



**Investigating immunotherapies for
endometrial cancer:
Working as an MDT to identify patients
and improve outcomes**

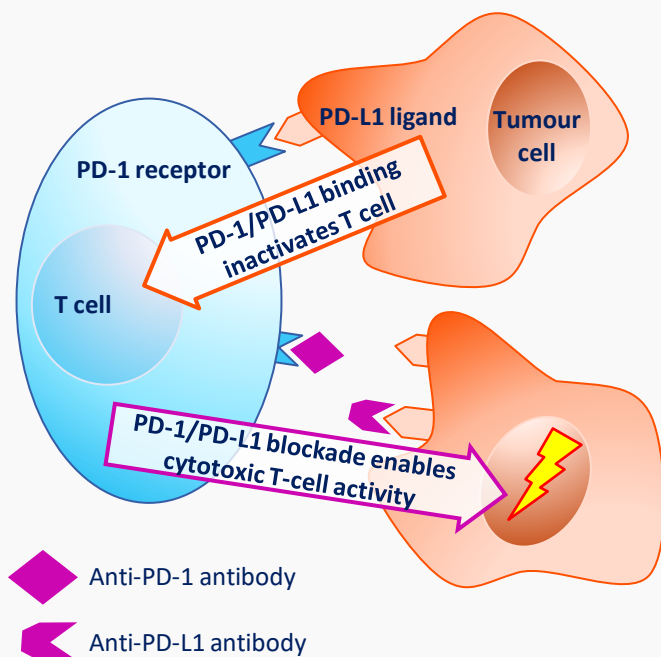
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Why is EC an ideal target for PD-1/PD-L1 inhibitors?¹

- ECs have the highest PD-1/PD-L1 expression among gynaecological cancers
- EC subtypes with MMRd and high mutational burden (e.g., *POLE*-mutant and MSI-H) are highly immunogenic, resulting in increased CD3+ and CD8+ lymphocyte tumour infiltration and an upregulated cytotoxic response
- Expression of PD-L1 by tumours inactivates infiltrating lymphocytes and protects the tumour

PD-1/PD-L1 signalling as a therapeutic target^{1,2}



Immunotherapy treatment options in EC

- **Dostarlimab monotherapy** (FDA and EMA approved)^{3,4}
- **Pembrolizumab monotherapy and combination with lenvatinib** (FDA approved)⁵
- Other treatments under investigation:⁶
 - Avelumab
 - Durvalumab
 - Nivolumab

Immunotherapy addressing an unmet need in recurrent EC

Single-agent salvage chemotherapy⁷



ORR 7–14%



Median OS <1 year

Single-agent immunotherapy

Pembrolizumab⁸



ORR 57% (n=49)



Median DOR not reached (range 2.9–27.0+ months)

