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Authors' Affiliation:
[1]Student's Scientific Association at the 1st Chair and Department of Oncological Gynecology and Gynecology, Medical University of Lublin, Staszic 16 St., 20-081 Lublin, Poland
[2]University Clinical Hospital No.2 of Medical University of Lodz, Pomorska 251 St., 92-213 Łódź, Poland
[3]1st Chair and Department of Oncological Gynaecology and Gynaecology, Medical University of Lublin, Staszic 16 St., 20-081 Lublin, Poland

***Corresponding author:**
Natalia Gierulska, Student's Scientific Association at the 1st Chair and Department of Oncological Gynecology and Gynecology, Medical University of Lublin, Staszic 16 St., 20-081 Lublin, Poland; e-mail: gierulskanatalia@gmail.com
Tel: (+48) 663 167 878

Contact List

Natalia Gierulska	- gierulskanatalia@gmail.com
Katarzyna Lachowska	- k.lachowska78@gmail.com
Joanna Ocicka	- ocickajoanna@gmail.com
Julia Orzelska	- j.orzelska811@gmail.com
Patrycja Wójcikiewicz	- wojcikiewiczpatrycja01@gmail.com
Amelia Trzcińska	- amelia.trzcinska33@gmail.com
Aleksandra Kubas	- a.kubas47@gmail.com
Rafał Tarkowski	- rafaltar@yahoo.com
Krzysztof Kułak	- krzysztof.kulak@gmail.com

Orcid List

Natalia Gierulska	- 0009-0005-8136-9997
Katarzyna Lachowska	- 0009-0004-2702-3461
Joanna Ocicka	- 0009-0009-6294-473X
Julia Orzelska	- 0009-0005-9589-6499
Patrycja Wójcikiewicz	- 0009-0004-0160-7020
Amelia Trzcińska	- 0009-0006-3577-3996
Aleksandra Kubas	- 0000-0003-0535-9832
Rafał Tarkowski	- 0000-0001-6926-5419
Krzysztof Kułak	- 0000-0001-9059-484X

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The role of innovative studies DUO-E treatment in recurrent endometrial cancer - case report

Natalia Gierulska[1*], Katarzyna Lachowska[1], Joanna Ocicka[1], Julia Orzelska[1], Patrycja Wójcikiewicz[1], Amelia Trzcińska[1], Aleksandra Kubas[2], Rafał Tarkowski[3], Krzysztof Kułak[3]

ABSTRACT

Recurrences of endometrial cancer occur in the early stages. Until now, the primary treatment has been platinum-based chemotherapy. However, there is hope in the use of immunotherapy. A 56-year-old patient went to the hospital for a planned ovariohysterectomy. Hystopathological examination performed after surgery revealed tubular endometrial adenocarcinoma G2. After the first stage of radiotherapy a patient had a complete response to treatment. CT-scan showed a remission of lesions after 36 months. After performing the appropriate tests, doctors qualified the patient for the DUO-E study, during which she received six cycles of Durvalumab. The treatment with Durvalumab resulted in a reduction of the tumor. The case highlights the benefits of combining surgery with radiotherapy and immunotherapy. The DUO-E study stands out for its use of a PARP inhibitor. This gives hope for the individualisation of therapy in the future.

Keywords: Recurrence, Endometrial Cancer, Clinical Trial, DUO-E study, Durvalumab

1. INTRODUCTION

Endometrial cancer ranks as the leading gynecologic malignancy, with a growing global burden in terms of both incidence and disease-related deaths (Grodhandas et al., 2023). Endometrial cancer is currently the most common gynaecological cancer with an overall 5-year survival rate of around 80% (for all stages considered together) (Crosbie et al., 2022; Concin et al., 2021). It is the third most prevalent malignant tumor in the female population. There are two types of this cancer. Type 1 is endometrial adenocarcinoma, which develops during the perimenopausal period. It has a good prognosis. Type 2 is a highly malignant tumour with a tendency to recur. It is not associated with hormonal stimulation and mainly affects women aged between 60 and 70. It is a serous, clear cell carcinoma which has worse prognosis (Crosbie et al., 2022).

Risk factors for endometrial cancer consist of increasing age, long-term exposure to unopposed oestrogens, high concentrations of oestrogens postmenopausally and metabolic syndrome. Factors that reduce the risk of endometrial cancer include

multiple births, the use of oral contraceptives, and physical activity (Concin et al., 2021; Tronconi et al., 2022). Complete gynecological examination with biopsy or curettage of the uterine cavity and transvaginal ultrasound will identify low-risk tumors in women. Although the most common sign of endometrial cancer is abnormal uterine bleeding, which is non-specific. Further diagnostic endometrial evaluation should be performed on all postmenopausal women who experience vaginal bleeding and abnormal uterine bleeding linked to risk factors for endometrial cancer or hyperplasia (Crosbie et al., 2022; Concin et al., 2021).

