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Supplement

Table S1 Site of primary tumor in patients in the dose-escalation part

	Avelumab 10 mg/kg Q2W				**Avelumab 800 mg QW → Q2W[a] plus M9241 16.8 µg/kg (n=7)**
	M9241 4 µg/kg (n=9)	**M9241 8 µg/kg (n=7)**	**M9241 12 µg/kg (n=7)**	**M9241 16.8 µg/kg (n=6)**	
Site of primary tumor, n (%)					
Anterior wall of bladder	0	0	0	1 (16.7)	0
Bladder, trigone	0	0	0	0	1 (14.3)
Choroid	0	0	1 (14.3)	0	0
Colon	0	2 (28.6)	1 (14.3)	0	0
Endocervix	0	0	1 (14.3)	0	1 (14.3)
Endometrium	0	0	1 (14.3)	0	0
Floor of mouth	0	1 (14.3)	0	0	0
Gastric antrum	1 (11.1)	0	0	0	0
Head, face, or neck	1 (11.1)	0	0	0	0
Intrahepatic bile duct	1 (11.1)	0	0	0	0
Kidney	1 (11.1)	0	0	0	0
Lateral wall of bladder	0	0	0	1 (16.7)	0
Liver	1 (11.1)	0	0	0	0
Nasopharynx	1 (11.1)	0	0	0	0
Oropharynx	0	0	1 (14.3)	0	0
Ovary	1 (11.1)	1 (14.3)	0	0	0
Overlapping lesion of hypopharynx	0	0	0	1 (16.7)	0
Pancreas	0	0	0	0	1 (14.3)
Pancreas, body	0	0	0	0	1 (14.3)
Pancreas, head	1 (11.1)	1 (14.3)	1 (14.3)	1 (16.7)	2 (28.6)
Prostate gland	0	0	1 (14.3)	1 (16.7)	0
Renal pelvis	0	1 (14.3)	0	0	0
Urachus	0	0	0	1 (16.7)	0
Ureter	0	0	0	0	1 (14.3)
Urethra	0	1 (14.3)	0	0	0
Uterus	1 (11.1)	0	0	0	0

[a]Avelumab QW for 12 weeks then Q2W thereafter.
QW, once weekly; Q2W, every 2 weeks.

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Table S2 Summary of baseline PD-L1 status in patients in the dose-expansion part

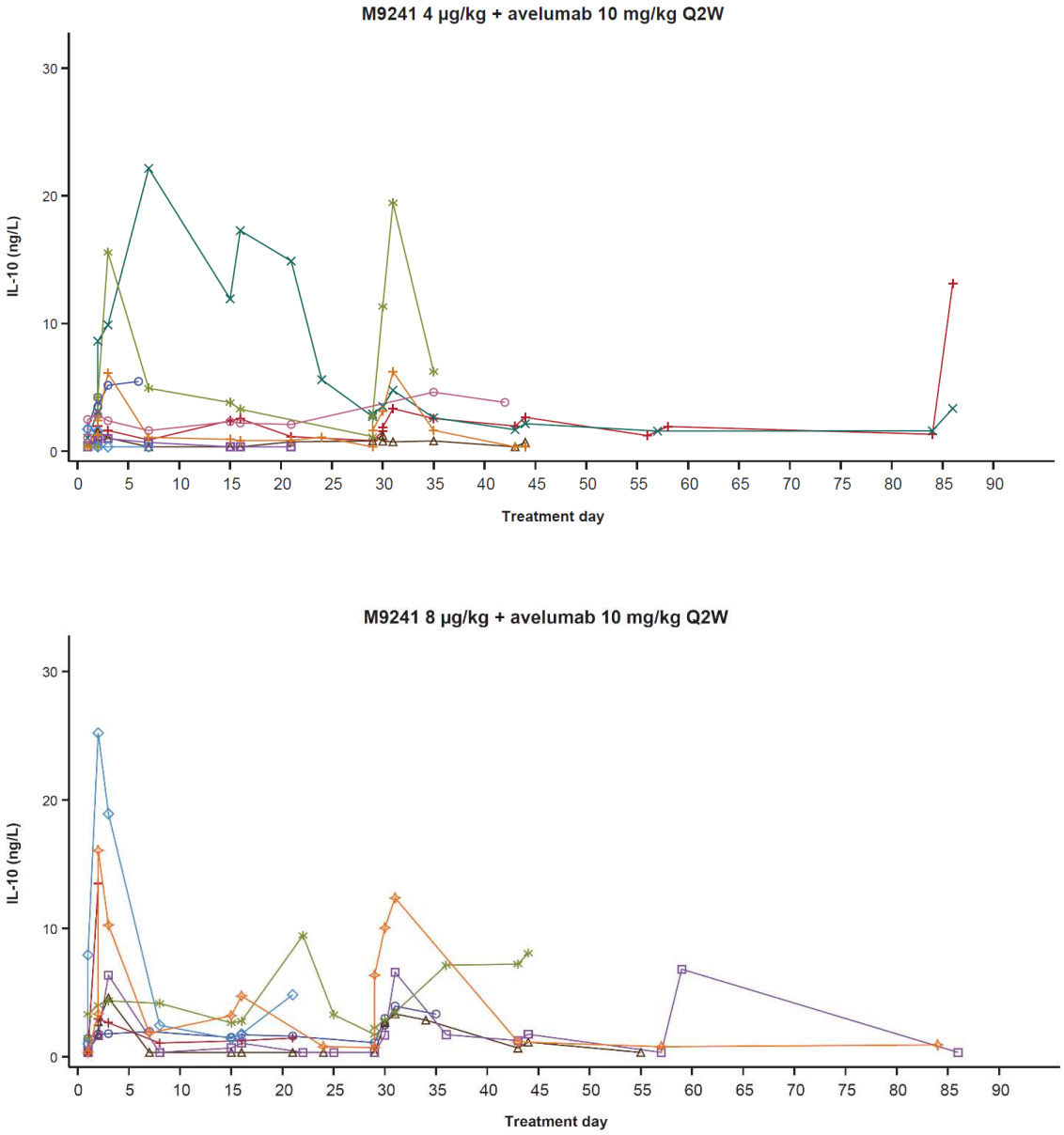
PD-L1 cutoff	**Patients, n (%) (N=16)**
≥1% of tumor cells, any membrane staining intensity	
Positive	6 (37.5)
Negative	9 (56.3)
Not evaluable	1 (6.3)
≥5% of tumor cells, any membrane staining intensity	
Positive	3 (18.8)
Negative	12 (75.0)
Not evaluable	1 (6.3)
≥50% of tumor cells, any membrane staining intensity	
Positive	2 (12.5)
Negative	13 (81.3)
Not evaluable	1 (6.3)
≥25% of tumor cells, any membrane staining; ≥25% of immune cells and percentage of immune cells present >1%; or 100% of immune cells and percentage of immune cells present = 1%	
Positive	4 (25.0)
Negative	11 (68.8)
Not evaluable	1 (6.3)

Strauss J, *et al. J Immunother Cancer* 2023; 11:e005813. doi: 10.1136/jitc-2022-005813

