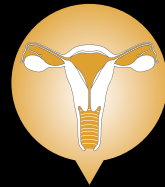


# Breakthrough Era in Endometrial Cancer Treatment: Highlights from ESMO 2023

EMJ Oncol. 2024; DOI/10.33590/emjoncol/10308392. <https://doi.org/10.33590/emjoncol/10308392>.

This infographic was funded by a medical educational grant from GSK, with the purpose of enhancing the fundamental understanding of oncology specialists of key data and the latest advancements in endometrial cancer care.

## Background



Treatment for endometrial cancer is rapidly evolving, with the development of molecular analysis and novel strategies<sup>1</sup>



FIGO staging now integrates molecular classification, tumour patterns, and histological staging<sup>2</sup>



Combining immunotherapy and chemotherapy has proved to be effective in the treatment of endometrial cancer, particularly dMMR disease<sup>3,4</sup>



March 2023

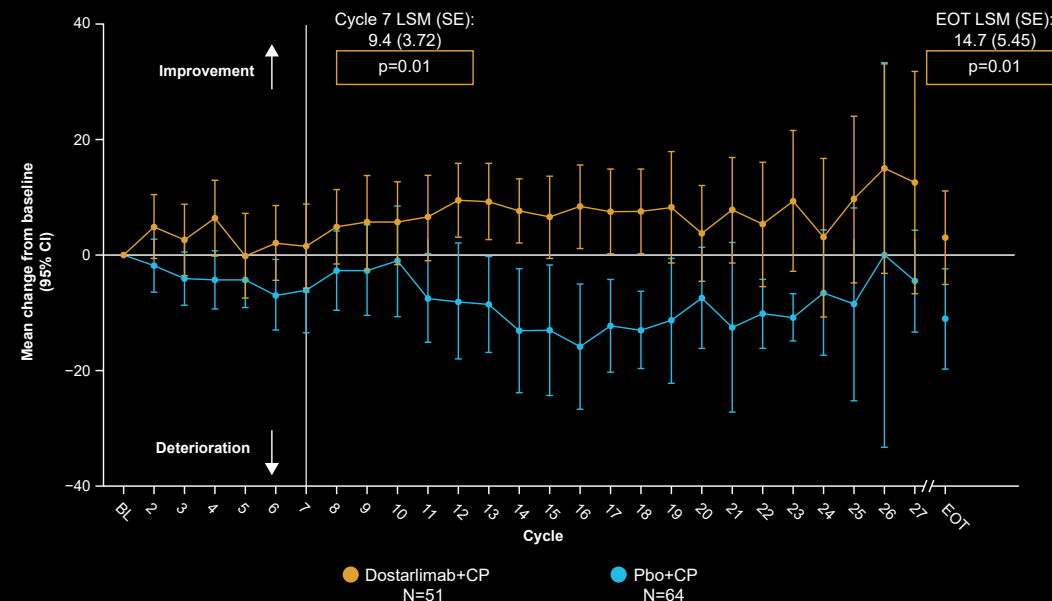
Unprecedented PFS data from RUBY<sup>3</sup> and NRG-GY018,<sup>4</sup> presented at SGO (now published), are changing the future of treatment for patients with endometrial cancer

October 2023

Presentations at ESMO provide updated data and additional analyses from RUBY and NRG-GY018 along with data from DUO-E<sup>8,9</sup>

