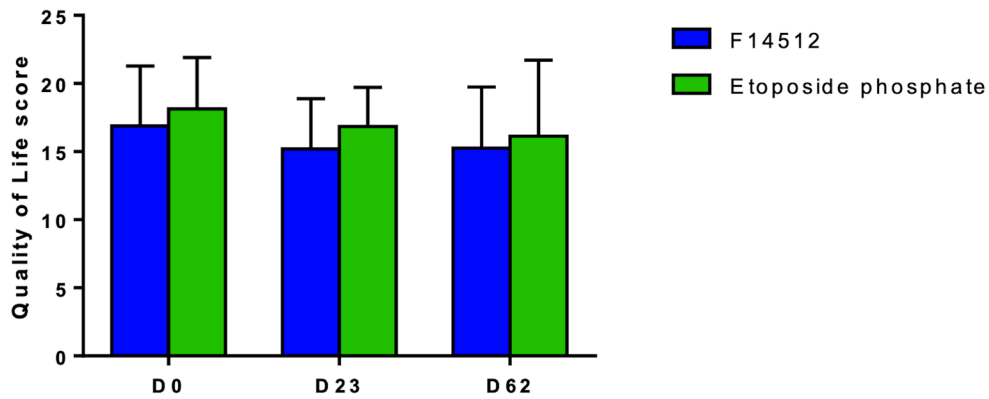


Randomized, double-blind trial of F14512, a polyamine-vectorized anticancer drug, compared with etoposide phosphate, in dogs with naturally occurring lymphoma

SUPPLEMENTARY MATERIALS



Supplementary Figure 1: Quality of life monitoring.

Supplementary Table 1: Serum thymidine kinase 1 activity measured prior to treatment according to clinical characteristics

Epidemiological characteristics	Number of dogs (%)	Pretreatment sTK1 activity, Du/L Median (range)	P value
All population	48 (100%)	1374 (20 – 60005)	
Prior treatment			0.15 ^a
Untreated	41 (85%)	1638 (20 – 60005)	
Prior chemotherapy	7 (15%)	334 (20 – 7269)	
Clinical stage			0.12 ^b
Stage II	2 (4%)	20 (20 – 20)	
Stage III	8 (17%)	1327 (20 – 3921)	
Stage IV	29 (60%)	1638 (20 – 60005)	
Stage V	9 (19%)	2994 (20 – 47453)	
Clinical substage			0.025 ^a
Substage a	26 (54%)	934 (20 – 47453)	
Substage b	22 (46%)	3018 (20 – 60005)	
Immunophenotype			< 0.001 ^a
B-cell lymphoma	37 (77%)	1688 (20 – 60005)	
T-cell lymphoma	7 (15%)	38 (20 – 834)	
Cytomorphological Subtype			0.18 ^a
DLBCL	33 (69%)	1688 (20 – 60005)	
Others	15 (31%)	834 (20 – 47453)	
Pgp			0.013 ^a
Pgp- (neg and low)	16 (33%)	280 (20 – 47453)	
Pgp+ (mid and high)	28 (58%)	2470 (20 – 60005)	
Treatment group			0.42 ^a
F14512	25 (52%)	1309 (20 – 47453)	
Etoposide phosphate	23 (48%)	2551 (20 – 60005)	

DLBCL: Diffuse large B-cell lymphoma. Pgp: P-glycoprotein. (a) Wilcoxon rank test, (b) Kruskal-Wallis test.

Supplementary Table 2. The clinical characteristics and outcome of dogs with low (≤ 0.5 mg/mL, $n = 27$) or high (> 0.5 mg/mL, $n = 21$) pretreatment D-dimer levels

Parameters	Number of dogs (%)	Number of dogs (%) with D-dimer ≤ 0.5 $\mu\text{g/mL}$	Number of dogs (%) with D-dimer > 0.5 $\mu\text{g/mL}$	P value
Overall	48 (100%)	27 (100%)	21 (100%)	
Clinical Stage				0.15 ^a
Stage II+III+IV	39 (81%)	24 (89%)	15 (71%)	
Stage V	9 (19%)	3 (11%)	6 (29%)	
Clinical Substage				0.24 ^a
Substage a	26 (54%)	17 (63%)	9 (43%)	
Substage b	22 (46%)	10 (37%)	12 (57%)	
Immunophenotype				0.44 ^a
B-cell	37 (77%)	22 (82%)	15 (71%)	
T-cell	7 (15%)	3 (11%)	4 (19%)	
Cytomorphological Subtype				0.76 ^a
DLBCL	33 (69%)	18 (67%)	15 (71%)	
Others	15 (31%)	9 (33%)	6 (29%)	
Prior treatment				0.12 ^a
Untreated	41 (85%)	21 (78%)	20 (95%)	
Prior chemotherapy	7 (15%)	6 (22%)	1 (5%)	
Treatment group				1.0 ^a
F14512	25 (52%)	14 (52%)	11 (52%)	
Etoposide phosphate	23 (48%)	13 (48%)	10 (48%)	
Pgp				0.53 ^a
Pgp- (neg and low)	16 (33%)	10 (37%)	6 (29%)	
Pgp+ (mid and high)	28 (58%)	14 (52%)	14 (67%)	
Outcome				
ORR at D62	22 (46%)	13 (48%)	9 (43%)	0.72 ^b
PFS (range)	86 (4-224)	104 (10-224)	54 (4-153)	0.011 ^c

DLBCL: Diffuse large B-cell lymphoma, ORR: overall response rate, PFS: progression-free survival, Pgp: P-glycoprotein. (a) Fisher's exact test; (b) Chi-square test; (c) Log-rank test.

Supplementary Table 3: Primary data. See Supplementary Table 3.