Findings	**Puppy-1 (Male)**	**Puppy-2 (Male)**
Anamnestic	Heterozygous *MDR1*-gene mutation (along with one other puppy – Puppy-4 – in litter; n=8)	Normal *MDR1* phenotype
	Whole litter received Milprovet® (2.5 mg milbemycin oxime/25 mg praziquantel) to treat severe intestinal parasitic infection 12-24 hrs after Milprovet® administration, symptoms appear and worsen: - Seizures - Tremors - Ataxia	
	Dies *en route* to veterinary hospital	
Clinical	Above-mentioned symptoms persist (40 hrs after Milprovet®). Additionally: - depression with hyper-excitability toward any external stimuli - Hyperthermia: 39-40 °C rectal temperature - Tachycardia - Mild dyspnea and tachypnea with homogeneous increase in vesicular sounds Littermates, including one other heterozygous *MDR1*-mutant, recover within 1.5 hrs of supportive therapy: flow-by oxygen, i.v. ringer-lactate (4 ml/kg/hr) and Intralipid®20% (1ml/kg) administration. 1 littermate (Puppy-3, with homozygous MDR1 wild type phenotype, has two convulsive crises 3 hrs after initiation of therapy, but recovers after repeated diazepam administration (1st dose endorectal, 2nd dose intravenous).	
		Dies 1hr after initiation of supportive therapy
Gross Pathology	Post mortem interval (PMI): 24 hr	PMI: 20 mins
	Both livers appearing mildly enlarged, with fragile consistency, light-red coloration and rounded edges	
		multifocal to coalescing pulmonary consolidation
Microscopic	Mild to moderate edema and congestion in all examined internal organs	

pathology	Cerebrum: cortical laminar necrosis, superficial spongiosis and meningeal congestion	
	mild to moderate	mild
	Cerebellum: multifocal Purkinje cell degeneration with perivascular edema of the molecular and Purkinje cell layers and the white matter	
	mild to moderate, coalescing, with multifocal Purkinje cell necrosis	mild
	Liver: mild to moderate, diffuse, micro- and macro-vesicular hepatic steatosis	
	Intestine: mild multifocal subacute lymphohistiocytic enteritis with reactive GALT	
	Lungs: mild to moderate, multifocal, subacute, histiocytic interstitial pneumonia.	
	mild emphysema at the lobe tip, multifocal interstitial and alveolar hemorrhages, and agonal edema	multifocal atelectasis, severe perivascular edema, interstitial hemorrhages, and a focal eosinophilic granuloma

Supplementary Table S1: Case summary for the two Australian Shepherd puppies that died following Milprovet® administration.