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An Open-label, Single Arm, Phase II Trial of Niraparib in Combination With Anti-PD1 Antibody in Recurrent/ Advanced Stage Endometrial Cancer Patients (SINI)

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Background

- Endometrial carcinoma is the most common malignancy of the female reproductive tract. The anti-tumor activity of second-line chemotherapy for recurrent or advanced endometrial cancer is poor, with an objective response rate of about 15%.
- PD-1 antibody was approved for the treatment of MSI-H/ dMMR unresectable or metastatic solid tumors, including endometrial cancer. Sintilimab is a high-affinity antibody against PD1 that was approved in China.
- Niraparib was approved for the maintenance treatment of ovarian cancer, and back-line rescue treatment for BRCA/HRD-positive advanced ovarian cancer.
- Recent studies demonstrated that PARP inhibitors might alleviate resistance and enhance the efficacy of immune checkpoint blockade therapy.

Table 1. Brief Inclusion and Exclusion Criteria

Inclusion Criteria:	Main Exclusion Criteria:
1.Patients volunteered to participate in this study, signed informed consent, good compliance, and cooperated with follow-up; 2. Recurrent or advanced endometrial cancer patients who were incurable via local therapies, and progressed after at least one line of platinum-based chemotherapy. 3. 18-70 years of age and female; 4. ECOG performance status of 0-1; 5.Expected survival longer than three months; 6. Histologically confirmed endometrial epithelial carcinoma; 7. At least one measurable lesion by irRECIST; 8. Pathologically confirmed epithelial endometrial cancer ; 9. Subjects provide formalin-fixed and paraffin-embedded tumor tissue samples for pathological consultation; 10. Life expectancy ≥ 16 weeks; 11. Good organ function, including: 12.Previous hormonal or immunotherapy was permitted. 13.The adverse effects of any previous treatment have returned to ≤ CTCAE grade 1 or baseline, except for symptomatically stable sensory neuropathy,hair loss, and anemiaa.	• 1. History of any PARP inhibitors; • 2. Patients with other invasive cancers within 5 years of enrollment, with the exceptions of cancers in situ within 2 years, such as squamous cell skin cancer, breast cancer, etc. • 3. The last systemic or radical anti-tumor therapies were completed within 4 weeks before the first dose • 4. Received immunomodulatory drugs or agents with anti-tumor effects within 2 weeks before enrollment. • 5. Had major surgery within 4 weeks before the start of the study or was expected to undergo major surgery during the study period. • 6. Uncontrollable pleural and ascites. • 7. Any active autoimmune disease or a history of autoimmune diseases; • 8.Known hypersensitivity to niraparib/PD-1 antibody or active or inactive ingredients of drugs with a similar chemical structure to niraparib/PD-1 antibody. • 9. Subjects who have severe or uncontrolled diseases • 10.Treatment with systemic corticosteroids (≥ 10 mg/day prednisone or equivalent) or other immunosuppressive drugs within 14 days prior to the initiation of the study treatment. • 11.Untreated or symptomatic brain metastases or leptomeningeal metastases.

Current status

- This study is currently enrolling patients.
- The estimated primary completion date is Sep 1st, 2022
- Clinical trial information: NCT04885413

Trial design

- The trial aims to evaluate the activity and safety of Niraparib plus Sintilimab in patients with recurrent/ advanced endometrial cancer.
- 37 patients were scheduled to be enrolled.
- Key eligibility criteria included: patients aged 18–70 years; measurable lesions per irRECIST; history of at least one line of chemotherapy and ECOG performance status of 0-1.
- Patients received niraparib 200 mg orally QD and intravenous sintilimab 200 mg d1 every 3 weeks until disease progression, intolerable toxicity, or withdrawal of consent.
- The primary endpoint was the objective response rate (ORR) assessed by irRECIST. Secondary endpoints included disease control rate (DCR), duration of response (DOR), PFS, and safety.

Study design

The aim of this study is to investigate the efficacy and safety Niraparib and Sintilimab dual therapy in Recurrent/ Advanced Stage Endometrial Cancer.

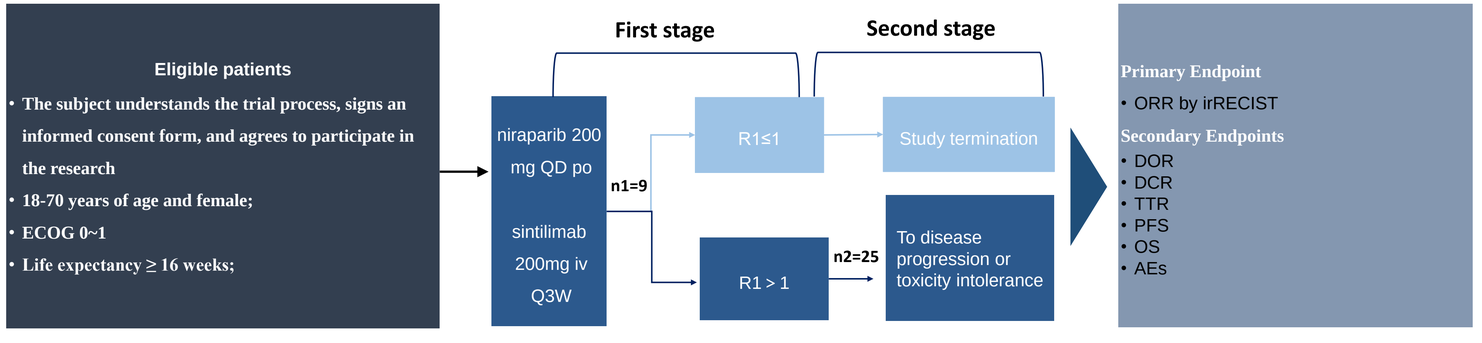

Figure 1. Study Design