cancer with no prior systemic treatment	Carboplatin/paclitaxel + placebo followed by placebo maintenance Carboplatin/paclitaxel + dostarlimab followed by dostarlimab maintenance Carboplatin/paclitaxel + dostarlimab followed by dostarlimab + niraparib maintenance	740	BICR-assessed PFS	Recruiting
KEYNOTE-B21/ GOG-3053 (NCT04634877)[51]	High-risk endometrial cancer with no prior systemic treatment	Carboplatin/paclitaxel + placebo followed by placebo maintenance +/- radiation therapy Carboplatin/paclitaxel + pembrolizumab followed by pembrolizumab maintenance +/- radiation therapy	990	Investigator-assessed PFS and OS	Recruiting
DUO-E/GOG-3041 (NCT04269200)[25]	Stage III-IV or recurrent endometrial cancer with no recent (>12 mo) systemic treatment	Carboplatin/paclitaxel + placebo followed by placebo maintenance Carboplatin/paclitaxel + durvalumab followed by durvalumab + placebo maintenance Carboplatin/paclitaxel + durvalumab followed by durvalumab + olaparib maintenance	699	Investigator-assessed PFS	Recruiting
Second-line setting					
NRG-GY018 (NCT03914612)[23]	Stage III-IV or recurrent endometrial cancer with no recent (>12 mo) systemic treatment	Carboplatin/paclitaxel + placebo followed by placebo maintenance Carboplatin/paclitaxel + pembrolizumab followed by pembrolizumab maintenance	810	Investigator-assessed PFS	Recruiting
AtTEnd (NCT03603184)[26]	Stage III-IV or recurrent endometrial cancer with no recent (>6 mo) systemic treatment	Carboplatin/paclitaxel + placebo followed by placebo maintenance Carboplatin/paclitaxel + atezolizumab followed by atezolizumab maintenance	550	Investigator-assessed PFS and OS	Active, not recruiting

BICR, blinded independent central review; GOG, Gynecologic Oncology Group; mo, months; NSGO, Nordic Society of Gynaecological Oncology; OS, overall survival; PFS, progression-free survival.

physician's choice of either doxorubicin or paclitaxel.[18] In the updated results of KEYNOTE-775, presented at the Society of Gynecologic Oncology 2021 annual meeting, the median PFS for all-comers was 7.2 months in the lenvatinib-plus-pembrolizumab group vs 3.8 months in the doxorubicin or paclitaxel group (hazard ratio [HR], 0.56; 95% CI, 0.47-0.66; *P*<.001). The median OS was also improved in the lenvatinib-plus-pembrolizumab group vs the doxorubicin or paclitaxel group, at 18.3 vs 11.4 months, respectively (HR, 0.62; 95% CI, 0.51-0.75; *P*<.001). Specifically, in the pMMR subgroup, benefits were still seen in the lenvatinib-plus-pembrolizumab arm, with a median PFS of 6.6 months vs 3.8 months in the doxorubicin or paclitaxel group (HR, 0.60; 95% CI, 0.50-0.72; *P*<.001). The median OS in the pMMR group was 17.4 months in the lenvatinib-plus-pembrolizumab group vs 12 months in the physician's choice of chemotherapy arm (HR, 0.68; 95% CI, 0.56-0.84; *P*<.001). An increase in ORR, 30.3% vs 15.1%, favored the lenvatinib-plus-pembrolizumab combination arm. Lastly, DOR was longer, at 9.2 months vs 5.7 months.[4]

Adverse events of grade 3 or higher occurred in 88.9% of patients in the lenvatinib-plus-pembrolizumab group vs 72.7% of those receiving physician's choice of chemotherapy. The most common serious adverse event was hypertension in the lenvatinib-plus-pembrolizumab group, with any adverse events leading to dose reduction in 66.5% of patients, treatment interruption in 69.2%, and discontinuation in 33%. The most common serious adverse event in the chemotherapy group was febrile neutropenia, with any adverse events leading to dose reduction in 12.9%, interruption in 27.1%, and discontinuation in 8.0%. No differences in reported quality of life were noted between the lenvatinib-plus-pembrolizumab group and the physician's choice group.[4] These results led to FDA approval of lenvatinib plus pembrolizumab in recurrent pMMR/non–MSI-H endometrial cancer in July 2021.[19]

In the frontline setting, the phase 3 LEAP-001 trial is looking to compare the combination of lenvatinib plus pembrolizumab with carboplatin/paclitaxel in patients who have advanced-stage or recurrent endometrial cancer and are chemotherapy-naive (NCT03884101).[36] The co-primary endpoints of the study are PFS and OS. Secondary endpoints include ORR, quality of life, and adverse events. Ultimately, the hope is to replace cytotoxic chemotherapy with alternate treatment strategies that are more effective.