## RUBY (dostarlimab+CP)<sup>3</sup>

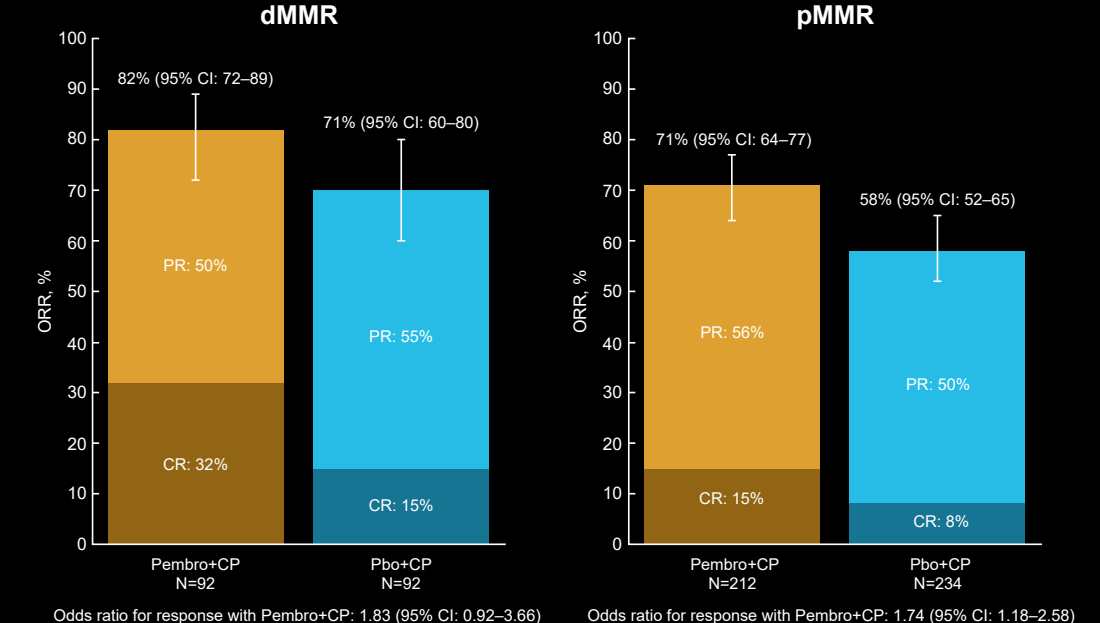
### Global QoL in the dMMR/MSI-H Population<sup>6</sup>



- Exploratory efficacy outcomes by molecular classification showed clinical benefit with dostarlimab+CP in dMMR/MSI-H, TP53mut, and NSMP molecular subgroups versus Pbo+CP<sup>5</sup>
- Based on the 400 patients (of the 494 randomised) for whom mutational data were available<sup>5</sup>
- Increased QoL seen in the dostarlimab+CP group in the dMMR/MSI-H population<sup>6</sup>

## NRG-GY018 (pembrolizumab+CP)<sup>4</sup>

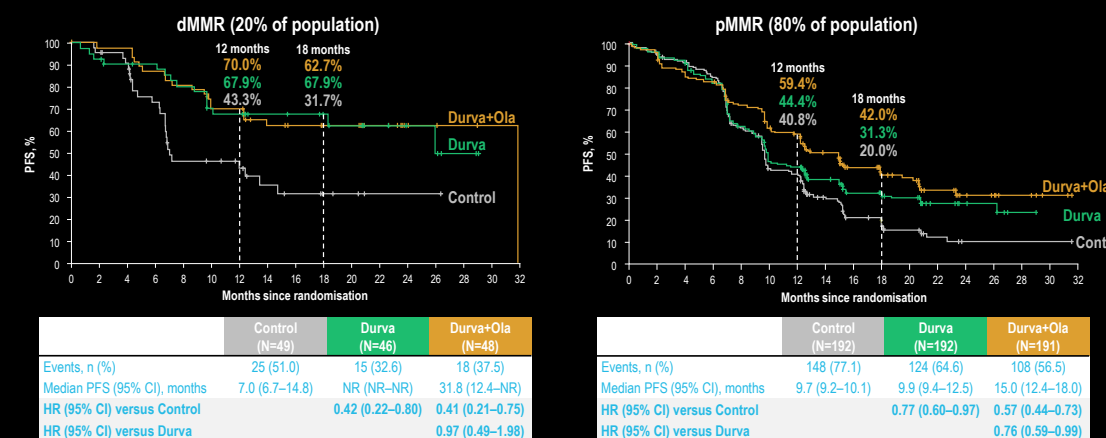
### ORR in dMMR and pMMR Populations<sup>7</sup>



- Clinical benefit with pembrolizumab maintained with more mature clinical follow-up in dMMR and pMMR populations<sup>7</sup>
- Mechanism of MMR loss does not appear to be prognostic of response to pembrolizumab<sup>7</sup>

