The use of lenvatinib and pembrolizumab after platinum-based chemotherapy in advanced endometrial cancer

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Endometrial cancer is a common cancer in women. While there are several treatment options, there is a need for newer, more effective therapies. One such option is combining lenvatinib, a targeted therapy, with pembrolizumab, an immunotherapy. This combination has shown promising results in treating advanced endometrial cancer, especially after patients have undergone chemotherapy with platinum-based drugs. However, more research is needed to fully understand its benefits and risks. This case report presents a patient with recurrent disease treated with lenvatinib and pembrolizumab, highlighting its potential efficacy.

Keywords: lenvatinib, pembrolizumab, platinum-based chemotherapy, advanced endometrial cancer

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Case report

A 52-year-old female patient presented with a three month history of recurrent vaginal bleeding and persistent pelvic pain after her initial diagnosis of advanced endometrial cancer.

She had previously undergone surgery (total abdominal hysterectomy) followed by chemotherapy with doxorubicin. Although her symptoms initially improved after chemotherapy, they returned and worsened in recent months. The patient reported significant vaginal bleeding and persistent pelvic pain.

The patient had completed four cycles of chemotherapy without any serious side-effects. She had no allergies, no family history of cancer, and did not smoke or drink alcohol. On examination, she appeared fatigued but was otherwise stable. Her blood pressure, heart rate, and other vital signs were within normal limits. During a pelvic exam, a friable (easily bleeding) lesion was found in the vaginal cuff, but no masses were felt. Her full blood count revealed a mild anaemia with haemoglobin of 10.8 g/dL, white blood cell count of 7,2 x 10^9/L, and a platelet count of 220 x10^9/L. Her collective metabolic panel were within normal limits.

A pelvic ultrasound was inconclusive due to the patient's post-hysterectomy status, and no definitive abnormalities were noted. The chest X-ray demonstrated no evidence of metastatic disease. However, a CT scan confirmed the presence of a recurrent mass in the pelvic area involving the vaginal cuff.

Based on the clinical presentation, physical examination findings, and imaging studies, the patient was diagnosed with recurrent advanced endometrial cancer and was referred to a gynaecologic oncologist.

Treatment options depend on several factors, including the extent of disease, previous treatment response, performance status, and overall health. Potential treatment modalities including surgical resection, radiation therapy, and systemic therapies such as targeted agents, immunotherapy, or participation in clinical trials were discussed.

Discussion

This case supports the growing body of evidence that lenvatinib and pembrolizumab can be effective for patients with recurrent endometrial cancer following platinum-based chemotherapy.

Recent studies, highlighted in Table I, including the KEYNOTE-775 trial, have shown that this combination therapy significantly improves both progression-free survival (how long the cancer doesn't worsen) and overall survival compared to other treatments.[1]

These studies suggest that lenvatinib, which blocks certain proteins involved in cancer growth, works well with pembrolizumab, an immunotherapy that helps the immune system fight cancer cells.

In a study by Yonmorei et al. (2022), the study findings were consistent with global data from the KEYNOTE-775 study, showing the effectiveness of lenvatinib and pembrolizumab in Japanese patients with advanced endometrial cancer. The safety profile of the combination therapy was manageable, and no new safety concerns were identified among the Japanese population.[1]

Another trial by Makker et al. (2022) also demonstrated improved progression-free survival and overall survival with lenvatinib and pembrolizumab, compared to placebo plus pembrolizumab. The study found that the combination resulted in a median progression-free survival of 16.7 months and overall survival of 33.2 months. The treatment was well-tolerated, with fatigue, diarrhoea, and hypertension being the most common side-effects.[2]

Lastly, a study by Ott et al. (2017) did not fully evaluate the long-term safety of pembrolizumab and differences in overall survival due to the study's shorter duration.[3]

However, the use of lenvatinib plus pembrolizumab has certain limitations. Many patients experience side-effects, leading to dose reductions or treatment discontinuation. In addition, some

Table I: Summary of key studies on lenvatinib and pembrolizumab in advanced endometrial cancer

Author, Year, Country	Study type	Key results	Study weaknesses
Yonemori et al. (2022), Japan[1]	RCT	- Lenvatinib plus pembrolizumab extended progression-free survival (PFS) in patients with proficient mismatch repair (pMMR) tumours. - Improved overall survival (OS) compared to Treatment of Physician's Choice (TPC). - Well-tolerated with manageable side-effects.	- No significant differences in overall survival. - Conducted in a single country. - Short follow-up for assessing long-term safety.
Makker et al. (2022), USA[2]	RCT	- Lenvatinib plus pembrolizumab significantly prolonged both PFS and OS compared to chemotherapy. - Median PFS: 16.7 months, Median OS: 33.2 months. - Manageable safety profile with fatigue, diarrhoea, and hypertension being common side- effects.	- No placebo arm, making it difficult to attribute results solely to the combination therapy. - Select population; generalisability may be limited. - No assessment of patient-reported outcomes.
Arora et al. (2020), USA[4]	RCT	- Pembrolizumab as monotherapy showed long-lasting efficacy against tumours. - Only four patients experienced grade 3 adverse events. No grade 4 or immune-mediated adverse events.	- Study not powered to detect differences in overall survival. - Single-country study; may not be generalisable. - Short follow-up for long-term safety assessment.
Ott et al. (2017), USA[3]	RCT	**- Objective Response Rate (ORR) of 26.3%. - Median PFS of 8.3 months. - Common adverse events included fatigue, pruritus, and pyrexia.**	**- No placebo arm. - Select population, limited generalisability. - No assessment of patient-reported outcomes.**

RCT = Randomised Controlled Trial

studies lacked patient-reported outcome (PROs) measures, making it unclear how the combination therapy affected the quality of life of patients. Future research should include PROs to better evaluate how these therapies affect patients beyond just survival outcomes.

Conclusion

In summary, the combination of lenvatinib and pembrolizumab has shown significant potential for treating recurrent advanced endometrial cancer, especially in patients who have already undergone platinum-based chemotherapy. The evidence indicates improvements in progression-free and overall survival, with manageable side-effects. This makes the combination a promising option for patients like the one presented in this case report, making her a suitable candidate for this treatment approach.

While lenvatinib plus pembrolizumab offers a promising treatment option, ongoing research and individual patient assessment remain essential to optimise treatment outcomes and minimise side-effects to ensure that the treatment is as effective and tolerable as possible.

Considering the clinical presentation, results of the physical examination, and findings from imaging studies, our patient is diagnosed with recurrent advanced endometrial cancer involving the vaginal cuff. This recurrence has occurred despite prior treatment with doxorubicin-based chemotherapy, which aligns with the inclusion criteria of the aforementioned studies. The use of lenvatinib plus pembrolizumab has shown improved progression-free survival compared to the physician's choice of treatment, as well as improved overall survival. Additionally, the combination therapy has demonstrated a manageable safety profile with adverse events that can be effectively addressed. Given these factors, it is evident that our patient is a suitable candidate for lenvatinib in conjunction with pembrolizumab.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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