

### **PHAEDRA Supplementary materials**

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Figure S2: Pain symptom score (single item) by MMR status (higher is more symptoms)

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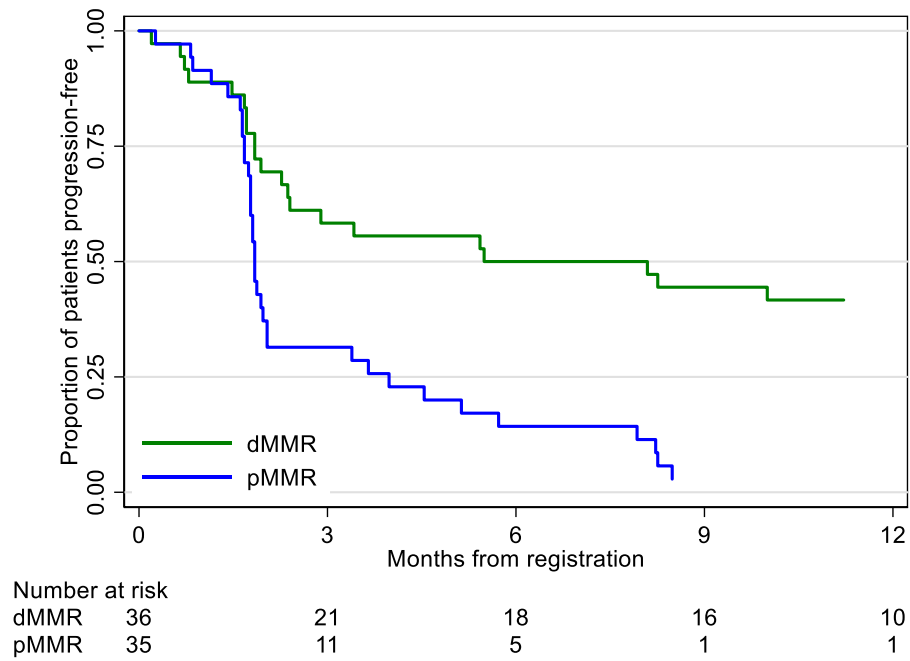
Figure S4: Nausea and vomiting symptom score (single item) by MMR status (higher is more symptoms)

Figure S5: Dyspnoea symptom score (single item) by MMR status (higher is more symptoms)

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**Table S1: Best objective tumor response and disease control rates according to RECIST by MMR status**

	<b>MMR deficient (n=36)</b>	<b>MMR proficient (n=35)</b>
<b>Best objective tumor response rate (OTRR)</b>	17 (47%; 95% CI: 32–63%)	1 (3%; 95% CI: 1–15%)
<b>OTRR according to previous lines of chemotherapy</b>		
None	12 (57%)	0 (0%)
One	5 (38%)	1 (5%)
Subsequent	0 (0%)	0 (0%)
<b>Best response</b>		
Non evaluable		1 (3%)
CR	5 (14%)	
PR	12 (33%)	1 (3%)
SD	6 (17%)	10 (29%)
PD	13 (36%)	23 (66%)
<b>DCR (overall)</b>	23 (64%)	11 (31%)
DCR at 16 weeks	21 (58%)	9 (26%)
DCR at 24 weeks	18 (50%)	7 (20%)

**Figure S1: PFS according to RECIST by MMR status**

**Table S2: Numbers of participants with adverse events**

	<b>Any grade</b>	<b>Grade 3-5</b>
Total participants who received at least one dose	69	69
Any adverse event	64 (93%)	25 (36%)
Events occurring in five or more patients:		
Fatigue	39 (57%)	1 (1%)
Nausea	23 (33%)	1 (1%)
Constipation	21 (30%)	1 (1%)
General disorders and administration site conditions (Other)	20 (29%)	
Skin and subcutaneous tissue disorders (Other)	14 (20%)	
Diarrhea	14 (20%)	
Pain	12 (17%)	1 (1%)
Urinary tract infection	10 (14%)	2 (3%)
Vomiting	10 (14%)	
Anorexia	9 (13%)	
Dyspnea	9 (13%)	
Gastrointestinal disorders (Other)	9 (13%)	1 (1%)
Anemia	8 (12%)	1 (1%)
Hyperthyroidism	8 (12%)	
Rash maculo-papular	8 (12%)	
Abdominal pain	7 (10%)	3 (4%)
Back pain	7 (10%)	
Cough	7 (10%)	
Hypothyroidism	7 (10%)	
Other infections	6 (9%)	2 (3%)
Musculoskeletal and connective tissue disorder (Other)	7 (10%)	
Respiratory, thoracic and mediastinal disorders (Other)	6 (9%)	
Upper respiratory infection	7 (10%)	
Arthralgia	5 (7%)	
Headache	5 (7%)	
Nervous system disorders (Other)	5 (7%)	
Pruritus	5 (7%)	

