Poster 798P

A phase 2 study of pembrolizumab in combination with doxorubicin in advanced endometrial cancer: TOPIC trial / VHIO10001

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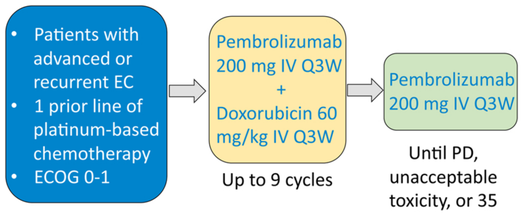
Background

- No standard second-line treatment is available for advanced endometrial cancer after failure to platinum-based chemotherapy in Europe.
- Cytotoxic therapies have shown an overall response rate (ORR) of 15% and progression-free survival rate at 6 months is less than 24%[1].
- Pembrolizumab conferred a 57% ORR in patients with mismatch repair-deficient (MMRd) advanced EC[2], however MMR-proficient (MMRp) advanced EC patients experience less benefit from immunotherapy[3].
- Doxorubicin produces an immunogenic cell death (ICD), which turns tumor cell destruction into a potent inducer of immune response[4].
- Our hypothesis was that pembrolizumab and doxorubicin could improve clinical responses in all advanced EC subtypes compared with historical data.

Methods

- This was an investigator-initiated, single-arm, multicentre, phase 2 (NCT03276013).



Abbreviations: EC, endometrial cancer; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; PD, progressive disease; Q3W, every 3 weeks

Primary endpoint

- Progression-free survival (PFS) rate at 6 months.

Secondary endpoints

- Overall survival (OS)
- Overall response rate (ORR)
- Duration of response (DOR)
- Safety & Tolerability

Results

- Patient demographics and baseline characteristics are listed in **Table 1**.

Table 1. Patient characteristics (N=48)

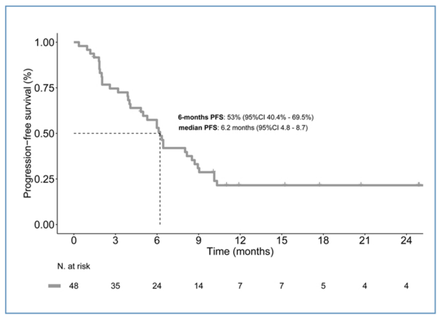
Characteristics	n (%)
Median age (range), years	65.7 (37-80)
Stage at diagnostic (FIGO)	
I-II	16 (33)
III-IV	41 (65)
Histology	
Carcinosarcoma	4 (8)
Endometrioid Adenocarcinoma	31 (65)
Mixed Carcinoma	2 (4)
Serous Carcinoma	10 (21)
Other	1 (2)
ECOG performance status	
0	33 (69)
1	15 (31)
Histological Grade	
Grade 1	6 (13)
Grade 2	11 (23)
Grade 3	21 (44)
Unknown	10 (21)
Prior radiotherapy	24 (50)
Prior chemotherapy	48 (100)
Paclitaxel with carboplatin	47 (98)
Cisplatin	10 (21)
Carboplatin	9 (19)
Paclitaxel	6 (13)
Others	3 (6)
Best response with prior chemotherapy	
Complete response	4 (8)
Partial response	18 (38)
Stable disease	7 (15)
Progressive disease	7 (15)
Unknown	12 (25)
Prior surgery	34 (71)

NOTE. Data reported as No. (%) unless otherwise indicated. Abbreviations: ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynaecology and Obstetrics system.

EFFICACY

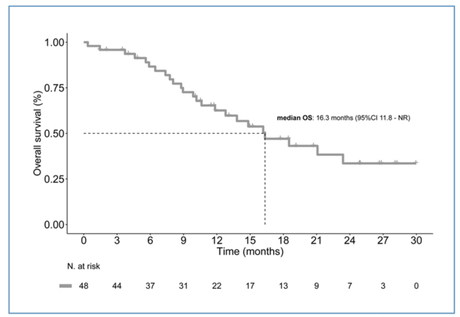
- Median follow-up was 19.1 months with a median PFS of 6.2 months (95%CI, 4.8 – 8.7) (**Figure 1**).
- The 6-months PFS was 53% (95%CI, 40.4% – 69.5%), which was a statistically significant improvement compared to the pre-defined 24% based on historical data (p< 0.001).
- Median OS was 16.3 months (95%CI, 11.8 – not reached); the OS at 24 months was 33.5% (**Figure 2**).
- The ORR was 31.3% (12.5% complete responses) (**Table 2**).
- Median DOR was 8.2 months (95%CI, 6.2 months to not reached).
  The 6-m PFS rate was higher for patients with endometroid vs patients with non-endometroid histological subtype (63% vs 35%) (**Figure 3**).

Figure 1. Kaplan-Meier estimate of progression-free survival by investigator assessment (N=48)



NOTE. Tick marks represent censored patients. Abbreviations: PFS, progression-free survival.

Figure 2. Kaplan-Meier estimate of overall survival (N=48)



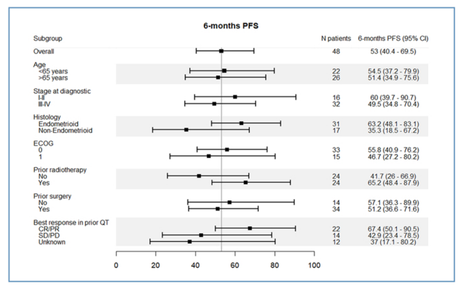
NOTE. Tick marks represent censored patients. Abbreviations: NR, not reached; OS, overall survival.

Table 2. Best response to study treatment

Objective response rate	15 (31)
Complete response	6 (12.5)
Partial response	9 (19)
Stable disease	22 (46)
Progressive disease	10 (21)
Median duration (95% CI) of response, months	8.2 (6.2 – NR)
Median time (range) to response, months	2.1 (1.6 – 22.9)

NOTE. Data reported as No. (%) unless otherwise indicated.

Figure 3. Forest-plot of 6-months progression-free survival in subgroups analysis (N=48)



Abbreviations: CR, complete response; ECOG, Eastern Cooperative Oncology Group; PD, progressive disease; PFS, progression-free survival; PR, partial response; QT, chemotherapy; SD, stable disease.

SAFETY

- Serious treatment-related adverse events (TRAE) occurred in 7 (15%) patients, and one treatment-related death due to intracranial haemorrhage was reported.

Table 3. Treatment-related adverse events occurring in ≥ 15% of patients (N=48)

TRAE, n (%)	Any grade	Grade ≥3
Asthenia	20 (42)	2 (4)
Anemia	20 (42)	2 (4)
Nausea	18 (38)	0
Neutropenia	18 (38)	12 (25)
Mucositis oral	16 (33)	1 (2)
Vomiting	10 (21)	3 (6)
Anorexia	7 (15)	1 (2)

Conclusions

The combination of pembrolizumab and doxorubicin showed promising antitumor activity with a manageable safety profile in women with EC after failure to platinum therapy.

Translational analyses are ongoing to correlate biomarkers with outcomes.

References

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Disclosures

Dra. L. Fariñas-Madrid has no conflicts of interest to declare