Supplementary Materials

Supplementary Table S1. Incidence of all-grade TEAEs occurring in ≥15% of patients by dose cohort.

Preferred term n (%)	0.01 mg/kg (n=2)	0.03 mg/kg (n=2)	0.1 mg/kg (n=6)	0.2 mg/kg (n=6)	0.4 mg/kg (n=5)	0.8 mg/kg (n=4)	1.6 mg/kg (n=3)	2.4 mg/kg (n=3)	3.6 mg/kg (n=28)	Total (N=59)
Any TEAE	2 (100)	2 (100)	6 (100)	6 (100)	5 (100)	4 (100)	3 (100)	2 (67)	26 (93)	56 (95)
Fatigue	1 (50)	2 (100)	4 (67)	2 (33)	4 (80)	3 (75)	0	0	8 (29)	24 (41)
Decreased appetite	2 (100)	0	1 (17)	2 (33)	4 (80)	1 (25)	2 (67)	2 (67)	7 (25)	21 (36)
Asthenia	0	0	3 (50)	2 (33)	0	1 (25)	2 (67)	1 (33)	8 (29)	17 (29)
Constipation	0	0	3 (50)	3 (50)	1 (20)	1 (25)	0	1 (33)	6 (21)	15 (25)
Dyspnea	0	0	1 (17)	2 (33)	3 (60)	0	0	0	9 (32)	15 (25)
Abdominal pain	0	0	4 (67)	1 (17)	1 (20)	1 (25)	0	0	6 (21)	13 (22)
Malignant neoplasm progression	1 (50)	0	3 (50)	3 (50)	1 (20)	0	2 (67)	0	1 (4)	11 (19)
Nausea	0	0	2 (33)	0	3 (60)	1 (25)	0	0	4 (14)	10 (17)
Anemia	1 (50)	0	1 (17)	1 (17)	0	0	1 (33)	0	5 (18)	9 (15)
Anxiety	0	0	1 (17)	2 (33)	3 (60)	1 (25)	1 (33)	0	1 (4)	9 (15)
Headache	0	0	0	3 (50)	1 (20)	1 (25)	0	1 (33)	3 (11)	9 (15)
Pleural effusion	0	0	0	1 (17)	2 (40)	1 (25)	2 (67)	0	3 (11)	9 (15)
Pyrexia	0	0	2 (33)	1 (17)	1 (20)	0	1 (33)	0	4 (14)	9 (15)

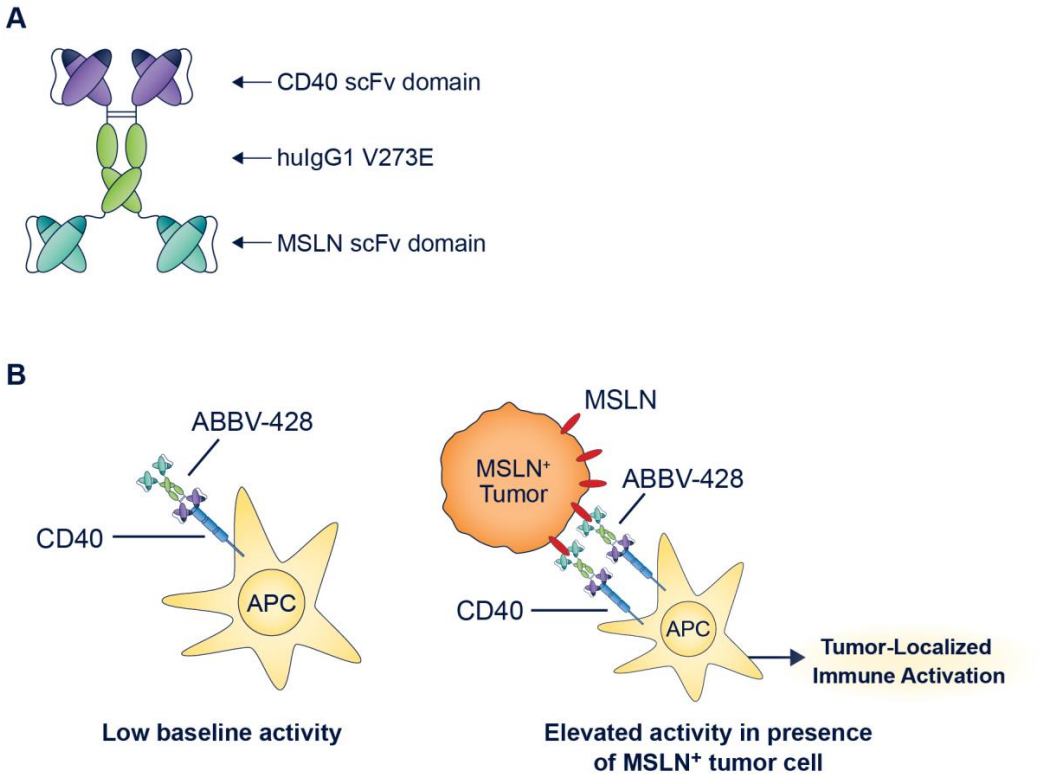
TEAE, treatment-emergent adverse event.