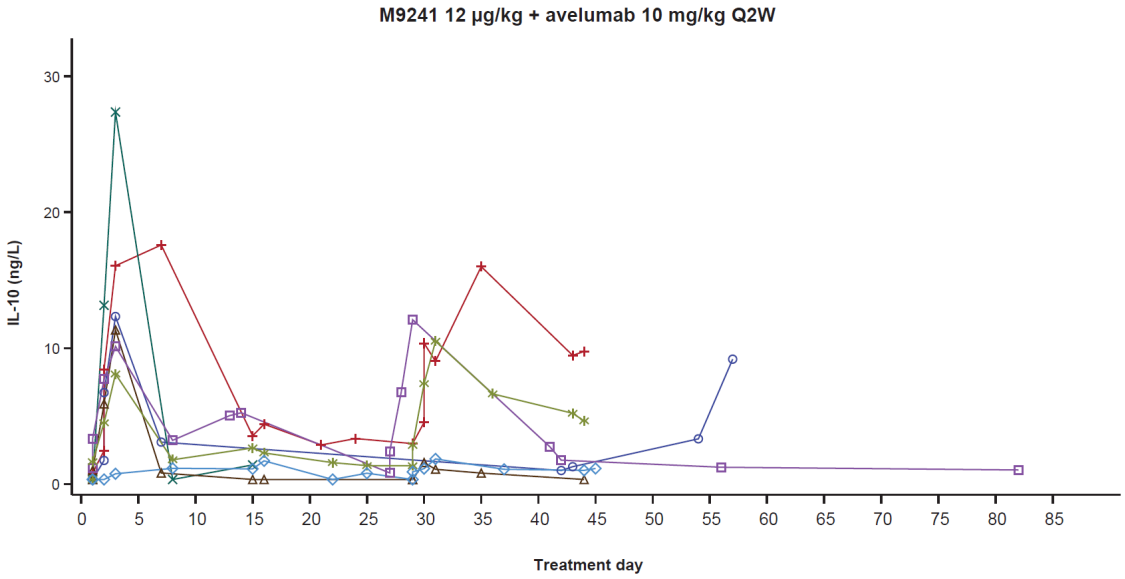
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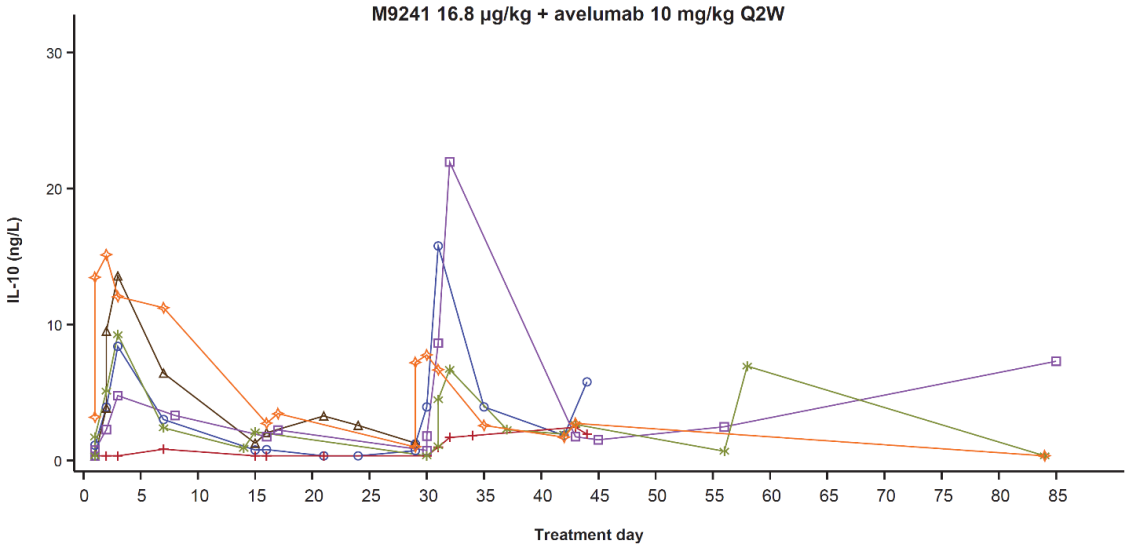
Figure S1 Serum levels of (A) IL-10, (B) IL-12p70, and (C) TNF-α in individual patients in each cohort in the dose-escalation part. Patients with a complete response (M9241 8 µg/kg plus avelumab 10 mg/kg Q2W [DL2] and M9241 16.8 µg/kg plus avelumab 10 mg/kg Q2W [DL4]) are depicted with orange lines.

A

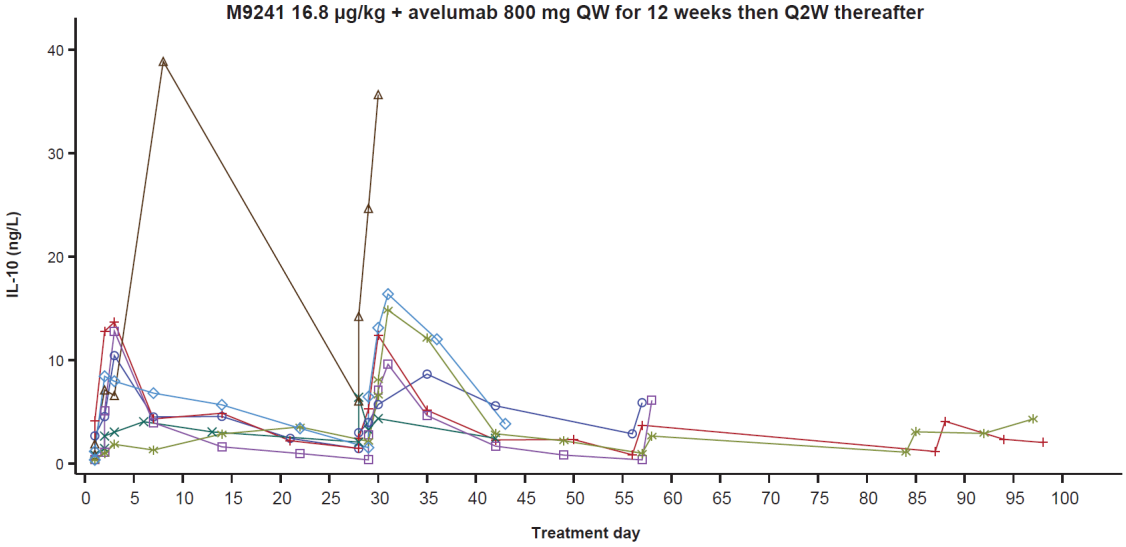


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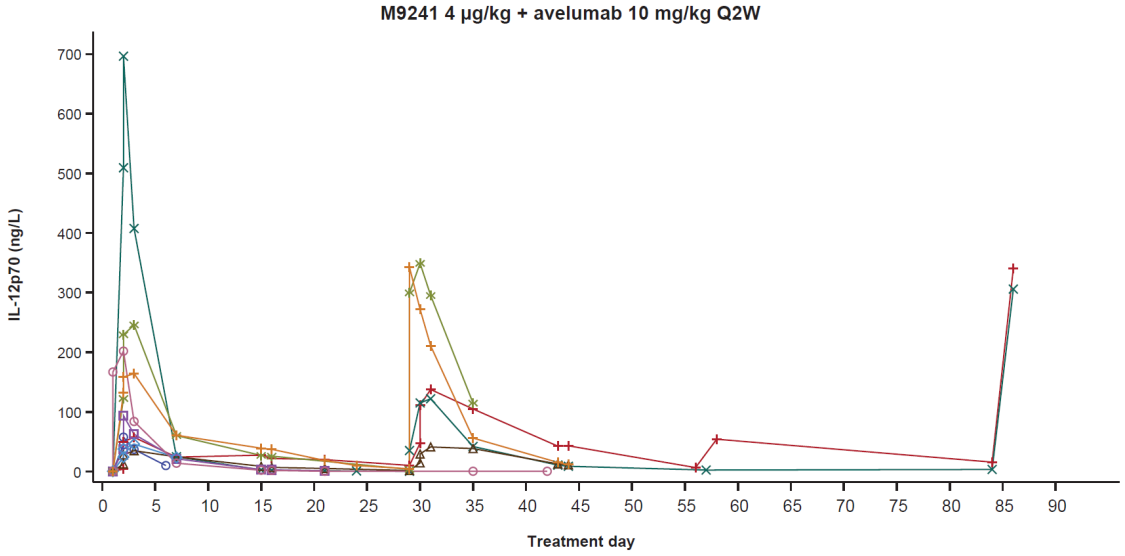




