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

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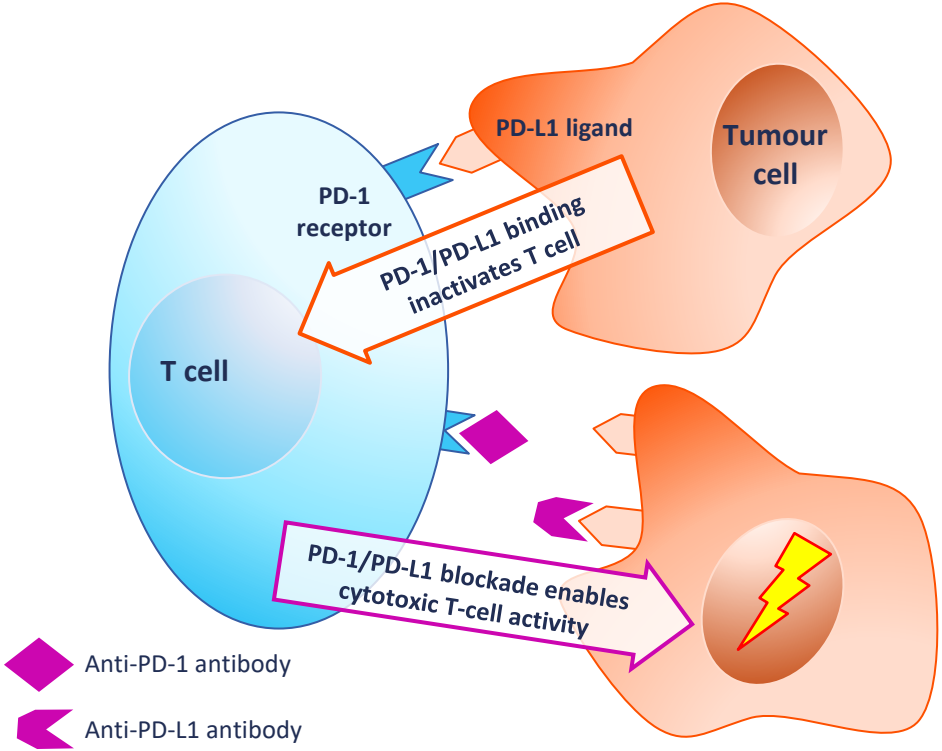
Why is EC an ideal target for PD-1/PD-L1 inhibitors?[1,2]



- ECs have the highest PD-1/PD-L1 expression among gynaecological cancers
- 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

EC, endometrial carcinoma; MMRd, mismatch repair deficient; MSI-H, microsatellite instability-high; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; POLE, DNA polymerase epsilon.

1. Green AK, et al. *Am Soc Clin Oncol Educ Book.* 2020;40:1–7; 2. Ganesh K, et al. *Nat Rev Gastroenterol Hepatol.* 2019;16:361–75.

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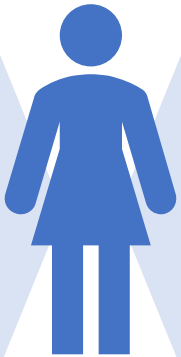
MDT tumour board

Patient profile

- Female
- 62 years old
- Endometroid EC
- FIGO stage IVB due to liver metastases
- High grade (grade 3 tumour)
- No molecular marker profiling at diagnosis
- Received systemic treatment with six cycles carbo/taxol
- Relapse after 12 months with progressive liver and new lung metastases
- Asymptomatic



MDT requirements to guide treatment

- Complete molecular classification
  - *POLE* (optional for low- or intermediate-grade)
  - MMR/MSI status
  - p53 status
- MMRd or MSI-H = potential for anti-PD-1 therapy
- Approved therapies available

Treatment options

- **Dostarlimab monotherapy** (FDA and EMA approved)[1,2]
- **Pembrolizumab monotherapy and combination with lenvatinib** (FDA approved)[3]
- Other treatments are under investigation: avelumab, durvalumab, nivolumab[4]

Carbo/taxol, carboplatin + paclitaxel; EC, endometrial carcinoma; EMA, European Medicines Agency; FDA, US Food and Drug Administration; FIGO, International Federation of Gynecology and Obstetrics; MDT, multidisciplinary team; MMRd, mismatch repair deficient; MSI-H, microsatellite instability-high; p53, tumour protein p53; PD-1, programmed cell death protein 1; POLE, DNA polymerase epsilon.