Supplementary Table S2. Incidence of Grade ≥3 TEAEs occurring in ≥5% of patients by dose cohort.

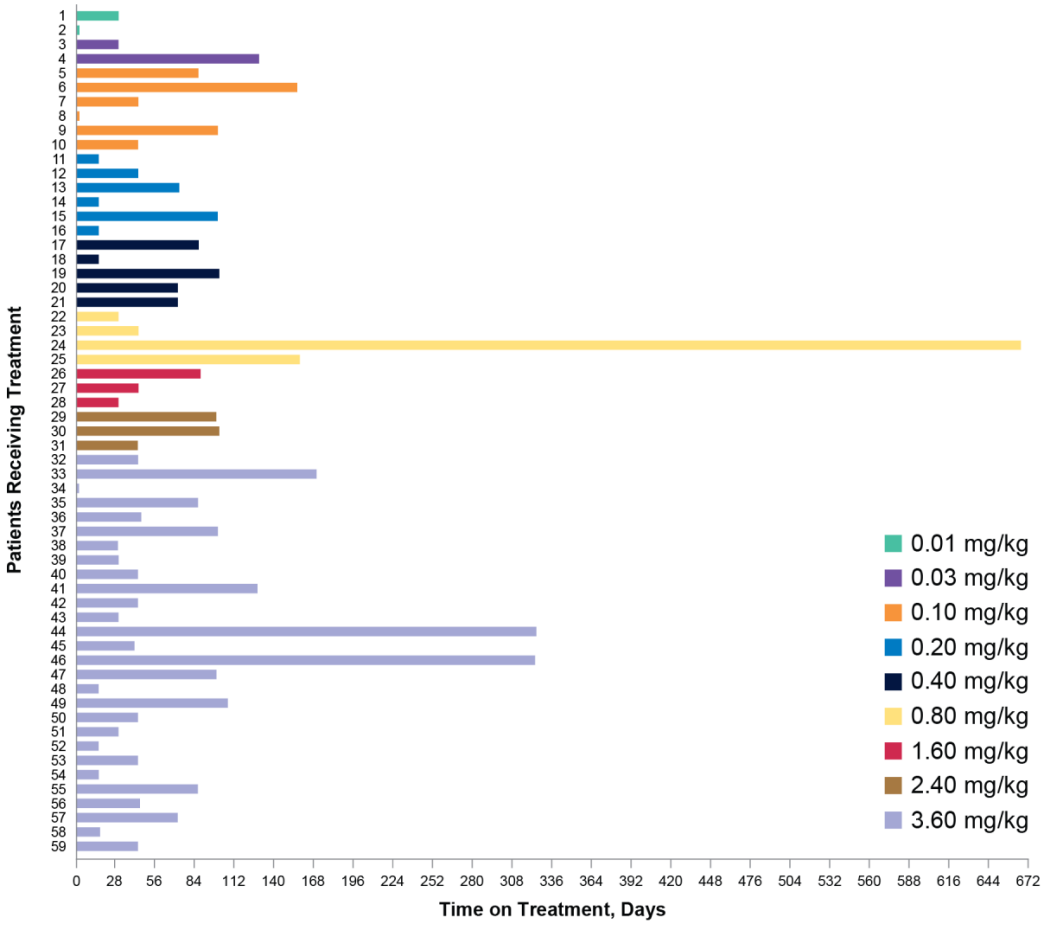
Preferred term n (%)	0.01 mg/kg (n=2)	0.03 mg/kg (n=2)	0.1 mg/kg (n=6)	0.2 mg/kg (n=6)	0.4 mg/kg (n=5)	0.8 mg/kg (n=4)	1.6 mg/kg (n=3)	2.4 mg/kg (n=3)	3.6 mg/kg (n=28)	Total (N=59)
Any Grade ≥3 TEAE	2 (100)	0	3 (50)	4 (67)	4 (80)	3 (75)	3 (100)	1 (33)	16 (57)	36 (61)
Malignant neoplasm progression	1 (50)	0	3 (50)	3 (50)	1 (20)	0	2 (67)	0	1 (4)	11 (19)
Anemia	1 (50)	0	1 (17)	1 (17)	0	0	1 (33)	0	1 (4)	5 (8)
Abdominal pain	0	0	2 (33)	0	0	0	0	0	2 (7)	4 (7)
Fatigue	1 (50)	0	0	1 (17)	1 (20)	1 (25)	0	0	0	4 (7)
Gamma-glutamyltransferase increased	2 (100)	0	0	0	0	1 (25)	0	0	1 (4)	4 (7)
Pleural effusion	0	0	0	0	1 (20)	1 (25)	1 (33)	0	1 (4)	4 (7)
Pneumonia	0	0	0	0	0	0	3 (100)	0	1 (4)	4 (7)
Asthenia	0	0	1 (17)	0	0	0	1 (33)	0	1 (4)	3 (5)
Blood bilirubin increased	2 (100)	0	0	1 (17)	0	0	0	0	0	3 (5)
Decreased appetite	1 (50)	0	0	1 (17)	1 (20)	0	0	0	0	3 (5)
Dyspnea	0	0	0	0	1 (20)	0	0	0	2 (7)	3 (5)
Hypokalemia	0	0	1 (17)	0	1 (20)	0	0	0	1 (4)	3 (5)
Lymphopenia	0	0	1 (17)	0	0	1 (25)	0	1 (33)	0	3 (5)

TEAE, treatment-emergent adverse event.