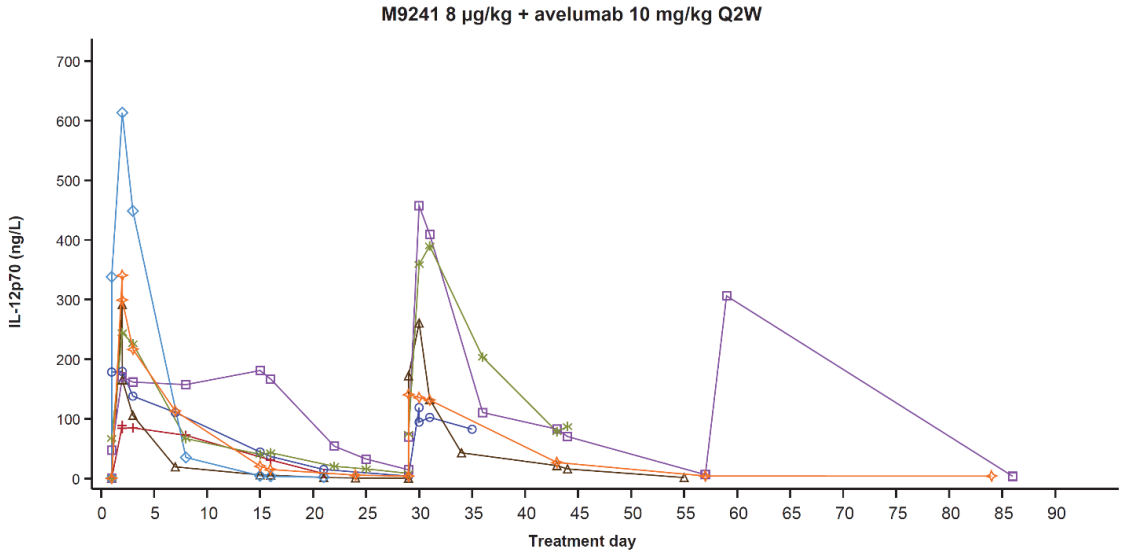
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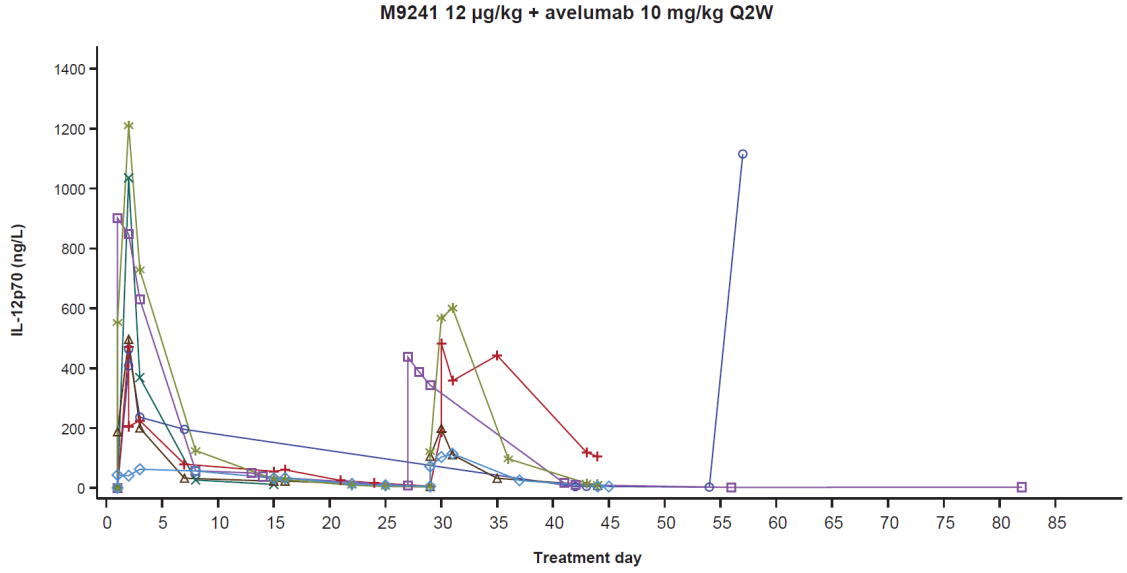


