Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work. Supplement to: Overman, Gelsomino, Aglietta, et al. Nivolumab plus relatlimab for patients with previously treated microsatellite instability high/mismatch repair-deficient metastatic colorectal cancer: the phase 2 CheckMate 142 study

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List of Sites and Investigators

Principal investigators for each site who participated in this trial (Cohort 5).

Country	**Principal investigator**
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Ireland	Gregory Leonard
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	Maria Diab
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	Heinz-Josef Lenz

Tables and Figures

Table S1 ORR in subgroups per investigator

	Objective response rate n (%)* [95% CI] (N=50)
Median age, years	
<65 (n=34)	14 (41) [24.6 to 59.3]
≥65 (n=16)	11 (69) [41.3 to 89.0]
≥65 and <75 (n=10)	6 (60) [26.2 to 87.8]
≥75 (n=6)	5 (83) [35.9 to 99.6]
Sex	
Male (n=28)	13 (46) [27.5 to 66.1]
Female (n=22)	12 (55) [32.2 to 75.6]
ECOG performance status	
0 (n=35)	20 (57) [39.4 to 73.7]
1 (n=15)	5 (33) [11.8 to 61.6]
Clinical history of Lynch syndrome†	
Yes (n=8)	4 (50) [15.7 to 84.3]
No (n=16)	7 (44) [19.8 to 70.1]
Unknown (n=26)	14 (54) [33.4 to 73.4]
Mutation status	
KRAS/BRAF wild type (n=15)	9 (60) [32.3 to 83.7]
BRAF mutation (n=12)	8 (67) [34.9 to 90.1]
KRAS mutation (n=17)	6 (35) [14.2 to 61.7]
KRAS/BRAF mutation (n=1)	0 [0.0 to 97.5]
Unknown (n=5)	2 (40) [5.3 to 85.3]

	Objective response rate n (%)* [95% CI] (N=50)
Number of prior systemic treatments‡	
0 (n=4)	3 (75) [19.4 to 99.4]
1 (n=11)	8 (73) [39.0 to 94.0]
2 (n=16)	8 (50) [24.7 to 75.3]
3 (n=15)	6 (40) [16.3 to 67.7]
≥4 (n=4)	0 [0.0 to 60.2]
Liver metastases	
Yes (n=18)	7 (39) [17.3 to 64.3]
No (n=32)	18 (56) [37.7 to 73.6]
Neutrophil-to-lymphocyte ratio§	
<3 (n=22)	11 (50) [28.2 to 71.8]
≥3 (n=28)	14 (50) [30.6 to 69.4]

*All patients had stage IV disease at study entry.
†Lynch syndrome designation was based on the clinical records of patients at sites in countries where this reporting was permitted.
‡Some patients may have been treated with more than one type of therapy.
§Neutrophil-to-lymphocyte ratio was derived by dividing absolute neutrophil count by absolute lymphocyte count.
CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; ORR, objective response rate.

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Table S2 Characteristics of patients who progressed after achieving disease control

