555P TQB2450 injection combined with anlotinib hydrochloride capsule in the treatment of advanced, recurrent or metastatic endometrial cancer: A multicohort, open label, multicenter phase II clinical trial: The TQB2450-II-08 trial

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Backgrounds

- The treatment options after first-line chemotherapy for endometrial cancer (EC) are very limited. There is a substantial need for second line and subsequent treatment of advanced EC. Several immune checkpoint inhibitors or combined with antiangiogenic drugs have shown antitumor activity and been approved in EC.
- Anlotinib is a multiple-targeted tyrosine kinase inhibitor that has been approved for the treatment of several solid tumors. TQB2450 is a humanized monoclonal antibody targeting programmed death-ligand 1 (PD-L1).
- This multicohort, open label, multicenter, phase II study aims to evaluate the efficacy and safety of TQB2450 injection or combined with anlotinib hydrochloride capsule in the treatment of recurrent or metastatic advanced EC.

Methods

- Patients with pathologically confirmed recurrent or metastatic advanced EC failed at 1 or 2 prior lines of therapy will be enrolled.
- All patients were treated with anlotinib orally (12 mg per day orally on days 1 to 14) plus TQB2450 (1200 mg intravenously on day 1), repeated every three weeks until progression or intolerant toxicity.
- The primary endpoint was the objective response rate (ORR) by independent review committee (IRC). Key secondary endpoints include ORR by investigator, disease control rate (DCR), duration of response (DoR), progression free survival (PFS), overall survival (OS) and safety.

Eligibility Criteria

- advanced, recurrent or metastatic endometrial cancer
- Age: ≥18 years
- ECOG PS: 0-1
- 1 or 2 prior lines of therapy
- Non-MSI-H/dMMR

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N=30

Anlotinib 12 mg, qd, day 1-14
TQB2450 1200mg, day 1
21 days/cycle

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Primary Endpoint
- ORR by IRC

Secondary Endpoints
- ORR by investigator
- DCR
- DOR
- PFS
- OS
- Safety

Figure 1. Study design

- Data Cut-off date: 18 Feb 2022

Results

As of February 18, 2022, 30 patients with a median age of 57.5 years (range, 47-78) were enrolled and received study treatment (Table 1). 29 patients had received at least one efficacy evaluation, and 1 patient was lost. At data cut-off, 10 of them achieved partial response, the confirmed ORR was 33.3% (10/30), DCR was 76.7% (23/30), and median PFS was 6.6 months (95%CI, 4.40m-9.63m).

Baseline characteristics

Table 1: Baseline characteristics (N=30)

Characteristics	N (%)
Age,years	
Median (range)	57.5 (47.0-78.0)
Prior history of pelvic radiation，%	12 (40.00)
FIGO stage	
I	1 (3.33)
IA	5 (16.67)
IB	5 (16.67)
II	2 (6.67)
III	3 (10.00)
IIIB	1 (3.33)
IIIC	2 (6.67)
IIIC1	2 (6.67)
IV	6 (20.00)
IVB	3 (10.00)
Histology at diagnosis	
Endometrioid carcinoma	22 (73.33)
Serous carcinoma	6 (20.00)
Mixed	2 (6.67)
ECOG Performance status	
0	13 (43.33)
1	17 (56.67)
Prior lines of systemic treatment	
1	19 (63.33)
≥2	11 (36.67)

Anti-tumor response

Table 2: Confirmed best overall response (N=30)

Response	% (n/N)
Partial Response (PR)	33.33% (10/30)
Stable Disease (SD)	43.33% (13/30)
Progressive Disease (PD)	20.00% (6/30)
Not Evaluated (NE)	3.33% (1/30)
ORR, % (95% CI)	33.33% (95% CI, 17.29–52.81)
DCR, % (95% CI)	76.67% (95%CI, 57.72-90.07)

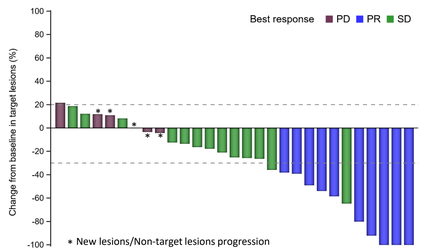

Figure 2: Waterfall plot of change from baseline in target-lesion (N=30)

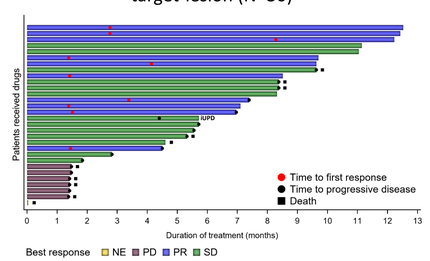

Figure 3: Swimming plot of duration of treatment (N=30)

Results

- **Median PFS was 6.6 months (95%CI, 4.40m-9.63m)**

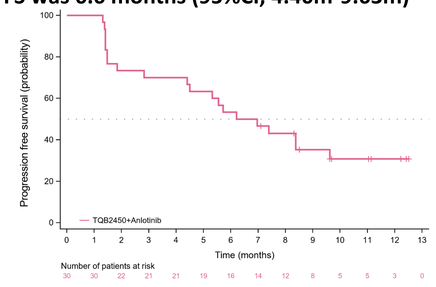

Figure 4. Kaplan-Meier curves for PFS (N=30)

- **Safety**

The most common treatment emergent adverse events (TEAEs) were hypertension (63.33%), leukopenia (53.33%), palmar-plantar erythrodysesthesia syndrome (53.33%), diarrhea (46.67%), increased blood corticotropin (43.33%) and palmar-plantar erythrodysesthesia syndrome (40.00%). The most common grade 3 TEAEs included hypertension (26.67%), and palmar-plantar erythrodysesthesia syndrome (6.67%).

Table 4: TEAEs with frequency ≥ 25% (N=30)

Adverse Events	Any Grade, n(%)	Grade 3, n(%)
Hypertension	19 (63.33)	8 (26.67)
Leukopenia	16 (53.33)	0 (0.00)
Increased thyroid stimulating hormone	16 (53.33)	1 (3.33)
Diarrhea	14 (46.67)	0 (0.00)
Increased blood corticotropin	13 (43.33)	0 (0.00)
Palmar-plantar erythrodysesthesia syndrome	12 (40.00)	2 (6.67)
Weight decrease	11 (36.67)	0 (0.00)
Hypertriglyceridemia	10 (33.33)	1 (3.33)
Increased alanine aminotransferase	10 (33.33)	0 (0.00)
Hyperthyroidism	10 (33.33)	0 (0.00)
Increased aspartate aminotransferase	9 (30.00)	0 (0.00)
Hypercholesterolemia	8 (26.67)	1 (3.33)
Hypothyroidism	8 (26.67)	0 (0.00)

Conclusions

TQB2450 plus anlotinib showed promising antitumor activity with a manageable safety profile in the treatment of recurrent or metastatic advanced EC.

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