1. EMA. Dostarlimab SmPC. Available at: www.ema.europa.eu/en/documents/product-information/jemperli-epar-product-information_en.pdf; 2. FDA. Dostarlimab PI. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2021/761174s000lbl.pdf; 3. FDA. Pembrolizumab PI. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s096lbl.pdf; 4. Ongoing interventional studies listed at www.ClinicalTrials.gov (all links accessed August 2021).

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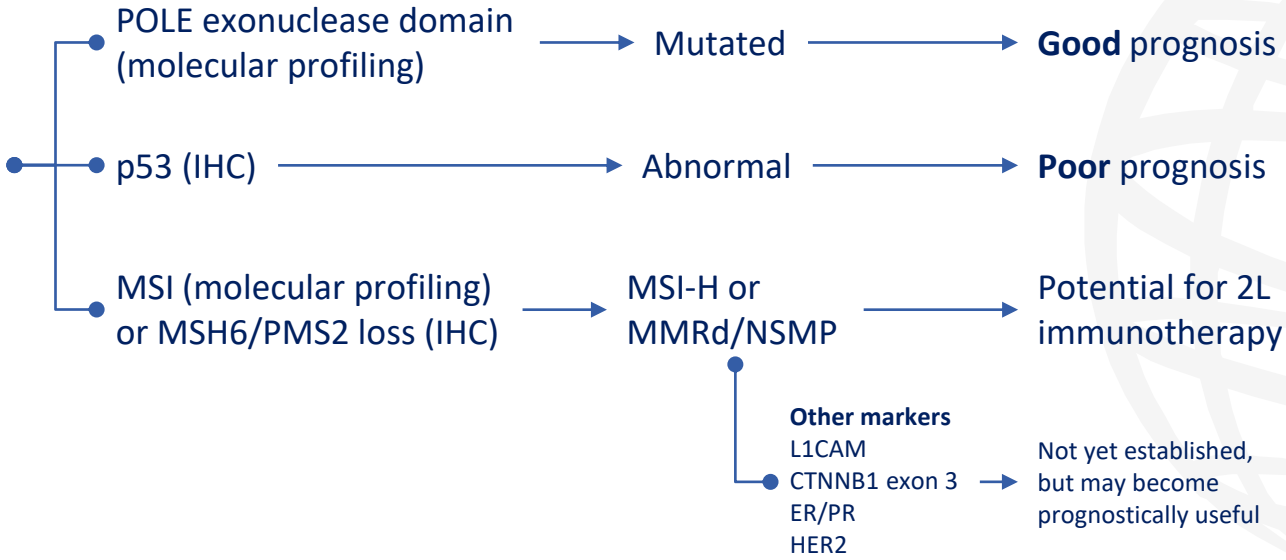
ESGO/ESTRO/ESP guideline recommendations for prognostic molecular testing of patients with EC

Endometrial carcinoma

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



2L, second-line; EC, endometrial carcinoma; CTNNB1, β-catenin gene; ER/PR, estrogen/progesterone receptor; ESGO, European Society of Gynaecological Oncology; ESP, European Society of Pathology; ESTRO, European SocieTy for Radiotherapy and Oncology; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; L1CAM, L1 cell adhesion molecule; MMRd, mismatch repair deficient; MSH6/PMS2, Lynch syndrome genes; MSI-H, microsatellite instability-high; NSMP, non-specific molecular profile; p53, tumour protein p53; POLE, DNA polymerase epsilon.

Concin N, et al. *Int J Gynecol Cancer.* 2021;31:12–39.

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