B

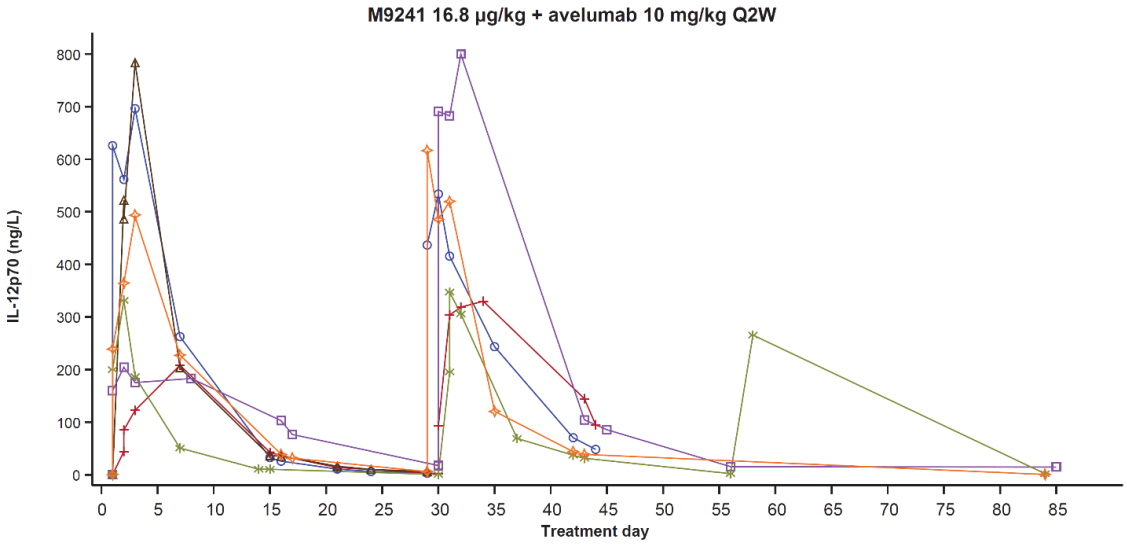


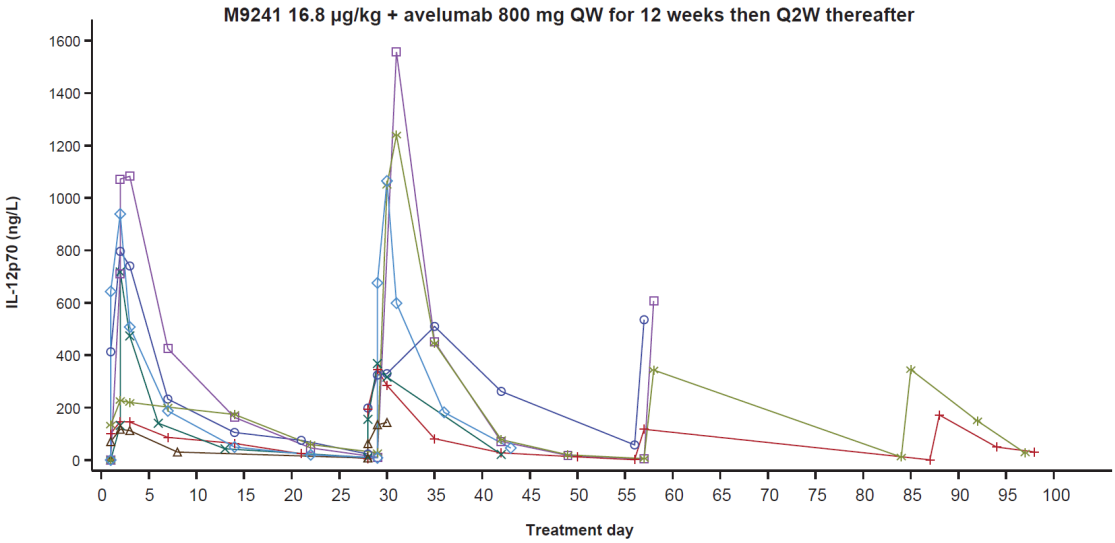
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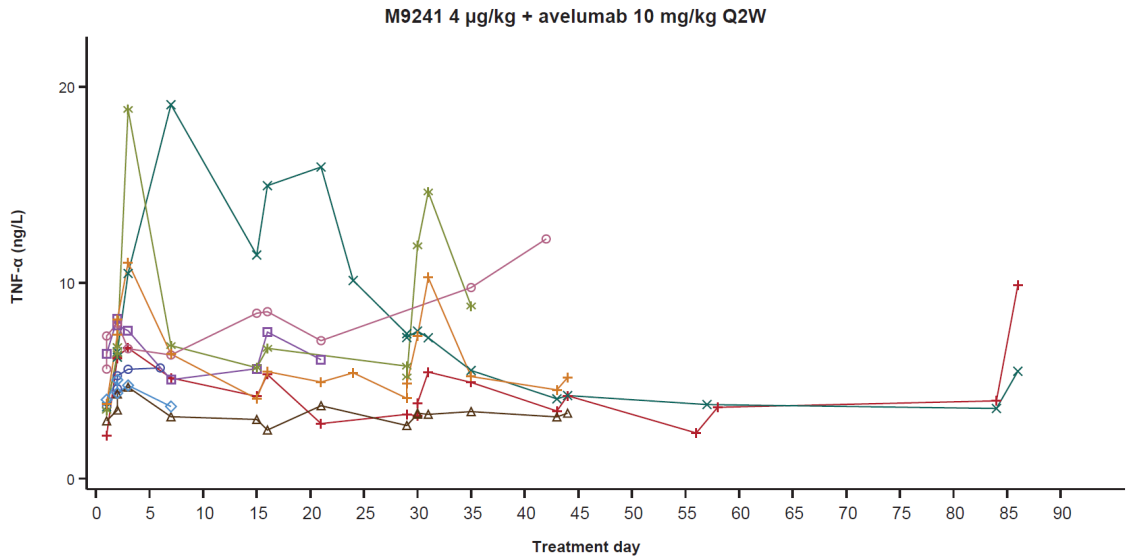
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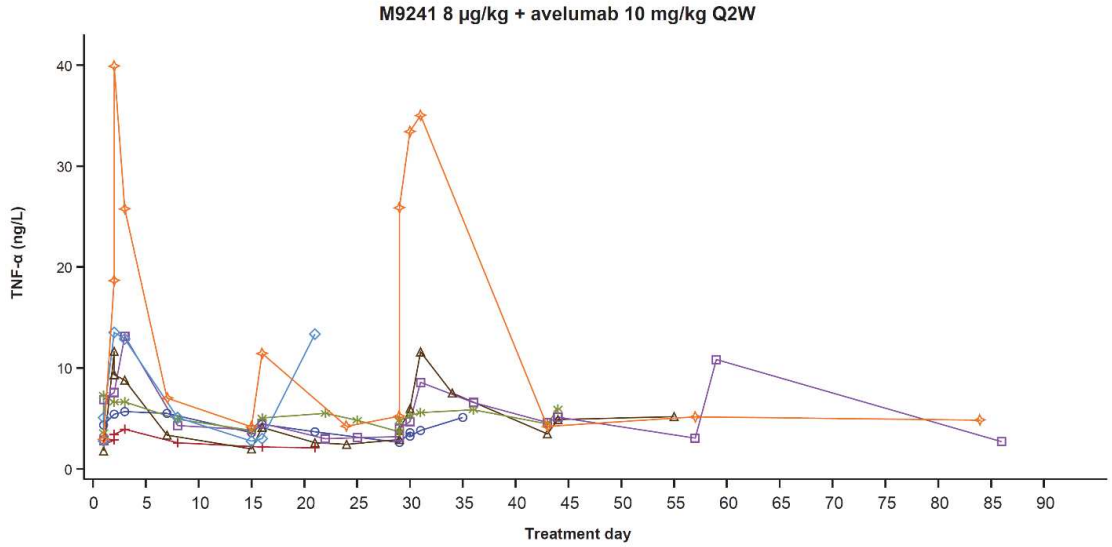




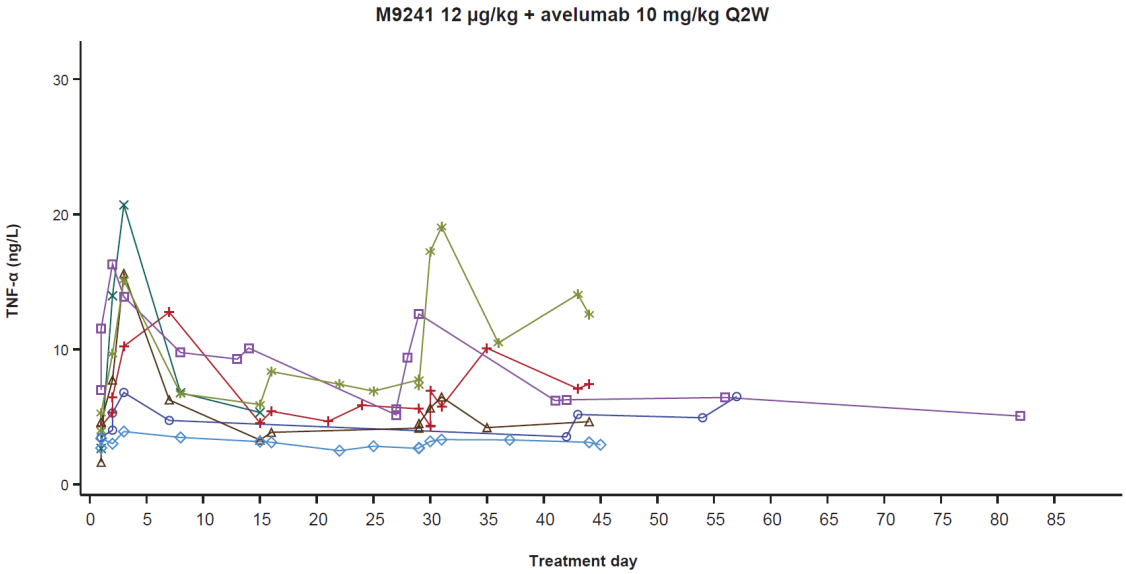
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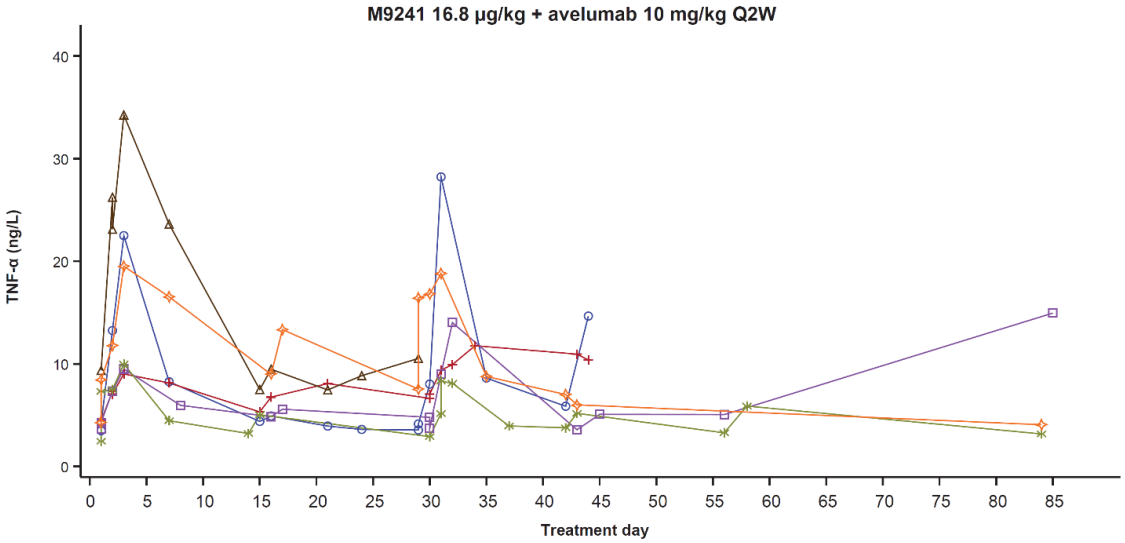
C