**Table S3: Completion rates of QLQ-C30 by MMR status\***

<b>Time point</b>	<b>MMR Deficient</b>	<b>MMR Proficient</b>	<b>Overall</b>
Baseline	32/36 (89%)	33/35 (94%)	65/71 (92%)
Month 1	31/32 (97%)	25/32 (78%)	56/64 (88%)
Month 2	27/29 (93%)	12/19 (63%)	39/48 (81%)
Month 3	20/24 (83%)	11/12 (92%)	31/35 (89%)
Month 4	18/22 (82%)	9/10 (90%)	27/32 (84%)
Month 5	17/21 (81%)	6/8 (75%)	22/29 (76%)
Month 6	15/19 (79%)	7/7 (100%)	23/26 (88%)
Month 7	17/19 (89%)	4/5 (80%)	21/24 (88%)
Month 8	15/19 (79%)	5/5 (100%)	20/24 (83%)
Month 9	14/18 (78%)	0/2 (0%)	14/20 (70%)
Month 10	13/17 (76%)	0/1 (0%)	13/18 (72%)
Month 11	11/16 (69%)	1/1 (100%)	12/17 (71%)

\*Forms are 'expected' until a patient progresses by iRECIST. Forms are considered completed if a global score can be obtained.

Improvement in QOL was defined as 2 or more visits with an improvement in that QOL measure of 10 points or more from baseline. This was calculated for each functioning QOL measure, but only for symptom scales Fatigue, Pain and Nausea and Vomiting as they are only composed of more than a single question. Patients that did not complete any QOL measures were considered to not improve.

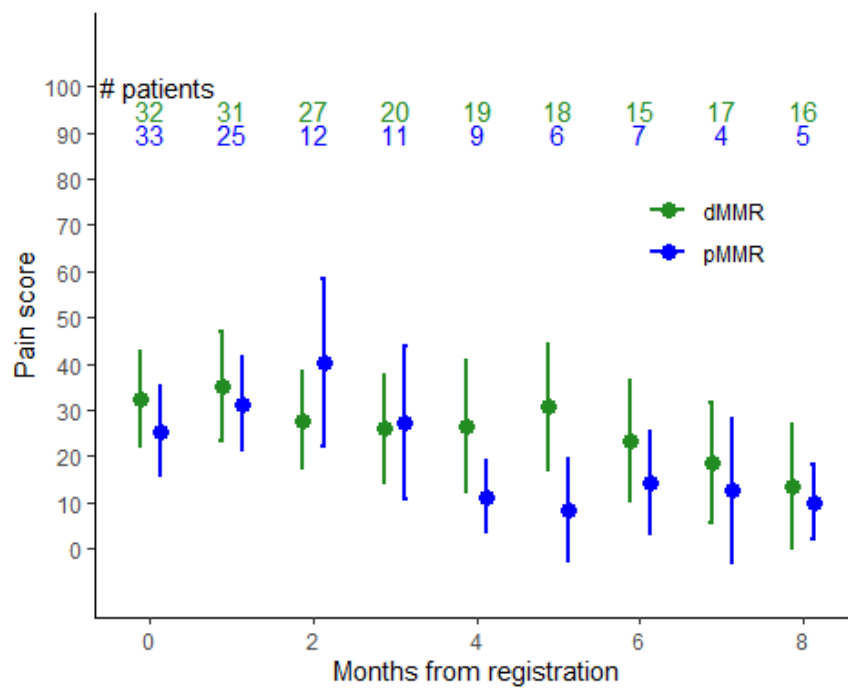
**Table S4: Proportion of patients that improved in each QOL domain by MMR status**

<b>Domain</b>	<b>MMR Proficient</b>	<b>MMR Deficient</b>
Global QOL	3 (9%)	9 (25%)
Physical functioning	2 (6%)	5 (14%)
Role functioning	2 (6%)	10 (28%)
Emotional functioning	2 (6%)	6 (17%)
Cognitive functioning	3 (9%)	4 (11%)
Social functioning	3 (9%)	13 (36%)
Fatigue symptoms	5 (14%)	10 (28%)
Pain symptoms	3 (9%)	12 (33%)
Nausea and vomiting symptoms	1 (3%)	5 (14%)

Compared to baseline, patients were categorized into decrease (10 points or more deterioration from baseline), stable (-9 to +9 inclusive), or increase (10 point or more improvement from baseline) at 3 and 6 months.