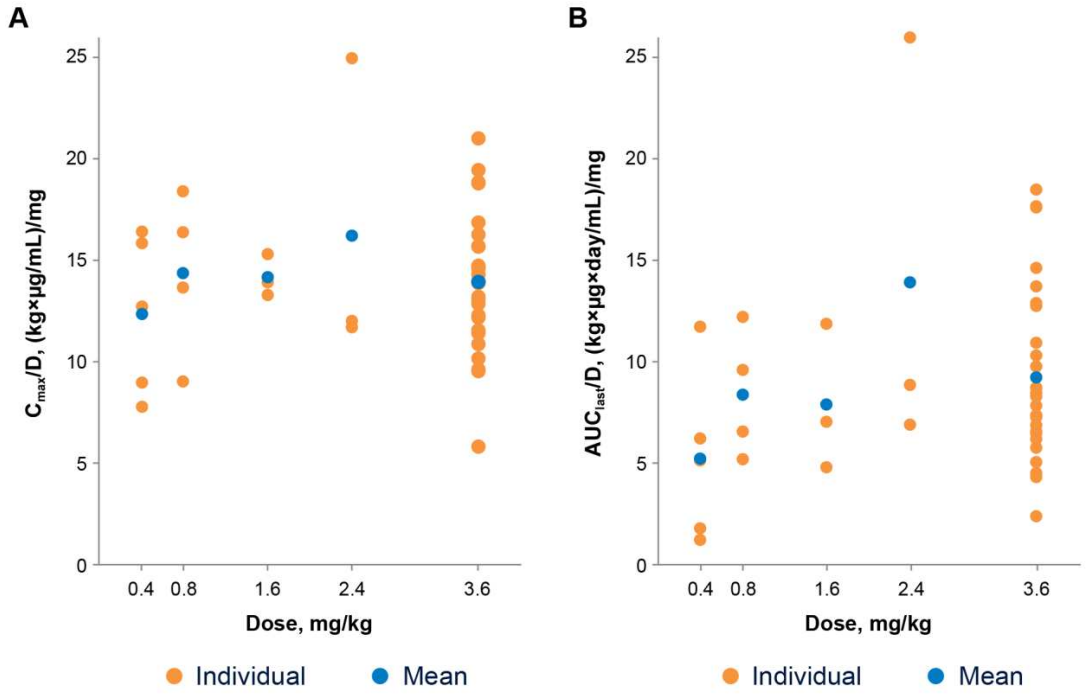
Supplementary Figure S1. (A) ABBV-428 structure and (B) mechanism of action. MSLN, mesothelin; scFv, single-chain