Recurrence occurs in the early-stage of the disease at a rate of 10-15%, and in as many as 40-70% of cases detected at an advanced stage. Most of these occur in the first 3 years of follow-up. Patients with recurrent endometrial cancer have a poor prognosis and limited therapeutic options (Tronconi et al., 2022). What's more, a lot of patients who are diagnosed with recurrence are resistant to treatment with platinum-based chemotherapy (Rubinstein et al., 2019).

The search strategy mainly included the PubMed and Scopus databases. There were no limitations regarding country of origin or data. The analysis includes publications in English released after 2019, available in full text.

2. CASE REPORT

Doctors referred a 56-year-old patient for a planned hysterectomy with bilateral removal of the adnexa due to atypical endometrial proliferation and uterine fibroids. She had been hospitalized in Zamość since March 2017. The result of the histopathological examination performed postoperatively showed the presence of endometrial tubular adenocarcinoma grade G2, FIGO II, confined to the uterus. As a result of the diagnosis, teleradiotherapy of the reproductive organ locus and regional nodes was performed in April 2017, using a dose of 50 Gy. In addition, two months later, the patient received intracameral HDR brachytherapy of the vaginal stump with a dose of 14 Gy, in 2 fractions. After the first line of treatment, a CT scan of the chest, abdomen, and pelvis confirmed complete remission.

The patient remained under regular follow-up. In January 2020, a CT scan showed lesions in the upper right lung and the anterior wall of the shell. A PET scan showed a neoplasm-like lesion in the rectus abdominis muscles measuring 32x28mm. Due to the pandemic, the patient neglected further management. The patient went to the Oncology Gynecology Department of University Clinical Hospital No 1 in Lublin in March 2021. A CT scan performed at the clinic showed an infiltrate measuring 86x42mm and 75mm in vertical dimension extending from the pubic conjunctiva to the umbilicus and from the rectus abdominis muscles to the supraperitoneal peritoneal capsule (figures 1 and 2). There was periaortic lymphadenopathy and lymph node enlargement in the right axillary cavity. Additional diagnostics evaluated the biological features of the patient's tumor. The presence of dMMR and PD-L1 protein allowed the patient to be included in the DUO-E clinical trial. The patient received six cycles of 1120 mg Durvulumab, Paclitaxel 306 mg, Carboplatin 665 mg and Olaparib. After the sixth cycle of therapy, a follow-up CT scan was performed in August 2021, which showed a reduction in tumor size to 17 x 15 mm and 40 mm in vertical dimension and regression of lymphadenopathy. Maintenance treatment included olaparyb/placebo 150 mg 1/d p.o. Durvalumab every 4 weeks. She received the treatment for 18 consecutive months. Subsequent follow-up examinations showed progressive enlargement of the tumor of the anterior abdominal wall and periaortic nodes. In addition, there was tissue infiltration on the anterior wall of the urinary bladder so doctors decided to stop the patient's treatment due to disease progression, according to RECIST 1.1 criteria. During the DUO-E study, patients experienced adverse events such as: G1 neutropenia, upper limb oedema, G1 anaemia, and hypothyroidism.

In July 2023, the patient had a CT scan, which showed progression of the lesion to 51 x 34 mm. Treatment with hormone therapy was attempted, but did not result in a significant response. In September of the same year, the tumor grew to 112 x 54 x 87 mm - a progression in size from the previous scan. In addition, there was an osteolytic infiltration of the left pubic bone branch with disruption of the cortical layer measuring 39 x 19 mm. The patient was qualified for Dostralimab treatment under the rescue access to drug technology (RTDL). In December of the same year, a CT scan showed an increase in the size of the lesion to 150 x 55 x 141 mm. There was also progression of infiltration of the pelvic wall and bony structures, and progression of infiltration through the continuity of the bladder wall. The patient did not respond positively to any of the proposed treatments. In January 2025, the patient was admitted urgently to the Oncology Gynecology Department of University Clinical Hospital No 1 in Lublin because of urethral bleeding, urinary disturbances, and thrombocytopenia. The patient received symptomatic treatment and doctors began further diagnosis of the lesion. Unfortunately, after a gynecological consultation, the gynecologists decided that they had exhausted all therapeutic options. Specialists decided to transfer the patient to another hospital, where he will continue palliative treatment.

