Abstract 80 Figure 1 Concordance between preoperative risk classification assessed by endometrial biopsy and magnetic resonance imaging with the final histological analysis of the surgical specimen

Abstract 83 Figure 1 Incidence of the most common irTRAEs and TRAEs in patients with dMMR and MMRp EC by cycle

wrongly classified, sentinel LN procedure instead of no LN dissection could be an option offered to preoperative low risk patients to decrease the indication of second surgery for re-staging and/or to avoid toxicity of adjuvant radiotherapy.

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occurrence seen at cycle 4. irTRAEs that were seen in ≥1% of patients included diarrhea (4.1%), amylase increased (2.2%), aspartate aminotransferase increased (2.2%), alanine aminotransferase increased (1.8%), colitis (1.5%), hyperglycemia (1.5%), lipase increased (1.5%), adrenal insufficiency (1.1%), and hyperthyroidism (1.1%).

Conclusion* When analyzed over the dMMR and MMRp EC safety population of the GARNET trial, dostarlimab has an acceptable safety profile with manageable adverse events. irTRAEs and TRAEs were seen in a low percentage of patients and were seen more frequently earlier in the time course of dostarlimab treatment. No increase in the rate of TRAEs or irTRAEs was seen when changing to the 1000-mg Q6W dose.

C, cycle; dMMR, mismatch mutation repair deficient; ir, immune-related; MMRp, mismatch mutation repair proficient; TRAE, treatment-related adverse event; W, weeks

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83 TIME COURSE OF ADVERSE EVENTS DURING DOSTARLIMAB TREATMENT IN PATIENTS WITH RECURRENT OR ADVANCED ENDOMETRIAL CANCER IN THE GARNET TRIAL

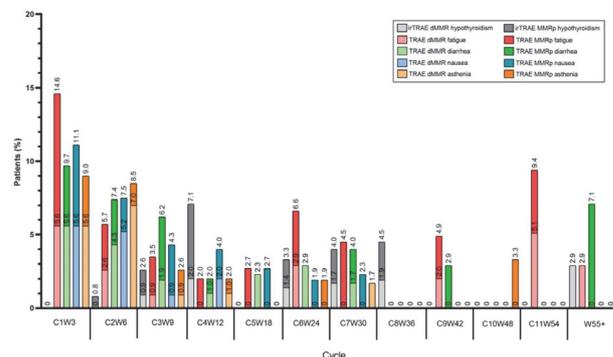[1]A Oaknin*, [2]L Gilbert, [3]A Tinker, [4]W Guo, [4]E Im, [5]B Pothuri. [1]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [2]McGill University Health Centre Research Institute, Montreal, Quebec, Canada; [3]BC Cancer, Vancouver, British Columbia, Canada; [4]GlaxoSmithKline, Waltham, MA, USA; [5]Gynecologic Oncology Group (GOG) and Department of Obstetrics/Gynecology, Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA

Introduction/Background* Dostarlimab is a humanized programmed death-1 (PD-1) receptor monoclonal antibody that blocks interaction with the PD-1 ligands. GARNET (NCT02715284) is a phase 1 study assessing antitumor activity and safety of dostarlimab monotherapy in patients with solid tumors. Dostarlimab has shown antitumor activity in patients with mismatch repair deficient (dMMR) and mismatch repair proficient (MMRp) advanced and recurrent endometrial cancer (EC). Here we report on the time of onset of treatment-related adverse events (TRAEs) and immune-related (ir) TRAEs over the course of dostarlimab treatment in patients with dMMR (cohort A1) and MMRp (cohort A2) EC in the GARNET trial.

Methodology Patients with advanced or recurrent dMMR or MMRp EC that progressed on or after a platinum regimen received 500 mg of dostarlimab every 3 weeks for 4 cycles, then 1000 mg every 6 weeks (Q6W) until disease progression or discontinuation.