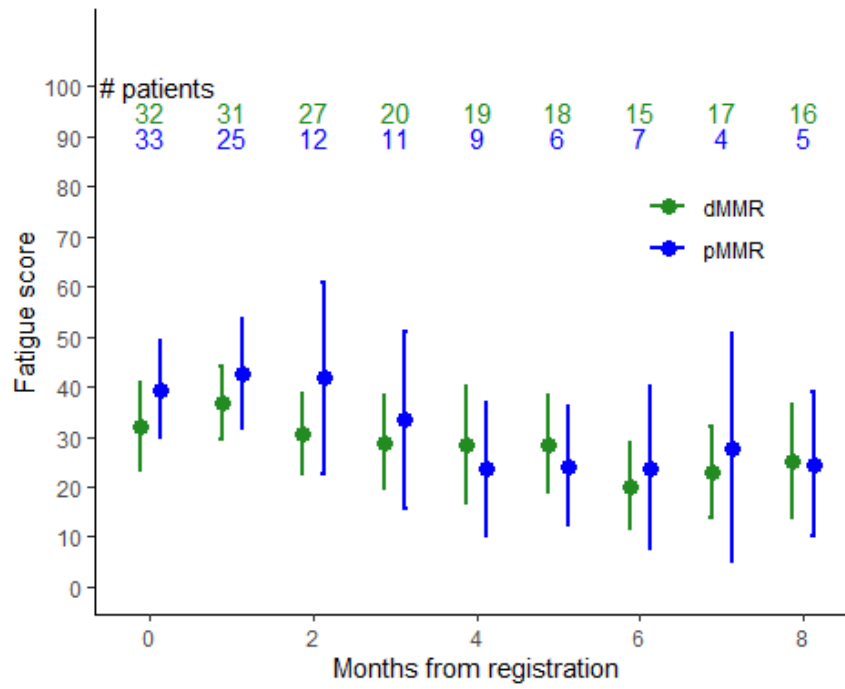
**Table S5: QOL status at 3 and 6 months by MMR status**

Domain	QOL status (compared to baseline)	Month 3		Month 6	
		pMMR	dMMR	pMMR	dMMR
Global QOL	Decrease	3 (25%)	5 (19%)	6 (38%)	
	Stable	8 (67%)	12 (46%)	4 (67%)	5 (31%)
	Increase	1 (8%)	9 (35%)	2 (33%)	5 (31%)
Physical functioning	Decrease	2 (17%)	8 (31%)	6 (35%)	
	Stable	7 (58%)	12 (46%)	4 (67%)	8 (47%)
	Increase	3 (25%)	6 (23%)	2 (33%)	3 (18%)
Role functioning	Decrease	2 (17%)	8 (31%)	5 (29%)	
	Stable	8 (67%)	9 (35%)	4 (67%)	8 (47%)
	Increase	2 (17%)	9 (35%)	2 (33%)	4 (24%)
Emotional functioning	Decrease	3 (25%)	4 (15%)	1 (6%)	
	Stable	8 (67%)	16 (62%)	5 (83%)	13 (76%)
	Increase	1 (8%)	6 (23%)	1 (17%)	3 (18%)
Cognitive functioning	Decrease	5 (42%)	7 (27%)	2 (33%)	3 (18%)
	Stable	5 (42%)	18 (69%)	2 (33%)	12 (71%)
	Increase	2 (17%)	1 (4%)	2 (33%)	2 (12%)
Social functioning	Decrease	2 (17%)	6 (23%)	3 (18%)	
	Stable	8 (67%)	11 (42%)	3 (50%)	8 (47%)
	Increase	2 (17%)	9 (35%)	3 (50%)	6 (35%)