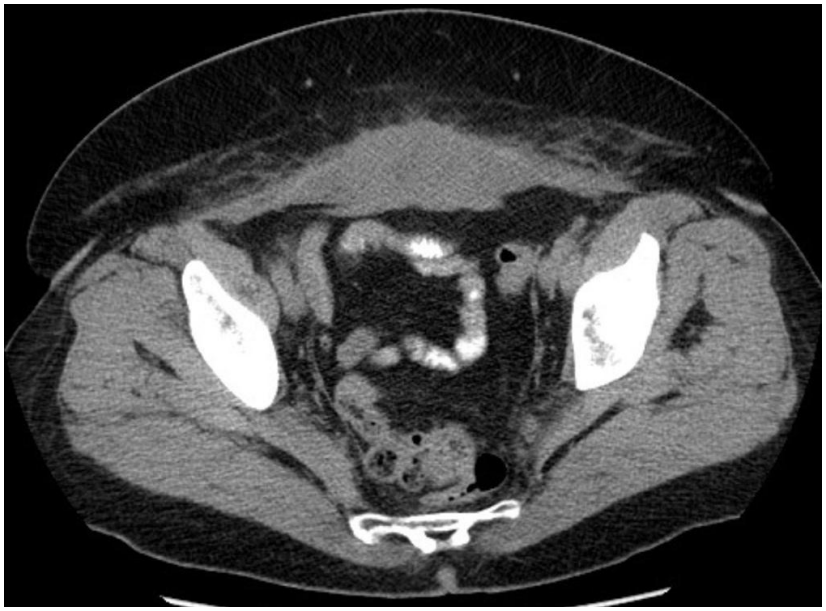

Fig.1. A CT scan showing a lesion in the rectus abdominis muscles (March 2021).

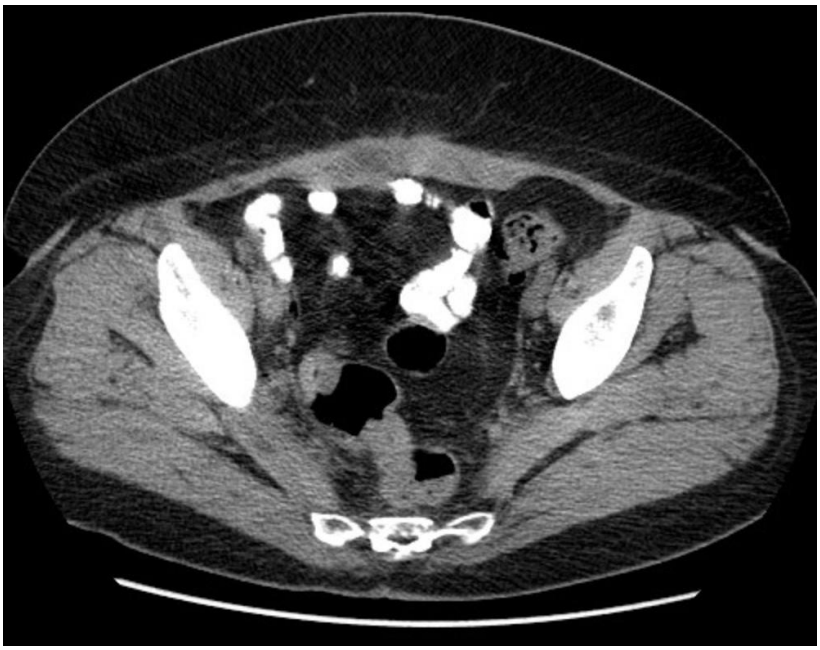

Fig 2. A CT scan showing a regression of the lesion in the rectus abdominis muscles after taking six cycles of Durvalumab with Paclitaxel, Carboplatin and Olaparib (August 2021).

3. DISCUSSION

Current treatment of recurrent endometrial cancer consists of platinum-based chemotherapy, being a first-line treatment, and hormonal therapy as a second-line treatment, with radiotherapy or surgery being an alternative (Tronconi et al., 2022). The most common type of first-line chemotherapy is the combined use of Carboplatin and Paclitaxel in six cycles, with Paclitaxel administered every three weeks. According to current ESMO guidelines, if there are contraindications or if Carboplatin and Paclitaxel are ineffective, Doxorubicin (in monotherapy or in combination with Cisplatin) can be used. Immunotherapy may be effective in patients with deficient mismatch repair (dMMR) positive and proficient mismatch repair (pMMR) positive patients (Oaknin et al., 2022).

Surgical treatment of recurrent endometrial cancer is used selectively and depends on some clinical factors. According to ESGO/ESTRO/ESP guidelines, surgery may be considered in patients with recurrent disease if complete macroscopic resection can achieve acceptable morbidity. It mainly applies to cases of recurrence confined to the pelvis or lymph nodes (Concin et al., 2021).