variable fragment.



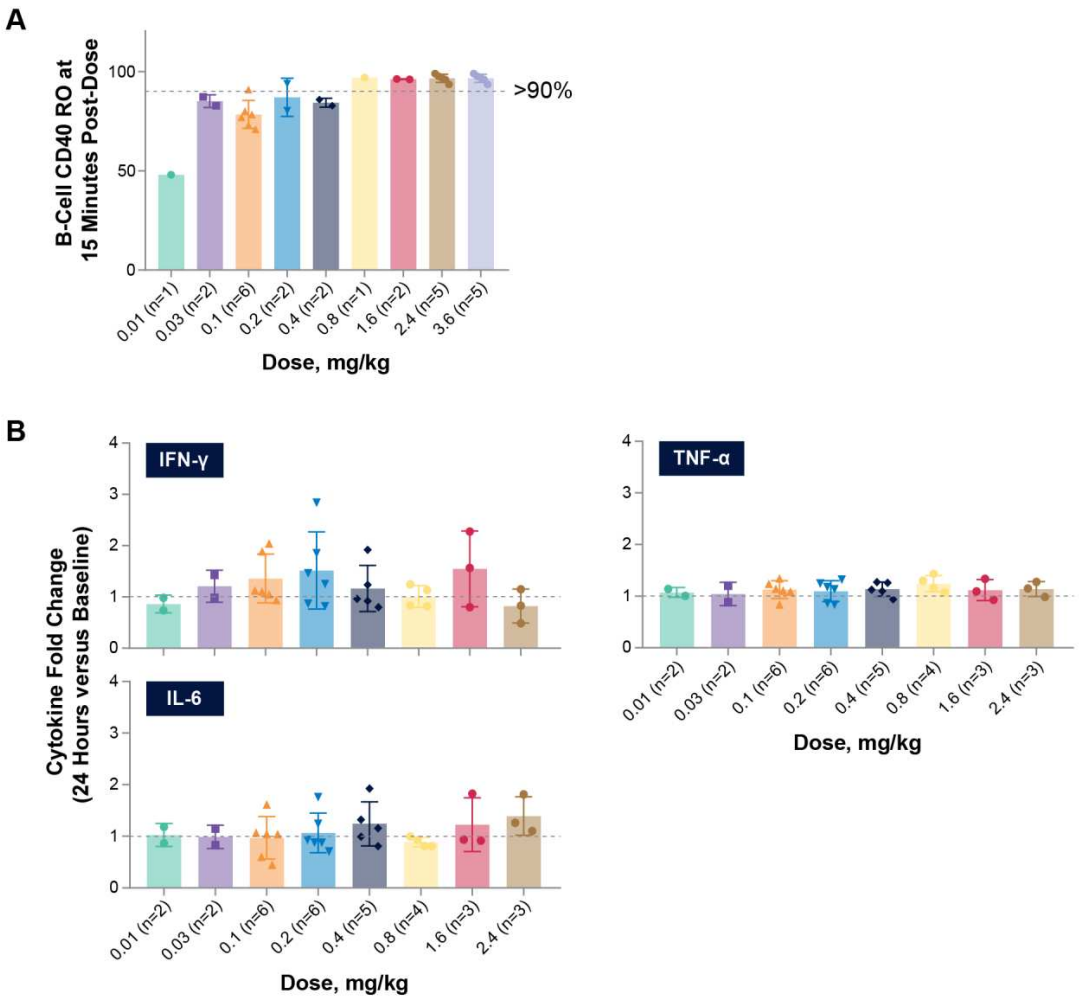
Supplementary Figure S2. Swimmers plot for the escalation and expansion cohorts.