Combining Immunotherapy and PARP Inhibitors

PARP inhibitors are thought to function via multiple mechanisms, although they lead to tumor cell death principally by interfering with high-fidelity DNA damage repair. Although significant gains have been achieved in the ovarian cancer arena with PARP inhibition, no indications for PARP inhibitors exist in the endometrial cancer space. Homologous recombination deficiency, a known biomarker for PARP inhibitor sensitivity in ovarian cancer, is hypothesized to occur in approximately 26% of cases of endometrial cancer.[37] With increased DNA damage by PARP inhibition, cytosolic DNA fragments increase. These interactions are thought to augment neoantigen formation and also may increase the secretion of interferon, which is thought to recruit an antitumor immune response.[38,39] Conversely, however, PARP inhibitors have been seen to upregulate PD-L1 expression in xenograft breast cancer and pancreatic cancer mouse models.[40,41]

The addition of immune checkpoint inhibitors might work synergistically with PARP inhibition by activating the immune system to recognize neoantigens and further the antitumor immune response.[38,42,43] PD-L1 inhibitors paired with PARP inhibitors in ovarian xenograft models were shown to offset the immunosuppressive upregulation of PD-L1 expression caused by PARP inhibitors, which would further potentiate the immune response.[44] As previously described, 2 ongoing phase 3 clinical trials are examining the synergistic relationship between immunotherapy and PARP inhibition: DUO-E and RUBY part 2.[25,45]

Future Directions

The incorporation of immunotherapeutics in the management of patients with advanced-stage or recurrent endometrial cancer has been transformative, achieving objective and durable responses that have clearly surpassed those in historical controls. It appears that this benefit is greatest in biomarker-selected patient populations (dMMR, MSI-H, or tumor mutational burden–high), although the combination of lenvatinib and pembrolizumab has shown efficacy in an all-comer patient population.

Furthermore, it will be important to determine if immunotherapy is a feasible replacement for chemotherapy in patients with dMMR endometrial cancer. This use of immunotherapy has been established in the colorectal cancer space. KEYNOTE-177 demonstrated the use of pembrolizumab alone as first-line therapy for MSI-H or dMMR colorectal cancers, leading to FDA approval for this indication.[46,47] MK-3475-C93/KEYNOTE-C93/GOG-3064/ENGOT-en15 is a multicenter, open-label phase 3 trial that is randomizing patients with advanced or recurrent, chemotherapy-naive, dMMR endometrial cancer to pembrolizumab monotherapy or carboplatin/paclitaxel.[48] This study is in addition to LEAP-001, which is looking potentially to replace chemotherapy

with up-front pembrolizumab and lenvatinib in the pMMR-selected population.[36]

Given the current ongoing phase 3 clinical trials, it is clear that we need to begin exploring treatment options in the post–immune checkpoint inhibitor patient population. A phase 2 trial by Lheureux and colleagues is examining cabozantinib and nivolumab in patients with heavily pretreated recurrent or advanced endometrial cancer. Early results demonstrated better PFS with the addition of cabozantinib (Cabometyx, Exelixis) than with nivolumab alone.[49] An exploratory arm in this trial included patients who had prior immune checkpoint exposure, with 6 patients having a response to the combined therapy and 8 patients exhibiting stable disease.[50] Lastly, the use of dual immunotherapy with combination CTLA-4 and PD-1 blockade has shown promising results in melanoma and may afford an alternate opportunity in endometrial cancer. Currently, the phase 2 NRG-GY025 trial is examining nivolumab and ipilimumab in patients with recurrent dMMR endometrial cancer and is allowing selected patients previously treated with immune checkpoint inhibitors to enroll.[51] This trial may inform the utility of dual checkpoint blockade in endometrial cancer.

The treatment landscape for endometrial cancer is rapidly evolving, and our molecular understanding of the disease has facilitated transformative gains. We eagerly await the results of the current phase 3 trials, which will ultimately inform future studies and may establish new standard-of-care treatment approaches for patients battling this aggressive disease.

Disclosures

Dr Hom-Tedla has no disclosures. Dr Eskander has received fees for research, educational, or advisory-related activities from AstraZeneca, Cardiff Oncology, Clovis Oncology, Daiichi-Sankyo, Eisai, Elevar Therapeutics, Lilly, Genentech/Roche, GSK/Tesaro, Immunogen, Merck, Mersana Therapeutics, Myriad Genetics, and MorphoSys.

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