

Supplemental Data

This is a supplement to Herrera AF, Burton C, Radford J, et al. Avelumab in relapsed/refractory classical Hodgkin lymphoma: phase 1b results from the JAVELIN Hodgkins trial

Supplemental Table 1. Summary of PK parameters for avelumab treatment groups

	Avelumab treatment group				
	70 mg Q2W	350 mg Q2W	500 mg Q2W	500 mg Q3W	10 mg/kg Q2W
Cycle 1 day 1					
AUC_{tau}, h•µg/mL					
Patients, n	4	6	6	6	6
Geometric mean (CV %)	1933 (64)	8450 (28)	15,436 (38)	15,392 (27)	23,780 (54)
Minimum-maximum	1020-4110	5190-11,400	9460-26,600	10,400-22,500	11,400-39,900
C_{max}, µg/mL					
Patients, n	3	3	4	4	3
Geometric mean (CV %)	24.0 (35)	68.4 (33)	143 (24)	126 (15)	271 (16)
Minimum-maximum	16.9-33.5	56.0-99.7	119-195	110-149	228-312
t_{1/2}, days					
Patients, n	3	4	5	6	5
Geometric mean (CV %)	3.49 (28)	3.25 (44)	4.38 (39)	4.04 (23)	3.88 (38)
Minimum-maximum	2.91-4.76	2.27-5.32	3.16-7.55	2.79-5.59	2.42-6.39
Cycle 2 day 1					
AUC_{tau}, h•µg/mL					
Patients, n	3	5	5	5	5
Geometric mean (CV %)	2067 (6)	8789 (39)	21,053 (47)	19,173 (23)	27,196 (59)
Minimum-maximum	1950-2200	5490-14,000	10,800-35,600	15,400-27,600	13,900-50,100
C_{max}, µg/mL					
Patients, n	3	3	4	3	2
Geometric mean (CV %)	26.1 (21)	78.7 (19)	195 (46)	135 (8)	273 (22)
Minimum-maximum	22.0-32.7	67.3-97.5	115-321	127-147	233-319
C_{trough}, µg/mL					
Patients, n	4	6	6	5	6
Geometric mean (CV %)	1.71 (163)	4.03 (110)	12.1 (93)	2.54 (125)	14.4 (170)
Minimum-maximum	BLQ-3.83	BLQ-11.3	4.86-36.7	0.714-8.95	2.20-54.5
t_{1/2}, days					
Patients, n	3	5	4	4	5
Geometric mean (CV %)	2.92 (13)	3.43 (43)	4.59 (36)	4.62 (17)	4.23 (37)
Minimum-maximum	2.68-3.37	2.32-6.13	3.07-7.03	3.95-5.89	2.71-6.25

AUC_{tau}, area under the plasma concentration-time profile from time zero (predose) to the next dose; BLQ, below limit of quantitation; C_{max}, maximum observed plasma concentration; C_{trough}, predose trough concentration during multiple dosing; CV %, coefficient variation for geometric mean; Q2W, every 2 weeks; Q3W, every 3 weeks; t_{1/2}, terminal half-life.