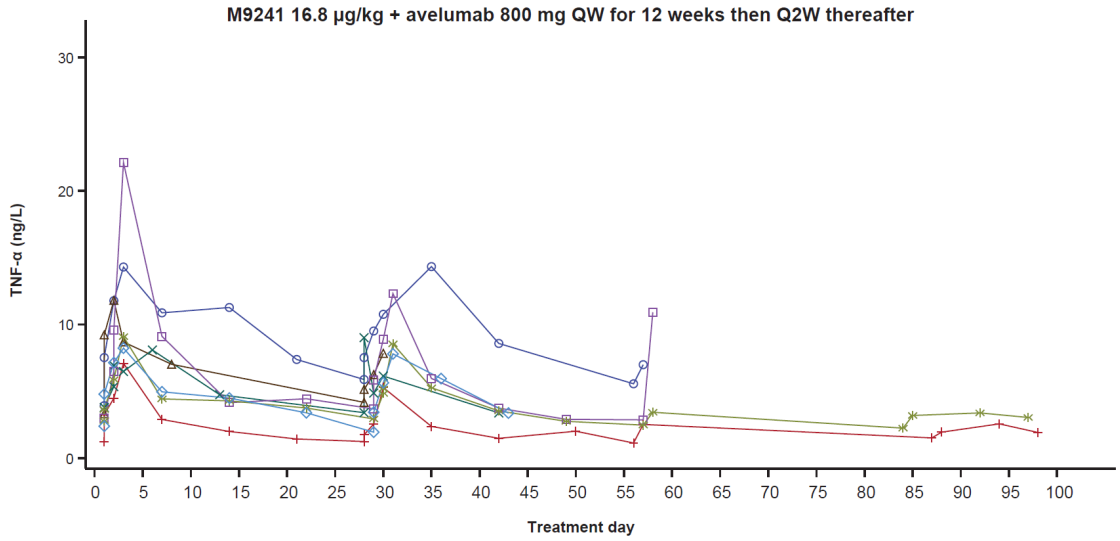


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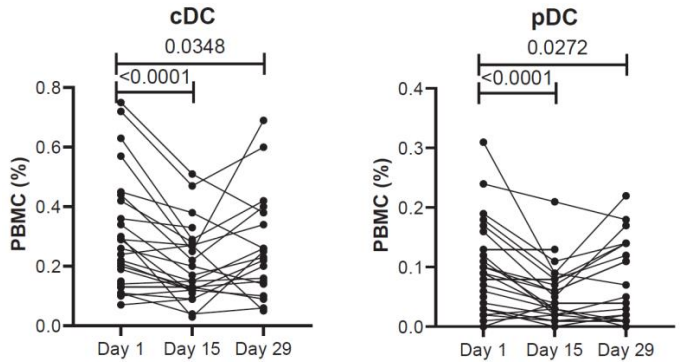
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IL, interleukin; TNF, tumor necrosis factor; QW, once weekly; Q2W, every 2 weeks.

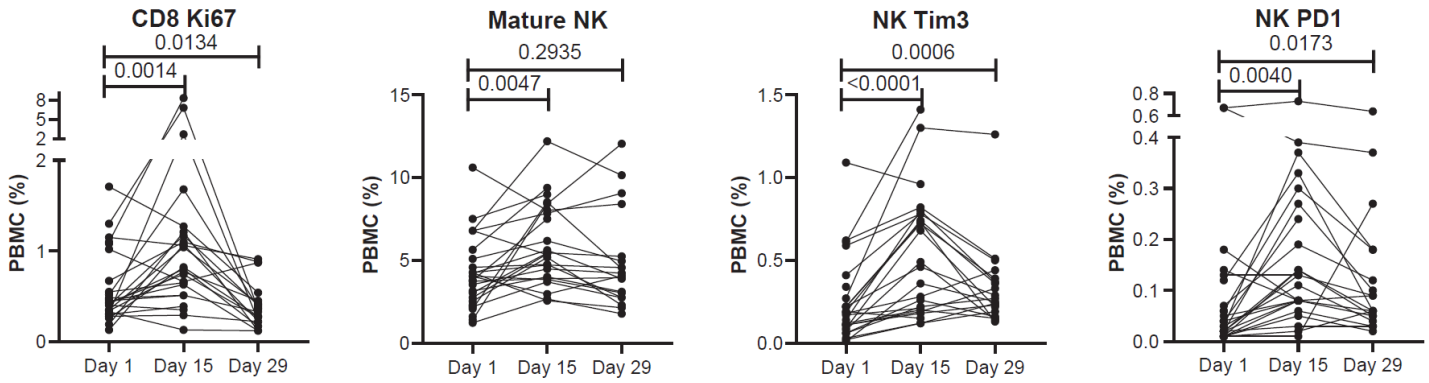
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Figure S2 Changes in peripheral immune cell (A) classic subsets and (B) refined subsets in samples from the dose-escalation part.



A

B



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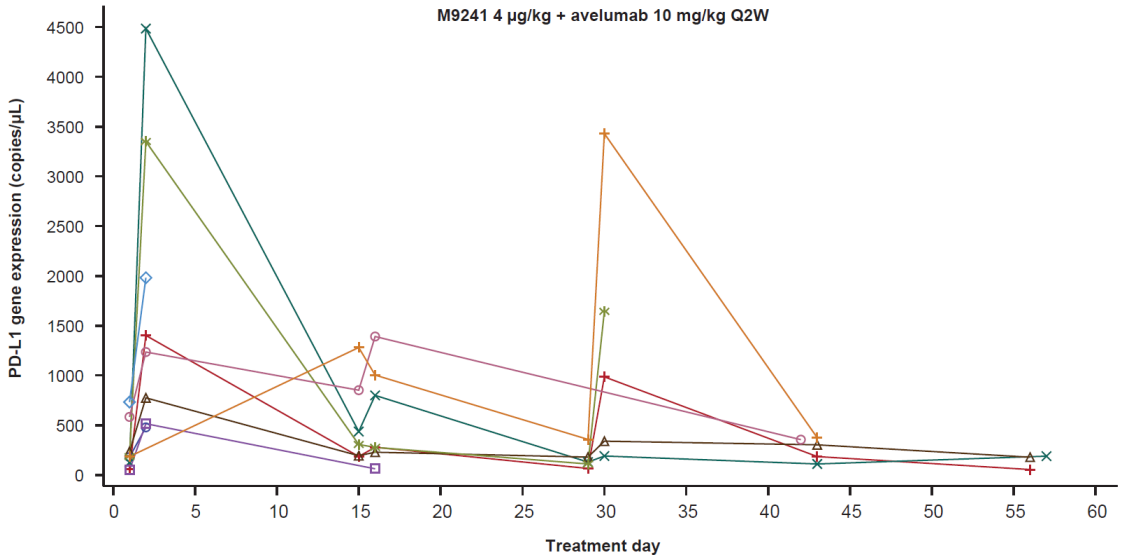
The frequency of all immune cell subsets was calculated as a percentage of PBMCs to eliminate potential bias in smaller populations with fluctuations in leukocyte subpopulations. Immune subsets with a potentially biologically relevant change following treatment were defined as those with $p<0.05$, most patients had a >25% change, and a difference in medians PBMCs >0.05%. P values are reported without adjustment for multiple comparisons; given the large number of PBMC subsets assessed and the small number of patients evaluated, p values <0.05 should be considered trends. cDC, conventional dendritic cell; PBMC, peripheral blood mononuclear cell; pDC, plasmacytoid dendritic cell; NK, natural killer.