## DUO-E (durvalumab+CP followed by durvalumab±olaparib)<sup>8,9</sup>

### Subgroup Analysis of PFS by MMR Status<sup>8,9</sup>



- Phase III study of 718 patients with newly diagnosed advanced or recurrent endometrial cancer randomised in a 1:1:1 ratio to control arm (durvalumab pbo+CP then durvalumab pbo+olaparib pbo), durvalumab arm (durvalumab+CP then durvalumab+olaparib pbo), or durvalumab+olaparib arm (durvalumab+CP then durvalumab+olaparib)<sup>9</sup>
- Adding a PARP inhibitor, e.g., olaparib, to immunotherapy–chemotherapy combinations may improve outcomes<sup>10</sup>
- Statistically significant and clinically meaningful improvement in PFS for durvalumab+CP followed by maintenance durvalumab±olaparib<sup>8,9</sup>
- PFS benefit with durvalumab was greatest in the dMMR subgroup<sup>8,9</sup>
- Adding olaparib to durvalumab enhanced PFS benefit in the pMMR subgroup<sup>8,9</sup>

## Conclusion

- Following the practice-changing findings from RUBY<sup>3</sup> and NRG-GY018<sup>4</sup> revealed at SGO 2023, data presented at ESMO 2023 show that research in endometrial cancer continues at a pace
- Observations of maintained clinical benefit, improved QoL, and efficacy of new treatment combinations are important steps towards improved outcomes in patients with endometrial cancer

## References:

1. Carr B et al. Endometrial cancer: molecular classification and future treatments. *BMJ Med.* 2022;1(1):e000152.
2. Berek JS et al.; Endometrial Cancer Staging Subcommittee; FIGO Women's Cancer Committee. FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet.* 2023;162(2):383–94. Erratum in: *Int J Gynaecol Obstet.* 2023;DOI:10.1002/ijgo.15193.
3. Mirza MR et al.; RUBY Investigators. Dostarlimab for primary advanced or recurrent endometrial cancer. *N Engl J Med.* 2023;388(23):2145–58.
4. Eskander RN et al. Pembrolizumab plus chemotherapy in advanced endometrial cancer. *N Engl J Med.* 2023;388(23):2159–70.
5. Mirza MR et al. 740MO Dostarlimab + chemotherapy for the treatment of primary advanced or recurrent endometrial cancer (pA/REC): Analysis of progression free survival (PFS) and overall survival (OS) outcomes by molecular classification in the ENGOT-EN6-NSGO/GOG-3031/RUBY trial. *Ann Oncol.* 2023;34(Suppl 2):S507.
6. Valabrega G et al. 749P Patient-reported outcomes (PROs) in patients (pts) with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (pA/REC) in

the ENGOT-EN6-NSGO/GOG3031/RUBY trial. *Ann Oncol.* 2023;34(Suppl 2):S513–4.

7. Eskander RN et al. LBA43 Updated response data and analysis of progression free survival by mechanism of mismatch repair loss in endometrial cancer (EC) patients (pts) treated with pembrolizumab plus carboplatin/paclitaxel (CP) as compared to CP plus placebo (PBO) in the NRG GY018 trial. *Ann Oncol.* 2023;34(Suppl 2):S1284.
8. Westin SN et al. LBA41 Durvalumab (durva) plus carboplatin/paclitaxel (CP) followed by maintenance (mtx) durva ± olaparib (ola) as a first-line (1L) treatment for newly diagnosed advanced or recurrent endometrial cancer (EC): Results from the phase III DUO-E/GOG-3041/ENGOT-EN10 trial. *Ann Oncol.* 2023;34(Suppl 2):S1282–3.
9. Westin SN et al.; DUO-E investigators. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: the Phase III DUO-E Trial. *J Clin Oncol.* 2024;42(3):283–99.
10. Wanderley CWS et al. Targeting PARP1 to enhance anticancer checkpoint immunotherapy response: rationale and clinical implications. *Front Immunol.* 2022;13:816642.

## Key:

BL: baseline; CI: confidence interval; CP: carboplatin–paclitaxel; CR: complete response; (d/p)MMR: (deficient/proficient) mismatch repair; Durva: Durvalumab; ESMO: European Society for Medical Oncology; EOT: end of treatment; FIGO: International Federation of Gynecology and Obstetrics; HR: hazard ratio; LSM: least square mean; MSI-H: microsatellite instability-high; mut: mutated; NR: not reached; NSMP: no specific molecular profile; Ola: Olaparib; ORR: objective response rate; PARP: poly adenosine diphosphate ribose polymerase; Pbo: pembrolizumab; Pbo: placebo; PFS: progression-free survival; PR: partial response; QoL: quality of life; SE: standard error; SGO: Society of Gynecologic Oncology; TP53: tumour protein 53.