Patient	Best overall response	*KRAS* mutation	*BRAF* mutation	Lynch syndrome	Local MSI test result	Duration of response, months	Time from first dose to progression, months	Treatment status at time of progression	Type of progression site	Organ with metastatic site progression
1	PR	Wildtype	Wildtype	Yes	MSI-H	33.1	35.7	On treatment	Target	Lymph node
2	SD	Mutant	Not Reported	Unknown	MSI-H	NA	4.1	Off treatment	Target New	Peritoneum Peritoneum
3	SD	Mutant	Not reported	Yes	MSI-H	NA	44.0	Off treatment	Target	Pelvis
4	SD	Unknown	Mutant	Unknown	Unknown	NA	4.4	Off treatment	Target New	Liver, peritoneum, lymph node Spleen
5	SD	Wildtype	Wildtype	Yes	MSI-H	NA	28.3	On treatment	Target	Lung, lymph node
6	PR	Wildtype	Wildtype	No	MSI-H	13.8	16.9	Off treatment	Target New	Peritoneum, lymph node Lung
7	SD	Wildtype	Mutant	No	MSI-H	NA	5.3	Off treatment	Target New	Lung, liver, lymph node, peritoneum Peritoneum
8	PR	Wildtype	Mutant	No	MSI-H	42.7	44.1	Off treatment	Target New	Lymph node Oblique transverse muscle
9	PR	Wildtype	Wildtype	No	MSI-H	46.2	47.6	Off treatment	Target New	Pericardium Peritoneum
10	PR	Wildtype	Wildtype	Unknown	MSI-H	27.1	43.7	Off treatment	Target	Peritoneum
11	PR	Wildtype	Wildtype	Unknown	MSI-H	32.9	35.7	Off treatment	Target	Lung, liver, lymph node
12	PR	Mutant	Wildtype	Unknown	MSI-H	29.5	30.9	Off treatment	Target	Lung, peritoneum
13	SD	Wildtype	Mutant	No	MSI-H	NA	8.2	Off treatment	Target New	Peritoneum Lymph node
14	PR	Wildtype	Mutant	No	MSI-H	2.8	5.5	On treatment	Target New	Subcutaneous Lymph node
15	PR	Wildtype	Mutant	Unknown	MSI-H	26.3	27.5	On treatment	Target	Liver, urethra
16	PR	Unknown	Mutant	Unknown	MSI-H	27.7	30.6	On treatment	Target New	Lymph node, other Lymph node
17	SD	Mutant	Wildtype	Unknown	MSI-H	NA	2.4	Off treatment	New	Central nervous system

MSI-H, microsatellite instability high; NA, not applicable; PR, partial response; SD, stable disease.

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Table S3 ORR, BOR, and DCR per investigator by tumor cell PD-L1 expression and LAG-3 expression

	Tumor cell PD-L1 expression		LAG-3 expression	
	≥1% (n=3)	<1% (n=24)	≥1% (n=8)	<1% (n=14)
Objective response rate, n (%)	1 (33)	15 (63)	5 (63)	5 (36)
95% CI	0.8 to 90.6	40.6 to 81.2	24.5 to 91.5	12.8 to 64.9
Confirmed best overall response				
Complete response, n (%)	1 (33)	1 (4)	2 (25)	0
Partial response, n (%)	0	14 (58)	3 (38)	5 (36)
Stable disease, n (%)	1 (33)	6 (25)	2 (25)	5 (36)
Progressive disease, n (%)	1 (33)	3 (13)	1 (13)	4 (29)
Unable to determine	0	0	0	0
Disease control rate,* n (%)	2 (67)	20 (83)	7 (88)	9 (64)
95% CI	9.4 to 99.2	62.6 to 95.3	47.3 to 99.7	35.1 to 87.2

*Complete response plus partial response plus stable disease (for at least 12 weeks); CI based on the Clopper-Pearson method.

BOR, best overall response; CI, confidence interval; DCR, disease control rate; LAG-3, lymphocyte-activation gene 3; ORR, objective response rate; PD-L1, programmed death ligand 1.