Strauss J, *et al. J Immunother Cancer* 2023; 11:e005813. doi: 10.1136/jitc-2022-005813

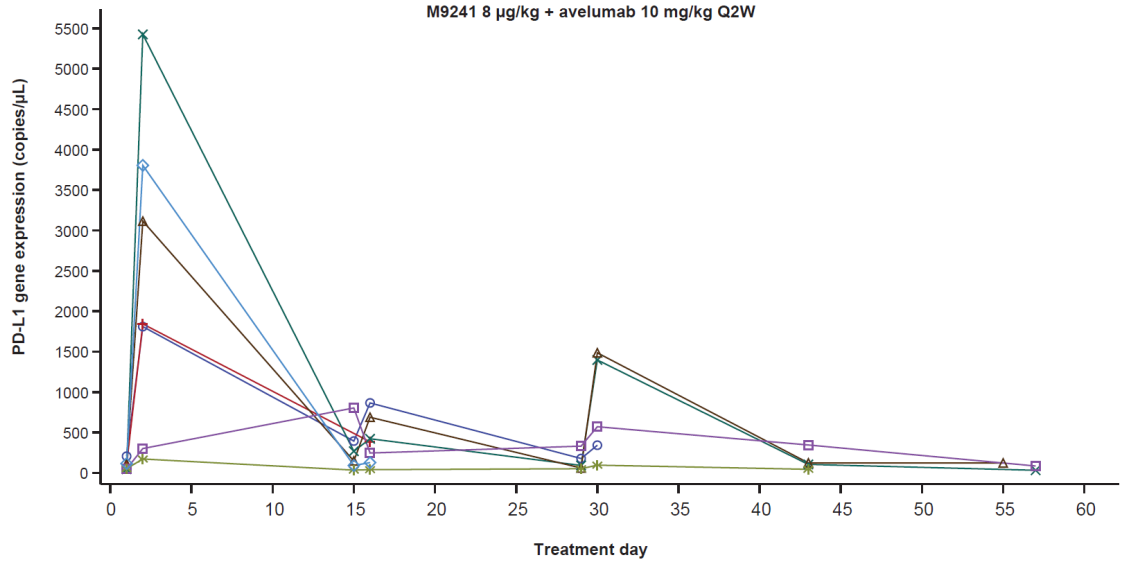
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Figure S3 PD-L1 gene expression in peripheral blood of individual patients from the dose-escalation part: (A) M9241 4 µg/kg + avelumab 10 mg/kg Q2W, (B) M9241 8 µg/kg + avelumab 10 mg/kg Q2W, (C) M9241 12 µg/kg + avelumab 10 mg/kg Q2W, and (D) M9241 16.8 µg/kg + avelumab 10 mg/kg Q2W.