Supplemental Table 2. Immune-related adverse events

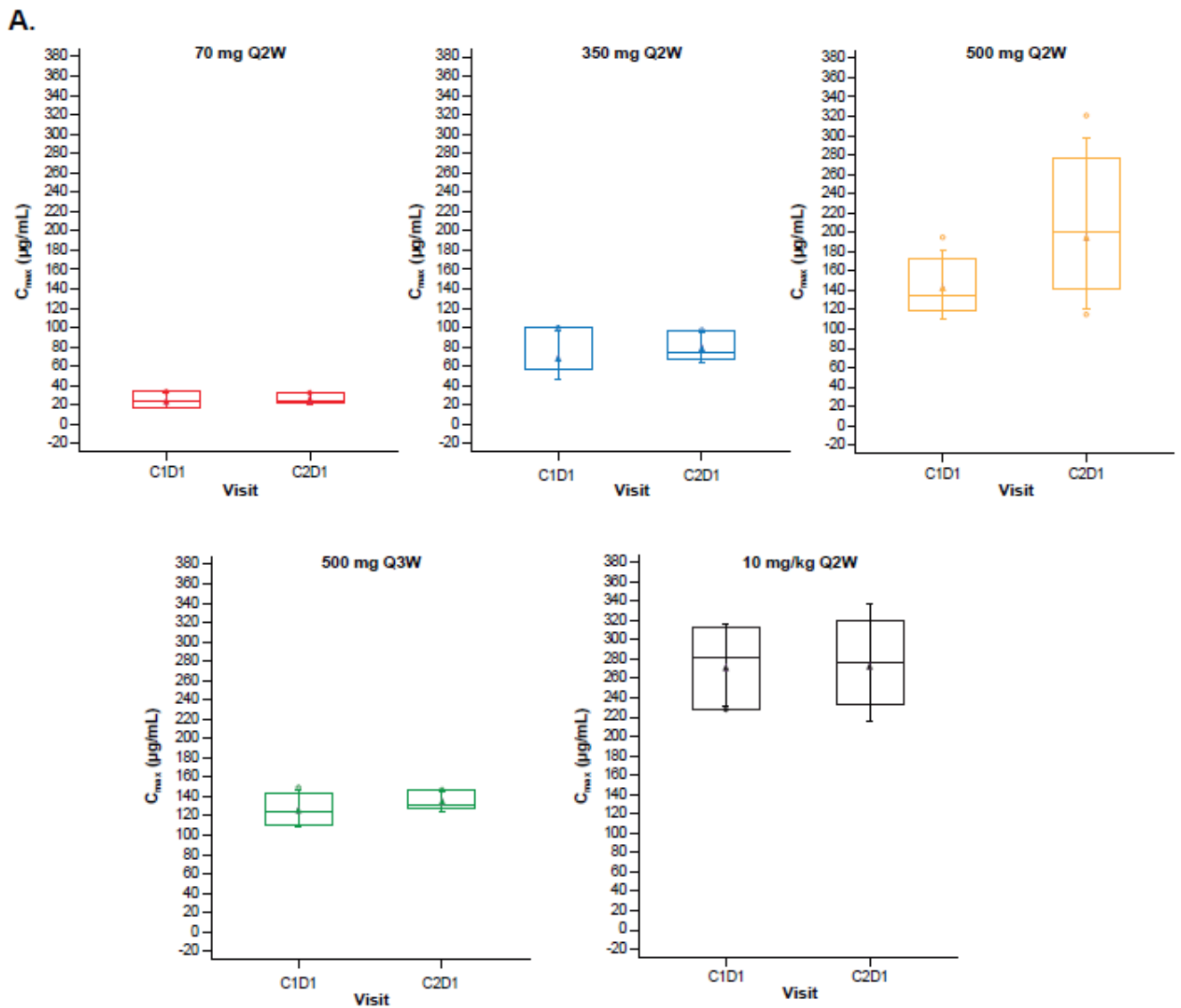
Cluster Preferred term	N=30	
	Any grade	Grade ≥3
Patients with events, n (%)	9 (30.0)	5 (16.7)
Immune-related rash, n (%)	3 (10.0)	–
Rash	2 (6.7)	–
Rash papular	1 (3.3)	–
Immune-related hepatitis, n (%)	2 (6.7)	1 (3.3)
Alanine aminotransferase increased	1 (3.3)	–
Aspartate aminotransferase increased	1 (3.3)	–
Transaminases increased	1 (3.3)	1 (3.3)
Other immune-related adverse events: GVHD, n (%)	2 (6.7)	2 (6.7)
GVHD in liver	2 (6.7)	2 (6.7)
Chronic GVHD in skin*	1 (3.3)	1 (3.3)
Immune-related endocrinopathies: thyroid disorders, n (%)	1 (3.3)	–
Blood thyroid-stimulating hormone increased	1 (3.3)	–
Immune-related pneumonitis, n (%)	1 (3.3)	1 (3.3)
Pneumonitis [†]	1 (3.3)	1 (3.3)
Other immune-related adverse events, n (%)	1 (3.3)	1 (3.3)
Immune thrombocytopenic purpura	1 (3.3)	1 (3.3)
Other immune-related adverse events: uveitis, n (%)	1 (3.3)	–
Iritis	1 (3.3)	–

GVHD, graft-versus-host disease.