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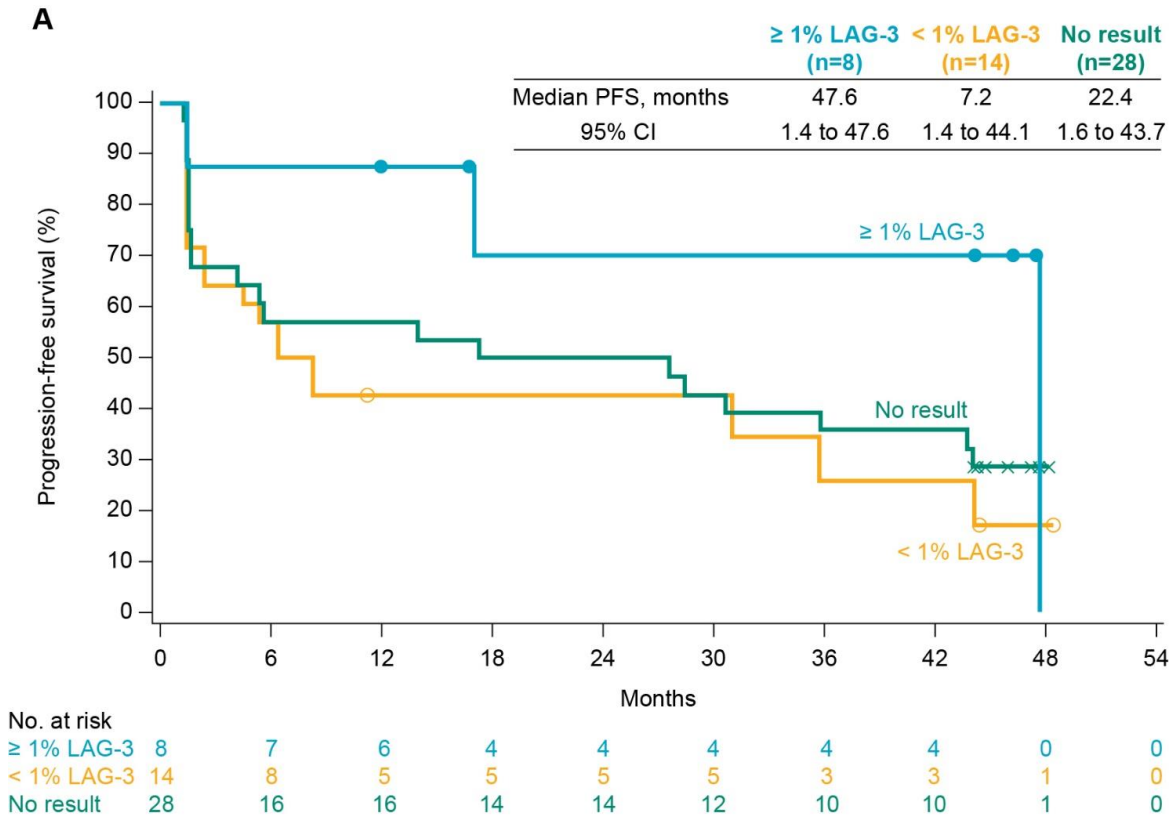
Figure S1 A) Kaplan-Meier curve of progression-free survival per investigator by baseline LAG-3 status. B) Kaplan-Meier curve of overall survival per investigator by baseline LAG-3 status. Symbols represent censored observations. LAG-3, lymphocyte-activation gene 3.



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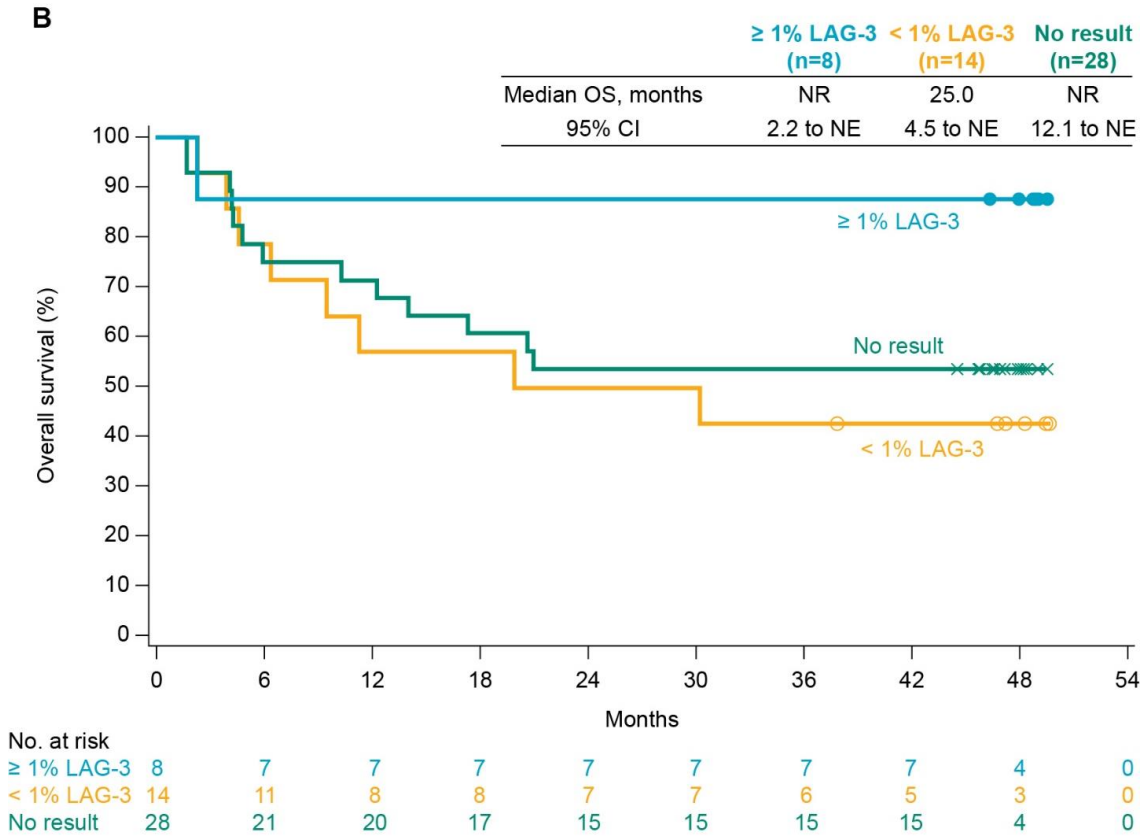