A

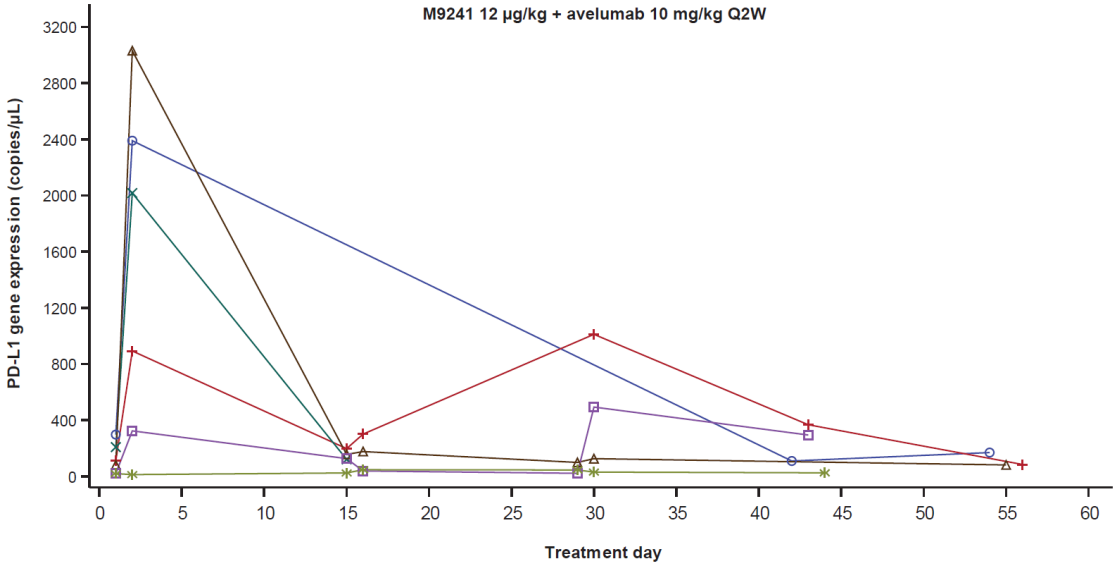


B

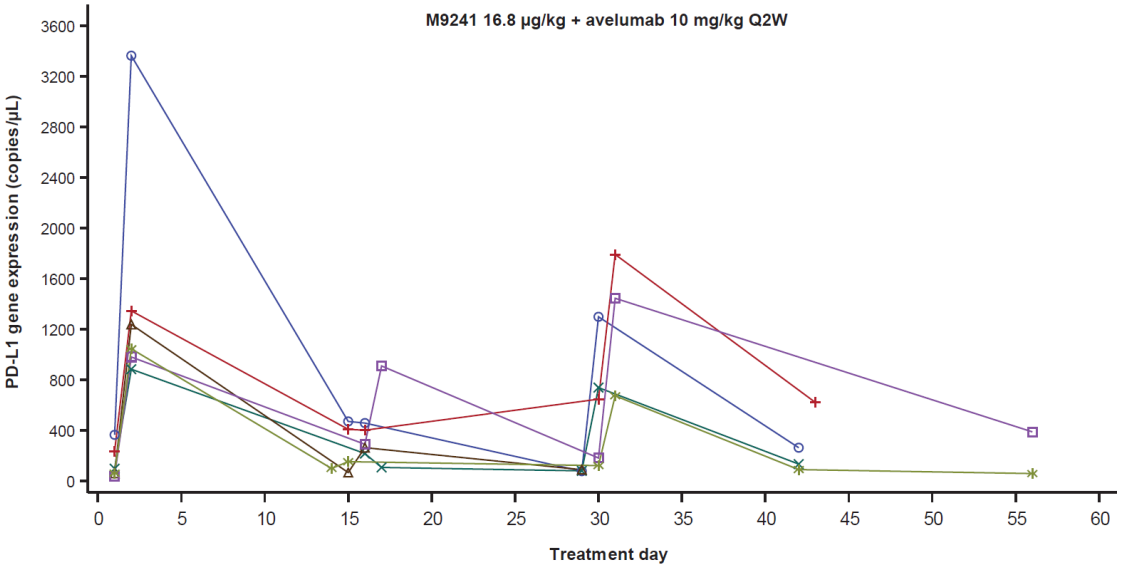


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C



D

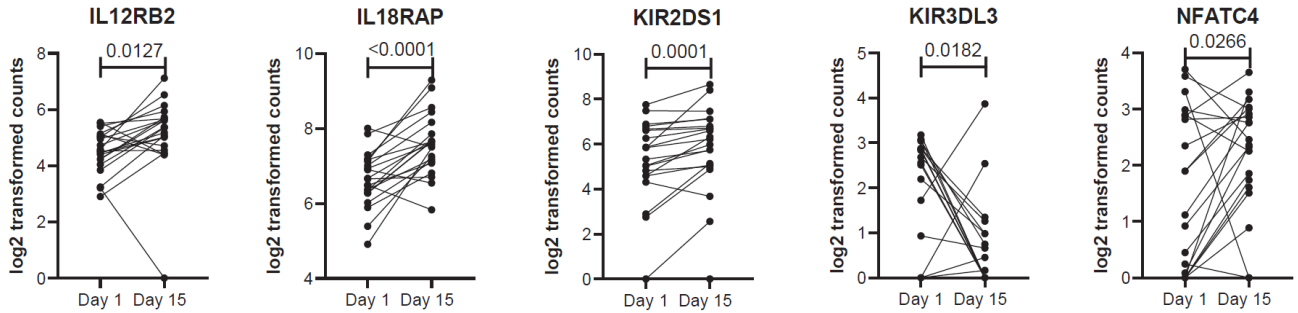


Q2W, every 2 weeks.

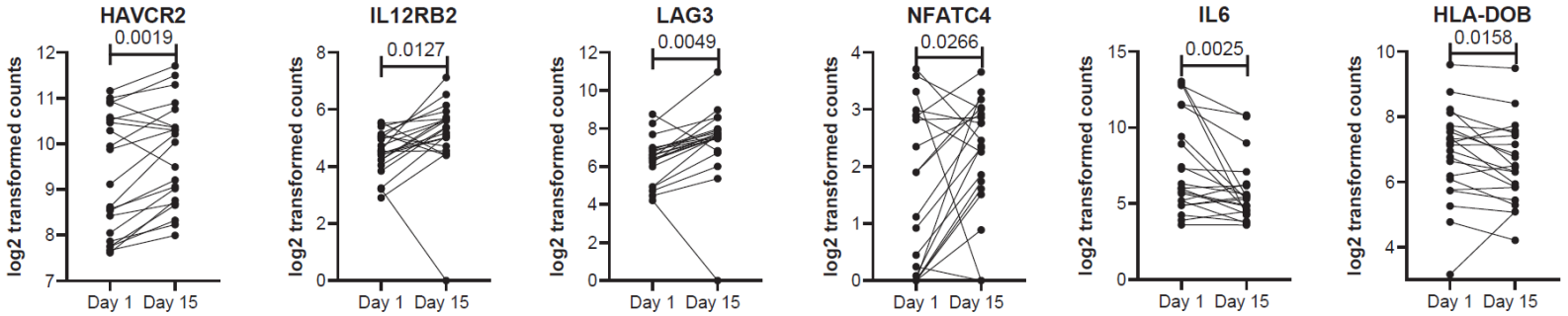
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Figure S4 Changes in gene expression from days 1 to 15 in samples from all evaluable patients in the dose-escalation part: (A) genes contributing to NK cell signaling pathways and (B) genes contributing to T-cell exhaustion signaling pathways.

A



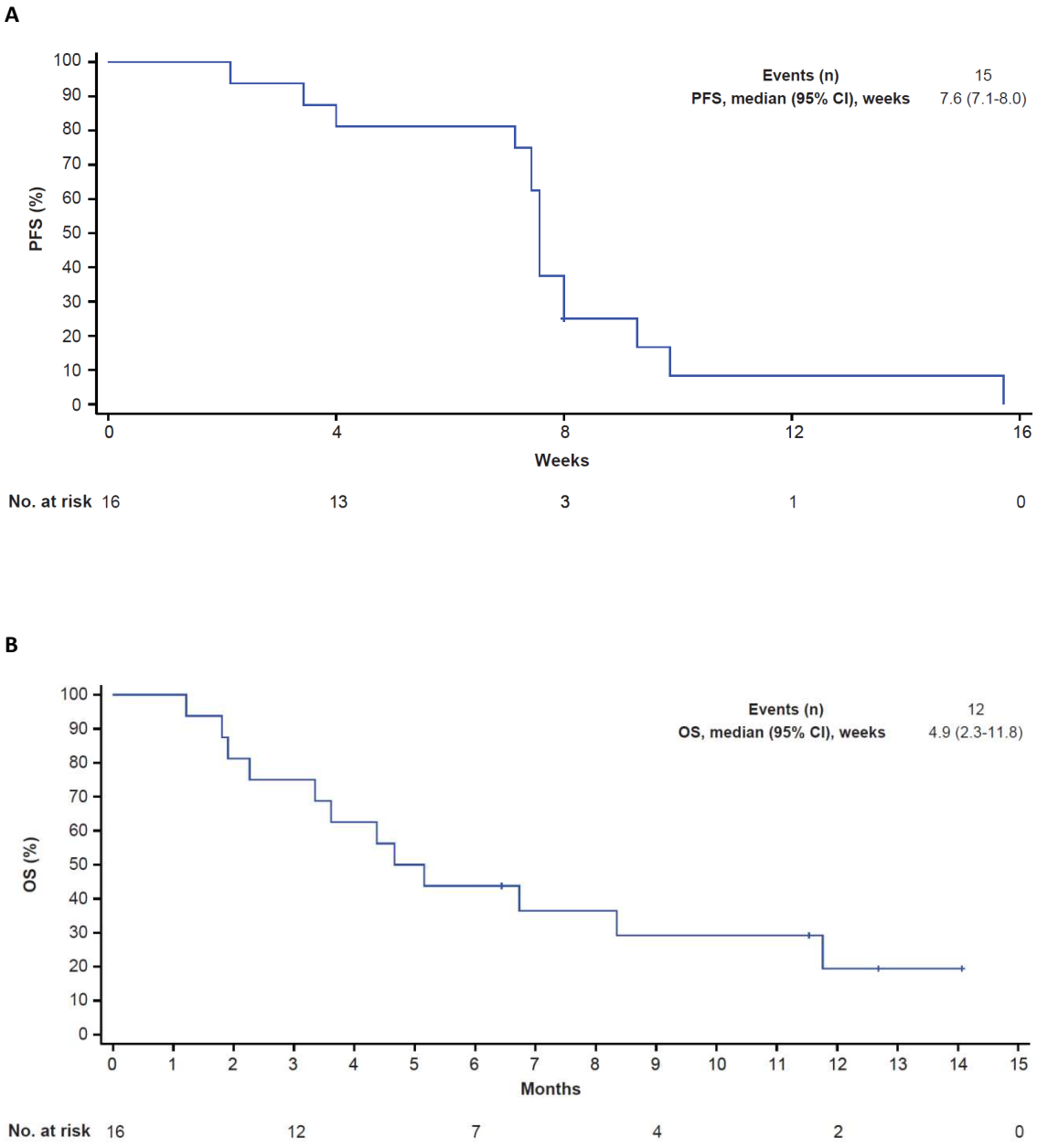
B



IL, interleukin; NK, natural killer.

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Figure S5 PFS (A) and OS (B) in the dose-expansion part.