Result(s)* A total of 126 patients with dMMR EC and 145 patients with MMRp EC were included in the safety population. Few TRAEs were seen in ≥10% of patients: fatigue (17.3%), diarrhea (14.4%), nausea (13.7%), and asthenia (11.1%). The majority of cases occurred during cycles 1–3, with a peak occurrence at cycle 1 for all 4 TRAEs. Hypothyroidism was the only irTRAE seen in ≥5% of patients, and 94% of cases occurred between cycles 2 and 8, with a peak

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86 ENDOMETRIAL CANCER IMMUNOHISTOCHEMICAL RISK STRATIFICATION IN A LARGE UTERINE-CONFINED CANCER SERIES

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Introduction/Background* Nowadays, after the recent insights about the molecular Endometrial cancer (EC) classification, the usual key histological parameters (i.e histotype and grade) have been shown to have poor reproducibility and adequacy in EC stratification risk. The need to define a more precise guidance of surgical and adjuvant approaches has suggested the possibility to refine the prognostic assessing, considering other EC characteristics. Inspired by these concepts, the aim of this study is to assess the clinical reproducibility and the oncological validity of the EC risk stratification based on the molecular information given by the immunohistochemistry (IHC). **Methodology** Retrospective IHC analyses were conducted in a large series of 778 pre-operative uterine-confined ECs, studying the presence/absence of MLH1, MSH2, MSH6, to define the mismatch repair (MMR) stable or instable phenotype; the

Abstract 86 Table 1 Distribution of clinicopathological parameters

	MMRs	MMRi	p53+	Total	p-value
Number of patients	480	170	128	778	
Age at diagnosis					< 0.001
Mean (SD)	61.4 (11.1)	63.8 (10.5)	68.8 (9.4)	63.1 (11.0)	
Range	25.0 – 87.0	29.0 – 88.0	46.0 – 89.0	25.0 – 89.0	
BMI					0.136
Mean (SD)	30.4 (8.9)	30.9 (8.1)	29.0 (6.7)	30.3 (8.4)	
Range	16.8 – 121.0	17.4 – 64.1	17.2 – 51.9	16.8 – 121.0	
FIGO_stage					< 0.001
IA	298 (62.1%)	86 (50.6%)	49 (38.3%)	433 (55.7%)	
IB	113 (23.5%)	44 (25.9%)	37 (28.9%)	194 (24.9%)	
II	28 (5.8%)	16 (9.4%)	19 (14.8%)	63 (8.1%)	
IIIA	5 (1.0%)	3 (1.8%)	3 (2.3%)	11 (1.4%)	
IIIB	5 (1.0%)	0 (0.0%)	3 (2.3%)	8 (1.0%)	
IIIC1	25 (5.2%)	14 (8.2%)	12 (9.4%)	51 (6.6%)	
IIIC2	1 (0.2%)	2 (1.2%)	0 (0.0%)	3 (0.4%)	
IVA	0 (0.0%)	3 (1.8%)	1 (0.8%)	4 (0.5%)	
IVB	5 (1.0%)	2 (1.2%)	4 (3.1%)	11 (1.4%)	
Early stage (I-II)					0.005
no	41 (8.5%)	24 (14.1%)	23 (18.0%)	88 (11.3%)	
yes	439 (91.5%)	146 (85.9%)	105 (82.0%)	690 (88.7%)	
Tumor grade					< 0.001
G1-2	420 (87.5%)	131 (77.1%)	6 (4.7%)	557 (71.6%)	
G3	60 (12.5%)	39 (22.9%)	122 (95.3%)	221 (28.4%)	
Histotype					< 0.001
Type I	450 (93.8%)	161 (94.7%)	16 (12.5%)	627 (80.6%)	
Type II	30 (6.2%)	9 (5.3%)	112 (87.5%)	151 (19.4%)	
LVSI					< 0.001
Negative	401 (83.7%)	128 (76.2%)	76 (61.3%)	605 (78.5%)	
Positive	78 (16.3%)	40 (23.8%)	48 (38.7%)	166 (21.5%)	
Myometrial invasion					0.003
≤ 50	324 (67.6%)	101 (59.8%)	67 (52.3%)	492 (63.4%)	
> 50	155 (32.4%)	68 (40.2%)	61 (47.7%)	284 (36.6%)	
Tumor dimension (class)					0.584
≤ 20 mm	117 (24.4%)	37 (21.8%)	27 (21.1%)	181 (23.3%)	
> 20 mm	360 (75.0%)	133 (78.2%)	101 (78.9%)	594 (76.3%)	
Tumor dimension					< 0.001
Mean (SD)	33.1 (18.1)	35.200 (16.314)	40.3 (25.9)	34.8 (19.4)	
Range	1.0 – 140.0	1.0 – 95.0	1.0 – 150.0	1.0 – 150.0	
Pathological lymph node status					0.057
Negative	468 (97.5%)	159 (93.5%)	123 (96.1%)	750 (96.4%)	
Positive	12 (2.5%)	11 (6.5%)	5 (3.9%)	28 (3.6%)	
Post-surgical treatment					0.082
None	212 (45.0%)	90 (54.9%)	55 (45.1%)	357 (47.2%)	
Any	259 (55.0%)	74 (45.1%)	67 (54.9%)	400 (52.8%)	
Adjuvant CHT					0.093
No	282 (59.9%)	113 (68.1%)	69 (56.6%)	464 (61.1%)	
Yes	189 (40.1%)	53 (31.9%)	53 (43.4%)	295 (38.9%)	
Adjuvant RT					0.540
No	229 (47.7%)	89 (52.4%)	65 (50.8%)	383 (49.2%)	
Yes	251 (52.3%)	81 (47.6%)	63 (49.2%)	395 (50.8%)	
Risk class 2020					< 0.001
Low	260 (54.2%)	72 (42.4%)	1 (0.8%)	333 (42.8%)	
Intermediate	79 (16.5%)	25 (14.7%)	11 (8.6%)	115 (14.8%)	
High/intermediate	80 (16.7%)	44 (25.9%)	8 (6.2%)	132 (17.0%)	
High	56 (11.7%)	27 (15.9%)	104 (81.2%)	187 (24.0%)	
Advanced/Metastatic	5 (1.0%)	2 (1.2%)	4 (3.1%)	11 (1.4%)	
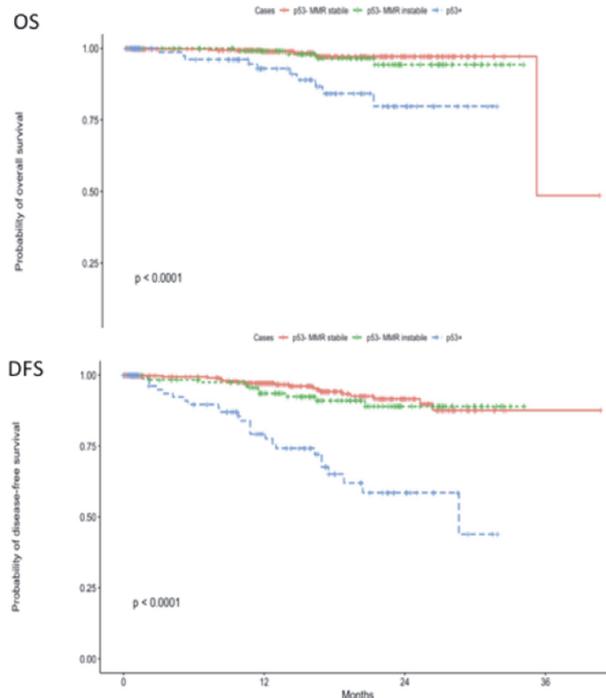
Abstract 86 Figure 1

