Breakthrough Era in Endometrial Cancer Treatment:

Highlights from ESMO 2023

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Background



Treatment for endometrial cancer is rapidly evolving, with the development of molecular analysis and novel strategies1



FIGO staging now integrates molecular classification, tumour patterns, and histological staging²



Combining immunotherapy and chemotherapy has proved to be effective in the treatment of endometrial cancer, particularly dMMR disease3,4



March 2023

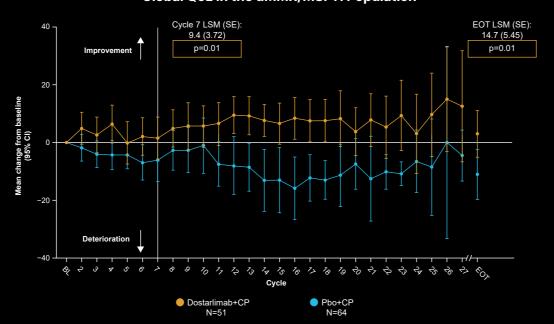
Unprecedented PFS data from RUBY³ and NRG-GY018,4 presented at SGO (now published), are changing the future of treatment for patients with endometrial cancer

October 2023

Presentations at ESMO provide updated data and additional analyses from RUBY and NRG-GY018 along with data from DUO-E8,9

RUBY (dostarlimab+CP)³

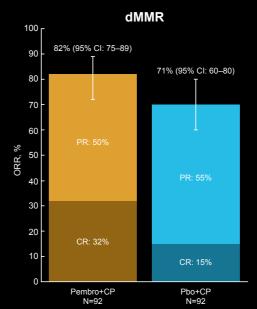
Global QoL in the dMMR/MSI-H Population⁶

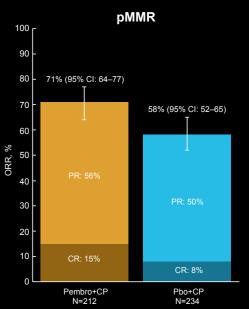


- Exploratory efficacy outcomes by molecular classification showed clinical benefit with dostarlimab+CP in dMMR/MSI-H, TP53mut, and NSMP molecular subgroups versus Pbo+CP5
- Based on the 400 patients (of the 494 randomised) for whom mutational data were available
- Increased QoL seen in the dostarlimab+CP group in the dMMR/MSI-H population6

NRG-GY018 (pembrolizumab+CP)4

ORR in dMMR and pMMR Populations7





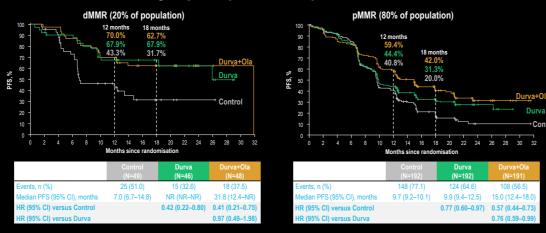
Odds ratio for response with Pembro+CP: 1.83 (95% CI: 0.92-3.66)

Odds ratio for response with Pembro+CP: 1.74 (95% CI: 1.18–2.58)

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

DUO-E (durvalumab+CP followed by durvalumab \pm olaparib) 8,9

Subgroup Analysis of PFS by MMR Status^{8,9}



- 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)9
- · Adding a PARP inhibitor, e.g., olaparib, to immunotherapy-chemotherapy combinations may
- · Statistically significant and clinically meaningful improvement in PFS for durvalumab+CP followed by maintenance durvalumab±olaparib8,9
- PFS benefit with durvalumab was greatest in the dMMR subgroup^{8,9}
- Adding olaparib to durvalumab enhanced PFS benefit in the pMMR subgroup^{8,9}

- Following the practice-changing findings from RUBY³ and NRG-GY018⁴ 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

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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; Pembro: pembrolizumab; Pbo: placebo; PFS: ression-free survival; PR: partial response; QoL: quality of life; SE: standard error; SGO: Society of Gynecologic Oncology