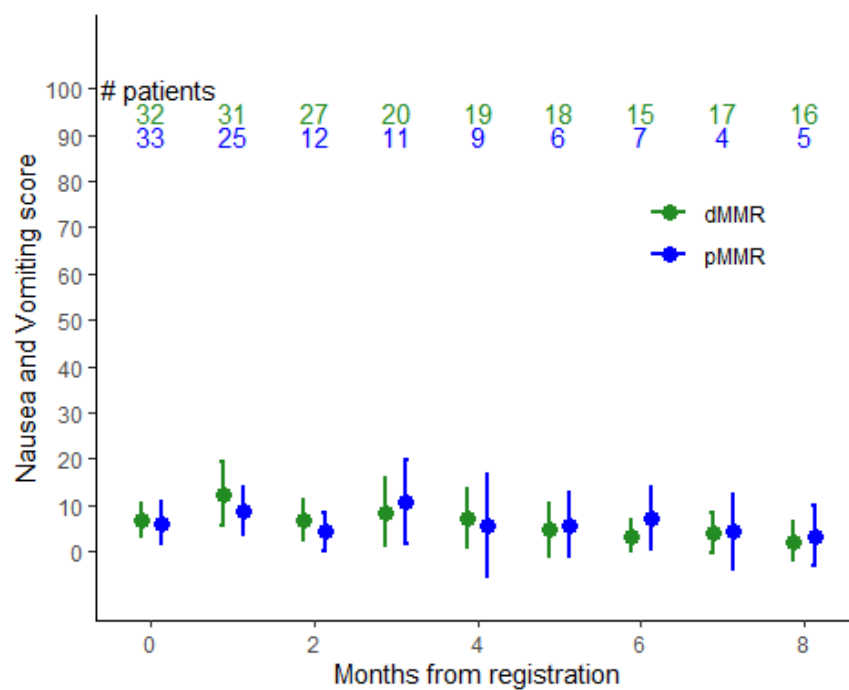
**Figure S2: Pain symptom score (single item) by MMR status (higher is more symptoms)**



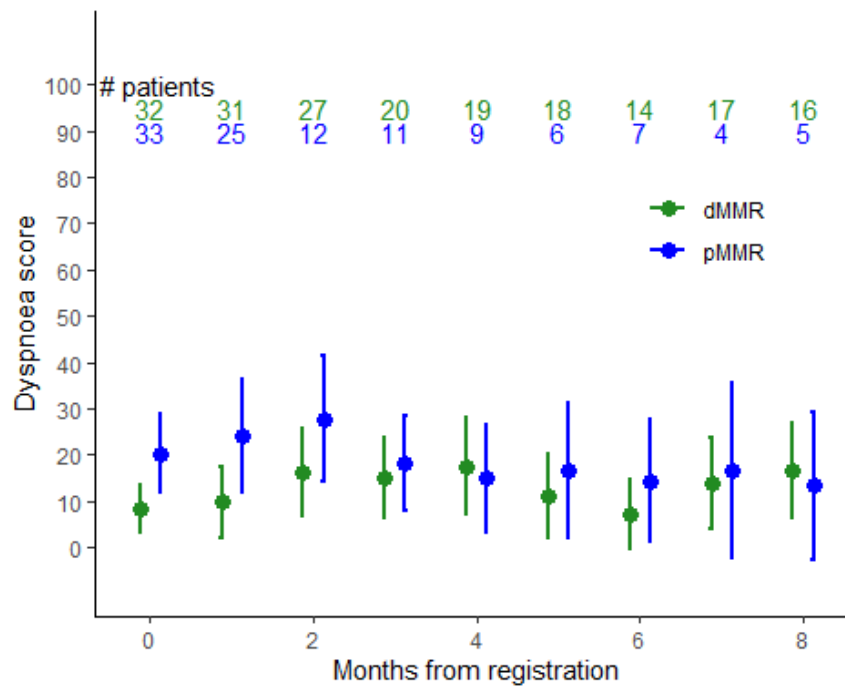
**Figure S3: Fatigue symptom score (single item) by MMR status (higher is more symptoms)**



**Figure S4: Nausea and vomiting symptom score (single item) by MMR status (higher is more symptoms)**



**Figure S5: Dyspnoea symptom score (single item) by MMR status (higher is more symptoms)**



**Figure S6: Diarrhoea symptom score (single item) by MMR status (higher is more symptoms)**