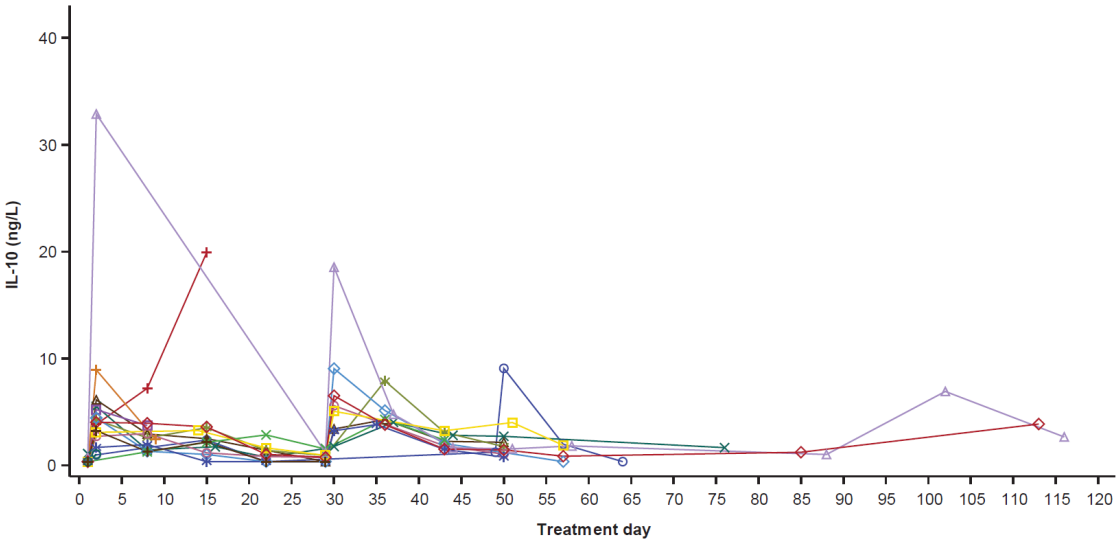


OS, overall survival; PFS, progression-free survival.

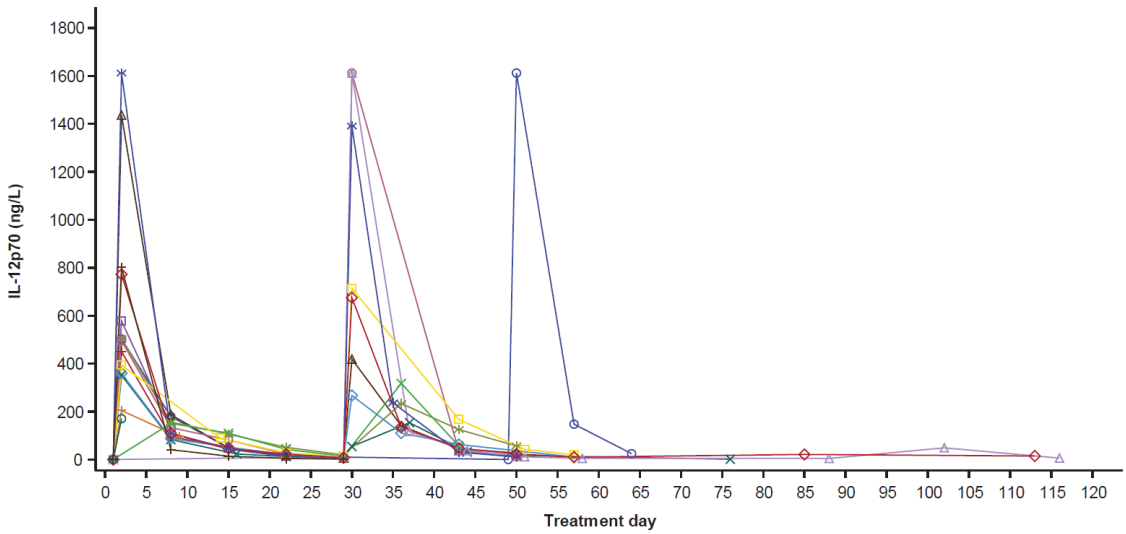
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Figure S6 Serum levels of (A) IL-10 and (B) IL-12p70 for individual patients in the dose-expansion part.

A



B

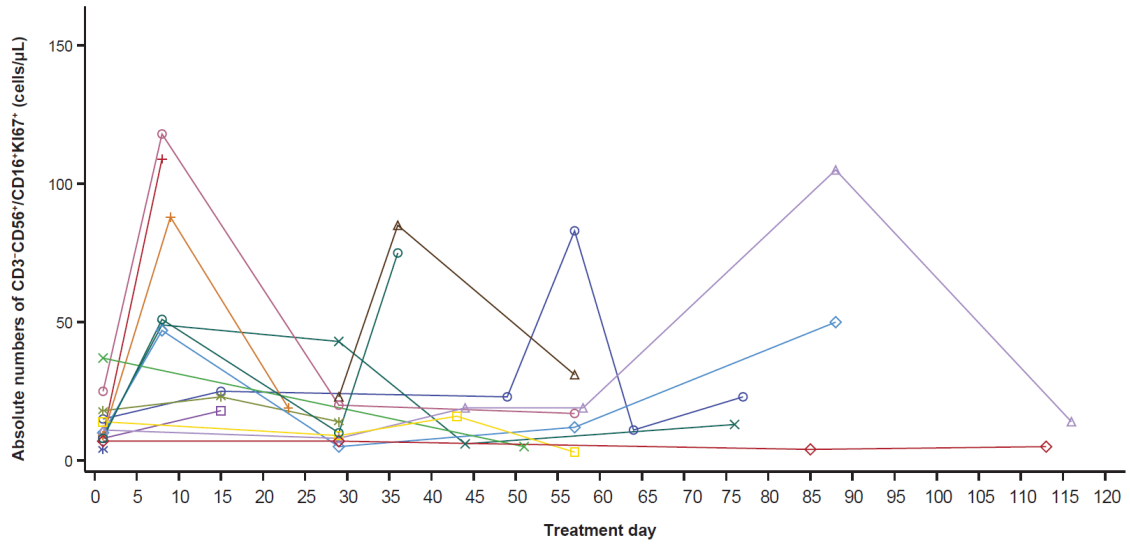


IL, interleukin.

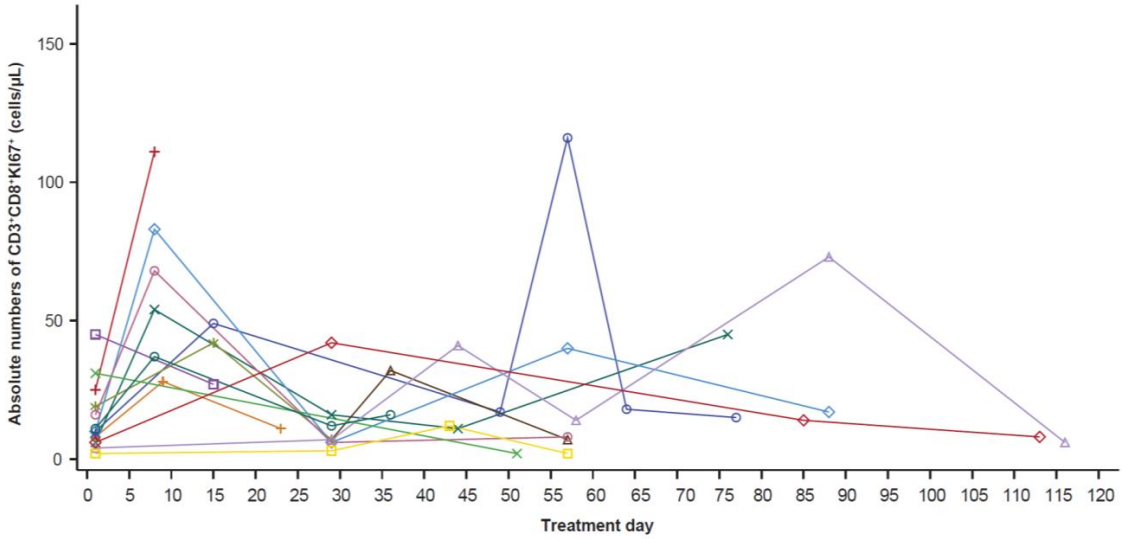
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Figure S7 Induction of proliferation in (A) NK cells and (B) $CD8^+$ T cells for individual patients in the dose-expansion part.

A



B



NK, natural killer.