Dostarlimab⁷



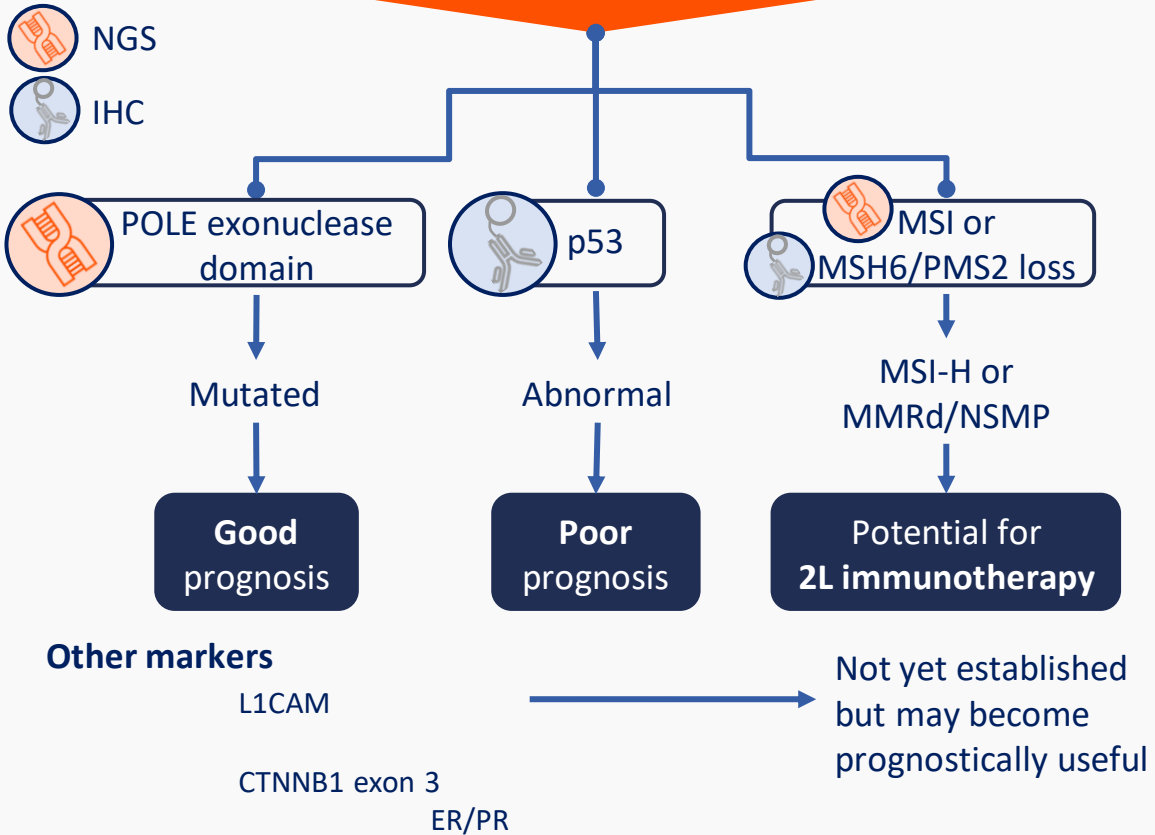
ORR 42% (n=104)



Median DOR not reached at 11 months' follow-up

ESGO/ESTRO/ESP guideline recommendations for prognostic molecular testing of patients with EC⁹

- Molecular classification encouraged in **all** cases
- POLE may be omitted if low/intermediate risk with low-grade histology
- Perform all tests as a group



Most common (≥8%) TRAEs with immunotherapies

Pembrolizumab (n=233) ⁸		
Event	Any grade (%)	Grade 3 or 4 (%)
Fatigue	14.6	0.9
Pruritus	12.9	0
Diarrhoea	12.0	0
Asthenia	10.7	0.4
Hypothyroidism	8.2	0

Dostarlimab (n=104) ⁷		
Event	Any grade (%)	Grade 3 or 4 (%)
Asthenia	15.4	0
Diarrhoea	15.4	1.9
Fatigue	14.4	0
Nausea	12.5	0
Pruritus	9.6	0
Hypothyroidism	8.7	0





Abbreviations:

2L	Second line	MMRd	Mismatch repair deficient
CTNNB1	β-catenin gene	MSH6/PMS2	Lynch syndrome genes
DOR	Duration of response	MSI-H	Microsatellite instability-high
EC	Endometrial carcinoma	NGS	Next-generation sequencing
ER	Estrogen receptor	NSMP	Non-specific molecular profile
ESGO	European Society of Gynaecological Oncology	ORR	Objective response rate
ESP	European Society of Pathology	OS	Overall survival
ESTRO	European Society for Radiotherapy and Oncology	p53	Tumour protein p53
FDA	US Food and Drug Administration	PD-1	Programmed cell death protein 1
HER2	Human epidermal growth factor receptor 2	PD-L1	Programmed cell death ligand 1
IHC	Immunohistochemistry	POLE	DNA polymerase epsilon
L1CAM	L1 cell adhesion molecule	PR	Progesterone receptor
MDT	Multidisciplinary team	TRAE	Treatment-related adverse event

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