At this moment, immunotherapy is yielding outstanding results, leading to a change in the approach to treating recurrent endometrial cancer. The average survival rate for clinical trial participants is approximately 12 months (Tronconi et al., 2022). DUO-E testing yields the most significant results in patients with a positive dMMR result (such as the patient), a positive pMMR result, and a positive PD-L1 result (Oaknin et al., 2022; Westin et al., 2024).

In addition to the DUO-e study, other studies such as RUBY and NRG-GY018 are also underway to evaluate the impact of immunotherapy on the treatment of endometrial cancer. RUBY concerns the use of Dostarlizumab as a first-line drug and has shown a significant improvement in survival time in women. NRG-GY018 evaluates the effect of Pembrolizumab (Lee et al., 2025; Powell et al., 2024).

Many adverse events were reported in studies: RUBY and NRG-GY018. However, in the RUBY study, there was greater improvement in both dMMR(+) and pMMR(+) patients (Powell et al., 2024; Eskander et al., 2025). In both the RUBY, DUO-E, and NRG-GY018 trials, the primary endpoint was PFS (Progression-Free Survival). In three of the studies mentioned above, the most significant number of patients (816) participated in the NRG-GY018 study. The others consisted of 699 in the DUO-E study and 494 in the RUBY study. Of the three trials, the DUO-E trial stands out in particular for its additional use of the PARP inhibitor-olaparib in the maintenance phase, which allows for greater individualization of treatment - especially for patients who have BRCA mutations, among other things (Westin et al., 2024; Powell et al., 2024; Eskander et al., 2025).

Modern immunotherapy strategies, including immune checkpoint inhibitors such as Pembrolizumab, Durvalumab, and Dostarlimab, used both as monotherapy and in combination with chemotherapy or other targeted drugs (e.g., Olaparib, Lenvatinib), have shown significant efficacy in the treatment of advanced and recurrent endometrial cancer. The results of recent clinical trials provide a basis for modifying current therapeutic recommendations and creating new treatment options for patients with limited therapeutic options (Mirza et al., 2023; Zhu et al., 2024). The DUO-E study complies with the principles of the Declaration of Helsinki (Westin et al., 2024). Table 1 shows a summary of the treatment of recurrent endometrial cancer.

Table 1. Treatment of recurrent endometrial cancer and key clinical trials.

Treatment / Study	Description	Notes
I-line Chemotherapy	Carboplatin + Paclitaxel (6 cycles)	ESMO standard (Tronconi et al., 2022)
Alternative	Doxorubicin ± Cisplatin	In the absence of effectiveness or contraindications
Hormone therapy	II-line treatment	For hormone-dependent tumours
Surgery	Possible with total resection	Mainly at the turn in the pelvis/nodes (Concin et al., 2021)
Immunotherapy	Pembrolizumab, Durvalumab, Dostarlimab	Particularly effective in dMMR+, also in pMMR+ (Oaknin et al., 2022; Mirza et al., 2023)
DUO-E	Durvalumab	699 patients, innovative maintenance therapy (Westin et al., 2024)
RUBY	Dostarlimab	494 patients, improvement in PFS and OS (Lee et al., 2025; Powell et al., 2024)
NRG-GY018	Pembrolizumab	816 patients, efficacy in dMMR+ and pMMR+ (Powell et al., 2024; Eskander et al., 2025)

4. CONCLUSION

The patient's case shows the effectiveness of surgical treatment in combination with radiotherapy, but also the risk associated with the possibility of relapse. Recurrences of endometrial cancer are really difficult to detect because symptoms are not pathognomic. That's why regular gynecological exams are crucial, especially for postmenopausal women and those in remission.

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Authors' Contributions

The Abstract, Keywords and the overall integration of the text of the case report was written and prepared by Natalia Gierulska and Aleksandra Kubas. The Introduction was written by Joanna Ocicka, Julia Orzelska and Amelia Trzcińska. Case Presentation was prepared by Katarzyna Lachowska and Joanna Ocicka. Natalia Gierulska and Patrycja Wójcikiewicz wrote the Discussion. Conclusions were prepared by Natalia Gierulska. Krzysztof Kułak was responsible for referring to the paper during the writing process and prepared figures 1 and 2. Rafał Tarkowski and Krzysztof Kułak conceived the idea for the review, supervised the project, provided critical revisions to the manuscript, and approved the final version. All authors read and approved the final manuscript.

Informed consent

The patient consented to the publication of photographs. Written & Oral informed consent was obtained from individual participant included in the study.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the corresponding author.

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