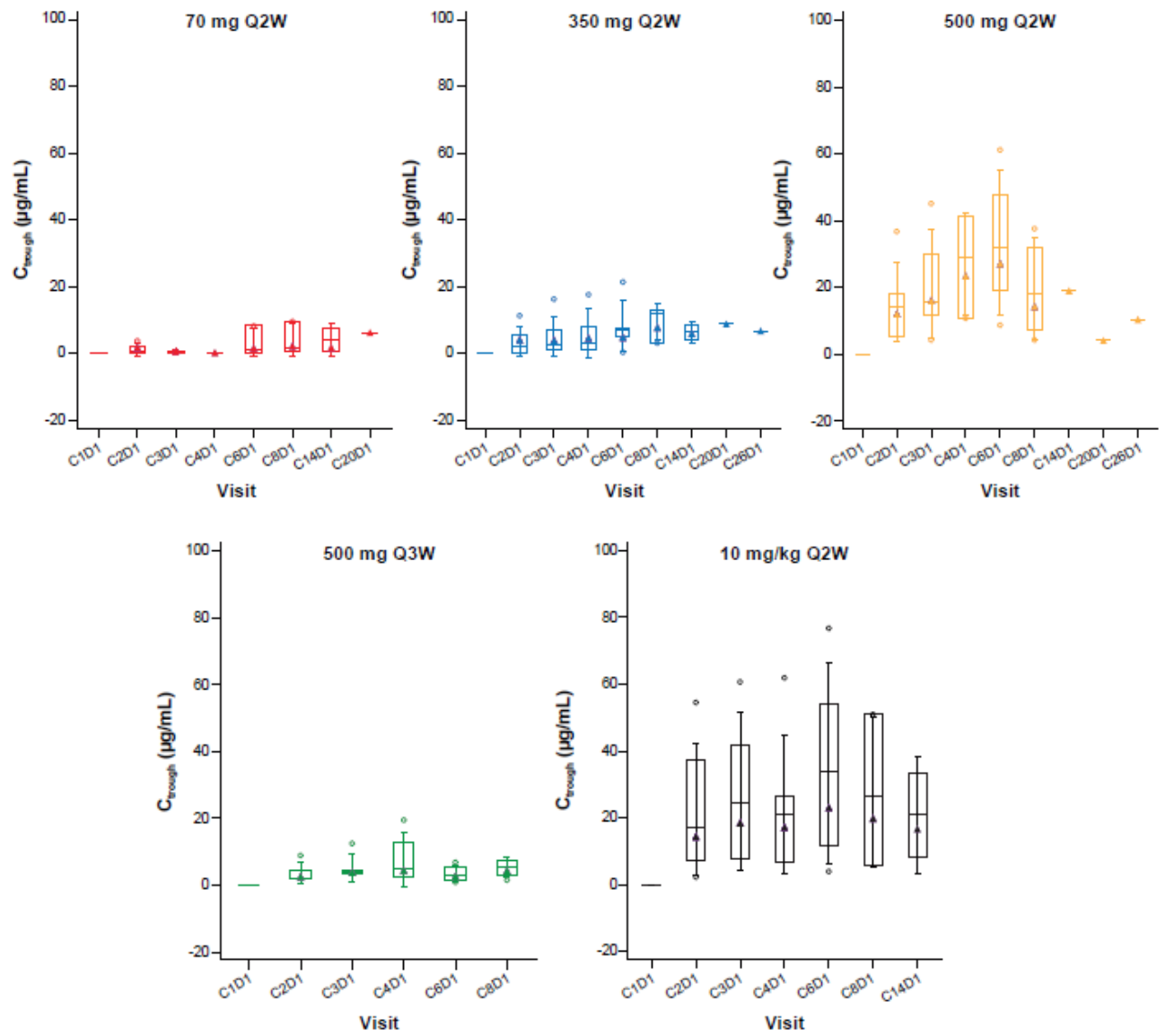
*Event occurred outside the on-treatment period.

[†]Grade 5 event.

Supplemental Figure 1. C_{max} (A) and C_{trough} (B) values per treatment group. The symbol in the box interior represents the geometric mean. The horizontal line in the box interior represents the median. Upper and lower box lines represent the 3rd and 1st quartiles, respectively. Ends of vertical lines represent 1 SD above and below the mean. Symbols outside the box represent measurements outside 1 SD from the mean total dose administered within $\pm 10\%$ of the planned dose. For C_{max} , summary statistics included concentration values from samples collected within 50 min to 2 h from the beginning of an uninterrupted infusion, with the total dose administered within $\pm 10\%$ of the planned dose. For median serum avelumab concentration, summary statistics were calculated by setting concentration values below the lower limit of quantification ($0.20 \mu\text{g/mL}$) to zero. C, cycle; D, day; C_{max} , maximum observed plasma concentration; C_{trough} , predose trough concentration during multiple dosing; Q2W, every 2 weeks; Q3W, every 3 weeks; SD, standard deviation.



B.



Supplemental Figure 2. Representative images of FISH detection of PD-L1/PD-L2 polysomy, amplification, and normal copy number cells. FISH, fluorescence in situ hybridization.