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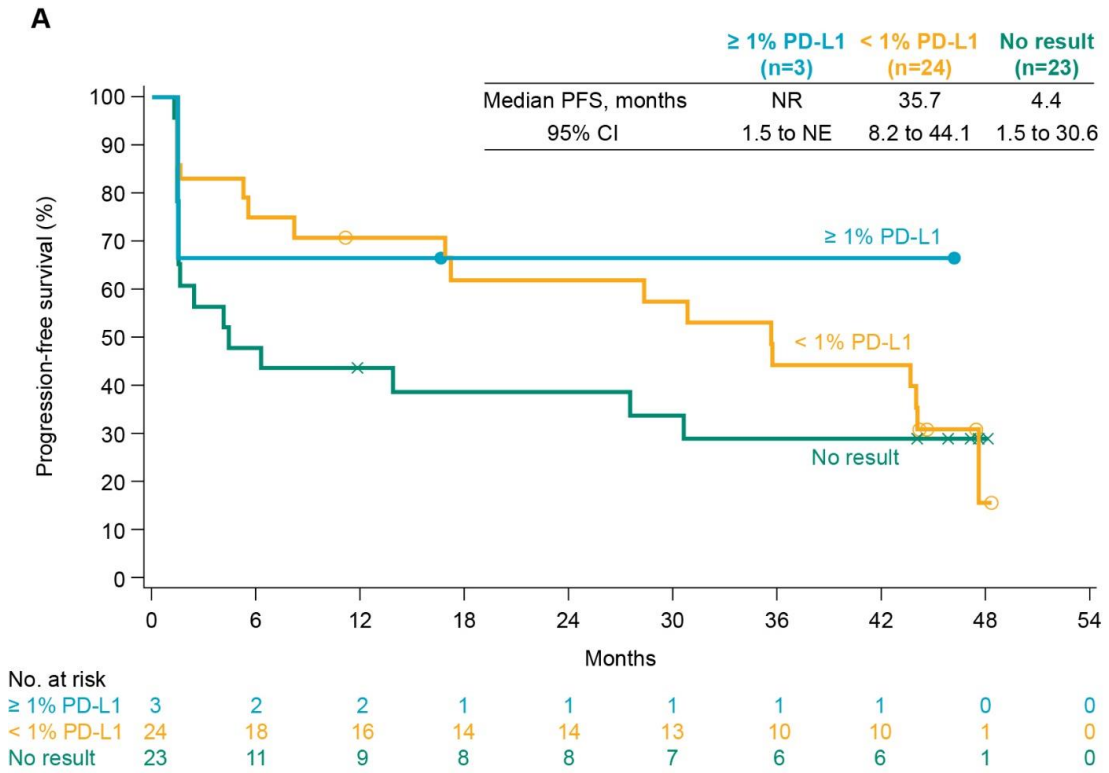
Figure S2 A) Kaplan-Meier curve of progression-free survival per investigator by baseline tumor cell PD-L1 expression status. B) Kaplan-Meier curve of overall-survival per investigator by baseline tumor cell PD-L1 expression status. Symbols represent censored observations. PD-L1, programmed death ligand 1.



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