presence of p53 mutations and other molecular features. The molecular profile was correlated with histological, clinical and prognostic EC patients data.

Result(s)* Based on the IHC, we defined 3 EC populations: MMR stable (MMRs), instable (MMRi) and p53 mutated (p53+) patients. Our result demonstrated that the IHC stratification statistically correlated with the most relevant anatomo-clinical features: FIGO stage (p<0.001), grading (12,5% G3 in MMRs vs 22.9% in MMRi vs 95.3% in p53+, p<0.001), histotype (Type II 6.2% in MMRs vs 5.3% in MMRi vs 87.5% in p53+, p<0.001), presence of LVSI (positive in 16.3% in MMRs vs 23.8% in MMRi vs 38.7% in p53+, p<0.001), myometrial invasion and tumor dimension (p=0.003 and p<0.001 respectively). Again, the 3 IHC populations statistically reflected the EC risk class ESGO-ESMO-ESP classification 2020 (p<0.001) (table 1). These results were confirmed also in Kaplan-Meier curves in terms of over-all survival (OS) and disease-free survival (DFS) (p<0.0001) (figure 1). Moreover, the multivariate analyses demonstrated that absence of estrogen receptor (ER) impacted the OS (p=0.011) and, the Age>60 years and the ER-status in DFS (p=0.004 and p=0.041).

Conclusion* In this large series, we demonstrated that the pragmatic and sistematic use of IHC may have an important role to properly stratify, in terms of histological features and clinical outcome, the pre-operative uterine-confined EC patients.