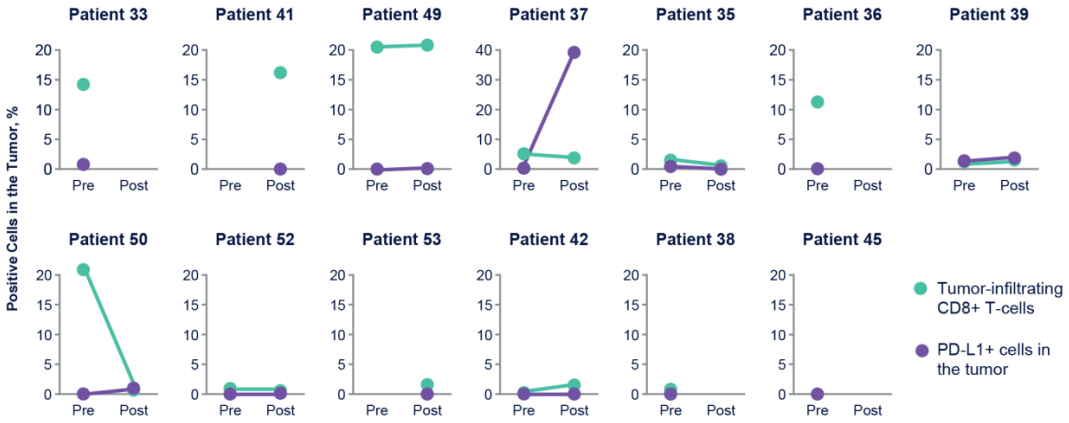
Supplementary Figure S3. Dose-normalized ABBV-428 pharmacokinetic parameters (C_{max} and AUC_{last}) between 0.4 and 3.6 mg/kg dose levels after the first dose. Orange circles represent individual values, and blue circles represent the mean value for each dose level. AUC_{last}, the area under the serum concentration-time curve from time zero to the last quantifiable concentration; C_{max}, maximum observed serum concentration; D, dose.



Supplementary Figure S4. (A) CD40 receptor occupancy on peripheral B-cells, and (B) cytokine secretion in the blood after ABBV-428 treatment. RO, receptor occupancy.



Supplementary Figure S5. Tumor-infiltrating CD8+ T-cells or PD-L1+ cells before and/or after ABBV-428 treatment.



Supplementary Figure S6. Immune-related gene expression in the tumor microenvironment before and after ABBV-428 treatment. Gene expression changes (analyzed using unsupervised clustering) are shown for 11 patients with ovarian cancer or mesothelioma treated with 3.6 mg/kg ABBV-428.